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THE DISPENSATORY
OF
THE UNITED STATES OF AMERICA

TWENTY-FIRST EDITION

THOROUGHLY REVISED, LARGELY REWRITTEN AND BASED UPON THE TENTH REVISION OF THE UNITED STATES PHARMACOPŒIA, NATIONAL FORMULARY FIFTH EDITION, AND THE BRITISH PHARMACOPŒIA 1914

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PREFACE.

The appearance of new revisions of both the United States Pharmacopœia and the National Formulary, as well as the many changes which have taken place in medical and pharmaceutical practice during the past decade, have necessitated an unusually extensive revision of this book.

While the general form and mode of presentation, the value of which have been so well established by the approval of the professions for many years, have not been departed from there are numerous changes to which attention may be directed. These alterations have been so great that large sections of the book have had to be completely rewritten. It may be remarked in this connection that the editors have spared no effort to bring the work abreast of the latest information concerning the subjects treated. Not only has advantage been taken of the numerous recent treatises in the various allied fields but thousands of articles, on specific topics, which have appeared in current journal literature of medicine and pharmacy have been utilized.

The U. S. Pharmacopœia X has admitted to official recognition 33 new drugs (not including preparations) some of which were practically unknown to the medical profession ten years ago. All of these, together with the recent admissions to the National Formulary, have been given thorough consideration. In addition a large number of other new remedial agents—some showing great promise of becoming of permanent value—have been introduced. These also have received careful attention—in Part II although not in quite so extensive detail as the official drugs.

The fact that the National Formulary is now a legal standard, on a parity with the Pharmacopœia in most parts of the country, has made it seem wise to include the drugs of that authority with the official substances in Part I, instead of in Part II as in previous editions of the Dispensatory. The galenical preparations of the N. F. are, however, described in summary in a separate place as heretofore.

For many years editors of the Dispensatory have been considerably disturbed by the continual increase in the size of the book, a growth which was threatening to make it too unwieldy to handle as a single volume. In the present edition a strenuous effort has been made to meet this situation by careful pruning and condensation. In the first place there has been a considerable elimination of repetition; for example, certain chemical constituents which occur in different plants, were, in previous editions, described in more or less detail in connection with several of the drugs in which they were found, whereas in the present edition their properties are set forth in detail only once and they are merely mentioned by name as principles present in the other plants in which they occur.

Much valuable space has also been saved by the omission of obsolete material, such as the discussions of chemical problems of past generations which are now solved, details of old formulas no longer employed, descriptions of abandoned methods of manufacture and similar topics which are chiefly of historical interest. In this pruning the editors have striven not to omit any information of real value, but to delete only those things which have been superceded by more modern knowledge or methods.

For the same reason it has been deemed wise to drop the translations of Metric into Apothecaries' measures and of Centigrade temperatures into Fahrenheit. In the preface of the Nineteenth edition of the Dispensatory the hope was expressed that the day was not far distant when the continuation of the duplex system of weights and measures would no longer be required. In the opinion of the present editors that day has arrived. Pharmacists, generally, are sufficiently acquainted with the internationally used Metric system —which has been for thirty years the only one recognized by the U. S. Pharmacopœia in its formulas—to make such translations unnecessary. Moreover any such translation to be even approximately accurate must be so cumbersome as to be of little real usefulness. In view of these facts it was felt that the space occupied could be more advantageously used for other purposes. Only in the case of doses was it deemed wise to continue double system. The great majority of American physicians are so firmly wedded to the Apothecaries' weights and measures, that practically all the prescriptions of the land are written in that system; and in a matter so intimately connected with the compounding of prescriptions as that of dosage it seems necessary to insert both quantities. It may be remarked in this connection that the equivalent doses given are not intended to be accurate translations, but merely to signify the ordinary limits which are employed by those who write in the Metric or in the English system respectively.

The references to the literature, which has been so conspicuous feature of past editions, we believe to be of much value in encouraging research and in aiding those who wish to find more detailed information concerning some special topic in which they may be peculiarly interested. Although many of the older references have been dropped the modern bibliography has been considerably extended. The aim of the editors has been not only to give the sources of the most recent studies in the fields of pharmacy and medicine but also to furnish, at least, the key which will unlock the door of the past to those who may wish to trace the history of the development of some phase of the subject. The same system of abbreviating the names of journals as was used in the 19th and 20th editions is continued.

In the cause of the more efficient utilization of the information of the Dispensatory we would urge the reader, especially one who may not be familiar with past editions, to a careful perusal of the *Introductory Matter* on page V; it not only explains the plan on which the book is constructed, but also gives certain definitions essential to an understanding of the text.

The editors desire to express their thanks to Mr. Ralph L. Calvert and Mr. Paul Card for their assistance in preparing the index.

It would not be fitting to let pass the occasion of a new edition of this old work without some mention of the editors who have gone from their labors since the last edition. Prof. Samuel P. Sadtler was for more than thirty years associated in the revising of the United States Dispensatory. His wide knowledge of chemistry, his long experience as a teacher and his high character had made him a well-known and highly respected authority. Prof. Henry Kraemer, who had charge of the botany and pharmacognosy in the last edition, brought to the work a breadth of knowledge and a scholarly spirit that made his contribution of great value to the whole profession. The achievements of both of these men will long rebound to the credit of pharmacy.

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EXPLANATORY INTRODUCTION.

That this work may be used to the best advantage there are certain matters of general information and concerning the scope of the book with which the reader should be acquainted.

General Arrangement.—The Dispensatory is divided into ~~to~~ three main divisions. In Part I are included all the drugs and preparations recognized by either the U. S. or British Pharmacopœias and all the crude drugs recognized by the National Formulary. These are arranged in alphabetical order according to their Latin titles.

In Part II are considered those substances not official in any of the above standards. These are arranged in alphabetical order according to their English names.

In Part III are included (1) General tests, Processes and Apparatus, Reagents Test Solutions and Tables of the U. S. Pharmacopœia. (2) The appendix of the British Pharmacopœia (3) a summary of the Galenical preparations of the National Formulary. (4) Formulas for reagents used in clinical examinations of the blood, urine, gastric contents etc. (5) Various tables showing the relative values of the Apothecaries, Troy and Imperial units, the size of drops of various liquids, and other subjects not included in the Pharmacopœial tables.

Arrangement of Part I.—In treating of the official substances an attempt is made to arrange the information according to the following order: The official titles and definitions; Unofficial synonyms; Source and history; Description and physical properties of the drug; Assay methods; Adulterants; Chemical constituents; Incompatibilities; Therapeutic uses; Toxicology; Dosage; List of official preparations. In a few cases it has been necessary to depart slightly from this order but the effort has been made to present the subject matter in a systematic manner so that it may be possible to find the answer to any specific question without reading the whole article.

General Tests.—Both the U. S. and British Pharmacopœias have adopted the plan of simply stating under the description of each drug that it does, or does not, "respond to the test for" this or that substance; instead of describing these identity tests over and over they are included in one place. These tests will be found in Part III of the Dispensatory. A similar condition holds for many of the Assay processes of the U. S. Pharmacopœia.

Constituents.—There are several chemical proximate principles which occur in a number of plants. In order to save space these are not described in detail in connection with each drug in which they are present but are simply mentioned by name and described in more detail under one or another title. For examples: Linalool is found in a number of volatile oils, its chemical formula and general properties are given once under the general article on *Olea Volatila;* the alkaloid berberine occurs in at least four official and several unofficial drugs, its detailed description is given in connection with the article on berberis. In those cases where cross reference to such descriptions may be lacking the interested reader should consult the Index.

We would also direct the attention to the following paragraphs from the "General Notices" of the U. S. P. as being essential to the interpretation of the official descriptions as quoted in this work:

U. S. Pharmaceutical Standards for Medicinal Substances.—"The standards of purity and strength prescribed in the monographs of this Pharmacopœia are intended to apply solely to substances which are used for medicinal purposes and when professedly bought, sold, or dispensed as such. Substances labeled with official synonyms must comply with the same standards, tests, and requirements that are demanded for the same substances under the official titles. Official preparations are to be made only from drugs that conform to the pharmacopœial standards, definitions, and descriptions.

"In the manufacture of products and preparations on a large scale deviation in detail from the official processes is permissible, provided the finished products conform to the definitions, descriptions, tests, and standards prescribed by the U. S. Pharmacopœia, Tenth. In the manufacture of pharmacopœia extracts and resins in which alcohol is used as a solvent only and does not remain in the finished product, it is permissible that alcohol made non-potable by the addition of from 5 to 10 per cent by volume of commercially pure methanol or of acetone be used in the place of ethyl alcohol in accordance with Federal Statutes and Regulations of the Internal Revenue Department, but the extracts and resins so made must be identical with those prepared by the processes in the monographs and must conform to the standards fixed by the tests of the U. S. Pharmacopœia, Tenth. This provision is not to be construed as permitting the use of specially denatured alcohol in the manufacture of any medicinal product other than extracts and resins." U. S.

Reagents.—"The reagents designated in this Pharmacopœia must conform to the standards established." (See *Reagents* Part III).

"*Moisture Tolerance.*—In most cases the allowable percentage of moisture in a chemical is specified in the monograph. When not specified, 5 per cent. of moisture is permitted, provided the chemical is dispensed in a condition of sensible dryness. For certain efflorescent chemicals, a limit of tolerance for loss of water of crystallization has been adopted analogous to the purity rubric described above.

"*Time Limitations.*—In testing chemicals for innocuous impurities in this Pharmacopœia (*chloride, sulphate, etc.*), it is understood that five minutes shall be allowed for the reaction to be observed unless otherwise specified. In the test for carbonizable impurities where sulphuric acid is used, it is understood that the time for observation is limited to fifteen minutes unless otherwise specified.

"*Solubilities.*—Solubility statements in the monographs are not intended as physical constants in the strict sense of this term, but primarily as information required by physicians and pharmacists in connection with the preparation and dispensing of medicines, except in the case of volatile oils where solubilities in alcohol of different strengths are used as tests for purity. For further statements concerning solubilities, see page 1547.

"Official chemicals, when brought into solution, may show slight mechanical impurities such as fragments of filter paper, fiber, and dust particles, unless excluded by definite tests in the monograph.

"*Melting, Boiling and Congealing Points.*—The figures given for these constants have been determined by the official methods and in estimating the physical constants of official products the pharmacopœial processes only are to be used. Where given with a range instead of a single figure, the figures are to be regarded as inclusive. For details and methods, see page 1236.

"*Negligible.*—The term, 'negligible,' where used in this Pharmacopœia, means a quantity not exceeding 0.0005 Gm.

"*Constant Weight.*—The term 'dried to constant weight,' where used in this Pharmacopœia, means that two consecutive weighings do not differ by more than 0.1 per cent, the second weighing following an additional hour of drying.

"*Quantities for Chemical Tests.*—In stating the quantities to be used for some assays and for quantitative tests for impurities a convenient amount is taken. The word 'about' is used to indicate that this need not be the exact quantity specified, but that it should be approximately that amount. This is then accurately weighed, and the result of the test or assay is to be based upon the exact weight. In those cases where the substances are corrosive, volatile, efflorescent, or hygroscopic, this plan will be found especially useful.

"Such phrases as '(1 in 10),' '(1 in 20),' etc., are understood to mean that 1 part by volume of a liquid is to be diluted with, or 1 part by weight of a solid dissolved in, 10 or 20 parts by volume of the solvent.

"'*Absence of' and 'Limit of'*.—The terms 'absence of' and 'limit of' following the tests indicating impurities are rarely used in this Pharmacopœia. Such words as (*chloride*), (*sulphate*) (*free alkali*), etc., in italics and parenthesis, which follow tests, are merely intended to give information as to the object of the test, the test itself indicating whether the substance is present in an amount which would be objectionable for medicinal use.

"*Temperatures.*—Statements of temperature are given in this Pharmacopœia in degrees of the centigrade thermometer, the equivalent Fahrenheit temperature being given in the Table of Thermometric Equivalents. The standard temperature for solubilities specific gravities, polarimetric determinations, and for the preparation of volumetric solutions is 25° C. For alcohol the former standard temperature of 60° F. (15.56° C.) has been retained, since the laws and regulations of the Internal Revenue Department of the United States, relating to alcohol and alcoholic liquids, are still based on this temperature.

"For refractive indices, viscosity, and for certain saccharimeters temperatures other than 25° C. have been directed as the special conditions require.

"When the Pharmacopœia directs the use of a water bath, it is understood that the water shall be boiling unless otherwise specified.

"*Specific Gravity.*—Except where otherwise stated, the specific gravity basis of this Pharmacopœia is $\frac{25° \text{ C.}}{25° \text{ C.}}$ (apparent), *i. e.*, the ratio of the apparent weight of a substance in air at 25° C. to that of an equal volume of distilled water at the same temperature.

"*Biological Assay Standards.*—In order to facilitate the adoption of the biological assay standards of the Pharmacopœia, and to provide a greater degree of uniformity in their application, the Bureau of Chemistry of the U. S. Department of Agriculture at Washington, D. C., has indicated its willingness to supply standard substances conforming to the pharmacopœial requirements.

"*Alcoholic Content in Preparations.*—In compliance with the instruction of the Pharmacopœial Convention there is given in the text accompanying each preparation containing alcohol, a range of alcohol content based upon numerous determinations and a compilation of data secured from pharmaceutical chemists and manufacturers. All statements of alcohol content under preparations are given in percentages of absolute alcohol. There is considerable variation in the amount of alcohol present in different lots of the same fluidextract due, to the varying proportions of moisture and extractive in the air-dried drug directed to be used, changing atmosphere conditions and the varying amounts of exposure; likewise if a process of 'percolation' or 'divided percolation' be adopted. Consequently, a much wider range of tolerance is necessary in some of the fluidextracts than would be permitted in a tincture or a spirit where the amount of drug and the exposure are much less.

"*Vegetable Drugs.*—The official definitions and standards for vegetable drugs, apply to all forms in which they may enter commerce, whether whole, cut, ground, powdered, or otherwise prepared for use, unless specifically exempted in the monograph or admitted under authority for manufacturing or for a special purpose. Vegetable drugs are to be as free as practicable from insects or other animal life, animal material or animal excreta. They are to be free from moldiness and show no discoloration, abnormal odor, sliminess, or deterioration due to any cause.

"For the preservation of vegetable or animal substances from the ravages of insects, it is directed in special cases that they be preserved in tightly-closed containers with a few drops of chloroform or carbon tetrachloride added. It is not intended that this precaution should be obligatory for drugs in bales or large original containers where it may be impracticable. The following drugs are particularly liable to the attack of insects: Aconite, althea, belladonna root, calumba, cantharides, capsicum, caraway, cardamom, ergot, ginger, glycyrrhiza, jalap, linseed, myristica, pumpkin seed, rhubarb, sarsaparilla, and strophanthus.

"In commerce it is not possible to obtain vegetable drugs in a state of absolute purity, and a limited amount of innocuous, extraneous, or foreign matter adhering to the drug or admixture with it is usually not detrimental. The presence or admixture of any poisonous or dangerous foreign substance, however, is not permissible. Foreign organic matter refers to any part of the plants or plants yielding the drug, except that part or those parts designated as constituting the drug, and to any other plant parts, vegetable tissues, or substances.

"In order that vegetable drugs be of uniform quality and as free as practicable from foreign substances, it is required that in each vegetable drug recognized in this Pharmacopœia the amount of foreign inorganic matter, estimated as acid-insoluble ash, be not more than 2 per cent of the weight of the drug unless otherwise specified in the monograph of the drug, and that amount of foreign organic matter be restricted to the allowable percentage specified in the monograph of the drug. Before vegetable drugs are ground or powdered, all lumps of dirt or other foreign inorganic matter which can be separated by mechanical means should be removed.

"*Weights and Measures.*—The metric system of weights and measures is the official system used in this Pharmacopœia. The units of the metric system are designated by abbreviations, as follows:

M. = meter
dm. = decimeter
cm. = centimeter
mm. = millimeter

L. = liter
dl. = deciliter
ml. = milliliter, or cubic centimeter, or cc.*

Kg. = kilogram
Gm. = gram
dg. = decigram
cg. = centigram
mg. = milligram

In measuring liquids, cylindrical graduates are preferred. Conical graduates, however, accurately graduated, are deemed suitable for the use of the pharmacist in compounding or dispensing medicines. The bottom of the meniscus is the point from which the reading is to be taken." *U. S.*

The Metric System of Weights and Measures, which is the only one recognized by either the United States or British Pharmacopœias in their formulæ, is based on the idea of a correlation between the units of length, capacity and weight, and multiples and subdivisions of these units according to the decimal system. The unit of length is the *meter*. The cube of the tenth part of a meter is taken as the unit of capacity and is called a *liter*. The one-thousandth part of a liter of distilled water at its maximum density is the unit of mass, and is denominated a *gramme*. The multiples of these measures, proceeding in the decimal progression, are distinguished by employing the prefixes *Deka*, *Hecto*, *Kilo*, (spelt with capitals) taken from the Greek numerals and the subdivisions, following the same order, by *deci*, *centi*, *milli*, (spelt with small letters) from the Latin numerals.

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*The cubic centimeter (cc.) used in this Pharmacopœia is intended to correspond to the one-thousandth part of a liter.

The following table shows the relative value of the linear measures; the equivalents of the Metric and Apothecaries weights and capacity measures are given in tables in Part III.

millimeter (mm.) = 0.001 meter = 0.039 inch
centimeter (cm.) = 0.01 meter = 0.394 inch
decimeter (dm.) = 0.1 meter = 3.937 inch
Meter (M.) = 39.37 inch
Dekameter (Dm.) = 10. meters = 10.94 yards
Hectometer (Hm.) = 100. meters = 109.36 yards
Kilometer (Km.) = 1000. meters = 0.621 mile

For equivalents of various multiples of the above measures see table of *Equivalents of Linear Measures*, Part III.

"*Apothecaries Weights and Measures.*—Physicians in prescribing, and pharmacists in dispensing medicines commonly employ the apothecaries weights and measures which were in use in England prior to 1825, the weights being orginally derived from the old English Troy weight, the fluid measures from the old wine gallon. The units of this system are designated in prescribing by signs or abbreviations as follows:

℥ = apothecaries ounce = 8 drachms = 480 grains
ʒ = drachm = 3 scruples = 60 grains
℈ = scruple = 20 grains
gr. = grain
O = pint = 16 fluidounces
f℥ = fluidounce = 8 fluidrachms = 480 minims
fʒ = fluidrachm = 60 minims
♏ = minim

"In writing prescriptions in the apothecaries system, Roman, not Arabic, numerals are employed, and these are always placed after the symbol or abbreviation, thus: f℥ii; gr.xv. In the case of metric abbreviations, the numerals precede the abbreviation, and are always written in Arabic characters, thus: 5 Gm.: 2 cc. Care is taken to distinguish the abbreviation for gram (Gm.) from that for grain (gr.) by writing the former with a capital, the latter with a small letter." U. S.

(For tables showing the relative value of the units of the various weights and measures employed in the United States and in Great Britain, also of the relations between the Apothecaries and metric systems see Part III.)

"*Approximate Measures.*—Physicians very commonly prescribe liquid medicines in teaspoonful, dessertspoonful, or tablespoonful doses. Inasmuch as spoons vary greatly in capacity, it is desirable that the more scientific practice should be always adopted, of prescribing doses in cubic centimeters, fluidrachms, or minims, to be measured with a suitable medicine measure. The following are the values conventionally attached to the several approximate measures above mentioned:

Metric System

A teaspoonful = 4 cc.
A dessertspoonful = 8 cc.
A tablespoonful = 15 cc.

Apothecaries System

A teaspoonful = 1 fluidrachm
A dessertspoonful = 2 fluidrachms
A tablespoonful = 4 fluidrachms or ½ fluidounce". U. S.

ABBREVIATIONS.

A. de P.—Archives de Physiologie normale et pathologique.

A. de S.—Académie des Sciences.

A. E. P. P.—Archiv für Experimentelle Pathologie und Pharmakologie.

A. G. M.—Archives générales de Médecine.

A. G. P.—Archiv der gesammte Physiologie.

A. I. B.—Archives Italiennes de Biologie.

A. I. P.—Archives internationales de Pharmacodynamique.

A. In. M.—Archives of Internal Medicine.

A. J. P.—American Journal of Pharmacy.

A. J. Phys.—American Journal of Physiology.

A. M. S. J.—Atlanta Medical and Surgical Journal.

A. Pharm.—Archiv der Pharmacie.

A. Phys.—Archiv für Anatomie und Physiologie, physiologisches Abteilung.

Aerzt. Rund.—Aerztliche Rundschau.

All. M. C. Z.—Allgemeine medicinische Central Zeitung.

All. W. M. Z.—Allgemeine Wiener medicinische Zeitung.

Am. Chem. J.—American Chemical Journal.

Am. Drug.—American Druggist and Pharmaceutical Record.

Am. J. M. S.—American Journal of Medical Sciences.

Am. J. Sci.—American Journal of Science (and Arts).

Am. Med.—American Medicine.

Am. Pract. and News.—American Practitioner and News.

An.—The Analyst.

Ann. Chem.—Liebig's Annalen der Chemie.

Ann. Ch. Ph.—Annalen der Chemie und Pharmacie. (Now Annalen der Pharmacie.)

Ann. Ch. Phys.—Annales de Chimie et de Physique.

Ann. In. Past.—Annales de l'Institut Pasteur.

Ann. Pharm.—Annalen der Pharmacie.

Ann. Thér.—Annuaire de Thérapeutique.

Ap. Ztg.—Apotheker Zeitung.

Apoth.—Apothecary.

Arch. I. C. M.—Archivio Italiano di Clinica Medica.

B. A. M.—Bulletin de l'Académie de Médecine de Paris.

B. A. R. B.—Bulletin de l'Académie Royale de Belge.

B. C. D.—British and Colonial Druggist.

B. Chem. G.—Berichte der Deutschen Chemischen Gesellschaft.

B. D. A. J.—Bulletin Department of Agriculture, Jamaica.

B. F. M. R.—British and Foreign Medical Review.

B. G. T.—Bulletin général de Thérapeutique, médicale et chirurgicale.

B. Hôp. Par.—Bulletin de la Société Médicale des Hôpitaux de Paris.

B. K. Ch.—Beitrage zur Klinische Chirurgie.

B. K. W.—Berliner klinische Wochenschrift. (Now Klinische Wochenschrift.)

B. M.—Le Bulletin Médicale.

B. M. J.—British Medical Journal.

B. M. N.—Bulletin Médicale du Nord.

B. M. S. J.—Boston Medical and Surgical Journal.

B. P. G.—Berichte der Deutschen Pharmaceutischen Gesellschaft.

B. S. Ph. Br.—Bulletin de la Société Royale de Pharmacie de Bruxelles.

B. Sc. Pharm.—Bulletin de la Société Pharmacologique.

B. Soc. Chim.—Bulletin de la Société Chimique de France.

B. Thier. W.—Berliner Thierärztliche Wochenschrift.

Biochem. J.—Biochemical Journal.

Biochem. Zeit.—Biochemische Zeitschrift.

Boston J. Chem.—Boston Journal of Chemistry.

Br.—British Pharmacopœia (1914).

Br. Add.—British Pharmacopœia, Indian and Colonial Addendum (1898).

Bull. Pharm.—Bulletin of Pharmacy.

C. D.—Chemist and Druggist.

C. R. A. S.—Comptes-rendus de l'Académie de Science de Paris.

C. R. S. B.—Comptes-rendus de le Société de Biologie de Paris.

Can. Drug.—Canadian Druggist.

Can. Pharm. Journ.—Canadian Pharmaceutical Journal.

Cb. B.—Centralblatt für Bacteriologie.

Cb. Chir.—Centralblatt für Chirurgie.

Cb. G. T.—Centralblatt für die gesammte Therapie.

Cb. Gyn.—Centralblatt für Gynekologie.

Cb. I. M.—Centralblatt für Innere Medicin.

Cb. M. W.—Centralblatt für medicinische Wissenschaften.

Cb. Path.—Centralblatt für Allgemeine Pathologie und Pathologisches Anatomie.

Cb. Phys.—Centralblatt für Physiologie.

Ch. Ph.—Chicago Pharmacist.

Chem. Abs.—Chemical Abstracts.

Chem. Cb.—Chemisches Centralblatt.

Chem. Gaz.—Chemical Gazette.

Chem. News.—Chemical News.

Chem. Ztg.—Chemiker Zeitung.

D. A. K. M.—Deutsches Archiv für Klinische Medicin.

D. C.—Druggists Circular.

D. M. W.—Deutsche medicinische Wochenschrift.

D. M. Ztg.—Deutsche medicinische Zeitung.

D. Z. Chir.—Deutsche Zeitschrift für Chirurgie.

Derm. Cb.—Dermatologisches Centralblatt.

Derm. Zeit.—Dermatologische Zeitschrift.

Dublin Q. J.—Dublin Quarterly Journal of Medical Science.

Ed. M. J.—Edinburgh Medical Journal.

Ephem.—Ephemeris (Squibb).

Fam.—Family.

F. Th.—Folia Therapeutica.

Fort. Med.—Fortschritte der Medicin.

France Méd.—La France Médicale.

Fr. Cod.—French Codex (Pharmacopée Française).

G.—German.

G. H. M. C.—Gazette Hebdomadaire de Médecine et de Chirurgie.

G. M. P.—Gazette Médicale de Paris.

G. Osp.—Gazetta degli Ospedale e delle Cliniche.

Hyg. Rund.—Hygienische Rundschau.

In. Dis.—Inaugural Dissertation.

Ind. Ann. Med. Sci.—Indian Annals of Medical Science.

Ind. L.—Indian Lancet.

Ind. Med. Jour.—Indiana Medical Journal.

Int. M. J.—Intercolonial Medical Journal.

It.—Italian.

J. A. C.—Journal of Applied Chemistry.

J. A. M. A.—Journal American Medical Association.

J. A. P.—Journal of Anatomy and Physiology.

J. A. Ph. A.—Journal of American Pharmaceutical Association.

J. Am. C. S.—Journal of the American Chemical Society.

J. Bi. Chem.—Journal of Biological Chemistry.

J. Chem. S.—Journal of the Chemical Society of London.

J. Cut. D.—Journal of Cutaneous Diseases.

J. Ex. M.—Journal of Experimental Medicine.

J. F. I.—Journal of the Franklin Institute.

J. H. H. B.—Johns Hopkins Hospital Bulletin.

J. I. and E. C.—Journal of Industrial and Engineering Chemistry.

J. Inf. D.—Journal of Infectious Diseases.

J. Lab. Clin. M.—Journal of Laboratory and Clinical Medicine.

J. M. R.—Journal of Medical Research.

J. M. S.—Journal of Mental Science.

J. Metab. R.—Journal of Metabolic Research.

J. P.—Journal of Physiology.

J. P. A.—Journal de Pharmacie d'Anvers.

J. P. C.—Journal de Pharmacie et de Chimie (Paris).

J. P. Ex. T.—Journal of Pharmacology and Experimental Therapeutics.

J. P. L.—Journal de Pharmacie de Liège.

J. P. P.—Journal de Physiologie et de Pathologie Genéralé.

J. Pr. Chem.—Journal für Praktische Chemie.

J. Pract.—Journal des Practiciens.

J. Soc. Chem. Ind.—Journal of the Society of Chemical Industry.

Jahresb.—Jahresberichte (Dragendorff's).

K. S. A.—Korrespondenzblatt für Schweizer Arzte.

K. T. W.—Klinisch - therapeutische Wochenschrift.

L. L.—The London Lancet.

L. M. R.—London Medical Recorder.

London Med. Gaz.—London Medical Gazette.

Lyons Méd.—Lyons Médicale.

M. A.—Merck's Archives.

M. B. D.—Meyer Brothers' Druggist.

M. Bull.—Merck's Bulletin.

M. Chem.—Monatshefte für Chemie.

Med. Chron.—Medical Chronicle.

Med. Klin.—Medicinisches Klinik.

Med. Mod.—La Médicine Moderne.

Med. Rec.—Medical Record.

M. H. S. A.—Monatsschrift der Harn und Sexual-Apparat.

Mil.—Milliliter, Cubic Centimeter.

Mm.—Millimeter.

M. M.—Medicinische Monatsschrift.

M. M. J.—Maryland Medical Journal.

M. M. W.—Münchner medicinische Wochenschrift.

M. News.—Medical News.

M. R.—Merck's Market Report and Pharmaceutical Journal.

M. S. Rep.—Medical and Surgical Reporter.

M. T. G.—Medical Times and Gazette.

Mit. Grenz. M. C.—Mitteilungen aus der Grenzgebeit der Medicin und Chirurgie.

Mon. Chem.—Monatshefte für Chemie.

Mont. Pharm. Jour.—Montreal Pharmaceutical Journal.

N. A. R. D. J.—Journal of National Association of Retail Druggists.

N. F.—National Formulary V.

N. I.—New Idea.

N. J. Med. Rep.—New Jersey Medical Reporter.

N. O. M. S. J.—New Orleans Medical and Surgical Journal.

N. P.—New Preparations.

N. R.—New Remedies.

N. R. Pharm.—Neues Repertorium für Pharmacie.

N. Y. M. J.—New York Medical Journal.

N. Y. M. R.—New York Medical Record.

Nat. Drug.—National Druggist.

Nouv. Rem.—Les Nouveaux Remèdes.

Off. Prep.—Official Preparations.

O. Z.—Oesterreichische Zeitschrift.

P. G.—German Pharmacopœia.

P. J.—Pharmaceutical Journal, London.

P. M. T.—Philadelphia Medical Times.

Pac. Drug.—Pacific Druggist.

Penna. M. J.—Pennsylvania Medical Journal.

Ph. Archiv.—Pharmaceutical Archives.

Ph. Cb.—Pharmaceutisches Centralblatt.

Ph. Centralh.—Pharmaceutische Centralhalle.

Ph. Era.—Pharmaceutical Era.

Ph. Post.—Pharmaceutische Post.

Ph. Rec.—Pharmaceutical Record.

Ph. Rev.—Pharmaceutical Review.

Ph. Rund.—Pharmaceutisches Rundschau.

Ph. Z. R.—Pharmaceutische Zeitschrift für Russland.

Ph. Ztg.—Pharmaceutische Zeitung.

Pharm.—The Pharmacist.

Philos. Mag.—Philosophical Magazine.

Philos. Trans.—Philosophical Transactions of the Royal Society of London.

Pr. M. W.—Präger medicinische Wochenschrift.

Pract.—Practitioner.

Pract. Drug.—Practical Druggist.

Press. Méd.—La Presse Médicale.

Proc. A. Ph. A.—Proceedings of the American Pharmaceutical Association.

Proc. Am. Med. Ass.—Proceedings of American Medical Association.

Proc. Chem. Soc.—Proceedings of the Chemical Society.

Proc. N. J. Ph. A.—Proceedings of the New Jersey Pharmaceutical Association.

Proc. P. Ph. A.—Proceedings of Pennsylvania Pharmaceutical Association.

Proc. Roy. Soc. N. S. W.—Proceedings of the Royal Society of New South Wales.

Prog. M.—Le Progrès Médicale.

R. C. C.—Revue des Cultures Coloniale.

R. M. Est.—Revue Médicale de l'Est.

R. M. S. R.—Revue Médicale de la Suisse Romande.

R. T.—Revue de Thérapeutique Médicale et Chirurgicale.

Rif. M.—La Riforma Medica.

S. Jb.—Schmidt's Jahrbücher der in- und auslandischen gesammten Medicin.

S. M.—La Semaine Médicale.

Sp.—Spanish.

Sp. Gr.—Specific Gravity.

S. W. P.—Schweizerische Wochenschrift für Pharmacie.

Schim. Rep.—Schimmel & Co.'s Semi-annual Report.

St. L. M. S. J.—St. Louis Medical and Surgical Journal.

St. P. M. W.—St. Petersburger medicinische Wochenschrift.

T. G.—Therapeutic Gazette.

T. Mod.—Terapia Moderna.

Th. M.—Therapeutische Monatshefte.

Ther. Geg.—Die Therapie der Gegenwart.

Ther. Prog.—Therapeutic Progress.

Ther. Woch.—Therapeutische Wochenschrift.

Tr. Am. Asso. Phys.—Transaction of the American Association of Physicians.

Tr. Chem. Soc.—Transactions of the Chemical Society of London.

Tr. Col. State Med. Soc.—Transactions of the Colorado State Medical Society.

Tr. Linn. Soc.—Transactions of the Linnæan Society.

Ungar. Med. Presse.—Ungarische medicinische Presse.

Union Méd.—L'Union Médicale.

U. P. M. B.—University of Pennsylvania Medical Bulletin.

U. S.—United States Pharmacopœia X. Other Editions are Indicated by Date or Number as: U. S. IX.

Var.—Variety.

V. A. P. A.—Virchow's Archiv für Pathologische Anatomie und Physiologie.

W. J. M. S.—Western Journal of Medicine and Surgery.

W. K. R.—Wiener klinische Rundschau.

W. K. W.—Wiener klinische Wochenschrift.

W. M. Bl.—Wiener medicinische Blätter.

W. M. P.—Wiener medicinische Presse.

West. Drug.—The Western Druggist.

Y. B. P.—Year-book of Pharmacy and Transactions of British Pharmaceutical Conference.

Z. B.—Zeitschrift für Biologie.

Zeit. An. Chem.—Zeitschrift für Analytische Chemie.

Zeit. Angew. Chem.—Zeitschrift für Angewandte Chemie.

Zeit. Anorg. Chem.—Zeitschrift für anorganischen Chemie.

Zeit. E. P. T.—Zeitschrift für Experimentelle Pathologie und Therapie.

Zeit. Hyg.—Zeitschrift für Hygiene und Infektionskrankheiten.

Zeit. K. M.—Zeitschrift für Klinische Medicin.

Zeit. Oest. Apoth. Ver.—Zeitschrift des Allgemeinen Oesterreichischen Apotheker-Vereines.

Zeit. P. C.—Zeitschrift für Physiologische Chemie.

Zeit. T. M.—Zeitschrift für thierische Medicin.

THE FOOD AND DRUGS ACT.

In force and effect from and after January 1, 1907.

AN ACT For preventing the manufacture, sale, or transportation of adulterated or misbranded or poisonous or deleterious foods, drugs, medicines, and liquors, and for regulating traffic therein, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That it shall be unlawful for any person to manufacture within any Territory of the District of Columbia any article of food or drug which is adulterated or misbranded, within the meaning of this Act; and any person who shall violate any of the provisions of this section shall be guilty of a misdemeanor, and for each offense shall, upon conviction thereof, be fined not to exceed five hundred dollars or shall be sentenced to one year's imprisonment, or both such fine and imprisonment, in the discretion of the court, and for each subsequent offense and conviction thereof shall be fined not less than one thousand dollars or sentenced to one year's imprisonment, or both such fine and imprisonment in the discretion of the court.

Sec. 2. That the introduction into any State or Territory or the District of Columbia from any other State or Territory or the District of Columbia, or from any foreign country or shipment to any foreign country of any article of food or drugs which is adulterated or misbranded, within the meaning of this Act, is hereby prohibited; and any person who shall ship or deliver for shipment from any State or Territory or the District of Columbia to any other State or Territory or the District of Columbia, or to a foreign country, or who shall receive in any State or Territory, or the District of Columbia from any other State or Territory or the District of Columbia, or foreign country, and having so received, shall deliver, in original unbroken packages, for pay or otherwise, or offer to deliver to any other person, any such article so adulterated or misbranded within the meaning of this Act, or any person who shall sell or offer for sale in the District of Columbia or the Territories of the United States any such adulterated or misbranded foods or drugs, or export or offer to export the same to any foreign country, shall be guilty of a misdemeanor, and for such offense be fined not exceeding two hundred dollars for the first offense, and upon conviction for each subsequent offense not exceeding three hundred dollars or be imprisoned not exceeding one year, or both, in the discretion of the court: *Provided,* That no article shall be deemed misbranded or adulterated within the provisions of this Act when intended for export to any foreign country and prepared or packed according to the specifications or directions of the foreign purchaser when no substance is used in the preparation or packing thereof in conflict with the laws of the foreign country to which said article is intended to be shipped; but if said article shall be in fact sold or offered for sale for domestic use or consumption, then this proviso shall not exempt said article from the operation of any of the other provisions of this Act.

Sec. 3. That the Secretary of the Treasury, the Secretary of Agriculture, and the Secretary of Commerce and Labor shall make uniform rules and regulations for carrying out the provisions of this Act, including the collection and examination of specimens of foods and drugs manufactured or offered for sale in the District of Columbia, or in any Territory of the United States, or which shall be offered for sale in unbroken packages in

First: In the case of mixtures or compounds which may be now or from time to time hereafter known as articles of food, under their own distinctive names, and not an imitation of or offered for sale under the distinctive name of another article, if the name be accompanied on the same label or brand with a statement of the place where said article has been manufactured or produced.

Second. In the case of articles labeled, branded, or tagged so as to plainly indicate that they are compounds, imitations, or blends, and the word "compound," "imitation" or "blend," as the case may be, is plainly stated on the package in which it is offered for sale: *Provided*, That the term blend as used herein shall be construed to mean a mixture of like substances, not excluding harmless coloring or flavoring ingredients used for the purpose of coloring and flavoring only: *And provided further*, That nothing in this Act shall be construed as requiring or compelling proprietors or manufacturers of proprietary foods which contain no unwholesome added ingredient to disclose their trade formulas, except in so far as the provisions of this Act may require to secure freedom from adulteration or misbranding.

Sec. 9. That no dealer shall be prosecuted under the provisions of this Act, when he can establish a guaranty signed by the wholesaler, jobber, manufacturer, or other party residing in the United States, from whom he purchases such articles, to the effect that the same is not adulterated or misbranded within the meaning of this Act, designating it. Said guaranty, to afford protection, shall contain the name and address of the party or parties making the sale of such articles to such dealer, and in such case said party or parties shall be amenable to the prosecutions, fines, and other penalties which would attach, in due course, to the dealer under the provisions of this Act.

Sec. 10. That any article of food, drug, or liquor that is adulterated or misbranded within the meaning of this Act, and is being transported from one State, Territory, District, or insular possession to another for sale, or, having been transported, remains unloaded, unsold, or in original unbroken packages, or if it be sold or offered for sale in the District of Columbia or the Territories, or insular possessions of the United States, or if it be imported from a foreign country for sale, or if it is intended for export to a foreign country, shall be liable to be proceeded against in any district court of the United States within the district where the same is found, and seized for confiscation by a process of libel for condemnation. And if such article is condemned as being adulterated or misbranded or of a poisonous or deleterious character, within the meaning of this Act, the same shall be disposed of by destruction or sale, as the said court may direct, and the proceeds thereof, if sold, less the legal costs and charges, shall be paid into the Treasury of the United States, but such goods shall not be sold in any jurisdiction contrary to the provisions of this Act or the laws of that jurisdiction: *Provided, however*, That upon the payment of the costs of such libel proceedings and the execution and delivery of a good and sufficient bond to the effect that such articles shall not be sold or otherwise disposed of contrary to the provisions of this Act, or the laws of any State, Territory, District, or insular possession, the court may by order direct that such articles be delivered to the owner thereof. The proceedings of such libel cases shall conform, as near as may be, to the preceedings in admiralty, except that either party may demand trial by jury of any issue of fact joined in any such case, and all such proceedings shall be at the suit of and in the name of the United States.

Sec. 11. The Secretary of the Treasury shall deliver to the Secretary of Agriculture, upon his request from time to time, samples of foods and drugs which are being imported into the United States or offered for import, giving notice thereof to the owner or consignee who may appear before the Secretary of Agriculture, and have the right to introduce testimony, and if it appear from the examination of such samples that any article of food or drug offered to be imported into the United States is adulterated or misbranded within the meaning of this Act, or is otherwise dangerous to the health of the people of the United States, or is of a kind forbidden entry into, or forbidden to be sold, or restricted in sale in the country in which it is made or from which it is exported, or is otherwise falsely labeled in any respect, the said article shall be refused admission, and the Secretary of the Treasury shall refuse delivery to the consignee and shall cause the destruction of any goods refused delivery which shall not be exported by the consignee within three months from the date of notice of such refusal under such regulations as the Secretary of the Treasury may prescribe: *Provided*, That the Secretary of the Treasury may deliver to the consignee such goods pending examination and decision in the matter on execution of a penal bond for the amount of the full invoice value of such goods, together with the duty thereon, and on refusal to return such goods for any cause to the custody of the Secretary of the Treasury when demanded, for the purpose of excluding them from the country, or for any other purpose, said consignee shall forfeit the full amount of the bond: *And provided further*, That all charges for storage, cartage, and labor on goods which are refused admission or delivery shall be paid by the owner or consignee and in default of such payment shall constitute a lien against any future importation made by such owner or consignee.

Sec. 12. That the term "Territory" as used in this act shall include the insular possessions of the United States. The word "person" as used in this Act shall be construed to import both plural and the singular, as the case demands, and shall include corporations, companies, societies and associations. When construing and enforcing the provisions of this Act, the act, omission, or failure of any officer, agent, or other person acting for or employed by any corporation, company, society, or association, within the scope of his employment or office, shall in every case be also deemed to be the act, omission, or failure of such corporation, company, society, or association as well as that of the person.

Sec. 13. That this Act shall be in force and effect from and after the first day of January, nineteen hundred and seven.

Approved, June 30, 1906.

REGULATIONS FOR THE ENFORCEMENT OF THE FOOD AND DRUGS ACT.

The regulations promulgated by the Department of Agriculture from time to time for the enforcement of this act have become so numerous and voluminous that it is impracticable to give even a summary of them. In these regulations are included definitions of certain terms used in the trade, standards for quality of foods, and of some drug products, as well as rules concerning the form of label etc. The food and drugs code has become so complex that the Bureau of Chemistry has recently (May 1925) issued a summary of the regulations for the guidance of manufacturers of and dealers in drugs. This circular follows.

INFORMATION ON DRUGS.

1. Scope of the Food and Drugs Act.

The Federal food and drugs act applies to all drugs which enter interstate or foreign commerce, or are made, sold, or offered for sale in any Territory of the United States (including the insular possessions) or the District of Columbia.

2. Definition of "Drug."

The term "drug," as defined by section 6 of the act, includes "all medicines and preparations recognized in the United States Pharmacopœia or National Formulary for internal or external use, and any substance or mixture of substances intended to be used for the cure, mitigation, or prevention of disease of either man or other animals."

3. Permit or License.

Nothing in the act provides for the issuance of permits or licenses or authorizes the approval of preparations or labels. Therefore, it is unnecessary to submit samples or formulas of medicinal preparations to the Bureau of Chemistry for examination or approval.

4. Ingredients Required to be Declared.

The act does not specify the substances that may or may not be used as ingredients, but it does require that the quantity or proportion of the substances referred to in section 8, second paragraph, under "In case of drugs" (Circular 21, page 25), present in drug products shall be plainly stated on the label of the container, and on the carton or wrapper (Regulation 24, Circular 21, page 12). The method of declaring the quantity or proportion of such substances or their derivatives mentioned in the paragraph cited above is set forth in Regulation 25. A declaration of the ingredients or formula is not ordinarily required, but if made it should be complete and correct (Regulation 14, (f), (g), and (h), Circular 21, page 9).

5. Declaration of Specially Denatured Alcohol.

The Bureau of Internal Revenue has authorized the use of specially denatured alcohol in the manufacture of certain drugs. Some of the denaturants permitted are derivatives of alcohol. For the present the requirements of the Federal food and drugs act relating to the declaration of alcohol and its derivatives will be considered satisfied by either:

(*a*) Declaration of the percentages of alcohol and of each of its derivatives present as a denaturant in the finished product, or

(*b*) Declaration of the percentage of specially denatured alcohol in the finished product.

If (*b*) is chosen, the number of the formula of the denatured alcohol used should be stated. For example, if a product contains 50 per cent. of specially denatured alcohol, formula 23-B, the declaration should be "Contains 50% Specially Denatured Alcohol, Formula 23-B."

6. Labeling.

(*a*) In section 8 the general paragraph and the three subparagraphs under the heading "In case of drugs" deal with misbrandings. The word "label" has been interpreted by the courts to cover any printed matter that accompanies the package, such as shipping container, wrapper box, carton, bottle label, booklet, or circular (Regulation 14, Circular 21, page 8).

(*b*) In a labeling the manufacturer should avoid any suggestion, hint, or insinuation, direct or indirect, by statement, design, or device, that may tend to convey a misleading impression in any particular, and also any unwarranted representations that are indefinite or of general sweeping character. It is the duty of the manufacturer to carefully consider whether the statements he proposed to put on his labeling are strictly in harmony with the facts.

(*c*) Care must be taken that on the labeling appears no misrepresentation, expressed or implied, as to the therapeutic effect of the product. In making statements of therapeutic efficacy on a label a manufacturer assumes the position of one having a special knowledge of disease and its treatment, and the United States Supreme Court has ruled that he can be held accountable accordingly. Under the law he is responsible for his statements or representations, and no one can relieve him of this responsibility. Personal belief, testimonials in general, dispensatories, scattered isolated excerpts from medical publications, obsolete medical books and discarded medical practices are not adequate authorities for therapeutic claims; the consensus of present-day medical opinion is the standard which should guide manufacturers in labeling. A preparation cannot properly bear promises of benefit unless as a matter of fact it can be reasonably depended upon to produce the results claimed for it.

7. Names of Diseases.

A judicial decision states: "Language used in the label is to be given the meaning ordinarily conveyed by it to those to whom it was addressed." The printing of names of diseases or disorders on the labeling of a medicine for public sale conveys to the purchaser the impression that the product in itself is a competent treatment for the diseases mentioned. One who is seeking something that will rid him of his trouble is more concerned with the names of the affections for which the product is recommended than with the style of language employed. Regardless of whether the product is recommended as a "cure," "remedy," "relief," "useful in the treatment of," "indicated for," or simply "for," certain affections, the question is whether or not the product in itself, by reason of the contained ingredients, constitutes a treatment for the disorders named. The names of diseases in a labeling, therefore, should be limited to those for which the article, in view of the recognized medicinal action of its ingredients, considered singly or in combination, is a treatment. Names of organs or portions of the body should not appear upon a labeling unless the product can properly be considered a treatment for any and all disorders to which such organs or parts may be subject.

8. Testimonials.

No statement relative to the therapeutic effect of a preparation should be made in the form of a testimonial for which the manufacturer is not willing to bear the full responsibility. Representations of curative or beneficial effect conveyed by testimonials are subject to the same requirements as other therapeutic claims. When a manufacturer publishes a testimonial to the effect that his medicine has produced certain results, he conveys to others the promise of a similar benefit, and he must assume the responsibility for all therapeutic claims made in this manner to the same extent that he does for promises of benefit made in his own words. That the testimonial may be bona fide and accurately quoted does not relieve him of this responsibility.

9. Collateral Advertising.

Collateral advertising in newspapers and elsewhere and claims made by agents determine the meaning of any indefinite or obscure statements or representations in the labeling. The wording of collateral advertising should in no instance exceed, in the impressions produced, the terms of the labeling. No interpretation of, or reference to, the terms of the label should be used to create an impression in the mind of the purchaser that the preparation is a remedy, treatment, or preventive for diseases for which, in fact, it is not.

10. Approval of Labeling.

Under the law there is no authority to approve or suggest labelings, formulas, trade names, or advertising literature. Numerous requests are referred to this department for the approval of labels. The act does not authorize the department to give such approval, and any printed matter upon the label implying that this department has approved it will be without warrant.

11. Important Quotation from Opinion of U. S. Supreme Court on Food and Drugs Act.

"The statute is plain and direct. Its comprehensive terms condemn every statement, design, and device which may mislead or deceive. Deception may result from the use of statements not technically false or which may be literally true. The aim of the statute is to prevent that resulting from indirection and ambiguity, as well as from statements which are false. It is not difficult to choose statements, designs and devices which will not deceive. Those which are ambiguous and liable to mislead should be read favorably to the accomplishment of the purpose of the act." (From Opinion of the Supreme Court of the United States in United States vs. 95 Barrells, Et Al., No. 559, October Term, 1923.)

12. Guaranty and Serial Number.

On May 5, 1914, all guaranties on file with the Secretary of Agriculture were stricken from the files and all serial numbers cancelled. It is, therefore, no longer permissible to use either the serial number or guaranty legend on the label or package of food or drug products that come within the jurisdiction of the Federal food and drugs act. In this connection your attention is called to Regulation 6, page 5, Circular 21, which explains the permissible use of a guaranty.

13. Requests for Information Regarding Specific Preparations.

The bureau is authorized to give out information concerning the quality and composition of preparations upon the market only in the form of notices of judgment, published after court action, as authorized by section 4, page 23, Circular 21. Requests for information concerning specific products can be complied with only in those instances where notices of judgment are available.

14. Requests for Analysis.

The examination of samples of medicinal preparations is limited to those of an official character, collected by authorized agents of the department. Requests for analysis can not be complied with, since no authority or appropriation exists for such work.

15. Statement of Weight, Measure, or Count.

The act does not require that the label of drugs shall bear a statement of the weight, measure, or numerical count of the contents of the package, but any statement of this nature should be correct and complete.

16. Toilet Preparations.

The act deals with foods and drugs, the term "drug" being defined in section 6, page 24, Circular 21. A toilet preparation that is not intended or represented, directly or indirectly, to be useful for the cure, mitigation, or prevention of disease is not subject to the law, but the manufacturer should exercise care that it does not contain any ingredient that might be injurious to health.

17. Narcotic Act and Prohibition Act.

Narcotics and alcohol are subject to the provisions of the Harrison narcotic act and the prohibition act, as well as to the provisions of the food and drugs act. Information regarding these two laws may be obtained from the Bureau of Internal Revenue, Washington, D. C.

18. Postal Laws.

The postal laws and regulations contain provisions as to drug products coming within their scope. Information on this subject can be obtained by addressing the Postmaster General, Washington, D. C.

19. Patents and Trade-marks.

The Department of Agriculture can give no advice on patents or trade-marks. Information on this subject may be obtained by addressing the Commissioner of Patents, Washington, D. C. As far as the Federal food and drugs act is concerned, no patent, trade-mark or copyright is necessary for the manufacture or sale of drug products.

20. Copyright.

Information regarding copyright privileges may be obtained by addressing the Copyright Division, Library of Congress, Washington, D. C.

21. Patents, Trade-marks and Copyrights Confer No Exemption.

The issuance of a trade-mark, copyright, or patent for a preparation does not exempt it from the provisions of the Federal food and drugs act.

22. State Laws.

State laws may contain additional requirements for the manufacture or sale of medicinal preparations.

HARRISON NARCOTIC ACT.

Production, Importation, Manufacture, Compounding, Sale, Dispensing, or Giving Away of Opium or Coca Leaves, their Salts, Derivatives, or Preparations.

THE LAW

By an act of Congress approved December 17, 1914, it is provided:

Persons who are required to register.

That on and after the first day of March, nineteen hundred and fifteen, every person who produces, imports, manufactures, compounds, deals in, dispenses, sells, distributes, or gives away opium or coca leaves or any compound, manufacture, salt, derivative, or preparation thereof, shall register with the collector of internal revenue of the district his name or style, place of business, and place or places where such business is to be carried on: *Provided*, That the office, or if none, then the residence of any person shall be considered for the purpose of this Act to be his place of business. At the time of such registry and on or before the first day of July, annually thereafter, every person who produces, imports, manufactures, compounds, deals in, dispenses, sells, distributes, or gives away any of the aforesaid drugs shall pay to the said collector a special tax at the rate of $1 per annum: *Provided*, That no employee of any person who produces, imports, manufactures, compounds, deals in, dispenses, sells, distributes, or gives away any of the aforesaid drugs, acting within the scope of his employment, shall be required to register or to pay the special tax provided by this section: *Provided further*, That the person who employs him shall have registered and paid the special tax as required by this section: *Provided further*, That officers of the United States Government who are lawfully engaged in making purchases of the above-named drugs for the various departments of the Army and Navy, the Public Health Service, and for Government hospitals and prisons, and officers of any State government, or of any county or municipality therein, who are lawfully engaged in making purchases of the above-named drugs for State, county, or municipal hospitals or prisons, and officials of and Territory or insular possession or the District of Columbia or of the United States who are lawfully engaged in making purchases of the above-named drugs for hospitals or prisons therein shall not be required to register and pay the special tax as herein required.

Special tax to be paid.

Exemption — Drugs purchased for U. S., etc.

Failure to register and to pay special tax.

It shall be unlawful for any person required to register under the terms of this Act to produce, import, manufacture, compound, deal in, dispense, sell, distribute, or give away any of the aforesaid drugs without having registered and paid the special tax provided for in this section.

Word "person" to include partnership, etc.

That the word "person" as used in this Act shall be construed to mean and include a partnership, association, company, or corporation, as well as a natural person; and all provisions of existing law relating to special taxes so far as applicable, including the provisions of section thirty-two hundred and forty of the Revised Statutes of the United States are hereby extended to the special tax herein imposed.

Regulations to be prescribed.

That the Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury, shall make all needful rules and regulations for carrying the provisions of this Act into effect.

Purchase orders required.

Section 2. That it shall be unlawful for any person to sell, barter, exchange, or give away any of the aforesaid drugs except in pursuance of a written order of the person to whom such article is sold, bartered, exchanged, or given, on a form to be issued in blank for that purpose by the Commissioner of Internal Revenue. Every person who shall accept any such order, and in pursuance thereof shall sell, barter, exchange, or give away any of the aforesaid drugs, shall preserve such order for a period of two years in such a way as to be readily accessible to inspection by any officer agent, or employee of the Treasury Department duly authorized for that purpose. and the State, Territorial District, municipal, and insular officials named in section five of this Act. Every person who shall give an order as herein provided to any other person for any of the aforesaid drugs shall, at or before the time of giving such order, make or cause to be made a duplicate thereof on a form to be issued in blank for that purpose by the Commissioner of Internal Revenue, and in case of the acceptance of such order, shall preserve such duplicate for said period of two years in such a way as to be readily accessible to inspection

Orders to be preserved for 2 years. Inspection of same by officers, agents, etc.

Duplicate orders to be retained by purchaser.

by the officers, agents, employees, and officials hereinbefore mentioned. Nothing contained in this section shall apply—

Exemptions—Drugs dispensed to patient, in certain cases.

(*a*) To the dispensing or distribution of any of the aforesaid drugs to a patient by a physician, dentist, or veterinary surgeon registered under this Act in the course of his professional practice only: *Provided:* That such physician, dentist, or veterinary surgeon shall keep a record of all such drugs dispensed or distributed, showing the amount dispensed or distributed, the date, and the name and address of the patient to whom such drugs are dispensed or distributed, except such as may be dispensed or distributed to a patient upon whom such physician, dentist or veterinary surgeon shall personally attend; and such record shall be kept for a period of two years from the date of dispensing or distributing such drugs, subject to inspection, as provided in this Act.

Prescriptions—how to be issued and signed.

Prescriptions to be preserved for 2 years.

(*b*) To the sale, dispensing, or distribution of any of the aforesaid drugs by a dealer to a consumer under and in pursuance of a written prescription issued by a physician, dentist, or veterinary surgeon registered under this Act: *Provided, however,* That such prescription shall be dated as of the day on which signed and shall be signed by the physician, dentist, or veterinary surgeon who shall have issued the same: *And Provided, further,* That such dealer shall preserve such prescription for a period of two years from the day on which such prescription is filled in such a way as to be readily accessible to inspection by the officers, agents, employees, and officials hereinbefore mentioned.

Exemption—drugs shipped to a foreign country.

(*c*) To the sale, exportation, shipment or delivery of any of the aforesaid drugs by any person within the United States or any Territory or the District of Columbia or any of the insular possessions of the United States to any person in any foreign country, regulating their entry in accordance with such regulations for importation thereof into such foreign country as are prescribed by said country, such regulations to be promulgated from time to time by the Secretary of State of the United States.

Sales, etc., to Department of Army, Navy, etc.

(*d*) To the sale, barter, exchange, or giving away of any of the aforesaid drugs to any officer of the United States Government or of any State, territorial, district, county, or municipal or insular government lawfully engaged in making purchases thereof for the various departments of the Army and Navy, the Public Health Service, and for Government, State, territorial district, county, or municipal or insular hospitals or prisons.

Blank forms to be provided.

Sale of same.

Collector to keep account of sales.

Blanks to be sold only to persons who have registered.

Unlawful use of forms.

The Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury, shall cause suitable forms to be prepared for the purposes above mentioned, and shall cause the same to be distributed to collectors of internal revenue for sale by them to those persons who shall have registered and paid the special tax as required by section one of this Act in their districts, respectively; and no collector shall sell any of such forms to any persons other than a person who has registered and paid the special tax as required by section one of this Act in his district. The price at which such forms shall be sold by said collectors shall be fixed by the Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury, but shall not exceed the sum of $1 per hundred. Every collector shall keep an account of the number of such forms sold by him, the names of the purchasers, and the number of such forms sold to each of such purchasers. Whenever any collector shall sell any of such forms, he shall cause the name of the purchaser thereof to be plainly written or stamped thereon before delivering the same, and no person other than such purchaser shall use any of said forms bearing the name of such purchaser for the purpose of procuring any of the aforesaid drugs, or furnish any of the forms bearing the name of such purchaser to any person with intent thereby to procure the shipment or delivery of any of the aforesaid drugs. It shall be unlawful for any person to obtain by means of said order forms any of the aforesaid drugs for any purpose other than the use, sale, or distribution thereof by him in the conduct of a lawful business in said drugs or in the legitimate practice of his profession.

Porto Rico and Philippine Islands.

Canal Zone.

The provisions of this Act shall apply to the United States, the District of Columbia, the Territory of Alaska, the Territory of Hawaii, the insular possessions of the United States, and the Canal Zone. In Porto Rico and the Philippine Islands the administration of this Act, the collection of the said special tax, and the issuance of the order forms specified in section two shall be performed by the appropriate internal-revenue officers of those governments, and all revenues collected hereunder in Porto Rico and the Philippine Islands shall accrue intact to the general governments thereof, respectively. The courts of first instance in the Philippine Islands shall possess and exercise jurisdiction in all cases arising under this Act in said islands. The President is authorized and directed to issue such Executive orders as will carry into effect in the Canal Zone the intent and purpose of this Act by providing for the registration and the imposition of a special tax upon all persons in the Canal Zone who produce, import, compound, deal in, dispense, sell, distribute, or give away opium or coca leaves, their salts, derivatives, or preparations.

Collector may require sworn statement as to drugs received.

Section 3. That any person who shall be registered in any internal-revenue district under the provisions of section one of this Act, shall whenever required so to do by the collector of the district, tender to the said collector a true and correct statement or return, verified by affidavit, setting forth the quantity of the aforesaid drugs received by him in said internal-revenue district during such period immediately preceding the demand of the collector, not exceeding three months, as the said collector may fix and determine; the names of the persons from whom the said drugs were received; the quantity in each instance received from each of such persons, and the date when received

Shipment of drugs unlawful, except—

Common carriers and employees exempt.

Section 4. That it shall be unlawful for any person who shall not have registered and paid the special tax as required by section one of this Act to send, ship, carry or deliver any of the aforesaid drugs from any State or Territory or the District of Columbia, or any insular possession of the United States, to any person in any other State or Territory or the District of Columbia or any insular possession of the United States: *Provided*, That nothing contained in this section shall apply to common carriers engaged in transporting the aforesaid drugs, or to any employee acting within the scope of his employment, of any person who shall have registered and paid the special tax as required by section one of this Act, or to any person who shall deliver any such drug which has been prescribed or dispensed by a physician, dentist, or veterinarian required to register under the terms of this Act, who has been employed to prescribe for the particular patient receiving such drug, or to any United States, State, county, municipal, District, Territorial, or insular officer or official acting within the scope of his official duties.

Orderforms, prescriptions, and statements filed to be open to inspection of officers.

Certified copies of statements and returns to be furnished by collectors.

Fees.

Penalty for disclosing information, except—

Certified list of names may be furnished.

Section 5. That the duplicate-order forms and the prescriptions required to be preserved under the provisions of section two of this Act, and the statements or returns filed in the office of the collector of the district, under the provisions of section three of this Act, shall be open to inspection by officers, agents, and employees of the Treasury Department duly authorized for that purpose; and such officials of any State or Territory, or of any organized municipality therein, or of the District of Columbia, or any insular possession of the United States, as shall be charged with the enforcement of any law or municipal ordinance regulating the sale prescribing, dispensing, dealing in, or distribution of the aforesaid drugs. Each collector of internal revenue is hereby authorized to furnish, upon written request, certified copies of any of the said statements or returns filed in his office to any of such officials of any State or Territory or organized municipality therein, or the District of Columbia, or any insular possession of the United States, as shall be entitled to inspect the said statements or returns filed in the office of the said collector, upon the payment of a fee of $1 for each one hundred words or fraction thereof in the copy or copies so requested. Any person who shall disclose the information contained in the said statements or returns or in the said duplicate-order forms, except as herein expressly provided, and except for the purpose of enforcing the provisions of this Act, or for the purpose of enforcing any law of any state or Territory of the District of Columbia, or any insular possession of the United States, or ordinance of any organized municipality therein, regulating the sale, prescribing, dispensing, dealing in, or distribution of the aforesaid drugs, shall, on conviction, be fined or imprisoned as provided by section nine of this Act. And collectors of internal revenue are hereby authorized to furnish upon written request, to any person, a certified copy of the names of any or all persons who may be listed in their respective collection districts as special tax payers under the provisions of this Act, upon payment of a fee of $1 for each one hundred names or fraction thereof in the copy so requested.

Act not to apply to certain preparations, etc.

Conditions imposed.

Decocainized coca leaves.

Section 6. That the provisions of this Act shall not be construed to apply to the sale, distribution, giving away, dispensing, or possession of preparations and remedies which do not contain more than two grains of opium, or more than one-fourth of a grain of morphine, or more than one-eighth of a grain of heroin, or more than one grain of codeine, or any salt or derivative of any of them in one fluid ounce, or, if a solid or semisolid preparation, in one avoirdupois ounce, or to liniments, ointments, or other preparations which are prepared for external use only, except liniments, ointments, and other preparations which contain cocaine or any of its salts or alpha or beta eucaine or any of their salts or any synthetic substitute for them: *Provided*, That such remedies and preparations are sold, distributed, given away, dispensed, or possessed as medicines and not for the purpose of evading the intentions and provisions of this Act. The provisions of this Act shall not apply to decocainized coca leaves or preparations made therefrom, or to other preparations of coca leaves which do not contain cocaine.

Certain revenue laws made applicable.

Section 7. That all laws relating to the assessment, collection, remission, and refund of internal-revenue taxes including section thirty-two hundred and twenty-nine of the Revised Statutes of the United States, so far as applicable to and not inconsistent with the provisions of this Act, are hereby extended and made applicable to the special taxes imposed by this Act.

Possession of drugs prohibited, except—

Certain persons exempt.

Burden of proof on defendant.

SECTION 8. That it shall be unlawful for any person not registered under the provisions of this Act, and who has not paid the special tax provided for by this Act, to have in his possession or under his control any of the aforesaid drugs; and such possession or control shall be presumptive evidence of a violation of this section, and also of a violation of the provisions of section one of this Act: *Provided,* That this section shall not apply to any employee of a registered person, or to a nurse under the supervision of a physician, dentist, or veterinary surgeon registered under this Act, having such possession or control by virtue of his employment or occupation and not on his own account; or to the possession of any of the aforesaid drugs which has or have been prescribed in good faith by a physician, dentist, or veterinary surgeon registered under this Act; or to any United States, State, county, municipal, District, Territorial, or insular officer or official who has possession of any said drugs, by reason of his official duties, or to a warehouseman holding possession for a person registered and who has paid the taxes under this Act; or to common carriers engaged in transporting such drugs: *Provided further*, That it shall not be necessary to negative any of the aforesaid exemptions in any complaint, information, indictment, or other writ or proceeding laid or brought under this Act; and the burden of proof of any such exemption shall be upon the defendant.

Penalties.

SECTION 9. That any person who violates or fails or comply with any of the requirements of this Act, shall, on conviction, be fined not more than $2,000 or be imprisoned not more than five years, or both, in the discretion of the court.

Appointment of agents, deputy collectors, etc.

SECTION 10. That the Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury, is authorized to appoint such agents, deputy collectors, inspectors, chemists, assistant chemists, clerks or messengers in the field and in the Bureau of Internal Revenue in the District of Columbia as may be necessary to enforce the provisions of this Act.

Appropriation.

SECTION 11. That the sum of $150,000, or so much thereof as may be necessary, be, and hereby is, appropriated, out of any moneys in the Treasury not otherwise appropriated, for the purpose of carrying into effect the provisions of this Act.

Act not to be construed as impairing or repealing certain acts.

SECTION 12. That nothing contained in this Act shall be construed to impair alter, amend, or repeal any of the provisions of the Act of Congress approved June thirtieth, nineteen hundred and six, entitled "An Act for preventing the manufacture, sale, or transportation of adulterated or misbranded, or poisonous, or deleterious foods, drugs, medicines, and liquors, and for regulating traffic therein, and for other purposes," and any amendment thereof, or of the Act approved February ninth, nineteen hundred and nine, entitled "An Act to prohibit the importation and use of opium for other than medicinal purposes," and any amendment thereof.

THE DISPENSATORY OF THE UNITED STATES

PART I

DRUGS RECOGNIZED BY THE UNITED STATES PHARMACOPŒIA, THE PHARMACOPŒIA OF GREAT BRITAIN, OR THE NATIONAL FORMULARY.

ACACIA. U. S. (Br.)

ACACIA Acac. [Gum Arabic]

"Acacia is the dried gummy exudation from the stems and branches of *Acacia Senegal* Willdenow or of some other species of *Acacia* (Fam. *Leguminosæ*). Acacia yields not more than 1 per cent. of water-insoluble residue, and not more than 15 per cent. of moisture." *U. S.* "A gummy exudation from the stem and branches of Acacia Senegal, *Willd.*, and of other species of Acacia, *Willd.*" *Br.*

Acaciæ Gummi, *Br.;* Gummi Africanum; Gummi Mimosæ; Gum Acacia; Galam Gum; Arabicum Gummi, *Fr. Cod,* Gomme Arabique Gomme du Sénégal, *Fr.;* Gummi Arabicum; *P. G.;* Arabisches Gummi, *G.;* Gomma Arabica, Gomma del Cordofan, *It.;* Goma Arabiga, *Sp.;* Samagh Arabee, *Arab.*

The name *Acacia* was employed by the ancient Greeks to designate the gum tree of Egypt, and has been appropriately applied to the genus in which that plant is included.

The most important of the gum-yielding Acacias is the official *A. Senegal* Willd. This is a small tree rarely exceeding a height of 6 m., with a grayish bark, the inner layers of which are strongly fibrous, bipinnate leaves, dense spikes of small yellow flowers longer than the leaves, and broad pods containing 5 or 6 seeds. It forms large forests in Western Africa, north of the river Senegal, and is abundant in Eastern Africa, Khordofan, and Southern Nubia. It is known by the natives of Senegambia as *Verek* and of Khordofan as *Hashab.*

Nearly all species of Acacia growing in Africa yield a gum. The commercial *Somali gum,* which is usually of fair quality, is yielded by *A. glaucophylla* Steud. and *A. abyssinica* Hochst., shrubs growing in Abyssinia and the Somali country. The following species yield a gum having a brownish or reddish color, and hence are less valuable, viz., *A. arabica* Willd. (*Amrad gum*), *A. stenocarpa* Hochst., *A. Seyal* Del. and *A. Ehrenbergiana* Hayne. Inferior gums are also yielded by the following: *A. horrida* Willd., which furnishes the so-called *Cape gum* and is distinguished by being very brittle and yielding a less adhesive mucilage. *Talca* or *Sennarr gum* is derived from *A. Fistula* Schweinf. This gum has a greenish tinge and yields a ropy mucilage. *Amritsar gum* is obtained from *A. modesta* Wall. It occurs in large brown tears and like *A. arabica* is used in calico printing. *Mogadore gum,* derived from *A. gummifera* Willd., occurs in dark brown tears which are little fissured. *Australian gum* has usually a reddish color, said to be due to the presence of tannin, although some specimens are light in color and scarcely distinguishable from acacia. This gum is also spoken of as *Wattle gum* or *Australian gum,* and is derived from the *Golden Wattle* (*A. pycnantha* Benth.), a shrub growing in New South Wales, Victoria and Southern Australia.

The bark and unripe fruit of the acacia contain both tannic and gallic acids. The dried juice of the pod was used by the ancient Greeks; and an extract is still sold in the bazaars of India under the name of *Akakia.* This extract is heavy, hard, of an agreeable odor, varying in color from greenish to dark-reddish, or, when seen in bulk, blackish. It has a sweet, astringent taste, and yields a mucilaginous infusion. A similar preparation, *acacia nostras,* has been prepared in Europe by expression and inspissation from the unripe fruit of *Prunus spinosa,* or wild plum tree.

The gum of the acacias exudes spontaneously from the bark, and hardens on exposure; but incisions are sometimes made in order to facilitate the exudation. The gum is said also to be found immediately under the bark, where it is sometimes collected in regular cavities. It is formed within the plant by metamorphosis of the cells of the inner bark. The tissues involved are chiefly those of the sieve and the cambium. While to some extent it is a natural change, yet it is usually looked upon as being in part a pathological production, as gummosus develops more largely upon the wounding of the trees. The attack of the Acacia plants by various parasites is held by some to account for the enormous production of gums in these plants. The investigations of Smith tend to show that all vegetable gums are of bacterial origin and that the differences in the several gums are due to the differences in the nature of the bacteria producing them. (*Proc. Linn. Soc. N. S. Wales,* 1904, p. 217.) For further discussion on the origin of acacia gum see Tschirch, *"Handbuch der Pharmakognosie,"* and Greenish, *"Materia Medica,"* 3rd ed.

The trees are not tapped for gum until they are about six years old. The annual yield varies very greatly, being from 188 to 2856 Gm. in young trees and from 379 to 6754 Gm. in large trees. The average annual yield of gum from young trees is about 900 Gm. and from old trees over 2 kilos. (Edie, 4th Report of the *Wellcome Tropical Research Laboratory.*)

It is stated by Jackson that, in Morocco, the greatest product is obtained in the driest and hottest weather, and from the most sickly trees. An elevated temperature appears to be essential, for in cooler climates, though the tree may flourish, it yields no gum. It is probable that some species of acacia yield finer gum than others, but it is also certain that the same tree will often yield some gum of the finest quality in regular tears or globular masses, and some irregular shaped, dark colored fragments of inferior value. Thus, from the same tree it will exude, frothy or thick, and clear or dark colored, and will assume, upon hardening, different shapes and sizes; so that the pieces, when collected, require to be assorted before being delivered into commerce. This sorting is usually done on its arrival in European ports and only the selected or picked gum corresponding to the U. S. P. description should be used.

Commercial History and Varieties.—There are two principal commercial varieties of gum arabic: 1. The Khordofan or Arabian Gum and 2. The Senegal or West African Gum, both of these being derived from *A. Senegal*. The former of these has the finer commercial qualities, being nearly white or faint yellowish-white and yielding a more or less transparent viscid mucilage.

KHORDOFAN OR ARABIAN GUM.—This is the finest variety of gum arabic obtainable. It was formerly the only kind designated as gum arabic and entered commerce almost exclusively through Egypt, being collected in Upper Egypt, Nubia, Khordofan, Darfur, and other regions of the Upper Nile, and carried to Alexandria, whence it passed directly into the world's commerce or entered the latter through Smyrna, Trieste, or some other Mediterranean entrepôt. At one time the more or less colored varieties were known as *gum gedda,* while the white and fine drug was known as *gum turic,* names derived from Jiddah and Tor, Red Sea ports, through which the varieties were supposed to be respectively exported. Three chief commercial varieties were formerly recognized. (*a*) *Hashabi* or *Khordofan gum,* the finest of these varieties, was collected in the country westward of the White Nile; formerly it constituted the bulk of the superior gum arabic of commerce. (*b*) *Sennari gum* was an inferior variety, yielding a mucilage which turned sour more quickly than that produced by Khordofan gum. It was collected in a country eastward of the White Nile, and in the region of the Blue Nile. (*c*) *Ghezzirah* or *Gezireh gum* is obtained from Ghezzirah and neighboring countries and sent to Trieste. It has much of the same appearance as the official Khordofan gum.

Formerly, Khordofan gum was collected in all parts of the Soudan and Upper Egypt, and forwarded on the backs of camels to Assouan, at the head of the Nile navigation, often being many months en route. The closure of the Soudan by the Mahdi caused Egyptian gum almost to disappear from commerce, but the reopening of the region by the British government has resulted in large quantities of the gum being brought by rail to Assouan, whence after being sorted into three varieties it is put in palm-leaf sacks and sent down the Nile. The finest Egyptian gum consists of large roundish or smaller more or less irregular fragments, transparent but usually rendered opaque upon the surface by innumerable minute fissures. The inferior gum varies from yellow to dark-reddish as the quality deteriorates, and often contains impurities. H. C. Wood found that the gum arabic comes into Assouan in sacks or mats which are simply piled in rectangular roofless spaces surrounded by walls about ten feet high, made of dry mud. He was informed by the traders that the gum is gathered during the months of January, February and March by collectors having vested rights in a certain portion of the forests. Long incisions are made vertically through the bark and the exuding gum allowed to harden, the trees not being injured by the process, the collections going on from year to year. *Gedda gum,* sometimes spoken of as an Egyptian gum, enters commerece through Geddah, or Jiddah, on the Arabian side of the Red Sea. It seems to be the same as *Mecca* or *El Wisch* or *Aden gums,* which are sometimes spoken of as Egyptian gums, but are probably produced in the triangular peninsula which forms the eastern extremity of Africa.

The best gum arabic is obtained near Khordofan from cultivated trees which are tapped from February to March. Strips of bark from 2 to 3 ft. long and 1 to 3 in. broad are torn from the trunks and larger branches, care being taken not to injure the cambium. The gum slowly exudes as a viscous liquid, collects in a tear at the base of the wound and gradually hardens. In from 2 to 4 weeks, depending upon the weather, the gum is collected by the natives who place the tears in leather bags which, when full, are emptied on a heap. The gum is later exposed to the bleaching action of the sun and garbled by native girls who remove bark and sand. It is then placed in sacks, carried by camel to railroad centers and consigned to Port Soudan for shipment.

Cairo and London are the chief markets of the world's supply of this drug.

Suakin gum, Talca or *Talha gum,* from *A. stenocarpa* and *A. Seyal,* is exceedingly brittle, and usually semi-pulverulent. It is a mixture of nearly colorless and brownish gums, is exported at Alexandria, and is sometimes termed *gum savakin.*

SENEGAL OR WEST AFRICAN GUM.—This commercial variety ranks second to the Khordofan gum. It is derived from *A. Senegal* and other species of *Acacia* growing in the Soudan and Senegal. It yields a good adhesive mucilage and is valuable for technical purposes. Some of the best qualities of Senegal gum are also adapted for certain pharmaceutical uses. It was introduced into Europe by the Dutch. The French afterwards planted a colony on the western coast of Africa, and took possession of the trade. St. Louis, at the mouth of the Senegal, and Portendie, considerably farther north, are the ports in which the commerce in gum chiefly centers. Immense forests exist in the interior, containing many species of the genus *Acacia,* all of which are said to yield gum, as is affirmed do also various trees belonging to other genera. The chief harvest begins in October and ends in December, although gum is also collected in March. The dry winds, which prevail after the rainy season, cause the bark to crack; the juice flows out and hardens in masses, which are often as large as a pigeon's egg, and sometimes as that of an ostrich. It is affirmed that the exudation is also largely caused by a parasitic plant, *Loranthus Acaciæ* Zucc., the gummy exudation freely oozing out at the point where the parasite penetrates the bark. (*Ph. Centralh.,* Aug., 1895.) Senegal gum is usually in roundish or oval unbroken tears, or in straight or curled cylindrical pieces of various sizes, in the finest grades whitish or colorless, but generally yellowish, reddish, or brownish-red. The pieces are generally larger than those of Khordofan gum, less brittle, fissured, and pulverizable, and breaking with a more conchoidal fracture. Vermiform tears are usually present and aid in diagnosing this variety. In recent years the commercial supply of gum Senegal has been a variable one. In 1911 the gum was extremely scarce, there was practically none on the market, owing to a failure of the crop. It is shipped from the Senegal river to Marseilles and Bordeaux, whence it enters the world's commerce.

According to the direction of the British Imperial Institute there are three qualities of Senegal gum as follows:

1. Gomme du bas du fleuve.
2. Gomme du haut du fleuve.
3. Gomme friable, Salabreda or Sadra beida.

INDIA GUM.—*Persian gum,* which is said to be sent from Persia to Assouan to be packed as genuine gum arabic, can be distinguished from the latter, which it closely resembles, by its not dissolving in water. Sickenberger thinks that it is the product of *Prunus bokharensis* or of *P. puddum. India gum* is not produced in India, but reaches Bombay from Aden and the Red Sea ports, and is almost certainly the product of the Soudan, being therefore identical with Egyptian gum. It occurs in India in two forms, "*Maklai,*" in large round tears or vermicular pieces, white, yellow or reddish, and much fissured; and "*Maswai,*" in fragments and vermicular pieces similar in color and fissuring to the other variety. It is often crudely adulterated before reaching Europe, especially with *Bassora gum,* distinguished by its insolubility in water. Of recent years various India gums have come into commerce in increasing quantities as substitutes for true gum arabic. India gum is brought to this country partly from Calcutta or Bombay, and partly by way of England. It usually comes in large cases. We have seen a parcel said to have come directly from the Red Sea, enclosed in large sacks made of a kind of matting, and bearing a close resemblance to the gum from Calcutta, except that it was more impure, and contained numerous large, irregular, very brittle masses, not much less than the fist in size. This India gum should not be confused with *India gum Tragacanth,* which is called simply by the name India gum in the confectionery and ice cream trades where it is used as a filler and to give bulk and firmness; nor with *India gum of the Br.* (See *Gummi Indicum.*)

During 1924, approximately two-thirds of all the Acacia imported into the United States came direct from Egypt, being shipped for the greater part through Cairo from Khartoum, Khordofan, El Obeid and Omdurman. The other third was imported from London with the exception of an occasional shipment from Bordeaux, Marseilles, Hamburg, Morocco and Bombay.

SUBSTITUTES FOR GUM ARABIC ARE: *Amrad, Amra* or *Oomra Gum.*—A name applied to various East Indian gums having a reddish color and being in more or less irregular stalactitic pieces. (See *U. S. D.,* 19th ed., p. 4.) For description of Ghatti gum see *Gummi Indicum.*

Small quantities of gum are produced in India by a large number of trees often having no botanical relations with the Acacias. For an account of these gums see *Pharmacographia Indica,* vol. i.

Under the names of *Brazilian gum, Para gum,* and *gum angico,* large quantities of a gum occurring in large dark-amber or dark-brown glossy drops, soluble in water, are occasionally found in commerce. It is said to be the product of *Acacia Angico* Mart. Its mucilage is very adhesive, but usually too dark in color for pharmaceutical purposes. It must be distinguished from the gum resin often known as *Brazilian gum,* which is said to be obtained from *Hymenæa courbaril,* and is used in making varnishes.

Chagual or *Magyey gum* of Chili occurs in hollow cylindrical pieces from 0.2 to 1.5 cm. in thickness, occasionally having the form of stalactites or irregular tubers. On their inner surface they are longitudinally streaked, while their outer surface is usually numerously fissured, the fissures penetrating deeply toward the interior. In the absence of these, the pieces are of glassy brightness, transparent, and of very dense structure internally. The color varies from colorless, through yellowish and brownish to a tolerably deep brown, isolated pieces being almost black. According to the experiments made by Guehm, the commercial drug is scarcely fitted for technical use as a gum, but the clear pieces when made into a concentrated mucilage by prolonged heating answer the purposes of the calico printer well. *Puya chilensis, P. lanuginosa,* and *P. lanata* are commonly said to be the sources of the gum, though the researches of Hartwich make this uncertain. The exudation is asserted to be the result of the bite of a caterpillar, *Kastina elegans.* (*Zeit. Oest. Apoth. Ver.,* Aug. 1, 1896.)

Specimens of gum arabic are sometimes found in commerce, which are soluble in water with difficulty. According to Köchlin, if ten parts of such gum, fifty parts of water, and three parts of a 12 per cent. solution of hydrogen dioxide be heated together for two or three hours, the gum is rendered easily soluble. (*Nat. Drug.,* 1894, 176.) Related to the acacia gums are *wood gum,* from the wood of foliage trees, yielding xylose on hydrolysis; *cherry gum,* the gum of cherry and almond trees, yielding β-arabinose on hydrolysis; *peach gum,* from the peach tree, yielding arabinose and galactose on hydrolysis; *barley gum,* obtained in the nitrogen-free extractive material of cereals, yielding galactose and xylose.

Thos. Maben (*P. J.,* March 1, 1890, p. 717) gives the following method of testing mucilage obtained from various gums sold for gum arabic as the best that he has been able to devise after much experimentation. Two or three drops of the mucilage prepared from the gum are placed on a glass or porcelain slab, and one or two drops of the following reagents added; these are then stirred together with a glass rod and the results compared. In the case of borax, acacia mucilage at once agglutinates or hardens into a gummy mass, similarly with basic lead acetate and ferric chloride, while it gelatinizes or forms a softer mass with potassium silicate. Similar reactions are given by the Senegal gums, the Indian Amrad gums, white Barbary, white and brown Cape, and Geddah gums. Barbary brown and Amrad give a jelly only with borax, otherwise they react as acacia. Australian gum agglutinates with borax, but only gelatinizes with basic lead acetate, and has no reaction with ferric chloride and potassium silicate. Brazilian gum has no reaction with potassium silicate, but gelatinizes with borax and ferric chloride and slightly with basic lead acetate. Ghatti gum gelatinizes with all four reagents, but in a slight degree only with potassium silicate. Oomra gum reacts similarly to acacia, except that it is entirely unaffected by basic lead acetate, and forms a softer jelly with ferric chloride. There are, of course, shades of difference in the various reactions which cannot be indicated by these terms, but, generally speaking, a fair idea is given of the nature of the gum.

It has been proposed to change the arabinic acid of the sugar beet, by the method of Scheibler, into metarabinic acid, as the foundation of a true artificial gum arabic, but the *artificial* gums of the market have no such close chemical relation with the natural gum; many of them are mixtures of various substances, others are produced from starch by the action sulphuric acid or by other means. *Universal gum,* a patented product obtained from potato starch, has been highly commended for the permanency and adhesiveness of its mucilage, but is said not to act well as an emulsifier; it is essentially a form of dextrin. Gelatin is sometimes added to acacia as an adulterant; formaldehyde has been recommended by Trillet (*Ph. Post,* 1899, 629) as an agent for its detection. (See also *Proc. A. Ph. A.,* 1900, 643.)

Description and Physical Properties.—"*Unground Acacia.*—In spheroidal tears up to 32 mm. in diameter or in angular fragments; color, yellowish-white to light amber; translucent; very brittle, the fractured surface glassy and occasionally iridescent; almost odorless; taste, mucilaginous.

"*Powdered Acacia.*—White; in angular microscopic fragments with but slight traces of starch or vegetable tissues present. Acacia is insoluble in alcohol, but almost completely soluble in twice its weight of cold water, the solution being acid to litmus paper.

"Add 0.2 cc. of basic lead acetate T.S. to 10 cc. of a 10 per cent. cold aqueous solution of Acacia: a gelatinous precipitate is produced. Add 0.1 cc. of ferric chloride T.S. to 10 cc. of a 2 per cent. aqueous solution of Acacia; no blackish coloration or blackish precipitate is produced (*tannin-bearing gums*). An aqueous solution of Acacia does not give a bluish or reddish color with iodine T.S. (*starch or dextrin*)." *U. S.*

"When dissolved in an equal weight of *water,* the solution is not glairy, and after admixture with more *water,* yields no gummy deposit on standing. An aqueous solution (1 in 10) exhibits slight lævorotation (absence of dextrin, certain sugars, etc.). 10 millilitres of the same solution are not precipitated by *solution of lead acetate;* are not, after previous boiling and cooling, colored blue or brown by 0.1 millilitre of *N/10 solution of iodine* (absence of starch and dextrin), or bluish-black by *T. Sol. of ferric chloride* (absence of tannin). Ash not more than 4 per cent." *Br.*

The commercial gum arabic contains 15 per cent. of water and 3 per cent. of ash, consisting almost entirely of calcium, potassium and magnesium carbonates.

The gum dissolves slowly, at ordinary temperature, in twice its weight of water, forming a thick glutinous liquid of distinctly acid reaction. It is insoluble in alcohol, ether, and the oils. One hundred parts of 22 per cent. alcohol, by volume, dissolve 57 parts of gum, diluted alcohol containing 40 per cent. alcohol takes up 10 parts, and 50 per cent. alcohol only 4 parts (Flückiger).

Constituents.—Gum arabic is composed essentially of the calcium salt of *arabin* or *arabic acid* which is obtained by adding hydrochloric acid to the aqueous solution and precipitating with alcohol. O'Sullivan says that arabin contains an acid nucleus which he has named *l-arabinosic acid* to which he gives the formula $C_{23}H_{28}O_{22}$ and further states that arabin is a compound of this nucleus with *arabinan* and galactan. Upon complete hydrolysis there is produced *arabinose,* galactose and arabinosic acid. The arabin (or arabic acid) may also be prepared by placing a solution of gum, acidulated with hydrochloric acid, on a dialyzer, when calcium chloride will diffuse out, leaving behind solution of arabin.

Arabin has a decided tendency to form acid salts. Concentrated nitric acid forms with it nitro-compounds; diluted nitric acid, on the other hand, gives rise to mucic and saccharic acids, together with oxalic and a little tartaric acid. Kiliani (*Ber. d. Chem. Ges.,* 1887, 339) first established the presence of arabinose which is one of the pentoses. These are not fermentable, and, on prolonged boiling with diluted hydrochloric acid, lose the elements of water and yield furfurol. Neutral lead acetate does not precipitate an aqueous solution of gum arabic, but the basic acetate forms, even in a very diluted solution, a precipitate.

Prolonged heating of the dry gum causes it to change readily into *metarabic* (*metagummic*) *acid,* which is identical with the *cerasin* found in the beet and in cherry gum. Sulphuric acid will also change arabic into metarabic acid. 25 Gm. pure gum arabic are covered with 50 cc. strong alcohol, 10 cc. water, and 5 cc. sulphuric acid, and allowed to stand twenty-four hours. On pouring off the fluid, and washing the residue with alcohol and with water, metarabic acid remains behind as a voluminous mass, which dries to a white, tasteless, and odorless powder of acid reaction. The *metapectic acid* which is prepared by Scheibler (*B. Chem. G.,* 1873, p. 612) from the sugar beet is identical with metarabic acid.

The similarity of the reaction and composition of arabinose and galactose (from sugar of milk by inversion) led Kiliani to assert the identity of these two varieties of sugar, but later studies by himself, Claesson, and Scheibler have shown that they are distinct. Thus, galactose is fermentable, while arabinose is not; galactose yields mucic acid when oxidized with nitric acid, and dulcite when reduced with sodium amalgam, while arabinose does not yield either; the fusing point of the crystallized galactose is given at 142° to 144° C., while that of arabinose is 160° C.; galactose yields with phenylhydrazin a light yellow compound, fusing at 170° to 171° C., while arabinose forms a brownish-yellow compound, fusing at 157° to 158° C. (Scheibler, *B. Chem. G.,* xvii, 1731.)

Gum arabic undergoes no change by age, when kept in a dry place. Its concentrated aqueous solution remains for a considerable time unaltered, but ultimately becomes sour, from the production of acetic acid. The disposition to sour is increased by employing hot water in making the solution. The tendency of a weak solution to become moldy is said to be obviated by adding a few drops of sulphuric acid, and decanting from the calcium sulphate deposited. (*A. J. P.,* 1872, 353.) Solution of gum arabic does not ferment upon the addition of yeast, saliva, or gastric juice; the addition of chalk and cheese, however, starts a fermentation which gives rise to lactic acid and alcohol, but not to mannite or glycerin. The addition of a solution of gum to an acidified albumin solution causes a precipitate, which disappears on further addition of gum, but the solution will then curdle and become flocculent on application of heat. Gum may be distinguished from dextrin by the following tests: 1. Gum contains no dextroglucose, which, however, is present in dextrin, and may be recognized by the copper test. (See *Alkaline Cupric Tartrate Volumetric Solution,* Part III.) 2. Gum contains a lime compound; hence its solution is rendered milky by oxalic acid, while a solution of dextrin remains almost clear. 3. Gum gives a slimy, yellow deposit when its solution is mixed with a neutral ferric salt.

J. Henry Schroeder examined twelve specimens of powdered acacia, and states that dextrin is not frequently used as an adulterant, and that if in using the alkaline cupric tartrate test the heat be prolonged during twenty minutes, a well defined reduction was produced even when pure Senegal gum was used. (*A. J. P.,* 1897, 195.) R. G. Shoults (*A. J. P.,* 1900, 267) supplemented the conclusions of Schroeder and proposed to use the difference in rotatory power of acacia and dextrin as a test. He found a solution of pure acacia to have a lævorotatory power of –18°, while one of dextrin was dextrorotatory varying to the extent of from +120°

to +138°. This method of testing the presence of dextrin may be replaced by the simpler one with the microscope. (See also Kebler's paper, *Am. Drug.*, 1901, 343.) The following test is given in the *Ph. Post,* 1894, 563. Add 3 cc. of a solution consisting of 15 drops of solution of ferric chloride, 15 drops of a saturated solution of potassium ferrocyanide, 5 drops of HCl (1–125), and 60 cc. of water to a 20 per cent. solution of the gum. If the gum arabic is pure, it will remain a clear yellow for from eight to ten hours. If there is dextrin present, the color changes to blue.

According to Roussin (*J. P. C.* (4), vii, 251), gum arabic and dextrin may be separated by means of ferric chloride which precipitates only the former. For this separation 1 Gm. of the material to be tested is dissolved in 10 cc. of water, the solution mixed with 30 cc. of proof spirit, 4 drops of ferric chloride solution (containing 26 per cent. of the anhydrous chloride) added, followed by a few decigrammes of powdered chalk; after stirring briskly the mixture is allowed to stand for a few minutes and filtered. If this filtrate becomes cloudy on the addition of strong alcohol it proves the presence of dextrin. If a quantitative estimation is desired, the precipitate containing the acacia should be washed with proof spirit and the washings added to the filtrate and then treated with strong alcohol which precipitates the dextrin. This mixture is allowed to stand for 24 hours, the spirituous liquid decanted and the precipitated dextrin dissolved in a small quantity of water and the resultant solution evaporated at 100° C. and the residue weighed. The first precipitate, resulting from the addition of the ferric chloride, which contains the gum arabic, should be dissolved in dilute hydrochloric acid. From this the arabin may be precipitated by strong alcohol; the precipitate, often being washed with alcohol, is then dissolved in water, the solution evaporated to dryness and the residue weighed.

C. W. Ballard (*J. A. Ph. A.*, 1920, p. 31) gives a comprehensive scheme for the identification of acacia and a number of other well known gums by the phenylhydrazine reaction. The reagent consists of 1 part of phenylhydrazine hydrochloride, 3 parts anhydrous sodium acetate, and 25 parts of water. The gum is dissolved in water (1 in 20) and united by boiling with HCl for 2 hours in a reflux condenser. Equal parts of the inverted gum solution and the reagent are heated to boiling for 1 hour and then allowed to cool slowly. The crystalline deposit is recrystallized if necessary. Characteristic crystalline forms were produced by each of the fourteen gums and mucilages which this author used in his work and the article contains illustrations of these crystals.

The properties above enumerated belong to gum arabic generally. There are, however, varieties with differences which deserve notice. 1. *Gum that is transparent and readily soluble.* This constitutes by far the greater portion of the commercial varieties distinguished by the names of Turkey and Senegal gum. It is characterized by its transparency, ready solubility, and the comparatively slight degree of thickness and viscidity of its solution. Under this head may be included the *gomme blanche fendillée* of Guilbourt. It is distinguished by the whiteness and deficient transparency of the pieces, attributable to the minute cracks or fissures with which they abound, and which render them very brittle and easily pulverizable. This peculiar structure is generally ascribed to the influence of solar heat and light, but is conjectured by Hayne to arise from the exudation of the juice in the frothy state noticed by Ehrenberg. Though the unbroken pieces are somewhat opaque, each minute fragment is perfectly, transparent and homogeneous. This variety, in consequence of its prompt and entire solubility, is usually preferred for medicinal use and for most purposes in pharmacy. 2. *Gum less transparent and less soluble.* Guilbourt has proposed for portions of this gum the name of *gomme pelliculée,* from the circumstance that the masses are always apparently covered, on some part of their surface, by a yellowish opaque pellicle. Other portions of it have a mammillary appearance on the surface. It is less transparent than the former variety, is less freely and completely dissolved by water, and forms a more viscid solution. It dissolves with difficulty in the mouth, and adheres tenaciously to the teeth. It is found in all the commercial varieties of gum, but least in that from Egypt. Its peculiarities have been ascribed to variable proportions of *bassorin* or *cerasin* associated with the soluble *arabin.* Between these two varieties there are insensible gradations, so that it is not always easy to classify specimens.

E. Bourquelot (*J. P. C.,* 1904, xix, 473, 474) states that acacia contains an active oxidizing ferment which renders it unsuitable for use in many pharmaceutical preparations, and that, notwithstanding the wide use of acacia as an excipient, it is possible that certain active ingredients may become altered in its presence. Nor is acacia the only gum which contains a ferment; myrrh, frankincense and bdellium also contain an oxydase. Among the substances stated as being incompatible with acacia are pyrogallol, morphine, vanillin, ordinary phenol, cresylol, ortho- and meta-xylol, thymol, carvol, *a*- and *b*-naphthol, pyrocatechol, guaiacol, phenols, lysol, cresols, acetylguaiacol, veratrol, creosol, eugenol, acetyleugenol, methylaniline, ethylaniline, paratoluidine, crude aniline, xylidine, *a*-naphthylamine, pyramidon apomorphine, eserine, adrenaline, isobarbaloin, caffeotannic acid, gallic acid and tannin. Paraxylenol, hydroquinone, resorcinol, anisol and phenetol do not appear to be affected. Nor is the action confined to chemical substances; acacia is incompatible with the opium and Calabar bean products, suprarenal extract, aloetic preparations, and all substances flavored with vanillin, tannin-containing extracts, such as those of rhatany, catechu, and rhubarb; fluidextract of viburnum prunifolium, and kola preparations. Obviously, in cases where mucilage of acacia is concerned, this oxidizing action may be eliminated by heatng the liquid to 100° C., and thus destroying the enzyme.

Impurities and Adulterations.—As gum arabic is usually collected in huge piles at Khartoum before being shipped to Port Soudan the sand and impurities are likely to sift to the bottom. As a consequence the first orders are likely to be filled with the cleaner article, while the latter containing the siftings may run as high as 4 per cent. of ash. The inferior grades are often mixed with, or substituted for, the better kinds, especially in powder.

The chief adulterant and substitute for acacia within recent years has been *Mesquite Gum,* from *Prosopis juliflora* (Fam. *Leguminosæ*), a plant indigenous to Mexico. It occurs in brownish to reddish-brown tears of variable size and differs from acacia in not precipitating from its aqueous solution when solutions of ferric chloride, lead sub-acetate or sodium borate are added.

Rarely flour or other starchy matter is fraudulently added to the powder, but may be easily detected by the use of the microscope and the blue color which it produces with tincture of iodine. In consequence of the impurities and difference in quality, gum arabic should generally be garbled. It is surprising what a good effect the removal of 1 to 2 per cent. of objectionable matter has upon the remainder of the drug.

Acacia is incompatible with strongly alcoholic liquids, solutions of ferric chloride and lead subacetate, and strong solutions of sodium borate.

Uses.—Acacia is used in medicine chiefly as a demulcent. Hence it is advantageously employed in catarrhal affections and irritation of the fauces, by being held in the mouth and allowed to dissolve slowly. It has been used as a food, but has very little if any nutritive value. In 1917 Bayliss suggested the use of a 7 per cent. solution of acacia for intravenous injection in the treatment of the posthemorrhagic conditions instead of the usual physiological salt solution. It was noted that after the use of the ordinary saline solution fluid escaped from the blood vessels so rapidly that the beneficial effects were too transitory to be of any practical value. This is generally attributed to the non-colloid nature of the salt solution; Bayliss after considerable experimentation finally recommended a 7 per cent. solution of acacia. The method has been attacked, especially on the grounds of possible anaphylactoid reactions or injurious effects on the kidney, but has, on the other hand, been highly praised by a number of surgeons. For references to the literature on this subject see *J. A. M. A.*, 1922, lxxviii, pp. 730, 1885 and 1897. It is essential for this purpose that only acacia in clear, colorless lumps be used. In pharmacy, gum arabic is extensively used for the suspension of insoluble substances in water, and for the formation of pills and troches. Two kinds of powdered gum arabic are used, one a coarse powder called *granulated,* the other *finely dusted.* The granulated dissolves more readily in water, according to Hager, because it has lost during desiccation only two per cent. of moisture, while in preparing the "finely dusted" powder the high heat necessarily used to thoroughly dry it drives off ten per cent. of water. Its easy solubility and absence of tendency to form "lumps" cause the coarse powder to be preferred for solutions, emulsions, etc.

Off. Prep.—Mucilago Acaciæ, *U. S., Br.*

ACACIÆ CORTEX. Br.

ACACIA BARK

"Acacia Bark is the dried bark of Acacia arabica, *Willd.,* and also the dried bark of Acacia decurrens, *Willd.;* obtained from wild or cultivated trees not less than seven years old, and, after being dried, kept for one year before use." *Br.*

Wattle Bark; Black Wattle; Babul Bark Neb-neb.

The Acacias are known not only for their gums, but a number of them contain large quantities of tannin and hence are used in tanning. Among the latter are the so-called wattle barks of Australia, and also catechu. The chief of the Australian trees is the black wattle (*A. decurrens*), the bark of which yields from 24 to 42 per cent. of tannin, and is employed as an astringent. More recently *A. arabica* has been similarly used in East Africa. It is a tree indigenous to India, Arabia and Africa.

Characters. "Bark of *A. arabica* hard and woody, rusty brown, and tending to divide into several layers. Outer surface of the older pieces covered with thick blackish periderm, rugged, fissured longitudinally and transversely. Inner surface red, longitudinally striated and fibrous. Taste astringent and mucilaginous."

"Bark of *A. decurrens* usually in curved or channelled pieces, 1.5 to 3 mm. thick. External surface greyish-brown, darkening with age; often with irregular longitudinal ridges, and, sometimes, transverse cracks. Inner surface reddish-brown, longitudinally striated; fracture irregular and coarsely fibrous, freshly fractured surface pale. Slight tan-like odor; taste astringent." *Br.*

Acacia bark owes its medicinal properties to the tannin it contains. It is used as an astringent in *diarrheas,* being usually employed in the form of a decoction (1:16), in *doses* of one-half to two fluidounces (15–60 cc.).

ACETANILIDUM. U. S., Br.

ACETANILID Acetanil. [Antifebrin]

"Monoacetyl aniline [$C_6H_5NH.CH_3CO$]." *U. S.* "Acetanilide, C_8H_9NO, may be obtained by the interaction of glacial acetic acid and aniline." *Br.*

Acetylamidobenzene, Phenylacetamide; Acétanilide, *Fr, Cod.*; Acetanilidum, *P. G.*; Antifebbrina, *It.*; Acetanilida. *Sp.*

Preparation.—Acetanilid is made, according to Yvon, as follows: 372 grammes of pure aniline and 240 grammes of glacial acetic acid are heated for four hours, to the boiling point, in a flask provided with a reversed condenser; the excess of both ingredients is then distilled off on a sand bath, this being completed when the temperature reaches 260° C. The cooled, congealed residue is crude acetanilid, which may be purified by sublimation or, better, by repeated crystallization from water.

This process has been criticized as not suitable for manufacturing acetanilid of pharmaceutical quality on account of the high temperature attained and the length of time of heating which yields a highly colored crude product difficult to purify.

It is found better on the large scale to mix the aniline and glacial acetic acid (500 lbs. each) in a steam jacketed enamelled still of 150 gallons capacity and to heat to 120°–125° C. for 8 or 9 hours, regulating the heat so that practically no vapor passes over into the condenser.

The progress of acetylation is followed by frequent tests for uncombined aniline. When the test for aniline is negative, usually in from 10 to 12 hours, the excess of acetic acid is distilled off under a vacuum. The residue is then blown into 200 gallons of water and allowed to cool. The crude acetanilid is centrifuged and recrystallized from boiling water, about 1000 gallons being required, using animal charcoal as a decolorizing agent. The mother liquors from both the centrifuging and crystallizing operations are used in succeeding batches.

The yield is about 400 Gm. It may also be prepared by acting on aniline with acetyl chloride (Gerhardt), or by heating aniline with acetamide (Kolbe). The sublimed salt is whiter and lighter than that obtained by crystallization from water, which has the appearance of boric acid. For Walters' method of preparing acetanilid, on a small scale, see *Bull. Pharm.*, 1899, 53.

Description and Physical Properties.—"Colorless, shining, crystalline leaflets, or a white, crystalline powder. It is odorless, and is stable in the air. One Gm. of Acetanilid is soluble in 190 cc. of water, 3.4 cc. of alcohol, 3.7 cc. of chloroform, 17 cc. of ether, 4 cc. of acetone, 47 cc. of benzene, and in about 5 cc. of glycerin, at 25° C. One Gm. is soluble in 20 cc. of boiling water and in 0.6 cc. of boiling alcohol. It is slightly soluble in petroleum benzin.

"Acetanilid melts between 113° and 115° C. Boil about 0.1 Gm. of Acetanilid with 5 cc. of sodium hydroxide T.S.: the characteristic odor of aniline becomes noticeable. Add 1 cc. of chloroform, and heat the mixture: the disagreeable odor of phenylisocyanide (a poisonous substance) is evolved. Boil about 0.1 Gm. of Acetanilid for several minutes with 2 cc. of hydrochloric acid: a clear solution results, which, when mixed with 3 cc. of an aqueous solution of phenol (1 in 20) and 5 cc. of a filtered, saturated solution of chlorinated lime, acquires a brownish-red color which becomes deep blue upon supersaturation with ammonia water. Bromine T.S. produces a white, crystalline precipitate in a saturated aqueous solution of Acetanilid.

"Ash: not more than 0.05 per cent. Shake 1 Gm. of Acetanilid with 20 cc. of distilled water for two minutes and filter: the filtrate is neutral to litmus paper. Add 5 drops of ferric chloride T.S. to 5 cc. of the filtrate: the color does not differ from that produced by adding 5 drops of ferric chloride T.S. to 5 cc. of distilled water (*aniline salts*). The solution of 0.5 Gm. of Acetanilid in 5 cc. of sulphuric acid is colorless or only faintly yellow (*readily carbonizable substances*)." *U. S.*

"Colorless, glistening lamellar crystals; inodorous; taste slightly pungent. Melting point 113° C. Soluble in 210 parts of *water*, and in 4.2 parts of *alcohol* (90 per cent.); soluble in *ether*, and in *chloroform*. Heated with *solution of sodium hydroxide* the odor of aniline is given off, and if the liquid is then warmed with a few drops of *chloroform* the unpleasant odor of phenyl isocyanide is developed. An aqueous solution mixed with *solution of bromine* gives a yellowish-white precipitate (distinction from phenacetin). Forms a colorless solution with cold *sulphuric acid* or with cold *nitric acid*. A cold saturated aqueous solution does not affect *solution of litmus* (absence of free acid), and is not affected by *T. Sol. of ferric chloride* (absence of phenazone, and salts of aniline). Ash not more than 0.1 per cent." *Br.*

Ritsert (*Ph. Ztg.*, 1890, 306) believes that the difference in melting point of acetanilid given by various writers is due to the almost constant presence of toluidine in aniline, and the production of acettoluids which have the following melting points: *ortho*, 170° C.; *meta*, 65.5° C.; and *para*, 147° C. A very important reaction, by which the presence of acettoluid may be detected in acetanilid, is in the use of a boiling solution of potassium permanganate. If the acetanilid be pure, it is not altered, and does not reduce the permanganate, but acettoluid, if it be present, is oxidized to acetamidobenzoic acid with reduction of the permanganate. Of a number of samples of acetanilid examined, in only one was the reduction slight, while all the others showed a decided reduction.

Methods for detection of acetanilid in mixtures of antipyretic drugs are frequently needed. R. Miller (*A. J. P.*, 1917, lxxxix, 156) outlines a rapid approximate method of determining phenacetine when mixed with acetanilid, which depends upon the yellow color produced when phenacetine is acted upon with nitric acid. The mixture of the antipyretics is dissolved in methyl alcohol and nitric acid added, a yellow color is produced, proportional to the amount of phenacetine present.

A method of assay for mixtures of acetanilid with various other synthetic remedies such as phenacetin, salol, etc., is suggested by A. D. Powell, *C. D.*, 1918, p. 1002.

Acetanilid is incompatible with alkalies (which liberate aniline) and when it is triturated with phenol, thymol, and many other organic drugs it forms a eutectic mixture which liquefies.

Uses.—Acetanilid is one of a numerous group of compounds which yield in the system paramido-phenol. Since these drugs owe their therapeutic virtues to the formation of this body the action of all of them is essentially the same. They differ, however, in the brusqueness of their effects according to the rapidity with which the paramido-phenol is formed from them.

The most striking actions of acetanilid are upon the heat regulating mechanism and the pain perception. The maintenance of the body temperature at a constant level is due to a delicate balance between the amount of heat generated in the system and that which is thrown off. The source of the bodily heat is chiefly from the oxidation of hydrocarbons in the organism; the dissipation of heat is accomplished partly by direct radiation from the skin and partly through the evaporation of the sweat. It is evident that the body temperature can be lowered either by diminishing oxidative processes or by increasing the rapidity in the dissipation of heat. There has been a great deal of experimental research to determine which of these functions acetanilid and the other antipyretics affected, but the conflicting results of various experimenters upon whether these drugs act upon heat formation or heat dissipation, and the observations of Stuhlinger (*A. E. P. P.*, 1899, xliii, p. 167) of the difference in the effects on heat dissipation between rabbits and guinea pigs, as well as clinical experience strongly suggests that the action of these antipyretics is not due primarily to effects either upon heat dissipation or heat formation but to some sort of narcotic action which lessens the irritability of the heat mechanism so that it does not respond to the irritation produced by poisons circulating in the blood. Hashimoto (*A. E. P. P.*, 1915, lxxviii, p. 414) has brought forward experimental evidence that the antipyretics lessen the irritability of the heat centers in the corpus striatum without, however, paralyzing it. It would seem that there is produced in the body in certain infections some poison which irritates the thermoregulator center and leads to a higher level of body temperature; the tendency of the system to maintain the temperature at a constant level is not lost but the level is higher than in health. It seems probable that acetanilid, perhaps by some sort of narcotic effect, lessens the irritability of the heat-regulating mechanism so that it does not respond to the irritation produced by poisons circulating in the blood. It is worthy of note that these drugs do not affect the body temperature in healthy persons unless given in poisonous quantities. Of the manner in which acetanilid lessens the sensibility towards pain, we are entirely ignorant. Barbour (*Proc. Soc. of Exp. Biology and Med.*, 1919, xvi, and *Proc. Nat. Acad. Sciences*, 1920, vi, p. 136) has recently brought forward a theory that the antipyretic action of the coal tar series is due to an effect upon carbohydrate metabolism whereby they increase the amount of blood sugar; this leads in turn to a relative hydremia which, through overfilling of the blood vessels, promotes heat dissipation.

In ordinary dose acetanilid has no demonstrable action upon the respiration or circulation in the lower animals, although in very large quantities it acts as a depressant to the heart. (Hale, *J. P. Ex. T.*, 1909, i, p. 185.) It appears also to be feebly depressant to the motor centers in the cord. When used continuously or given in toxic quantity, it acts upon the hemoglobin of the blood producing a new compound known as methemoglobin, which does not yield its oxygen to the tissues with sufficient readiness to maintain their function.

Locally acetanilid is mildly antiseptic and to some degree anesthetic.

Acetanilid is used in medicine chiefly as an analgesic or as an antipyretic. As a pain relieving drug its greatest value is in cases of *neuralgia* whether of the head or other portions of the body. It is, however, an agent of much usefulness even in those pains in which there are actual anatomical lesions in the nervous system, such as *neuritis* or crises in *locomotor ataxia*. When, however, the pain is due to conditions outside of the nervous system, although it may enhance the potency of the opiates, by itself it is of little service.

There has been a great deal of difference of opinion as to the advisability as to the use of antipyretic drugs for the purpose of lowering *fever* temperature. One of their great disadvantages is a liability of overaction; at times they produce such a sudden or excessive change in body temperature as to lead to a condition of collapse.

Locally acetanilid has been used as a dusting powder in various types of *ulcers*, but its use is not free from danger and it does not appear to have any great advantage over a number of other safer remedies for this purpose.

Toxicology.—Two distinct types of acetanilid poisoning must be recognized, one in which the symptoms are caused by a single large dose, and the other by repeated use of the drug over long periods of time. Under ordinary circumstances acetanilid is a relatively safe remedy, but there are not a few persons who possess an idiosyncrasy towards the drug and are liable to show toxic symptoms after doses which cannot be regarded as excessive. In poisoning from single doses of acetanilid there is marked fall of the body temperature with the symptoms of collapse, rapid feeble pulse, cold, clammy skin, more or less drowsiness or even coma, sometimes tinnitus aurium, or mydriasis; there is frequently a peculiar eruption of the skin resembling that of measles; sometimes there is cyanosis, although this is less common than in the more chronic types of intoxication.

The frequency with which the laity employ various mixtures containing acetanilid for the relief of the minor discomforts of life is a serious danger to the welfare of the community. In the first place, acetanilid is to be ranked among the habit-forming drugs; there are a number of well-authenticated instances on record of acetanilid habit. In the second place the prolonged use of the drug leads to chemical changes in the blood, as has been pointed out above. When acetanilid is taken regularly and frequently these changes in the blood are frequently manifest, even to the casual observer, by a peculiar dusky cyanotic color of the skin and especially of the lips. Probably because of the diminished oxygen carrying power of the blood there is a tendency towards degenerative changes in various organs, especially the heart muscle, and sudden death from slight overexertion is liable to occur.

Dose, three to eight grains (0.2–0.5 Gm.).

Off. Prep.—Pulvis Acetanilidi Compositus, *N. F.*

ACETONUM. U. S., Br.

ACETONE. Aceton. [Dimethyl-ketone]

"Acetone contains not less than 99 per cent. of $CH_3.CO.CH_3$," *U. S.* "Acetone, or dimethylketone, C_3H_6O, may be obtained by the dry distillation of calcium acetate, or barium acetate." *Br.*

Pyroacetic Spirit; Acétone, Ether (Esprit) pyroacétique *Fr.;* Acetone, Essiggeist, Mesitalkohol, *G.;* Acetone, Chetone Metilacetone, *It.*

Preparation.—Acetone is found in small amount in normal urine, in blood, etc., and in larger amount in certain pathological conditions. It is produced during the dry distillation of sugar, gum, cellulose, etc., and therefore is always contained in crude wood-naphtha.

E. R. Squibb has also prepared it on a large scale by passing acetic acid vapor through a rotating iron cylinder heated to from 500° to 600° C., and containing pumice stone with precipitated barium carbonate. (*J. Am. C. S.*, 1895, 197.) It is made commercially by the dry distillation of calcium acetate at a temperature not exceeding 300° C. The crude acetone thus obtained is purified by digestion with quicklime and again distilled from sodium hydroxide. Acetone of even higher purity is obtained by a subsequent distillation from sodium sulphite.

The outbreak of the World War brought a large demand for acetone as a solvent in the smokeless powder industry which could not be satisfied by the facilities of the wood distillation industry. Acetone was produced to meet this demand by a process of fermentation known as the Fernbach process. A special ferment is employed which produces a mixture of acetone and butyl alcohol from starch. More than 300 tons per month were made in Canada and the U. S. alone during the latter part of the war, by this method.

Description and Physical Properties.—"A transparent, colorless, mobile and volatile liquid, having a characteristic odor. It is inflammable. Acetone is miscible without cloudiness with water, alcohol, ether, chloroform, and most volatile oils.

"Specific gravity: about 0.790 at 25° C. It boils between 56° and 58° C., but volatilizes even at low temperatures. Add 1 cc. of sodium hydroxide T.S. to 1 cc. of an aqueous dilution of Acetone (1 in 200), warm the mixture, and add a few cc. of iodine T.S.: a yellow precipitate of iodoform is formed at once. Mix 1 cc. of the same Acetone dilution with 5 drops of sodium nitroprusside T.S. and 2 cc. of sodium hydroxide T.S., and add a slight excess of acetic acid: a deep red liquid is produced which develops a violet tint when diluted with several volumes of water.

"Acetone diluted with an equal volume of distilled water does not affect the color of blue or red litmus paper previously moistened with water. Evaporate 50 cc. of Acetone in a dish on a water bath, and dry to constant weight at 100° C.: the weight of the residue does not exceed 0.002 Gm. Mix 20 cc. of Acetone with 0.1 cc. of tenth-normal potassium permanganate in a clean, glass-stoppered bottle: the pink tint produced does not wholly disappear in less than fifteen minutes (*empyreumatic substances*).

"Preserve in well-closed containers, in a cool place, remote from fire." *U. S.*

"A colorless, transparent, mobile and volatile liquid. Characteristic odor; taste pungent and sweetish. Forms clear mixtures with *water, alcohol* (90 per cent.), *ether* and *chloroform* in all proportions. Specific gravity 0.795 to 0.798. Not less than 95 per cent. distils between 55° and 57° C. Leaves no residue when evaporated on a water-bath. 10 millilitres, to which a few drops of *solution of phenolphthalein* have been added, require not more than 1 drop of *N/1 solution of sodium hydroxide* to produce a permanent pink coloration. 20 millilitres do not completely decolorize 0.1 millilitre of *N/10 solution of potassium permanganate* within fifteen minutes (limit of readily oxidizable impurities). Yields a clear mixture with an equal volume of *petroleum spirit* (limit of water)." *Br.*

Distilled with water and chlorinated lime, it yields nearly 200 per cent. of its weight of chloroform, and hence largely used in the manufacture of this substance, both in this country and in Germany. In the presence of an alkali, iodine converts it into iodoform, so that a trace of acetone in methyl alcohol can be detected by iodoform formation. This reaction is taken advantage of in the quantitative determination of acetone. It may also be determined by Strache's phenyl-hydrazine method. (*Zeit. An. Chem.*, 1892, p. 573.)

Reagents for detecting acetone in the urine are described under *Diagnostic Reagents,* Part III.

Acetone oil, largely a mixture of higher ketones, obtained as a by-product in the manufacture of acetone and suggested by Lang as an addition to alcohol and spirits to denaturize them, cannot be used on a large scale as pointed out by Klar, as the commercial supply would probably be insufficient. (*Chem. News,* 1899, 205.)

Assay.—"Determine the exact weight of a glass-stoppered weighing bottle containing 15 cc. of distilled water, add about 1 cc. of Acetone, and again weigh accurately. Transfer the contents of the bottle to a 1000 cc. graduated flask, rinse the weighing bottle with several portions of distilled water, and add the rinsings to the flask. Fill to the mark with distilled water, and mix thoroughly. Place 25 cc. of normal sodium hydroxide in a 250 cc. glass-stoppered flask, add exactly 25 cc. of the Acetone solution and 35 cc. of tenth-normal iodine, with constant agitation of the flask, and allow the mixture to stand for fifteen minutes. Add 26 cc. of normal hydrochloric acid, and at once titrate the residual iodine with tenth-normal sodium thiosulphate, adding starch T.S. as indicator when the liquid is nearly decolorized. Conduct a blank test with the same quantities of the reagents, and subtract the quantity of tenth-normal iodine consumed in the blank test from that consumed in the assay. Each cc. of the difference, which represents the iodine consumed by the reaction with the Acetone, corresponds to 0.0009677 Gm. of $CH_3.CO.CH_3$." *U. S.*

Uses.—Acetone is used chiefly as a solvent for fats, resins, and camphors, and was used as a menstruum for extracting oleoresins in the U. S. P. VIII. As a solvent it is particularly valuable in that it possesses the fat dissolving power of the immiscible solvents and the miscibility with water which makes it similar to alcohol. It is present in a number of the denatured alcohols of commerce, both in those intended for general use and in those used by special permit only. As a drug it has been employed locally to a certain extent in inoperable *carcinomata of the uterus* for the purpose of relieving hemorrhage and discharge. (Gellhorn, *Cb. Gyn.,* 1911, 1240.)

In a general way, the physiological effects of acetone seem to resemble those of alcohol. Salant and Kleitman (*J. P. Ex. T.,* 1922, xix, 293) have found that the intravenous injection of 1 cc. per kilo caused in the rabbit narcosis with primary stimulation and secondary depression of respiration and a fall in the blood pressure. Elimination is slow but its rate varies in different animals. In cats they detected it in the blood 24 hours after injection, but in dogs it had disappeared within 4 hours. The toxicity of acetone is not very high, as is shown not only by the experiments of Salant and Kleitman upon rabbits but also by the studies of Albertoni who found that *doses* of 15 to 20 Gm. of acetone produced no symptoms in man beyond slight narcosis.

Off. Prep.—Petroxolinum Iodoformi, *N. F.*

ACETPHENETIDINUM. U. S. (Br.)

ACETPHENETIDIN Acetphen. [Phenacetin]

"Monoacetyl para-aminophenetol [$C_6H_4(OC_2H_5).NH.CH_3CO$ 1:4]." *U. S.* "Phenacetin or para-acet-phenetidin, $C_{10}H_{13}NO_2$, may be obtained by the interaction of glacial acetic acid and paraphenetidin." *Br.*

Phenacetinum *Br., P. G.;* Para-acetphenetidin, Para-ethoxyacetanilide; Phenacetin; Acet-Phénétidine, *Fr. Cod.;* Phénacetine, Para-acétophénétidine, Amide Acétique de l'amido-Phénétol, *Fr.;* Fenacetina, *It., Sp.*

The chemical relationship of this body to phenol is seen by an examination of its formula and the formulas of the intermediate compounds obtained as stages in its preparation.

Phenol, $C_6H_5.OH$, is converted into *nitrophenol,* $C_6H_4(NO_2)OH$. Only the paranitrophenol is available, and this is separated by distilling off the ortho-nitrophenol by steam distillation. The residual *paranitrophenol,* in the form of the sodium compound, is treated with ethyl chloride, when ethyl paranitrophenol or *paranitrophenetol,* $C_6H_4(NO_2)OC_2H_5$, is produced. This is now reduced by the action of hydrochloric acid and iron turnings to *paraphenetidin,* $C_6H_4(NH_2)OC_2H_5$ or the reduction may be carried out by the use of sodium sulphide. Glacial acetic acid then serves to introduce the acetyl group, and *para-acetamidophenetol* (phenacetin), $C_6H_4(NHC_2H_3O)OC_2H_5$, is obtained. It is also prepared commercially by starting with para-acetamino-phenol which is later subjected to ethylation by the use of ethyl bromide.

The crude phenacetin by either of these methods is purified by recrystallization from water or 90 per cent. alcohol, with the use of animal charcoal or sulphur dioxide as decolorizing agents.

Description and Physical Properties.—"White, glistening, crystalline scales, or a fine white, crystalline powder. It is odorless, has a slightly bitter taste, and is stable in the air. One Gm. of Acetphenetidin is soluble in 1310 cc. of water, 15 cc. of alcohol, 14 cc. of chloroform, and in about 130 cc. of ether, at 25° C. One Gm. is soluble in 82 cc. of boiling water and in 2.8 cc. of boiling alcohol. Acetphenetidin melts between 134° and 135° C. Boil about 0.1 Gm. of Acetphenetidin for one minute with 1 cc. of hydrochloric acid, dilute with 10 cc. of distilled water, cool, filter, and add a drop of potassium dichromate T.S. to the filtrate: a ruby-red color results.

"Ash: not more than 0.05 per cent. Shake about 1 Gm. of Acetphenetidin with 20 cc. of distilled water during two minutes, and filter: the filtrate is neutral to litmus paper. A mixture of about 0.005 Gm. of Acetphenetidin and 1 cc. of nitric acid develops a yellow color which becomes darker on standing. A solution of 0.5 Gm. of Acetphenetidin in 5 cc. of sulphuric acid is only faintly yellow (*readily carbonizable substances*). Boil 0.5 Gm. of Acetphenetidin with 10 cc. of distilled water for one minute, cool, filter, and add bromine T.S. to the filtrate, drop by drop, agitating after each addition until the solution remains permanently yellow: neither turbidity nor precipitation results (*acetanilid*). A mixture of 0.3 Gm. of Acetphenetidin with 1 cc. of alcohol and 1 drop of tenth-normal iodine does not acquire a red tint when diluted with three times its volume of distilled water and boiled (*paraphenetidin*)." *U. S.*

The British Pharmacopœia gives the following tests for phenacetin. "Small, colorless, glistening, scaly crystals. Inodorous; tasteless. Melting point 135° C. Very sparingly soluble in cold *water,* more freely in boiling *water;* soluble in 21 parts of *alcohol* (90 per cent.), the solution being neutral to *litmus.* 0.1 gramme boiled with 2 millilitres of *hydrochloric acid* for half a minute yields a liquid which, diluted with 10 times its volume of *water,* cooled and filtered, assumes a deep-red color on the addition of *solution of chromic acid. Sulphuric acid* dissolves Phenacetin without coloration. A cold saturated aqueous solution does not become turbid on the addition of *solution of bromine* (absence of acetanilide). A mixture of 0.3 gramme of Phenacetin with 1 millilitre of *alcohol* (90 per cent.) does not acquire a red tint when diluted with 3 times its volume *of water,* and boiled with 1 drop of *N/10 solution of iodine* (absence of paraphenetidin). No appreciable ash." *Br.*

The test with chromic acid will serve to distinguish it from acetanilid and exalgin; that with bromine water will indicate the absence of phenol and acetanilid, both of which will show a white turbidity, owing to the formation of difficultly soluble bromine derivatives. The presence of unchanged paraphenetidin may be detected by melting 2.5 Gm. of hydrated chloral in a test tube and adding 0.5 Gm. of the acetphenetidin to be tested. If pure, it will remain colorless; if paraphenetidin be present, it will become violet or reddish-blue in tint. For further information see a paper in *Proc. A. Ph. A.,* 1903, 180, on an examination of samples of commercial phenacetin by G. M. Beringer, and *Proc. A. Ph. A.,* 1903, 365, for a paper by L. F. Kebler on its history, methods of manufacture, and chemical constitution.

Acetphenetidin is incompatible with strong acids and alkalies, and also with oxidizing agents, such as chlorine, bromine, and iodine. It forms a liquid eutectic mixture when rubbed with chloral, phenol, etc. It conceals the fluorescence of dilute quinine sulphate solutions.

Uses.—Acetphenetidin, like acetanilid, yields in the body paramido-phenol and its physiological action and therapeutic effects are therefore essentially the same as those of acetanilid (*q. v*). Its action, however, is more gradual and more prolonged and it is less likely to give rise to undesirable symptoms. Enormous quantities of it can be administered to the lower animals without disturbances of the vital functions: H. C. Wood, Jr. (*U. M. M.,* July, 1900), found that 0.5 Gm. per kilo could be injected intravenously into the dog before the occurrence of serious disturbances of either respiration or circulation. In large quantities it is mildly depressant to the spinal cord. The relative safety of acetphenetidin as shown both by animal experimentation and clinical experience, is probably dependent upon the slowness with which it undergoes chemical change in the blood and consequent gradual formation of the active phenylamine. It is, however, capable of causing serious poisoning; we are cognizant of a case in which five powders of 2 grains each taken over an interval of ten hours, produced death in a baby one year old, and Hollopeter reports serious collapse from 22½ grains in a woman. Acephenetidin is useful as an antipyretic and analgesic in the same group of cases in which acetanilid is of service. It requires, however, somewhat larger doses to produce the same degree of action.

Dose, five to fifteen grains (0.32–1.0 Gm.).

ACETUM CANTHARIDINI. Br.

Vinegar of Cantharidin

Vinaigre cantharidé, *Fr.;* Cantharidin-Essig, *G.*

"Cantharidin, 1 gramme; Glacial Acetic Acid, 200 millilitres; Acetic Acid sufficient to produce 2000 millilitres. Dissolve the Cantharidin in the Glacial Acetic Acid with the aid of a water-bath; cool, and add sufficient Acetic Acid to produce the required volume." *Br.*

This preparation contains approximately the same proportion of cantharidin as the *Acetum Cantharidis* of the British Pharmacopœia, 1898. The latter was made by macerating and then percolating bruised cantharides with diluted glacial acetic acid.

Procter found that, by digestion at a temperature of 100° C., the active principle of the flies is readily taken up by official acetic acid, though a portion of the cantharidin is deposited upon cooling. (*A. J. P.*, xxiv, 299.) It would seem, therefore, that the vinegar of Spanish flies would be best prepared with the aid of heat; and, to a certain extent, this advantage is enjoyed in the present process.

Uses.—This preparation is intended exclusively for external use, as a speedy epispastic. It is said, when lightly applied by a brush, to act as a rubefacient; and, when rubbed freely upon the skin for three minutes, to be followed in two or three hours by full vesication. The pain produced by the application, though more severe, is also more transient than that occasioned by the blistering cerate.

ACETUM SCILLÆ. U. S., Br.

VINEGAR OF SQUILL Acet. Scill.

Aceticum scilliticum; Meerzwiebel-Essig, *G.;* Vinaigre de scille, *Fr. Cod.;* Vinaigre scillitique, *Fr.;* Aceto scillitico, *It.;* Vinagre de escila, *Sp.*

" Squill, in coarse powder, 100 Gm.; Diluted Acetic Acid, a sufficient quantity to make 1000 cc. Macerate the squill with 900 cc. of diluted acetic acid during seven days with frequent agitation. Then strain the mixture, and wash the mass on the strainer with enough diluted acetic acid to make the strained liquid measure nearly 1000 cc. Heat this liquid to boiling, filter while hot, and when cold add sufficient diluted acetic acid to make the product measure 1000 cc." *U. S.*

" Squill, bruised, 1000 grammes; Acetic Acid, 1000 millilitres; Distilled Water, 3200 millilitres. Macerate for seven days; press and filter.

" *Tests.*—Specific gravity 1.070. 10 millilitres require for neutralisation not less than 10.8 millilitres of *N/1 solution of sodium hydroxide.*" *Br.*

The British preparation is of approximately twice the strength of the Acetum Scillæ of the British Pharmacopœia 1898 or of the U. S. P.

Vinegar of Squill may also be prepared by percolating the Squill with the diluted acetic acid after previous maceration with an equal bulk of the diluted acetic acid (this precaution being necessary in order to satisfy thoroughly its tendency to swell) and filtering through paper.

The process now official differs from that of the U. S. Pharm. of 1890 in directing the heating of the strained liquid to coagulate albuminous matter and filtering, so that when the vinegar is mixed with sugar and water, in making syrup of squill, a transparent syrup may be secured.

As vinegar of squill is apt to be injured by keeping, it should be prepared in small quantities, as wanted for use.

Uses.—Vinegar of squill is certainly inferior to the alcoholic preparations of this drug in its effects upon the heart and kidneys. It is used chiefly for making syrup of squill.

Dose, of the U. S. preparation, from fifteen to thirty minims (1–2 cc.), but the latter quantity would be apt to nauseate; of the Br., five to fifteen minims (0.3–0.9 cc.).

Off. Prep.—Syrupus Scillæ, *U. S., Br.;* Oxymel Scillæ, *N. F.*

ACETUM URGINEÆ. Br.

VINEGAR OF URGINEA Vinegar of Indian Squill

" Urginea, bruised, 1000 grammes; Acetic Acid, 1000 millilitres; Distilled Water, 3200 millilitres. Macerate for seven days; press and filter.

" *Tests.*—Specific gravity 1.070. 10 millilitres require for neutralisation not less than 10.8 millilitres of *N/1 solution of sodium hydroxide.*" *Br.*

Vinegar of Urginea was admitted to the Indian and Colonial Addendum of the British Pharmacopœia in 1900, but the strength was doubled approximately in the Br. Pharm., 1914. It is used to make syrup of urginea in the same way that vinegar of squill is used by the addition of sugar. It is to be regretted that the end product was not definitely stated in the above process, as some loss during expression cannot be avoided. Under these circumstances the requirement that the specific gravity shall be exactly 1.070 cannot always be met satisfactorily.

Dose, five to fifteen minims (0.3–0.9 cc.).

ACIDUM ACETICUM. U. S., Br.

ACETIC ACID Acid. Acet.

" Acetic Acid is an aqueous solution containing not less than 36 per cent. and not more than 37 per cent. of CH_3COOH." *U. S.* " Acetic Acid may be obtained by the destructive distillation of wood, and contains 33 per cent. by weight of hydrogen acetate, $HC_2H_3O_2$, and 67 per cent. by weight of water." *Br.*

Acetum Concentratum; Ethanoic Acid; Acide acétique, *Fr Cod.;* Acidum Aceticum Dilutum, *P. G.;* Essigsäure, *G.;* Acido acetico, *It., Sp.*

For account of this see under *Acidum Aceticum Glaciale.*

ACIDUM ACETICUM DILUTUM. U. S., Br.

DILUTED ACETIC ACID Acid. Acet. Dil.

" Diluted Acetic Acid is an aqueous solution containing not less than 5.7 and not more than 6.3 per cent. of $CH_3.COOH$." *U. S.* " Diluted Acetic Acid contains 5 per cent. by weight of hydrogen acetate, $HC_2H_3O_2$." *Br.*

Acetum Destillatum; Acide Acétique dilué, *Fr.;* Acetum, *P. G.;* Reiner Essig, Verdünnte Essigsäure, *G.*

See under *Acidum Aceticum Glaciale.*

ACIDUM ACETICUM GLACIALE.
U. S., Br.

GLACIAL ACETIC ACID Acid. Acet. Glac.

"Glacial Acetic Acid contains not less than 99 per cent. of CH_3COOH." *U. S.* "Glacial Acetic Acid contains not less than 98.9 per cent. by weight of hydrogen acetate, $HC_2H_3O_2$." *Br.*

Acidum Aceticum Concentratum; Radical Vinegar; Acidum Aceticum, *P. G.;* Acide acétique crystallisable, *Fr. Cod.;* Acide acetique concentré, Vinaigre glacial, Esprit de vinaigre, *Fr.*, Essigsäure, Eisessig, *G.;* Acido acetico concentrato, *It.*

Three strengths of acetic acid are now official in the U. S. and Br. Pharmacopœias. These are *Acidum Aceticum Glaciale,* of sp. gr. 1.047 to 1.050 at 25° C., *U. S.; Acidum Aceticum,* of sp. gr. 1.045, *U. S.,* at 25° C., and 1.044, *Br.,* at 15.5° C., and *Acidum Aceticum Dilutum,* sp. gr. 1.008, *U. S.,* at 25° C., and 1.007, *Br.,* at 15.5° C.

We shall consider these grades separately, in the order of their strength.

Acidum Aceticum Glaciale.—A process for this preparation was given in the British Pharmacopœia of 1864, but was not satisfactory, as the resulting acid was not truly glacial, and always contained sulphurous acid. The following modification of the process does, however, yield a pure product. Crystallized sodium acetate is in an iron dish in its own water of crystallization, dried out, again brought to fusion by increased heat, whereby, if the heat applied be not too strong, no acid is decomposed or vaporized. The anhydrous salt is then treated with half a molecule of sulphuric acid (for 82 parts anhydrous acetate 49 parts of strongest sulphuric acid), which, according to Mohr and Buchner, suffices, instead of twice the amount, usually employed. No sulphurous acid is liberated in this case. A process to be followed on a large scale, practically the counterpart of this, is given in the *U. S. D.,* 14th ed., p. 8.

Acetic acid of maximum strength may also be obtained by distilling acid potassium acetate at a heat between 199° C. and 299° C. One molecule of monohydrated acetic acid distils over, and neutral potassium acetate is left. The acid acetate may be formed by evaporating a mixture of the neutral acetate with an excess of aqueous acetic acid. In this process, the same potassium acetate serves repeatedly for conversion into acid acetate, and subsequent decomposition. This process is said to be employed by manufacturers on a large scale in some parts of the continent of Europe. It originated with Melsens. It is customary in the preparation of the very pure acid to construct the head of the still and the entire condensing system of pure silver.

Description and Physical Properties.—"A clear, colorless liquid, having a strong, characteristic odor, and a very pungent, acid taste. Glacial Acetic Acid is miscible with water, alcohol, and glycerin. Specific gravity: from 1.047 to 1.050 at 25° C.

"Congealing point: not below 14.5° C. It boils between 117° and 118° C. Glacial Acetic Acid responds to the reactions for acetates, page 440. It conforms to the tests for purity under *Acidum Aceticum* when diluted to that strength, except in the following respects: The pink color produced by the addition of 0.1 cc. of tenth-normal potassium permanganate to 2 cc. of Glacial Acetic Acid, which has been diluted with 10 cc. of distilled water and is contained in a glass-stoppered bottle, is not changed to brown within two hours (*readily oxidizable impurities*). Evaporate 20 cc. of Glacial Acetic Acid to dryness on a water bath, and dry to constant weight at 100° C: the weight of the residue does not exceed 0.002 Gm.

"Preserve in glass-stoppered bottles." *U. S.*

"At summer temperatures [about 15° to 20° C.] it is a clear, colorless liquid with a very pungent odor. Yields, when neutralised, the *reactions* characteristic of acetates. Crystallizes when sufficiently cooled, and does not entirely re-melt until the temperature rises above 14.7° C. 1 gramme diluted with 50 millilitres of *water* requires for neutralisation not less than 32.9 millilitres of *N/2 solution of sodium hydroxide.* Leaves no residue on evaporation, and yields no characteristic *reactions* for lead, copper, arsenic, chlorides, nitrates, sulphates, or sulphites. Does not immediately darken in color when neutralised with *solution of ammonia* and warmed with *solution of silver nitrate* (absence of formates). 2 millilitres of Glacial Acetic Acid do not completely decolorize a mixture of three drops of *solution of potassium permanganate* and 10 millilitres of *water* within half a minute (limit of empyreumatic matter)." *Br.* The anhydride was first isolated by C. Gerhardt, who found it to be a limpid liquid, heavier than water, and having the constant boiling point of 138° C. Glacial acetic acid should be kept in carefully stoppered glass containers, as it otherwise loses strength.

The U. S. and Br. acids are identical in strength (99 per cent.) but the temperature at which the sp. gr. is taken is 25° C. in the U. S. and 15° C. in the Br. It possesses the property of dissolving a number of substances, such as volatile and fixed oils, camphor, resins, gelatin, etc. As it attracts humidity from the atmosphere, it should be preserved in well-stoppered bottles.

The percentage of water in glacial acetic acid is generally determined by titration or by taking the melting and congealing points. N. Schoorl discovered that a solubility test with iodine and carbon tetrachloride gives very close results. Carbon tetrachloride is soluble in water-free glacial acetic acid in all proportions and its solubility is affected in proportion to the amount of water present. Iodine is used to intensify the end point of the reaction. (*Ph. Wb.*, 1917, 945.) The official method is as follows:

"**Assay.**—Proceed as directed under the assay for acids, using about 2.5 Gm. of the Acid, accurately weighed, and phenolphthalein T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.06004 Gm. of $CH_3.COOH$." *U. S.*

ACIDUM ACETICUM. *U. S., Br.* (sp. gr. 1.045, *U. S.*, 1.044, *Br.*). *Acetic Acid.*—This is the acid usually resulting from the purification of the crude acetic acid obtained by the destructive distillation of wood. It is the strength most useful to the apothecary, and is employed in making numerous pharmaceutical preparations. As this acid often has its source in acetic acid made by destructive distillation it will be proper to premise some account of the crude acid, called *pyroligneous acid.*

Wood, when charred, yields many volatile products, among which are an acid liquor, an empyreumatic oil, and tar containing creosote and some other proximate principles (see *Pix Pini.*) When the carbonization is performed in closed vessels, these products, which are lost in the ordinary process of charcoal burning, may be collected, and, at the same time, a large amount of charcoal be obtained.

Senff has furnished some comparative results in respect to the dry distillation of wood. It was found that when similarly distilled the yield by weight of crude acid, tar, charcoal, and gas from the most diverse species of wood does not essentially differ, but that the percentage of real acid in the crude acid obtained varies considerably, and in this respect the wood from orginary foliage trees compares favorably with that from needle-leaved trees; also that stem-wood yields more acid than branch-wood, that wood yields more acid than bark, and that sound wood yields more acid than unsound wood. (*B. Chem. G.*, 1885, xviii, p. 60.)

The following table gives the amounts of the various fractions yielded by 1 cord of wood, 128 cu. ft.

	Charcoal in bushels	Wood alcohol in gallons	Calcium acetate in lbs.	Tar in gallons
Hard woods.....	40-50	8-12	150-200	8-20
Resinous woods..	25-40	2-4	50-100	30-60

In the case of resinous woods from 30 to 80 gallons of wood oil and turpentine oil are obtained before the charring temperature is reached.

Crude pyroligneous acid, sometimes called *pyroligneous vinegar*, or *wood vinegar*, is a dark brown liquid, having a strong smoky odor, and consists of acetic acid, diluted with more or less water, and holding in solution some creosote and empyreumatic oil, with methyl alcohol, methanol, and acetone. It is from this crude acid that the U. S. and British acetic acid, corresponding to the acetic acid of commerce, is usually obtained. The purification is effected as follows: The acid is saturated with milk of lime, whereby calcium acetate is formed in solution, and thus most of the tarry matter is precipitated. The solution of calcium acetate is then mixed with a concentrated solution of sodium sulphate, and, by double decomposition, sodium acetate is formed in solution, and calcium sulphate precipitated. The solution of sodium acetate is next subjected to evaporation, during which further impurities that separate on the surface are skimmed off. The solution, being duly concentrated, is set aside to crystallize, and the impure salt thus obtained, after having been partially purified by solution and recrystallization, is fused in an iron vessel, stirred until it dries, and, the heat being carefully raised, subjected to incipient carbonization, whereby remaining empyreumatic matters are carbonized, with little damage to the salt. The mass is then dissolved in water, and the solution, being strained and recrystallized, furnishes pure sodium acetate. Sometimes soda ash is used directly for the neutralization of the distillate instead of milk of lime. (See *Sodii Acetas.*) Finally, this salt, distilled with from 34 to 35 per cent. of its weight of sulphuric acid, yields the acetic acid of commerce, the residue being sodium sulphate, which is reserved for decomposing fresh portions of calcium acetate. The acid has still an empyreumatic flavor, which is removed by filtering it through animal charcoal or rectifying with potassium dichromate. The odor is due to furfurol, which, as Victor Meyer has shown, can be detected even in glacial acetic acid by the red coloration it gives with aniline. It may be removed from pyroligneous acid by agitating the liquid with 2 or 3 per cent. of benzene. The aqueous layer, after separation from the benzene, is stated to give, by a single distillation, a palatable table vinegar.

Acetic acid, according to E. R. Squibb, improves very much by age, and a sample examined for odor when freshly distilled would not be recognized as the same three months afterward.

An excellent quality of acetic acid was made by E. R. Squibb by an improvement on the process of Schwartz, the principal feature being the careful regulation of the heat, whereby the excessive charring of the wood is prevented and the formation of the tarry substances so reduced as to leave the acetic acid almost entirely free from empyreuma. The retorts, which are rectangular in shape, are supported by wheels secured to shafts, rotating in bearings connected with the sides, and are run upon car tracks into the ovens, after they have been loaded with some billets of oak wood from the transfer car, in an ingenious and simple manner. In the construction of the ovens, care is taken to economize the fuel and to secure control of the temperature by the use of corrugated bottoms to the retorts and dampers in the flues; when necessary, the vapors are condensed in earthenware air condensers. Experience has shown that the production and liberation of acetic acid take place at a considerably lower temperature than that sufficient to convert the wood into charcoal, Squibb having proved that wood begins to char at 218.3° C.; indeed, the wood which is removed from the retorts after the operation is over is sold as kindling wood, and has the color of black walnut. The crude acetic acid does not require the tedious method of purification usually employed, but is treated with soda ash, forming sodium acetate, which is decomposed by sulphuric acid, and the acetic acid recovered in a purified condition by distillation.

A higher yield of acetic acid may be obtained in the distillation of hard woods by the use of a small amount of phosphoric acid which acts as a catalyzing agent. Almost three times the normal yield of acid has been reported and an increase of from 40 to 90 per cent. in the yield of wood alcohol.

It has also been discovered that if wood tar from former distillations be placed in the still with fresh wood, in starting a new distillation, the methoxy groups in the tar split off yielding an additional amount of wood alcohol. (*J. Ind. Chem.*, 1918, p. 264.)

Experiments with hard woods seasoned for different periods showed that beech and maple give the best wood alcohol yields when wet, but the best results are obtained from birch when dry. (*J. I. and E. C.*, 1918, 262.)

Cocoanut shells and native woods are being employed in Ceylon for destructive distillation for the production of acetic acid. (*C. D.*, 1918, p. 82.)

During the World War the facilities of the wood distillation industry were found to be entirely inadequate to supply the demand for acetic acid and it was made from molasses which had been fermented into alcohol. The conversion of the molasses alcohol into acetic acid was accomplished by the quick fermentation process by passing the weak alcohol through percolators filled with beech wood shavings which had been inoculated with *Mycoderma Aceti.* Another method for the rapid production of acetic acid during the World War, was by converting acetylene into acetaldehyde which is then readily oxidized into acetic acid. (*Chem. Met. Eng.*, 1918, 397.)

The sp. gr. of the different acetic acids increases with their strength up to the density of 1.0681 at $\frac{25°C.}{25°C.}$ (maximum), after which it decreases until it reaches 1.0471 at $\frac{25°C.}{25.C.}$, the density of the strongest acid (*glacial acid*). The specific gravities of the glacial (100 per cent.) and the 39 per cent. acid are practically the same, and this applies also to the 74 and 81 per cent.; the 76, 77, and 78 per cent. acids have exactly the same density, the variations between 71 and 83 per cent. being very slight. It will thus be seen that specific gravity cannot be relied upon as a criterion for strength. The glacial acid may, however, be distinguished from the 39 per cent. acid by adding 10 per cent. of water, when, if the density increases, the specimen is the stronger acid.

For U. S. Pharmacopœia tables of specific gravity of various strengths of acetic acid, see Part III.

Description and Physical Properties.—" A clear, colorless liquid, having a strong, characteristic odor, and a sharply acid taste. Acetic Acid is miscible with water, alcohol, and glycerin. Specific gravity: about 1.045 at 25° C.

" Preserve in glass-stoppered bottles." *U. S.*

" Acetic Acid is strongly acid to litmus paper and responds to the reactions for acetates.

" Evaporate 20 cc. of Acetic Acid on a water bath, and dry to constant weight at 100° C.: the weight of the residue does not exceed 0.002 Gm. Mix 5 cc. of the Acid with 10 cc. of ammonia T.S., add 5 cc. of silver nitrate T.S., and boil the solution for one minute: the color of the solution is not changed (*formic or sulphurous acid*). Dilute 4 cc. of the Acid in a glass-stoppered bottle with 20 cc. of distilled water, and add 0.5 cc. of tenth-normal potassium permanganate: the pink color is not changed to brown at once, and the liquid does not become entirely brown or free from a pink tint in less than one-half minute (*empyreumatic substances*). Separate portions of 1 cc. each of Acetic Acid diluted with 10 volumes of distilled water show no turbidity on the addition of 5 drops of barium chloride T.S. (*sulphate*), and no opalescence with 5 drops of silver nitrate T.S. (*Chloride*). Acetic Acid diluted with 20 volumes of distilled water meets the requirements of the test for *heavy metals*.

" **Assay.**—Proceed as directed under the assay for acids, using about 6 cc. of the Acid, accurately weighed, and phenolphthalein T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.06004 Gm. of $CH_3.COOH$.

The British Pharmacopœia requires that acetic acid shall be " a clear, colorless liquid with pungent odor, yielding, when neutralised with an alkali, the *reactions* characteristic of acetates. Specific gravity 1.044. Yields no residue on evaporation, and no characteristic *reactions* for copper, chlorides, nitrates, sulphates, or sulphites. Does not immediately darken in color when exactly neutralised with *solution of ammonia* and warmed with *solution of silver nitrate* (absence of formates). 5 millilitres require for neutralisation 28.7 millilitres of *N/1 solution of sodium hydroxide*. 2 millilitres do not completely decolorize a mixture of one drop of *solution of potassium permanganate* and 10 millilitres of *water* within half a minute (limit of empyreumatic matter). When tested for lead according to the quantitative method described in Appendix V, using 10 grammes in each Nessler glass, no difference in color is observed on the addition of the *solution of sodium sulphide* to one of the solutions (absence of lead). *Arsenic limit* 2 parts per million." *Br.*

Of the British acid (sp. gr. 1.044) the strength in hydrogen acetate is 33 per cent. The U. S. official acid is somewhat stronger than the British. In the arts *Acetic Acid No. 8* (sp. gr. 1.049) has long been used; it derives its name from the fact that one part added to sufficient water to make eight parts, by measure, constitutes so-called distilled vinegar, used in pickling; the latter is not equal to the official diluted acetic acid in strength (one-fifth weaker).

Charles F. Squibb has made numerous experiments proving the value of many strengths of acetic acid as menstrua for exhausting the valuable organic principles of drugs by percolation; he found even diluted acetic acid a reliable menstruum. J. P. Remington preferred a 10 per cent. acetic acid, and suggested a class of preparations termed *"acetracts"* to replace solid extracts. Acetic acid is a powerful solvent and can frequently be made to take the place of the more expensive alcoholic menstrua. (*A. J. P.*, 1897, p. 121.)

ACIDUM ACETICUM DILUTUM. *U. S., Br. Diluted Acetic Acid.*—

"Acetic Acid, 165 Gm.; Distilled Water, 835 Gm.; to make 1000 Gm. Mix them.

"Acetic Acid, 152.6 grammes; Distilled Water, sufficient to produce 1000.0 millilitres. Mix." *Br.*

"**Description and Physical Properties.**—A clear, colorless liquid, having a characteristic odor. Diluted Acetic Acid is miscible with water and with alcohol. Specific gravity: about 1.008 at 25° C.

"Preserve in glass-stoppered bottles." *U. S.*

"Diluted Acetic Acid is acid to litmus paper and responds to the reactions for acetates. It conforms to the tests for purity under *Acidum Aceticum,* allowance being made for the difference in strength.

"**Assay.**—Proceed as directed under the assay for acids, using about 25 cc. of the Acid, accurately weighed, and phenolphthalein T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.06004 Gm. of $CH_3.COOH$.

"Specific gravity 1.007. 20 millilitres require for neutralisation 16.7 millilitres of *N/1 solution of sodium hydroxide.* Free from the impurities indicated under 'Acidum Aceticum.'" *Br.*

Uses. *Crude Pyroligneous Acid.*—This acid having been incidentally described as the source of the acetic acid of commerce, it may be proper in this place to notice its uses. It is an active disinfectant and stimulant, the former property being mainly due to the presence of creosote. It has been used as a local application to *gangrene* and ill-conditioned *ulcers.* Kolipinski recommends it internally in doses of one to two teaspoonfuls (3.75–7.5 cc.) three times a day in the treatment of *arthritis deformans.* (*Trans. American Therap. Soc.,* 1907.) It has also been suggested for the preservation of food-stuffs, especially meat and fish. Its use, however, is specifically prohibited by the food laws of most states because of the presence of methyl alcohol which is absorbed by the food and particularly because of the fact that foods treated by immersion in pyroligneous acid rather than by "smoking" do not shrink in weight as do the latter (often 15 or 20 per cent.) and are therefore of less food value although they usually sell for the same price.

Glacial Acetic Acid.—Glacial acetic acid has been employed externally as a vesicant and as a caustic. For the former purpose it may be applied by means of a blotting paper moistened with the acid. It requires, however, considerable carefulness in its use and is generally inferior to cantharides. As an escharotic it is useful for the destruction of *warts* and *corns,* but has been largely replaced by the trichloracetic acid (see *Acidum Trichloraceticum*).

Strong acetic acid is also a useful agent for detecting small quantities of albumin and is used in the examination of urine, especially in conjunction with potassium ferrocyanide.

Diluted Acetic Acid.—The object of making diluted acetic acid official is to make available a weak solution of *pure* acetic acid which may be substituted for "distilled" vinegar in all formulas in which accuracy is required. For a long period diluted acetic acid has been made by mixing one part of acetic acid with seven parts of water by measure. *Acetic acid No. 8* is the commercial designation of an acid of 30 per cent. strength. The official diluted acid was made considerably stronger in the U. S. P., 1880, and the strength has not been altered in the subsequent revisions. "Distilled" vinegar is not vinegar made by distillation as is popularly supposed. The designation is applied to vinegar made by the beech-wood shaving or quick fermentation process from a weak alcoholic liquid which has been produced by distillation. Such a product contains a little organic matter, which is always darkened or precipitated when its acid is saturated with an alkali, a change which does not take place when diluted acetic acid is employed.

Either in the form of the official diluted acetic acid or in the form of natural or "distilled" vinegar, acetic acid is useful as a refrigerant drink in febrile conditions. As it is entirely oxidized in the system, escaping through the breath as carbonic acid, it does not tend to increase the acidity of the urine. It is also of service as an astringent and styptic. As an emergency remedy it may prove life-saving in *hemorrhage* from the stomach or uterus. For the former condition the diluted acetic acid should be further weakened by the addition of one or two parts of water, and this mixture taken in doses of a tablespoonful every few minutes. Owing to its volatility and pungency the vapor of acetic acid is frequently applied to the nostrils as an excitant in *syncope* or *headache* as a substitute for smelling salts. Used in this manner it has been recommended for the purpose of quieting post-anesthetic *nausea.*

Acetic acid is incompatible with carbonates, free chlorine, and ferric salts, the latter producing a deep red color which is destroyed by excess of mineral acids.

Dose, of diluted acetic acid, twenty to sixty minims (1.3–3.9 cc.).

Off. Prep.—From *Acetic Acid,* Acidum Aceticum Dilutum, *U. S.;* Acetum Aromaticum, *N. F.;* Linimentum Terebinthinæ Aceticum, *N. F.* From *Glacial Acetic Acid,* Linimentum Terebinthinæ Aceticum, *Br.*

ACIDUM ACETYLSALICYLICUM. U. S., Br.

ACETYLSALICYLIC ACID

"Acetylsalicylic Acid contains not less than 99.5 per cent. of $C_6H_4.O(CH_3CO)COOH$ 1:2." *U. S.*

"Acetylsalicylic Acid, $C_9H_8O_4$, may be obtained by the action of acetic anhydride or of acetyl chloride on salicylic acid." *Br.*

Aspirinum; Aspirin; Acide Acetylsalicylique, *Fr. Cod.;* Acidum Acetylo-salicylicum, *P. G.*

The name aspirin, by which this substance is popularly known, is not purely fanciful nor arbitrary. It is derived from the fact that salicylic acid as originally obtained from *Spiræa ulmaria* was at first known as *acidum spiricum.* Acetylsalicylic acid is made by heating together 50 parts of salicylic acid and 75 parts of acetic acid anhydride at about 150° C. It is said that this method does not give results and that no trustworthy method has ever been published for its preparation.

Another method suggested is by the acetylation of salicylic acid with acetyl chloride using one molecule of the former to 2½ molecules of the latter, keeping the reaction below 70°.

Aspirin cannot be purified by crystallization from water or solvents containing it on account of its tendency to undergo hydrolysis. It may be crystallized from benzene, methyl acetate, chloroform, or strong ethyl or methyl alcohol. It is then purified by recrystallization.

Description and Physical Properties.—"Small, colorless crystals or needles, or a white, crystalline powder. It is odorless, and in dry air is stable, but in contact with moisture it gradually decomposes into salicylic and acetic acids. One Gm. of Acetylsalicylic Acid is soluble in about 300 cc. of water, 5 cc. of alcohol, 17 cc. of chloroform, and in from 10 to 15 cc. of ether, at 25° C. It is less soluble in absolute ether. It is also soluble with decomposition in solutions of alkali hydroxides and carbonates.

"Preserve in well-closed containers." *U. S.*

"The melting point of Acetylsalicylic Acid, when determined in a bath previously heated to 120° C., is not below 132° C. When the Acid is heated with water for several minutes, then cooled and a drop or two of ferric chloride T.S. added, a violet-red color is produced. Boil about 0.5 Gm. of Acetylsalicylic Acid with 10 cc. of sodium hydroxide T.S. for a few minutes, cool, and add 10 cc. of diluted sulphuric acid: a white precipitate of salicylic acid is produced, and the odor of acetic acid is perceptible. Filter, add to the filtrate 3 cc. of alcohol and 3 cc. of sulphuric acid, and warm: the odor of ethyl acetate becomes noticeable.

"Ash: not more than 0.05 per cent. A solution of 0.5 Gm. of Acetylsalicylic Acid in 10 cc. of sulphuric acid is not darker than light yellow (*readily carbonizable substances*). A solution of 0.5 Gm. of the Acid in 10 cc. of warm sodium carbonate T.S. is clear. Shake 1 Gm. of Acetylsalicylic Acid with 20 cc. of distilled water and 1 cc. of nitric acid for one minute, and filter: five cc. portions of the filtrate yield no opalescence or turbidity at once on the addition of a few drops of silver nitrate T.S. (*chloride*) or barium chloride T.S. (*sulphate*). Warm 1 Gm. of Acetylsalicylic Acid with 10 cc. of distilled water and 1 cc. of hydrochloric acid for two minutes, dilute with 40 cc. of distilled water, cool, and filter: the filtrate meets the requirements of the test for *heavy metals.* Dissolve 1 Gm. of Acetylsalicylic Acid in 5 cc. of alcohol, and allow the solution to evaporate spontaneously in a dish protected from dust: a white crystalline residue is obtained (*coloring matter, resinous substances*). Dissolve 0.1 Gm. of Acetylsalicylic Acid in 1 cc. of alcohol, dilute the solution with 48 cc. of cold distilled water, and add at once 1 cc. of a freshly prepared diluted ferric ammonium sulphate solution (made by adding 1 cc. of normal hydrochloric acid to 2 cc. of ferric ammonium sulphate T.S. and diluting with water to 100 cc.): the coloration, if any, produced in one-half minute, is not greater than that produced in a control test, using 1 cc. of a solution containing 0.1 Gm. of salicylic acid and 1 cc. of glacial acetic acid in 1 liter of water (*free salicylic acid*).

"**Assay.**—Add 50 cc. of half-normal sodium hydroxide to about 1.5 Gm. of Acetylsalicylic Acid, previously dried for three hours over sulphuric acid and accurately weighed, and boil gently for ten minutes. Titrate the excess of sodium hydroxide with half-normal sulphuric acid, using three drops of phenolphthalein T.S. as indicator. Make a blank test, using 50 cc. of half-normal sodium hydroxide, and from the comparisons make any necessary corrections. Each cc. of half-normal sodium hydroxide corresponds to 0.04503 Gm. of $C_6H_4.O(CH_3CO).COOH$.

The British Pharmacopœia described acetylsalicylic acid as follows: "A white, crystalline powder; taste slightly acid. Sparingly soluble in *water;* soluble in 5 parts of *alcohol* (90 per cent.); soluble in *ether.* Melting point from

133° to 135° C. When 0.5 gramme is boiled for two or three minutes with 10 millilitres of *solution of sodium hydroxide* and to the cooled solution excess of *diluted sulphuric acid* is added, a crystalline precipitate is produced which, after washing and drying, responds to the tests described under 'Acidum Salicylicum,' and the filtrate, after neutralisation, yields the *reactions* characteristic of acetates. When 0.5 gramme is shaken with 20 millilitres of *water* and 1 drop of *T. Sol. of ferric chloride* is added, no violet coloration is produced (absence of salicylic acid). *Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million. No appreciable ash." *Br.*

Many discrepancies have been noted with regard to the melting point of aspirin, some authorities claiming it to be 131° to 132° C., while others claim 134° to 135° C. The rate of heating seems to have considerable effect upon this factor.

Acetylsalicylic acid has been one of the most popularly used drugs of the last two decades. It has been known under many names such as: *xaxa, coxpyria, helicon, atonin, acetosal, regipyrin, asposal, empirin, nupyrin, salcetin, salacetol, anglopirin* and *salaspin.* It has been grossly and variously adulterated, especially abroad, during the World War. Among the adulterants reported have been, sugar, starch, talc, tartaric acid, acetanilid, phenacetin, milk sugar, salol, acid calcium phosphate, bone acid and cream of tartar.

Uses.—Although it has been shown that salicylic acid occurs in the urine within from twenty minutes to half an hour after the ingestion of acetylsalicylic acid, there is strong reason to believe that the drug circulates in the blood in large part unbroken; in other words, the action is not purely that of salicylic acid but there is also a different effect of acetylsalicylic acid. Christone and Lapresa (*P. J.*, lxxxv) have found that it requires forty minutes for the decomposition of acetylsalicylic acid by the gastric juice and that its toxicity is three times as great as that of sodium salicylate. Hanzlik and Presho (*J. P. Ex. T.*, 1923, xxi, 246) recovered from the urine undecomposed acetylsalicylic acid amounting to about 25 per cent. of the ingested dose. Moreover, there have been reported a very considerable number of cases of acetylsalicylic acid poisoning in human beings with symptoms very different from those caused by the salicylates and in many of these cases of poisoning the dosage has been so small as to practically exclude salicylic acid poisoning; in a case reported by Graham (*J. A. M. A.*, 1911), after two doses of five grains each there occurred marked cardiac weakness with pulse rate of 136 and edematous swelling of the face and mucous membranes with eversion of the lids and lips from the swelling; Shelby (*J. A. M. A.*, 1918, lxxi, 1381) has reported alarming edema of the face and throat from a single dose of 5 grains. In the third place, clinical experience has demonstrated that the range of therapeutic usefulness of acetylsalicylic acid is not the same as that of the salicylates.

Acetylsalicylic acid has been used in medicine (1) as an antirheumatic, (2) as an analgesic, (3) as an antipyretic, (4) locally.

In *inflammatory rheumatism,* it is generally of less value than ammonium or sodium salicylate. On the other hand, in those *myalgias* or *neuralgias* of dubious origin commonly diagnosed as *chronic rheumatism,* acetylsalicylic acid is often of great usefulness. In a general way it may be said that the more nearly these types of pain approach to true rheumatism the more likely it is that sodium salicylate will be a superior drug to acetylsalicylic acid. As an analgesic acetylsalicylic acid comes in competition with acetanilid and other coal tars for the relief of *headaches, neuritis,* and similar painful conditions. As an antipyretic, as has been shown by Chambers (*B. M. J.*, 1912), Bondi (*Th. M.*, 1911, p. 179) and others, it far exceeds the salicylates in power. It has been used for the reduction of the temperature in *typhoid fever* and *rheumatic fever* but in some cases it is liable to produce serious collapse. Locally it has been recommended by Fetterolf (*T. G.*, November, 1908) in *acute tonsillitis* and has also been employed to a lesser extent in *eczema* and other *skin diseases.*

Overdoses of acetylsalicylic acid commonly produce ringing in the ears as do the inorganic salicylates. Frequently, however, even in quantities not excessive it produces a very different type of intoxication. Among the most common symptoms are profuse sweating, cold extremities, either with or without a fall in body temperature, rapid or irregular pulse and occasionally albuminuria. In many reported cases there has been marked facial edema involving not only the skin but the mucous membrane of the mouth and throat.

Cooke (*J. A. M. A.*, Sept. 6, 1919) reports a group of a familial idiosyncrasy to acetylsalicylic acid. In these patients there was urticaria and violent bronchial asthma.

Acetylsalicylic acid readily undergoes hydrolysis with aqueous solvents with the liberation of free salicylic and acetic acids. In pure water complete decomposition takes place in 100 days. Acids hasten the rapidity of such change. In the presence of moisture acetylsalicylic acid unites with various bases to form salts (acetylsalicylates), with many organic substances it forms liquid entectic mixtures, when triturated.

The statement that quinine and acetylsalicylic acid react upon each other to form the poisonous quinotoxin has been contradicted by the experiments of Sollmann. Ruddiman and Lanwermeyer (*J. A. Ph. A.*, 1924, xiii, p. 1009; *J. A. M. A.*, 1921, April 9) experimented with mixtures of acetyl salicylic acid with basic quinine and also the sulphate, bisulphate, hydrochloride and other cinchona alkaloids. They found that the mixture with quinine alkaloid, after several months, changed to a brownish red viscid mass if exposed to the light, but when kept in the dark the change was less rapid; this mixture tested on frogs was not more poisonous than the freshly made mixture nor than the equivalent dose of acetyl salicylic acid. It has of course the characteristic color incompatibilities of the salicylates.

The *dose* of acetylsalicylic acid is from five to fifteen grains (0.3–1.0 Gm.).

ACIDUM ACETYLTANNICUM. U. S.

ACETYLTANNIC ACID

Acid. Acetyltan. **[Diacetyltannic Acid, Tannyl Acetate, Acetannin.]**

"Acetyltannic Acid is a product obtained by the acetylization of tannic acid." *U. S.*

Tannigen.

Acetannin is prepared by heating tannin with acetic anhydride in the presence of glacial acetic acid; after the reaction is completed the product is poured into water and the resultant precipitate washed and dried.

Leech (*J. A. M. A.*, 1920, lxxv, 1123) has shown that the commercial samples of acetannin differ greatly among themselves. The proportion dissolved by water varied from six to eighteen per cent. of the sample tested. The amount dissolved by 1 per cent. solution of sodium bicarbonate ranged from 30 to 90 per cent. of the sample. Their solubility in artificial gastric juice was slightly less than in plain water.

Description and Physical Properties.—"A yellowish-white, or a grayish-white powder which darkens on exposure to light. It is odorless or has a slight acetous odor. Acetyltannic Acid is only slightly soluble in water and in alcohol, but is soluble in ethyl acetate. It is soluble with gradual decomposition in aqueous solutions of alkali hydroxides and carbonates. It is also soluble in aqueous solutions of sodium borate and of sodium phosphate.

"Warm 0.2 Gm. of Acetyltannic Acid with 2 cc. of alcohol and 2 cc. of sulphuric acid: the odor of ethyl acetate is noticeable. A solution of Acetyltannic Acid in sodium phosphate T.S. (1 in 100) after standing for several hours precipitates albumin solution, but this property is destroyed by the presence of an excess of alkali. When dissolved in an aqueous solution of sodium borate (1 in 25), it does not precipitate albumin.

"Ash: not more than 0.3 per cent. Dry about 1 Gm. of Acetyltannic Acid, accurately weighed, for three hours at 100° C.: the loss does not exceed 3 per cent. Shake 1 Gm. of Acetyltannic Acid with 50 cc. of distilled water during five minutes and filter: a 25 cc. portion of the filtrate requires for neutralization not more than 1.2 cc. of tenth-normal sodium hydroxide, using 3 drops of phenolphthalein T.S. as indicator (*free acid*). To the remainder of the filtrate add 2 drops of ferric chloride T.S.: a green but not a blue color is produced (*free tannic acid*). Digest 1 Gm. of Acetyltannic Acid with a solution of 2 Gm. of sodium bicarbonate in 200 cc. of distilled water for three hours at about 40° C., filter through a counterbalanced filter or a Gooch crucible, wash the insoluble residue with 4 portions of distilled water, 10 cc. each, and dry to constant weight at 110° C. The weight of the residue does not exceed 0.15 Gm. Digest 1 Gm. of Acetyltannic Acid with 200 cc. of distilled water for two hours, shaking at frequent intervals. Filter through a dry filter into a dry flask, rejecting the first 20 cc. of the filtrate, evaporate 100 cc. of the subsequent filtrate to dryness on a water bath and dry the residue for three hours at 100° C. The weight of the residue does not exceed 0.03 Gm. (*soluble substances*).

"Preserve in well-closed containers, protected from light." *U. S.*

Uses.—Acetyl tannin has a very mild astringent effect due to the presence of a small amount of free tannic acid. In alkaline solutions it is slowly hydrolized, liberating its combined tannic acid to exercise the characteristic astringent effect. According to Sollmann (*J. P. Ex. T.*, 1921, xvii, 87) this decomposition takes place rather slowly, the astringency reaching its maximum in about two hours. This would mean that the drug would exercise very little astringent effect in the stomach or duodenum; that in the lower part of the intestinal canal it would exert a mild continuing effect as it was gradually hydrolized. Acetannin is used exclusively in the treatment of *diarrheas* of various types, such as chronic *enteritis, cholera infantum, dysentery,* etc. It has even been asserted to have a beneficial effect in relieving symptoms of *intestinal tuberculosis.*

The *dose* is five to fifteen grains (0.3 to 1 Gm.).

ACIDUM BENZOICUM. U. S., Br.

BENZOIC ACID **Acid. Benz.**

"Benzoic Acid, dried at 100° C. for two hours, contains not less than 99.3 per cent. of $C_6H_5.COOH$." *U. S.*

"Benzoic Acid, $HC_7H_5O_2$, may be obtained from benzoin, or prepared synthetically." *Br.*

Acidum Benzoicum Sublimatum, Flores Benzoes; Flowers of Benzoin; Flowers of Benjamin; Acide benzoïque; Fleurs de Benjoin, *Fr.;* Acidum Benzoïcum, *P. G.;* Benzoesäure, Benzoeblümen, *G.;* Acido benzoico, *It., Sp.*

Although most of the benzoic acid on the market is manufactured synthetically the older method of preparing it from benzoin is still used commercially to some extent despite the much higher price of the product. The acid made from the natural resin is distinguished commercially as "English benzoic acid" while the synthetic product is designated as "German benzoic acid." The latter term was formerly applied to a product made from hippuric acid of the urine of cattle; this does not appear, however, to be any longer an article of commerce. During the World War the suggestion was made to revive this process and it was estimated that one pound of benzoic acid could be produced from the daily urine of 15 cows. This yield would hardly be profitable and as far as we know was not actually practised.

The acid which exists in benzoin combined with resin may be volatilized by heat and collected in a condenser. Formerly the benzoin was mixed with sand before sublimation; but this is now usually omitted as not only useless but probably injurious by favoring the production of empyreumatic substances. Unless the temperature be very carefully regulated, a portion of the resin is decomposed, and an oily substance generated, which rises with the acid, and gives it a brown color, from which it cannot be entirely freed by bibulous paper; and this result, even with the greatest caution, sometimes takes place. Mohr, after experimenting, recommended the following plan as unobjectionable: In a round cast iron vessel, eight or nine inches in diameter and two inches deep, a pound or less of coarsely powdered benzoin is placed, and uniformly strewed over the bottom. The top of the vessel is closed by a sheet of filter paper or some fabric as muslin or cheese cloth through which the vapors may pass but which prevents the sublimed material from falling back into the exhausted resin. A cylinder of thick paper in the form of a hat, just large enough to fit closely around the sides of the pot, is then placed over it, and in like manner secured by paste. A moderate heat is now applied by means of a sand bath and continued for three or four hours. The vapors pass through the porous diaphragm, which absorbs the empyreumatic oil, and are condensed within the upper chamber in brilliant white crystals, having an agreeable odor of benzoin. (*Ann. Pharm.*, xxix, 178.) The heat must be kept below 120° C. during the operation. Strips of paper passed at irregular intervals across the cap prevent the falling back of crystals. The remaining acid of the benzoin may be extracted, if deemed advisable, by treating the residue of the benzoin with lime or sodium carbonate. From the mode of preparing benzoic acid by sublimation, it was formerly called *flowers of benzoin* or *flowers of Benjamin.*

Another mode of separating the acid from benzoin is by combining it with a salifiable base and precipitating with an acid. Such is the process of Scheele. It consists in boiling the powdered benzoin with calcium hydroxide and water, filtering the solution of calcium benzoate thus obtained, and precipitating the benzoic acid with hydrochloric acid. The crude benzoic acid is then purified by sublimation.

Several other modes of extracting the acid have been recommended. The following is the process of Stolze. One part of the benzoin is dissolved in three parts of alcohol, the solution filtered and introduced into a retort, and the acid saturated by sodium carbonate dissolved in a mixture of eight parts of water and three of alcohol. The alcohol is distilled off and the sodium benzoate contained in the residual liquid is decomposed by sulphuric acid, which precipitates the benzoic acid. This is purified by solution in boiling water, which deposits the acid when it cools. By this process Stolze obtained 18 per cent. of acid from benzoin containing 19.425 per cent. By the process of Scheele he obtained 13.5 per cent.; by the agency of sodium carbonate, 12 per cent.; by sublimation, only 7.6 per cent. Scharling prepared benzoic acid by means of heated steam, and obtained 8 per cent. (*A. J. P.*, xxiv, 236.)

The acid is manufactured very cheaply by several synthetic methods. The processes most commonly employed start with *toluene*, $C_6H_5CH_3$. In the first method the toluene is changed to benzotrichloride, $C_6H_5CCl_3$, by passing chlorine into rectified toluene heated to 110°, and contained in an earthenware or lead lined vessel, until the product possesses a specific gravity of 1.35. Iron and moisture must be carefully excluded during this stage of the operation. The benzotrichloride is then heated with milk of lime with a trace of powdered iron added as a catalyzer. Benzaldehyde is produced to some extent and is recovered by distillation. The calcium benzoate which is produced is then decomposed with hydrochloric acid and the crude benzoic acid purified by sublimation or by recrystallization from water.

In the second method the benzoic acid is obtained as a by-product in making benzaldehyde from toluene (see *Benzaldehydum*); in the process of manufacturing much of the benzaldehyde is converted into benzyl alcohol and calcium benzoate by the excess of lime used. This latter salt is then treated with hydrochloric acid, and the benzoic acid thus set free after which it is purified as previously described. In a third method the toluene is only chlorinated to the point where benzylchloride is formed. The benzylchloride is then heated in an apparatus provided with a reflux condenser with lime or caustic soda and some calcium hypochlorite is gradually added. The resulting calcium benzoate is purified as in the previous processes. The synthetic acid is frequently resublimed in contact with benzoin, in order to give it the vanilla-like odor of the acid sublimed from the gum. A method of making benzoic acid from tannin or gallic acid is described in *Ph. Era*, 1892, 172. P. Schulze produced benzoic acid by heating benzyl chloride or benzotrichloride in the presence of ferric benzoate or metallic iron. The process is patented. (*Ph. Centralh.*, 1896, 221.)

Owing to the scarcity in the market of benzoin yielding paying quantities of benzoic acid, it was asserted that the English manufacturers used certain varieties of Botany Bay gum (see *Gum acroides*, Part II), and obtained a larger yield of an acid which was at one time regarded as cinnamic, but has been shown to be benzoic acid. (*N. R.*, Feb., 1879.) Benzoic acid is also found as a decomposition product of benzaldehyde or of oil of bitter almond in the bottom of containers of these substances which have been exposed for some time.

Description and Physical Properties.—"Lustrous scales or friable needles. The synthetic Acid is white and odorless, or it may have a slight odor of benzaldehyde. The natural Acid is white or yellowish, acquiring a darker color on exposure to light, and has a slight odor of benzoin. Benzoic Acid is somewhat volatile at moderately warm temperatures, and freely volatile with steam. One Gm. of Benzoic Acid is soluble in 275 cc. of water, 2.3 cc. of alcohol, 4.5 cc. of chloroform, 3 cc. of ether, 10 cc. of benzene, 30 cc. of carbon disulphide or carbon tetrachloride, and in 23 cc. of oil of turpentine, at 25° C. One Gm. is soluble in 18 cc. of boiling water, and in 1.5 cc. of boiling alcohol. It is soluble in fixed or volatile oils and is sparingly soluble in petroleum benzin.

"Benzoic Acid melts between 120° and 122° C. Benzoic Acid responds to the reactions for benzoates.

"Ash: not more than 0.05 per cent. A solution of 0.1 Gm. of the synthetic Acid in 2 cc. of sulphuric acid does not become darker than light yellow when warmed for five minutes at 50° C. The color produced by the Acid from benzoin tested in the same manner does not become darker than light brown (*readily carbonizable substances*). Dissolve 0.3 Gm. of the Acid in 15 cc. of hot water, and add to the solution 2 cc. of tenth-normal potassium permanganate: the odor of benzaldehyde is not perceptible (*cinnamic acid*). Mix 0.5 Gm. of Benzoic Acid and 0.7 Gm. of calcium carbonate with a little distilled water in a crucible, dry the mixture, and incinerate it at a low red heat. Dissolve the residue in 20 cc. of diluted nitric acid, filter, wash the filter and insoluble residue with 15 cc. of distilled water, add to the filtrate 0.5 cc. of tenth-normal silver nitrate, and dilute with distilled water to 50 cc. Dissolve 0.7 Gm. of the same calcium carbonate in 20 cc. of diluted nitric acid; filter if necessary, add 0.5 cc. of tenth-normal silver nitrate, and dilute with distilled water to 50 cc. Add to this solution fiftieth-normal hydrochloric acid, drop by drop, mixing well after each addition, until the turbidity matches that in the test with the Benzoic Acid. If the synthetic Acid is tested, not more than 0.6 cc. of fiftieth-normal hydrochloric acid is required in the control test to match the turbidity, and, if the natural Acid is tested, not more than 0.3 cc. of fiftieth-normal hydrochloric acid is required (*chlorinated compounds*).

"Preserve in well-closed containers, in a cool place, protected from light.

"**Assay.**—Dry about 1 Gm. of Benzoic Acid at 100° C. for two hours, and dissolve 0.5 Gm. of the dried Acid, accurately weighed, in 25 cc. of diluted alcohol, which has previously been neutralized with tenth-normal sodium hydroxide, using three drops of phenolphthalein T.S. as indicator. Titrate this solution with tenth-normal barium hydroxide until the pink color is restored. From the number of cc. of tenth-normal barium hydroxide consumed, subtract one-fifth of the volume of fiftieth-normal hydrochloric acid used in the test for chlorinated compounds. Each cc. of tenth-normal barium hydroxide corresponds to 0.01221 Gm. of $C_6H_5.COOH$." *U. S.*

"Soluble in 450 parts of *water*, in 3 of *alcohol* (90 per cent.), in 2.5 of *ether*, and in 7 of *chloroform*. Melting point 121.5° C., but if sublimed from benzoin about 120° C. Heated in a dry test-tube it melts and sublimes leaving only a slight residue. Volatilises in the vapor of *water*. The solution obtained by gently warming 0.2 gramme with 20 millilitres of *water* and 1 millilitre of *N/1 solution of sodium hydroxide* and filtering yields a pale reddish precipitate with *T. Sol. of ferric chloride*. When 0.5 gramme is heated in a closed crucible with twice its weight of *calcium carbonate*, the mass dissolved in *diluted nitric acid*, and *solution of silver nitrate added*, not more than the slightest cloudiness results (absence of chlorobenzoic acid). Yields no characteristic *reactions* for oxalates. Does not develop the odor of benzaldehyde when warmed with its own weight of *potassium permanganate* and ten times its own weight of *diluted sulphuric acid* (absence of cinnamic acid). *Arsenic limit* 2 parts per million." *Br.*

It is entirely soluble in solutions of potassium, sodium, or ammonium hydroxides, from which it is precipitated by hydrochloric acid. On carefully neutralizing any of these solutions and adding solution of ferric sulphate previously diluted with water, a flesh-colored precipitate is produced.

Potassium permanganate has been depended upon more than any other reagent to distinguish between benzoic acids as obtained from different sources. Schacht proposes the following test: If 3 grains of benzoic acid be dissolved in 96 minims of solution of potassium hydroxide, sp. gr. 1.777, diluted with 96 minims of distilled water, and 10 drops of a solution made by dissolving 1 grain of potassium permanganate in 200 grains of water be added to it and the whole heated to boiling, dark green liquids (in which brown precipitates gradually appear) are produced if the benzoic acid be obtained from urine, from toluene, or from commercial benzoin, while if the benzoic acid be from Siam benzoin (sublimed or made by wet process) decoloration of the liquids and brown precipitates are produced, due to the presence of cinnamic acid. (*Ph. Centralh.*, 1881, 565.) The odor of bitter almonds confirms the presence of cinnamic acid. Essell (*Ph. Ztg.*, 1904, 272) modifies this test to secure greater accuracy as follows: 0.2 Gm. of the *finely* powdered benzoic acid and 5 cc. of tenth-normal permanganate solution are mixed in a test tube of wide diameter and securely corked. When the red color is discharged (usually after a few minutes) 5 cc. more of tenth-normal permanganate solution are added, and the tube is set aside from fifteen to thirty minutes, with frequent shaking. If then the cork be removed the odor of benzaldehyde will be strongly perceptible in the presence of 5 per cent. of cinnamic acid, and distinctly recognizable if only 1 per cent. is present. It is claimed that benzoic acid from benzoin can be distinguished from that from other sources by adding resorcinol and sulphuric acid to the alcoholic solution of the acid; the benzoin-benzoic acid gives a beautiful red color, due probably to a trace of vanillin or other aldehyde in the natural product. (Göldner, *Ph. Ztg.*, 1892, 697.)

The principal impurities to be looked for in the synthetic acid are the chlorinated compounds which contaminate the resulting end product. It is sometimes difficult to detect these chlorobenzoic acids and it is stated that the high assays sometimes recorded in the analysis of sodium benzoate are accounted for by their presence.

Benzoic acid is incompatible with salts of iron, silver, lead, and mercury. It precipitates a solution of quinine sulphate and is decomposed by hydrogen dioxide in the presence of inorganic acids with the production of salicylic acid.

Uses.—When benzoic acid is taken into the system it appears in the urine chiefly as hippuric acid. This conversion would appear to take place in the kidneys, since, after the exhibition of large doses, benzoic and not hippuric acid can be detected in the blood, while even small amounts of hippuric acid injected into the blood produce violent poisoning. Moreover, Bunge and Schmiedeberg have succeeded in converting benzoic acid into hippuric acid by passing blood containing benzoic acid slowly through the kidneys immediately after their removal from the body. In rare cases, according to Meissner and Shepard, the benzoic acid is converted into succinic instead of hippuric acid. When it is given very freely a portion of the benzoic acid escapes unchanged. Where the nitrogen necessary for the conversion of the benzoic into hippuric acid comes from, is at present unknown. *A priori* it would seem probable that the source of this nitrogen was the urea, but the testimony as to the effect of benzoic acid upon the urea and uric acid excretion is contradictory. The most recent investigations indicate that benzoic acid has practically no effect on the elimination of either urea or uric acid, although Denis (*J. P. Ex. T.*, 1915, vii, 601) finds that in large doses the output of uric acid is increased.

The only advantageous uses of benzoic acid as a remedy are connected with its antibacterial properties. As small quantities as one part in a thousand have a distinctly inhibiting action on the growth of many micro-organisms, and in somewhat stronger solution it is actively germicidal. It is a popular ingredient in many of the supposedly antiseptic mouth washes. It has also been used internally as a urinary antiseptic but because of its irritant action upon the stomach is much better administered for such purpose in the form of one of its salts. For a discussion of the use of benzoic acid as a food preservative, see *Sodii Benzoas.*

Dose, ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Tinctura Opii Ammoniata, *Br.;* Tinctura Opii Camphorata, *U. S.* (*Br.*); Trochiscus Acidi Benzoici, *Br.;* Nebula Aromatica, *N. F.*

ACIDUM BORICUM. U. S., Br.

BORIC ACID Acid. Bor. [Boracic Acid]

"Boric Acid, when dried to constant weight over sulphuric acid, contains not less than 99.5 per cent. of H_3BO_3." *U. S.* "Boric Acid may be obtained by the interaction of sulphuric acid and borax, and contains not less than 99.5 per cent. of orthoboric acid, H_3BO_3." *Br.*

Hydrogen Borate; Acidum Boracicum; Acidum Orthoboricum; Boracic Acid, Acide Borique Cristallisé, *Fr. Cod.;* Acidum Boricum Cristallisatum, *P. G.;* Borsäure, *G.;* Acido borico, *It., Sp.*

Boric acid occurs in small amount, most probably in combination as a magnesium salt, in sea water and in certain mineral waters, as the hot springs of Wiesbaden, Aix-la-Chapelle, and Vichy; in certain mineral substances, such as the *borocalcite* which occurs in considerable quantities in the niter beds of Chile; in the natural borax or *tincal,* first found in the basins of dried-up lagoons in Central Asia, and afterwards in large amount in Clear Lake, California; in *ulexite* (sodium and calcium borate) and *colemanite* (calcium borate). The last of these minerals yields by far the largest amount of the boric acid now obtained on the Pacific coast. It is found in a large vein deposit in San Bernardino County, California, where it is mined and shipped to the works of the Borax Consolidated Co. (Limited), at Alameda, California. (See *Sodii Boras.*)

Boric acid itself is extracted, under the name of *sassolin,* from the lagoons of the volcanic districts of Tuscany, and from the crater of Vulcano, one of the Lipari Islands. In the neighborhood of Monte Rotondo, Lago, Zolforeo, Sasso, and Larderello are found numerous hillocks and fissures, the latter of which emit hot aqueous vapor containing boric acid and certain gases. Around one or several of these fissures, called *suffioni,* a circular basin of masonry is built, which is filled with water and called a lagoon. By the jets of vapor constantly breaking through it, the water becomes gradually impregnated with boric acid and heated. A series of such lagoons are made to communicate with each other on the declivity of a hill, and the lowest to discharge itself into a reservoir, where the solution is allowed to rest and deposit mechanical impurities. It is still very dilute, containing only about 2 per cent. of boric acid. From this reservoir the solution is made to pass into leaden evaporating pans, heated by the natural vapor, where it is sufficiently concentrated to fit it for being conducted into wooden tubs, where it is allowed to cool and crystallize. The crude acid thus obtained contains from 74 to 84 per cent. of boric acid, the impurities consisting chiefly of alum, the double ammonium and magnesium sulphate, and calcium sulphate.

Considerable amounts of a calcium borate known as *pandermite* are produced in Turkey, but the chief foreign producer at present is Cnile.

The native borax minerals of California supply, at present, the entire American demand for boric acid. Boric acid is obtained from borax by acidulating a hot saturated solution of borax with hydrochloric or sulphuric acid. Upon cooling the mixture, crystals of boric acid separate from the more soluble sodium chloride or sulphate. The crystals thus obtained may be purified by recrystallization from water and if a small amount of albuminous matter be added before crystallizing, large, light, shining crystalline scales of the acid may be obtained.

Description and Physical Properties.—"Transparent, colorless scales of a somewhat pearly luster, or six-sided, triclinic crystals, or a white, bulky powder, slightly unctuous to the touch. It is stable in the air. One Gm. of Boric Acid is soluble in 18 cc. of water, 18 cc. of alcohol, and in 4 cc. of glycerin, at 25° C. One Gm. is soluble in 4 cc. of boiling water and in 6 cc. of boiling alcohol. Heated to 100° C., Boric Acid loses water, forming metaboric acid (HBO_2), which slowly volatilizes at that temperature. Heated to about 160° C., Boric Acid fuses to a glassy mass of tetraboric or pyroboric acid ($H_2B_4O_7$). At about 185° C. the fused mass swells, loses all of its water, and becomes boron trioxide (B_2O_3), which fuses into a transparent non-volatile, hygroscopic mass. Boric Acid volatilizes from a boiling aqueous or alcoholic solution.

"An aqueous solution of Boric Acid (1 in 50) is slightly acid to litmus paper. Boric Acid responds to the reactions for borates.

"One Gm. of Boric Acid dissolves completely in 10 cc. of boiling alcohol (*insoluble substances*). An aqueous solution of Boric Acid meets the requirements of the test for *heavy metals.* An aqueous solution of Boric Acid meets the requirements of the test for *arsenic.*

"**Assay.**—Dry about 2.5 Gm. of Boric Acid to constant weight over sulphuric acid, weigh accurately, dissolve in 50 cc. of distilled water and 50 cc. of glycerin, and titrate with normal sodium hydroxide, phenolphthalein T.S. being used as indicator. Each cc. of normal sodium hydroxide corresponds to 0.06192 Gm. of H_3BO_3." *U. S.*

"Soluble in 25 parts of *water,* in 4 of *glycerin,* and in 30 of *alcohol* (90 per cent.), the solutions being clear. *Turmeric paper* moistened with an aqueous solution slightly acidified with *hydrochloric acid* becomes brownish-red on gently drying, and this color changes to a greenish-black on the addition of *solution of potassium hydroxide.* The alcoholic solution burns with a flame tinged with green. 1 gramme dissolved in a mixture of 25 millilitres of *water* and 20 millilitres of *glycerin* requires for neutralisation not less than 16.0 millilitres of *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. Yields no characteristic *reactions* for copper, and not more than the slightest *reactions* for iron, calcium, magnesium, chlorides, or sulphates. *Lead limit* 25 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Boric acid has a sp. gr. of 1.434, dissolves in three parts of boiling water and in volatile oils, but is insoluble in ether. On evaporation of the alcoholic solution, the boric acid volatilizes even more readily than from the aqueous solution. Glycerin, when heated, dissolves a very large quantity of boric acid. (See *Glyceritum Boroglycerini,* Part I; also *Boroglyceride,* Part II.) Its aqueous solution tastes somewhat acid, colors litmus paper a wine red, and changes turmeric paper to a reddish color, analogous to that produced by alkalies, even when hydrochloric acid is present. On moistening the paper so reddened and then dried, with ammonia water or caustic alkali solution it turns first blue and then a dirty gray color. This reaction has been taken advantage of by Chamot and Cole in the development of a micro-chemical test for boric acid and borates. Fibers of viscose silk, cellulose xanthate, are dyed with turmeric solution. These sensitized fibers are then used in testing by placing one drop of a suspected solution, acidified with diluted hydrochloric acid solution, on a glass slide, add one of the turmeric stained fibers and apply gentle heat until the liquid has evaporated. If boric acid be present the fibers will have a rose tint which is changed to a deep blue by the application of a 1 per cent. solution of an alkali. This test will show 0.000025 mgm. of boric acid in 1 drop of solution. Cassol and Gerraus (*Chem. News,* 1903, 27) use curcumin with oxalic acid for determining the presence of boric acid when used as a preservative for foods.

Bori acid is a weak acid, or may even act as a base. Thus, with sulphuric and phosphoric acids it forms compounds which may be considered as salts. Its compounds with bases, when in solution, are readily decomposed by other acids, but at red heat boric acid will other acids, but at red heat boric oxide will displace many of the stronger but more volatile acids.

Boric acid requires 18 parts of cold water to dissolve it, and this fact has led to many attempts to increase its solubility without interfering with its usefulness. The use of glycerin has been officially sanctioned. Scholz and Mansier recommended the use of magnesium carbonate (11 per cent.), but such an addition is not always permissible. When equal parts of boric acid and borax are dissolved in boiling water a crystalline mass separates on cooling, which has been termed *boro-borax.* Its advantages are increased solubility and neutral reaction. Thus 12 parts of borax and 13 parts of boric acid will dissolve in 75 parts of water, making a solution containing the equivalent of 19 per cent. of boric acid. The tendency of the crystals of boric acid to slip from under the pestle renders the process of pulverization very tedious. It is essential that the acid be in an impalpable powder when it is desired to make an ointment. The gradual addition of ether to the acid has been suggested as a valuable aid to trituration. Manufacturers at the present time supply boric acid made by precipitation in an impalpable powder. The remarkable volatility of boric acid when in alcoholic solution has been observed by Schneider and the fact utilized in its quantitative determination. (*Zeit. Oest. Apoth. Ver.*, 1896, 791.)

Methyl alcohol gives better results than ethyl alcohol in the flame test for boric acid.

"**Assay.**—Dissolve about 2.5 Gm. of Boric Acid,

B. H. St. John noted an unsatisfactory end point in this titration and suggests the use of methyl red as an indicator with some slight change in manipulation details. (*A. J. P.*, 1917, p. 8.)

Uses.—Boric acid in single dose is about as near physiologically inert as a substance can be, indeed, the assertion has been made on reputable authority that, in the frog, at least, it is less poisonous than sodium chloride. In very large doses, however, it has some depressant action upon the spinal centers. When taken by the mouth it is absorbed, somewhat slowly but completely, and eliminated unchanged through the kidney. According to Rost (*A. I. P. T.*, xv, p. 291) it may be detected in the urine for some days after a single dose and when taken repeatedly tends to accumulate in the system.

Although it has been abundantly shown that boric acid has no germicidal effect, in concentrated solutions it is distinctly antiseptic. Because of freedom from toxic properties or local irritant influence its solution is widely used as a detergent wash in inflammations of mucous membranes, such as *rhinitis, conjunctivitis,* and *stomatitis.* It is also useful as an internal antiseptic in *fermentative cystitis.* It differs from most urinary antiseptics in that it is almost as efficacious in alkaline as in acid urine and has the further advantage that it tends to restore the acidity. Although its antibacterial properties are too feeble to make boric acid generally useful as a surgical disinfectant it appears to have considerable value as a local application, either in the form of the ointment or solution, in local infections. Ochsner (*Trans. Southern Surg. and Gynecol. Ass.*, 1916) believes that while it does not inhibit the growth of pathogenic bacteria it greatly reduces their virulence, and affirms that dressings of saturated solution of boric acid are almost specific in infections by *streptococcus* or *staphylococcus albus* or *pneumococcus.* So potent is its antagonism against the latter micro-organism that he has found it of value (*Illinois Med. Jour.*, June, 1917) as an internal remedy in various pneumococcus infections. He asserts that after the local application of wet dressings of saturated solution of boric acid there is considerable absorption of the drug, boric acid appearing within the urine within an hour. Internally it has from time to time been recommended in the treatment of *epilepsy* but is probably without value.

Boric acid and the borates have been used to a considerable extent as food preservatives and there has waged an acrimonious dispute as to their harmfulness when used for this purpose. Although as mentioned above their toxicity is very low, yet there have been reported a few cases in which death was apparently induced from washing out internal cavities with solutions of boric acid. These instances, however, are so rare and the dose of boron ingested probably so large as to have little bearing on the harmfulness of the boric acid food preservatives. A considerable number of cases of skin eruptions have been reported from the continued use of the boron derivatives over long periods of time. It must be acknowledged, however, that even in these cases the quantity ingested has been larger than would be at all probable from the use of any food containing it. The question of whether or not its use in smaller quantities over long periods of time is injurious can scarcely be considered as definitely settled, but in the elaborate investigation of the U. S. Department of Agriculture under H. A. Wiley, it was found that quantities of less than 0.5 Gm. daily, if continued over long periods of time, caused disturbances of digestion and assimilation (see also Lindet, *P. J.*, 1920, civ, 46). The question, however, is not merely whether it is theoretically possible for boric acid used in the preservation of food to have an injurious action upon the system, but whether the danger from this preservative is any greater than from other agents which are used for the same purpose. Certainly if it is possible to obtain undecomposed food free from preservatives they are preferable, but we do not believe that boric acid is any more injurious to the system than, for instance, is saltpeter.

For the detection of boric acid in food products, see *Chem. News,* 1903, 27; *A. Pharm.*, 1904, 194; *J. Am. C. S.*, 1904, 91.

The only important incompatibility of boric acid is the fact that in combination with salicylic acid it sometimes acts as an alkaloidal precipitant. A solution containing two and one-half grains of boric acid and one-fourth grain of salicylic acid to the fluidounce will precipitate quinine, strychnine, and other alkaloids.

Dose, of boric acid, five to twenty grains (0.3–1.2 Gm.).

Off. Prep.—Glyceritum Boroglycerini, *U. S.* (*Br.*); Liquor Antisepticus, *N. F.;* Unguentum Acidi Borici, *U. S., Br.;* Cataplasma Kaolini, *N. F.;* Liquor Antisepticus, *N. F.;* Pulvis Talci Compositus, *N. F.*

ACIDUM BROMAURICUM. N. F.

BROMAURIC ACID Acid. Bromaur.

"It contains $HAuBr_4.5H_2O$ (607.97) corresponding to not less than 32 per cent. of gold, Au." *N. F.*

This is a compound of gold and bromine corresponding to chlorauric acid $HAuCl_4$. It may be considered as a combination of gold bromide and hydrobromic acid, $AuBr_3 + HBr$, crystallizing with 5 molecules of water of crystallization.

Bromauric acid is prepared by the action of *bromine* on metallic gold. *Auric bromide* is first produced, which is dissolved in hydrobromic acid and upon concentration the compound $HAuBr_4.5H_2O$ crystallizes out.

Description and Physical Properties.—"Bromauric Acid occurs as dark red-brown, flat, needle-shaped crystals, or as irregular, coarse, granular masses; odorless, and having a metallic and acid taste. Permanent in the air when pure; when chloride is present the salt is deliquescent. Bromauric Acid melts at about 27° C. It is very soluble in water and in alcohol. Its aqueous solution is strongly acid to litmus, and yields with silver nitrate T.S. a yellowish white precipitate, insoluble in nitric acid and but slightly soluble in ammonia water.

"Ignite 0.1 Gm. of Bromauric Acid, heat the resulting residue of gold with 5 cc. of nitric acid, add 15 cc. of distilled water and filter; no weighable residue remains on evaporating the filtrate and igniting. Dissolve 0.2 Gm. of Bromauric Acid in 10 cc. of distilled water, add 16 cc. of tenth-normal silver nitrate V.S. and 12 cc. of ammonium carbonate T.S., digest the mixture for ten minutes on a water-bath, then cool and filter. The filtrate, on supersaturating with nitric acid, does not become more than slightly opalescent (*chloride*). Bromauric Acid is decomposed on exposure to red heat and leaves a residue of metallic gold equivalent to not less than 32 per cent. of the weight taken.

"Preserve it in glass-stoppered, amber-colored bottles." *N. F.*

Uses.—This preparation is in the National Formulary only because it is an ingredient in the so-called *gold and arsenic bromide* (see *Liquor Auri et Arseni Bromidi,* Part III). This combination is similar to a proprietary solution that at one time enjoyed a considerable popularity as a remedy for *diabetes.* That this solution is of any greater value in this condition than other arsenicals is open to question.

Dose, of bromauric acid, one-twentieth to one-eighth of a grain (0.003–0.008 Gm.).

Off. Prep.—Liquor auri et arseni bromidum, *N. F.*

ACIDUM CITRICUM. U. S., Br.

CITRIC ACID Acid. Cit.

"Citric Acid contains not less than 99.5 per cent. of $C_3H_4(OH)(COOH)_3.H_2O$." *U. S.* "Citric Acid may be obtained from the juice of the fruit of various species of Citrus, and contains not less than 99.5 per cent. of hydrogen citrate, $H_3C_6H_5O_7,H_2O$." *Br.*

Acidum Citri, s. Limonis, s. Limonum, s. Limonorum; Acide citrique, *Fr. Cod.;* Acide du Citron, *Fr.;* Acidum citricum, *P. G.;* Citronensäure, Citronsäure, *G.;* Acido citrico, *It., Sp.*

Citric acid is the peculiar acid to which lemons and other citrus fruits owe their sourness. It is present also as one of the constituent organic acids in the juice of other fruits, such as the cranberry, the red whortleberry, the berry of the bittersweet, the red gooseberry, the currant, the strawberry, the raspberry, the tamarind, and the red elderberry (fruit of *Sambucus pubens* Michx.). The latter berry contains citric acid so abundantly that it has been proposed as a source of the acid by Thibierge, of Versailles. It is contained also largely in the fruit of *Cyphomandra Hartwegi* Sendt., a solanaceous plant, indigenous in Mexico, Peru, and other parts of South America, where it is called *tomato de la paz.* Citric acid is now known to be a normal constituent of fresh, whole cows' milk; the amount present is about 0.19 Gm. per 100 cc., and it may be estimated by a method given in *Arch. Chem. Micros.,* 1915, viii, 120. It also occurs in the shoots and leaves of grape vine, tobacco, and as a calcium salt in the beet, willow, etc. The commercial source of citric acid is lime, lemon, and bergamot juice; large quantities of *lime juice* are made in Sicily, concentrated, and exported to England and the United States. Citric acid, which was formerly imported in large quantities from Great Britain, is now made extensively in the United States, especially in California. Culls and damaged oranges and lemons afford a source for raw material that promises soon to supply the entire need of the country.

The acid is extracted from lemon or lime juice by a very simple process, for which we are indebted to Scheele; it is one requiring some careful manipulation.

On the large scale the juice is placed in a wooden vat, closed at top, and is saturated with whiting (calcium carbonate.) Carbonic acid gas is thus evolved, which passes out by an exit pipe, and may be used in the manufacture of sodium bicarbonate, while calcium citrate precipitates. The supernatant liquor, containing much extractive matter, is drawn off, and the calcium citrate is decomposed by diluted sulphuric acid, liberating the citric acid, and precipitating the lime as a sulphate. The mixture of citric acid and calcium sulphate is run off into a wooden filter-rack, lined with lead, furnished with a perforated false bottom, and lined throughout with stout twilled flannel. The solution of citric acid passes off through a pipe leading from the bottom of the back to suitable reservoirs.

The sulphate is washed until it becomes tasteless, and the washings are run off into the same reservoirs. The filtered acid solution is then concentrated by evaporation in wooden vessels lined with lead, through which steam is made to pass by means of coiled lead pipes. As citric acid is liable to decomposition if subjected to a very high temperature, the use of the vacuum pan is highly advantageous in concentrating the solution. When the liquor is sufficiently concentrated, it is transferred to cylindrical sheet-lead vessels, placed in a warm situation, to crystallize. The crystals at first obtained are colored. In order to purify them, they are redissolved in a small quantity of water, with the assistance of heat, and the solution is digested with purified animal charcoal, filtered, evaporated, and the crystals, after having been washed and drained, are dried on wooden trays lined with sheet-lead, in a room heated by steam. It is desirable to have a slight excess of sulphuric acid, as this rather favors than otherwise the crystallization of the citric acid. It is found necessary, also, to add occasionally a small proportion of sulphuric acid to the citric acid liquor, during the progress of its concentration. From 8000 lemons are obtained 600 liters of juice containing from 4.5 to 6 per cent. of citric acid. The more recent the juice the better the quality. That which is stale will sometimes be quite sour, without containing any citric acid, in consequence of having undergone the acetous fermentation.

Processes for producing citric acid by fermentation of carbohydrates have been patented in Germany. The earlier of these (1893) involved species of citromyces (*Citromyces pfefferienus* and *C. glaber*). Later (1897) it was discovered that the same result may be obtained by means of *Mucor pyroformis*. The latter fungus is found on decomposing fruit, especially on pears and apples; its spore carriers grow only in a moist atmosphere and form long white filaments, terminated by brownish-black heads. It can be readily obtained in pure culture by sowing the spores in a suitable medium, such as sugar solutions, beer wort, steamed rice, starch paste, etc., the ordinary room temperature being favorable for its growth. The solution becomes acid from the formation of citric acid. (*J. Soc. Chem. Ind.*, June 30, 1897; see also *P. J.*, 1894, 893; 1902, 551; *A. J. P.*, 1916, p. 337.)

Ohley (*Ph. Era*, 1901, 706) has devised a process which consists in diluting fresh concentrated lemon juice with twice its volume of water, filtering after standing over night to remove albumen, then adding a calculated quantity of calcium chloride, followed by solution of sodium hydroxide, gradually added, until the solution is exactly neutral, when, upon stirring, a magma of calcium citrate is quickly deposited. From this the sodium chloride formed is readily removed by hot water, and the calcium citrate is then decomposed by the calculated quantity of sulphuric acid. The main advantages of this process are: convenience, a yield approximating to theoretical figures, and decidedly superior purity of product. In the manufacture of citric acid, the quantity of alkaline salt added to the juice must be sufficient to combine with all of the citric acid, and the amount of sulphuric acid added should thoroughly decompose the calcium citrate and not be in excess, to avoid contaminating the crystals with sulphuric acid.

Synthetic citric acid may be prepared by the action of hydrocyanic acid upon acetone-dicarboxylic acid and subsequent hydrolysis of the product, but the process is not economical.

Description and Physical Properties.—" Colorless, translucent crystals, or a white powder. It is odorless, has an acid taste, and is efflorescent in warm air. One Gm. of Citric Acid is soluble in 0.5 cc. of water, 1.8 cc. of alcohol, and in about 30 cc. of ether, at 25° C. One Gm. is soluble in 0.5 cc. of boiling water.

" An aqueous solution of Citric Acid is acid to litmus paper and responds to the reactions for citrates. When slowly ignited, Citric Acid is gradually decomposed without emitting an odor resembling that of burning sugar (*difference from tartaric acid*).

" Ash: not more than 0.05 per cent. Neutralize 10 cc. of an aqueous solution of the Acid (1 in 10) with ammonia T.S., add 5 drops of diluted hydrochloric acid, cool, and add 2 cc. of calcium chloride T.S.: no turbidity is produced (*oxalic acid*). The addition of 1 cc. of barium chloride T.S. to 10 cc. of an aqueous solution of the Acid (1 in 100), to which 3 drops of hydrochloric acid have previously been added, causes no turbidity (*sulphate*). Mix 1 Gm. of powdered Citric Acid with 10 cc. of sulphuric acid in a test tube previously rinsed with sulphuric acid, and maintain the temperature of the mixture at 90° C. for one hour: no color darker than yellow develops (*tartaric acid*). Ten cc. of an aqueous solution of the Acid (1 in 50) mixed with 0.5 cc. of hydrochloric acid meets the requirements of the test for *heavy metals*, page 439. Dissolve 10 Gm. of Citric Acid in 20 cc. of distilled water, add 2 cc. of sulphurous acid T.S., and boil the mixture until the odor of sulphur dioxide is barely perceptible. Cool the solution, mix it with 1 cc. of sodium cyanide T.S., and follow this immediately with stronger ammonia water until the solution possesses a slight odor of ammonia. Cool, transfer the solution to a 50 cc. graduated cylinder, dilute with sufficient distilled water to measure 50 cc., and add 3 drops of sodium sulphide T.S. After mixing well, the color produced in the solution, if any, when viewed downward against a white surface, is not darker than the color of a control solution prepared as follows: dissolve 2 Gm. of reagent ammonium chloride in 20 cc. of distilled water, add 4 cc. of a solution containing 0.08 Gm. of lead nitrate in 1000 cc. of distilled water, and 1 cc. of diluted hydrochloric acid. Treat this solution with the same quantity of sulphurous acid, sodium cyanide T.S., and stronger ammonia water, as directed above; transfer the mixture to another 50 cc. cylinder, dilute it with sufficient distilled water to make 50 cc., and add 3 drops of sodium sulphide T.S. Before adding the sodium sulphide T.S., the liquid must possess a distinct odor of ammonia. The two cylinders used must be matched, be of practically colorless glass, and have the same internal diameter (*lead*)." *U. S.*

"Soluble in about 0.5 part of *water*, somewhat less soluble in *alcohol* (90 per cent.), and slightly soluble in *ether*. Yields, when neutralised, the *reactions* characteristic of citrates. 1 gramme dissolved in *water* requires for neutralisation 14.2 millilitres of *N/1 solution of sodium hydroxide*. Yields no characteristic *reactions* for copper or iron, and not more than very slight *reactions* for calcium or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 1.4 parts per million. 1 gramme of powdered Citric Acid mixed with 10 millilitres of *sulphuric acid* in a test-tube previously rinsed with *sulphuric acid* acquires not more than a pale yellow color when kept at a temperature of 90° C. for one hour (absence of tartaric acid). Ash not more than 0.05 per cent." *Br.*

Assay.—"Proceed as directed under the assay for acids, using about 3 Gm. of Citric Acid and phenolphthalein T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.07004 Gm. of $C_3H_4(OH)(COOH)_3.H_2O$." *U. S.*

It is nearly insoluble in chloroform, benzene and petroleum benzin. A weak solution of it has an agreeable taste, but cannot be kept, as it undergoes spontaneous decomposition.

Sometimes crystals of tartaric acid are substituted for or mixed with the citric, or the two acids may be mixed in powder, a fraud which is detected by adding a solution of potassium acetate to that of the suspected acids, when, if tartaric acid be present, a crystalline precipitate of potassium bitartrate will be formed.

Another method of detecting tartaric acid is to digest the suspected acid with ferric hydroxide in a test tube, afterwards to raise the heat slowly to the boiling point, and, having allowed the excess of hydroxide to subside, to decant the clear liquid, and evaporate it to a syrupy consistence. If the acid be pure, the liquid remains limpid, and of a fine red color; if contaminated with tartaric acid, even to the extent of only one per cent., it becomes cloudy, and deposits tartrate. Another test is potassium permanganate, of which an alkaline solution is without action on citric acid, while under the influence of tartaric acid the manganese peroxide is deposited. Still another method takes advantage of the fact that when citric acid is oxidized with potassium permanganate in an acetic acid solution acetone is formed which can readily be detected qualitatively or estimated quantitatively. Tartaric acid does not undergo this decomposition but malic acid does and must be separated from the citric acid by taking advantage of the differences in the barium salts. The tartaric acid also may be removed by converting in the usual way into the comparatively insoluble acid potassium tartrate (*Pharm. Weekblad.*, 1917, p. 686.)

Lead is often found in the metallic state in citric acid in small quantity, and this arises from small portions being detached in breaking off the crystals from the crystallizing vats. The presence of lead or copper may be detected as above, or by igniting in a porcelain crucible a small quantity of the acid, dissolving the ash in a few drops of nitric acid, diluting largely, and passing hydrogen sulphide through it, a black precipitate indicating the impurity. A most delicate test for lead is that of the U. S. P. given above. Some interesting observations in relation to the presence of lead in citric acid and citrates are recorded by Haussmann in *A. J. P.*, 1894, 173.

The formula of the anhydrous acid is $C_6H_5O_7H_3$. It is a tribasic acid, and may therefore yield three classes of citrates according as one, two, or three atoms of hydrogen are replaced by metal, the first two classes being acid citrates, and the third class neutral citrates. When crystallized from its solution by cooling, it contains one molecule of water. Crystals of the formula $(C_6H_8O_7)_2 + H_2O$ have also been formed. (Flückiger, *Pharm. Chem.*, 1879, p. 157.) Witter (*Ph. Centralh.*, 1892, 1003) has obtained anhydrous citric acid, in crystals melting at 153° C., by heating aqueous solutions of the hydrated acid to 130° C. If citric acid be further heated after all its water of crystallization has been driven off, there will be produced *aconitic acid* ($H_3C_6H_3O_6$), which is found naturally in aconite, larkspur, black hellebore, equisetum, yarrow, and other plants. For method of preparation of aconitic acid see *U. S. D.*, 20th ed., p. 28.

Uses.—Except for its local irritant action citric acid is almost without effect upon the system. In any ordinary quantity it is entirely oxidized in the body and eliminated through the lungs as carbonic acid. For this reason the citrates of sodium and potassium, although neutral salts in themselves, tend to alkalize the system, appearing in the urine as carbonates. This change probably occurs in nearly all the tissues of the body so that after the ingestion of a citrate, carbonates can be found in the blood. According to Bence Jones, however, when sufficiently large quantities are given some of the citric acid appears in the urine unchanged.

Citric acid, is mildly astringent and is popularly used to a large extent in various inflamed conditions of the skin, such as *sunburn.* It is, however, inferior in this regard to acetic acid. Although it has been suggested as a substitute for lemon juice in *scurvy,* it is entirely without value as it contains no vitamine.

A substitute for lemonade may be made by dissolving from two to four parts of the acid, mixed with sugar and a little oil of lemon, in nine hundred parts of water; or twenty grains of the acid may be dissolved in a pint of water, and sweetened with sugar which has been rubbed on fresh lemon-peel. Citric acid is used as one of the ingredients in the effervescent salts on account of the presence of the water of crystallization which is an essential factor in the process. In the experiments of Strong, one-half to one per cent. of citric acid was found to be so poisonous to the cholera germ as to make impure water to which it was added probably a safe drink. It was further found that a large Philippine lemon, containing 40 cc. of juice, was the equivalent of 2.74 grammes of citric acid. (*Report Government Laboratories, Philippine Islands,* Sept. 1, 1903.)

Citric acid is incompatible with alkali hydroxides and carbonates, converting them into citrates, in the latter case with effervescence; with calcium and strontium salts citric acid and its compounds produce white precipitates of the insoluble citrates of these respective elements.

It possesses the valuable property of lessening or entirely preventing the coloration incompatibility of iron salts with tannin.

Dose, of the acid, from five to thirty grains (0.32–2.0 Gm.).

Off. Prep.—Syrupus Acidi Citrici, *U. S.;* Syrupus Aurantii, *U. S.*

ACIDUM FORMICUM. N. F.

FORMIC ACID Acid Formic.

“An aqueous solution containing not less than 24 per cent. of and not more than 26 per cent. of HCOOH (46.02).” *N. F.*

Aminic Acid; Hydrogen Carboxylic Acid; Ameisensaure, *G.;* Acide Formique, *Fr.*

This acid, although deriving its name from having first been obtained from the ant (*Formica rufa*), is remarkable for the number of sources of its production. It can be made from some species of caterpillars, from the blood or urine, of human beings; it is found in the products of decomposition of a number of vegetable substances, in common oil of turpentine, as a decomposition product of tartaric acid contained in various fruits and in the juice of the stinging nettle. It may be produced artifically in many ways: by the oxidation of methyl alcohol, the saponification of chloroform, and the hydrolysis of hydrocyanic acid; the following process yields good results: 50 Gm. of glycerine and 50 Gm. of crystallized oxalic acid are placed in a suitable retort attached to a condenser and the mixture carefully heated until the temperature rises to 105° C., it is then allowed to cool to about 50° C. and 50 Gm. more of oxalic acid are added and the mixture heated very slowly to 115° C. The condensed liquid may be drawn off and another addition of oxalic acid made and the distillation continued almost indefinitely. When oxalic acid and glycerin are distilled together, chemical reaction occurs, glyceryl formate being produced; this is saponified by the water which is separated, formic acid distils over and glycerin is reproduced.

The pure formic acid occurs as a colorless liquid with a pungent odor, a boiling point of about 100.8° C., is soluble in all proportions in water, alcohol, ether or glycerin. Its specific gravity is about 1.22.

The 25 per cent. solution of formic acid which is official in the National Formulary is described as follows:

Description and Physical Properties.—“Formic Acid is a clear colorless liquid, having a strongly acid reaction and a characteristic pungent odor. Specific gravity about 1.058 at 25° C. It is miscible with water or alcohol. A white precipitate of mercurous chloride is formed on warming formic acid with mercuric chloride T.S.

“When Formic Acid is diluted with five times its volume of distilled water, separate portions yield no precipitate or turbidity on the addition of silver nitrate T.S. after adding nitric acid (*chloride*); or of barium chloride T.S. (*sulphate*); or of calcium chloride T.S. after supersaturating with ammonia water. Formic acid is volatilized on heating and evaporating 20 cc. to dryness on a water bath, not more than 0.002 Gm. of a residue remains (*oxalic acid*). Formic Acid when supersaturated with solution of sodium hydroxide develops no pungent or empyreumatic odor (*acrolein, allyl formate*). Heat 1 cc. of Formic Acid on a water bath with 1.5 Gm. of yellow mercuric oxide and 10 cc. of distilled water for ten minutes shaking frequently and filter the liquid; the filtrate does not show an acid reaction (*acetic acid*). Add 1 drop of tenth-normal Iodine to 10 cc. of Formic Acid; the iodine color is not destroyed (*sulphurous acid*). Formic Acid does not respond to the test for heavy metals.

“**Assay.**—Pour about 5 cc. of Formic Acid into a weighing bottle, stopper, weigh accurately, dilute with about 50 cc. of distilled water and titrate with normal potassium hydroxide using phenolphthalein T.S. as indicator. Each cc. of normal potassium hydroxide corresponds to 0.04602 Gm. of HCOOH.” *N. F.*

An aqueous solution of formic acid, usually the crude or unrefined product containing from 15 to 20 per cent. of the acid, is used in the textile industries under the name of *scroop liquid.* Certain fabrics, when rinsed in this solution, acquire the crisp, punging sound characteristic of silk when squeezed or twisted, which is known in the industries as scroop.

Uses.—Pure formic acid is an active caustic. In diluted condition it is locally irritant and astringent. It is used to a considerable extent on the European continent as a counter-irritant in strengths of from 5 to 10 per cent. Formic acid has also been recommended for its astringent effect, especially for the purpose of lessening excessive *sweating of the feet.* It has been used in the same manner as smelling salts in the treatment of *fainting spells,* its effects in this condition being due to local irritant effect of the vapors on the nasal mucosa.

An old folk lore that bee sting was beneficial in *rheumatism* has led to the use of formic acid and its salts in the treatment of this condition but there is no sufficient evidence of their value. Fleig (*A. G. M.,* 1905) could obtain no physiological basis for the use of the formates except as stimulants to the gastric mucous membrane and to the kidney. It has been employed as a diuretic either alone or in combination with theobromine. It has been employed by Stern and others (*J. A. M. A.,* 1906) internally for the treatment of inoperable *cancers, diphtheria* and *tuberculosis.* Berret (*K. T. W.,* 1906) reports good results from sodium formate in the treatment of muscular *tremors* such as *paralysis agitans* and senile or toxic tremors.

The *dose* of the N. F. solution of formic acid is from two to five minims (0.12 to 0.3 cc.).

Off. Prep.—Spiritus acidi formici. *N. F.*

ACIDUM HYDRIODICUM DILUTUM
U. S., Br.

DILUTED HYDRIODIC ACID Acid. Hydriod. Dil.

"Diluted Hydriodic Acid is an aqueous solution containing not less than 9.5 per cent. and not more than 10.5 per cent. of HI." *U. S.*

"Diluted hydriodic Acid is an aqueous liquid containing, when freshly prepared, 10 per cent. by weight of hydrogen iodide, HI, and 1 per cent. by weight of hydrogen hypophosphite, HPH_2O_2. It may be obtained by the action of hydrogen sulphide on a solution of iodine, with the subsequent addition of hydrogen hypophosphite." *Br.*

Acide hydroidique dilué, *Fr.;* Verdünnte Jodwasserstoffsäure, *G.*

Hydriodic acid was discovered by Clement and Desormes in 1813. The strong aqueous solutions, from 49° to 60° Baumé, are used in organic chemistry as reducing agents. The stronger acids are prepared by the reaction of phosphorus and iodine to produce phosphoric and hydriodic acids, the latter being separated from the former by distillation.

The weaker solution (ten per cent.) only is used in pharmacy and medicine. Several methods for making this have been suggested. The old process consisted in passing hydrogen sulphide into a bottle containing iodine and water until the iodine disappeared and the liquid was colorless, it was then filtered to separate the precipitated sulphur and the filtrate heated to drive off the excess of hydrogen sulphide. H. Kolbe (*J. Pr. Chem.,* 1879, 172, and *A. J. P.,* June, 1877) adds phosphorus to iodine in a retort filled with carbon dioxide. Heat is applied, and water added; on application of moderate heat, hydriodic acid gas free from iodine is produced. C. Winckler (*A. J. P.,* May, 1880) dissolves iodine in carbon disulphide, adds sufficient water to form a layer on top of the solution of iodine, and passes a stream of hydrogen sulphide through the mixture; when this has acquired a yellow color, the layers are separated, the aqueous hydriodic acid is boiled a few minutes to expel hydrogen sulphide, and it is then supposed to be chemically pure.

Neither the U. S. nor the Br. at present give any formula for the preparation of this acid. That of the U. S. IX was as follows: "Potassium Iodide, *one hundred and thirty-five grammes;* Potassium Hypophosphite, *ten grammes;* Tartaric Acid, *one hundred and thirty-six and five-tenths grammes;* Distilled Water, Diluted Alcohol, each, *a sufficient quantity,* to make *one thousand grammes.*

"Dissolve the Potassium Salts in *two hundred and fifty mils* of Distilled Water with the aid of heat, and the Tartaric Acid in *four hundred mils* of Diluted Alcohol. Having poured the solution of Tartaric Acid into a bottle of about one thousand mils capacity, add the solution of the Potassium Salts and shake the mixture briskly. Cool the mixture to about 5° C. for several hours and, having inserted a pledget of purified cotton tightly in the throat of a funnel, transfer the contents, of the bottle to the funnel. When all the liquid has passed through, wash the bottle and crystalline precipitate with Diluted Alcohol in successive small portions until the *filtrate* weighs *one thousand grammes.* Evaporate the liquid at a moderate temperature, on a water-bath, until all of the Alcohol has evaporated, and add sufficient Distilled Water to make the product weigh *one thousand grammes.*" *U. S. IX.* The hypophosphite is added in order to provide a small quantity of hypophosphorous acid which acts as a preservative, while the diluted alcohol aids in the precipitation of the potassium bitartrate because of the insolubility of the latter in alcohol. The cooling of the mixture is also used to assist in the separation of the potassium bitartrate.

$$KI + 2H_2C_4H_4O_6 + KPH_2O_2 = HI + 2KHC_4H_4O_6 + HPH_2O_2$$

Description and Physical Properties.—"A colorless or not more than pale yellow, odorless liquid. Specific gravity: about 1.100 at 25° C.

"It is strongly acid to litmus paper. Diluted Hydriodic Acid responds to the reactions for iodides.

"A 5 cc. portion of Diluted Hydriodic Acid, when evaporated to dryness on a water bath and ignited at dull red heat (about 750° C.), leaves not more than 0.165 Gm. of residue. No blue color is produced on adding a few drops of starch T.S. to 5 cc. of the Acid (*free iodine*). The addition of 1 cc. of potassium sulphate T.S. to 10 cc. of the Acid causes no turbidity (*barium*). Mix 0.5 cc. of Diluted Hydriodic Acid with 10 cc. of distilled water, add 8 cc. of silver nitrate T.S. and 6 cc. of ammonium carbonate T.S., digest the mixture for ten minutes on a water bath, cool, and filter: the filtrate upon supersaturation with nitric acid shows no more *chloride* than corresponds to 0.5 cc. of fiftieth-normal hydrochloric acid. A 10 cc. portion of Diluted Hydriodic Acid shows no more *sulphate* than corresponds to 1.0 cc. of fiftieth-normal sulphuric acid. A 10 cc. portion of Diluted Hydriodic Acid without further acidulation meets the requirements of the test for *heavy metals*. Mix 5 cc. of Diluted Hydriodic Acid with 1 cc. of nitric acid, and evaporate the liquid to dryness on a water bath: the residue meets the requirements of the test for *arsenic*.

"Preserve in amber-colored, glass-stoppered bottles, protected from light. Do not dispense if it contains free iodine.

"**Assay.**—Pour about 5 cc. of Diluted Hydriodic Acid into a tared flask, weigh accurately, dilute with 20 cc. of distilled water, add 50 cc. of tenth-normal silver nitrate, and shake the mixture well. Then add 5 cc. of nitric acid, heat the mixture on a water bath until the precipitate has a bright yellow color, cool, add 2 cc. of ferric ammonium sulphate T.S., and determine the residual silver nitrate by titration with tenth-normal potassium thiocyanate. Each cc. of tenth-normal silver nitrate corresponds to 0.01279 Gm. of HI." *U. S.*

"A clear, colorless liquid. Yields, when neutralized, the *reactions* characteristic of iodides. Yields no characteristic *reactions* for barium, calcium, potassium, sulphates, or sulphides. When to 5 grammes of the Acid, diluted with a little *water,* 45 millilitres of *N/10 solution of silver nitrate,* 5 millilitres of nitric acid, and 0.5 millilitre of *solution of ferric sulphate* are added, not less than 5 or more than 7 millilitres of *N/10 solution of ammonium thiocyanate* are required to produce a permanent pink coloration. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Diluted hydriodic acid is incompatible with oxidizing agents in general, such as chlorates, nitrates, permanganates, hydrogen dioxide, etc., which liberate iodine. It is also incompatible with salts of mercury, bismuth, and cupric and ferric salts.

Uses.—Diluted hydriodic acid was introduced into use as a medicine by Andrew Buchanan, of Glasgow. There can be little doubt that hydriodic acid is capable of producing the alterative effects of iodine, and it may be given in all cases to which that medicine is applicable. When the solution becomes discolored it may be irritant through the liberated iodine, and should not be dispensed. It need not be thrown away, however, as exposure to strong sunlight for several days will usually effect a reduction of the iodine and the restoration of its original colorless condition.

Dose, ten minims (0.6 cc.) three times a day, well diluted.

Off. Prep.—Syrupus Acidi Hydriodici, *U. S.; Br.*

ACIDUM HYDROBROMICUM DILUTUM. Br.

DILUTED HYDROBROMIC ACID

"Diluted Hydrobromic Acid is an aqueous liquid containing 10 per cent. by weight of hydrogen bromide, HBr. It may be obtained by the interaction of bromine and sulphurous acid, and subsequent distillation." *Br.*

Acidum Bromhydricum Dilutum, Acidum Bromohydricum Solutum, *Fr. Cod.;* Acide Bromhydrique dissous, Acide hydrobromique dilué, *Fr.;* Acidum hydrobromicum, *P. G.;* Verdünnte Hydrobromsäure, Bromwasserstoffsäure, *G.*

Hydrobromic acid was discovered by Balard in 1830. The strong acid (48 to 50 per cent.) is used in organic chemistry both in manufacturing and for analytical purposes.

The weaker acid (10 per cent.) only is used in pharmacy and medicine. It was official in the U. S. IX, but was dismissed at the last revision.

Dr. E. R. Squibb published a process (*A. J. P.*, 1878, 116) for making this acid which was based on the decomposition of potassium bromide with sulphuric acid. (See *U. S. D.*, 19th ed., p. 32.) A more convenient process is that of Dewitt C. Wade (*Peninsular Medical Journal,* Feb., 1875), modelled after Buchanan's method of making hydriodic acid, which directs that 120 grains of potassium bromide be dissolved in one fluidounce of water, and 153 grains of tartaric acid be added to the solution; acid potassium tartrate is produced, the greater part of which crystallizes out on standing twelve hours at a low temperature, and a solution of hydrobromic acid is formed, sp. gr. 1.228, containing about 80 grains pure hydrobromic acid to the fluidounce, equivalent to nearly 15 per cent. Fothergill's method although based upon Wade's formula, yields a weaker acid. Diluted hydrobromic acid made in this way is open to the objection of containing cream of tartar, and probably some undecomposed potassium bromide in solution, and thus is not strictly pure. To lessen this, Charles Rice proposed the addition of a double quantity of alcohol to facilitate the precipitation, recovering the alcohol by distillation subsequently. (*N. R.*, 1877, p. 107.) Other processes have been suggested for the preparation of hydrobromic acid.

Edward Goebel (*N. R.*, Sept., 1880) proposed a method based on Glover's process, which is to decompose 148 grains of barium bromide dissolved in half an ounce of water, with 50.6 grains of sulphuric acid, diluted with two drachms of distilled water; the precipitated barium sulphate is washed with distilled water until the filtrate weighs 810 grains to make the 10 per cent. acid solution. Markoe (*Proc. A. Ph. A.*, 1875, p. 686) recommends an economical process, based upon the reaction which takes place between phosphorus and bromine producing hydrobromic and phosphoric acids, the former being subsequently separated by distillation. A convenient method for obtaining a small amount of hydrobromic acid gas or solution was described by L. H. Friedburg, in a communication before the New York Section of the American Chemical Society (May, 1905). Bromine is allowed to trickle into paraffin which is kept in a melted condition by placing the flask containing it in a shallow steam bath. A portion of the bromine reacts with the hydrocarbon to form hydrobromic acid. The vapors from this reaction are carried to a second flask containing paraffin, joined to the first flask and standing with it in the steam bath, which absorbs part of the free bromine. (See also Gassman's process, *S. W. P.*, 1893, 107.) Marshall proposed a method which depends on the easy solubility of bromine in hydrobromic acid, the conversion of the bromine into sulphur bromide by the addition of sulphur, and the ready decomposition of sulphur bromide when shaken with water.

Properties.—Hydrobromic Acid is of a pungent and irritating odor, and fuming on contact with the atmosphere when concentrated, but in its diluted state it is odorless. On adding chlorine or nitric acid to diluted hydrobromic acid, there is liberated bromine, which is soluble in chloroform or carbon disulphide, imparting to these liquids a red or yellow color. On distilling it, weak acid passes over first; when the temperature of 126° C. is reached, an acid of 48 per cent. remains, which may be distilled unchanged.

Diluted hydrobromine acid is officially described as follows:

"Yields, when neutralised, the *reactions* characteristic of bromides. Specific gravity 1.077. 10 millilitres require for neutralisation 13.3 millilitres of *N/1 solution of sodium hydroxide*. 2 millilitres require for complete precipitation 26.6 millilitres of *N/10 solution of silver nitrate*. Yields no characteristic *reactions* for barium, chlorides, phosphates, or sulphites, and only a slight *reaction* for sulphates. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million. Leaves not more than 0.01 per cent. of residue on evaporation." *Br.*

The U. S. IX gave the following additional tests:

"Silver nitrate T.S. produces a yellowish-white precipitate, which is insoluble in diluted nitric acid, slowly soluble in an excess of stronger ammonia water, but readily soluble in a 10 per cent. solution of sodium thiosulphate. Evaporate 25 cc. of Diluted Hydrobromic Acid from a platinum or porcelain dish and afterwards dry it at 110° C.; not more than 0.0025 Gm. of residue remains. The addition of 1 cc. of barium chloride T.S. to 10 cc. of the Acid produces not more than a slight cloudiness (*sulphuric acid*); the addition of 1 cc. of potassium sulphate T.S. to 10 cc. of the Acid causes no turbidity (*barium*). Shake 10 cc. of the Acid with 2 cc. of chloroform; no color is imparted to the latter (*free bromine*). Now add 5 drops of ferric chloride T.S. and shake the mixture; the chloroform does not acquire a violet tint (*iodine*). Ten cc. of Diluted Hydrobromic Acid, without further acidulation, does not respond to the Test for heavy metals (see Part III, Test No. 3). Mix 5 cc. of Diluted Hydrobromic Acid with 1 cc. of nitric acid and evaporate the liquid to dryness on a water bath; the residue meets the requirements of the Test for arsenic (see Part III, Test No. 1). Mix 0.5 cc. of Diluted Hydrobromic Acid with 10 cc. of distilled water, add 8 cc. of silver nitrate T.S., and 6 cc. of ammonium carbonate T.S., digest the mixture for ten minutes on a water bath, cool and filter. The filtrate, on supersaturating with nitric acid, does not at once become more than slightly turbid (*chloride*).

"**Assay.**—Pour about 20 mils of Diluted Hydrobromic Acid into a tared flask, weigh accurately, dilute with 30 mils of distilled water, and titrate the liquid with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 9.5 per cent. nor more than 10.5 per cent. of HBr.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.08093 Gm. of HBr. Each gramme of Diluted Hydrobromic Acid corresponds to not less than 1.17 mils nor more than 1.30 mils of normal potassium hydroxide V. S." *U. S. IX.*

Concentrated hydrobromic acid has been furnished by manufacturing chemists containing from 20 to 50 per cent. of absolute hydrobromic acid; C .T. Tyrer states that the stronger acids are prone to show discoloration in a few days after being made, but that even the highly colored acids, when diluted to the official strength, become colorless; the concentrated acid attacks glass rapidly and the silica is not thrown out on dilution; he recommends acid of the sp. gr. 1.250 as having the most suitable limit of concentration for pharmaceutical purposes. (*Y. B. P.*, 1896, 296.)

The following table by Biel will be found useful in showing from the specific gravities of solutions the percentage of absolute hydrobromic acid.

Biel's Table of Percentage and Specific Gravity of Hydrobromic Acid

Per cent. HBr.	Specific gravity at 15° C.	Per cent. HBr.	Specific gravity at 15° C.
1	1.0082	26	1.219
2	1.0155	27	1.229
3	1.0230	28	1.239
4	1.0305	29	1.249
5	1.038	30	1.260
6	1.046	31	1.270
7	1.053	32	1.281
8	1.061	33	1.292
9	1.069	34	1.303
10	1.077	35	1.314
11	1.085	36	1.326
12	1.093	37	1.338
13	1.102	38	1.350
14	1.110	39	1.362
15	1.119	40	1.375
16	1.127	41	1.388
17	1.136	42	1.401
18	1.145	43	1.415
19	1.154	44	1.429
20	1.163	45	1.444
21	1.172	46	1.459
22	1.181	47	1.474
23	1.190	48	1.490
24	1.200	49	1.496
25	1.209	50	1.513

Uses.—The action of hydrobromic acid upon the system is practically identical with that of the alkaline bromides, (see *Potassii Bromidum.*) but the acid is too irritant to the stomach to be used freely. Two fluidrachms contain about 12 grains of bromine, equivalent to 18 grains of potassium bromide, and may be given at once, well diluted with water or syrup. The addition of a trace of oil of lemon to the mixture will impart a flavor to this dose closely similar to lemonade.

Diluted Hydrobromic Acid is incompatible with many oxidizing agents, as is hydriodic acid; it is also incompatible with salts of lead, silver, mercury, and bismuth.

Dose, from one-half to two fluidrachms (1.8 to 7.5 cc.).

Off. Prep.—Elixir Calcii Bromidi. *N. F.*

ACIDUM HYDROCHLORICUM. U. S., Br.

HYDROCHLORIC ACID. Acid. Hydrochl.

"Hydrochloric Acid is an aqueous solution containing not less than 31 per cent. and not more than 33 per cent. of HCl." *U. S.* "Hydrochloric Acid is a liquid containing 31.79 per cent. by weight of hydrogen chloride, HCl, and 68.21 per cent. by weight of water. It may be obtained by dissolving in water the gas produced by the interaction of sulphuric acid and sodium chloride." *Br.*

Acidum Muriaticum, *U. S.*, 1870; Acidum Hydrochloratum, Spirit of Sea Salt, Marine Acid, Muriatic Acid, Chlorhydric Acid· Acidum Chlorhydricum, *Fr. Cod.;* Acide chlorhydrique, Acide muriatique, *Fr.;* Acidum hydrochloricum, *P. G.;* Salzäure, Chlorwasserstoffsäure, *G.;* Acido cloridrico concentrato, Acido muriatico, *It.;* Acido clorhidrico, Acido muriatico, *Sp.*

Preparation.—Hydrochloric acid was originally described by Valentine in the 15th century. He obtained it by distilling sodium chloride and ferrous sulphate together and called it *spirit of salt.* Glauber, in the 17th century prepared it by the method by which it is yet mainly obtained, *i.e.*—by the action of sulphuric acid on sodium chloride or common salt. In England it is produced in enormous quantities during the decomposition of common salt for the purpose of making sodium sulphate, from which soda ash and sodium carbonate are afterwards manufactured in immense quantities. The decomposition of the sea salt is performed in semi-cylindrical vessels, the curved part, next the fire, being made of iron, and the upper or flat surface, of stone. The acid gas is conveyed by a pipe to a double-necked stoneware receiver, half filled with water, and connected with a row of similar receivers, likewise containing water. As carried out on a larger scale, the decomposition of the salt takes place in hemispherical iron pans, 9 feet in diameter, covered by a brick-work dome; upon the mass of salt the requisite quantity of sulphuric acid is allowed to run from a leaden cistern placed above the decomposing pan. Volumes of hydrochloric acid gas are evolved, which collect in the space between the pan and the brick-work dome, whence they pass by a brick-work or earthenware flue into upright towers or condensers. These towers are filled with bricks or coke, down which a small stream of water is allowed to trickle. The gas, passing upward, meets the water and is dissolved by it, and as the acid liquor approaches the bottom, it becomes more and more nearly saturated with gas.

The development of this process and indeed of the increased use of hydrochloric acid was the outcome of legislation against the manufacturing plants for sodium sulphate, which permitted the acid vapors to escape into the air to the detriment of surrounding vegetation and property.

Next in importance is the Hargreaves and Robinson process which has recently been made successful in a mechanical way. It depends upon the following reaction between sodium chloride, sulphur dioxide, steam and atmospheric oxygen.

$$2NaCl + SO_2 + H_2O + O = Na_2SO_4 + 2HCl.$$

It is carried out as a continous process, the temperature of the reaction being from 400° to 500° C.

Under former industrial conditions chlorine was largely manufactured from hydrochloric acid. These conditions are now occasionally reversed, owing to the immense amount of chlorine which is obtained as a by-product in the manufacture of caustic soda by electrolysis. The subsequent conversion of chlorine into hydrochloric acid takes place when chlorine and steam are heated to 1000° C. in the presence of an excess of carbon, and is according to the following reaction: $Cl_2 + H_2O + C = 2HCl + CO$. (*Ch. Ztg.,* 1912, p. 54.)

An electrolytic process is now being operated at Niagara Falls by the Roberts Chemical Company, who electrolyze potassium chloride and obtain as products potassium hydroxide and hydrochloric acid. This is done by burning the chlorine direct with the hydrogen set free at the cathode. This is known as *Synthetic Hydrochloric Acid.*

The acid, when required to be pure, is generally prepared by saturating distilled water with the gas in Woulff's apparatus. A quantity of pure fused sodium chloride is introduced into a retort or flask, placed on a sand-bath. The vessel is then furnished with an S-tube, and connected with a series of bottles, each two-thirds full of water. A quantity of sulphuric acid is then gradually added, equal in weight to the common salt employed, and diluted with one-third of its weight of water. The materials ought not to occupy more than half the body of the retort. When the evolution of the gas slackens, heat is applied, and gradually increased until the water in the bottles refuses to absorb any more, or until no more gas is found to come over. As soon as the process is completed, boiling water should be added to the contents of the retort or flask, in order to facilitate the removal of the residue. During the progress of the saturation, the water in the several bottles increases in temperature, which lessens its power of absorption. It is, therefore, expedient, in order to obtain a strong acid, to keep the bottles cool by means of water or ice. The connecting tubes need not plunge deeply into the acid.

In the process for hydrochloric acid, theory calls for a little less than 90 parts of liquid sulphuric acid to 100 of common salt. A moderate excess of the former may be useful to insure the complete decomposition of the salt. The reaction for its formation is:

$$NaCl + H_2SO_4 = HCl + HNaSO_4$$

If only half the amount of sulphuric acid be used, the reaction is:

$$2NaCl + H_2SO_4 = 2HCl + Na_2SO_4$$

In the first of these reactions, as only one molecule of salt is taken, it is obvious that there is not enough sodium furnished to neutralize the sulphuric acid completely and make the normal sulphate, Na_2SO_4, so the result is the acid sulphate, $HNaSO_4$. On the other hand, in the second reaction, the two molecules of salt furnish just the sodium necessary to neutralize the one molecule of sulphuric acid and make the neutral sulphate, Na_2SO_4.

As hydrochloric acid, prepared in the ordinary mode, often contains arsenic, so as to obscure its indications when employed in testing for that poison, it is of interest to the practical toxicologist to know that it may be obtained free from that impurity by distilling sodium or potassium chloride with oxalic acid in equivalent proportions.

A method of freeing hydrochloric acid from arsenic trioxide is recommended by Engel (*J. P. C.*, 1873, p. 10) as easy and efficacious. It is founded on the fact that arsenic trioxide is reduced to arsenic by hypophosphorous acid. In another method the acid is first treated with MnO_2 and then diluted with water and allowed to stand in contact with bright copper sheets, after which it is distilled in the presence of copper. Arsenic may also be removed by taking advantage of the fact that in the presence of ferrous chloride the arsenic volatilizes easily and passes over with the first portions distilled. Traces of arsenic may also be removed by adding solution of stannous chloride, and after the precipitate of impure arsenic has settled, the clear liquid is redistilled. (Bettendorf, *Zeit. An. Chem.* [2], v, p. 492.) The best results in the removal of arsenic seem to be obtained by the process of Meister Lucius and Bruning of Hoechst (1905), in which cheap vanadous salts are employed which may be regenerated and recovered electrolytically.

Description and Physical Properties.—" A colorless, fuming liquid having a pungent odor. The fumes and odor disappear on diluting the Acid with 2 volumes of water. On distilling Hydrochloric Acid at normal barometric pressure, a stronger acid passes over first, until at 110° C. an acid of about 20 per cent. remains and this distils unchanged. Specific gravity: about 1.155 at 25° C.

" It is strongly acid to litmus paper, even when highly diluted. When Hydrochloric Acid is heated with manganese dioxide, chlorine is evolved. Hydrochloric Acid responds to the reactions for chlorides.

" Hydrochloric Acid when diluted with 2 volumes of water conforms to the following tests: Evaporate 25 cc. of the dilution and dry at 110° C.: not more than 0.003 Gm. of residue remains. Add 1 cc. of chloroform to 10 cc. of the dilution, and cautiously add, a drop at a time with constant agitation, chlorine T.S. which has been diluted with an equal volume of distilled water: the chloroform remains free from even a transient yellow, orange or violet color (*bromide or iodide*). Add 1 cc. of potassium iodide T.S. and 1 cc. of chloroform to 10 cc. of the dilution, and agitate the mixture: the chloroform remains free for at least one minute from any violet coloration (*free chlorine or bromine*). A 2 cc. portion of the dilution further diluted with 14 cc. of distilled water meets the requirements of the test for *heavy metals,* page 439. A 5 cc. portion of the dilution further diluted with 12 cc. of distilled water (without the treatment with sulphuric and sulphurous acids) meets the requirements of the test for *arsenic,* page 428. Add 5 drops of barium chloride T.S. to a mixture of 3 cc. of the dilution and 5 cc. of distilled water: neither turbidity nor precipitation appears within one hour (*sulphuric acid or sulphate*). At the end of this period, the further addition to the liquid of 2 drops of tenth-normal iodine produces neither turbidity nor decoloration of the iodine (*sulphurous acid*).

" **Assay.**—Proceed as directed under the assay for acids, page 430, using about 3 cc. of the Acid, accurately weighed, and methyl orange T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.03647 Gm. of HCl. "Preserve in glass-stoppered bottles." *U. S.*

"Yields, when neutralised, the *reactions* characteristic of chlorides. Specific gravity 1.160. 5 millilitres, diluted with *water,* require for neutralisation 50.6 millilitres of *N/1 solution of sodium hydroxide.* When diluted with *water* yields no characteristic *reactions* for bromides, iodides, sulphates, or sulphites, and only slight *reactions* for iron. Diluted with *water* and *solution of potassium iodide* added, no blue color is produced on the addition of *mucilage of starch* (absence of free chlorine). *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million. Leaves not more than 0.01 per cent. by weight of residue on evaporation." *Br.*

Exposed to the air it emits white fumes, owing to the escape of the acid gas and its union with the moisture of the atmosphere. When concentrated, it blackens organic substances, as does sulphuric acid. Its sp. gr. varies with its strength. When as highly concentrated as possible, its density is 1.21. The U. S. acid has the specific gravity of 1.155 at 25° C., which is practicaly equivalent to the figure given in the British Pharmacopœia, which is 1.160 at 15.5° C. When exposed to heat, it continues to give off hydrochloric acid gas, with the appearance of ebullition, until its sp. gr. falls to 1.094, when it properly boils, and may be distilled unchanged, or entirely volatilized.

Hydrochloric Acid of Commerce. Muriatic Acid.—So-called by Priestley, from *murum,* the old name of chlorine, which in turn was derived from the Latin *murias,* brine. It has a yellowish color owing to the presence of ferric chloride, or of a minute proportion of organic matter, such as cork, wood, etc. It usually contains traces of sulphuric acid, and sometimes free chlorine and nitrous acid. Sulphurous Acid was formerly a frequent impurity (for methods for its detection see tests under *Acidum Hydrochloricum Dilutum,* but is not at present an important adulterant. Arsenic, derived from sulphuric acid, used in its manufacture, and lead, from the vessels used, were also often present. The official tests will exclude these impurities for all purposes but in toxicological analysis. (For other tests see *U. S. D.,* 19th ed., p. 38.) A small proportion of thallium has been detected in commercial hydrochloric acid by Wm. Crookes, being derived from sulphuric acid, in the manufacture of which pyrites was employed. Selenium has been found in French hydrochloric acid, causing the acid to have a bad odor.

Properties of Hydrochloric Acid Gas.—Hydrochloric acid gas is colorless and elastic, possessing a very pungent odor, and the property of irritating the organs of respiration. It destroys life and extinguishes flame. It reddens litmus powerfully, and has the other properties of a strong acid. Its sp. gr. is 1.278 (Gay-Lussac and Biot). Subjected to a pressure of 40 atmospheres, at the temperature of 10° C., it is condensed into a transparent liquid, to which alone the name of *liquid hydrochloric acid* properly belongs. Water absorbs this gas with the greatest avidity.

Hydrochloric acid is found in nature in volcanic exhalations and in the waters of streams in volcanic regions, the water of the Vinagro River in the Andes containing 0.111 per cent. of HCl. It is a normal constituent of the gastric juice of all mammals and serves an important purpose in digestion.

Toxicological Properties.—Hydrochloric acid, when swallowed, is highly irritating and corrosive, but less so than sulphuric or nitric acid. It produces hiccough, violent efforts to vomit, and agonizing pain in the stomach. There is much thirst, with great restlessness, a dry and burning skin, and a small concentrated pulse. If the acid has been recently swallowed, white vapors of a pungent odor will be emitted from the mouth. The best antidote is magnesia, but sodium bicarbonate, chalk, soap or any sufficiently diluted alkaline solution which is immediately at hand may be used. In the course of the treatment, bland and mucilaginous drinks must be freely given. When inflammation supervenes, it must be treated on general principles.

Uses.—Stronger hydrochloric acid is rarely used in medicine. For a discussion of the therapeutic properties, incompatibilities, etc., see *Acidum Hydrochloricum Dilutum.*

Dose, five to ten minims (0.3–0.6 cc.) well diluted.

Off. Prep.—Acidum Hydrochloricum Dilutum, *U. S., Br.;* Acidum Nitrohydrochloricum, *N. F.;* Acidum Nitrohydrochloricum Dilutum, *N. F., Br.*

ACIDUM HYDROCHLORICUM DILUTUM. U. S., Br.

DILUTED HYDROCHLORIC ACID Acid. Hydrochl. Dil.

"Diluted Hydrochloric Acid is an aqueous solution containing not less than 9.5 per cent. and not more than 10.5 per cent. of HCl." *U. S.*

"Diluted Hydrochloric Acid contains 10 per cent. by weight of hydrogen chloride, HCl." *Br.*

Acidum Muriaticum Dilutum, U. S., 1870: Diluted Muriatic Acid; Acide chlorhydrique dilué, *Fr.;* Acidum hydrochloricum dilutum, *P. G.;* Verdünnte Salzsäure, *G.;* Acido cloridrico diluito, *It.*

"Hydrochloric Acid, 313 Gm.; Distilled Water, 687 Gm.; to make 1000 Gm. Mix them." *U. S.* "Hydrochloric Acid, 330 grammes; Distilled Water, sufficient to produce 1000 millilitres. Mix." *Br.*

The official description is as follows: "A colorless, odorless liquid. Specific gravity: about 1.049 at 25° C.

"Diluted Hydrochloric Acid is strongly acid to litmus paper. Diluted Hydrochloric Acid conforms to the tests for identity and purity under *Acidum Hydrochloricum.*

"**Assay.**—Proceed as directed under the assay for acids, using 10 cc. of Diluted Hydrochloric Acid, accurately weighed, and methyl orange T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.03647 Gm. of HCl.

"Preserve in glass-stoppered bottles." *U. S.*

"Yields, when neutralised, the *reactions* characteristic of chlorides. Specific gravity 1.048. 10 millilitres require for neutralisation 28.7 millilitres of *N/1 solution of sodium hydroxide.* Free from the impurities indicated under 'Acidum Hydrochloricum.'" *Br.*

Delort and Roche have proposed a colormetric method of assay for free hydrochloric acid taking advantage of the color produced when it is mixed with a solution of brilliant green.

Uses.—As is well known, hydrochloric acid is secreted by the glands of the stomach and is essential in gastric digestion for the purpose of activating pepsinogen. It probably also plays an important part in the digestive processes by determining the rapidity of the discharge of the gastric contents in the duodenum. Cannon has shown that free acid in the pyloric portion of the stomach leads to a relaxation of the pylorus and that when the duodenal contents have become acid through the discharge of the gastric contents there is a closing of this orifice. Moreover, hydrochloric acid forms with the duodenal mucous membrane a hormone known as *secretin* which stimulates the pancreas. In many cases of gastric indigestion, and probably also of intestinal indigestion, the cause of the disturbance is a diminution in the amount of hydrochloric acid secreted. The most important use of hydrochloric acid in medicine is for the purpose of replacing at least in part the lack of the natural acid in the treatment of *fermentative gastritis, nervous dyspepsia,* and similar conditions. For the same reason it is often of service to improve the digestion, and thereby the nutrition, in various *low fevers, phthisis,* and other forms of *malnutrition.* The doses which are sometimes employed are absurdly small. When we remember that the normal acidity of the stomach during gastric digestion ranges from 0.2 to 0.3 per cent. of hydrochloric acid—which would necessitate nearly two grammes of absolute hydrochloric acid for an ordinary meal—the futility of administering five to ten drops of a 10 per cent. solution of this acid is evident. Hydrochloric acid has also been highly recommended in *pernicious anemia* by Beebe and by Croftan (*J. A. M. A.,* August, 1910, p. 593), and in the treatment of *gout* by Falkenstein and others. Its value in these vases is probably due to improvement of the patient's nutrition.

Hydrochloric Acid and diluted hydrochloric acid are incompatible with lead, silver, and mercury salts; with antimony and potassium tartrate solution, a precipitate of basic chloride of antimony is produced. In bismuth and ammonium citrate, bismuth citrate is precipitated. The strong acid decomposes chlorates, nitrates, etc., with the evolution of chlorine, and other irritating gases.

Dose, ten to sixty minims (0.6–3.75 cc.) well diluted.

Off. Prep.—Acidum Hydrochloricum.

ACIDUM HYDROCYANICUM DILUTUM. Br.

DILUTED HYDROCYANIC ACID Acid. Hydrocyan. Dil.

"Diluted Hydrocyanic Acid is an aqueous solution containing 2 per cent. by weight of hydrogen cyanide, HCN. It may be obtained by the interaction of diluted sulphuric acid and potassium ferrocyanide, and subsequent distillation. Should be stored in a dark place, in small, inverted stoppered bottles of amber-coloured glass." *Br.*

Cyanhydric Acid; Diluted Prussic Acid: Acidum Hydrocyanatum, s. Borussicum; Acidum Cyanhydricum Solutum, *Fr. Cod.;* Acide cyanhydrique, dissous, *Fr.;* Cyanwasserstoffsäure, Blausäure, *G.;* Acido cianhidrico Medicinal, *Sp.*

Diluted hydrocyanic acid is no longer recognized by the U. S.

Hydrocyanic acid must be handled with great caution because of the poisonous character of its fumes even in the diluted form. No process for making this acid is official. The U. S. P. VIII gave the following extemporaneous process: "Silver Cyanide, *six grammes;* Diluted Hydrochloric Acid, *fifteen and fifty-four hundredths cc.;* Distilled Water, *forty-four and one-tenth cc.* Mix the Diluted Hydrochloric Acid with the Distilled Water, add the Silver Cyanide, and shake the whole together in a glass-stoppered bottle. When the precipitate has subsided, pour off the clear liquid." *U. S. VIII.*

The U. S. P., 1890, process, which may be used on a larger scale, is carried out by distilling potassium ferrocyanide with diluted sulphuric acid under carefully specified conditions. (See *U. S. D.,* 20th ed., p. 38.)

When potassium ferrocyanide is decomposed by sulphuric acid, the residue in the retort is potassium sulphate, mixed with an insoluble compound of iron cyanide and potassium cyanide (*Everitt's Salt*). The reaction is expressed by the following equation:

$$2K_4FeC_6N_6 + 3H_2SO_4 = 3K_2SO_4 + 2KFeC_3N_3 + 6HCN$$

Half of the cyanogen present in the potassium ferrocyanide goes to form the hydrocyanic acid, while the other half remains in the white residue. Everitt's salt, so named from its discoverer, is a yellowish-white powder. Like potassium ferrocyanide, it is a double salt (iron and potassium cyanide), but of different molecular ratio. As it appears in practice, it is apt to be greenish, owing probably to the presence of a little Prussian blue.

Investigations have shown that potassium ferrocyanide is decomposable not only by the weakest acids but also by numerous non-acid organic substances, hydrocyanic acid being liberated; thus the diluted mineral acids (containing even less than 0.1 per cent.), formic, acetic, butyric, lactic, tartaric, benzoic acids, even carbon dioxide and hydrogen sulphide, phenols, peptones, casein, etc., will decompose potassium ferrocyanide more or less quickly at temperatures below 100° C., liberating a portion of the hydrocyanic acid. (*A. J. P.*, 1893, p. 283.)

Hydrocyanic acid may also be made by passing a mixture of trimethylamine and ammonia through a red hot tube. $N(CH_3)_3 + 2NH_3 = 3HCN + 12H$.

The processes thus far given are intended to furnish a *diluted* hydrocyanic acid for medicinal purposes. For processes for making the *anhydrous* acid, see U. S. Dispensatory, 19th ed., p. 40.

Berthelot has made hydrocyanic acid synthetically. He first prepared, by a direct synthesis of its elements, *acetylene* (C_2H_2). He then mixed this gas with pure nitrogen, passed a series of electric discharges from a Ruhmkorff coil through the mixture, and, when the odor of prussic acid was perceptible, agitated with a solution of potassium hydroxide to get the fixed cyanide. It has also been made by heating chloroform with ammonia and potassium hydroxide solution. (Hofmann.)

Properties of the Diluted Acid.—Diluted hydrocyanic acid is officially described as "a colorless liquid with a characteristic odor. Specific gravity is 0.997. Only slightly acid to litmus. Yields when neutralised the reactions characteristic of cyanides. 5 millilitres, mixed with 50 millilitres of *water,* 5 millilitres of *solution of ammonia,* and 3 drops of *solution of potassium iodide,* require the addition of not less than 18.4 and not more than 19 millilitres of *N/10 solution of silver nitrate* before a permanent precipitate begins to form. 5 millilitres evaporated in a platinum dish leave no appreciable residue. Yields not more than the slightest characteristic *reactions* for sulphates or chlorides." *Br.*

It is liable to undergo decomposition if exposed to the light, but it may be kept for a longer time in a bottle covered with black paint or black paper. From experiments carefully conducted by Bussy and Buignet, it appears that, when the alteration in the acid under the influence of light has begun, it will afterwards go on very rapidly in the dark; and that after exposure for a certain time to the light, though no alteration may be apparent, an influence has nevertheless been exerted which disposes to change, and promotes decomposition even in the absence of light. Hence the necessity of immediately enclosing the acid in bottles from which the light is excluded. Experience has shown that it is best preserved in cork-stoppered bottles of amber glass; when glass and rubber stoppers were used, decomposition frequently takes place rapidly.

Leivcock (*P. J.*, 1918, p. 50) discusses the various causes of decomposition of hydrocyanic acid, which are mainly due to the presence of alkalies. He states that the best preservatives are small amounts of sulphuric or tartaric acid. The U. S. IX permitted the presence of 0.1 per cent. of hydrochloric acid.

"**Assay.**—Pour about 5 mils of Diluted Hydrocyanic Acid into a 100 mil flask containing 25 mils of distilled water and 5 mils of potassium hydroxide T.S., the whole having been previously tared, and weigh the Acid accurately. Then add 3 drops of potassium iodide T.S. and titrate with tenth-normal silver nitrate V.S. to the production of a slight, permanent precipitate. It shows not less than 1.9 per cent. nor more than 2.1 per cent. of HCN.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.005404 Gm. of HCN. Each gramme of Diluted Hydrocyanic Acid corresponds to not less than 3.5 mils nor more than 3.9 mils of tenth-normal silver nitrate V.S." *U. S. IX.*

Formerly the medicinal acid was of different strengths, as ordered by the different pharmaceutical authorities, but the Br. now conforms with the International Protocol. At one time its strength was indicated by its specific gravity, which is lower in proportion as it is stronger; but this inaccurate method is not now relied on, though the British Pharmacopœia gives the sp. gr. of its diluted acid at 0.997.

In connection with the determination of the minute amounts of hydrocyanic acid encountered in work on cyanogenetic plants, Viehoever and Johns have published a method in *J. Am. C. S.*, 1915, based upon a colorimetric comparison with a standard suspension of Prussian blue.

Properties of the Anhydrous Acid.—*Hydrocyanic acid,* perfectly free from water, is a colorless, transparent, inflammable liquid, of extreme volatility, boiling at 27° C., and congealing at –15° C. Its sp. gr. as a liquid is 0.6969, at the temperature of 18° C.; and as a vapor 0.9423. Its vapors are highly poisonous.

Anhydrous prussic acid is now supplied, commercially, compressed in metal cylinders. Large quantities are used in California in combating certain diseases of the citrus trees.

It was discovered in 1815 by Gay-Lussac, who viewed it as a compound radical which when combined with hydrogen becomes hydrocyanic acid. Hydrocyanic acid, in a diluted state, was discovered in 1780 by Scheele, who correctly stated its elements to be carbon, nitrogen, and hydrogen; but the peculiar way in which they are combined was first pointed out by Gay-Lussac by whom also the anhydrous acid was first obtained.

Hydrocyanic acid is one of the products of the decomposition of the cyanogenetic glucosides. These plant principles are widely distributed being found in at least a dozen natural orders of plants. The *Prunus* family is especially noted for the occurrence of this cyanogenetic glucoside *amygdalin.* Others are *dhurrin* from sorghum, *cotusin* from Lotus *arabicus,* and *phaseolunatin* from the seeds of certain beans and in species of Manihot which yield tapioca. A method for the detection of minute amounts of hydrocyanic acid based upon the formation of a sulphocyanide, is proposed by Lavaille and Varenne (*J. P. C.,* 1918, p. 97). It is stated that .005 milligramme can be detected by this test.

Uses.—Moderate doses of hydrocyanic acid and the cyanides cause marked increase in both the rate and depth of respiration and with a marked rise in blood pressure accompanied by a slowing of the pulse. These effects are due to increased activity of the respective centers in the medulla. Gepper (*Z. K. M.,* 1889, xv, 208–307) has shown that the cyanides lessen oxidative processes in the body and Gasser and Loevenhart (*J. P. Ex. T.,* 1914, v, 139) attribute the stimulation of the medullary centers to the deficiency in oxygen. The stimulation of these centers lasts but a very short time and if the dose has been large enough is followed by a marked depression. According to Loevenhart (*A. I. M.,* 1918, xxi, 109) by giving small doses at short intervals it is possible to maintain the stimulating effects for a long period of time. Somewhat paradoxically Loevenhart (*J. P. Ex. T.,* 1922, xix, 13) has shown that when the respiratory center is depressed by cerebral ischemia the cyanides are still capable of acting as respiratory stimulants. Diluted hydrocyanic acid has been much used in respiratory diseases and to quiet *cough,* but its action is so fugacious that it has really very little medicinal value except as a local remedy in sick stomach of nervous origin and in *gastrodynia.* Externally, it may be of occasional service in *pruritus,* but should be used circumspectly, as its vapors are poisonous.

It should be administered with the greatest caution, on account of its minute dose and its variable strength as usually found. The proper plan, therefore, is to begin with a small dose, two drops, for example, and gradually to increase the quantity until some obvious impression is produced. On account of the rapidity and uncertainty of its action, it should be given at intervals of not more than two hours; indeed, it is very improbable that the largest therapeutic dose of the substance exerts any influence whatever upon the system one hour after its ingestion. If giddiness, weight at the top of the head, sense of tightness at the stomach, or faintness come on, its use should be discontinued. In all cases in which a fresh portion of medicine is used, the dose should be lowered to the minimum quantity, lest the new sample should prove stronger than that previously employed. As a lotion it may be diluted with from eight to fifteen parts of water.

Gaseous hydrocyanic acid is used in public hygiene for the destruction of vermin in buildings (see *J. Soc. Chem. Med.,* 1920, xxxix, 794). It is also used by trappers by placing a small triangular ampule containing a few drops of the acid, in a bait in such a manner that the ampule is crushed by the teeth of the animal when the bait is taken.

Diluted Hydrocyanic Acid is incompatible with the strong mineral acids which decompose it to formic acid and a salt of ammonium. Calomel is changed into mercuric chloride. It is also incompatible with salts of silver, lead and mercury. Oxidizing agents destroy it with the formation of a number of compounds.

Toxicology.—Hydrocyanic acid is an exceedingly powerful poison acting with great rapidity. After large doses death may take place in from two to ten minutes, but from minimal fatal quantities may be delayed as long as two or three hours. The smallest fatal quantity upon record seems to be that reported by Garstang (*L. L.,* 1888, ii, p. 15), in which 2 drachms of the 2 per cent. solution proved fatal. The ordinarily fatal does is about 1 to 1½ grains of the pure acid. Of potassium cyanide the ordinarily fatal dose is about five grains.

After large doses the progress of the poison is so rapid that one can scarcely speak of symptoms; the patient gives a cry and falls down insensible and respirations which are at first hurried become in a few seconds slow and gasping and death may occur in a few minutes either with or without preceding convulsions. In the majority of cases, however, the poison progresses somewhat more slowly and the symptoms will be as follows: Immediately after swallowing the poison there is a sense of constriction in the throat followed by salivation and nausea with vertigo and headache. The respirations are at first rapid and then become slow and irregular, with expiration often being greatly prolonged. The pulse is slow and at first bounding, the pupils dilated and insensible to light, the eyes wide open and staring, the skin cold and cyanotic, and violent convulsions with foaming of the mouth are not uncommon. This stage is followed by one of weakness, the patient becoming unconscious, the temperature falling, the pulse growing feeble, the respirations very slow and gasping in character. Death is the result of asphyxia and the symptoms are those, in general, characteristic of interference with oxygenation. Post mortem the blood may be either of a uniform arterial hue in both veins and arteries or the dark blood of cyanosis, according as to whether death has taken place rapidly or slowly.

The treatment of prussic acid poisoning to be of any avail must be undertaken with great promptness. The stomach should be immediately emptied with the pump, as emetics often fail to produce the desired effect. Among the chemical antidotes which have been suggested the most useful are the ferric salts suggested by T. and H. Smith. Martin and O'Brien (*Pro-*

ceedings of the Soc. for Chemical Industry, Victoria, i, p. 119) recommend that in mines, etc., where accidental poisoning is likely to occur, there should be kept on hand one ounce each of a 23 per cent. solution of ferrous sulphate, of a 5 per cent. solution of potassium hydroxide, and 30 grains of magnesium oxide. These are to be mixed in a half pint of water before being used. Cobaltous nitrate has been recommended, but, although an efficient antidote, it is so poisonous that its use in the human subject seems hardly justifiable. Kobert and Krohl (*Arb. d. Pharm. Inst. z. Dorpat,* 1891, vii; *Ph. Centralh.,* 1891) have found that in the lower animals good results may be achieved in the poisoning by the conversion in the system of the prussic acid into oxamide by means of peroxide of hydrogen. The oxamide is itself somewhat poisonous, and after its production it is essential to give large draughts of water to wash it out of the system. It is affirmed that in various mining and extracting establishments, and in certain chemical works, where the cyanides are used in enormous quantities, Kobert's method is practically employed, and Merck furnishes what is known as an "antidote-box," containing the necessary apparatus and the supply of hydrogen peroxide. (See *M. A.,* ii, p. 94.) When the cyanide has been taken into the system the peroxide must be introduced by means of a stomach tube into the stomach itself, and the latter should then be washed out. Before or immediately after the administration by the mouth the salts should be given hypodermically. In cases of poisoning by inhalation the antidote should be used subcutaneously. The poison's action is, however, so rapid that there is rarely time for any antidote to be of value. Atropine, which has been suggested as physiologically antagonistic to hydrocyanic acid, has no antidotal value.

Dose, of diluted hydrocyanic acid, one to four minims (0.06–0.25 cc.).

Off. Prep.—Tinctura Chloroformi et Morphinæ Composita, *Br.*

ACIDUM HYPOPHOSPHOROSUM. U. S.

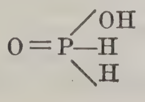
HYPOPHOSPHOROUS ACID Acid. Hypophos.

"Hypophosphorous Acid is an aqueous solution containing not less than 30 per cent. and not more than 32 per cent of HPH_2O_2." *U. S.*

Acide hypophosphoreux, *Fr.;* Unterphosphorigesäure, *G.*

Hypophosphorous acid is obtained by heating a concentrated solution of sodium hydroxide or other alkali with phosphorous. The alkaline hypophosphite is converted into a barium salt which is then decomposed with sulphuric acid and purified by crystallization.

Hypophosphorous acid is a monobasic acid since the molecule contains only one ionizable hydrogen atom as shown by the following structural formula:



It has a great affinity for oxygen which transforms it into phosphoric acid. It is therefore one of the most valuable reducing agents in chemistry and is frequently used in pharmacy as a preservative for easily oxidizable compounds. When heated, it is resolved into hydrogen phosphide and phosphoric acid. Its salts are generally soluble in water and deliquescent, and many are soluble in alcohol. They are converted into phosphates by heat, with the escape of hydrogen phosphide; some are explosive. *Calcium hypophosphite* has been most largely employed.

Description and Physical Properties.—"A colorless or slightly yellow, odorless liquid. When the Acid is heated in a suitable dish, water evaporates, leaving a more concentrated acid. On further heating between 130° and 140° C., it decomposes, forming spontaneously combustible hydrogen phosphide and phosphorous acid. The latter, between 160° and 170° C., decomposes into hydrogen phosphide and phosphoric acid. The pasty residue finally reddens, ignites, and the last portions of unoxidized phosphorus burn out at a higher temperature. Specific gravity: about 1.130 at 25° C.

"It is acid to litmus paper even when highly diluted. Hypophosphorous Acid responds to the reactions for hypophosphites. Hypophosphorous Acid diluted with 3 volumes of water conforms to the following tests for identity and purity: Neutralize 30 cc. of the dilution with ammonia T.S.: not more than a slight precipitate results. Filter, acidulate 10 cc. of the filtrate with hydrochloric acid, and add 2 cc. of potassium sulphate T.S.: no turbidity is produced (*barium*). Another 10 cc. portion of the filtrate shows no turbidity upon the addition of 1 cc. of calcium chloride T.S. (*oxalate*). One cc. of the dilution mixed with 9 cc. of distilled water meets the requirements of the test for *heavy metals.* Mix 5 cc. of the dilution with 3 cc. of nitric acid and 10 cc. of distilled water, and evaporate the liquid to dryness on a water bath: the residue meets the requirements of the test for *arsenic.*

"**Assay.**—Proceed as directed under the assay for acids, page 430, using about 7 cc. of the Acid, accurately weighed, and methyl orange T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.06606 Gm. of HPH_2O_2.

"Preserve in glass-stoppered bottles." *U. S.*

A new method of assay for hypophosphorous acid and the hypophosphites has been proposed by T. T. Cocking and J. T. Kettel (*Tr. Br. Ph. Conf.,* 1913, 518), which is more accurate and expeditious than any hitherto proposed. It is as follows: Two and one half Gm. of the hypophosphite (or the acid) are dissolved in 40 cc. of water and an excess of lead acetate solution (10 per cent.) added to precipitate phosphites (5 cc. is usually sufficient) and the solution is made up to 50 cc., well shaken and allowed to stand until the supernatant liquid is clear. Then 10 cc., representing 0.5 Gm. of the material taken, is carefully pipetted off, 50 cc. of normal potassium dichromate and 10 cc. of sulphuric acid added and the mixture heated on a water bath. After one hour the solution is cooled and diluted with distilled water to 250 cc. The excess of dichromate is then determined in 50 cc. of the solution by titration with tenth normal sodium thiosulphate V.S., after adding potassium iodide. The reaction upon which calculations are based is as follows:

$$R'.PH_2O_2 + O_2 = R'H_2PO_4.$$

The authors gave the method a thorough trial with a number of samples of hypophosphites obtained in the market.

The U. S. IX also recognized under the name of *Acidum Hypophosphorosum Dilutum* (*Diluted Hypophosphorus Acid*) a solution containing 10 per cent. of hypophosphorus acid which was made by mixing 100 grams of the strong acid with 210 Gm. of distilled water.

Hypophosphorous Acid is incompatible with many substances on account of its powerful reducing properties, and in exercising these effects it is oxidized to phosphoric acid and thus loses its own identity. It reduces bismuth, mercuric, and mercurous compounds to the metallic state. Ferric and cupric compounds are reduced to ferrous and cuprous. Permanganates are changed to managanous compounds; arsenates are reduced to arsenites and sometimes to metallic arsenic. With some oxidizing agents like potassium chlorate, it must not be triturated for fear of causing an explosion.

Uses.—Hypophosphorus acid was formerly believed to exert upon the nervous system a tonic effect like that of elemental phosphorus, but it has been demonstrated that the salts of this acid pass through the system unchanged and therefore cannot exert the influence of phosphorus. The present Pharmacopœia recognizes this acid only because of its use in the preparation of syrup of ferrous iodide.

ACIDUM LACTICUM. U. S., Br.

LACTIC ACID Acid. Lact.

"A mixture of lactic acid and lactic anhydrides equivalent to a total of not less than 85 per cent. and not more than 90 per cent of $CH_3.$-CHOH.COOH." *U. S.*

"Lactic Acid is an aqueous solution containing not less than 75 per cent. by weight of hydrogen lactate, $HC_3H_5O_3$, and not less than 10 per cent. by weight of lactide, $C_6H_8O_4$. It may be obtained by the fermentation of lactose." *Br.*

Alphahydroxypropionic Acid, Oxypropionic Acid, Ethylidenelactic Acid, Isolactic Acid; Acide lactique, *Fr. Cod.;* Acidum lacticum, *P. G.;* Milchsäure, *G.;* Acido lactico, Sp.

Lactic acid was discovered in 1780 by Scheele. It exists in sour milk, and is a product of the viscous or lactic fermentation of rice water, or of the juices of the beet, turnip, and carrot, and is a normal constituent of sauer kraut and of ensilage. Pasteur demonstrated that the lactic acid fermentation, like the vinous, is caused by a peculiar micro-organism. It is attended with the production not only of lactic acid, but of other substances also, and among them a peculiar gum-like substance, in abundance, which, first noticed by Kirchof, has been isolated in a pure state by Brüning. Though similar to arabin and dextrin, with the formula $C_6H_{10}O_5$, it is not exactly identical with either. The lactic acid of fermentation is one of four isomeric acids possessing the formula $C_3H_6O_3$. The *first* of these is the official lactic acid, and is inactive optically. The *second* is identical chemically with this, but dextrorotatory, and is found in the juice of flesh. It is called *paralactic acid.* The *third,* or *ethylene lactic acid,* is found mixed with the second in the so-called *"sarcolactic"* acid extracted from meat. The *fourth* acid has only been obtained synthetically, and is known as *hydracrylic acid.*

Preparation.—Lactic acid occurs in milk as a result of the decomposition of lactose. The earlier methods for its manufacture were all of them based upon the fermentation of milk or whey (for details see *U. S. D.,* 20th Ed., p. 43). It is now known that other saccharine matters such as glocose or sucrose can be made to undergo the lactic fermentation.

There are a number of species of bacteria which will produce more or less lactic acid when cultivated in a sugar-containing medium. The one generally regarded, however, as the special lactic acid ferment is the *Bacillus acidi lactici.* (See also under *Lac Fermentatum.*)

Alan A. Claflin thus describes the manufacture of lactic acid as carried out on a large scale under the patent of Charles E. Avery (*J. Soc. Chem. Ind.,* June 30, 1897): A saccharine solution varying in density from 1.05 to 1.075 is taken. This will contain from 7.5 to 11 per cent. of saccharine matter. It is advantageous to have from 10 to 15 per cent. of this, cane sugar, the rest being grape sugar. The saccharine solution, having been made up and boiled for an hour to insure sterilization, is conveyed into the fermentation tank and cooled to from 55° to 45° C., and then impregnated with nitrogenous matter (such as is extracted from bran by the action of boiling water and diluted acid) in amount equal to about 8 per cent. of the saccharine matter, and inoculated with the *Bacillus acidi lactici.* In continuous manufacture the ferment solutions are impregnated from a preceding ferment liquor in which a lively fermentation is in progress; 20 per cent. of such impregnating liquor may be added. The impregnation having taken place at 45° C. or over, the temperature is allowed to decrease somewhat as the fermentation proceeds. The glucose is practically all decomposed, and the yield of lactic acid is over

98 per cent. of the theoretical amount. As the fermentation progresses the solution must be neutralized with milk of lime, as the limits of acidity in which lactic acid bacteria are healthy are rigidly confined between 0.02 and 0.5 per cent. If the fermenting solution is overneutralized, the butyric ferment will immediately begin to act, and once active is difficult to control. The lactic fermentation is best completed in from three to six days, and when the fermentation is ended, the liquor must be heated sharply to kill all bacteria and spores and prevent subsequent fermentation. The solution is now filtered and evaporated, when calcium lactate may be crystallized out; or if commercial syrupy acid only is required, the solution may be at once decomposed by sulphuric acid. Chemically pure lactic acid is obtained by converting calcium lactate into zinc lactate with zinc carbonate, precipitating the zinc with H_2S, passing through animal charcoal and evaporating *in vacuo.*

Kiliani (*B. Chem. G.*, 1882, xv, 136 and 699) has found that lactic acid may be readily prepared by the action of potassium or, preferably, sodium hydroxide upon either grape sugar or invert sugar (*i.e.*, cane sugar after treatment with diluted acids.). He found that invert sugar gave a better yield than ordinary glucose.

His method for the preparation of lactic acid is as follows: 500 grammes of cane sugar are placed with 150 grammes of water and 10 cc. of the sulphuric acid, in a stoppered flask of 2 liters' capacity and heated for 3 hours to about 50° C. The solution of invert sugar so obtained is colorless, or at most faintly yellow. After cooling there is to be added to it in portions of 50 cc. at a time 400 cc. of a caustic soda solution made by dissolving 1 part of caustic soda in 1 part of water. The strong alkali settles at first as a slimy mass on the bottom, and a new portion is only to be added when the mixture has become perfectly homogeneous by shaking. The flask should also be cooled with water while the alkali is being added. The mixture nevertheless becomes colored and greatly heated. Finally the mixture is heated to 60° or 70° C. until a portion heated over a boiling water bath does not separate cuprous oxide from Fehling's solution, but gives it only a slight greenish tinge. Into the cooled mixture the calculated amount of sulphuric acid (made by mixing 3 parts of sulphuric acid with 4 of water) is then run. As soon as the acid liquid has cooled to the temperature of the room a crystal of sodium sulphate is dropped in and the flask dipped in cold water until a thin crystalline crust forms on the sides, which is removed by a rapid shaking of the flask. Cooling and shaking are continued until the crust no longer forms, when the mixture is allowed to stand at rest for twelve to twenty-four hours. At the end of this time the contents of the flask appear to consist of a crystalline cake soaked with a reddish liquid. There is then added alcohol of 93 per cent., and the whole is shaken up until on further addition no precipitate separates out. The precipitated sodium sulphate is freed from the alcoholic solution by a vacuum filter, and can be washed with relatively very little alcohol. The half of the alcoholic solution is neutralized over the water bath with zinc carbonate, filtered boiling hot, and united with the other half. The crystallization begins immediately upon cooling, and is complete after standing 36 hours. The zinc lactate so obtained can be pressed free from mother liquor and crystallized once, when it is perfectly pure. The weight of this first crystallization amounts to from 30 to 40 per cent. of the sugar used. The concentrated mother liquor yields yet another portion of nearly pure, although slightly yellowish, crystals. The zinc lactate may then be treated with hydrogen sulphide to remove the zinc.

Beckers (*Ap. Ztg.*, 1899, 400) patented a process for making lactic acid from the liquors obtained in the manufacture of "sauer kraut" which were formerly wasted. The liquor is neutralized with lime, filtered, evaporated and set aside to crystallize; the calcium lactate is purified, if necessary, by washing or recrystallization and then dissolved in cold water and the solution treated with sufficient sulphuric acid to set free the lactic acid. Lactic acid is also made from the liquid cheese residues. For a method of making lactic acid from corn meal, see *N. R.*, 1882, p. 235.

Description and Physical Properties.—"A colorless, or slightly yellow, nearly odorless, syrupy liquid. It absorbs moisture on exposure to air. Lactic Acid is miscible with water, alcohol, and ether, but is insoluble in chloroform, petroleum benzin, and carbon disulphide. Specific gravity: about 1.206 at 25° C. Lactic Acid cannot be distilled without decomposition.

"Lactic Acid is strongly acid to litmus paper and responds to the reactions for lactates.

"Ash: not more than 0.006 Gm. from 5 cc. of the Acid. Ten cc. portions of an aqueous dilution of the acid (1 in 100) remain unaffected by the addition of 1 cc. of silver nitrate T.S. (*chloride*), or 1 cc. of barium chloride T.S. (*sulphate*). The addition of 1 cc. of copper sulphate T.S. to 10 cc. of an aqueous dilution of the acid (1 in 20) causes no turbidity (*sarcolactic acid*). No turbidity is produced on heating the Acid with an excess of calcium hydroxide T.S. (*citric, oxalic, phosphoric, or tartaric acid*). Add a few drops of Lactic Acid to 10 cc. of hot alkaline cupric tartrate V.S.: no red precipitate is produced (*sugars*). Carefully superimpose 5 cc. of Lactic Acid upon an equal volume of sulphuric acid in a clean test tube, and keep the temperature at 15° C.: no dark color develops at the zone of contact of the two liquids upon standing for fifteen minutes (*readily carbonizable substances*). An aqueous dilution of the Acid meets the requirements of the test for *heavy metals*.

"Preserve in glass-stoppered bottles." *U. S.*

"Specific gravity about 1.21. Warmed with one-tenth of its weight of *potassium permanganate* it yields the odor of aldehyde. 1 gramme diluted with 10 millilitres of *water* requires for neutralisation not less than 8.3 millilitres of *N/10 solution of sodium hydroxide.* After the further addition of 10 millilitres of the alkaline solution and boiling for fifteen minutes, not more than 8.6 millilitres of *N/1 solution of sulphuric* acid are required to neutralise the excess of alkali. Yields no characteristic *reactions* for copper, iron, chlorides, citrates, oxalates, phosphates, sulphates, or tartrates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million. Diluted with *water* gives no precipitate with *solution of copper sulphate* (absence of sarco-lactic acid), and none, or only the slightest traces, with excess of *solution of potassio-cupric tartrate,* even after prolonged boiling (absence of more than traces of various sugars). The mixture obtained by heating Lactic Acid with excess of *zinc carbonate* and evaporating to dryness, when exhausted with *absolute alcohol* and the latter evaporated, does not leave any sweet residue (absence of glycerin). Yields no rancid odor when gently warmed (absence of fatty acids). When carefully poured upon an equal volume of *sulphuric acid* contained in a clean test tube, little or no darkening in color occurs (absence of organic impurities). No turbidity, whether permanent or transient, is produced when the Acid is added drop by drop to twice its volume of *ether* (absence of gum, sugars, mannite, calcium phosphate). Yields no precipitate with *solution of lead subacetate* (absence of malic acid and sulphuric acid)." *Br.*

Exposed to a temperature of 150° C., it is for the most part converted into a new body, which is called concrete lactic acid or *lactide,* an anhydride having the formula $C_6H_8O_4$. It coagulates albumin and dissolves a large quantity of freshly precipitated calcium phosphate, a property which doubtless renders it important in the animal economy.

Assay.—"Add 50 cc. of normal sodium hydroxide to about 2.5 cc. of Lactic Acid, accurately weighed, in a tared 250 cc. flask, and boil for twenty minutes. Titrate the excess of alkali in the hot solution with normal sulphuric acid, using phenolphthalein T.S. as indicator. Make a blank test, using 50 cc. of half-normal sodium hydroxide, and from the comparisons make any necessary corrections. Each cc. of normal sodium hydroxide corresponds to 0.09006 Gm. of $CH_3.CHOH.COOH$." *U. S.*

Of the organic acids lactic acid is the only one oxidized by chromic acid in the presence of sulphuric acid, to acetic acid and carbonic acid. An assay process based upon this principle has been devised by Szberenyi who claims results within three per cent. of the theoretical amount. (*Pharm. Weekblad.*, 1918, lv, 1041).

Lactic acid has the incompatibilities of the organic acids in general, but is also incompatible with oxidizing agents which convert it into aldehyde, oxalic acid etc. Hydriodic acid decomposes lactic acid with the production of propionic acid.

Uses.—Lactic acid was formerly used for the removal of *phosphatic deposits* in the urine and in certain types of *diarrhea.*

Hypnotic properties have also been ascribed to lactic acid, but the claim has not been verified. It is no longer employed as an internal remedy.

In concentrated form lactic acid is an active caustic; when diluted it is stimulant and germicidal. The 50 to 80 per cent. solution has been used as a caustic antiseptic in *infected wounds, ozena, laryngeal tuberculosis,* etc.; the 20 per cent. solution has been used for the destruction of false membrane in *diphtheria;* the three per cent. solution has been strongly recommended by Sneguirewa for irrigation in foul *leucorrheas.* (For consideration of the therapeutic uses of the lactic acid forming bacteria see under *Kephir,* Part II.)

Dose, from fifteen to forty-five minims (1–3 cc.).

ACIDUM NITRICUM. U. S., Br.

NITRIC ACID Acid. Nitric.

"Nitric Acid contains not less than 67 per cent. nor more than 69 per cent of HNO_3." *U. S.* "Nitric Acid contains 70 per cent. by weight of hydrogen nitrate, HNO_3, and 30 per cent. by weight of water. It may be obtained by the interaction of sulphuric acid and sodium nitrate." *Br.*

Acidum Nitri, s. Azoticum, Spiritus Nitri Acidus; Spirit of Nitre; Aqua Fortis; Acide azotique officinal, *Fr. Cod.;* Acide nitrique, *Fr.;* Acidum nitricum, *P. G.;* Salpetersäure, *G.;* Acido nitrico concentrato, *It.;* Acido nitrico, *Sp.;* Zaltpeterzuur, Sterkwater, *Dutch;* Shedwater, *Sw.*

Nitric acid oxide is one of the five compounds formed by nitrogen and oxygen. These are, nitrogen monoxide or hyponitrous oxide (laughing gas), N_2O; nitrogen dioxide, N_2O_2, or NO; nitrous oxide, N_2O_3; nitrogen tetroxide or peroxide, N_2O_4; and nitric oxide, N_2O_5. From this latter by the addition of water is formed nitric acid:

$$N_2O_5 + H_2O = 2HNO_3$$

The nitric acid of the British Pharmacopœia is slightly stronger than that of the U. S. containing 70 per cent. of HNO_3 as against 67 to 69 per cent.

Preparation.—Nitric acid is made by decomposing sodium nitrate with sulphuric acid. The reaction is as follows:

$$NaNO_3 + H_2SO_4 = NaHSO_4 + HNO_3.$$

This reaction takes place below 200° C.

At higher temperatures the sodium acid sulphate may be made to react with another molecule of sodium nitrate and normal sodium sulphate, Na_2SO_4, is produced, but in practice the reaction is rarely forced up to the second phase on account of some practical disadvantages connected with the removal of the by-product from the still.

The by-product, acid sodium sulphate, has found but a limited use and is practically given away free of charge to get rid of it. Formerly it was the custom to use glass retorts in the manufacture of nitric acid, but they have been abandoned in favor of cast iron retorts, the vapors being condensed in stoneware vessels. These condensers are so arranged that the various gases produced as variants or by-products of the reaction, such as N_2O_3, HCl, NOCl, O, and the halogens, if present, are collected and obtained separately, so that instead of the first distillation producing a very impure nitric acid which required subsequent redistillation and purification, a pure nitric acid is obtained directly. This method is now said to yield 650,000 tons annually in the United States alone.

During recent years nitric acid has been manufactured from atmospheric nitrogen by causing it to combine directly with oxygen through the heat of an electric arc. This is known as the Birkeland-Eyde process. This forms nitric oxide which, as the temperature falls, is converted into nitrogen peroxide. This latter gas is led into granite towers filled with broken quartz where it meets with falling water, with the elements of which it unites to form a dilute nitric acid. (See Strong, *A. J. P.*, 1915, p. 39.) A modification of this method in which rarified air and an excess of oxygen are used, is the Haber process. Another method of utilization of atmospheric nitrogen is by burning carbon monoxide in the presence of air in closed chambers, under pressure, and by rapidly cooling the flame against a cold surface. Still another method is by transforming ammonia into nitric acid by mixing it with air and passing it over spongy platinum heated to 300° C. Other catalyzing agents, such as thorium or tellerium oxides, have been employed. This method is said to be six times as efficient as the arc process, especially when nitrogen concentrated from liquid air is employed. Nitric acid has also been prepared industrially from synthetic calcium nitrate which is one of the modern products of the electric furnace.

Lunge and Rey obtained pure, colorless, concentrated nitric acid by the following method: A quantity of nitric acid, prepared and deprived of coloring impurities in the usual manner, and containing 98.7 per cent. of absolute nitric acid, was put into a retort together with twice its volume of absolute sulphuric acid (H_2SO_4), and distilled *in vacuo*, the pressure being reduced to 20 mm. by means of a water-jet pump. This was found to be the only way to prevent the acid from becoming yellow. The connection between the neck of the retort and the receiver was effected by wrapping with asbestos paper and an external coat of moulder's clay. Great care was taken to insure the absence of organic matter. The distillation takes place at a temperature of 35° C. and the distillate was completely colorless. It contained 99.7 per cent. of HNO_3. (*Am. Drug.*, June 1, 1891, 170; from *Zeit. An. Chem.*)

Monohydrated Nitric Acid. Hydrogen Nitrate.—This is the strongest liquid nitric acid that can be procured, and may be obtained by distilling one molecule of pure and dry sodium nitrate with one molecule of monohydrated sulphuric acid. One molecule of monohydrated nitric acid distils over, and one molecule of sodium bisulphate remains behind: Acid of this strength is very difficult to make, and requires for its preparation the most elaborate attention to separate the superabundant water. According to Arthur Smith, of London, acid dehydrated as far as possible is perfectly colorless, boils at 84° C., and has the sp. gr. 1.517 at 15.4° C., and nearly approaches, in composition, to a monohydrate. Acid of this strength, even at the boiling temperature, has not the slightest action on tin or iron. According to Kolb (*Ann. Ch. Phys.* [4], x, 140), the true HNO_3 has a sp. gr. at 15° C. as high as 1.530.

The acid of a former Br. Pharmacopœia, having the sp. gr. 1.5, is of a yellowish color, and strongly corrosive. Strictly speaking, it is hydrogen nitrate diluted with half a molecule of water. An acid of this strength is inconveniently strong, is constantly undergoing decomposition under the influence of light. Besides, acid of this density was not necessary for any process of the Pharmacopœia. These considerations led to a reduction in the strength of both the U. S. and British Pharmacopœias to their present strengths. The specific gravity 1.40 given in the U. S. Pharmacopœia is practically equivalent to that given in the U. S. Pharmacopœia of 1890 (1.414), the temperature used in the U. S. Pharmacopœia for specific gravity being 25° C. instead of the lower one of 15.6° C.

For official tables of specific gravity of various strengths of nitric acid, see Part III.

Description and Physical Properties.—"A fuming liquid, very caustic and corrosive and having a characteristic, highly irritating odor. It boils at about 120° C., but volatilizes completely when heated on a steam bath. Specific gravity: about 1.40 at 25° C.

"Nitric Acid is strongly acid to litmus paper, even when highly diluted. Nitric Acid responds to the reactions for nitrates. Nitric Acid acts upon copper, mercury, silver, and many other metals with the evolution of brownish-red fumes, and stains woolen fabrics and animal tissues a bright yellow.

"Evaporate 20 cc. of Nitric Acid from a platinum or porcelain dish, and dry at 110° C.: not more than 0.003 Gm. of residue remains (*non-volatile substances*). Shake 2.5 cc. of Nitric Acid, diluted with 7.5 cc. of distilled water, with 2 cc. of chloroform: the latter remains colorless (*iodine or bromine*) even after the introduction of a small piece of metallic tin (*iodic or bromic acid*). Nitric acid diluted with 25 volumes of distilled water and neutralized with ammonia T.S., meets the requirements of the test for *heavy metals.* The residue remaining from the evaporation of 0.5 cc. of Nitric Acid to dryness on a water bath meets the requirements of the test for *arsenic.* Separate portions of Nitric Acid diluted with 10 volumes of distilled water do not yield a precipitate upon the addition of barium chloride T.S. (*sulphate*), or of silver nitrate T.S. (*chloride*).

"Preserve in dark amber-colored, glass-stoppered bottles, protected from light." *U. S.*

"A clear, colorless, or almost colorless liquid emitting corrosive fumes. Yields, when neutralised, the *reactions* characteristic of nitrates. Specific gravity 1.42. 1 gramme diluted with *water* requires for neutralisation 11.1 millilitres of *N/1 solution of sodium hydroxide.* When diluted with *water* yields no characteristic *reactions* for copper, iron, chlorides, bromates, iodates, or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million. Leaves not more than 0.05 per cent. by weight of residue on evaporation." *Br.*

Acid of the density 1.42 at 15° C. is the most stable of the hydrated compounds of nitric acid, and boils at 121° C., the U. S. P. acid boiling at 120.5° C. When either stronger or weaker than this, it distils over at a lower temperature, and, by losing more acid than water in the first case, and more water than acid in the second, constantly approaches to the sp. gr. 1.42, when its boiling point becomes stationary. Dalton first observed these facts in relation to nitric acid of this strength, which have been confirmed by Arthur Smith, of London. This acid may be assumed to have the composition $HNO_3 + 1\frac{1}{2}H_2O$.

The reddish acid called *aqua fortis* or *nitrous acid* is nitric acid containing more or less nitrogen tetroxide (N_2O_4). The same acid may be formed by impregnating, to a limited extent, nitric acid with nitrogen dioxide (N_2O_2). If the saturation be complete, every two molecules of nitric oxide become three molecules of nitrogen tetroxide by the aid of one molecule of nitrogen dioxide ($2N_2O_5 + N_2O_2 = 3N_2O_4$). More commonly it is obtained by distilling a mixture of 4 parts of starch and 100 parts of potassium nitrate with 100 parts of sulphuric acid. In this way the nitrogen tetroxide produced is at once taken up in the concentrated nitric acid and an acid of sp. gr. 1.50 is obtainable. This acid is sometimes sold under the name of *fuming nitric acid.*

The ordinary commercial acid has a specific gravity of from 1.30 to 1.41, and is usually prepared by means of chamber sulphuric acid; but if a more concentrated acid is required, a stronger sulphuric acid must be employed. The strongest nitric acid occurring in commerce has a sp. gr. of 1.43, and this is obtained by distilling well dried Chili saltpetre with sulphuric acid having a specific gravity of 1.85.

Nitric acid, so called from nitre, is an extremely sour and corrosive liquid. It was discovered by Raymond Lully, in the thirteenth century, and its constituents by Cavendish, in 1784. When perfectly pure it is colorless; but, as usually obtained, it has a straw color, owing to the presence of hyponitric acid. The concentrated acid, when exposed to the air, emits white fumes, possessing a disagreeable odor. By the action of light it undergoes a slight decomposition, and becomes yellow. It acts powerfully on animal matter, causing its decomposition. On the living tissue it operates as a strong caustic. It stains the skin and most animal substances an indelible yellow color. The compound produced being a nitrogen derivative of protein called *xanthoproteic acid.* On vegetable fiber it acts peculiarly, abstracting hydrogen or water, and oxidizing the remaining elements. When diluted, nitric acid converts most animal and vegetable substances into oxalic, malic, and carbonic acids. The general character of its action is to impart oxygen to other bodies, which it is enabled to do, as oxygen in the nascent state is liberated in its decomposition. If this liberation takes place while in contact with bodies capable of oxidation, the oxygen goes to effect this oxidation. Free nitric acid, however, will evolve oxygen at a red heat, according to the following reaction:

$$4HNO_3 = 2N_2O_4 + O_2 + 2H_2O$$

It oxidizes sulphur and phosphorus, giving rise to sulphuric and phosphoric acids, and all the metals, except chromium, tungsten, columbium, cerium, titanium, osmium, rhodium, gold, platinum, and iridium. It combines with salifiable bases and forms nitrates. When mixed with hydrochloric acid, mutual decomposition takes place, according to the reaction

$$HNO_3 + 3HCl = NOCl + Cl_2 + 2H_2O$$

and nitrohydrochloric acid is formed.

Great care must be used in transporting nitric acid, for if the strong acid comes in contact in quantity with vegetable substances like hay, tow, excelsior, paper, etc., fire will be apt to occur. The cause of such accidents was proved by the official inquiry of R. Hass. (*B. Chem. G.*, 1881, 597.)

Nitric oxide or anhydride consists of two atoms of nitrogen and five atoms of oxygen; or, in volumes, of two volumes of nitrogen and five volumes of oxygen, which on combining condense into two volumes of nitric oxide vapor. In 1849 Deville isolated nitric acid oxide or anhydride. The method pursued was to pass perfectly dry chlorine over silver nitrate. The oxide is in the form of colorless brilliant limpid crystals which melt at 29.5° C. and boil at 45° C. In contact with water they form a colorless solution with evolution of heat, without the disengagement of gas.

Assay.—"Proceed as directed under the assay for acids, using 2 cc. of the Acid, accurately weighed, and methyl orange T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.06302 Gm. of HNO_3." *U. S.*

Uses.—Nitric acid is capable of replacing the hydrochloric acid in the activation of the peptic enzyme and may therefore be used in the treatment of those types of *indigestion* in which hydrochloric acid is of service. It differs from hydrochloric acid in being astringent and is therefore often preferred where there is looseness of the bowels associated with digestive failure. It has also been found of service in chronic *hepatitis,* but is probably inferior to the nitro-hydrochloric acid. For internal use it should be well diluted and taken through a glass tube to avoid injury to the teeth.

Externally, diluted solutions of nitric acid in the proportion of about 12 minims of the stronger acid to a pint of water have been employed as astringent and antiseptic applications to *ulcers.* The most important external use of this acid, however, is as an escharotic. It has been especially employed as combining both caustic and disinfectant properties to *venereal ulcers* and poisoned *wounds,* especially the *bites* of rabid animals. It is also of service for destruction of small tumors, such as *warts;* for this purpose one or two drops of the official nitric acid may be applied by means of a glass rod, repeating in two or three days if necessary. Too deep caustic action may be prevented by washing the part in an alkaline solution as soon as the proper degree of effect has been obtained. In *cancrum oris,* concentrated nitric acid, freely applied, is one of the best local remedies that can be employed for arresting the phagedænic ulceration and disposing the sore to heal, but great care must be exercised to protect the teeth.

Toxicology.—The swallowing of concentrated nitric acid is immediately followed by burning heat in the mouth, esophagus, and stomach, acute pain, disengagement of gas, abundant eructations, nausea, and hiccough. These effects are soon followed by repeated and excessive vomiting of matter having a peculiar odor and taste, tumefaction of the abdomen with exquisite tenderness, a feeling of coldness on the surface, horripilation, icy coldness of the extremities, small depressed pulse, great anxiety, continual tossings and contortions, and extreme thirst. The cases are almost always fatal. Sometimes the collapse has been immediate and has masked all the other symptoms. The best remedies are repeated large doses of alkaline solutions, especially magnesia, or chalk, as antidotes, mucilaginous drinks, olive or almond oil in large doses, emollient fomentations, etc.

Nitric acid is an energetic oxidizing agent and its incompatibilities are usually shown along that line. It decomposes most organic principles when brought in contact with them, sometimes with the production of dangerous explosive compounds, as with the volatile oils, glycerin, etc.

Dose, three to eight minims (0.2–0.5 cc.), largely diluted.

Off. Prep.—Acidum Nitricum Dilutum, *Br.;* Acidum Nitrohydrochloricum, *N. F.;* Acidum Nitrohydrochloricum Dilutum, *N. F., Br.*

ACIDUM NITRICUM DILUTUM. Br.

DILUTED NITRIC ACID

"Diluted Nitric Acid contains 10 per cent. by weight of hydrogen nitrate, HNO_3." *Br.*

"Nitric Acid, 151 grammes; Distilled Water, sufficient to produce 1000 millilitres. Mix." *Br.*

"Specific gravity 1.057. 10 millilitres require for neutralisation 16.8 millilitres of a *N/1 solution of Sodium Hydroxide.* This Diluted Acid is approximately three-fifths the strength of the corresponding preparation of the British Pharmacopœia, 1898, and contains 10 per cent. by weight of hydrogen nitrate, HNO_3." *Br.*

Dose, from ten to twenty minims (0.6–1.2 cc.).

ACIDUM NITROHYDROCHLORICUM DILUTUM. Br.

DILUTED NITROHYDROCHLORIC ACID

Acidum Nitromuriaticum Dilutum, U. S. P. 1870; Diluted Nitromuriatic Acid; Acide chlorazotique dilué, *Fr.;* Verdünnte Salpetersalzsäure, *G.*

"Nitric Acid, 60 millilitres; Hydrochloric Acid, 80 millilitres; Distilled Water, 500 millilitres. Mix the Acids with the Distilled Water, and keep the mixture in a glass-stoppered bottle for fourteen days before use." *Br.*

The U. S. IX recognized two strengths of this acid but both of them were dismissed at the latest revision, which was, in our judgment, an unfortunate omission. They are, however, recognized by the N. F. (see Part III).

The stronger of these, *Acidum Nitrohydrochloricum,* is the fluid known to the ancients as *aqua regia* from its power of dissolving gold. It differs from the Br. solution not only in being much stronger but in having a very different proportion of the two acids. The diluted nitrohydrochloric acid of the N. F. is decidedly weaker than the British formula.

$$HNO_3 + 3HCl = NOCl + Cl_2 + 2H_2O$$

Nitrosyl chloride is a ruby-red volatile liquid. In aqueous solution it is decomposed forming nitrous and hydrochloric acids.

It is evident, therefore, that aqua regia is a very complex mixture containing, besides some undecomposed hydrochloric and nitric acids, varying amounts of nitrosyl chloride, free chlorine and nitrous acid, according to the age of the mixture and the conditions under which it has been preserved. The age of the mixture can be approximately gaged by the color. When freshly made it is of a deep golden-yellow verging almost on the orange. The color gradually becomes less and less passing through a lemon-yellow to almost complete colorlessness.

As the peculiar virtues of the mixture probably reside largely in the nitrosyl chloride and free chlorine only solutions of a golden-yellow color should be dispensed; it is preferably made fresh at the time of dispensing.

For an apparatus for making nitrohydrochloric acid upon a large scale, see *P. J.*, xi, 422.

The power of nitrohydrochloric acid to dissolve gold and similar metals having a weak affinity for oxygen, is owing exclusively to the free chlorine present, and is in no wise dependent on the compound above referred to, which remains entirely passive during the solution of the metal. When nitrohydrochloric acid is made from too strong acids, there is always a loss of the nitrosyl chloride and of free chlorine by effervescence, in consequence of the acids not containing sufficient water to hold the gaseous products in solution; on the other hand when diluted acids are used the reaction does not take place and no nitrosyl chloride or chlorine are produced.

Properties.—The strong "Nitrohydrochloric Acid is a golden-yellow, fuming, and very corrosive liquid; it has a strong odor of chlorine and is intensely acid to litmus, afterwards bleaching it. It readily dissolves gold leaf." *U. S. IX.*

The diluted acid is pale yellow or colorless. "Specific gravity 1.07. 10 millilitres require for neutralisation about 26.6 millilitres of *N/1 solution of sodium hydroxide.*" *Br.*

It should be kept in a cool dark place, on account of its liability to lose chlorine by heat, and to have its chlorine converted into hydrochloric acid by the action of light and the decomposition of water. On account of its tendency to decomposition, it should not be made in large quantities, nor be kept very long by the apothecary; and care should be taken not to transfer it to the bottle in which it is to be dispensed, until effervescence has ceased, lest the pressure within should drive out the stopper or an explosion should occur.

Uses.—Nitrohydrochloric acid, like other mineral acids, is capable of activating pepsin and may be used in cases of *subchlorhydria.* In addition, there is considerable evidence that it increases the flow of bile and is useful in cases of mild *cholangitis* and other conditions in which there is deficiency of this secretion in the intestinal tract. There is reason to believe that its power in increasing the flow of bile is due to a relaxing of the sphincters of the bile duct and permitting the easier emptying of the gall bladder. It has therefore been employed in cases of *cholecystitis* and has even been asserted to be effective in promoting the passage of *biliary calculi.* Formerly it was applied externally either by sponging or in the form of a local or general bath but is at present rarely so used. It has also been lauded as a valuable remedy in *oxaluria.*

The best results are obtained from a freshly prepared acid. It should be given well diluted, after meals, care being exercised to prevent its injuring the teeth. It should never be prescribed in combination with strong alcoholic liquids undiluted, as gases may be generated in sufficient volume to cause explosion. Its incompatibilities are the same as strong nitric acid and strong hydrochloric acid with the added factor of the free chlorine which liberates bromine and iodine from bromides and iodides respectively.

Dose, of the Br. preparation, five to twenty minims (0.3–1.2 cc.)

ACIDUM OLEICUM. U. S., Br.

OLEIC ACID Acid. Oleic.

"Oleic Acid is obtained from fats, and consists chiefly of $C_{17}H_{33}COOH$." *U. S.* "Oleic Acid may be obtained by the saponifying action of alkalies and subsequent action of acids, or by the action of superheated steam upon commercial oleins." *Br.*

Acidum oleinicum, Acidum elainicum; Elaic acid; Acide oléique, *Fr.;* Oleinsäure, Elainsäure, Oelsäure, *G.*

This acid, although known for many years, was not used medicinally until 1872 (*L. L.*, 1872, 709), when John Marshall introduced the oleates to the profession as substitutes for some of the older ointments. (See *Oleata.*)

Preparation.—The difficulty in preparing oleates of good quality arises usually from the use of the commercial oleic acid, which, being obtained as a by-product in the manufacture of glycerin and candles, has a reddish-brown color and a disagreeable fatty odor. It is almost always contaminated with stearic and palmitic acids, with undecomposed glycerides when obtained by the autoclave process, and hydrocarbons when obtained by the distillation of the fat acids. Various processes have been suggested for the purification of oleic acid. Charles Rice (*A. J. P.*, xlv, 2) exposes the commercial acid to a temperature of 4° C., and expresses the liquid portion which is oleic acid deprived of the greater part of the contaminating substances. The odorous and coloring principles are not removed by this process. A writer in *A. J. P.* (xlv, 97) prepares oleic acid for making oleates by saponifying almond oil with potassium hydroxide; decomposing by tartaric acid, separating the precipitated bitartrate, heating for several hours on a water bath with half its weight of finely powdered lead oxide; after cooling, mixing with three times its volume of ether, settling, decanting, and treating the residue with ether as before; agitating the mixed ethereal solution with diluted hydrochloric acid; skimming off the ethereal solution of oleic acid, washing it with water, reskimming, and recovering the ether by distillation. Modifications of this method are described in *U. S. P.*, 20th ed., p. 53. Commercially, oleic acid is now obtainable by the process of decomposition of fatty oils by the action of enzymes. For this purpose, the ferment of the castor oil bean has proven most efficient. Connstein has described the technical application of this process in a paper read at the *International Congress of Applied Chemistry,* held at Berlin in 1903. (Vol. ii, p. 537.) For a paper on the esterification of oleic acid in the presence of a pancreatic ferment, by H. Pottevin, see *P. J.,* 1904, 492.

Low grade oleic acids, obtained by the distillation of wool-grease, etc., may contain cholesterin and other unsaponifiable materials from this source (Allen). Commercial oleic acid is often adulterated with linoleic acid. Hazura claims to be able to show the presence of one per cent. of this by saponifying the mixture and then adding potassium permanganate. (For details see *A. J. P.,* 1889, p. 356.) Grandval and Valser (*Chem. News,* 1890, p. 85) give the following tests for linoleic acid: If a thin layer of the fraudulent oleic acid be placed upon a slip of lead scraped quite clean, and some pure oleic acid be put upon a similar slip of lead for comparison, the next day the impure acid will be more or less resinified, while the pure acid will be scarcely altered. If some drops of oleic acid adulterated with linoleic acid be mixed with an equal volume of soda lye, an intense yellow color will be produced; pure oleic acid, if similarly treated, will merely take a grayish tint.

Description and Physical Properties.—" A pale yellow or brownish-yellow, oily liquid. It has a peculiar lard-like odor and taste, but is free from disagreeable odor. On exposure to air it absorbs oxygen and becomes darker. Oleic Acid is almost insoluble in water, but is miscible with alcohol, chloroform, ether, benzene, petroleum benzin, and with fixed or volatile oils. Specific gravity: about 0.895 at 25° C. On heating strongly, Oleic Acid is decomposed with the formation of acrid vapors.

" When cooled to about 4° C., it congeals to a whitish solid or nearly solid mass. The ash from 5 cc. does not exceed 0.005 Gm. When gradually cooled, Oleic Acid does not become cloudy above 10° C. (*stearic acid*). Shake 5 cc. of Oleic Acid with an equal volume of distilled water, allow the liquids to separate, and filter through a paper filter moistened with water: the filtrate is not reddened by the addition of a drop of methyl orange T.S. (*mineral acids*). Boil 1 cc. of Oleic Acid with about 0.5 Gm. of sodium carbonate and 30 cc. of distilled water in a capacious flask: the resulting solution, while hot, is clear or at most opalescent (*neutral fat or mineral oils*).

" Preserve in well-closed glass or stoneware containers, in a cool place." *U. S.*

According to Dieterich, pure oleic acid has the iodine figure 89.8 to 90.05 and commercial oleic acid 65.03 to 86.18.

" A straw-colored liquid, occasionally with a faintly rancid odor. Insoluble in *water,* but readily soluble in *alcohol* (90 per cent.), in *chloroform,* or in *ether.* When cooled it does not become semi-solid until the temperature has fallen below 9° C. Specific gravity 0.890 to 0.910." *Br.*

Oleic acid has been the originating factor in spontaneous combustion of fibers to which it had been applied. The primary cause was attributed to the presence of ferric oxide as a contamination. This acted as a catalyzer. (*J. I. E. C.,* 1918.)

Chemical Constitution.—Oleic acid, $C_{18}H_{34}O_2$, does not belong to the " fatty acid " series, but differs from the corresponding acid of that series, stearic acid, $C_{18}H_{36}O_2$, by having two atoms less of hydrogen. It belongs to a series derived by oxidation from alcohols which, like allyl alcohol, C_3H_5OH, have two atoms of hydrogen less than the normal monatomic alcohols, like propyl alcohol, C_3H_7OH. The alcohol from which oleic acid is in theory derivable is not, however, known. Oleic acid is monobasic, as shown in the formula $HC_{18}H_{33}O_2$. Oleic acid and its compounds are now converted into fatty acid of the higher series, which are solid instead of liquid, by a method known as " hydrogenation " which consists of the application of nascent hydrogen in the presence of metallic nickel which is used as a catalyzing agent. (For further information see under *Olea Fixa.*)

Uses.—Oleic acid is used only in preparing the oleates and in ointments.

Oleic acid is incompatible with alkalies with which it forms soaps, and with oxidizing agents which effect its decomposition.

ACIDUM PHOSPHORICUM. U. S. (Br.)

PHOSPHORIC ACID Acid. Phos.

" Phosphoric Acid contains not less than 85 per cent. and not more than 88 per cent. of H_3PO_4." *U. S.* " Concentrated Phosphoric Acid is a liquid containing 66.3 per cent. by weight of hydrogen orthophosphate, H_3PO_4, and 33.7 per cent. by weight of water. It may be obtained by the oxidation of phosphorus." *Br.*

Acidum Phosphoricum Concentratum, *Br.;* Concentrated Phosphoric Acid; Orthophosphoric Acid; Acide Phosphorique, *Fr.;* Acidum phosphoricum, *P. G.;* Phosphorsäure, *G.;* Acido fosforico, *It., Sp.*

The U. S. P. has very properly abandoned the former official process for this acid; it is more profitably and conveniently made on a large scale, and with such precautions and safeguards as cannot be easily used by the apothecary; the U. S. P. 1880 process will be found upon page 77, U. S. D., 18th edition.

The U. S. X retained the strong acid termed " 85 per cent. phosphoric acid " and the Br. (1914) retained the 66.3 per cent. acid so that the U. S. acid is about 20 per cent. stronger than that of the Br. That of the German Pharmacopœia is only 25 per cent. The glacial phosphoric acid is no longer official, it having been shown that it is practically impossible to obtain it of sufficient purity to be reliable. The present syrupy acid is a great improvement in every way, as it can be obtained of undoubted purity and strength, and by the addition of water, diluted phosphoric acid of any desired strength can easily be produced from it.

The process for its preparation is the well-known one of oxidizing phosphorus by the use of nitric acid, the former British method not differing materially from that of the U. S. Pharmacopœia of 1880, except in the absence of the use of hydrogen sulphide for precipitating the arsenical compounds usually found in phosphorus, and in the greater strength of the finished product.

It has been suggested that red phosphorus might be substituted for common phosphorus, as producing the same results, with less danger of explosion; but the former official process, when carefully followed in reference to due dilution and a moderate heat, is not dangerous. Phosphorus is oxidized at the expense of the nitric acid, any excess of nitric acid and all the lower oxides of nitrogen being driven off by heat. Strong nitric acid acts too energetically on phosphorus, producing explosion and rapid combustion, but when diluted it yields its oxygen slowly, and it is even desirable to aid the operation with a gentle heat. It may also be made by dissolving phosphorus pentachloride or phosphorous oxychloride in hot water.

$$P_2Cl_5 + 4H_2O = H_3PO_4 + 5HCl$$

or

$$POCl_3 + 3H_2O = H_3PO_4 + 3HCl$$

Another method of manufacture is by the use of bone ash and sulphuric acid in molecular proportions.

Much dissatisfaction was at one time caused among pharmacists by the fact that diluted phosphoric acid frequently produces a white precipitate in solutions of ferric salts. An examination proved that this occurred when the glacial acid is used, or when high heat had been employed in the concentration. Experiments conducted by Louis Dohme and Remington indicated that the precipitation resulted from the presence of pyrophosphoric acid. (*Proc. A. Ph. A.*, 1874, 431, 511; 1875, 667.) Considerable difficulty was experienced in driving off all the nitric acid, and in the attempt to do so the temperature became so elevated as to reconvert some of the tribasic acid to the dibasic form. This occurred slightly at 148.8° C., but to a much greater extent between 176.6° C. and 204.4° C. The diluted acid, made from phosphorus, can be brought to the boiling point of 232.2° C. and will then only produce a slight cloud with tincture of ferric chloride, but if diluted, when cool, with about half its bulk of cold water, which causes considerable elevation of temperature, it forms a clear solution. The same acid evaporated, heated to redness, allowed to congeal, and then dissolved in water, precipitated the iron solution. The addition of twenty per cent. of sodium pyrophosphate to the same diluted acid made a preparation which in all respects resembled that made from the glacial acid, thus giving evidence that the presence of this contamination was the cause of the difference in the two preparations.

Description and Physical Properties.—" A colorless, odorless liquid of a syrupy consistence. Phosphoric Acid is miscible with water and with alcohol. When heated, the liquid loses water, and at 200° C. gradually changes to pyrophosphoric acid. At a still higher temperature (about 300° C.) it is converted into metaphosphoric acid, which either volatilizes as dense fumes, or forms, on cooling, a transparent mass of metaphosphoric acid. Specific gravity: about 1.71 at 25° C.

" Phosphoric Acid is strongly acid to litmus paper, even when highly diluted. Phosphoric Acid carefully neutralized with sodium hydroxide T.S. responds to the reactions for phosphates. Render 3 cc. of the dilution alkaline with ammonia T.S., and add magnesium sulphate T.S. (or magnesia mixture T.S.): a white, crystalline precipitate of magnesium-ammonium phosphate is produced. Collect this precipitate, wash it, and then dissolve it in diluted acetic acid: the solution yields a yellow precipitate with silver nitrate T.S. (*distinction from metaphosphoric or pyrophosphoric acid*).

" Phosphoric Acid diluted with 14 volumes of distilled water conforms to the following tests: Warm 5 cc. of the dilution gently, and add 2 cc. of silver nitrate T.S.: the mixture does not become brown (*phosphorous or hypophosphorous acid*). A 10 cc. portion of the dilution meets the requirements of the test for *heavy metals.* A 2 cc. portion of the dilution meets the requirements of the test for *arsenic.* The dilution is not immediately affected by silver nitrate T.S. (*hydrochloric acid*), nor is it affected even after one hour by the addition of an equal volume of tincture of ferric chloride (*pyrophosphoric or metaphosphoric acid*). Mix 1 cc. of the dilution with 6 cc. of distilled water, and add 1 cc. of barium chloride T.S.: no precipitate is produced immediately (*sulphate*). Mix 5 cc. of the dilution with an equal volume of ferrous sulphate T.S., and superimpose the mixture upon 3 cc. of sulphuric acid contained in a test tube: the zone of contact does not assume a brown or brownish-red color (*nitrate*). Transfer 1 cc. of Phosphoric Acid to a graduated cylinder, and add 6 cc. of ether and 2 cc. of alcohol: no turbidity appears (*phosphates*).

" Preserve in glass-stoppered bottles." *U. S.*

Assay.—" Pour about 1 Gm. of Phosphoric Acid into a tared, 100 cc. volumetric flask, weigh accurately, and add enough distilled water to make 100 cc. Transfer 10 cc. of this solution to a 100 cc. volumetric flask, add a drop of phenolphthalein T.S., and neutralize the mixture with special sodium hydroxide T.S. Add 50 cc. of tenth-normal silver nitrate from a burette while gently shaking. Mix a small amount of reagent zinc oxide with distilled water and gradually add the mixture, in small portions, until the liquid is neutral to litmus paper. Now add distilled water to make the liquid measure 100 cc., mix well, and filter through a dry filter, rejecting the first 5 cc. Transfer 50 cc. of the filtrate with a pipette to a flask, add 2 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S., and determine the excess of silver nitrate by titration with tenth-normal potassium thiocyanate to the production of a permanent red color. Each cc. of tenth-normal silver nitrate corresponds to 0.003269 Gm. of H_3PO_4." *U. S.*

"A colorless, syrupy liquid with an acid taste and reaction. Leaves, on evaporation, a residue which melts at a low red heat, and when cold forms a glass-like mass. Yields, when neutralised, the *reactions* characteristic of phosphates. Specific gravity 1.5. 1 gramme mixed with a solution of 5 grammes of *sodium chloride* in 20 millilitres of *water* requires for neutralisation 13.5 millilitres of *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. Yields when diluted with *water* no characteristic *reactions* for copper, calcium, chlorides, or nitrates, and not more than slight *reactions* for iron or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Uses.—This acid is used in making phosphates and lactophosphates. It has the same medicinal properties and uses as the diluted phosphoric acid making allowance for the difference in strength but is practically never prescribed.

Off. Prep.—Acidum Phosphoricum Dilutum, *U. S., Br.;* Liquor Phosphatum Acidus, *N. F.;* Liquor Phosphatum Compositus, *N. F.*

ACIDUM PHOSPHORICUM GLACIALE.—(*Glacial Phosphoric Acid; Metaphosphoric Acid; Monobasic Phosphoric Acid; Monohydrated Phosphoric Acid; Acide phosphorique glaciale,* Fr.; *Glasige Phosphorsaure,* G.) Formula HPO_3; mol. wt. 79.41.—Phosphoric oxide consists of two atoms of phosphorus and five atoms of oxygen, P_2O_5, and can be obtained only by the direct union of its constituents, which takes place when phosphorus is burned in perfectly dry oxygen gas. Thus procured, it is in the form of a white amorphous powder, extremely deliquescent, volatilizable at a red heat, and assuming, when it cools after fusion, a vitreous appearance. The classic researches of Graham first established clearly the character of the several varieties of phosphoric acid, which may be considered as derived from this oxide.

When amorphous phosphorus is boiled with nitric acid, or when phosphoric oxide is boiled with water, the oxide takes up three molecules of water, and yields tribasic or *ordinary phosphoric* acid according to the reaction:

$$P_2O_5 + 3H_2O = H_6P_2O_8 \text{ or } (H_3PO_4)_2$$

If this acid be heated for a considerable time to 215° C., the two molecules lose one molecule of water and yield *pyrophosphoric acid,* a tetrabasic variety, according to the reaction:

$$H_6P_2O_8 - H_2O = H_4P_2O_7$$

Lastly, at a red heat the ordinary phosphoric acid is converted into *metaphosphoric acid,* a monobasic variety, according to the reaction:

$$H_3PO_4 - H_2O = HPO_3$$

This last variety may also be obtained direct from the oxide by dissolving it in cold water, when it takes up one molecule of water:

$$P_2O_5 + H_2O = H_2P_2O_6 \text{ or } (HPO_3)_2$$

An aqueous solution of either of the two acids of higher basicity, heated so long as water escapes, yields the metaphosphoric acid; and as, upon cooling, it becomes a transparent ice-like solid, it has received in this state the name of glacial phosphoric acid. Conversely, this monobasic acid is slowly transformed, in aqueous solution, and more rapidly if the solution is heated, into the tribasic form. John M. Maisch ascertained that nitric acid, added to the solution of the monobasic acid, with the aid of heat, caused the change from the monobasic to the tribasic form, *i.e.,* to the common phosphoric acid, without the intermediate production of the tetrabasic variety. *Pyrophosphorous acid,* $H_4P_2O_5$, has been obtained by V. Auger in the form of colorless needles, melting at 38° C. (*C. R. A. S.,* cxxxvi, 814.)

The three forms of phosphoric acid are distinguishable by peculiar reactions. Thus, the monobasic is characterized by coagulating albumin, and giving white, gelatinous, uncrystallizable precipitates with the soluble salts of barium, lime, and silver; the tetrabasic does not coagulate albumin, and, though it causes a white precipitate with silver nitrate, must first be neutralized; the tribasic does not coagulate albumin, and, until neutralized, does not precipitate silver nitrate, but after neutralization throws down a yellow precipitate of silver phosphate.

Glacial phosphoric acid is most advantageously obtained from calcined bones, by first treating them with sulphuric acid, which produces an insoluble calcium sulphate and soluble acid phosphate; then dissolving out the latter salt, and saturating it with ammonium carbonate, which generates ammonium phosphate in solution; and, finally, obtaining the ammonium phosphate by evaporation to dryness, and then igniting it in a platinum crucible. The ammonia and all the water except the one molecule needed for the formation of metaphosphoric acid are driven off, and the glacial acid remains.

Properties.—Glacial phosphoric acid is in the form of a white, uncrystallizable, fusible solid; inodorous, very sour to the taste, slowly deliquescent, slowly soluble in water, and soluble also in alcohol. Its formula is HPO_3, and it is made up of 11.2 per cent. of water in combination with 88.8 per cent. of phosphoric oxide.

Impurities.—Glacial phosphoric acid is very little used at the present time. For further information concerning its adulterations, etc. See *U. S. D.*, 20th ed., p. 58.

ACIDUM PHOSPHORICUM DILUTUM. U. S., Br.

DILUTED PHOSPHORIC ACID Acid. Phos. Dil.

"Diluted Phosphoric Acid is an aqueous solution containing not less than 9.5 per cent. and not more than 10.5 per cent of H_3PO_4." *U. S.* "Diluted Phosphoric Acid contains 10 per cent. by weight of hydrogen orthophosphate, H_3PO_4." *Br.*

Acide phosphorique médicinale, *Fr.*: Verdünnte Phosphorsäure, *G.*

"Phosphoric Acid, 116 Gm.; Distilled Water, 884 Gm.; to make 1000 Gm. Mix them." *U. S.* "Concentrated Phosphoric Acid, 159.5 grammes; Distilled Water sufficient to produce 1000.0 millilitres. Mix." *Br.*

Properties.—Diluted phosphoric acid is a colorless, inodorous, sour liquid, acting strongly on litmus, and possessing powerful acid properties, although when evaporated so as to become dense, it is not corrosive like the other mineral acids. Neubauer found that the strong acid, when pure and warm, was capable of dissolving calcium oxalate.

Description and Physical Properties.—"A clear, colorless, odorless liquid. Specific gravity: about 1.057 at 25° C.

"Diluted Phosphoric Acid is strongly acid to litmus paper. Evaporate 20 cc. of Diluted Phosphoric Acid on a water bath to a volume of 4 cc. Cool, transfer 2 cc. to a graduated cylinder, and add 6 cc. of ether and 2 cc. of alcohol: no turbidity appears (*phosphate*). Diluted Phosphoric Acid conforms to the other tests for identity and purity under *Acidum Phosphoricum.*

"Preserve in well-stoppered bottles.

"**Assay.**—Pour about 1 Gm. of Diluted Phosphoric Acid into a tared, 100 cc. volumetric flask, weigh accurately, add a drop of phenolphthalein T.S., and neutralize the mixture with special sodium hydroxide T.S. Add 50 cc. of tenth-normal silver nitrate, and proceed as directed in the assay under *Acidum Phosphoricum.* Each cc. of tenth-normal silver nitrate corresponds to 0.003269 Gm. of H_3PO_4." *U. S.*

"Specific gravity 1.057. 10 millilitres mixed with a solution of 5 grammes of *sodium chloride* in 20 millilitres of *water* require for neutralisation 21.6 millilitres of *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator." *Br.*

Bauzil suggests the assay of phosphates by precipitation with magnesia mixture and titration of the suspended precipitate with tenth-normal hydrochloric acid. He also gives minute directions for assaying for phosphates in urine. (*J. P. C.*, 1917, p. 321.)

Phosphorous acid may be detected by testing the medicinal acid with a solution of corrosive sublimate, which will be converted into calomel if this impurity be present.

Old diluted phosphoric acid is very apt to contain microscopic plants. The presence of traces of hydrochloric acid is said to prevent their formation. (Rother, D. C., 1886, p. 99; L. E. Sayre, *Proc. A. Ph. A.*, 1885.)

Uses.—Diluted phosphoric acid, like other mineral acids, is capable of replacing the hydrochloric acid in peptic digestion and is a useful drug, therefore, in certain types of *dyspepsia.* It is doubtful, however, whether it possesses any advantage over diluted hydrochloric acid.

It has been shown that the utilization of calcium by the body is dependent upon an ample supply of phosphates and consequently, phosphoric acid and its salts may be useful in various diseases of the bone in which there is a deficiency of lime deposition. It may, perhaps, have a similar value in certain nervous diseases when there is calcium deficiency. Schmitz (*B. K. W.*, 1922, l, 432) has found, from experiments on soldiers and mine-workers, that the salts of phosphoric acid increase muscular vigor.

The neutrality of the blood is maintained in part by the "buffer" action of the phosphates; when there is an abundance of base the phosphoric acid exists in the blood as a neutral salt, but if, for any reason there is an increased formation of acid in the body, the blood yields a part of the base from its phosphate the excess of phosphoric acid being excreted by the kidney. For this reason phosphoric acid affords one of the least injurious means of increasing the acidity of the urine and it has therefore been used in the treatment of *phosphatic deposits* and certain types of *cystitis.* Generally, however, the monobasic sodium phosphate is preferred for this purpose to the acid itself. (See *Sodii Phosphas Acidum*).

Diluted phosphoric acid is incompatible with salts of silver, lead, and mercury, and also with many compounds of iron, aluminum and calcium, insoluble precipitates being formed unless the acid be much in excess in which case the precipitate may redissolve.

Dose, from fifteen to sixty minims (0.9–3.75 cc.) well diluted.

ACIDUM SALICYLICUM. U. S., Br.

SALICYLIC ACID Acid. Salicyl.

"Salicylic Acid, dried at 100° C. for two hours, contains not less than 99.5 per cent. of $C_6H_4(OH).COOH$ 1:2." *U. S.* "Salicylic Acid, $HC_7H_5O_3$, may be obtained from natural salicylates such as the oils of winter-green (Gaultheria procumbens, *Linn.*) and sweet-birch

(Betula lenta, *Linn.*), or by the interaction of sodium phenate and carbon dioxide." *Br.*

Ortho-oxybenzoic Acid; Acidum Spiricum; Acidum oxybenzoicum; Acide Salicylique, *Fr.;* Acidum salicylicum, *P. G.;* Salicylsäure, Spirsäure, Salicoylsäure, Spiroylsäure, *G.;* Acido salicilico, *It., Sp.*

In 1834 *salicyl aldehyde* (so-called *salicylous acid*) was discovered by Pagenstecker in the flowers of *Spiræa Ulmaria,* L. In 1837, Piria and Ettling found that by oxidizing agents salicyl aldehyde was converted into a new body, salicylic acid, and in 1839, Löwig and Weidmann derived the latter principle directly from the flowers of the *Spiræa Ulmaria* L. Shortly afterwards Procter (*A. J. P.*, 1843; Aug., 1875) discovered that the acid could be procured from the oil of wintergreen (*Gaultheria procumbens* L.), which is now known to contain over 98 per cent. of methyl salicylate. Methyl salicylate is indeed obtainable by distillation from very many plants, but the probabilities are that it never exists already formed in the plant, but is produced during the process of distillation. (See *Oleum Gaultheriæ.*) When potassium hydroxide is added to methyl salicylate, potassium salicylate is formed, and methyl alcohol is also produced. If this latter be volatilized by heating, the acid is readily obtained by means of hydrochloric acid. Notwithstanding the discovery of this fact, and also the invention of still another process of manufacture by Ettling in 1845, salicylic acid remained so expensive as to be of no value in the arts until Kolbe and Lautemann discovered that it could be prepared by uniting phenol with carbon dioxide through the instrumentality of sodium. The article now began to attract some attention, but remained beyond the reach of general use until Kolbe, by continuing his researches, succeeded, in 1874, in producing it at a moderate cost. Traphagen and Burke found salicylic acid to be a natural constitutent of many fruits, as follows: strawberries, raspberries, blackberries, currants, plums, black cherries, apricots, peaches, grapes, crab apples, apples, and oranges. (*J. Am. C. S.*, 1903, 242.) In none of these, however, can it be detected by the ordinary tests in the proportions in which these substances are used in testing for the presence of salicylic acid which may have been used as a preservative.

Preparation.—While salicylic acid may be prepared from salicin by fusion with potassium hydroxide, or from oil of wintergreen by saponification with potassium hydroxide solution, practically it is usually obtained, according to Kolbe's patent, by treating sodium phenate (or carbolate) with carbon dioxide gas. For this purpose, the most concentrated caustic soda solution is evaporated with the corresponding amount of phenol to a dry powder, which is then heated to 100° C., while a stream of dry carbon dioxide gas is passed over it. The temperature is gradually raised to 180° C., increased to 220° C. as soon as phenol distils over, and finally raised to 250° C., until no more phenol distils. In the retort, the half of the phenol used remains as basic sodium salicylate, while the other half has distilled over unchanged. The reaction is as follows:

$$2C_6H_5ONa + CO_2 = C_6H_5OH + C_6H_4(ONa)COONa$$

The sodium salt thus obtained is dissolved in water, decomposed by hydrochloric acid, the salicylic acid filtered off, washed, and crystallized out of hot water, or purified by sublimation in a current of superheated steam. P. W. Hofmann subsequently patented a process whereby distillation with superheated steam, with its attendant loss, is obviated; to the crude solution is added stannous chloride, which precipitates a dark mass containing the impurities, the clear supernatant liquid is then decomposed with hydrochloric acid and the crystals of salicylic acid purified by washing and the use of centrifugals. (*Ph. Centralh.*, 1892, 412.) An important improvement was subsequently made in Kolbe's process whereby all, instead of only half, of the phenol-sodium is converted into salicylate. R. Schmitt has found (Wagner's *Jahresbericht für Chem. Tech.*, 1885, p. 490) that if dry sodium phenolate and dry carbon dioxide are allowed to act on each other at ordinary temperatures, as long as absorption takes place a phenyl-sodium carbonate, $CO\left\{\begin{matrix}OC_6H_5\\ONa\end{matrix}\right.$, is formed. If this is heated for several hours in a closed vessel to 140° C., a molecular rearrangement takes place, and simple sodium salicylate, $C_6H_4(OH)COONa$, is formed without any separation whatever of phenol.

Lloyd's process for preparing salicylic acid from oil of wintergreen is as follows: Pure wintergreen oil, 3 parts; white potassium hydroxide, 3 parts; hydrochloric acid, 8 parts; water, q. s. Dissolve the potassium hydroxide in two parts of water in a glass or porcelain vessel, and heat to the temperature of 82.2° C. Stir into this gradually the oil, using a glass or porcelain spatula. Into another vessel place 64 parts of cold distilled water, and add the hydrochloric acid. Then with constant stirring add the solution of the potassium salicylate. The magma of minute crystals of salicylic acid must be separated with a thin muslin strainer (previously moistened) and pressed, then dried by exposure to a temperature of 65.5° C. Dissolve this crude acid in six parts of cold alcohol, filter through a funnel stopped with cotton and, with constant stirring, pour the filtrate into 32 parts of cold water. The purified crystals may be separated by straining through muslin, and dried by exposure to a heat of 65.5° C. The yield is a trifle less than 2 parts. For Walter's process, see *Bull. Pharm.*, 1899, 54.

Salicylic acid has also been obtained synthetically from copper benzoate and water, which, when heated together in sealed tubes, yield cuprous oxide, free benzoic acid, and salicylic acid. (E. F. Smith, *Am. Chem. J.*, ii, p. 338). A. Rautert has found that the acid volatilizes with steam of 170° C., and has devised a process of purification based upon this, which yields at very little cost a beautiful product. Biel (*Ph. Z. R.*, 1876) reports that the sublimed acid is liable to decompose spontaneously. Dialyzed salicylic acid of beautiful appearance has been in the market since 1876. All traces of tarry matter can be removed by dialysis, and this acid is unexceptionable. Kolbe also obtained salicylic acid from barium and calcium carbolates, but the yield was less than when sodium salt was employed. Potassium phenol yielded only a trace of salicylic acid, but an abundance of *paraoxybenzoic* acid.

Description and Physical Properties.—" Fine needles, or a bulky crystalline powder. It has a sweetish, afterwards acrid taste, and is stable in the air. Synthetic Salicylic Acid is white and odorless. When prepared from natural methyl salicylate, the Acid may have a slightly yellow or pink tint, and a faint, gaultheria-like odor. One Gm. of Salicylic Acid is soluble in 460 cc. of water, 2.7 cc. of alcohol, 42 cc. of chloroform, 3 cc. of ether, 3 cc. of acetone, 135 cc. of benzene, and in 52 cc. of oil of turpentine, at 25° C. One Gm. is soluble in about 15 cc. of boiling water.

" Salicylic Acid melts between 157° and 159° C. Salicylic Acid responds to the reactions for salicylates, page .

" Ash: not more than 0.05 per cent. Allow a solution of 1 Gm. of Salicylic Acid in 3 cc. of alcohol to evaporate spontaneously in a glass or porcelain dish, protected from dust: the synthetic Acid yields a white, crystalline residue, while the Acid prepared from natural methyl salicylate yields a white, or not more than a slightly yellow, or a slightly pink residue (*coloring matter*). Dissolve 1 Gm. of Salicylic Acid in an excess of cold sodium carbonate T.S., agitate the liquid with an equal volume of ether, separate the ether layer, and allow it to evaporate spontaneously: the residue, if any, is free from the odor of phenol. A solution of 0.5 Gm. of the synthetic Salicylic Acid in 10 cc. of sulphuric acid acquires not more than a light yellow color. The Acid prepared from natural methyl salicylate under similar conditions may produce a slightly brown color (*readily carbonizable substances*). Dissolve 0.5 Gm. of Salicylic Acid in 10 cc. of alcohol containing a few drops of nitric acid: the solution is unaffected by the addition of a few drops of silver nitrate T.S. (*chloride*).

" **Assay.**—Dissolve about 0.5 Gm. of Salicylic Acid, previously dried at 100° C. for two hours and accurately weighed, in 25 cc. of diluted alcohol, which previously has been neutralized with tenth-normal sodium hydroxide, using phenolphthalein T.S. as indicator. Titrate the solution with tenth-normal barium hydroxide until the pink color is restored. Each cc. of tenth-normal barium hydroxide corresponds to 0.01381 Gm. of $C_6H_4(OH).COOH$." *U. S.*

" Distinct, prismatic, colorless crystals. Taste at first sweetish, then acid, leaving a burning sensation in the throat. Soluble in about 500 parts of *water*, in 3.5 of *alcohol* (90 per cent.), or in 2 of *ether*. Melting point 156° to 157° C. Carefully heated it volatilises without decomposition. Dissolves in *solution of ammonium acetate*, and in *solution of sodium phosphate*. *T. Sol. of ferric chloride* gives with the aqueous solution a violet color, or, if the solution be largely diluted, a reddish-violet color. Shaken with a small proportion of water, the mixture filtered, and the solution evaporated, there remains a white residue, having no buff-tinted fringe (absence of iron, organic impurities, and coloring matter). Salicylic Acid dissolves in cold *sulphuric acid*, imparting to the liquid not more than a faint brownish tint in fifteen minutes (absence of certain organic impurities). When 1 gramme of the Acid is dissolved in an excess of cold *solution of sodium carbonate*, the liquid shaken with an equal volume of *ether*, and the ethereal solution allowed to evaporate spontaneously, the residue, if any, is free from the odor of phenol (absence of phenol). *Arsenic limit* 2 parts per million. No appreciable ash." *Br.*

When heated rapidly it is converted into phenol and carbon dioxide. Although salicylic acid requires 500 parts of water for its solution at 20° C. it is stated that, by careful heating, glycerin can be made to dissolve 1 part in 50, and that the solution not only remains clear on cooling, but also may be diluted with water without separating. Goldsborough affirms that a mixture of the acid with alcohol, 1 to 10, may be diluted with 150 parts of water without crystallizing. By the presence of various neutral salts its solubility is increased without its antiseptic value being interfered with. It dissolves when mixed with 1 part of potassium nitrate, in 50 parts water; 1½ parts of ammonium citrate, in 60 parts water; 2 parts sodium sulphite, in 50 parts water; 2 parts sodium phosphate, in 50 parts water; 2½ parts sodium phosphate, in 12½ parts water. (See Allen, *Com. Org. Anal.*; also Rother, *A. J. P.*, 1886, p. 420.) The solubility of salicylic acid in fixed oils is very slight with the exception of castor oil with which a solution containing as much as 15 per cent. can be made.

On distilling salicylic acid or one of its salts with methyl alcohol and sulphuric acid, acid methyl salicylate is formed, having an agreeable aromatic odor. The reaction with ferric salts is much more delicate (1 in 100,000) than that of phenol with the same reagent (1 in 3000). Commercial salicylic acid was formerly very impure. Sodium chloride, phenol, cresotic acid, and oxybenzoic and paraoxybenzoic acids were the usual impurities. These may be detected by the official tests.

The most sensitive test for it is a ferric salt, with which it develops a beautiful violet color. Goldsborough states that to insure the delicacy of this reaction it is necessary that the iron salt be perfectly neutral; also that with this precaution he has clearly detected 1 part of the acid in 400,000 parts of water. On the addition of ammonia the violet color is changed to a reddish-brown, then to an orange, then to a permanent greenish-yellow. Sulphuric and nitric acids change the violet to a light brown (Goldsborough). It must be remembered that *salicylous acid* (salicylic aldehyde, C_6H_4OHCHO) reacts similarly with ferric salts. Salicylous acid, however, precipitates the silver potassio- or ammonio-nitrate white, the salicylic acid yellow. A. Fagans (*A. J. P.*, 1893, p. 133) points out that salicylic acid cannot be colorimetrically estimated in aqueous solutions in presence of phenols, but that in alcoholic solution only the former reacts with ferric chloride. M. Claasz (*A. Pharm.*, 1915, p. 360) has made an exhaustive study of the *iron salicylates* and has prepared the following varieties: *Ferrous disalicylate,* colorless crystals; *ferrous cresstinate,* white salt; *ferrous para-oxybenzoate* colorless crystals; *ferrous methoxy salicylate,* yellowish crystals; basic *ferrous salicylate,* yellowish green crystals; ferric disalicylate, a black mass; ferric ferri-salicylate, blackish crystals; basic ferric ferri-salicylate, rust colored crystalline powder; dibrom-compound of ferric ferri-salicylate violet powder; ferrous ferro-salicylate, yellow crystals. He states that the purple compound which is so characteristic of the identifying test for salicylic acid is a tetra-chlor compound of ferric ferri-salicylate.

By distilling with alcohol and strong sulphuric acid, salicylic acid forms methyl- and ethyl-salicylic acids.

Uses.—Salicylic acid is an active disinfectant distinctly superior to phenol in its antiseptic properties and probably also in its germicidal effects. De LaCroix (*A. E. P. P.*, 1881, xiii) found that in the proportion of one part in a thousand it was sufficient to prevent the growth of various bacteria, and Kolbe has shown that as little as 0.04 per cent. is sufficent to retard souring of milk. In the experiments of H. C. Wood, Jr. (*U. P. M. B.*, February, 1907), 0.5 per cent. killed the colon bacillus in five minutes' exposure, and De LaCroix found that one in four hundred was germicidal after one and one-half days' exposure. Like many other disinfectants it retards, and if in sufficient concentration arrests, enzymic fermentation. Locally salicylic acid is strongly irritant to mucous membranes and its irritant action can be demonstrated upon the skin. It has the peculiar property of softening and finally causing the separation of the horny matter of the epiderm.

In ordinary quantities when taken internally the salicylates exercise practically no effect upon the circulation nor respiration. It appears to act upon the central nervous system somewhat like the anilin derivatives, lessening painful sensation and also causing reduction in febrile temperature; in both of these actions, however, it is inferior in power to the coal-tar antipyretics. After full doses of salicylates there is a marked increase in the elimination of uric acid and in some cases also of other nitrogenous waste products. This seems to be due to increased activity of the kidney and not to hastened catabolism. This view is strongly indicated by the observations of Fine and Chase (*J. Bi. Chem.*, 1915, xxi, 371) that the uric acid of the blood is diminished, and by the studies of Hanzlik and Scott (*A. I. M.*, 1917, xix and xx) which have shown that large doses of salicylates have a markedly irritating effect upon the kidney—shown in human beings by the appearance of albumin and casts in the urine and a diminished ability to excrete phenolsulphonphthalein and confirmed in the lower animals by pathological evidence of nephritis.

Whether administered in the form of the acid itself or as one of its salts salicylic acid circulates in the blood almost entirely in the form of sodium salicylate. It was formerly believed that most of it united with glycocoll and appeared in the urine in the form of a new compound known as salicyluric acid but Hanzlik (*J. P. Ex. T.*, 1917, x, 461) maintains that this opinion was founded on improper chemical methods and that no salicyluric acid can be demonstrated in the urine. The urine often shows a greenish tinge from a small amount the salicylate being changed to pyrocatechin. According to Hanzlik and Wetzel (*J. P. Ex. T.*, 1919, xiv, 25) over 80 per cent. of the salicylic acid administered can be recovered as a salicylate from the urine in normal men. In diseased conditions accompanied with a heightened catabolism, such as fever and hyperthyroidism, the larger portion is destroyed in the body.

After large doses salicylic acid causes symptoms resembling those seen after quinine; there is fulness of the head, roaring in the ears often with headache and sometimes disturbances of hearing and vision. Nausea and vomiting—due to an action upon the emetic center—are also frequent symptoms of large doses. With toxic quantities these symptoms are intensified and there is usually a fall in the bodily temperature with profuse sweating, excessive restlessness passing into delirium, a slow pulse, with at first hurried and later depressed respiration.

Salicylic acid is used both for its local effect and its systemic action. Because of its relative insolubility in water it is rarely of service as a direct surgical germicide but *salicylated cotton* and gauze are widely used. This may be prepared by dissolving two ounces (62 Gm.) of salicylic acid in two pints (1 liter) of alcohol, diluting with twenty pints (9.5 liters) of water and saturating with this six and one-half pounds (2–4 kilogm.) of absorbent cotton, and drying. Wadding so prepared contains about 2.53 per cent. of salicylic acid. It is also widely used in the form of lotions and ointments in the treatment of various *skin diseases,* especially chronic *eczemas.* Its beneficial action in these conditions is due in part to its antiseptic effect and in part to its softening action upon the corneous layer of the skin. Because of this latter property it is also widely employed for the purpose of removing *corns.* Weinbrenner (*M. M. W.,* lxi) has obtained good results from the local application of crystalline salicylic acid to superficial *cancers* of the skin.

Internally salicylic acid and its salts are used as urinary antiseptics, analgesics, antipyretics, and in the treatment of various forms of rheumatism. As the neutral salicylates are almost without antiseptic influence and as salicylic acid in whatever form exhibited circulates in the blood only in combination with a base, it is evident that any antiseptic action in the urine must depend upon the decomposition of its salt by urinary acids with the liberation of free salicylic acid; therefore it is of service as a urinary antiseptic only when the urine is acid in reaction. As an analgesic or antipyretic it has the same range of usefulness as the aniline derivatives, but except in rheumatic conditions is distinctly inferior to them.

The most important use of the salicylates is in the treatment of various rheumatic conditions. There are two distinct groups of conditions to which the term *rheumatism* is applied. One of these groups, which includes *acute articular rheumatism* and *tonsillitis,* is of infectious origin; in the other group, are included various painful conditions of the muscles, nerves, or joints, occurring in persons of a *lithemic diathesis.* The cause of this latter group of disturbances is unknown. There has been a great deal of difference of opinion as to the mode of action and precise value of the salicylates in rheumatism. Some have maintained that the relief seen after their use was purely symptomatic and to be attributed entirely to the analgesic and antipyretic effects of the drug, while others have maintained that the action is truly curative and probably due to a direct influence upon the causative agent. Against the former view are the positive opinions of practitioners of wide experience based upon clinical observations and the failure of other analgesics, such as acetphenetedin, to produce similar effects; while against the theory of specificity stands the opinion of almost equally experienced clinicians and the failure of any acceptable explanation of its mode of action. Formerly the benefit of the salicylates in rheumatism was attributed to their power to increase the elimination of uric acid but as our present theories regard this as a result rather than a cause, at least in rheumatic fever, the explanation no longer suffices. Rheumatic fever to-day is commonly viewed as an infectious disease and some have attempted to ascribe the value of the salicylates to their antibacterial powers. Against this view, however, it has been urged that although the salicylic acid is a powerful germicide the neutral salts are but very feebly disinfectant and because of the alkalinity of the system the salicyl radical must circulate only in combination with a base. The theory, suggested in previous editions of this work, that there might be a local liberation of free acid in the inflamed joints due to a local excess of carbon dioxide, seems to be disproven by the observations of Boots and Cullen (*Proc. of the Soc. for Exp. Biol.,* 1912., xix, 287) who showed that the joint exudates in rheumatic fever are alkaline, and the observations of Hanzlik (*J. P. Ex. T.,* 1921, xvii, 385) who has found that in fatal asphyxiation the hydrogen ion concentration of the blood is still too low to liberate free salicylic acid. It is of course within the realms of possibility that the specific germs responsible for rheumatic fever may have a peculiar susceptibility to the salicylates. While no direct evidence of such a view has been brought forward it is not uncommon to find substances of relatively low disinfectant powers very poisonous to one or two species of bacteria. Closely allied to rheumatic fever, and probably due to the same micro-organism, are certain types of *acute tonsillitis* and some cases of *chorea;* in these conditions the salicylates are often of great service, although their action is neither so certain nor so prompt as in the case of joint involvement. It is probable also that there is a type of *chronic arthritis* which is caused by the germ of rheumatic fever. Perhaps also certain inflammations of serous membranes, as *iritis,* may be due to the same cause. In this latter group of diseases the salicylates are often of service.

In *lumbago, pleurodynia* and other myalgias, in certain inflammations of nerves as *sciatica,* in some cases of *chronic arthritis,* and the host of similar conditions which for lack of better diagnostic acumen we are wont to call *rheumatism,* salicylic acid is a valuable palliative and often appears to exercise even a curative effect.

Moulton (*J. A. M. A.,* 1920, lxxv, 725) recommends the salicylates in the treatment of sympathetic *ophthalmia* occurring after injuries to the other eye. According to Hanzlik (*A. J. M.,* 1917, xix, and 1918, xx) full therapeutic doses of salicylates have an injurious effect upon the kidneys, as shown by albuminuria, diminished excretory power of the kidney, and even the appearance of œdema.

There has been a great deal of discussion concerning the relative value and toxicity of salicylic acid obtained from plants and that manufactured from phenol. There is a widespread belief among clinicians that the so-called "natural salicylates" are superior in power and less prone to cause unpleasant symptoms than those manufactured synthetically. The toxic properties of the synthetic salicylates have been attributed to various phenol bodies, especially *cresotinic acid,* which are present as impurities, but Stockmann (*J. P. Ex. T.,* 1912, iv) has shown that these substances are scarcely more actively poisonous than salicylic acid and are possessed of similar curative properties in rheumatism. In an elaborate investigation undertaken under the auspices of the Council of Pharmacy and Chemistry of the American Medical Association, which included an historical, chemical, pharmacological, and clinical investigation of this subject, the conclusion was reached that there was no trustworthy evidence of any kind that the natural salicylates were superior to those prepared from phenol. (See *J. A. M. A.,* 1913, lx and lxi.)

Salicylic acid itself is so irritant to the stomach that it is rarely used internally. Because the neutral salicylates are so much less powerfully antiseptic some have believed that the salicylic acid is theoretically preferable in those cases where an antiseptic influence is desired as in *cystitis* and *rheumatic fever,* but as the acid must immediately combine with the excess of alkali in the blood, this theory is erroneous. There is no justification for the internal use of the free acid.

The use of salicylic acid or its salts as preservatives of beer, or milk, or other articles of food, is to be strongly condemned and its use is prohibited under the Federal and most state food and drugs acts.

Salicylic acid is incompatible with compounds of lead, silver, mercury, bismuth, zinc, and some other metals with which it produces insoluble precipitates. With ferric salts it produces the well-known violet color which is used as a test for its identity. Oxidizing agents destroy its identity and produce various derivatives. It is frequently thrown out of solution when the salicylates are prescribed with either organic or inorganic acids which set it free.

Dose, five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Unguentum Acidi Salicylici, *Br.;* Collodium Salicylici Compositum, *N. F.;* Glycerogelatinum Acidi Salicylici, *N. F.;* Mulla Creosoti Salicylata, *N. F.;* Mulla Acidi Salicylici, *N. F.;* Pasta Zinci, *N.F.;* Pulvis Antisepticus, *N. F.;* Pulvis Talci Compositus, *N. F.;* Stili Acidi Salicylici Dilubilis, *N. F.*

ACIDUM STEARICUM. U. S.

STEARIC ACID Acid. Stear.

"Stearic Acid is obtained from tallow and other solid fats, and consists chiefly of $C_{17}H_{35}$.-COOH." *U. S.*

Acidum Stearinicum; Acide Stéarique, *Fr.;* Talgsäure, Stearinsäure, *G.*

Preparation.—Stearic acid is obtained from tallow soap by treating it with sulphuric or hydrochloric acid, whereby sodium sulphate or chloride is produced and stearic acid liberated; it is also made on a large scale by purifying the residue left after making glycerin by acting on stearin with superheated steam. (See *Glycerinum.*)

Properties.—A hard, white or faintly-yellowish, somewhat glossy and crystalline solid. It is odorless, or has a slight, tallow-like odor, and is stable in the air. Stearic Acid is almost insoluble in water. One Gm. dissolves in 21 cc. of alcohol, 2 cc. of chloroform, and in 3 cc. of ether, at 25° C. It is freely soluble in carbon disulphide and in carbon tetrachloride.

"Melting point: not below 56° C. Congealing point: not below 54° C. Ash: not more than 0.1 per cent. Boil 1 Gm. of Stearic Acid and 0.5 Gm. of sodium carbonate with 30 cc. of distilled water in a capacious flask: the resulting solution while hot is not more than opalescent (*neutral fat or paraffin*). Shake melted Stearic Acid with an equal volume of hot distilled water, cool, and filter: the filtrate is not reddened by the addition of a drop of methyl orange T.S. (*mineral acids*)." *U. S.*

The melting point, 56° C., is an important factor in testing stearic acid, as a lower melting point would unfit it for use in making glycerin suppositories.

Uses.—This acid was introduced into the U. S. P. solely because of its use in making glycerin suppositories. Stearic acid combines with alkalies to form the corresponding salts and is decomposed by oxidizing agents.

Off. Prep.—Suppositoria Glycerini, *U. S.;* Linimentum Saponati Camphoratum, *N. F.*

ACIDUM SULPHURICUM. U. S., Br.

SULPHURIC ACID Acid. Sulphuric.

"Sulphuric Acid contains not less than 93 per cent. and not more than 95 per cent. of H_2SO_4." *U. S.* "Sulphuric Acid may be obtained by the combustion of sulphur or pyrites and the oxidation and hydration of the resulting sulphur dioxide by means of nitrous and aqueous vapours, and contains not less than 95 per cent. by weight of hydrogen sulphate, H_2SO_4." *Br.*

Oil of Vitriol, Vitriolic Acid; Hydrogen Sulphate; Acide sulfurique; Huile de Vitriol, *Fr.;* Acidum Sulfuricum, *P. G.;* Vitriolöl, Schwefelsäure, *G.;* Acido solforico, *It.;* Acido sulfurico, *Sp.*

Preparation.—Sulphuric acid is obtained by burning sulphur or iron pyrites, FeS_2, and allowing the product of combustion, SO_2, to mix with nitrous fumes obtained from the decomposition of sodium nitrate, which change SO_2 into SO_3, and this uniting with steam yields H_2SO_4. If the sulphur were burned by itself, the product would be sulphurous oxide, which contains only two-thirds as much oxygen as sulphuric oxide. The object of the sodium nitrate is to furnish, by its decomposition, the requisite additional quantity of oxygen. To understand the process, it is necessary to remember that several oxides of nitrogen have oxidizing power. Thus, the main reactions of the sulphuric acid process are

$$2SO_2 + N_2O_3 + O_2 + H_2O = 2SO_2OH.NO_2$$
$$2SO_2OH.NO_2 + H_2O = 2H_2SO_4 + N_2O_3$$

in which the sulphurous oxide from the burning pyrites or sulphur is oxidized to sulphuric oxide by the nitrogen trioxide, passing through the intermediate stage of the formation of nitrosyl sulphuric acid which upon contact with water vapor produces sulphuric acid and regenerates the nitrogen trioxide. If the supply of steam be insufficient, white crystals of the nitrosyl sulphuric acid (*lead chamber crystals*) will also form; when steam enters in larger amount they disappear, with formation of sulphuric acid, while red fumes are given off, thus:

$$2HSO_3(NO_2) + H_2O = 2H_2SO_4 + N_2O_3$$

Preparation on the Large Scale.—Large quantities are manufactured in the United States, England, France, and Germany. Smaller amounts are prepared in Austria, Italy, Belgium, Russia and Japan, and additional amounts in Spain and in Scandinavian countries.

As made from pyrites, the process is as follows: Beginning with the pyrites-kilns, or burners, the broken mineral is placed in moderate-sized lumps on the bars of the burners, which have previously been heated to redness, and when the burning is once started, the fire is kept up by placing a new charge on the top of that nearly burned out. The ordinary charge for each burner of pyrites, containing about 48 per cent. of sulphur, is from 5 to 6 cwt., which is burnt out in twenty-four hours. The hot sulphur dioxide and air are drawn from the pyrites-burners through the whole system of tubes, towers, and chambers by help of the powerful draught from a large chimney which is placed in connection with the apparatus. These gases then pass either into a tall tower (called the Glover or denitrating tower), where they meet a descending stream of strong sulphuric acid charged with nitrous fumes, which at this moment of descent is mixed with a weaker sulphuric acid, thereby liberating the nitrous fumes which then mix with the sulphur dioxide and air, or they are charged with nitrous fumes direct from the nitre-pots, where a mixture of Chili saltpetre and sulphuric acid liberates them. The mixed gases are then delivered at a temperature of about 75° C. into the first of the leaden chambers. These chambers, of which there are three, are now made of much larger size than was formerly the case, having often a capacity of 38,000 cubic feet. Here the gases meet jets of steam and deposit liquid sulphuric acid, as also in the second chamber. In the third or exhaust chamber all the sulphur dioxide should have been converted into sulphuric acid, and red nitrous fumes must always be visible. These must not be lost, but are drawn into a so-called Gay-Lussac tower filled with coke, over which a finely divided shower of strong acid is allowed to fall. The nitrous fumes are absorbed by this, and give the so-called nitrated acid used as before mentioned in the Glover tower. The acid obtained in the leaden chambers has a sp. gr. of 1.55, or contains 64 per cent. of H_2SO_4. The acid which comes from the Glover tower (or, in case this is not used, is obtained by further concentration of chamber acid in leaden pans) has a sp. gr. of 1.71, and contains 78 per cent. H_2SO_4. The strongest acid must be procured by still further concentration in glass or platinum vessels, and will contain 98 per cent. H_2SO_4. (Roscoe and Schorlemmer, *Chem.*, vol. i, pp. 321–338.) Within recent years it has been found that to continue the concentration to the limit of 98 per cent. acid in platinum vessels is very destructive to these. Therefore it has been proposed, after a strength of 65° B. or about 90 per cent. acid has been reached, to finish in vessels of cast iron. It is found that the concentrated acid does not attack this, and therefore it can be substituted for platinum to advantage. Another method of concentrating is that of Gaillard in which the weak acid is made to fall in the form of a fine spray from the top of a tall tower, being met by a current of hot gases from a coke generator which cause the vaporization of the water, and the acid is thus concentrated to a strength ranging from 92 to 97 per cent. Hundreds of plants are now using this method of concentration. The Schwarzenberg tower is an apparatus used to aid in the removal of arsenic for specially pure acid. In it the sulphuric acid meets a current of H_2S which converts the arsenic into sulphide.

According to theory, 100 parts of sulphur burnt should yield 305.9 parts of pure sulphuric acid. In practice the yield is 290 to 294. The amount of sodium nitrate used varies very much. Manufacturers who employ Glover and Gay-Lussac towers require from 3.5 to 6.5 parts of nitrate for every 100 of sulphur burnt, while works unprovided with these appliances may take from 12 to 13 parts. (Roscoe and Schorlemmer, *Chem.*, vol. i, p. 337.)

In 1901, the "Badische Anilin and Sodafabrik" began on a large scale the manufacture of sulphuric acid by what is known as the "contact process," and since then this process has developed very successfully, and is now in use in this country in a number of the newer chemical works. It is rather a process for the manufacture, on a commercial scale, of sulphur trioxide, which then can be allowed to take up the necessary amount of water to form acid of any strength. A mixture of sulphur dioxide and purified air is passed over heated platinized asbestos, which is the so-called "contact material." To make the process successful, the sulphur dioxide gas must be washed to free it from dust, and all traces of volatile arsenic compounds (arising from arsenical pyrites) must be absent; in addition, the temperature must be regulated with great care to avoid the dissociation of the sulphur trioxide formed. The sulphur trioxide can be marketed as anhydride or as concentrated sulphuric acid of any desired strength.

What is said above relates to the mode of preparing common sulphuric acid; but there is another kind, known on the continent of Europe by the name of the *fuming sulphuric acid of Nordhausen,* so-called from its properties, and a place in Saxony where it was first manufactured. This product is known in commerce, in the industries where it is used, simply as *oleum.* It is also called *pyro sulphuric acid* or *di-sulphuric acid.* This acid is obtained by distilling dried ferrous sulphate in large stoneware retorts, heated to redness, and connected with receivers of glass or stoneware. The fuming acid distils over, and ferric oxide is left in the form of *colcothar* or *polishing rouge,* a material used for polishing metals, particularly gold and silver. The formula usually given for fuming sulphuric acid is $H_2S_2O_7$ or $H_2SO_4 + SO_3$. This would demand about 45 per cent. of sulphuric oxide or SO_3. In fact, the so-called Nordhausen acid seldom contains more than 10 per cent. of SO_3, and to obtain that demanded by the formula a re-distillation is necessary. This product is semi-solid and is now obtainable in commerce; put up in sealed glass flasks. Its sale has been largely curtailed lately, owing to the introduction into commerce of the *anhydride* under the name of *solid sulphuric acid. Sulphuric oxide* (*solid sulphuric acid*) under 18° C. is in small, colorless crystals, resembling asbestos. It is tenacious, difficult to cut, and may be moulded in the fingers like wax, without acting on them. Exposed to the air, it emits a thick opaque vapor of an acid odor. Above 18° C. it is a liquid, very nearly of the density 2.

When moisture is rigidly excluded, the acid has little action on metals, and it is put up in soldered boxes of tinned sheet-iron; it is used largely in the arts in the manufacture of artificial alizarin and indigo. *Persulphuric acid* and the *persulphates* are among recent products of electrolysis. The ammonium persulphate, $(NH_4)_2S_2O_8$, and potassium persulphate, $K_2S_2O_8$, both form white crystalline salts. The former has already found a considerable technical application as an energetic oxidizing agent in the manufacture of organic dye-stuffs and the cyanide extraction of gold.

The fuming sulphuric acid is also prepared by passing the SO_3 of the contact method through strong sulphuric acid. In this way *oleum* containing as high as 80 per cent. of free SO_3 may be obtained.

Kohlrausch (*Pogg. Ann. Erganzungs,* Bd. viii, p. 675, Lunge) found the specific gravity of pure sulphuric acid, to be 1.8342, and believes that a higher sp. gr. than this is due to impurities (probably lead sulphate). The commercial acid is seldom of this strength. According to Phillips, it has generally the sp. gr. 1.8433, and this is about the strength of the Br. acid, of which the sp. gr. is stated to be 1.841 at 15.6° C. The specific gravity of the U. S. P. acid is about 1.83 at 25° C.; the British acid contains about 95 per cent. of absolute sulphuric acid and the U. S. P. X acid not less than 93 per cent. nor more than 95 per cent. of H_2SO_4. Mendelejeff, after a careful determination, found that pure monohydrated sulphuric acid had the specific gravity 1.8371 at 15° C. compared with water at its maximum density, 4° C. (*Am. Drug.,* 1885, p. 16.) The strong acid boils at 338° C., and freezes at $-26°$ C. When diluted, its boiling point is lowered. When of the sp. gr. 1.78 it deposits crystals of the formula $H_2SO_4 + H_2O$ at about 0° C., and hence it is hazardous for manufacturers to keep an acid of that strength in glass vessels in cold weather, as they are liable to burst. With salifiable bases it forms a numerous class of salts, called sulphates. It acts powerfully on organic bodies, whether vegetable or animal, depriving them of the elements of water, liberating carbon, and turning them black. A small piece of cork or wood dropped into the acid will for this reason render it of a dark color. It absorbs water with avidity, and is used as a desiccating agent. It has been ascertained by W. B. and R. E. Rogers to be capable of absorbing 94 per cent. of carbon dioxide, a fact having an important bearing on analytical operations.

Description and Physical Properties.—" A colorless, odorless liquid of oily consistence, very caustic and corrosive. Sulphuric Acid is miscible with water and with alcohol with the evolution of much heat. The Acid must be added with great caution to the diluent. When strongly heated, the Acid is vaporized with the evolution of dense, white fumes. Specific gravity: about 1.83 at 25° C.

" It is strongly acid to litmus paper even when highly diluted. Sulphuric Acid responds to the reactions for sulphates. Sulphuric Acid with or without the aid of heat chars cane sugar, wood, and many other organic substances.

" No precipitate is formed within an hour on mixing 1 volume of Sulphuric Acid with 5 volumes of alcohol (*lead*). Sulphuric Acid diluted with 15 volumes of distilled water conforms to the following tests: Evaporate 25 cc. of the dilution from a platinum or porcelain dish, and ignite: not more than 0.0015 Gm. of residue remains after ignition (*non-volatile substances*). A 10 cc. portion of the dilution does not at once discharge the color of 0.1 cc. of tenth-normal potassium permanganate (*sulphurous or nitrous acid*). Mix 5 cc. of the dilution with an equal volume of ferrous sulphate T.S., and superimpose it upon reagent sulphuric acid: the zone of contact does not assume a brown or brownish-red color (*nitrate*). The dilution is not immediately affected by silver nitrate T.S. (*chloride*). A 10 cc. portion of the dilution meets the requirements of the test for *heavy metals.* A 2 cc. portion of the dilution meets the requirements of the test for *arsenic.*

" **Assay.**—Proceed as directed under the assay for acids, using about 1 cc. of the Acid, accurately weighed, and methyl orange T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.04904 Gm. of H_2SO_4.

"Preserve in glass-stoppered bottles." *U. S.*

"A colorless, corrosive, intensely acid liquid of oily consistence, evolving much heat on the addition of *water.* Yields, when neutralised, the *reactions* characteristic of sulphates. Specific gravity about 1.841. 1 gramme diluted with 20 or 30 millilitres of *water* requires for neutralisation not less than 19.3 millilitres of *N/1 solution of sodium hydroxide.* Yields no characteristic *reactions* for copper, iron ammonium, chlorides, nitrates, nitrites, or sulphites. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million. *Hydrochloric acid* to which *sodium sulphite* has been added, when poured carefully upon an equal volume of Sulphuric Acid contained in a test-tube, does not cause a red coloration at the junction of the two liquids, and no red precipitate forms on warming the tube (absence of selenium). Leaves not more than 0.05 per cent. by weight of solid residue on evaporation." *Br.*

For official tables showing specific gravity of various strengths of sulphuric acid, see Part III.

Occasionally potassium nitrate is added to render dark samples of acid colorless. This addition gives rise to the impurity of potassium sulphate. These impurities often amount to 3 or 4 per cent. The commercial acid cannot be expected to be absolutely pure; but when properly manufactured it should not contain more than one-fourth of 1 per cent. of impurity. The fixed impurities are discoverable by evaporating a portion of the acid, when they will remain. If lead sulphate be present, the acid will become turbid on dilution with an equal bulk of water. This impurity is not detected by hydrogen sulphide unless the sulphuric acid be saturated with an alkali. If only a scanty white turbidity arise, the acid is of good commercial quality.

Arsenic is sometimes present in sulphuric acid. In consequence of the high price of Sicilian sulphur, most English manufacturers have employed iron pyrites for the purpose of furnishing the necessary sulphurous acid in the manufacture of oil of vitriol. As the pyrites usually contains arsenic, it happens that the sulphurous acid fumes are accompanied by arsenous oxide, and thus the sulphuric acid becomes contaminated. From 22 to 35 grains of arsenic trioxide have been found in 20 fluidounces of oil of vitriol, of English manufacture, by G. O. Rees and Watson, and a still larger proportion by J. Cameron of South Wales. It may readily be discovered by the official tests for arsenic.

Until within recent years all the sulphuric acid produced in the United Sates was made from sulphur. At the present time many of the sulphuric acid works are using pyrites. Most of the American pyrites ore is entirely free from arsenic. Another impurity occasionally existing in French sulphuric acid is selenium, supposed to be derived from copper pyrites sometimes substituted for sulphur in the manufacture of the acid.

Apart from the destructive effect which strong sulphuric acid has upon almost all forms of organic matter, its incompatibilities in general are those of the diluted acids, which see.

Uses.—For the therapeutic powers and uses of sulphuric acid when administered internally, see *Acidum Sulphuricum Dilutum.* Externally it is sometimes employed as a caustic; but, from its liquid form, it is very inconvenient for that purpose, and should be applied with caution. A plan, however, has been proposed by Simpson by which it becomes very manageable. This consists in mixing it with dried and powdered zinc sulphate sufficient to give it a pasty consistence. *Michel's Paste* consists of strong sulphuric acid three parts, and finely powdered asbestos one part, thoroughly rubbed together. Mixed with saffron to the consistence of a ductile paste, Velpeau found it a convenient caustic not liable to spread or be absorbed, and producing an eschar which is promptly detached.

Toxicological Properties.—The symptoms of poisoning by this acid are the following: Burning heat in the throat and stomach, extreme fetidness of the breath, nausea and excessive vomitings of black or reddish matter, excruciating pains in the bowels, difficulty of breathing, extreme anguish, a feeling of cold on the skin, great prostration, constant tossing, convulsions, and death. Sometimes there is no pain whatever in the stomach, sensibility being apparently destroyed by the violence of the caustic action. The intellectual faculties remain unimpaired. Frequently the uvula, palate, tonsils, and other parts of the fauces are covered with black or white sloughs. The treatment consists in the administration of large quantities of magnesia, or, if this be not at hand, of solution of soap or other alkali. The safety of the patient depends upon the greatest promptitude in the application of the antidotes. After the poison has been neutralized, mucilaginous and other bland drinks must be taken freely.

Upon the skin sulphuric acid acts as a very rapid and powerful corrosive. When it has been spilled or thrown upon the person the part should be immediately washed with a weak solution of sodium carbonate or bicarbonate, or soap may be well rubbed into the surface. After the removal and neutralization of the acid, Carron oil or similar protective may be applied. Further treatment is that of a burn.

The holes burnt in linen by sulphuric acid, so long as the texture is undisturbed, are distinguished from those produced by red-hot coals, by the paste-like characters of their edges.

Uses in the Arts.—Sulphuric acid is more used in the arts than any other acid. It is employed to obtain many of the other acids; to make alum and ferric sulphate; to refine petroleum and paraffin; to decompose the neutral fats; to dissolve indigo; to prepare phosphorus, chlorinated lime, magnesium sulphate, etc. Petroleum refining, manufacture of smokeless powder and other nitrated explosives, and manufacture of fertilizers from phosphatic materials consume the largest amounts of sulphuric acid in the United States.

Off. Prep.—Acidum Sulphuricum Aromaticum, *U. S., Br.;* Acidum Sulphuricum Dilutum, *U. S., Br.;* Acidum Sulphurosum, *Br.*

ACIDUM SULPHURICUM AROMATICUM. U. S., Br.

AROMATIC SULPHURIC ACID Acid. Sulph. Arom.

"Aromatic Sulphuric Acid contains free sulphuric acid and ethyl-sulphuric acid together equivalent to not less than 19 per cent. nor more than 21 per cent. of H_2SO_4." *U. S.*

Tinctura Aromatica Acida; Elixir of Vitriol; Elixir vitriolique, Teinture (alcoolé) aromatique sulphurique, *Fr.;* Saure Aromatische Tinktur, Elixir Vitrioli Mynsichti, Mynsicht's Elixir, G.

"Aromatic Sulphuric Acid contains free sulphuric acid and ethylsulphuric acid together equivalent to not less than 19 per cent. and not more than 21 per cent. of H_2SO_4. Sulphuric Acid, 109 cc.; Tincture of Ginger, 50 cc.; Oil of Cinnamon, 1 cc.; Alcohol, a sufficient quantity to make 1000 cc. Add the sulphuric acid gradually and with great caution to 700 cc. of alcohol, and allow the mixture to cool. Then add to it the tincture of ginger and the oil of cinnamon, and afterwards enough alcohol to make the product measure 1000 cc." *U. S.*

"Tincture of Ginger, 250 millilitres; Spirit of Cinnamon, 15 millilitres; Sulphuric Acid. 70 millilitres; Alcohol (90 per cent.), sufficient to produce 1000 millilitres. Mix the Sulphuric Acid gradually with six hundred millilitres of the Alcohol; cool to 15.5° C.; add the Spirit of Cinnamon and Tincture of Ginger and sufficient of the Alcohol to produce the required volume." *Br.*

The British formula is similar in flavor but weaker in acid containing only about 12.5 per cent.

Description and Physical Properties.—"A clear, reddish-brown liquid having a pleasant aromatic odor. Specific gravity: about 0.94 at 25° C. Aromatic Sulphuric Acid is strongly acid to litmus paper. Aromatic Sulphuric Acid responds to the reactions for sulphates.

"Preserve in glass-stoppered bottles." *U. S.*

Aromatic sulphuric acid of the older Pharmacopœias was of a deep reddish-brown, but it is a straw-colored liquid when freshly prepared according to the directions of the U. S. Pharmacopœia IX, of a peculiar aromatic odor, and, when sufficiently diluted, of a grateful acid taste. It cannot, however, be viewed merely as a sulphuric acid diluted with alcohol and containing essential oils, for the difference between fresh and old preparations is quite marked, and a peculiar and agreeable ethereal odor is developed by age. The U. S. official definition recognizes the presence of ethyl sulphuric acid.

"**Assay.**—Transfer about 5 cc. of Aromatic Sulphuric Acid, accurately weighed, to a tall beaker. Add exactly 30 cc. of normal sodium hydroxide, and evaporate the mixture to complete dryness on a sand bath. Dissolve the residue in 30 cc. of distilled water, and titrate the excess of alkali with normal sulphuric acid, using methyl orange T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.04904 Gm. of H_2SO_4." *U. S.*

"Specific gravity 0.917 to 0.923. 10 millilitres require for neutralisation not less than 24.9 millilitres of *N/1 solution of sodium hydroxide.*" *Br.*

Uses.—This valuable preparation is tonic and astringent. It acts precisely as does the *Acidum Sulphuricum Dilutum.* Water produces a turbidity in this preparation owing to the precipitation of the oil and resin of the aromatics, otherwise the incompatibilities are the same as those of diluted sulphuric acid, which see.

Dose, from five to fifteen minims (0.32–1.0 cc.), in a wineglassful of water, repeated two or three times a day. Care must be taken that the teeth are not injured.

ACIDUM SULPHURICUM DILUTUM. U. S., Br.

DILUTED SULPHURIC ACID Acid. Sulph. Dil.

"Diluted Sulphuric Acid is an aqueous solution containing not less than 9.5 per cent. nor more than 10.5 per cent of H_2SO_4." *U. S.* "Diluted Sulphuric Acid contains 10 per cent. by weight of hydrogen sulphate, H_2SO_4." *Br.*

Acide sulphurique dilué *Fr.;* Acidum sulphuricum dilutum, *P. G.;* Verdünnte Schwefelsäure, *G.*

"Sulphuric Acid, 107 Gm.; Distilled Water, 893 Gm.; to make 1000 Gm. Pour the Acid gradually, with constant stirring, into the distilled water, and allow the solution to cool." *U. S.*

"Sulphuric Acid, 112.5 grammes; Distilled Water, 940.0 millilitres, or a sufficient quantity. Add the Sulphuric Acid very gradually to one-half of the Distilled Water contained in a glass flask; cool to 15.5° C. and add sufficient Distilled Water to make the resulting liquid respond to the following tests." *Br.*

Description and Physical Properties.—"A colorles, odorless liquid having a strongly acid taste. Specific gravity: about 1.067 at 25° C.

"Diluted Sulphuric Acid is strongly acid to litmus paper. Diluted Sulphuric Acid conforms to the tests for identity and purity under *Acidum Sulphuricum.*

"**Assay.**—Proceed as directed under the assay for acids, using 20 cc. of the Acid, accurately weighed, and methyl orange T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.04904 Gm. of H_2SO_4.

"Preserve in glass-stoppered bottles." *U. S.*

"Specific gravity 1.069. 10 millilitres require for neutralisation 21.7 millilitres of *N/1 solution of sodium hydroxide.*" *Br.*

This preparation is sulphuric acid diluted to such an extent as to make it convenient for prescription. The British Pharmacopœia, 1914, lowered slightly the specific gravity of this acid and now corresponds with that of the U. S. The difference is not so great as to be of practical importance. The strong acid is added gradually to the water, to guard against the too sudden production of heat, which might cause the fracture of the vessel.

Uses.—Diluted sulphuric acid is tonic, refrigerant, and astringent. It is given in *typhoid fever,* and often with advantage. In the convalescence from protracted fevers it acts beneficially as a tonic, exciting the appetite and promoting digestion. It is a valuable astringent in *serous diarrheas* and is also frequently used, but with less reason, in *colliquative sweats.* Buxton, of London, called attention to its great value in *choleraic diarrheas;* his assertions have received abundant confirmation both in this country and in England. It has even been recommended in *asiatic cholera.* It is added with advantage to infusions of cinchona, the alkaloids of which it tends to hold in solution. As it is injurious to the teeth, it is best taken through a glass tube. It is much less used in the United States than is the aromatic sulphuric acid.

All forms of sulphuric acid show incompatibility with salts of lead, barium, strontium, and calcium, forming insoluble precipitates of the corresponding sulphates. With hypophosphorous acid or hypophosphites, it is reduced to sulphurous acid and finally to sulphur.

Dose, ten to thirty minims (0.6–1.8 cc.).

ACIDUM SULPHUROSUM. Br.

SULPHUROUS ACID

" Sulphurous Acid is an aqueous solution containing 6.4 per cent. by weight of hydrogen sulphite, H_2SO_3, corresponding to 5 per cent. by weight of sulphur dioxide, SO_2. The sulphur dioxide may be obtained by heating sulphuric acid with charcoal or sulphur." *Br.*

Acide sulfureux, *Fr.;* Schwefligsäure, Schwefligsäurewasser, *G.*

Sulphurous acid was not admitted to Part I of the U. S., but was placed among the reagents (see Part III). There is no process for making it at present official. The U. S. VIII method of preparation is:

"Sulphuric Acid, *sixty cc.;* Charcoal, in coarse powder, *twenty grammes;* Distilled Water, *five hundred cc.* Introduce the Charcoal into a glass flask having a capacity of about *five hundred cc.,* add the Acid, and mix them well. Connect the flask by means of bent glass tubing, about fifty centimeters in length, with a wash bottle having a capacity of about two hundred cc. containing about *fifty cc.* of water, so that the end of the inlet tube shall be below the surface of the water. Through the triply perforated rubber stopper of the wash-bottle pass a safety tube, which should reach nearly to the bottom of the bottle, and connect the latter, by means of a glass tubing, with a bottle provided with a doubly perforated rubber stopper, having a capacity of about one thousand cc., and containing *five hundred cc.* of well-cooled Distilled Water. The inlet tube should dip about twenty-five millimeters below the surface of the Distilled Water. By means of a second tube connect this bottle with another containing water, the end of the tube extending five centimeters below the surface. Having ascertained that all the connections are air-tight, apply a moderate heat to the flask containing the Sulphuric Acid and Charcoal, until the evolution of gas has nearly ceased, and, during the passage of the gas, keep the bottle containing the Distilled Water at or below 10° C., by surrounding it with cold water or ice. Assay a small portion of the Sulphurous Acid by the method given below. Then add to the remainder sufficient Distilled Water to bring the product to the strength of 6.4 per cent., by weight, of sulphur dioxide. Finally pour the Sulphurous Acid into dark, amber-colored, glass-stoppered bottles, which should be completely filled, and kept in a cool place, protected from light. Owing to its rapid deterioration, Sulphurous Acid should be frequently assayed, and none should be dispensed, if it fails to conform to the assay given below." *U. S. VIII.*

This process is essentially that of Wittstein.

For further details concerning this process and its modifications see *U. S. D.,* 20th ed., p. 73.

F. L. Cheney devised a method of making sulphurous acid extemporaneously as follows: Dry acid sodium sulphite, 5.7 Gm.; dilute hydrochloric acid, 18.5 cc.; water, 25 cc. Add the acid to the salt, placed in a half pint glass-stoppered bottle, stopper immediately and set aside in a cool place. Agitate slowly to aid in the solution of the salt, and when bubbles cease to arise, add the water and shake the bottle for a few minutes. The product should measure 40 cc. and assay from 6 per cent. to 6.5 per cent. SO_2. When it is necessary to have a fresh solution of sulphurous acid and the presence of a small amount of sodium chloride is admissible, this process will be found convenient. (*A. J. P.,* 1906, 333.) This process was modified by Otto Raubenheimer (*J. A. Ph. A.,* 1917, vi, 352. R. W. Terry proposes a still different method in which SO_2 is generated from anhydrous Na_2SO_3 with H_2SO_4 and the gas collected in a Woulffe bottle. (*J. A. Ph. A.,* 1917, vi, 484.)

Sulphur dioxide in liquefied form in cylinders is now commercially available even in small amounts, so it is rarely necessary at present to make the sulphurous acid by any of the older processes as all that is necessary is to pass the SO_2 into water with suitable precautions.

Properties.—Sulphurous acid is a solution of sulphurous oxide gas. The oxide is an irrespirable gas, of a suffocating odor familiar to every one as that of burning sulphur, which is converted into it by combustion. If inhaled in the concentrated state, it proves fatal. Cold reduces it to a colorless liquid, which boils at –10.5° C. It has the sp. gr. 2.21, liquefies at –10° C., has a strong acid reaction, extinguishes burning bodies, has the power of bleaching many colored substances, and has a strong affinity for oxygen, with which it gradually combines in the presence of water, forming sulphuric acid. Water at 18° C takes up about 50 volumes of gas, and the solution has the sp. gr. 1.04. (Brande and Taylor.)

Sulphurous acid sometimes exists as an impurity in hydrochloric, acetic, and other acids; according to P. Schweitzer, the minutest quantity may be detected by dissolving zinc in the suspected acid, when, if sulphurous acid be present, hydrogen sulphide will be evolved, recognizable by its odor. (*Chem. News,* xxviii, 293.)

When sulphurous acid is exposed to the air it slowly absorbs oxygen, with the formation of sulphuric acid, and acquires a sour taste, and the property of changing vegetable blues to red differing in this respect from the original sulphurous acid which bleaches vegetable colors. When kept in closed vessels exposed to the sunlight, a portion of it is decomposed, sulphur being deposited and sulphuric acid formed by the union of the liberated oxygen with other portions of the acid. (*A. J. P.,* xlii, 352.) It should be entirely volatilized by heat. It decolorizes iodine by producing hydriodic acid, and on this fact is based the Br. test given below. It decomposes calcium phosphate.

"A colorless liquid with a pungent, sulphurous odor. Yields, when neutralised, the *reactions* characteristic of sulphites. Yields not more than a slight precipitate with *solution of barium chloride* (limit of sulphates), but a copious precipitate if *solution of chlorine* is also added. Leaves no appreciable residue on evaporation. Specific gravity 1.025. 1 gramme, diluted with 100 millilitres of recently boiled and cooled *water,* requires 15.5 millilitres of *N/10 solution of iodine* for complete oxidation, *mucilage of starch* being used as indicator. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Assay.—A process for its assay will be found in Part III, where this acid appears as a reagent.

Uses.—Sulphurous acid in concentrated solutions is a powerful germicide, but probably no more so than are the other mineral acids. The disinfectant value of burning sulphur is due to the formation of this acid; during the process of combustion sulphur dioxide is formed and if there be present in the air an abundance of aqueous vapors this will unite with the water to form sulphurous acid which has a destructive action on many forms of life including the less resistant bacteria. It is, however, difficult to generate sufficient sulphurous acid by this method to have any real bactericidal effect, and the method of disinfecting sick rooms has been almost completely abandoned in favor of the more efficient and less destructive formaldehyde. It is, however, often useful for the destruction of vermin. It is quite impossible to hope for any true disinfectant action by burning sulphur candles in the manner which is so popularly resorted to; the most that can be hoped for is a deodorizing effect. By virtue of its reducing properties sulphurous acid decomposes hydrogen sulphide, and like other acids will unite with ammonia to form relatively inodorous compounds. It must also be remembered that sulphurous acid has a bleaching effect due to its reducing power and is therefore likely to be injurious to various kinds of clothing and furniture which are exposed to its fumes. Sulphurous acid and sulphites have been widely used for preserving food, but are now prohibited by the laws of many states. They are still permitted for the preservation of dried fruits where the function is to prevent darkening during drying and from which they are largely removed by the preliminary washing and subsequent cooking to which these foods are subjected before being eaten. So-called "sulphite powders" containing either sodium sulphite or calcium or magnesium bi-sulphites have figured largely as food preservatives. Sulphurous acid is also used for its bleaching properties to decolorize various products and make them look pure and colorless, and as a preliminary step to their subsequent dyeing, as in so-called "maraschino" or cocktail cherries. For a method of determining sulphurous acid in foodstuffs and allied products, see *Circular of the U. S. Dept. of Agriculture,* 1906, No. 28, pp. 11–12.

Its use in food products, however, should not be encouraged as it is well demonstrated that the contined ingestion of sulphites is injurious to the kidneys.

Externally sulphurous acid is used in various *skin diseases,* such as *scabies, ringworm* and *impetigo contagiosa* for its parasiticide effect. For local application it should be diluted with two or three parts of water or glycerin and applied as a lotion or by cloths wet with this solution. Intenally it has been used as a gastric antiseptic in *pyrosis* and in cases of *sarcinæ ventriculi,* but has been almost entirely replaced by the acid sulphite of sodium.

The incompatibilities of sulphurous acid are those of any powerful reducing agent. It will decompose many metallic salts, as of mercury, with the liberation of metallic mercury. Oxidizing compounds readily change it to sulphuric acid.

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

ACIDUM TANNICUM. U. S., Br.

TANNIC ACID Acid. Tann. [Gallotannic Acid, Tannin]

"A tannin usually obtained from nutgall." *U. S.* "Tannic Acid, $C_{14}H_{10}O_9$, may be extracted by water-saturated ether from galls which have been subjected to a special fermentation." *Br.*

Digallic Acid; Acidum Gallo-tannicum Tanninum; Acide tannique, *Fr.;* Acidum tannicum, *P. G.;* Gerbsäure, Gallusgerbsäure, *G.*; Acido tannico, *It.;* Acido tanico, *Sp.*

The U. S. and the Br. do not give a detailed process for preparing tannic acid; the former British Pharmacopœia adopted a process which was almost identical with that of the U. S. P., 1870, both being essentially the process of Leconnet, modified by Dominé, which had been substituted for that of Pelouze previously employed in both Pharmacopœias. The process of the British Pharmacopœia (1855) was as follows: "Galls in powder, Ether, of each a sufficient quantity. Expose the powdered galls to a damp atmosphere for two or three days, and afterwards add sufficient ether to form a soft paste. Let this stand in a well-closed vessel for twenty-four hours, then, having quickly enveloped it in a linen cloth, submit it to strong pressure in a suitable press, so as to separate the liquid portion. Reduce the pressed cake to powder, mix it with sufficient ether, to which one-sixteenth of its bulk of water has been added, to form again a soft paste, and press this as before. Mix the expressed liquids, and expose the mixture to spontaneous evaporation until, by the aid subsequently of a little heat, it has acquired the consistence of a soft extract; then place it on earthen plates or dishes, and dry it in a hot-air chamber at a temperature not exceeding 212° F." *Br.* (1885).

While the Pelouze process yields the tannic acid probably in a somewhat purer state than Leconnet's, it is less easy of performance, and much less productive, and the product of the above formula is sufficiently pure for all practical purposes. The addition of a little alcohol —8 per cent., for example—to the ethereal menstruum still further increases the product. The exposure of the powdered galls to a damp atmosphere for two or three days is for the purpose of inducing a special fermentation, whereby the yield of tannin is materially increased. There appear to be two coloring principles in galls, one soluble in ether and not in alcohol, the other in alcohol and not in ether. Hence, while the tannic acid, in whichever way procured, is yellowish, that obtained by ether has a greenish tint, while that obtained by the addition of alcohol is slightly brownish. In consequence of the mode in which the acid is dried, in thin layers, on tinned or glass plates, and equally exposed to the heat above and below, it froths up on the escape of the ether, and concretes in a soft, cellular, friable form, which is strikingly characteristic of the preparation made in strict accordance with the formula. Further discussion of these methods will be found in the *U. S. D.*, 20th ed., p. 75.

From 30 to 35 per cent. of tannic acid is obtained from galls by Pelouze's method; 60 per cent. by that of Leconnet. Alcohol tannin and water tannin are terms used to indicate the method of extraction; in the former the powdered nutgall is percolated with alcohol (50 per cent.) and the solution of tannin evaporated in a vacuum apparatus; in the water tannin, water is used as in the ether process as above described and the aqueous solution evaporated *in vacuo*. Gartenmeister used acetic ether for a solvent and a patent was secured for this process in Germany.

"Crystallized" tannic acid is said to be made by forcing a thick syrupy tannin solution through finely perforated sieves and dropping the threads from a height upon rapidly revolving wooden cylinders and scraping off the product. The term crystallized is, of course, a misnomer, as tannin is amorphous.

Henry Trimble and J. C. Peacock recommend acetone as a valuable solvent for extracting tannin from oak bark (*Proc. A. Ph. A.*, 1893, p. 110), and acetone is now largely used by manufacturers as a solvent in extracting tannin from galls. B. L. DeGraffe (*A. J. P.*, 1896, 313) recorded investigation upon the plants of the Ericaceæ to determine the character of their tannins; acetone and acetic ether were used as solvents. For Sisley's method of preparing *pure* tannin, see *Proc. A. Ph. A.*, 1894, 1087.

Composition.—The term "tannin" is applied to a group of vegetable principles which have the following chemical properties: (1) They are mostly uncrystallizable colloidal substances with astringent properties; (2) They precipitate gelatin-yielding tissues, a property which enables them to convert hide into leather; (3) They all give blackish-blue or blackish-green colors with ferric salts, a fact which is made use of in the manufacture of ink; (4) They are precipitated from solution by many metallic salts such as copper or lead acetates or stannous chloride, etc.; (5) They are precipitated from solution by a strong aqueous solution of potassium bichromate or by a 1 per cent. solution of chromic acid; (6) They precipitate from aqueous solution both alkaloids and other organic substances of a basic nature, such as basic organic coloring matters; (7) In alkaline solution, the tannins, and many of their derivatives, readily absorb oxygen, becoming dark in color; (8) With a solution of potassium ferricyanide and ammonia they give a deep red color. It must be borne in mind, however, that none of these reactions, taken separately, are specific for tannins; they may be given by other substances as well, but all true tannins answer them as a whole.

Some authors include also among the tannins vegetable principles which have all of these properties except that of precipitating gelatin; on the other hand Dekker prefers to regard those substances which do not give this reaction as *pseudo-tannins* and includes under this heading caffetannic acid and the tannins of *Portlandia grandiflora, Asperula odorata, Rubia tinctorum, Scrophularia nodosa, Humulus Lupulus, etc.* Similarly, Procter points out that such substances as moringatannic acid, or maclurin, and caffetannic and lupulotannic acids, are more closely related to the coloring matters than to the tannins; maclurin which is a pentahydroxybenzophenone is the yellow coloring matter occurring in the substance known as fustic, obtained from the wood of *Chlorophora tinctoria* (see *Fustic,* Part II). The tannin used in pharmacy and medicine is called, for the sake of distinction, *gallotannic acid.* According to Pettenkofer, it is found only in perennial plants, indicating some relation to the production of woody fiber. (*Buchner's Neues Repert.,* iii, 74–76.) Henry Trimble (*The Tannins,* vol. ii, p. 132, Phila., 1894) classifies the tannins into two main groups: Group *a.* Gallotannic acid, chestnut wood tannin, chestnut bark tannin, pomegranate bark tannin and sumac tannin. Group *b.* Oak bark tannin, mangrove tannin, canaigre tannin, rhatany tannin, kino tannin, catechu tannin, and tormentil tannin. Group *a.* Give blue-black precipitates with iron salts, group *b.* greenish or brownish.

For another scheme of classification of the tannins, based on the products they yield when heated alone, when heated with diluted acid, and when fused with caustic alkali, see Allen, *Com. Org. Anal.,* 2d ed., vol. iii, part i, p. 77.

We have as yet comparatively little certain knowledge concerning the chemical constitution of even the simplest tannins. Gallo-tannic acid is generally regarded as an anhydride formed by the removal of one molecule of water between two molecules of gallic acid according to the equation:

$$2C_7H_6O_5 - H_2O = C_{14}H_{10}O_9$$

These are differences, however, of opinion with regard to the exact position from which the H and O have been removed. (See also *Acidum Gallicum.*)

Description and Physical Properties.—"An amorphous powder, glistening scales, or spongy masses, varying in color from yellowish-white to light brown. It is odorless, or has a faint, characteristic odor, and a strongly astringent taste. Tannic Acid is very soluble in water, acetone, and alcohol. It is freely soluble in diluted alcohol and slightly soluble in dehydrated alcohol. It is almost insoluble in benzene, chloroform, ether, and in petroleum benzin. One Gm. of Tannic Acid dissolves in about 1 cc. of warm glycerin.

"The addition of a small quantity of ferric chloride T.S. to an aqueous solution of the Acid produces a bluish-black color or precipitate. An aqueous solution of Tannic Acid produces precipitates in solutions of most of the alkaloids and glucosides, and also in solutions of gelatin, albumin, and starch.

"Tannic Acid loses not more than 12 per cent. of its weight when dried to constant weight at 100° C. Ash: not more than 0.5 per cent. Dissolve 2 Gm. of Tannic Acid in 10 cc. of hot distilled water: the solution is not more than slightly turbid, and no turbidity is produced upon diluting separate 5 cc. portions of the cooled and filtered solution with 10 cc. of alcohol (*gum or dextrin*), or with 10 cc. of distilled water (*resinous substances*).

"Preserve in well-closed containers, in a cool place, protected from light." *U. S.*

"A light brownish powder consisting of thin glistening scales. Characteristic odor; taste strongly astringent. Reaction acid. Soluble in 1 part of *water* or of *alcohol* (90 per cent.), and, slowly, in 1 part of *glycerin.* It is precipitated from an aqueous solution by many mineral salts and acids. The aqueous solution precipitates *solutions of isinglass, albumen,* alkaloids, and *tartarated antimony,* and gives with *T. Sol. of ferric chloride* a bluish-black color. Ash not more than 0.2 per cent." *Br.*

Commercial tannic acid often has a decided odor, which is probably owing chiefly to the presence of the odorous principle of the galls, though sometimes to matter derived from the ether with which it is prepared. According to Heinz, the odor is due to a greenish resinous principle, which may be separated by dissolving the acid in twice its weight of hot water, adding one-fourth part of ether, agitating slowly, allowing the coagulated coloring matter to precipitate, filtering, and evaporating. (*J. P. C.,* xv, 308.)

When tannic acid, iodine, and water are mixed, a reaction takes place, by which the water is decomposed, its hydrogen forming with the iodine hydriodic acid, which combines with a portion of the tannic acid and remains in solution, while the oxygen of the water combines with another portion of the tannic acid to form a compound, which, being insoluble, is precipitated. The iodized solution thus obtained is capable of dissolving more iodine, and holding it in permanent solution, however, much diluted. This compound is the basis of the preparation known as *syrupus Iodotannicus* of the National Formulary. Iodine in a liquid containing tannic acid cannot be detected by starch, but if the liquid is placed in a watch-glass, ferrous sulphate added, and the glass covered with starch paper, ferric tannate being precipitated, the blue color soon appears.

Griessmayer (*Zeit. An. Chem.,* 1873) proposes a test for tannin and free alkalies. On mixing a drop of a solution of tannin with 1 cc. of 1/100 normal solution of iodine, the reddish color of the iodine solution instantly disappears; if one drop of solution of ammonia be now added (previously diluted with ten times its bulk of water), a brilliant red color is produced which is quite permanent. Tannic acid precipitates solutions of starch, albumin, and gluten, and forms with gelatin an insoluble compound, which is the basis of leather. J. Napier Spence (*J. Soc. Chem. Ind.,* 1891, p. 1114) has reviewed all the current tests for distinguishing between tannic acid and gallic acid. (See *Proc. A. Ph. A.,* 1892, p. 1032.)

Various plans have been proposed for estimating the quantity of tannic acid, which is an object of importance to tanners, as enabling them to judge of their tanning materials. John H. Yocum, after reviewing various methods of estimating tannin, believes the "hide-powder" method most practical and useful. (*J. Am. C. S.*, Jan. 9, 1897.) This was the one adopted by the International Congress of Leather Trades Chemists at Turin, Italy, in 1904, and is still used. For other methods, see *P. J.*, 1885, pp. 121, 850; *J. P. C.*, 1874, p. 445; *West. Drug.*, 1891, p. 445; and a monograph on the *"The Tannins,"* by Henry Trimble. (J. B. Lippincott Company, 1894.)

Uses.—Tannic acid is a powerful astringent and but slightly irritant. It is not capable of being absorbed nor, indeed, of circulating in the blood, because of its property of precipitating all albumin. When taken by the mouth, however, a portion of it combines with the alkalies of the intestinal tract and is probably absorbed as sodium tannate—which is not astringent—and a portion of it is hydrolized to gallic acid which may also be absorbed. As an astringent it is employed locally in chronic *congestions of the throat*, in local *relaxations, as of the uvula* or in *hemorrhoids*, to check excessive secretion, as in mercurial *salivation* or weeping *ulcers*, and as a styptic in various local *hemorrhages*. In *diarrheas* it is often of much service but is not so generally employed in the pure form as in one of the galenicals of crude vegetables containing it, or as some synthetic derivative. The preference of these various drugs which contain tannic acid over the pure substance is owing to their being less readily precipitated by the albumins of the prima viae before they reach the diseased point. Tannic acid is also widely recommended as a chemical antidote to various poisons, especially to the alkaloids and heavy metals. The tannates of the alkaloids are, however, soluble in dilute acids and the use of tannic acid in alkaloidal poisoning can at best be only partially antidotal.

Tannic acid produces insoluble compounds with many metallic salts such as copper, lead, tin and especially iron where the compound possesses the well known inky coloration. Tannic acid is also incompatible with solution of alkaloidal salts from which it throws down the insoluble tannates of the alkaloids, which are not physiologically inert but which need to be suspended or incorporated by shaking in order to avoid danger in dispensing.

Gelatin, albumin and other organic compounds form insoluble combinations with tannic acid. Alkaloids and oxidizing agents decompose tannic acid upon standing in contact in aqueous solutions.

Dose, from three to twenty grains (0.20–1.3 Gm.).

Off. Prep.—Glyceritum Acidi Tannici, *U. S.* (*Br.*); Suppositoria Acidi Tannici, *Br.*; Trochisci Acidi Tannici, *U. S.* (*Br.*); Ungentum Acidi Tannici, *U. S.*; Collodium Stypticum, *N. F.*; Syrupus Iodotannicus, *N. F.*

ACIDUM TARTARICUM. U. S., Br.

TARTARIC ACID Acid. Tart.

"Tartaric Acid contains not less than 99.5 per cent. of $C_2H_2(OH)_2(COOH)_2$." *U. S.* "Tartaric Acid may be obtained from acid potassium tartrate, and contains not less than 99 per cent. of hydrogen tartrate, $H_2C_4H_4O_6$." *Br.*

Dextrotartario Acid; Sal Essentiale Tartari; Acide Tartrique, *Fr. Cod.*; Acide du Tartre, Acide dextroracémique, *Fr.*; Acidum tartaricum, *P. G.*; Weinsteinsäure, Weinsäure, *G.*; Acido tartarico, *It.*; Acido tartrico, *Sp.*

No formula for the preparation of tartaric acid is given in either Pharmacopœia. It is prepared from *wine lees*, a by-product of the process of making wine, which is obtained in the initial stages of the process. It is also extracted from *tartar*, or *argol*, a peculiar substance which is deposited on the inside of wine casks during the fermentation. Tartar, when purified and reduced to powder, is the cream of tartar of commerce, and consists of acid potassium tartrate. (See *Potassii Bitartras.*) The following is the former British process:

"Take of Acid Tartrate of Potassium *forty-five ounces* [av.]; Distilled water a *sufficiency;* Prepared Chalk *twelve ounces and a half* [av.]; Chloride of Calcium *thirteen ounces and a half* [av.]; Sulphuric Acid *thirteen fluidounces.* Boil the Acid Tartrate of Potassium with two gallons [Imp. measure] of the Water, and add gradually the Chalk, constantly stirring. When the effervescence has ceased, add the Chloride of Calcium dissolved in two pints [Imp. meas.] of the Water. When the tartrate of calcium has subsided, pour off the liquid, and wash the tartrate with Distilled Water until it is rendered tasteless. Pour the Sulphuric Acid, first diluted with three pints [Imp. meas.] of the Water, on the tartrate of calcium, mix thoroughly, boil for half an hour with repeated stirring, and filter through calico. Evaporate the filtrate at a low temperature until it acquires the sp. gr. of 1.21, allow it to cool, and then separate and reject the crystals of sulphate of calcium which have formed. Again evaporate the clear liquid till a film forms on its surface, and allow it to cool and crystallize. Lastly, purify the crystals by solution, filtration (if necessary), and recrystallization." *Br.* (1885).

Tartaric acid was first obtained in a separate state by Scheele in 1770. The process consists in saturating the excess of acid in potassium bitartrate or cream of tartar with calcium carbonate, and decomposing the resulting insoluble calcium tartrate by sulphuric acid, which causes the precipitation of calcium sulphate, and liberates the tartaric acid. The equivalent quantities are two molecules of the acid tartrate and one molecule of calcium carbonate. The process, when thus conducted, furnishes one-half of the tartaric acid. The other half may be procured, as in the British process, by decomposing the neutral potassium tartrate remaining in the solution after the precipitation of the calcium tartrate, by calcium chloride in excess. By double decomposition, potassium chloride will be formed in solution, and a second portion of calcium tartrate will precipitate, which may be decomposed by sulphuric acid together with the first portion. The process, when thus conducted, will furnish twice as much tartaric acid as when the acid salt only is decomposed. The reactions are:

$$2KHC_4H_4O_6 + CaCO_3 = K_2C_4H_4O_6 + CaC_4H_4O_6 + H_2O + CO_2$$
$$CaC_4H_4O_6 + H_2SO_4 = CaSO_4 + H_2C_4H_4O_6$$
$$K_2C_4H_4O_6 + CaCl_2 = 2KCl + CaC_4H_4O_6$$
$$CaC_4H_4O_6 + H_2SO_4 = CaSO_4 + H_2C_4H_4O_6$$

Scarlata (*Chem. News,* 1899, 296) has devised a method of making tartaric acid based on the decomposition of potassium and calcium tartrates by *fluosilicic acid;* tartaric acid is liberated and corresponding fluosilicates are formed; the latter may then be decomposed by sulphuric acid and fluosilicic acid reproduced for use in a subsequent operation. By this method tartaric acid of 99 per cent. purity may be obtained. Zinno has prepared tartaric acid synthetically by passing carbon dioxide under pressure over potassium glycerate. (*Proc. A. Ph. A.,* 1902, 263.)

Preparation on the Large Scale.—To obtain tartaric acid from the crude materials (argol and wine lees), the method still largely used is the precipitation of the acid potassium tartrate as calcium tartrate and subsequent preparation of the tartaric acid from the latter. The methods of obtaining the calcium tartrate vary according to the nature of the crude material. A suitable method of producing it from argol is to mix the argol, preferably in the form of a powder, with water, and boil, after the addition of some hydrochloric acid. Milk of lime is then added to the boiling mass until this is nearly neutral, when calcium tartrate is precipitated and neutral potassium tartrate and calcium chloride left in solution. The neutral potassium tartrate is decomposed either by boiling with a sufficient amount of calcium sulphate or by adding calcium chloride solution, an excess of the precipitant being avoided in either case. The small amount of acid potassium tartrate purposely left in the liquid, when treating the latter with milk of lime, is decomposed with pure precipitated calcium carbonate. The object of not adding the milk of lime to the neutral point or in excess is to avoid the precipitation of iron or aluminum oxides. The solution must still remain perceptibly acid after the addition of the calcium carbonate. When cooled to about 40° C., the liquid is filtered with the aid of a suction pump, and the residue washed with water.

In the oldest methods of obtaining calcium tartrate from wine lees the latter were boiled with water and hydrochloric acid, the clear solution removed, and the residue treated with more water. As the extraction was very incomplete, these methods have not been employed of late years. When filtration of the lees was first attempted it was found that the pores of the filter became clogged, and that even under a pressure of four or five atmospheres no liquid would pass through. This difficulty was overcome by the process of Dietrich and Schnitzer, in which the albuminoid substances are coagulated by heating for about six hours under a pressure of four or five atmospheres. Wet lees, when thus treated, can be readily filtered. Dried lees are crushed, stirred in a tank with water, and heated by steam for some time, until air is completely expelled, before being heated in the pressure boiler.

During the process of heating the lees, the steam passing from the apparatus carries with it volatile empyreumatic products derived from the decomposed albuminoids. These have a very offensive odor, and should be conveyed into a factory chimney of sufficient height, so that the evil-smelling vapors are drawn up and decomposed by the furnace gases.

When the heating is finished, the steam outlet pipe is opened and the pressure allowed to fall to from one to one-half atmosphere, this pressure being required to force the lees from the boiler into a tank, which may be suitably constructed of wood. Here they are mixed with water, which has previously been put into the tank, and the requisite quantity of crude hydrochloric acid (21° to 22° B.). Experience has shown that for every 100 parts by weight of argol in the lees 100 parts of acid are required. Too little acid causes deposition of argol in the cloths of the filter-press, while too much destroys the cloths, and more lime is needed to neutralize the filtrate. If the conditions are right, the filtered liquid should have a specific gravity of about 6° B.

The acidified lees are pressed and washed, the washings being used instead of clear water for mixing with the next charge of lees from the pressure boiler. The tartaric acid in the filtrate is precipitated with lime and calcium carbonate, and the remainder of the process is the same as in the case of the argol, with the exception that there is no necessity to add calcium chloride or calcium sulphate.

Calcium tartrate obtained from wine lees is of a clear gray color, which is considerably purer than the dark gray or dark brown product from argol.

L. H. Baekeland patented, in 1916, a synthetic method for the production of tartaric acid: From carbon monoxide and an alkali is obtained an alkaline formate; this is changed into an oxalate by heating under pressure; the latter to glyoxalate by potassium amalgam in the presence of an acid. The glyoxalate is reduced electrolytically to tartaric (racemic) acid.

Oscar Ficinus, of Bensheim, proposed the following process to procure a pure tartaric acid.

Saturate the crude tartar with calcium carbonate, and decompose the resulting calcium tartrate with solution of zinc chloride, whereby calcium chloride and zinc tartrate are produced. The latter is almost insoluble, and is completely decomposed by hydrogen sulphide. The liquid filtered from the precipitated zinc sulphide, containing tartaric and sulphydric acids in solution, is heated for some time to 60° to 80° C., in order to dissipate the latter acid, filtered from the precipitated sulphur, and concentrated to the point of crystallization. (*A. Pharm.*, 1879.)

Description and Physical Properties.—"Colorless, translucent crystals, or a white, granular or fine powder. It is odorless, has an acid taste, and is stable in the air. One Gm. of Tartaric Acid is soluble in 0.75 cc. of water and in 3 cc. of alcohol, at 25° C. One Gm. is soluble in 0.5 cc. of boiling water. The Acid is almost insoluble in chloroform and only slightly soluble in ether.

"When slowly ignited, Tartaric Acid gradually decomposes, emitting an odor resembling that of burning sugar (*difference from citric acid*). An aqueous solution of Tartaric Acid is acid to litmus paper and responds to the reactions for tartrates.

"Ash: not more than 0.05 per cent. Nearly neutralize 10 cc. of an aqueous solution of the Acid (1 in 10) with ammonia T.S., and add 10 cc. of calcium sulphate T.S.: no turbidity is produced (*oxalate*). The addition of 1 cc. of barium chloride T.S. to 10 cc. of an aqueous solution of the Acid (1 in 100), to which 3 drops of hydrochloric acid have previously been added, causes no turbidity (*sulphate*). A 10 cc. portion of an aqueous solution of the Acid (1 in 50) mixed with 0.5 cc. of hydrochloric acid meets the requirements of the test for *heavy metals.* Dissolve 10 Gm. of Tartaric Acid in 20 cc. of distilled water, add 2 cc. of sulphurous acid T.S., and boil the mixture until the odor of sulphur dioxide is barely perceptible. Cool the solution, mix it with 1 cc. of sodium cyanide T.S., and follow this immediately with stronger ammonia water until the precipitate formed is redissolved and the solution has a slight odor of ammonia. Cool, transfer the solution to a 50 cc. graduated cylinder, dilute with sufficient distilled water to measure 50 cc., and add 3 drops of sodium sulphide T.S. After mixing well, the color produced in the solution, if any, when viewed downward against a white surface, is not darker than the color of a control solution prepared as follows: Dissolve 2 Gm. of reagent ammonium chloride, in 20 cc. of distilled water, add 4 cc. of a solution containing 0.08 Gm. of lead nitrate in 1000 cc. of distilled water, and 1 cc. of diluted hydrochloric acid. Treat this solution with the same quantity of sulphurous acid, sodium cyanide T.S., and stronger ammonia water, as directed above; transfer the mixture to another 50 cc. cylinder, dilute it with sufficient distilled water to make 50 cc., and add 3 drops of sodium sulphide T.S. Before adding the sodium sulphide T.S., the liquid must possess a distinct odor of ammonia. The two cylinders used must be matched, be of practically colorless glass, and have the same internal diameter (*lead*).

"**Assay.**—Proceed as directed under the assay for acids, using about 3 Gm. of Tartaric Acid and phenolphthalein T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.07504 Gm. of $C_2H_2(OH)_2(COOH)_2$." *U. S.*

"Soluble in less than 1 part of *water,* and in 3 parts of *alcohol* (90 per cent.). Yields, when neutralised, the *reactions* characteristic of tartrates. An aqueous solution is dextrorotatory. 1 gramme dissolved in *water* requires for neutralisation not less than 13.2 millilitres of *N/1 solution of sodium hydroxide.* Yields no characteristic *reactions* for copper, iron, or oxalates, and not more than the slightest *reactions* for calcium. *Lead limit* 20 parts per million. *Arsenic limit* 1.4 parts per million. 1 gramme dissolved in 50 millilitres of *water,* on addition of 0.5 millilitre of *solution of barium chloride,* does not yield a greater opalescence than 1 millilitre of *N/100 solution of sulphuric acid* when precipitated under the same conditions (limit of sulphates). Ash not more than 0.1 per cent." *Br.*

The powder is sometimes directed to be kept in well-stoppered vials; but Otto has shown that this method tends to spoil it. A better plan is to keep the powder in ordinary boxes. The tendency of the powder to form hard masses on keeping has been largely obviated of late years. This was formerly due to the presence of traces of sulphuric acid which caused the absorption from the air of water, but with the greater purity of the commercial product and absence of sulphuric acid the powder retains it pulverulent form much better than formerly.

Denigés gives the following modification of Mohler's test for tartaric acid. A solution of 2 Gm. of resorcinol in sufficient diluted sulphuric acid (1 per cent.) is added to 20 times its volume of strong sulphuric acid. In the presence of tartaric acid this liquid gives with a few drops of the fluid to be tested (which must be free from carbohydrates) a characteristic violet-red color when the mixture is heated to 115° to 140° C. (*Am. Drug.*, 1896, 182.)

Modifications of Tartaric Acid.—Five distinct modifications of tartaric acid exist. Their chief physical and chemical differences are:

a. Dextro-tartaric acid, or ordinary tartaric acid, forms anhydrous, hemihedral, rhombic crystals, the aqueous solution of which turns the plane of polarization of a luminous ray to the *right.* The crystals fuse at 135° C., have a sp. gr. of 1.74 to 1.75, and are readily soluble in absolute and aqueous alcohol.

b. Lævo-tartaric acid forms anhydrous, hemihedral, rhombic crystals, the aqueous solution of which turns the plane of polarization of a luminous ray to the *left.*

c. Racemic or *para-tartaric* acid forms hydrated, holohedral, triclinic crystals of $H_2C_4H_4$-

$O_6 + H_2O$, which are optically *inactive.* The crystals have a sp. gr. of 1.69, and are soluble in five parts of cold water and with difficulty in cold alcohol. The calcium racemate is less soluble in water than calcium dextro-tartrate, and is also distinguished by its insolubility in acetic acid and in ammonium chloride solution. Racemic acid can be prepared by mixing *d-* and *l*-tartaric acids, and can be resolved into them by appropriate methods. Racemic acid exists naturally in small proportion in the juice of grapes growing in particular localities, and was first obtained artificially in 1853 by Pasteur.

d. Inactive or *meso-tartaric* acid, optically inactive, but not resolvable in to *a* and *b* acids.

Uses.—Tartaric acid is sometimes used for citric acid in the preparation of refrigerant drinks, especially for decomposing sodium bicarbonate in the preparation of effervescent salts. It differs sharply from citric, acetic, and many other vegetable acids in that it is not oxidized in the system, appearing in the urine unchanged. Acid tartrates, therefore, tend to increase the acidity of the system. Tartaric acid is also more irritant than citric acid and decidedly more laxative in effects.

Tartaric acid is incompatible with salifiable bases and their carbonates; with salts of potassium, with which it produces a crystalline precipitate of bitartrate, and with the salts of calcium and lead, with which it also forms precipitates.

Dose, five to thirty grains (0.32–2.0 Gm.).

ACIDUM TRICHLORACETICUM. U. S.

TRICHLORACETIC ACID Acid. Trichloracet.

"Trichloracetic Acid, dried to constant weight over sulphuric acid, contains not less than 99 per cent. of $CCl_3.COOH$." *U. S.*

Acide trichloracétique, *Fr.;* Acidum trichloraceticum; *P. G.;* Trichloressigsäure, *G.*

Three forms of chloracetic acid are known, mono-, di-, and tri-chloracetic acids, having the following formulas, respectively, $C_2H_3ClO_2$, $C_2H_2Cl_2O_2$, and $C_2HCl_3O_2$. *Monochloracetic acid* may be prepared by acting upon glacial acetic acid containing 10 per cent. of iodine with dry chlorine, reserving the portion distilling over between 180° C. and 188° C. *Dichloracetic acid* distils over between 189° and 191° C. *Trichloracetic acid,* discovered by Dumas in 1838, may be most conveniently prepared by treating hydrated chloral with three times its volume of fuming nitric acid, and placing the whole mixture in the sunlight until the red fumes have disappeared; the liquid is then distilled, and the portion coming over at 195° C. is pure trichloracetic acid. They form various salts, most of which are easily soluble in water. The mono- and tri- acids are solid, crystalline, deliquescent bodies; dichloracetic acid is a colorless liquid having a suffocating odor, and crystallizing at 0° C.

While trichloracetic acid is usually formed by the oxidation of hydrated chloral with nitric acid, it may also be obtained by the action of potassium permanganate in concentrated solution upon hydrated chloral, the potassium trichloracetate crystallizing out in white silky crystals. The reduction of trichloracetic acid to acetic acid can be accomplished by the use of nascent hydrogen.

Description and Physical Properties.—Deliquescent crystals having a slight, characteristic odor. One Gm. of Trichloracetic Acid is soluble in about 0.1 cc. of water at 25° C. It is very soluble in alcohol and in ether.

"Trichloracetic Acid heated with a solution of an alkali hydroxide is decomposed with the formation of alkali carbonate and chloroform, the latter being recognizable by the odor of phenylisocyanide (a poisonous substance), when a few drops of a saturated, aqueous solution of aniline are added to the heated mixture.

"Ash: not more than 0.05 per cent. Dissolve about 0.5 Gm. of ferrous sulphate in 5 cc. of an aqueous solution of Trichloracetic Acid (1 in 20), and superimpose it upon 5 cc. of sulphuric acid: no brownish-red color develops at the zone of contact (*nitric acid*). One Gm. of Trichloracetic Acid shows no more *chloride* than corresponds to 0.5 cc. of fiftieth-normal hydrochloric acid.

"**Assay.**—Proceed as directed under the assay for acids, using about 4 Gm. of the Acid, previously dried to constant weight over sulphuric acid, and phenolphthalein T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.1634 Gm. of $CCl_3.COOH$. Each Gm. of Trichloracetic Acid, previously dried to constant weight over sulphuric acid, corresponds to not less than 6.06 cc. and to not more than 6.12 cc. of normal sodium hydroxide.

"Preserve in well-stoppered bottles, in a cool place, protected from light." *U. S.*

Uses.—In dilute solution (1 per cent. or less) trichloracetic acid is strongly astringent and has been used as a local application in *hyperhydrosis* and congestion of the mucous membranes. In concentrated form it destroys vitality of tissue through its active precipitation of protein and also has the power of dissolving keratin. This combination of properties makes it a valuable caustic, especially in the treatment of various forms of keratosis such as *warts, moles,* etc. It has also been used as a caustic in vascular *naevi, chancroids, lupus,* etc. Its caustic action is accompanied with relatively little pain and it leaves a white leathery eschar. Gallaher (*Laryngoscope,* 1918, xxviii, p. 551) has highly praised it as a local application in *Vincent's angina.*

As an astringent trichloracetic acid may be applied in strengths of from 1/10 to 1 per cent. When used as a caustic a few drops of water may be added to the crystals to liquefy them and this solution applied by means of a glass rod, the surrounding parts being protected with vaseline or collodion. When the caustic has penetrated deeply enough the parts should be washed with a solution of carbonate of soda. It is also actively antiseptic and is used in diluted solution, 1 in 1000 to 1 in 2000, in *ozena* and other forms of chronic *inflammation of the nose, pharynx* and *tonsils.*

ACONITINA. U. S., Br.

ACONITINE Aconitin.

"An alkaloid [$C_{34}H_{47}O_{11}N$] obtained from aconite. Aconitine, administered subcutaneously to guinea pigs, has a minimum lethal dose of not less than 0.00,000,005,5 Gm. and not more than 0.00,000,006,5 Gm. for each gram of body weight of guinea pig." *U. S.* "Aconitine, $C_{34}H_{45}NO_{11}$, is an alkaloid obtained from Aconite Root." *Br.*

Aconitia, Aconitinum, Aconitin, Aconitine, *Fr. Cod.;* Aconitin, *G.;* Aconitina, *It., Sp.*

Formerly a process for the manufacture of aconitine was given in the U. S. and Br. Pharmacopœias, but is no longer given by either authority.

Crystallized aconitine was first made known by the researches of Groves (*P. J.,* 2d ser., viii, 121), but it was elaborately studied by Duquesnel. The methods of obtaining it differ, but, according to Patrouillard (*J. P. C.,* 4e sér., xix, 151), that of Duquesnel gives much the larger yield. It is as follows: 100 parts of the powdered roots having been mixed with one part of tartaric acid, and the whole exhausted by repeated percolation with cold alcohol, the liquid is evaporated at a low temperature on a water bath to the consistence of a fluidextract. To this, distilled water is added, and the precipitated resinous and oily matters removed by filtration. The solution of aconitine tartrate is then precipitated with a slight excess of potassium bicarbonate, agitated with washed ether, and the two fluids separated with a siphon. The ethereal solution is shaken four or five times with a 10 per cent. solution of hydrochloric acid, which takes up the alkaloids from the ethereal solution. The acid liquids are treated with calcium carbonate to saturation in order to prevent the prolonged and injurious action of the acid upon the crystallizable aconitine, the mixture is evaporated at a very gentle heat, filtered, and while still warm mixed with a solution of sodium nitrate (2 of salt to 3 of water) having the same temperature. The whole is allowed to cool slowly during several hours, and set away for several days' rest, when the crystals separate out as a crust on the bottom.

Pure aconitine may exist in an amorphous or in a crystalline form. The official product is always crystalline, but of amorphous aconitine there are two varieties, the hydrated and the anhydrous. When the alkaloid is dried at ordinary temperature, it retains 20 (Hager) or 25 (Hottot) per cent. of water; but when dried at the temperature of the water bath, it is anhydrous, and is then *not* soluble in 50 parts of boiling water. (Hager, *A. J. P.,* xlvii, 210.) For Hottot's process of preparing aconitine, see 15th ed., U. S. D.

The amorphous aconitine of commerce is of very uncertain composition and value, and should never be substituted for official aconitine. The official aconitine, however, of the Pharmacopœia is not pure aconitine of the chemist, but is a more or less variable mixture of the alkaloids of aconite. As these individual alkaloids differ greatly in their toxicity, it is obvious that aconitine will vary in its power almost as widely as aconite itself.

Description and Physical Properties.—"Colorless or white crystals. It is odorless, and is stable in the air. *Caution—Aconitine is extremely poisonous.* Aconitine is very slightly soluble in water. One Gm. dissolves in 28 cc. of alcohol, in about 65 cc. of ether, and in 7 cc. of benzene, at 25° C. It is almost insoluble in petroleum benzin.

"Aconitine melts at about 195° C. when heated rapidly. Solutions of Aconitine in neutral solvents are slightly alkaline to litmus paper. About 0.001 Gm. of Aconitine mixed with 2 or 3 drops of nitric or sulphuric acid on a white porcelain surface dissolves without coloration. Under the same conditions, 0.001 Gm. of Aconitine mixed with 2 drops of sulphuric acid containing 0.005 Gm. of ammonium vanadate in each cc. produces an orange color. Dilute solutions of Aconitine salts yield precipitates with mercuric potassium iodide T.S., tannic acid T.S., and gold chloride T.S., but only concentrated solutions yield precipitates with platinic chloride T.S., mercuric chloride T.S., and trinitrophenol T.S.

"The ash from 0.05 Gm. is negligible. Evaporate to dryness on a water bath about 0.01 Gm. of Aconitine with 5 drops of fuming nitric acid, cool, and treat the resulting yellow residue with alcoholic potassium hydroxide T.S.: no violet color develops (*pseudaconitine or atropine*).

"**Assay.**—Dissolve the Aconitine in distilled water with the aid of a little acetic acid and proceed as directed under *Tinctura Aconiti.*

"Preserve in well-closed containers, protected from light." *U. S.*

Aconitine as defined by the Br. Pharmacopœia is in "colorless, transparent, hexagonal crystals belonging to the rhombic system, prismatic and tabular. Melting point 198° C., at which temperature evolution of acetic acid occurs. Almost insoluble in *water, petroleum spirit,* and *carbon disulphide;* readily soluble in *benzene* and in *chloroform,* less readily in *ether* and in *absolute alcohol.* Forms a crystalline hydrochloride which melts at 149° C. A drop of an aqueous solution (1 in 10,000) placed upon the tongue produces a characteristic tingling and numbing sensation. An aqueous solution, not more dilute than 1 in 4000, faintly acidified with *acetic acid,* yields a reddish precipitate on the addition of a few drops of *N/10 solution of potassium permanganate.* The ethereal solution obtained by boiling Aconitine with *N/2 alcoholic solution of potassium hydroxide,* removing most of the alcohol by evaporation, diluting with *water,* acidifying, and extracting with *ether,* leaves on evaporation a crystalline residue of benzoic acid. When 0.0002 gramme of Aconitine is gently warmed with 4 drops of *sulphuric acid* an odor of benzoic acid is evolved, and if after five minutes a few crystals of *resorcin* are added and the heat continued, a reddish-yellow color, changing to intense red, is produced. No appreciable ash." *Br.*

Aconitine is precipitated from its solution by caustic alkalies, but not by ammonium carbonate or potassium and sodium bicarbonates. A spurious substance has sometimes been sold under the same name, which is nearly or quite inert; and at best the alkaloid is apt to be of uncertain strength as found in commerce.

Monti proposes a color test for aconitine with resorcinol which is now official in the Br. Pharm., 1914, after some modification. (See *P. J.,* 1908, 596.)

For E. R. Squibb's physiological test for aconitine and aconite preparations, see under *tinctura aconitum.* Its only peculiar color reaction is obtained with difficulty by dissolving in diluted phosphoric acid and evaporating, when at a certain degree of concentration a violet coloration appears.

Uses.—Aconitine produces effects on the system similar to aconite. Because of its extreme toxicity, as well as its variability, its use is not to be encouraged.

Dose, one eight-hundredth to one four-hundredth of a grain (0.000075–0.00015 Gm.).

Off. Prep—Unguentum Aconitinæ, *Br.;* Oleatum Aconitinæ, *N. F.*

ACONITUM. U. S. (Br.)

ACONITE Aconit. [Monkshood Aconite Root Aconiti tuber P. I.]

"Aconite is the dried tuberous root of *Aconitum Napellus* Linné (Fam. *Ranunculaceæ*). Aconite, in the form of the tincture, administered subcutaneously to guinea pigs, has a minimum lethal dose not exceeding 0.004 cc. of tincture for each gram of body weight of guinea pig. Aconite contains not more than 5 per cent. of its stems or 2 per cent. of other foreign organic matter." *U. S.*

"Aconite Root is the dried root of Aconitum Napellus, *Linn.*" *Br.*

Aconiti Radix, *Br.;* Aconite Root, Monkshood, Wolfsbane, Wolfroot, Friar's cap, Cuckoo's cap, Blue rocket; Racine d'Aconite, Aconit, Coqueluchon, Aconit Napel, *Fr.;* Tubera Aconiti, *P. G.;* Eisenhut, Eisenhutknollen, Sturmhut, Mönchskappe, Akonitknollen, *G.;* Aconito, *It., Sp.*

The name Aconite is derived, according to Pliny, from the Black Sea port, Aconie. While the drug was used by the ancient Chinese as well as by the hill tribes of India, it was introduced into modern medicine by Störck, of Vienna, in 1763. The genus *Aconitum* is a relatively large one, there being some sixty well-defined species, nearly half of which have been used in medicine. The species which is official and recognized by nearly all the Pharmacopœias is *Aconitum Napellus.* It is indigenous to the mountainous regions of Middle Europe and is found growing in Northern Europe, Siberia and Central Asia. It is extensively cultivated in temperate climates for its foliage and flowers and has been successfully grown in the testing garden of the U. S. Department of Agriculture. Schneider reports that it has become naturalized to some extent in California. There are five species of Aconitum which are indigenous to the mountainous regions of the Northern United States, two of these being found in the Rocky Mountains and on the Pacific Coast. Holm describes the morphology and structural characteristics of the wild Monkshood of the United States, *A. uncinatum* L., in *Merck's Rep.,* 1907, p. 65.

The roots or rhizomes of several other species of Aconitum are found in commerce, these being chiefly used in the manufacture of the alkaloids. (1) The tuberous roots of *A. variegatum* L. and of *A. Stoerkianum* Reich, are sometimes found in the commercial drug. These are smaller, not so pungent, although quite active. (2) Japanese Aconite is derived from *A. Fischeri* Reich. and *A. uncinatum* L. var. *japonicum* Regel. The roots are light to dark gray or brownish in color, fleshy, being smaller than the official tubers. They have a more or less circular cambium and the starch grains are more numerous than in the official root. They are largely imported into Europe and to some extent to this country. (3) Indian Aconite is derived from *A. ferox* Wall., a plant growing in the Himalayas and in Nepal. The roots are from 5 to 10 cm. long and from 2 to 4 cm. in diameter, being externally grayish-brown and deeply furrowed. They are hard, the fracture being horny or mealy and the inner surface is either yellowish-brown or whitish. The cambium is 7- to 9-rayed and the taste resembles that of the official Aconite. (4) Another species of Aconitum that is very poisonous is *A. Lycoctonum* L., of Europe and Northern Asia. This, however, does not produce a tuberous root, but develops an oblique rhizome surrounded with numerous roots. (5) The fleshy roots of *A. heterophyllum* Wallich., a plant growing in the West Himalayas, are somewhat ovoid and flattened at the summit and base. Externally they are grayish-brown. The odor resembles that of black pepper and the taste is bitter and acrid. The rhizome contains an amorphous bitter alkaloid, *atisine,* which is not toxic. Under the name of *Nepaul aconite* there enters European commerce the roots of species of aconite grown in India. It is by some believed that these are identical with those roots known in India as "Bikh" or "Bish," the latter apparently being derived from the *A. spicatum* Lam. Under the name of *Utees, Atees,* or *Atis,* the rhizome and roots of *A. heterophyllum* are said to be largely employed in doses of 20 grains as an antiperiodic. *Wakhma* is the root of *A. Palmatum* Don, in which Jowett found *aconitic acid* and the alkaloid *atisine,* $C_{22}H_{33}NO_3$, which, according to Cash, is physiologically very feeble. (*J. Chem. S.,* 1896.) While most of the species of *Aconitum* are more or less closely related in their physiological effects, the use of other species in medicine, even for the purpose of extracting alkaloids, is to be condemned. According to Fraser (*P. J.,* 1917, xcviii, 209) the various aconites may be divided into two classes, those in which aconitine is the prevailing alkaloid and those in which pseudo-aconitine predominates; since these two alkaloids are not identical in their effects it follows that the alkaloids obtained from unofficial species may exercise a different effect from the official aconitine.

Aconitum Napellus is a perennial herbaceous plant, with a fusiform to conical tuberous root, seldom exceeding 10 cm. in length and 2 cm. in thickness near the summit, brownish externally, whitish and fleshy within, and sending forth numerous long, thick, fleshy rootlets. When the plant is in full growth, there are usually two roots joined together, of which the older is dark brown, fusiform, wrinkled, and supports the stem, while the younger of a light yellowish-brown color and conical shape is destined to furnish the stem of the following year, the old root decaying. The stem is erect, round, smooth, leafy, usually simple, and from two to six or even eight feet high. The leaves are alternate, petiolate, divided almost to the base, from two to four inches in diameter, deep green upon their upper surface, light green beneath, somewhat rigid, and more or less smooth and shining on both sides. Those on the lower part of the stem have long footstalks and five or seven divisions; the upper, short footstalks and three or five divisions. The divisions are wedge-form, with two or three lobes, which extend nearly or quite to the middle. The lobes are cleft or toothed, and the laciniæ or teeth are linear or linear-lanceolate and pointed. The flowers are of a dark violet-blue color, large and beautiful, and are borne at the summit of the stem upon a thick, simple, straight, erect, spike-like raceme, beneath which, in the cultivated plant, several smaller racemes arise from the axils of the upper leaves. There are 2 lanceolate bracts beneath each pedicelled flower. The sepals are five, the upper helmet-shaped and beaked, nearly hemispherical, open or closed, the two lateral roundish and internally hairy, the two lower oblong-oval. They enclose two to eight hammer-like petals, the 2 posterior ones being nectariferous and covered by the hood of the posterior sepal. The carpels are 3 to 4 with bilobed stigma.

The fruit consists of three to four beaked follicles. The seeds are angular, wrinkled and very acrid. They rapidly lose their germinating power upon drying and storing and are for the greater part non-viable after a year.

This plant is abundant in the mountain forests of France, Switzerland, and Germany. It is also cultivated in the gardens of Europe, and has been introduced into this country as an ornamental plant. All parts of the plant are acrid and poisonous. The leaves and root are used. The leaves should be collected when the flowers begin to appear, or shortly before. After the fruit has formed, they are less efficacious. The *fresh leaves* have a faint narcotic odor, most sensible when they are rubbed. Their taste is at first bitterish and herbaceous, afterwards burning and acrid, with a feeling of numbness and tingling, on the inside of the lips, tongue, and fauces, which is very durable, lasting sometimes many hours. When long chewed, they inflame the tongue. The *dried leaves* have a similar taste, but the acrid impression commences later. Their sensible properties and medicinal activity are impaired by long keeping. The root is much more active than the leaves, and an extract from the latter is said to have only one-twentieth of the strength of one made from the former. It should be gathered in autumn or winter after the leaves have fallen, and is not perfect until the second year. It has been mistakenly substituted for horseradish root, as a condiment, with fatal effects. The wild plant is said to be more active than the cultivated. (Schroff.) The studies of P. W. Squire seem to show that in the autumn the root is the most active. So far, however, as concerns the whole plant, the practical difficulty is that the root of *A. paniculatum* Lam. cannot be distinguished by the ordinary collector from that of *A. Napellus,* except by taste; so that the custom which seems to prevail of gathering the root about the flowering period is probably well founded. The plant is being cultivated to some extent for medicinal purposes in England, but much of the stock is of doubtful nature, owing to the extraordinary tendency of *A. Napellus* to hybridize with other species and to alter under cultivation. (See *P. J.,* 1889, 645.) For Keller's test for aconite root and leaves, see *Proc. A. Ph. A.,* 1895, 539.

Aconite root is collected chiefly from plants growing wild in the cool mountainous regions of Germany, Switzerland, Spain and France. The tuberous roots are dug up in autumn, washed and carefully dried. The present commercial supplies coming to the United States are shipped chiefly from Trieste, Hamburg, Leghorn, Barcelona and Marseilles.

A number of substitutes and adulterants for official aconite root have appeared in commerce within recent years. Chief among these have been the roots of *Aconitum Fischeri* Reichb., *A. chasmanthum* Stapf. and *A. Laciniatum* Stapf.

The root of *A. Fischeri* Reichb., commonly known as *"Japanese Aconite"* has been a very common article of commerce. It is smaller than the official aconite for which it has been substituted, and may be further distinguished from the genuine article by its lighter weight, short conical shape generally more mealy interior and usually dark greyish; less deeply wrinkled exterior. Cross sections exhibit a less pronounced stellate cambium and more numerous fibro-vascular bundles arranged in a wavy circle.

The root of *A. chasmanthum* Stapf. is generally smaller than the official article, about 2 cm. long and about 0.75 cm. in diameter, less wrinkled with rootlet stubs usually clustered at the basal end. It contains *indacinatine.*

The root of *A. laciniatum* Stapf., commonly known as "*Nepaul Aconite*" or to the natives of India as "*Bikh*" or "*Bish Aconite*" is larger than that of *A. napellus,* being up to 15 cm. in length and 4 cm. in diameter near the crown; it is fusiform to irregularly cylindrical in shape, coarsely wrinkled and brown externally, usually yellowish and horny internally, showing gelatinized starch when scrapings are examined under the microscope. It contains *pseudaconitine.*

Commercial aconite root shows considerable variation and is usually a mixture of six or seven different kinds of tubers, as follows: 1. Single fleshy tubers which are smooth, light brown and full of starch. 2. Single tubers which are single, somewhat elongated fusiform, crowned with short stems, dark brown and longitudinally furrowed. 3. Twin tubers, one of which is bud-crowned and the other having a short stem at the summit. 4. Very small single tubers usually crowned with stems, the lower portion being acute or pointed. 5. Single tubers which are almost cylindrical, crowned with stems and either fleshy and nearly smooth or more or less shrunken and furrowed. 6. Dark brown resinous tubers. 7. And finally fragments of small and nearly filiform roots.

The *root* has a feeble earthy odor. Though sweetish at first, it has afterwards the same effect as the leaves upon the mouth and fauces. It shrinks much in drying, and becomes darker, but does not lose its acridity.

Description and Physical Properties.—"*Unground Aconite.*—More or less conical or fusiform, from 4 to 10 cm. in length, and from 1 to 3.5 cm. in diameter at the crown; externally dark brown or grayish-brown, smooth or longitudinally wrinkled, the upper end with a bud, or remains of bud-scales and a stem-scar, the other portions with numerous root-scars or short rootlets; fracture short, horny or somewhat mealy; internally whitish, light brown, or dark brown; bark, 1 to 2 mm. in thickness, cambium zone usually 5- to 8-angled; odor very slight; taste sweetish, soon becoming acrid and developing a tingling sensation, followed by numbness. (*Taste cautiously.*)

"*Structure.*—An outer layer of one or more rows of suberized cells with blackish-brown walls; a primary cortex of parenchyma and characteristic stone cells, separated by a modified endodermis from an inner layer of starch-bearing parenchyma interspersed with a few small vascular bundles; in the cambium zone a 2- to 4-rayed collateral vascular bundle at each angle or a number of small bundles in an irregular circle; pith of large starch-bearing parenchyma cells.

"*Powdered Aconite.*—Grayish-brown; starch grains numerous, spherical, somewhat planoconvex, single, or 2- to 5-compound, the individual grains from 0.003 to 0.020 mm. in diameter and frequently with a central cleft; tracheæ mostly with slit-like, simple pores, sometimes with spiral or reticulate thickenings or with bordered pores; stone cells single, or in small groups, tabular, irregular, rectangular or elongated in shape, from 0.1 to 0.4 mm. in length, walls strongly lignified and having large simple pores; a few fragments of cells with brownish walls; fragments of parenchyma numerous, the cells being filled with starch grains; bast-fibres from stems few, very long, with lignified walls and marked by transverse or oblique, slit-like pores.

"**Assay.**—Prepare a tincture by the official process, and assay as directed under *Tinctura Aconiti.*" *U. S.*

The following standards for aconite root are given in the British Pharmacopœia: "From four to ten centimetres long, and from one to two centimetres wide at the upper extremity. Conical, dark brown, with numerous root scars, and crowned with base of the stem or the remains of a bud. Internally solid and starchy. In transverse section a stellate cambium with small vascular bundles at the projecting angles; primary cortex narrow, with isolated thick-walled sclerenchymatous cells; cells of parenchymatous tissue contain numerous small simple or compound starch grains. No marked odor; taste at first slight, followed by persistent sensation of tingling and numbness." *Br.*

The British Pharmacopœia formerly recognized the flowering tops of the Aconite (*Aconiti Folia*). To be effective they should be collected just as the flowers are beginning to expand, at which time they are richest in alkaloid. The dried leaves are stated to contain about 0.3 per cent. and the flower-buds about 0.4 per cent. of aconitine. For an account of the chemistry of aconite, see *Aconitina.*

Chemical Assay.—According to Roth (*J. A. Ph. A.,* 1913, ii, p. 705) the chemical assay of aconite does not offer any measure of its activity; and Haskell (*Am. Drug.,* 1916, lxiv, 129) asserts that the chemical aconitine assay is not only useless but dangerously misleading. The U. S. has therefore, entirely omitted the chemical standard but it is still recognized by the Br. Probably the most satisfactory test yet devised is the toxicity of the guinea pig, as recommended by the U. S. P. X. Even this is far from satisfactory, as according to Dohme (*Proc. Amer. Drug. Man. Assoc.,* 1919) the fatal dose may range from 66 to 133 per cent. of standard in the hands of different experimenters. The chemical assay recommended by the Br. is as follows:

"Yields not less than 0.40 per cent. of ether-soluble alkaloids when assayed by the following process, provided with a glass tap and suitably plugged with cotton wool, introduce 10 grammes of Aconite Root in No. 40 powder and 75 millilitres of *alcohol* (70 per cent.). Macerate for four hours, shaking occasionally. Then allow percolation to proceed slowly until the liquid ceases to drop. Continue the percolation by the addition of more of the same menstruum until 150 millilitres have been collected or the Root is exhausted. Evaporate the percolate to dryness in a shallow porcelain evaporating basin, at a temperature not exceeding 60° C. Dissolve the residue in 5 millilitres of *N/10 solution of sulphuric acid* diluted with 20 millilitres of *water*. Filter into a separating funnel, washing the dish and filter with about 30 millilitres of *water*. Add to the mixed filtrate and washings 25 millilitres of *ether* and 2 millilitres of *solution of ammonia*, and shake for one minute. After separation draw off the lower layer into a flask, and filter the ethereal solution into a beaker. Return the contents of the flask to the separator, add 20 millilitres of *ether* and again shake for one minute, separating the aqueous liquid and filtering the ethereal solution into the beaker. Repeat the operation with two other portions, each of 20 millilitres, of *ether*. Evaporate the mixed ethereal solutions to dryness, dry the residue at 60° C., dissolve it in 5 millilitres of *N/20 solution of sulphuric acid* diluted with 20 millilitres of *water*, and titrate back with *N/20 solution of sodium hydroxide*, *tincture of cochineal* being used as indicator. Deduct the number of millilitres of the alkaline solution required from 5, multiply the difference by 0.3217; the result will be the percentage of ether-soluble alkaloids in the powdered Root." *Br.*

Constituents.—Our present knowledge of the chemistry of aconite is based chiefly on the investigations of Dunstan (*Tr. Chem. Soc.*, 1892, lxi, p. 285 and 1905, lxxxvii, p. 1622; *P. J.*, 1893, p. 625), Schulze (*A. Pharm.*, 1906, ccxliv, p. 169 and 1916, ccliv, p. 567), Wright (*J. Chem. S.*, 1875, xxix and 1879, xxxv, p. 387).

Aconitum Napellus contains at least three distinct alkaloids. The alkaloid *aconitine*, which was first separated in a pure state by Groves in 1860, is the most important of these principles. It has been assigned various formulæ; Wright gives $C_{33}H_{43}O_{12}N$; the U. S. accepts the formula of Freund and Beck, $C_{34}H_{47}O_{11}N$, but the Br. that of Schulze, $C_{34}H_{45}O_{11}N$. It has been shown that pure aconitine crystallizes in rhombic prisms, has a melting point of 197° to 198° C. and is dextrorotatory. When its solution is heated under pressure to a temperature of 120° C. it undergoes hydrolysis into benzoyl aconine and acetic acid. Subsequently the first of these bases is split up into benzoic acid and aconine.

Benzoyl-aconine (also called *benzaconine*) seems to be identical with *napelline* or *isaconitine*. Its formula is given by Schulze as $C_{32}H_{43}O_{10}N$, its melting point 130° C. It is amorphous but forms crystalline salts. It is dextrorotatory but furnishes laevorotary salts. It occurs naturally in aconite root or can be formed by hydrolysis from aconitine. Its toxicity is very much less than that of aconitine and it appears to differ somewhat in the type of its physiological action as well as in the degree.

Aconine is one of the final products of hydrolysis and also occurs naturally in aconite root. Dunstan gives its formula as $C_{26}H_{41}O_{11}$ but Schulze gives $C_{25}H_{39}O_9N$. Its melting point is 132° C. It is actively dextrorotatory but yields laevorotary salts. Neither it nor its salts have been crystallized because of their hygroscopic properties.

Picraconitine of Wright is probably a mixture.

Other species of aconitum yield allied but different alkaloids from the official. We shall list briefly the more important of these: *Aconitum ferox* Wall contains according to Wright the alkaloid *pseudaconitine*. The same alkaloid is found also in the Nepaul aconite whose exact botanical origin is somewhat doubtful. Its formula is $C_{36}H_{51}O_{12}N$. It hydrolyzes into acetic acid and veratroyl-pseudaconine. According to Cash and Dunstan (*Phil. Trans. Roy. Soc.*, 1902, cxcv, p. 39) it is more active than aconitine.

Of the two Japanese aconite roots the *A. uncinatum* contains, according to Wright, the alkaloid *japaconitine*. This is stated by Freund and Beck (*B. Chem. G.*, 1894, xxvii, p. 723) to be identical with aconitine, but Dunstan and Read (*Tr. Chem. Soc.*, 1900, lxxvii, p. 49) and Makoshi (*A. Pharm.*, 1909, ccxlvii, p. 242) maintain that, although closely allied to, it differs from aconitine. The *A. Fischeri* contains *jesaconitine*.

From *A. Lycoctonum*, Hübschman in 1866 obtained an alkaloid *lycoctonine*, but Dragendorf and Spohn (*J. P. C.*, 1884, x, p. 361) state that this is a decomposition product of *lycaconitine*. The latter authors also found myoctonine in this root.

Dustan and Andrews (*Tr. Chem. Soc.*, 1905, lxxxvii, p. 1636) found *bikhaconitine* in *A. Spicatum* and *indaconitine* in *A. chasmanthum*. *Aconitum septentrionale* contains *lappaconitine* (Schulze and Ulfert, *A. Pharm.*, 1922, clx, p. 230) and *septentrionaline* (Weidemann, *A. E. P. P.*, 1922, xcv, p. 136).

Uses.—Aconite was well known to the ancients as a powerful poison; it appears to have been used as an arrow poison early in Chinese history and perhaps also by the inhabitants of ancient Gaul. Although mentioned in the *Meddygon Myddfai*, published in Wales in the 12th century, it was introduced into regular medicine by Baron Störck of Vienna, whose experiments were published in the year 1762.

Locally aconite is actively irritant and also a paralyzant to the peripheral sensory nerves. When applied to a mucous surface it produces at first a burning tingling sensation followed in a few minutes by a numbness. This sensation may even be perceptible after the systemic ingestion of very large doses. When administered internally the most marked changes are seen in the circulation. The first effect is generally a slowing of the pulse due to stimulation of the cardio-inhibitory centers, with consequent fall in the blood pressure. After somewhat larger doses, however, there is a weakening of the force as well as reduction of the rate of the pulse brought about by a direct action on the heart muscles. After poisonous doses various irregularities of heart action are produced and often there will be complete lack of harmony between the contraction of the auricle and ventricle. After fatal doses the heart is arrested in complete diastole and will respond to neither electrical nor mechanical irritation. In the frog, large quantities of aconite produce a loss of reflex activity, which is apparently due to a paralysis of sensation as voluntary motion is preserved for some time later, although it too may eventually be abolished. The drug appears to affect both the sensory nerves and the receptive side of the spinal cord, although the latter is involved comparatively late in the poisoning. In mammals this depressant action upon the nervous system can scarcely be demonstrated because of the powerful depressant effect upon the circulation.

Aconite is used internally for the purpose of quieting overaction of the heart either due to essential diseases of the circulatory system or to various febrile complaints. For example, in certain cases of *valvular lesions* of the heart where, although the muscular compensation is apparently good, the pulse rate is abnormally rapid, apparently from loss of nerve control; and in the analogous condition of so-called *irritable heart,* seen in improperly trained athletes and military recruits and the like, in which despite the absence of any demonstrable organic lesion the heart rate tends to become very rapid on the slightest exertion aconite has long been a favorite remedy. Although its effects in these conditions are generally less certain than those of veratrum, because of its freedom from nauseating properties it is preferred by many clinicians. In cases of *high blood pressure* by slowing the pulse it will often lead to a sensible reduction in the arterial tension; it should be remembered in this connection, however, that there is no action upon the vasomotor center (see Pilcher and Sollmann, *J. P. Ex. T.,* 1915, vi, 366). Aconite has also been used in various mild *febrile conditions.* Whatever value it possesses in such states, however, must be ascribed to its action in preventing excessive rapidity of the heart or to a slight tendency towards the production of diaphoresis from slowing of the circulation.

Aconite is also frequently employed for its local effects. The combination of local irritant effects with anesthetic action suggests strongly its use in peripheral *neuralgias.* It must not be forgotten, however, that if used too freely for this purpose it may be absorbed through the skin in sufficient quantities to cause serious poisoning. It is also occasionally employed as a local anesthetic to the stomach in various types of *vomiting* or *gastralgia* but on account of its systemic effect is of secondary value.

For internal use the best preparation is the tincture which may be given in doses of from five to fifteen minims (0.3–0.9 cc.). For external application and fluidextract may be employed, but generally an ointment is preferred. This may be made by rubbing up the extract with two or three parts of lard, or the *ointment of aconitine* of the British Pharmacopœia may be used. The U. S., 1870, recognized a *plaster of aconite.*

Toxicology.—Aconite is a rapidly acting and powerful poison. The symptoms produced by overdose of it are sensations of warmth in the stomach, sometimes with nausea but usually without vomiting, with slowing of the pulse and of the respiration; the skin is cool and moist and there is profound prostration. As the poisoning progresses the respirations become more slow and shallow, the pulse more and more feeble and towards the end may become rapid or very irregular. A characteristic symptom, in fact the only symptom of diagnostic importance, is the peculiar numbness and tingling first felt in the lips and mouth, but later also often in the fingers. At times here is dimness of vision, the pupils may be either contracted or dilated, and occasionally delirium and stupor or convulsions may precede the fatal termination.

In the treatment of aconite poisoning the patient should be kept absolutely in a horizontal position or with the feet higher than the head. For the purpose of emptying the stomach the stomach pump is preferable to emetics as the latter involve a more or less serious strain upon circulation. Hartung (*A. E. P. P.,* 1912, lxix, 176) has shown experimentally the great value of atropine. Other circulatory stimulants such as strychnine, and ammonia, may also be used. Body temperature should be maintained by external application of heat.

Dose, of aconite root, one-half to one grain (0.032–0.065 Gm.).

Off. Prep.—Fluidextractum Aconiti, *U. S.;* Linimentum Aconiti, *Br.;* Tinctura Aconiti, *U. S., Br.*

ADEPS. U. S. (Br.)

LARD

"The purified internal fat of the abdomen of the hog (*Sus scrofa,* var. *domesticus* Gray, Fam. *Suidæ*)." *U. S.* "Prepared Lard is the purified internal fat of the hog, Sus scrofa, *Linn.*" *Br.*

Adeps Præparatus, *Br.;* Axungia Porci, s. Porcina, Axungia; Prepared Lard, Hog's Lard; Axonge, *Fr. Cod.;* Graisse, Graisse de Porc, Saindoux, *Fr.;* Adeps Suillus, *P. G.;* Schweineschmalz, *G.;* Grasso suino, Sugno, Grasso di Porco, Lardo, *It.;* Grasa de cerdo, Manteca de puerco, Lardo, *Sp.*

Preparation.—Lard is the prepared fat of the hog. The Br. Pharmacopœia (1898) gave a process for its preparation; but in this country it is generally purchased already prepared by the druggists. The adipose matter of the omentum and mesentery and that around the kidneys, are usually employed, though the subcutaneous fat is said to afford lard of a firmer consistence. In the crude state it contains membranes and vessels, and is more or less contaminated with blood, from all of which it must be freed before it is fit for use. For purification, the fat, having been deprived of membranous matter as far as possible by the hand, is cut into pieces, washed with water till the liquor ceases to be colored, and then, after carefully separating the water, it is melted in a copper or iron vessel, over a slow fire, or, on the large scale, by steam heat. The heat is continued until all the moisture is evaporated, which may be known by the transparency of the melted fat, and the absence of crepitation when a small portion of it is thrown into the fire. This operation is technically known as "rendering." In the western packing houses this operation is performed upon a tremendous scale. The rendering tanks holding nearly 100,000 lbs. Care should be taken that the heat be not too great, as otherwise the lard may be partially decomposed, acquire a yellow color, and become acrid. The process is completed by straining the liquid through linen, and pouring it into suitable vessels, in which it hardens upon cooling. It has been suggested that for the complete removal of tissue the lard should be remelted over a water bath and then filtered through filter paper by means of a hot water funnel. Lard may be rendered inodorous by melting it, on a salt-water bath, with a little alum or common salt and continuing the heat until a scum rises which is skimmed off. The lard is then allowed to cool and the saline matter separated by washing it thoroughly with water. For a particiular account of the process, see *A. J. P.*, xxviii, 176.

Lard, as offered for sale, sometimes contains common salt, which renders it unfit for pharmaceutical purposes. This may be detected, when the quantity is insufficient to be sensible to the taste, by means of silver nitrate, which will produce a precipitate of silver chloride with water in which the salted lard has been boiled, after cooling and filtration. To free it from this impurity, it may be melted with twice its weight of boiling water, the mixture well agitated and set aside to cool, and the fat then separated. Lard was formerly adulterated with water, starch, and a small portion of alum and quicklime, which rendered it whiter, but unfit for medicinal use. But by far the most common adulteration of lard in recent years is through the use of cotton seed stearin. Crookes (*Analyst*, 1893, p. 221) gives the following very delicate modification of Milliau's test. Pure white filtering paper is first moistened with 12 per cent. solution of silver nitrate and held over a small sample of the lard, which is gradually heated in an oil bath to 115.5° C., when, if even less than 1 per cent. of cottonseed oil is present, the paper will turn light brown to nearly black. Pure fresh lard does not affect the paper. The best test for detecting imitation lard is the Halphen test for cottonseed fat, see under *Oleum Olivæ.*

The food laws recognize both *compound lard* and *imitation lard.* The latter consists of beef stearin and cotton seed oil with no lard whatever present. The former must contain at least 50 per cent. of genuine hog fat. The *compound lard* is rarely seen at present but the *imitation lard* or *lard substitute* as it is also called is freely sold at a lower price than lard. The regulations regarding its sale require that it be plainly labeled so as to designate its character, but much of it is sold as pure lard by unscrupulous grocers.

It may be readily distinguished by applying the U. S. P. tests which detect cotton seed stearin and also by the crystallization test which enables beef stearin to be detected.

Lard from hogs which have been fed with cottonseed meal will not only show the tests for cottonseed oil (Becchi and Halphen tests), but even the presence of physosterin or vegetable cholesterin can be shown. (Emmett & Grindley, *J. Am. C. S.*, 1905, 270.)

The slight reaction shown under these conditions is not likely to be confused, however, with the marked reaction which occurs in a sample of lard which is actually adulterated, as has been shown in the examination of hundreds of samples in the enforcement of the food laws.

Although it is possible at this time to obtain lard of excellent quality in the American market, if due care is observed (Gordon, *Proc. Pa. Pharm. Assoc.*, 1901, 126), there are many grades of lard to be found in commerce, designated by the dealers as follows: 1. Neutral (or Kettle) lard. 2. Leaf lard; made by melting the whole flare with steam, followed by pressure. 3. Choice kettle-rendered lard, chiefly from fat from the back of the hog. 4. Prime steam lard, from all the fatty parts of the hog. 5. Butcher's lard, melted on an open fire. 6. Off grade lard, from salt fat. 7. Dead hog grease from diseased hogs. 8. Brown grease from the intestines. 9. White grease, from the other parts. 10. Yellow grease, from the waste of packing warehouses. 11. Pig's foot grease, from glue factories.

Description and Physical Properties.—"A soft, white, unctuous mass, having a faint odor, and a bland taste. It is free from rancidity. Lard is insoluble in water; very slightly soluble in alcohol; readily soluble in ether, chloroform, carbon disulphide, and in petroleum benzin.

"Lard melts between 36° and 42° C., forming a clear liquid from which no aqueous layer separates. Distilled water boiled with lard shows no alkaline reactions to litmus paper (*alkalies*). Dissolve 10 Gm. of Lard in 30 cc. of chloroform, mix the solution with 10 cc. of neutralized alcohol, and add 1 drop of phenolphthalein T.S.: not more than 2 cc. of tenth-normal sodium hydroxide is required to produce a pink tint when shaken vigorously (*free fatty acids.*) Boil 1 Gm. of Lard with 20 cc. of alcohol under a reflux condenser for ten minutes, cool, filter, and add to the filtrate 5 drops of an alcoholic solution of silver nitrate (1 in 50): the turbidity, if any, is not greater than that produced by the same quantity of the silver nitrate solution in a mixture of the same volume of alcohol and 0.5 cc. of fiftieth-normal hydrochloric acid (*chloride*). Agitate in a test tube 5 cc. of melted and filtered Lard, while warm, with 5 cc. of an alcoholic solution of silver nitrate (made by dissolving 0.1 Gm. of silver nitrate in 10 cc. of alcohol, and adding 2 drops of nitric acid), and heat this mixture for five minutes on a water bath: the liquid fat acquires no reddish or brown color, nor is any dark color produced at the line of contact of the hot liquids (*cottonseed fats*). Dissolve 5 Gm. of Lard in 20 cc. of ether in a test tube, close the tube loosely with purified cotton, and allow it to stand for about eighteen hours at a temperature of about 20° C. Collect some of the crystals which have separated at the bottom of the test tube, mount them either in alcohol or in a fixed oil, and examine under a microscope having a magnifying power of about two hundred diameters: lard stearin crystallizes in the form of flat, rhomboidal plates, cut off obliquely at one end and grouped irregularly. (Beef stearin crystallizes in the form of cylindrical rods or needles with sharp ends and grouped in fan-shaped clusters.) Saponification value: not less than 195 and not more than 203. Iodine value: not less than 46 and not more than 70.

"Preserve in a cool place, in well-closed containers which are impervious to fat." *U. S.*

"A soft, white, homogeneous, unctuous substance. Odor faint but not rancid. Entirely soluble in *ether*. *Acid value* not more than 1.2; *saponification value* 192 to 198; *iodine value* 52 to 63; *unsaponifiable matter* not more than 0.5 per cent.; *refractive index* at 60° C. 1.4530 to 1.4550. Forms on melting a clear liquid which does not deposit water on standing. *Water* boiled with it does not acquire an alkaline reaction (absence of alkalies), and, after filtering and acidifying with *nitric acid,* does not yield any reaction with *solution of silver nitrate* (absence of chlorides). When a mixture of 20 millilitres of the melted and filtered Lard with 10 millilitres of *hydrochloric acid* containing 1 per cent. of *refined sugar* is shaken for half a minute and allowed to stand, the acid layer does not become pink (absence of sesame oil). In India, Prepared Suet (Sevum Præparatum) should be employed in making the official preparations for which Prepared Lard is directed to be used." *Br.*

When melted, it readily unites with wax and resins. Like most animal fats and oils, it consists of stearin, palmitin, and olein its consistence, when pure, depending largely upon the relative proportions of these principles.

Lard oil, which was formerly recognized by the U. S. P. VIII under the name of *Oleum Adipis,* is made by exposing lard to low temperatures and then subjecting it to powerful pressure. In this way the stearin of the lard is separated from the olein, the latter oozing out from the presses in the form of a yellowish-white oil; the stearin left behind is found in the market in large cakes and is largely used in making soap. Lard oil is colorless or pale yellow liquid which, at a temperature below 10° C. begins to deposit a white granular fat and forms a solid white mass at approximately the temperature of freezing water. Its specific gravity is from 0.905 to 0.915; it shows a saponification value of 195 to 197 and an iodine value between 56 and 74. It is not pure olein but contains varying proportions of stearin and is sometimes adulterated with paraffin oil.

Olein may also be separated by means of boiling alcohol, which, on cooling, deposits the concrete principles of the lard.

Exposed to the air, lard absorbs oxygen and becomes rancid. It should, therefore, be kept in well-closed vessels, or procured fresh when wanted for use. In the rancid state, it irritates the skin, and sometimes exercises an injurious reaction on substances mixed with it. Rancidity in lard and other fats is prevented by digesting them with benzoin or poplar buds (see *Adeps Benzoinatus*), and rancid lard may often be greatly improved by washing it with lime water. (See *Unguenta.*) Lard even when fresh is slightly acid, as was proved by Dieterich. (*A. Pharm.,* 1887.)

Uses.—Lard is emollient, and is occasionaly employed by itself in frictions, or in connection with poultices to preserve their soft consistence; but its chief use in pharmacy is as an ingredient in the preparation of ointments and cerates. (See under *Unguenta.*)

Off. Prep.—Adeps Benzoinatus, *U. S.* (*Br.*).

ADEPS BENZOINATUS. U. S., (Br.)

BENZOINATED LARD Adeps Benz.

Adeps Benzoatus, *Br., P. G.;* Benzoated Lard; Ointment of Benzoin; Unguentum Benzoini, *U. S.* 1870; Axungia Balsamica, s. Benzoinata, s. Benzoata; Axonge (Graisse) benzoinée (balsamique), *Fr.;* Benzoinirtes Schmalz, Benzoeschmalz, *G.;* Grasso con benzoino, *It.*; Manteca benzoada, Manteca con benjui, *Sp.*

"Lard, 1000 Gm.; Siam Benzoin, in coarse powder, 10 Gm.; to make about 1000 Gm. Melt the lard on a water bath, add the benzoin, mix thoroughly, and continue the heat for two hours, covering the vessel and not allowing the temperature to rise above 60° C. Strain the liquid through muslin, and stir it occasionally while it cools. Preserve in a cool place, in well-closed containers which are impervious to fat.

"NOTE.—For use in southern latitudes and during the heated season in other localities, 50

Gm. of the lard (or more, if necessary) may be replaced by an equal weight of white wax." *U. S.*

"Prepared Lard, 1000 grammes; Benzoin, in coarse powder, 30 grammes. Melt the Lard, add the Benzoin, and maintain at a temperature of 60 C. for one hour, stirring frequently; strain, and stir until nearly cold. In India, Benzoated Suet (*Sevum Benzoatum*) should be employed in making the official preparations for which Benzoated Lard is directed to be used." *Br.*

That the balsamic or resinous principles, in certain substances like benzoin, exercise a valuable function in preserving fats has been proved by abundant experience. The present U. S. formula differs somewhat from the British in the amount of benzoin directed. The name "benzoinated lard" is preferred by the U. S. Pharmacopœia to that used by the British Pharmacopœia "benzoated lard" because benzoin is used as a preservative; the word benzoated might imply that a benzoate or benzoic acid is employed. A much pleasanter and agreeable product is insured by heeding the U. S. directions as to limiting the temperature, a high heat volatilizing the odorous principles and communicating an empyreumatic odor.

ADEPS LANÆ. U. S., Br.

WOOL FAT Adeps Lan. [Anhydrous Lanolin, Refined Wool Fat]

"The purified, anhydrous, fat-like substance from wool of sheep (*Ovis aries* Linné Fam. *Bovidæ*)." *U. S.* "Wool Fat is the purified fat of sheep's wool, freed from water." *Br.*

Anhydrous wool-fat, *E.;* Suint de laine, *Fr.;* Adeps Lanæ, anhydricus, *P. G.;* Wollfett, *G.;* Lanolinum Anhydricum.

Both the United States and the British Pharmacopœias now recognize wool fat (anhydrous) and hydrous wool fat.

Preparation.—The wool of sheep contains from 10 to 50 per cent. of its weight of fat, which must be removed before the wool can be used in the manufacture of woolen fabrics. The crude fat was termed *æsypus* and *æsypum* by the ancients but the modern name for it is *suint.* This fat is a mixture of *cholesterin,* $C_{26}H_{43}(OH)$, esters of the several fatty acids contained in ordinary fats. Darmstaedter and Lifscheitz obtained from the alkaline washings of partially saponified wool fat two unsaturated alcohols, $C_{10}H_{20}O$ and $C_{11}H_{22}O$, both being colorless, odorless and tasteless powders; *lanolin alcohol,* also a colorless, odorless powder, was isolated by G. Marchetti (*B. Chem. G.,* 1895, No. 19); by the action of chromium trioxide the latter is converted into *lanolinic acid,* $C_{12}H_{22}O_3$, a white crystalline powder. (*P. J.,* 1895, p. 75.) Wool fat may be obtained by treating the wool with petroleum benzin and distilling off the benzin. The objection to the latter process is the difficulty of getting rid of the benzin odor. Liebreich's patented process for obtaining it from the washings of wool is as follows: The fresh undecomposed waste liquor or lye is passed through a centrifugal machine, in which the dirt and fat are separated from each other, while the cleansed soap liquor is continually drawn off by means of a pipe and led directly into the vat which serves for the acidulation. The raw lanolin thus obtained is thoroughly kneaded by suitable machinery in cold flowing water until the water which flows off is as clear as the water which flows in. The raw lanolin is then heated with water, thereby it is split up into water and fat. The latter is skimmed off from the surface and cooled, and for further purification it can be treated in the centrifugal machine in a melted condition, or it can be dissolved in ether, ethylated or methylated spirits, or other solvents and the solution can be separated from the residue by filtration or other means. The solvents can be recovered by treatment in suitable stills. After the fat has been cleaned as above stated, it is thoroughly kneaded with water for a long time, and a perfectly white neutral ointment is obtained. From the deposit in the lowest part of the centrifugal machine a further portion of lanolin can be obtained by stirring the same with clean or salt water and again treating it in the centrifugal machine, or extracting it, either in a wet or a dry condition, by means of a solvent, after which it is treated as above.

Instead of producing lanolin from wool-washing water it may be obtained from commercial wool fat by stirring this wool fat together with water containing sodium carbonate, caustic soda, or a mixture of these to form a thin milky solution, which is treated in the manner above described.

The practical difficulties in the way of purifying commercial wool grease so as to make a product which shall conform to the requirements for a medicinal article are very great. Solvents, bleaching agents and other material aids are necessary and the mechanical difficulties are also of importance. Many firms attempted the task during the war when the price was high but only a few were successful. (See *Ph. Era,* 1917, p. 279.)

Description and Physical Properties.—"A brownish-yellow, tenacious, unctuous mass, having not more than a slight odor. Wool Fat is insoluble in water, but mixes without separation with about twice its weight of water. It is sparingly soluble in cold alcohol, more soluble in hot alcohol, and freely soluble in ether and in chloroform.

"Wool Fat melts between 38° and 42° C. Dried to constant weight on a water bath with frequent stirring, Wool Fat loses not more than 0.5 per cent. of its weight (*water*). Ash: not more than 0.1 per cent. Dissolve 2 Gm. of Wool Fat in 10 cc. of ether, and add 2 drops of phenolphthalein T.S.: the liquid is not colored red (*free alkalies*), but on the addition of 0.2 cc. of tenth-normal sodium hydroxide a deep red color is produced (*free fatty acids*). Boil 1 Gm. of Wool Fat with 20 cc. of alcohol under a reflux condenser, cool, filter, and add to the filtrate 5 drops of an alcoholic solution of silver nitrate (1 in 50): the turbidity, if any, is not greater than that produced by the same quantity of the silver nitrate solution in a mixture of the same volume of alcohol and 0.5 cc. of fiftietn-normal hydrochloric acid (*chloride*). Warm 10 Gm. of Wool Fat with 50 cc. of distilled water on a water bath, constantly stirring the mixture until the Wool Fat is melted: the fat separates completely on cooling, leaving the aqueous layer nearly clear and neutral to litmus paper. A 10 cc. portion of the filtered aqueous layer leaves no sweet residue on evaporation (*glycerin*). Another 10 cc. portion of the filtrate emits no *ammonia* vapors when boiled with 1 cc. of sodium hydroxide T.S., and a further 10 cc. portion does not completely decolorize 0.05 cc. of tenth-normal potassium permanganate within ten minutes (*soluble oxidizable impurities*). About 0.5 Gm. of Wool Fat dissolves completely in 40 cc. of boiling dehydrated alcohol (*petrolatum*). Iodine value: not less than 18 and not more than 28, using 0.8 to 0.85 Gm. of Wool Fat.

"Preserve in a cool place in well-closed containers which are impervious to fat." *U. S.*

"A yellowish, tenacious, unctuous substance. Almost inodorous. Melting point about 40° C. When a solution of 0.1 gramme in a mixture of 5 millilitres of *chloroform* and 0.5 millilitre of *acetic anhydride* is gently poured upon the surface of 5 millilitres of *sulphuric acid* in a test-tube, a purplish-brown ring, the upper layer of which gradually becomes green, is developed at the surface of contact (presence of cholesterol). A solution of 0.2 gramme in 10 millilitres of *ether* remains colorless on the addition of 2 drops of *solution of phenolphthalein* (absence of free alkali), but becomes deep red on the addition of 1 drop of *N/1 solution of sodium hydroxide* (limit of free acid). Heated with *solution of sodium hydroxide* no ammoniacal odor is evolved (absence of organic nitrogenous matter). Ash not more than 0.3 per cent." *Br.*

For account of uses see under *Adeps Lanæ Hydrosus.*

Off. Prep.—Adeps Lanæ Hydrosus, *U. S., Br.*

ADEPS LANÆ HYDROSUS. U. S., Br.

HYDROUS WOOL FAT Adeps Lan. Hyd. [Lanolin]

"Hydrous Wool Fat consists of wool fat incorporated with not less than 25 per cent. and not more than 30 per cent of water." *U. S.*

Lanoline; Lanolin, Adeps lanæ cum aqua, *P. G.*; Wasserhaltiges Wollfett, *G.*; Lanolina, *It.*, *Sp.*

"Wool Fat, 70 grammes; Distilled Water, 30 millilitres. Mix." *Br.*

Description and Physical Properties.—"A yellowish-white, or nearly white, ointment-like mass, having not more than a slight odor. Hydrous Wool Fat is insoluble in water.

"With ether and with chloroform Hydrous Wool Fat yields turbid solutions which are neutral to moistened litmus paper. Hydrous Wool Fat heated on a water bath separates into an upper oily and a lower aqueous layer. When the heating is continued with frequent stirring until it ceases to lose weight, not less than 70 per cent. and not more than 75 per cent. of residue remains, which, when melted, is transparent and when cold, is a yellowish, tenacious, unctuous mass completely soluble in ether or chloroform and only sparingly soluble in alcohol. Hydrous Wool Fat thus deprived of water meets the requirements of the test for *petrolatum* under *Adeps Lanæ.* Hydrous Wool Fat complies with the tests for *free alkalies, free fatty acids, chloride, glycerin,* and *ammonia* described under *Adeps Lanæ,* allowance being made for the proportion of water present.

"Preserve in a cool place, in well-closed containers which are impervious to fat." *U. S.*

"10 grammes heated on a water-bath, with stirring, until the weight is constant, yield not less than 7 grammes of a residue which responds to the tests described under 'Adeps Lanæ.'" *Br.*

Uses.—As an ointment base wool fat has the following advantages over lard: it will absorb a larger quantity of water; it is less likely to become rancid; because of its stickiness it adheres more pertinaciously to the skin, and because of the difficulty in saponifying it it is less liable to be washed off. Because of its consistence it usually requires some thinning with cottonseed or other oil. It has been claimed for wool fat that it passes through the skin more readily than other ointment bases and is therefore especially suitable when it is desired to have medicaments absorbed. The fact, however, that this is a sebaceous secretion intended by nature to soften fibers of the wool and not for absorption, a priori would seem to render such a view improbable, and in the experiments of Sutton and of Gardiner it was found that wool-fat penetrated the skin much less readily than did lard. (See under *Unguenta.*)

ADONIS. N. F.

ADONIS Adon.

"Adonis is the overground portion of *Adonis vernalis* Linné (Fam. *Ranunculaceæ*). Adonis contains not more than 5 per cent. of foreign organic matter." *N. F.*

Pheasant's Eye, Vernal Pheasant's Eye, False Hellebore Spring Adonis. Sommerteufelsauge, *G.*

The *Adonis vernalis* is an erect perennial herb a little less than one foot high, with light green, pinnatifid leaves and conspicuous yellow solitary flowers and achene fruits. It is a native of northern Europe and Asia. Its rhizome sometimes occurs in commercial black Hellebore as an adulterant.

The commercial supply of Adonis comes to the United States from Hamburg, Germany.

Adonis aestivalis L. or *summer adonis* has recently been offered as a substitute for the genuine article. It may be distinguished from the latter by its crimson flowers and by its stem which unlike that of *A. vernalis* is branched at the top.

Description and Physical Properties.—"*Unground Adonis.*—Glabrous, with the exception of the younger portions which may be slightly grayish puberulent; stems from 15 to 50 cm. in length, longitudinally grooved, soft and weak, shining, simple or branched, the branches mostly from near the base and similar to the main stem, naked below, except for some scale-like leaf vestiges, densely leafy above; leaves from 2 to 4 cm. in length and two-thirds or more as broad, pinnately divided into several segments, the larger again divided, the ultimate segments being narrowly linear and acute; flowers terminal, yellow but usually drying to a cream color, from 3 to 6 cm. in breadth; sepals five, green or grayish puberulent, more than half the length of the petals, oblong, obtuse, finely nerved; petals from five to twenty, oblong, obtuse, finely nerved; stamens indefinite; pistils numerous, in fruit forming an ovoid, obtuse, dense head of ovoid achenes, which are tipped with the very small persistent styles. Odor faint; taste bitterish, slightly acrid.

"*Powdered Adonis.*—Grayish green; abundant pith parenchyma, the cells up to 0.050 mm. in width and 0.250 mm. in length, and with few simple pores; groups of long narrow fibers, mostly with lignified walls, the latter 0.005 to 0.007 mm. in thickness and having a few rounded or oblique simple pores; tracheæ spiral or with bordered pores and up to 0.017 mm. in width; epidermal cells from the stem and petiole elongated in surface view or from the blade composed of finely striated cells with wavy, vertical walls; elliptical stomata, the latter up to 0.064 mm. in length; brownish colored fragments from the scales at the base of the stem, composed of elongated cells with rounded ends and yellowish-brown walls; starch grains and calcium oxalate crystals few or absent." *N. F.*

Constituents.—Cervelo, in 1882, obtained from the plant a glucoside, to which he gave the name of *adonidin*. For improved method of preparation, see *P. J.*, vol. xvi, 145, and *A. J. P.*, 1887, 609. This glucoside occurs in the form of a somewhat hygroscopic, canary-yellow powder of an intensely bitter taste; soluble in water, alcohol, and in amyl alcohol; insoluble in anhydrous ether, chloroform, oil of turpentine, or petroleum benzin. Podwyssotzki found commercial samples of adonidin to be mixtures containing the active substance *picroadonidin*, which he describes as an amorphous glucoside having an excessively bitter taste easily soluble in water and alcohol and entirely soluble in ether. (*P. J.*, 1888, xix, 346.) According to Fuckelman, confirmed by Mercier (*Nouv. Rem.*, 1914), commercial adonidin is a mixture of a neutral body with a hemolytic acid, *adonic acid.*

Merck has described another crystalline principle, which fuses at 102° C., is very soluble in water and warm alcohol, and crystallizes in clear needle-like prisms. It has a neutral reaction, does not reduce Fehling's solution, and is not colored brown by alkalies. Its analysis formula is $C_5H_{12}O_5$, and Merck considers it to be a hitherto undescribed pentatomic alcohol, and calls it *adonite.* Whether it be identical with the *adonidulcite* announced in a preliminary communication by Podwyssotzki shortly before his death, Merck is not able to state, as no details of fusing point, formula, or chemical reaction were given by the former. (*M. Bull.*, Jan., 1893.) E. Fischer (*B. Chem. G.*, 1893, 633) has confirmed the findings of Merck.

Other species of adonis seem to possess similar properties to the official. Cervello (*A. E. P. P.*, xv) states that the glucoside adonidin exists in the *A. cupaniana.* Tahara (*B. Chem. G.*, 1891, xxiv) found an allied glucoside *adonin* in the *A. autumnalis* and Inoko (*A. E. P. P.*, xxviii) a glucoside also related to adonidin in the *A. amurensis* of Japan. Borgiotti (*D. M. Ztg.*, 1888) from clinical experience has found the *A. aestivalis* physiologically active.

Uses.—Adonidin belongs physiologically to the digitalis group. Although in Hare's experiments (*T. G.*, 1886) the frog's heart was arrested in diastole, Cervello (*A. E. P. P.*, xv) Schmidt (*A. J. P.*, 1920, xcii, 702) found that the arrest is systolic. The pulse is slowed by stimulation of the inhibitory apparatus. In the experiments of Henrijean (*B. A. R. B.*, 1909, xxiii, p. 363) in the early stages of the action, electrical stimulation of the pneumogastric nerve produced an unwonted degree of retardation of the pulse rate, which would indicate an increased excitability of the peripheral ends of the nerves. All investigators are in accord that the slowing of the pulse is to a large extent abolished by section of the vagi, so that the inhibitory influence must be largely also of central origin. There occurs also a pronounced rise of the blood pressure, which, according to Hare, is due partly to a stimulant action upon the heart, and partly to an effect upon the vasomotor mechanism. In the more exact experiments of Henrijean, vaso-constriction appeared only late in adonidin poisoning. After large toxic doses, the heart becomes irregular, and the blood pressure falls. According to Kakowski (*A. I. P. T.*, xv, p. 21), adonidin differs from most of the other digitalis group in that it dilates the coronary arteries, while most of these drugs produce constriction.

Adonis vernalis was introduced as a cardiac tonic by Bubnow in 1879. Clinical experience confirms the conclusion of the pharmacologist, that it resembles digitalis in its action, and is a useful agent in the treatment of chronic *heart disease.* The advantages which have been claimed for it are, that it is more prompt in its action, and that it manifests less cumulative tendency than digitalis, but it appears to be less certain in its effect. Bechterew asserts that it is a useful remedy in *epilepsy* when used in conjunction with the bromides. Under the name of *panadonine,* a preparation of the Japanese *A. Davurica* has been introduced into medicine, not only for its cardiac effect but also as an analgesic in *neuralgia.*

The *dose* of *Adonis vernalis* is from one to five grains (0.06–0.3 Gm.). The glucoside adonidin may be given in doses of one-twelfth to one-fourth of a grain (0.005–0.015 Gm.).

Off. Prep.—Fluidextractum Adonis, *N. F.*

ÆTHER. U. S. (Br)

ETHER

"Ether contains from 96 per cent. to 98 per cent. of $(C_2H_5)_2O$, the remainder consisting of alcohol and water. *Caution.*—Ether to be used for anesthesia must be preserved only in small well-closed containers, and is not to be used for this purpose, if the original container has been opened longer than twenty-four hours." *U. S.* "Ether, also known as ethylic ether, $C_4H_{10}O$, may be obtained by distilling a mixture of ethylic alcohol or industrial methylated spirit and sulphuric acid, and rectifying the distillate. It should be preserved in a cool dark place." *Br.*

Æther Purificatus, *Br.*, Purified Ether; Stronger Ether; Anesthesia Ether, Æther sulphuricus, Æther Oethylicus; Sulphuric Ether, Naphtha Vitrioli, Hydrate of Ethylen, Oxide of Ethyl; Ethoxyethane; Ether officinal, Ether pur, *Fr. Cod.;* Ether hydrique, ou vinique, ou sulphurique, *Fr.;* Aether, *P. G.;* Reiner Aether, Schwefeläther, *G.;* Etere, *It.;* Eter, Eter sulfurico, *Sp.*

Attention should be directed to the unfortunate difference in nomenclature between the British and American Pharmacopœias. The former authority recognizes two grades of ether, the inferior of which is denominated simply ether and the superior grade, corresponding to the ether of the U. S. P., is known as "purified ether."

Ether is the oxide of ethyl (C_2H_5). It is commonly formed from alcohol (ethyl hydroxide) by the action of sulphuric acid, according to the following reactions:

$$C_2H_5OH + SO_2OH.OH = SO_2OH.OC_2H_5 + HOH$$

that is, alcohol reacting with sulphuric acid yields ethyl-sulphuric acid (*sulphovinic acid*) and water. In the presence of an excess of alcohol and at the proper temperature the ethyl-sulphuric acid then reacts with another molecule of alcohol, as follows:

$$C_2H_5OH + SO_2OH.C_2OH_5 = C_2H_5OC_2H_5 + SO_2OH.OH$$

whereby ethyl oxide (ether) is formed, and sulphuric acid is regenerated. These reactions take place best at a temperature of about 140° C., and if the mixture in the still is kept at this temperature a steady stream of alcohol can be converted into ether, whence the process has been called "the continuous etherification process."

Preparation.—A process for preparing ether upon the small scale was given in the U. S. P., 1870, and a former British Pharmacopœia, (see *U. S. D.*, 18th ed., p. 118), but it was properly abandoned by both Pharmacopœias, as the production of this inflammable and very volatile liquid should be undertaken only in buildings properly safeguarded, and it is now made of excellent quality on a large scale with special apparatus. Ether was made officially by the action of sulphuric acid upon alcohol, in a glass flask, at a temperature ranging between 130° C. and 137.7° C., the distillate being afterwards rectified to remove impurities.

In the apparatus employed by E. R. Squibb the ether is made in one operation; the vapors of ether and unchanged alcohol are first washed by a solution of caustic potash maintained at a temperature above the boiling point of alcohol, the alcoholic vapor being condensed in a worm condenser kept at a suitable temperature and runs back into the still, while the ether vapor, retaining about 4 per cent. of alcohol, is condensed in a well-cooled apparatus. Three hundred and sixty pounds of concentrated sulphuric acid are sufficient to etherify 120 barrels of clean spirit; the acid has then to be changed, chiefly because the impurities of the spirit render the mixture dark and tarry and liable to froth in the still. One of the wartime ether plants run on the continuous principle as above described showed the following figures of materials and labor used for each ton (2240 lbs.) of ether produced: 3200 lbs. alcohol, 3 lbs. sodium hydroxide, 3 lbs. sulphuric acid, 9000 gallons water, 6000 lbs steam, one foreman and four laborers. The capacity of this plant was 25 tons per day. Kraft proposes to manufacture ether by heating alcohol in contact with the alkyl esters of sulphonic acid. He states that benzene-sulphonic acid under favorable conditions is capable of converting several thousand times its weight of alcohol into ether. The advantage claimed for this method is greater purity of the resulting ether. (*Chem. Ztg.*, 1893, 1876.) Methionic acid, $CH_2(HSO_3)_2$, is used in manufacturing ether under the patents of Schroeter and Sondag. In Senderens' process the alcohol vapor is transformed into ether by passing it over alumina (Al_2O_3) heated to exactly 260° C. Ekenberg purifies ether by mixing it with 5 or 10 per cent. of liquid paraffin, which has a boiling point of about 300° C. and distilling at a temperature of from 40° to 50° C. The liquid paraffin holds the impurities and permits the pure ether to distill over. (*Chem. Ztg.*, 1894, 1240.)

It is necessary to draw a sharp distinction between the official ethers of the two Pharmacopœias. The strength of the official ether of both Pharmacopœias is practically the same, that of the American having specific gravity of 0.713 to 0.716 at 25° C., that of the British 0.720 at 15.5° C. The British "Aether" differs from the substance official in the U. S. P. under the same name in that there is no official test for limit of aldehyde or methyl compounds. The substance intended for anesthetic purposes and corresponding to the ether of the U. S. P. is known in the Br. P. as "Aether purificatus."

Description and Physical Properties.—"A transparent, colorless, mobile liquid, having a characteristic odor, and a burning, sweetish taste. It is highly volatile and inflammable. Its vapor when mixed with air and ignited may explode violently. It is slowly oxidized by the action of air, moisture, and daylight with the formation of peroxides. Ether is soluble in about 12 times its volume of water at 25° C., with slight contraction of volume. It is miscible with alcohol, benzene, chloroform, petroleum benzin, and fixed or volatile oils.

"Specific gravity: 0.713 to 0.716 at 25° C. Boiling point: about 35° C.

"The color of light blue litmus paper moistened with water is not changed to red when the paper is immersed in Ether for ten minutes. Allow 50 cc. of Ether to evaporate spontaneously from a shallow dish, and dry at 100° C. for one hour: the residue does not exceed 0.001 Gm. Place 10 cc. of 80 per cent. alcohol in a 50 cc. glass-stoppered flask, add 0.5 cc. of phenolphthalein T.S., and just sufficient fiftieth-normal sodium hydroxide to produce a pink color which persists after shaking for one-half minute. Then add 25 cc. of Ether, stopper the flask, mix gently, and add again fiftieth-normal sodium hydroxide until the pink color persists after shaking for one-half minute: not more than 0.4 cc. additional fiftieth-normal sodium hydroxide is required to neutralize the Ether (*acid*). Pour 10 cc. of Ether, in portions, upon clean, odorless blotting paper, and allow it to evaporate spontaneously: no foreign odor is perceptible when the last traces of Ether evaporate from the paper. Shake 10 cc. of Ether occasionally during two hours with 1 cc. of potassium hydroxide T.S. in a glass-stoppered container, protected from light: no color is developed in either liquid (*aldehyde*). Shake 10 cc. of Ether occasionally during one hour with 1 cc. of a freshly made solution of cadmium and potassium iodide (1 in 10), in a glass-stoppered cylinder, previously rinsed with the Ether under examination and protected from light: no color develops in either liquid (*peroxide*).

"Preserve in partially filled, well-closed, light-proof containers, in a cool place, remote from fire." *U. S.*

Under the title "Ether" the British Pharmacopœia gives the following description:

"A colorless, very volatile and inflammable liquid. Odor and taste strong and characteristic. Slightly soluble in *water;* miscible in all proportions with *alcohol* (90 per cent.), *chloroform,* and fixed and volatile oils. Specific gravity 0.720. Boiling point from 34° to 36° C. Its vapor mixed with air is explosive in contact with flame. 5 millilitres, on spontaneous evaporation in a glass dish, leave a film of moisture which does not redden or bleach *blue litmus paper* (absence of free acid, sulphurous acid)." *Br.*

The British Pharmacopœia gives the following tests for purified ether: "Purified Ether possesses the characters and responds to the tests described under 'Æther,'" with the following requirements in addition: "Kept in contact with *potassium hydroxide* freshly broken into small fragments, in a well-stoppered white glass bottle in the dark, no yellow coloration is developed within one hour. Mixed with one-tenth of its volume of freshly prepared *solution of potassium iodide,* it does not develop a yellow color within three hours when kept in a completely filled white glass-stoppered bottle in the dark and frequently shaken. Yields no reaction with the following test for methyl compounds: Well shake 2 volumes of the Purified Ether in a separating funnel with 1 volume of *alcohol* (20 per cent.) and 1 volume of *water,* allow the mixture to separate, and draw off the lower layer. Mix 5 millilitres of this lower layer in a wide test-tube with 2.5 millilitres of an aqueous solution (1 in 50) of *potassium permanganate* and 0.2 millilitre of *sulphuric acid.* At the end of three minutes add to the contents of the tube 0.5 millilitre of an aqueous solution (9.6 in 100) of *oxalic acid,* followed by 1 millilitre of *sulphuric acid,* and then by 5 millilitres of *decolorised solution of fuchsin;* mix thoroughly and set aside for twenty minutes. No violet color is produced (absence of methyl compounds)." *Br.*

Commercial ether, which is sometimes used as a solvent, varies in sp. gr. from 0.733 to 0.765. The impurities found in it are excess of alcohol, water, sulphurous and other acids, heavy oil of wine, and various fixed substances.

According to R. Boettger, water may be detected in ether by agitating the suspected liquid with carbon disulphide; if water be present the mixture becomes milky and turbid, otherwise it remains clear. The most delicate test, however, according to George B. Frankforter and E. A. Daniels (*J. Am. C. S.,* 1915, p. 2560) is anhydrous aluminum chloride which when dropped into ether produces a delicate white cloud or a milky layer according to the amount of water present. For the detection of alcohol Stefanelli (*B. Chem. G.,* viii, 439) proposed to shake ether with a small fragment of aniline-violet, which does not impart color to ether free from alcohol. One per cent. of alcohol may be thus detected. A delicate test for the presence of alcohol in ether is that of Lieben, founded on the formation of iodoform by alcohol but not by ether. The mere keeping of ether in the presence of moisture is said to generate sufficient alcohol to produce the reaction. (Allen, *Com. Org. Anal.*) Ether is usually made anhydrous by allowing it to remain in contact with dry calcium chloride or by distilling it with a small quantity of metallic sodium in a flask or retort.

The extreme volatility of ether causes it to evaporate speedily in the open air, with the absorption of considerable heat. Its inflammability is very great, and the greatest care should be used not to bring it in the vicinity of a naked flame; ether vapors may ignite from a flame several feet away from the ether. When too long kept it undergoes decomposition, and is converted in part into acetic acid and organic peroxides. It dissolves iodine and bromine freely, and sulphur and phosphorus sparingly. Its power to dissolve corrosive sublimate makes it a useful agent in the manipulations for detecting that poison. It is also a solvent of volatile and fixed oils, many resins and balsams, tannic acid, caoutchouc, and most of the vegetable alkaloids. It does not dissolve potassium or sodium hydroxide, in which respect it differs from alcohol.

On filtering an ethereal liquid with free access of air, a frost-like congelation is observed on the upper part of the filter, its appearance and quantity depending upon the temperature and the hygrometric state of the atmosphere. Tanret has collected some of this *ether hydroxide,* and found that after it had been completely freed from ether by strongly blowing upon it, it had the temperature –3.5° C., and on fusion yielded 17 to 18 parts of water for 37 of ether; the formula $(C_2H_5)_2O,2H_2O$ requires 18 parts.

Uses.—As early as 1805, inhalations of ether were recommended by Warren, of Boston, to relieve pulmonary distress in advanced *phthisis,* and in 1812 ether intoxication by inhalation is said to have been frequently practiced. It seems to have been first used as anesthetic by Dr. C. W. Long, of Georgia, but it was not until October, 1846, that Warren, at the instance of W. T. G. Morton, of Boston, used ether as a surgical anesthetic at the Massachusetts General Hospital and made its value public knowledge. A few days subsequently, C. T. Jackson, of Boston, claimed to have first made known to Morton the use of ether for the prevention of pain in dental operations.

Locally, ether is a violent irritant. It is absorbed through the lungs with very great rapidity, and less quickly, but with equal certainty, through the mucous membrane of the gastro-intestinal tract, and is eliminated through the lungs.

Ether is predominantly a paralyzant to the central nervous system affecting first the cerebral centers, then the spinal cord, and at last the vital centers in the medulla. The condition of surgical anesthesia is really one of advanced poisoning which is made reasonably safe only by the fact that the vital centers are involved so late and that the volatility of the ether allows it to be rapidly eliminated through the lungs. Although eventually both sensory and motor apparatus are paralyzed, the effect occurs much earlier in the sensory side of the organism than in the motor. The action upon the circulation is of relatively minor importance, although it is probable that this drug affects the circulatory apparatus much as does alcohol; that is, after small doses there is a slight stimulation of the heart with dilatation of the peripheral blood vessels and generally a slight increase in the blood pressure. After large doses both the heart and vascular system are depressed and the arterial tension greatly reduced. When pushed to a fatal termination ether poisoning nearly always causes death from respiratory failure.

As a practical anesthetic, ether is inferior to chloroform in being distinctly slower in action, more disagreeable to the patient by producing greater excitement and in being more apt to cause prolonged nausea and vomiting after its use. Statistics show, however, that the proportion of deaths due to chloroformization is four to five times greater than after etherization; and only in rare circumstances is the surgeon justified for the sake of convenience in selecting the more dangerous anesthetic.

It being impossible in the space which can be allotted to the subject in the present work to discuss to any advantage the subject of surgical etherization, either in its general, theoretical, or practical aspects, the reader is referred to H. C. Wood, Jr.'s *Textbook of Pharmacology.*

Given by the mouth, ether may be used in *nausea* dependent upon gastric depression, in excessive *flatulence,* especially when attended by colic, and in *gastrodynia.* It has also been recommended by Andrain (*Press. Med.,* Aug. 16, 1919) by intramuscular injection for the relief of *whooping-cough.* As a constituent of Hoffmann's anodyne it is much used as a stimulant antispasmodic. For administration by the mouth it is best given floating on ice-cold water, though it is sometimes administered in a syrup which may be made by shaking together in a bottle 440 parts of sugar, 490 parts of distilled water, 50 parts of alcohol (sp. gr. 0.833), 20 parts of ether. If the parts taken are grains the formula would give one dose.

Dose, from one-half to one fluidrachm (1.8–3.75 cc.).

Off. Prep.—Spiritus Ætheris, *N. F.;* Spiritus Ætheris Compositus, *N. F.*

ÆTHER ACETICUS. N. F., Br.

ACETIC ETHER Æth. Acet. [Ethyl Acetate]

"Acetic Ether is a liquid obtained by distilling a mixture of ethylic alcohol, acetic acid, and sulphuric acid, and purifying the product. It contains not less than 90 per cent. of ethyl acetate, $C_2H_5C_2H_3O_2$." *Br.* "A liquid containing not less than 96 per cent., by volume, of $C_4H_8O_2$ or $CH_3CO.OC_2H_5$ (88.08), the remainder consisting of alcohol and a little water." *N. F.*

Naptha Aceti; Vinegar Naptha; Acetas Ethylicus; Æthylium Aceticum, *Fr. Cod.;* Acétate d'Ethyl, Ether acétique, Naphte acétique, *Fr.;* Aether aceticus, *P. G.;* Essigäther, Essignaphtha, *G.;* Etere acetico, *It.;* Eter acetico, *Sp.*

Acetic ether is not official in the U. S. X. The Br. Pharm., 1914, and N. F. V retain it.

Preparation.—A process for preparing this ether will be found in a former British Pharmacopœia (1885). It is a modification of the process recommended by W. I. Clark (*P. J.*, 1883, p. 777), and is as follows: "Take of Rectified Spirit, 32¼ fluidounces [Imp. meas.]; Sulphuric Acid, 31½ fluidounces [Imp. meas.]; Acetate of Sodium, 40 ounces [av.]; Carbonate of Potassium, freshly dried, 6 ounces [av.]. To the spirit slowly add the acid, keeping the fluid cool, and, the product being cold, add the acetate, mixing thoroughly. Distil forty-five fluidounces [Imp. meas.]. Digest the distillate with the carbonate of potassium for three days in a stoppered bottle. Separate the ethereal fluid, and again distil until all but about four fluidounces have passed over. Preserve the resulting acetic ether in a well-closed bottle and in a cool place." *Br.*, 1885. In adition to this method, acetic ether may be made by several processes, the chief of which are the following: 1. Mix 100 parts of alcohol (sp. gr. 0.83) with 63 parts of concentrated acetic acid, and 17 parts of strong sulphuric acid, and distil 125 parts into a well-cooled receiver. 2. Distil to dryness a mixture of three parts of sodium acetate, three of alcohol, and two of sulphuric acid, mix the distilled product with one-fifth of sulphuric acid, and distil a second time an amount of ether equal to the alcohol employed. 3. Distil two parts of efflorescent lead acetate with one part of alcohol and a little more than one part of sulphuric acid. In the last two processes, the acetic acid is set free by the action of the sulphuric acid on the acetate employed. J. A. Pabst has devised a process for acetic ether in imitation of that for the preparation of common ether. Fifty cc. of sulphuric acid and the same quantity of alcohol are heated together in a retort to 140° C., and then a mixture of one liter of 96 per cent. alcohol and one liter of acetic acid (93 per cent.) is allowed to flow in slowly. At first some ethyl ether goes over, and then a liquid which contains, with considerable uniformity, 85 per cent. ethyl acetate. The reaction takes place between 130° C. and 135° C.; at 145° C. some sulphurous acid is produced. The yield is about 1350 grammes, or 78 per cent., which is 90 per cent. of the theoretical amount. The *methyl acetate* can be prepared exactly as the ethyl compound, but in the attempt to prepare the amyl acetate in an analogous manner, side reactions were found to interfere. In order to study the proportional power of combination possessed by the two alcohols, Pabst allowed a mixture of 100 cc. methyl alcohol and 100 cc. acetic acid to flow into a mixture of 50 cc. sulphuric acid and 50 cc. ethyl alcohol. The first distillates contained essentially methyl acetate and the latter pure ethyl acetate. In the flash were found remaining nearly equal amounts of sulphuric and ethyl-sulphuric acids, and in addition alcohol, acetic acid, and some residual ethyl acetate. (*Bull. Soc. Chim.*, xxxiii, p. 350; *A. J. P.*, 1880.)

Ethyl acetate often forms in galenical preparations which contain both acetic acid and alcohol in the menstruum and which have been allowed to stand for some time. This sometimes is a disadvantage, for it causes differences between a freshly made and an old preparation which require an explanation when a change is made from one to the other, as in refilling a prescription.

Description and Physical Properties.—"Acetic Ether is a transparent, colorless liquid, of a fragrant and refreshing, slightly acetous odor, and a peculiar acetous and burning taste. Specific gravity: 0.890 to 0.896 at 25° C. One cc. of Acetic Ether is soluble in about 10 cc. of water at 25° C., miscible with alcohol, ether, or fixed or volatile oils.

"It does not immediately redden blue litmus paper. Boiling point: from 72° to 77° C. Acetic Ether is readily volatilized, even at a low temperature. It is inflammable, burning with a yellowish flame and an acetous odor.

"No weighable residue remains on evaporating 10 cc. of acetic ether. Allow 10 cc. of Acetic Ether to evaporate spontaneously from clean, odorless blotting paper; the final odor does not resemble that of pineapple (*butylic* or *amylic derivatives*). Pour carefully 2 cc. of Acetic Ether on 10 cc. of sulphuric acid; no dark ring is developed at the point of contact of the two layers within fifteen minutes (*readily carbonizable organic impurities*). Mix 20 cc. of Acetic Ether with a solution of 20 Gm. of sodium hydroxide in 50 cc. of distilled water, allow the mixture to stand, agitating occasionally, or heat it gently under a reflux condenser, until a homogeneous liquid results, and then distil about 25 cc. This distillate complies with the Test for absence of methanol under Alcohol in the U. S. Pharmacopœia X. Shake 25 cc. of Acetic Ether in a graduated cylinder with 25 cc. of distilled water just previously saturated with Acetic Ether; the ethereal layer when separated measures not less than 24 cc. (undue proportion of *alcohol* or *water*).

"Preserve it in well-stoppered bottles, in a cool place, remote from fire and protected from light." *N. F.*

The British Pharmacopœia describes it as "a colorless liquid with a fragrant odor. Soluble in all proportions in *alcohol* (90 per cent.), in *ether* and in *chloroform*, and in not less than 11 parts of *water*. Specific gravity 0.900 to 0.907 at 15.5° C. Moistened *blue litmus paper* introduced into it is not immediately reddened. A little allowed to evaporate from filter paper leaves no extraneous odor. When carefully poured over *sulphuric acid* no dark ring is formed within fifteen minutes at the surface of contact. Contains not less than 90 per cent. of ethyl acetate as determined by the following process: Introduce about 5 grammes into a tared stoppered flask, weigh, and make up to 100 millilitres with *water*. Transfer 10 millilitres of this solution to a titration flask and neutralise with *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. Then add 20 millilitres of the alkaline solution, set aside for five minutes, rotating occasionally, dilute with *water* and titrate back with *N/1 solution of sulphuric acid.* Deduct from 20 the number of millilitres of the acid solution required. Each millilitre of the difference corresponds to 0.088 gramme of ethyl acetate." *Br.*

With reference to the solubility of acetic ether in saturated calcium chloride solution, it is to be remarked that pure acetic ether is not dissolved, except when it is mixed with 90 per cent. alcohol. One volume acetic ether, one volume alcohol, and two volumes calcium chloride solution give a homogeneous liquid.

Uses.—Acetic ether is occasionally used in medicine as a stimulant and antispasmodic. Its action upon the system is probably very similar to that of ether; but as it is less volatile it is less rapidly absorbed and eliminated, and consequently is much less prompt and fugacious in its influence than is ether. It is locally irritating. H. C. Wood found it to be capable of being used as an anesthetic, but to be too slow in its action for practical purposes. It is sometimes employed externally, by friction, as a resolvent, and for *rheumatic pains.*

Its most important use is as a flavoring agent.

Off. Prep.—Elixir Gentianæ Glycerinatum, *N. F.;* Spiritus Odoratus, *N. F.;* Tinctura Antimonii, *N. F.*

Dose, fifteen to thirty minims (1–2 cc.).

ÆTHYLIS AMINOBENZOAS. U. S.

ETHYL AMINOBENZOATE

Æthyl. Aminobenz.—[Benzocaine]

$C_6H_4NH_2COO(C_2H_5)1:4$

This base, which was introduced under the proprietary name of *anesthesin,* is the ethyl ester of paraminobenzoic acid. It is prepared by the following method: Para-nitrobenzoic acid is heated with sodium sulphide and solution of sodium hydroxide. This solution, after cooling and acidulating, is boiled to expel SO_2 and sodium acetate is then added which causes the crystallization of paramidobenzoic acid, which is then esterified by heating with ethyl alcohol and sulphuric acid.

Description and Physical Properties.—"Small white or colorless crystals, or a white crystalline powder. It is odorless, and is stable in the air. One Gm. of Ethyl Aminobenzoate is soluble in about 2500 cc. of water, 5 cc. of alcohol, 2 cc. of chloroform, 4 cc. of ether, and in from 30 to 50 cc. of expressed oil of almond or olive oil, at 25° C. It is soluble in dilute acids.

"Ethyl Aminobenzoate melts between 88° and 90° C. When boiled with alkali hydroxides, alcohol is liberated. Dissolve about 0.02 Gm. of Ethyl Aminobenzoate in 10 cc. of distilled water with the aid of a few drops of diluted hydrochloric acid, and add to the solution 5 drops of a 10 per cent. sodium nitrite solution, followed by 2 cc. of a solution of 0.1 Gm. of beta-naphthol in 5 cc. of sodium hydroxide T.S.: an orange-red precipitate is produced. Its aqueous solution (1 in 50), prepared with the aid of a slight excess of diluted hydrochloric acid, yields a precipitate with iodine T.S., and instantly reduces potassium permanganate T.S.

"Ash: not more than 0.1 per cent. A solution of 0.1 Gm. of Ethyl Aminobenzoate in 1 cc. of sulphuric acid is colorless (*readily carbonizable substances*). Dissolve 1 Gm. of Ethyl Aminobenzoate in 10 cc. of neutral alcohol: a clear solution results. Dilute this solution with 10 cc. of distilled water, add 2 drops of phenolphthalein T.S. and 1 drop of tenth-normal sodium hydroxide: a red color is produced (*free acid*). The addition of a few drops of silver nitrate T.S. to a solution of 0.2 Gm. of Ethyl Aminobenzoate in 5 cc. of alcohol, previously acidulated with a few drops of diluted nitric acid, produces no immediate turbidity (*chloride*). An aqueous solution of Ethyl Aminobenzoate (1 in 20) prepared with the aid of just sufficient hydrochloric acid meets the requirements of the test for *heavy metals.* Heat a crucible to redness, and add, in small portions, an intimate mixture of 0.2 Gm. of Ethyl Aminobenzoate, about 0.5 Gm. of potassium nitrate, and about 0.3 Gm. of anhydrous sodium carbonate. Maintain a red heat until the reaction ceases, then boil the cooled residue for five minutes with 10 cc. of diluted sulphuric acid, filter, and wash the undissolved residue with 10 cc. of distilled water. Evaporate the filtrate and washings until sulphuric acid vapors begin to evolve: the residue, dissolved in 5 cc. of distilled water, meets the requirements of the test for *arsenic.*" *U. S.*

Benzocaine is decomposed by prolonged boiling with water, but its oily solution can be boiled without change. It is incompatible with acids and acid salts.

Uses.—Ethyl aminobenzoate is remarkable among the local anesthetics first for its comparative insolubility, and secondly for its lack of toxicity. Closson (*Journ. Michigan State Med. Soc.,* 1914, xiii, 587) found that in oily solution, injected hypodermically, it required the enormous dose of 1.2 Gm. per kilo of body weight to kill the guinea pig, which would make it about one-twentieth as poisonous as cocaine. Kennel (*B. K. W.,* December, 1902) has reported a case in which 40 grains were administered to a patient without apparent ill-effect. It also appears to be almost free of local irritating action, although the soluble salts that it forms with acids give rise to considerable irritation. According to the investigations of Closson, the anesthetic effect is almost entirely on the nerve terminals; that is, it has very little effect upon nerve trunks as compared, for example, to cocaine. Despite its sparing solubility, it is capable of passing through mucous membranes to a sufficient extent to lessen sensation. Sollmann (*J. P. Ex. T.,* 1919, xiii, 429) found that a dusting powder containing 5 per cent. of benzocaine caused almost complete loss of sensation when applied to the gums of human beings.

Benzocaine is employed for its local anesthetic action, an ingredient of dusting powders—in the proportions of from 10 to 20 per cent. for ulcerated surfaces as *burns* and *wounds.* According to Hartmann (*Ther. Geg.,* Oct., 1902) it has a distinctly antiseptic effect. In *tuberculous laryngitis* a similar powder may be insufflated or it may be used in the form of lozenges each containing from one-third to two-thirds of a grain (0.02 to 0.04 Gm.). In *gastric ulcer* it will generally give complete relief from pain and it is useful to relieve *gastralgia* even in the absence of ulcerative conditions. Reiss (*Ther. Geg.,* 1905) highly recommends it for the relief of *vomiting* when due to gastric irritation. He has found that it counteracts the emetic effects of antimony but not those of apomorphine, indicating that its antiemetic action is not central. Dentists have found it of much service to lessen the after pains of various dental operations such as extraction of the teeth.

The hydrochloride is soluble in 100 parts of water. Although Binz has shown that this salt like the base itself is of very low toxicity it is too irritant to be of great value as a local anesthetic.

Externally, ointments containing 10 per cent. of benzocaine have been used to relieve various types of itching as *pruritus vulvæ* of *diabetes,* and *eczema.* In painful *hemorrhoids,* suppositories containing 3 to 5 grains in Oil of Theobroma are often of much value. Duhot (*Ann. de la Policlin. Centrale de Bruxelles,* February, 1903) has reported excellent results in painful *cystitis* from the injection of a solution of benzocaine in oil of sweet almonds into the bladder.

Dose, three to eight grains (0.2 to 0.5 Gm.).

ÆTHYLIS CHAULMOOGRAS. U. S.

ETHYL CHAULMOOGRATE Æthyl. Chaulmoog.

“ The ethyl esters of the fatty acids of chaulmoogra oil.” *U. S.*

Chaulmestrol. Antileprol.

As pointed out elsewhere (see *Oleum Chaulmoogras*) the therapeutic action of chaulmoogra oil seems to reside in its peculiar fatty acids known as chaulmoogric and hydnocarpic acids. The compound recognized by the U. S. under the name of Ethyl Chaulmoograte is really the ethyl ester of all the fatty acids of the oil and is therefore a mixture of ethyl chaulmoograte and *ethyl hydnocarpate.*

Description and Physical Properties.—“ A clear, pale yellow liquid, having a slight, fruity odor. It is insoluble in water, but is miscible with alcohol, chloroform, and ether.

“ Specific gravity: about 0.904 at 25° C. The specific rotation $[\alpha]_D$ of Ethyl Chaulmoograte, determined at 25° C. in chloroform, containing in each 10 cc. of solution 5 cc. of the Ethyl Chaulmoograte, and using a 100 mm. tube, is not less than $+44.5°$. A solution of 1 cc. Ethyl Chaulmoograte in 10 cc. of neutralized alcohol requires not more than 0.1 cc. of tenth-normal sodium hydroxide for neutralization, using 2 drops of phenolphthalein T.S. as indicator (*free acid*). Saponification value: not less than 190 and not more than 196. Iodine value: not less than 90 and not more than 100.

“ Preserve in well-closed containers.” *U. S.*

Uses.—The therapeutic properties of ethyl chaulmoograte are precisely those of the chaulmoogra oil (which see). It has the advantage over the oil for oral administration of being less objectionable to the taste and for intramuscular injection of being somewhat less irritant locally.

Dose, either by injection or by mouth, from eight to seventy minims (0.5–5.0 cc.).

ÆTHYLIS CHLORIDUM. U. S. (Br.)

ETHYL CHLORIDE Æthyl. Chlor.

“ Monochlorethane α[C_2H_5Cl].” *U. S.* “ Ethyl Chloride, C_2H_5Cl, may be obtained by the action of hydrochloric acid on ethylic alcohol or on industrial methylated spirit; in the latter case it will contain a small but variable proportion of methyl chloride, CH_3Cl.” *Br.*

Ethyl Chloridum, *Br.;* Hydrochloric Ether; Chlorethyl, Monochlorethane; Æthyllium Chloratum, *Fr. Cod.;* Chlorure d'éthyle, Ether Hydrochlorique, *Fr.;* Æther Chloratus, *P. G.;* Aethylchlorid, Chlorwasserstoffäther, Chloräthyl, *G.*

Preparation.—Ethyl chloride was discovered by Rouelle, but first obtained in sufficient quantities to permit the examination of its properties by Basse. It consists of one atom of chlorine combined with the monatomic radical or group C_2H_5, *ethyl,* and its composition is sufficiently shown by the reaction for its production:

$$C_2H_5OH + HCl = C_2H_5Cl + H_2O$$

It may be procured by several processes, but the following is recommended. Distil a mixture of equal measures of concentrated hydrochloric acid and alcohol, and receive the product, by means of a curved glass tube, in a tubulated bottle, half filled with water at a temperature between 21.1° C. and 26.6° C., and connected by means of a second tube with another bottle, loosely corked, and surrounded by a mixture of common salt with snow or pounded ice. The ethyl chloride, as it enters the first bottle, is mixed with alcohol and acid, which are retained by the water; while the pure ester passes forward, and is condensed in the refrigerated bottle. It must be kept in strong bottles, well secured with ground stoppers covered with leather or in sealed containers. Before being opened, the bottle should be cooled to the freezing point.

On the large scale it is manufactured by a process essentially the same as above described in lead lined autoclaves and employing molecular proportions of hydrochloric acid and alcohol. In another process part of the hydrochloric acid is replaced by calcium chloride and an earthenware still is employed.

Like ether some of the other ethyl esters and ethers it dissolves sulphur, phosphorus, the fixed and volatile oils, and many other substances.

Description and Physical Properties.—" At low temperatures or under pressure it is a colorless, mobile, very volatile liquid. It has a characteristic, ethereal odor, and a burning taste. When Ethyl Chloride is liberated at ordinary room temperature from its sealed container, it vaporizes at once. *As its vapor is very inflammable, do not use it near fire.* It burns with a smoky, greenish flame with the production of hydrogen chloride. Ethyl Chloride is slightly soluble in water, and is freely soluble in alcohol and in ether. Specific gravity: about 0.921 at 0° C. Boiling point: between 12° and 13° C.

" Add a few drops of silver nitrate T.S. to 10 cc. of alcohol, cool to the temperature of melting ice, and add to the clear liquid about 0.5 cc. of Ethyl Chloride cooled in the same manner: no turbidity is produced at once (*chloride*). Shake 10 cc. of Ethyl Chloride with 10 cc. of distilled water, both previously cooled to the temperature of melting ice, and allow the supernatant stratum of Ethyl Chloride to evaporate spontaneously: the residual liquid is neutral to litmus paper, and on adding to it a few drops of potassium dichromate T.S., followed by 2 cc. of diluted sulphuric acid, and boiling the mixture, no odor of aldehyde is developed, and no greenish or purplish color is produced (*alcohol*). Allow 5 cc. of Ethyl Chloride to evaporate spontaneously from a shallow dish: no foreign odor is noticeable while the last portions evaporate, and only a negligible residue remains.

" Preserve in hermetically sealed containers, in a cool place, remote from fire, protected from light." *U. S.*

" Gaseous at normal temperature and pressure, but as usually supplied it is condensed into a colorless, mobile, inflammable, and very volatile liquid. Odor pleasant and ethereal, not alliaceous; if kept in vessels provided with rubber fittings, it may acquire a slight odor of rubber. Specific gravity at 0°C., 0.920 to 0.960. *Water* which has been shaken with twice its volume of liquid Ethyl Chloride is neutral to *litmus*, and gives no opalescence or precipitate with *solution of silver nitrate* (absence of sulphur dioxide and of hydrochloric acid). *Sulphuric acid* does not become colored when shaken with ten times its volume of liquid Ethyl Chloride and, after separation and dilution with an equal volume of *water*, has no unpleasant odor, or odor of ether, and does not become turbid on the addition of *solution of silver nitrate* (absence of ether, empyreumatic matter, and certain other substances). When 0.4 gramme is saponified by heating in a stoppered bottle in a water-bath with 10 millilitres of *N/1 alcoholic solution of potassium hydroxide,* the liquid requires for neutralisation not more than 38.2 millilitres of *N/10 solution of sulphuric acid,* corresponding to a proportion of not less than 99.5 per cent. by weight of esters calculated as ethyl chloride, C_2H_5Cl." *Br.*

Uses.—Ethyl chloride is used in the manufacture of synthetic organic chemicals as an ethylating agent. Ethyl chloride is so extremely volatile that when sprayed upon the skin it absorbs sufficient heat in its vaporization to cause superficial freezing in the area to which it is applied. This freezing destroys functional activity of the peripheral nerve endings and therefore the application of ethyl chloride produces local anesthesia. It is used for this purpose for a large variety of conditions where a short and superficial anesthesia is desired as, for instance, in inserting trocar for the removal of fluid, and for the application of cautery. This method of anesthesia has also been applied for opening boils and abscesses, but is not to be recommended as it more or less interferes with the nutrition of the part. Seidelin (*L. L.,* 1913, i, 1663) destroys superficial *epithelioma* by freezing them with ethyl chloride. Ethyl chloride has also been used by inhalation as a general anesthetic. Its action in this regard is extremely rapid and fugacious, comparable to that of nitrous oxide, but it is a much more dangerous anesthetic. The statements concerning the mortality after ethyl chloride anesthesia have been extremely varied. In a critical study of the statistics of fifty thousand cases H. C. Wood, Jr. (*J. A. M. A.,* 1910, lv) reaches the conclusion that the death rate is in the neighborhood of one in six thousand anesthesias. It is perhaps less dangerous than chloroform but is certainly less safe than ether. According to Guedel (*J. A. M. A.,* 1921, lxxvii, 427) there are two types of intoxications from over doses of ethyl chloride. About 90 per cent. of the cases belong to the spasmodic type in which there are contractions of the muscles of the face, neck and larynx, and sometimes other muscles of the body with consequent obstruction to respiration and cyanosis. These cases are very difficult of treatment because the muscular spasm interferes with efforts at artificial respiration. In the rarer group of cases the symptoms are those of progressive depression similar to those caused by other anesthetics. In its physiological action it closely resembles chloroform, although it is less powerfully depressant to the heart. On account of its great inflammability it should not be used near a light or flame.

A proprietary form of ethyl chloride supplied in a special form of container is known as *Kelene.*

Dose, five to ten minims (0.3–0.6 cc.) in alcoholic solution.

ÆTHYLMORPHINÆ HYDROCHLORIDUM U. S.

ETHYLMORPHINE HYDROCHLORIDE

Æthylmorph. Hydrochl.

" The hydrochloride of a synthetic alkaloid prepared from morphine by ethylation [$C_{17}H_{18}O_2N(OC_2H_5).HCl.2H_2O$]." *U. S.*

Dioninum; Dionin; Morphinum æthylatum hydrochloricum; Æthylmorphium Chlorhydricum, *P. G.*

It is the hydrochloride of the ethyl ester of morphine, and is made by acting on morphine in the presence of an alkali with ethyl iodide. The product is purified by treatment with hot alcohol and crystallization from its solution in hydrochloric acid.

Description and Physical Properties.—" A white or faintly yellow, microcrystalline powder, having no odor. One Gm. of Ethylmorphine Hydrochloride is soluble in 8 cc. of water, and in 22 cc. of alcohol, at 25° C. It is slightly soluble in ether and in chloroform.

" It melts at about 123° C. with decomposition. Add a drop of ferric chloride T.S. to a solution of about 0.01 Gm. of the salt in 10 cc. of sulphuric acid, and warm it on a water bath: upon the addition of a drop of nitric acid the color of the mixture becomes at first green, then deep violet-blue, and finally deep red. Silver nitrate T.S. produces in an aqueous solution of the salt (1 in 20) a white precipitate which is insoluble in nitric acid.

" An aqueous solution of the salt (1 in 20) is neutral to litmus paper. The ash from 0.2 Gm. is negligible. Ethylmorphine Hydrochloride loses not more than 10 per cent. of its weight when dried to constant weight at 100° C. (*water*). Heat 5 cc. of an aqueous solution of the salt (1 in 20) with 5 cc. of sodium hydroxide T.S. on a water bath: no vapors showing an alkaline reaction to litmus paper are evolved at once (*ammonium compounds*). Dissolve about 0.05 Gm. of potassium ferricyanide in 10 cc. of distilled water, add 1 cc. of diluted ferric chloride solution (1 volume of ferric chloride T.S. to 9 volumes of water), and 1 cc. of an aqueous solution of Ethylmorphine Hydrochloride (1 in 100): no green or blue color is produced at once (*morphine*). Add 1 cc. of ammonia T.S. to 5 cc. of an aqueous solution of Ethylmorphine Hydrochloride (1 in 25): a white turbidity is produced at once (*difference from codeine hydrochloride*).

" Preserve in well-closed containers, protected from light." *U. S.*

The incompatibilities of dionin and its salts are the same as those of alkaloids and their salts in general.

Uses.—Ethyl morphine hydrochloride, in its general effect, stands between morphine and codeine, but is somewhat closer to the latter. Although it is more powerful as an analgesic and hypnotic than codeine it is greatly inferior to morphine. Internally ethyl morphine is a useful drug to allay *cough* and to relieve *pain.* As a cough sedative it is inferior in power to either morphine or diacetylmorphine, but has the advantages of being less constipating and less liable to habit formation. As an analgesic, although greatly inferior to morphine, it is useful in the same class of cases. It has also been highly recommended for the quieting of nervousness following the withdrawal of opiates in those who have been accustomed to the habitual use of this drug. Lindenmayr (*B. K. W.*, 1912) reports good results from the use of ethylmorphine in acute *coryza,* stating that it not only relieves the symptoms, but has a true curative action.

Locally ethylmorphine is decidedly irritant to the more delicate mucous membranes, as conjunctiva or nose, but seems to increase the lymph flow to an extent not explicable purely on its local irritant action. It is widely employed as a local lymphagogue in various inflammations of the eye, such as *iritis, glaucoma, corneal ulcers,* and the like. It has also been employed to a lesser extent for a similar effect upon the mucous membrane of the nose, especially in *ozena.*

Dose, one-eighth to one grain (0.008–0.065 Gm.).

AGAR. U. S.

AGAR [Agar-agar]

" Agar is the dried mucilaginous substance extracted from *Gelidium corneum* (Hudson) Lamouroux and other species of *Gelidium* and closely related Algæ. (Class *Rhodophyceæ.*)

" Agar contains not more than 1 per cent. of foreign organic matter, and yields not more than 1 per cent. of acid-insoluble ash, and not more than 16 per cent. of moisture." *U. S.*

Vegetable Gelatin, Vegetable Glue, Gelosine, Japanese (Chinese, Bengal or Ceylon) Isinglass, Japanese Gelatin, Thav, Mousse de Chine, *Fr.;* Layor Caranga.

Quite a number of the algæ belonging to the *Rhodophyceæ,* growing on the coast of Southern and Eastern Asia, contain large quantities of mucilage which is extracted and sold under the name of agar-agar. The most important species are those recognized by the U. S. Pharmacopœia. The algæ are collected, spread out upon the beach until they are bleached and then dried. They are then boiled with water and the mucilaginous solution strained through a cloth with pressure. The strained mucilage is cooled, cut into strips and thoroughly dried in the sun. The algæ are usually collected during the summer and fall, bleached and dried, but the process of the manufacture of agar-agar does not take place until cold weather and usually extends from November to February.

Most of the agar used in the United States is imported from Japan, although considerable is now being manufactured at Glendale, California, from red algæ growing along the coast of lower California. (*Pract. Drug.*, Feb., 1921.)

The following varieties of agar are known:

1.—*Ceylon Agar-agar,* consisting chiefly of *Gracilaria lichenoides,* Greville, the alga used by the *Hirundo esculenta* in the formation of its edible nest.

2.—*Macassar Agar-agar,* coming from the straits between Borneo and Celebes, consisting of impure *Eucheuma spinosum,* Ag., incrusted with salt.

3.—*Japanese Agar-agar,* known as *Japanese* *isinglass,* derived from several algæ, especially *Sphærococcus compressus,* Ag., *Gloiopeltis tenax,* J. Ag., *Gelidium corneum* Lam. and *G. cartilagineum* Gaill and other species of *Gelidium.* It occurs in European commerce either in transparent pieces, two feet long and as thick as a straw, prepared in Singapore by putting the algæ named in hot water, or, more frequently, in yellowish-white masses, a foot long and upward of an inch in width. It is the latter kind of agar-agar that is suitable for the culture of bacteria, and is employed in medicine. (*P. J.,* 1885, 188.)

Morin has investigated the *gelose* of Payen, contained in the agar-agar. When a solution of gelose is cooled, even that of 1 in 500 parts of water, a colorless, transparent, and stiff jelly is obtained, which, when heated with moderately strong nitric acid, yields *mucic* and oxalic acids. It dissolves on heating with acidulated water without yielding a jelly on cooling.

Gelose leaves 3.88 per cent. of ash, and when air-dried contains 22.85 per cent. of moisture. When dissolved there also separates out a flocculent mass amounting to 1.9 per cent. Alcohol precipitates gelose, but it cannot be obtained pure in this manner, as the precipitate contains some ash. Ellery H. Harvey (*A. J. P.,* 1925, pp. 66 and 447) by electro-dialysis was able to reduce the ash of agar content from nearly 4 per cent. to 0.81 per cent. He also gives data on adsorption, viscosity, specific gravity and other factors.

Under the name of *gelosine* a mucilaginous substance, extracted from a Japanese alga, has entered commerce in the form of dry, whitish leaves. Gelosine is soluble in alcohol and water, and is said when wet to gradually contract and expel water and the medicinal substances which it may contain. It has been proposed as a pharmaceutical basis for various preparations for local use. (See *B. M. J.,* 1886, vol. ii.) Glycerin suppositories have been made with agar-agar as a vehicle, but they contain only 70 per cent. of glycerin as compared to 90 per cent. in the official suppositories made with sodium oleate.

Description and Physical Properties.—"*Unground Agar.*—Usually in bundles from 3 to 6 dm. in length, consisting of thin, translucent, membranous, agglutinated pieces 4 to 10 mm. in width; externally yellowish-white or brownish-white, tough when damp, brittle when dry, with a slight odor and a mucilaginous taste.

"*Structure.*—Granular and somewhat filamentous; a few fragments of the spicules of sponges and a few diatoms, notably the frustules of *Arachnoidiscus Ehrenbergii* Baillon which are disk-shaped and 0.1 to 0.3 mm. in diameter, may be present.

"*Powdered Agar.*—Pale buff; in chloral hydrate T.S., fragments transparent, more or less granular, striated, angular, occasionally containing frustules of diatoms. Agar is insoluble in cold water, but slowly soluble in hot water. Boil 1 part of Agar for ten minutes with 100 parts of water and replace the water lost by evaporation. It yields a stiff jelly upon cooling.

"Iodine T.S., colors some of the fragments of Agar bluish-black with some areas bright red. A solution made by boiling 0.1 Gm. of Agar in 100 cc. of water upon cooling yields no precipitate upon the addition of tannic acid T.S. (*gelatin*), and does not produce a blue color upon the addition of iodine T.S. (*starch*)." *U. S.*

To detect agar in jams, jellies, etc., in which it is often used as an adulterant, it was formerly usually considered necessary to ash the sample and examine the acid insoluble ash for presence of the characteristic diatoms. Albert Schneider (*Pac. Pharm.,* 1912, p. 35) states that the ashing is unnecessary and often destructive of the diatoms and that they may be collected by dissolving 10 Gm. of the sample in 200 cc. of distilled water and centrifuging for thirty minutes, after which the sediment may be placed on a microscopic slide and examined.

Uses.—Under the name of agar-agar a jelly-like substance has been used as a culture medium by bacteriologists for many years. Although agar contains 60 per cent. of carbohydrates, according to Saiki (*J. B. C.,* 1906), the human digestive tract is able to utilize but a very small percentage of the food value. Its therapeutic importance depends upon the ability of the dry agar to absorb and retain moisture. Being indigestible, it passes through the intestinal tract, swelling up somewhat, owing to the absorption of water from the stomach, and gives bulk to the intestinal contents. In other words, it acts mechanically in an analogous manner to the cellulose of vegetable foods, and aids in maintaining the regularity of the bowel movements. It has been widely used in the treatment of *chronic constipation.* Of itself, when there is more or less atony of the intestinal muscles, it does not originate peristaltic movements, and therefore is frequently combined with small doses of cascara, or one of the other vegetable cathartics. It is best administered cut up in small pieces, and eaten like a cereal with the addition, if desirable, of cream and sugar. A chocolate coated form of agar is also available for those who do not like the plain agar. It is also combined with mineral oil emulsions in a number of proprietary preparations, but in these very little agar is present.

Dose, ordinarily, from two to four drachms (7.7–15.5 Gm.) of the dry agar may be administered once a day.

AGARICUS. N. F.

AGARIC [White Agaric, Larch Agaric]

"Agaric is the dried fruit body of *Polyporus officinalis* Fries (Fam. *Polyporaceæ*) deprived of its outer rind. Agaric contains not more than 5 per cent. of foreign organic matter.

It yields to boiling alcohol not less than 50 per cent. of a non-volatile resinous extract." *N. F.*

Agaricus Albus; White Agaric; Larch Agaric; Touchwood; Spunk; Tinder; Boletus Laricis; Fungus Laricis; Agaricum, *Fr. Cod.;* Funpurgatif, *Fr.;* Larchenschwamm, *G.*

The term "Agaric" is more properly applied to the fungi of the genus *Agaricus,* but most medical writers and the N. F. limit it to the fungus from *Polyporus officinalis* Fries (*Boletus laricis* Jacquin; *B. purgans* Persoon), which is found upon the old trunks of the European larch and upon *Larix sibirica* Ledebour, of Asia. The same species is found on various coniferous trees in some of the western United States and British Columbia. It is of various sizes, from that of the fist to that of a child's head, or even larger, hard and spongy, externally brownish or reddish; but, as found in commerce, it is deprived of its exterior coat, and consists of a light, white, spongy, somewhat farinaceous, friable mass, which, though capable of being rubbed into powder upon a sieve, is not easily pulverized in the ordinary mode, as it flattens under the pestle. Agaricus is collected chiefly in larch forests near Archangel, dried and exported to Hamburg.

When prepared polyporus (so-called agaric) is steeped in a solution of niter, and afterwards dried, it constitutes *spunk, punk,* or *tinder,* the *amadou* of the French, which occurs in flat pieces, of a consistence somewhat like that of very soft, rotten buckskin leather, of a brownish-yellow color, capable of absorbing liquids, and inflammable by the slightest spark. It is said to be prepared also from various other species of *Polyporus,* as *P. ungulatus, P. ribis,* etc.

Description and Physical Properties.—"*Unground Agaric.*—Light, fibrous, somewhat spongy pieces of irregular shape; grayish white to pale brown externally; yellowish and resinous internally; fracture tough, fibrous; friable but difficult to powder. Odor faint; taste, sweetish, acrid and bitter.

"*Powdered Agaric.*—Numerous non-septate, narrow, mycelial threads and few prismatic or cubical crystals of calcium oxalate from 0.010 to 0.040 mm. in diameter." *N. F.*

Agaric owes its medicinal virtues to *Agaric acid,* which is also called *laricic* and *agaricinic acid.* This is a tribasic acid, $C_{19}H_{36}OH(COOH)_3 + 1\frac{1}{2}H_2O$, occurring as an odorless, tasteless, micro-crystalline powder, melting at 141.5° C. According to J. Schmieder, agaric contains a small amount of soft resin, $C_{15}H_{20}O_4$, extracted with petroleum benzin, and from 4 to 6 per cent. of a fatty body, which is made up of (1) *agaricol,* $C_{10}H_{16}O$, fusing at 223° C.; (2) *phytosterin,* $C_{26}H_{44}O$; (3) solid hydrocarbons, $C_{23}H_{46}$ and $C_{29}H_{54}$; (4) cetyl alcohol; (5) a liquid aromatic alcohol, $C_9H_{18}O$; (6) a fatty acid, $C_{14}H_{24}O_2$; and (7) ricinoleic acid. (Schmidt, *Lehrbuch der Pharm. Chem.*, ii, 3te Auf., 1528.) J. D. Riedel has produced two phenetidides of agaric acid, for which antipyretic and anhidrotic properties are claimed. (*Ph. Ztg.,* xlvii.) *Sodium, lithium* and *bismuth agaricinates* have been prepared and introduced into medicine. An agaric growing on the *Larix leptolepis,* and used in Japan as a sacred medicine under the name of *Toboshi* or *Eburiko,* has been found by Y. Inoko to contain agaric acid. (*Sei-I-Kwai,* April, 1891.)

Fungus chirurgorum. Boletus chirurgorum, Wundschwamm, G.—*Surgeon's agaric* is the product of *Polyporus fomentarius* (L.) Fries, which is found upon the oak and beech trees of Europe. It is shaped somewhat like the horse's foot, with a diameter of from six to ten inches. It is soft like velvet when young, but afterwards becomes hard and ligneous. It usually rests immediately upon the bark of the tree, without any supporting foot-stalk. On the upper surface it is smooth, but marked with circular ridges of different colors, more or less brown or blackish; on the under surface, it is whitish or yellowish, and full of small pores; internally it is fibrous, tough, and of a tawny-brown color. It is composed of short tubular fibers compactly arranged in layers, one of which is added every year. The best is that which grows on the oak, and the season for collecting the fungus is August or September. It has neither taste nor odor. Among its constituents, according to Bouillon-Lagrange, are extractive, resin in very small proportion, nitrogenous matter also in small quantity, potassium chloride, and calcium sulphate, and in its ash is found iron, and calcium and magnesium phosphate. It is prepared for use by removing the exterior rind or bark, cutting the inner part into thin slices, and beating these with a hammer until they become soft, pliable, and easily torn by the fingers. In this state it was formerly much used by surgeons for arresting *hemorrhage,* being applied with pressure. *P. ignarius* (L.) Fries and *P. marginatus* Fries yield similar products.

Uses.—According to Hoffmeister (*A. E. P. P.*, 1889, xxv, p. 189), in a moderate dose, agaric acid has no effect upon the system, except to paralyze the nerves of the sweat glands. When given in very large doses, it produced primary excitation of the medulla, followed by paralysis, increasing at first the blood pressure and the respiratory rate, which was followed by diminishing activity in both. The large doses also acted as an irritant to the stomach and intestine, causing vomiting and purging. The depressant action shown on the sweat glands was not shared by the other glands of the body. McCartney (*J. P. Ex. T.,* 1917, x, 83) offers the remarkable theory that its antihydrotic action is due to spasm of the muscular layer of the skin.

The most important use of agaric is in the treatment of the *colliquative sweats* of wasting conditions, such as *phthisis.* Its value in these conditions has been abundantly confirmed by clinical experience. Aside from the solanaceous drugs, it is probably the most reliable remedy that we possess for this purpose. Rosenbaum has found the *fluidextract of agaric* (*Med. Klin.,* 1906) of service in various catarrhal conditions of the alimentary tract, even in *intestinal tuberculosis.*

Under the name of *agaricin* are marketed preparations containing the active *agaric acid,* with larger or smaller amount of impurities. The *dose* of the pure principle is from one-sixth to one-half of a grain (0.01–0.03 Gm.).

Dose, of agaric, five to fifteen grains (0.3–1.0 Gm.).

Off. Prep.—Pilulæ Antiperiodica, *N. F.;* Pilulæ Antiperiodica sine Aloe, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.*

ALBUMINI TANNAS. U. S.

ALBUMIN TANNATE Album. Tan.
[Albutannin]

"A compound of albumin and tannic acid." *U. S.*

Various compounds of tannin with protein substances have been introduced into medicine under proprietary names. These proprietary compounds, which probably do not differ greatly in their therapeutic properties, are described in Part II under their respective names. Because of certain advantages of these tannates of albumin in the treatment of diarrhea and of the considerable variations in their physical properties the U. S. P. X has recognized an official type which offers the advantages of the proprietary articles in a standardized form.

Leach (*J. A. M. A.,* 1920, lxxv, 1129) has tested the solubility of a number of brands of tannin albuminate. He finds that while only partially soluble in 0.2 per cent. hydrochloric acid, in artificial gastric juice they are slowly digested and become almost completely soluble at the end of 3½ hours. While a somewhat larger proportion (30 to 50 per cent.) of the drug is dissolved by a 1 per cent. solution of bicarbonate of soda they are not as completely digested by pancreatin as by pepsin; from 45 to 85 per cent. of the various specimens tested became soluble after pancreatic digestion.

Tannalbin is prepared by mixing 10 parts of a 10 per cent. aqueous solution of egg albumen with 6½ parts of a 10 per cent. aqueous solution of tannic acid. The precipitate is filtered and washed until free from excess of tannin; is then dried, powdered and heated to a temperature of 126° C. for six hours.

Description and Physical Properties.—"A yellowish-white, odorless powder. It is almost insoluble in water, alcohol, chloroform, and in ether. It is decomposed by aqueous solutions of alkali hydroxides and carbonates.

"Ash: not more than 0.3 per cent. Dry about 1 Gm. of Albumin Tannate for three hours at 100° C.: the loss does not exceed 6 per cent. Shake 1 Gm. of Albumin Tannate with 50 cc. of distilled water for five minutes and filter: a 25 cc. portion of the filtrate requires for neutralization not more than 1 cc. of tenth-normal sodium hydroxide, using 3 drops of phenolphthalein T.S. as indicator (*free acid*). Digest 1 Gm. of Albumin Tannate with 200 cc. of distilled water for two hours, shaking at frequent intervals. Filter through a filter, which has not been previously moistened, into a dry flask, rejecting the first 20 cc. of the filtrate. Evaporate 100 cc. of the subsequent filtrate to dryness on a water bath and dry the residue for three hours at 100° C.: the weight of the residue does not exceed 0.06 Gm. (*soluble substances*). Place 1.5 Gm. of Albumin Tannate in a 500 cc. glass-stoppered flask. Dissolve 2.5 Gm. of sodium bicarbonate in 250 cc. of distilled water, warm the solution to 40° C., and gradually add it with agitation to the Albumin Tannate. Then add a filtered aqueous solution of 0.25 Gm. of pancreatin in 5 cc. of distilled water. Place the flask in a suitable bath, maintain at 40° C. for two hours, inverting the flask every ten minutes. Allow to remain in the bath for one-half hour longer without inverting. Filter through a counterbalanced filter, wash the undissolved residue with four 10 cc. portions of cold distilled water, and dry to constant weight at 110° C.: the weight of the residue does not exceed 0.45 Gm. Place 1.5 Gm. of Albumin Tannate in a 500 cc. glass-stoppered flask. Mix 20 cc. of normal hydrochloric acid with 230 cc. of distilled water, warm the mixture to a temperature of 40° C., and add it gradually with agitation to the Albumin Tannate. Then add a filtered aqueous solution of 0.25 Gm. of pepsin in 5 cc. of distilled water. Place the flask in a suitable bath and maintain at 40° C. for two hours, inverting the flask during the digestion every ten minutes. Allow the flask to remain in the bath for another half hour without inverting. Filter through a counterbalanced filter, wash the undissolved residue with four 10 cc. portions of cold distilled water, and dry at 110° C. to constant weight: the weight of the residue is not less than 0.6 Gm.

"Preserve protected from light." *U. S.*

Uses.—Although as shown by Sollmann (*J. P. Ex. T.,* 1921, xvii, 63) most of the commercial preparations of albumin tannate are more or less soluble in water and slightly astringent, this effect is probably due to presence of uncombined tannin as an impurity. When submitted either to peptic or pancreatic digestion the compounds are gradually broken up, liberating tannic acid, which exercises its characteristic astringent effect. The digestion by pepsin is, however, so slow that under ordinary conditions it is not probable that any considerable amount of tannin will be liberated in the stomach. Therefore, the astringent effect is felt mostly in the intestinal tract. According to the experiments of Sollmann the pancreatic digestion which takes place in the intestines is also very slow, so that an astringent action will be continued throughout almost the whole of the alimentary canal. As the tannin is liberated gradually the astringency will evidently be comparatively mild in its effect.

Albutannin is used in medicine solely as an astringent in the treatment of *diarrheas.* It has the advantage over the vegetable astringents in that it is much less likely to produce gastric disturbances. While more mild in its action than the vegetable astringents it probably continues its effect throughout the whole length of the alimentary canal and is especially used in those cases of *chronic enteritis* involving the lower portions of the small bowel and even of the colon.

Dose, from fifteen to sixty grains (1–4 Gm.) three or four times a day.

ALCOHOL. U. S. (Br.)

ALCOHOL. [Ethanol]

"Alcohol contains not less than 92.3 per cent. by weight, corresponding to 94.9 per cent. by volume, at 15.56° C., of C_2H_5OH." *U. S.*

"Alcohol (90 per cent.) is a mixture of ethyl hydroxide and water containing in 100 parts by volume 90 parts by volume of ethyl hydroxide, C_2H_5OH, and is obtained by the distillation of fermented saccharine liquids." *Br.*

Spiritus Rectificatus, *Br.;* Ethyl alcohol, Ethyl hydroxide, Rectified Spirit; Spiritus Vini Rectificatus vel Rectificatissimus, Alcohol ethylicum, Alcohol Vini; Spirit of Wine; Alcool, *Fr. Cod.;* Esprit de Vin, *Fr.;* Spiritus, *P. G.;* Rectificirter Weingeist, Aethyl alkohol, Alkohol, *G.;* Alcool, Acquavite rectificata, *It.;* Alcohol, Espiritu rectificado de vino, *Sp.*

ALCOHOL DEHYDRATUM. U. S. (Br.)

DEHYDRATED ALCOHOL. Alcohol Dehyd. [Alcohol Absolutum, Dehydrated Ethanol]

"Dehydrated Alcohol contains not less than 99 per cent. by weight of $C_2H_5.OH$." *U. S.* "Absolute Alcohol is ethyl hydroxide, C_2H_5OH, with not more than 1 per cent. by weight of water; obtained by the dehydration of less strong ethylic alcohol, and subsequent distillation." *Br.*

Alcohol Absolutum, *Br.;* Alcohol absolutus, *P. G.;* Absoluter Alkohol, *G.;* Alcool absolu, *Fr.;* Alcool assoluto, *It.;* Alcohol anhidro, *Sp.*

The term dehydrated alcohol should be exclusively applied to this, the strongest commercial form of ethyl alcohol, and the term "absolute alcohol" should be reserved for the theoretical 100 per cent. ethyl hydroxide referred to in the alcohol tables.

ALCOHOL DILUTUM. U. S. (Br.)

DILUTED ALCOHOL. Alcohol Dil.

Alcohol Dil. [Diluted Ethanol]

"Diluted Alcohol contains not less than 41 per cent. and not more than 42 per cent. by weight, corresponding to not less than 48.4 per cent. and not more than 49.5 per cent. by volume, at 15.56° C., of C_2H_5OH." *U. S.*

"The four official liquids obtained by diluting alcohol (90 per cent.) with Distilled Water, contain, respectively, 70, 60, 45, and 20 per cent. of ethyl hydroxide by volume." *Br.*

Spiritus Tenuior, *Br.* 1885, Proof Spirit; Alcool dilué, *Fr.;* Spiritus Dilutus, *P. G.;* Verdünnter Spiritus, Verdünnter Weingeist, *G.*

From the titles and definitions above given, which include all the forms of alcohol recognized by the U. S. and Br. Pharmacopœias, it will be perceived that there are three strengths of alcohol official in the U. S. while the Br. recognizes six. Those preparations of the British Pharmacopœia which are of nearly the same strength and used for similar purposes as solutions official in the U. S. are considered in the same place.

The extensive use of alcohol in pharmacy renders it desirable not only to group the official kinds together here, but to consider each in detail in the subsequent pages.

Alcohol, in the chemical sense, is a peculiar liquid generated for the most part in vegetable juices and infusions by a fermentation, called the "vinous" or alcoholic. The liquids which have undergone it are called vinous liquors, and are of various kinds. Thus, the fermented juice of the grape is called *wine;* of the apple, *cider;* and the fermented infusion of malt and hops, *ale, porter* or *beer.*

With regard to the nature of the liquids susceptible of the vinous fermentation, however various they may be in other respects, one general character prevails; that, namely, of containing sugar in some form or other. It is found, further, that after they have undergone the vinous fermentation the sugar they contain has either wholly or in part disappeared; and it was long believed that the only new products are alcohol which remains in the liquid, and carbonic acid which escapes during the process, and that these, when taken together, are equal in weight to the sugar lost. It was hence inferred that sugar is the subject matter of the changes occurring during the vinous fermentation, and that it is resolved into alcohol and carbon dioxide, $C_6H_{12}O_6 = 2C_2H_5OH + 2CO_2$. It has, however, been shown by Pasteur that, along with alcohol and carbon dioxide, glycerin and succinic acid are generated in small amount, and that the process is not so simple as at first supposed. One of the theories earlier held was that some definite intermediate product was always formed between the sugar and the alcohol. Some authorities, including Baeyer and Buchner, believed this product to be lactic acid. One of the more recent views is that of Fernbach, who holds that the intermediate product is *pyruvic acid,* $CH_3COCOOH$, which is capable of being converted into alcohol by yeast, which lactic acid is not. This theory has been further elaborated by Neuberg and Reinfurth (*B. Chem. G.,* 1919, lii, 1677). They state that the first action during fermentation is the rearrangement of the glucose molecule with the formation of one molecule of glyceric acid and one molecule of dihydroxyacetone. These each lose water with the formation of methyl glyoxal ($CH_3.CO.CHO$). This compound is then hydrolized into pyruvic acid and glycerol. The pyruvic acid is then acted upon by a carboxylase in the yeast yielding acetic aldehyde and carbon dioxide. The acetic aldehyde then is reduced to ethyl alcohol.

The accelerating factor in the early stages of alcoholic fermentation is a phosphate, according to Harden and Young (*Proc. Roy. Soc. Lond.,* 1906–1911). This forms a hexose phosphate in the presence of the enzyme.

Much work has been done lately in determining the nutrient factors for the optimum development of the yeast, a combination of phosphates, calcium and magnesium salts and ammonium salts seem to give the best results so far.

Sugar will not undergo the vinous fermentation by itself, but requires to be dissolved in water, subjected to the influence of a ferment, and kept at a certain temperature. Accordingly, sugar, water, the presence of a ferment, and the maintenance of an adequate temperature may be deemed the prerequisites of the vinous fermentation. The water acts by giving fluidity, and the ferment and temperature by commencing and maintaining the chemical changes. The fermentative change is intimately connected with the multiplication of a microscopic plant, *Saccharomyces cerevisiæ.* Pasteur has shown that the yeast plant lives and grows at the expense of the sugar, which is converted partly into the plant's tissue, partly into alcohol and other products. The proper temperature for conducting vinous fermentation ranges from 15.5° C. to 32.2° C.

Any starchy material may be converted into alcohol if the starch be first converted into soluble carbohydrates, on the commercial scale this is usually accomplished by the use of malt, the diastase of which converts the starch according to the following reactions:

$$(C_6H_{10}O_5)_3 + H_2O = \underset{\text{Dextrin.}}{(C_6H_{10}O_5)_2} + \underset{\text{Dextrose.}}{C_6H_{12}O_6}$$

$$(C_6H_{10}O_5)_3 + 2H_2O = \underset{\text{Maltose.}}{C_{12}H_{22}O_{11}} + \underset{\text{Dextrose.}}{C_6H_{12}O_6}$$

The two compounds, *dextrin* and *maltose,* then pass gradually into dextrose, according to the reactions:

$$(C_6H_{10}O_5)_2 + 2H_2O = 2C_6H_{12}O_6$$

$$C_{12}H_{22}O_{11} + H_2O = 2C_6H_{12}O_6$$

Neither dextrin nor maltose is directly fermentable. In this respect they resemble sucrose which must first be inverted before fermentation can occur. Arnoult has succeeded in obtaining alcohol by fermenting sugar (glucose), formed by the action of sulphuric acid on poplar wood sawdust, which yielded from 70 to 80 per cent. of this kind of sugar. Simmson (*Ap. Ztg.,* 1898, 776) obtained 6.5 liters of absolute alcohol from 100 kilogrammes of air dried sawdust. The action of sulphurous acid upon wood fiber has been found by Clássen to be more satisfactory as a saccharifying agent than sulphuric acid, and the process has been successfully used in practice.

The industrial production of alcohol from wood waste or sawdust has not been commercially successful up to the present time. According to S. H. Tomlinson (*Chem. Met. Eng.,* 1918, 552) the difficulty has been due to the unsuitable commercial conditions under which the attempts have been made. He gives cost figures and processes confirming the belief that it is possible to obtain a product of high quality and low cost and states that the unconverted residue of the wood waste, amounting to about 70 per cent., still possesses a high fuel value. T. E. Thorpe (*P. J.,* 1918, 203) directs attention to the value of the seaweeds (*Laminaria* species) as sources of alcohol. He states that 50 kilogrammes of the seaweed dried, converted to sugars with diluted sulphuric acid and then fermented with yeast, will yield 6 liters of alcohol. In Australia a species of palm (*Macrozamia Spiralis*) has been used as a source of alcohol. The roots, which are very starchy, are ground to a fine powder, boiled with water, converted to sugar by the agency of diastatic enzymes and then fermented with yeast. The yield is 45 gallons of alcohol to the ton of material used and the cost is about 4½ pence per gallon of proof spirit (*Commerce Reports,* 1918). In the Philippines distillers are preparing alcohol from the nipa-palm, a swamp plant growing over 100,000 acres in the archipelago (*J. I. E. C.,* 1918, 313).

A valuable table of the sources whence alcohol may be obtained commercially, together with the estimated yield, was published in the *Kew Bulletin* for 1912, No. 3, and will be found reprinted in the *A. Ph. A. Yearbook of Pharmacy* for 1912, p. 354. A similar article also appeared in the *Scientific American* (supplement, May 4, 1918, p. 287) and a more recent one in the *Kew Bulletin,* 1925, v, 193.

In vinous liquors, the alcohol is largely diluted with water, and associated with coloring matter, volatile oil, extractive, ethereal substances, and various acids and salts. In purifying it, advantage is taken of its volatility, which enables it to be separated by distillation, combined with some of the principles of the vinous liquor employed, and more or less water. The unrectified distilled product of vinous liquors forms the different *ardent spirits* of commerce. When obtained from wine, it is called *brandy;* from fermented molasses, *rum;* from grain, such as corn, malted barley, or rye, *whisky;* from malted barley and rye meal with hops, and rectified from juniper berries, *Holland gin;* from malted barley, rye, or potatoes, and rectified from turpentine, common *gin;* and from fermented rice, *arrack.* These spirits are of different strengths, that is, contain different proportions of alcohol, and have various peculiarities by which they are distinguished by the taste. Their strength is accurately judged by the specific gravity, which is always less in proportion as their concentration is greater. When they have the sp. gr. 0.920 (0.91984, Drinkwater), they are designated in commerce by the term *proof spirit.* This *English proof spirit* contains about 49 per cent. by weight of alcohol which corresponds to over 57 per cent. by volume. United States *proof spirit* is considerably weaker as United States Custom House and Internal Revenue Service defines the term proof spirit to be alcohol containing 50 per cent. by volume of absolute alcohol at 15.6° C.

Commercial proof spirit is still very far from being pure, being a diluted alcohol, containing about half its weight of water, together with amylic alcohol and other foreign matters. It may be further purified and strengthened by redistillation, or *rectification* as it is called. The average strength of rectified spirit (sp. gr. 0.835), corresponds very nearly with the *Spiritus Rectificatus* of the Br. Pharm. When this is once more cautiously distilled, it may be further purified from water, and the specific gravity attained will be about 0.820, which is the strongest spirit that can be obtained by ordinary distillation, and is practically the pure spirit of the British system of excise. It still, however, contains 11 per cent. of water. In the meanwhile, the spirit, by these repeated distillations, becomes more and more freed from the contaminating oil, called *grain oil* or *fusel oil.* (See *Alcohol Amylicum.*)

The direct synthesis of alcohol from calcium carbide has been commercially accomplished in Switzerland according to the following reactions:

$$CaC_2 \text{ (calcium carbide)} + 2H_2O = Ca(OH_2 + C_2H_2) \text{ (acetylene)}$$

Acetylene may be converted by catalytic action of certain substances into acetaldehyde.

$$C_2H_2 \text{ (acetylene)} + H_2O = CH_3CHO \text{ (acetaldehyde)}$$

The catalytic agents used are sulphuric or phosphoric acids or certain metallic salts.

The acetaldehyde is finally converted into ethyl alcohol by catalytic hydrogenation, using reduced nickel as the catalyst.

$$CH_3COH \text{ (acetaldehyde)} + H_2 = CH_3CH_2OH \text{ (ethyl alcohol)}$$

It is said that by this method, which is being perfected at the Longa Electric Co. at Visp, it will soon be possible to satisfy the total alcohol consumption of Switzerland.

Alcohol can be prepared synthetically from ethylene by simple hydration but it has not been possible thus far to obtain an economic yield of synthetic ethylene, which is one of the normal constituents of coal gas.

Alcohol combines in all proportions with water and ether, and, when diluted with distilled water, preserves its transparency. Its density varies with the proportion of water it contains. (See alcohol tables, Part III.) Its value depends upon the quantity of absolute alcohol contained in it; and, as this is greater in proportion as the specific gravity is less, it is convenient to take the density of a sample as a means of estimating its strength.

This is done by instruments called hydrometers or alcoholometers, which, when allowed to float in the spirit, sink deeper into it in proportion as it is lighter. Each hydrometer degree has a corresponding specific gravity, and, by referring to tables constructed for the purpose, the percentage of absolute alcohol is at once shown. Hydrometer manufacturers graduate instruments showing specific gravity and Baumé's degrees upon the same scale in parallel columns, with a thermometer inserted or taking the place of the bulb; these are exceedingly convenient. Alcoholometers are also constructed to show the alcohol percentage by weight directly, as well as percentage of proof spirit.

The alcoholometer, however, cannot be used to determine the alcoholic strength of wines, flavoring extracts or of any preparations containing more than traces of anything but alcohol and water. For such liquids distillation must be first resorted to. (See *Alcohol Determination,* Part III); also C. R. Hares (*J. A. Ph. A.,* 1918, 594).

Alcohol is used enormously in the arts as a solvent and for other purposes, and the U. S. government has established suitable regulations permitting the proper use of alcohol in manufacturing and forbidding its sale as a beverage. The liquid treated so that it is rendered unfit for use in beverages is termed *denatured alcohol.* Among the denaturants thus permitted are tartar emetic, salicylic acid, quinine sulphate, colocynth extract, diethylphthalate, brucine and iso-propyl alcohol. Owing to the dishonesty of some manufacturers of toilet preparations and perfumes these supplies are occasionally diverted from their original purpose and turned over for sale for medicinal use or for beverage purposes, either with or without rectification. Even the most careful attempts at rectification sometimes fail to remove all traces of the denaturant and careful tests are necessary to determine the fitness of a sample of alcohol for use in manufacturing operations. The French excise directs that alcohol should be denatured or deprived of its natural properties by the addition of 500 cc. of petroleum benzin and 1 Gm. of malachite green to each hectoliter; it has been found, however, that the color can be destroyed by calcium hypochlorite.

The U. S. Internal Revenue Department has authorized the use of a number of formulas for denaturing alcohol, but it must be prepared under the supervision of an official of the Department, in special plants. Some of these formulas provide an alcohol for burning purposes or for use as special solvents, others are the preliminary steps to manufacturing processes, such as a mixture of sulphuric acid and alcohol for the subsequent production of ether, while other formulas have now been authorized which are identical with official formulas, such as tincture of iodine, soap liniment, etc., thus making it possible to have these products manufactured from duty-free alcohol at greatly reduced cost. These preparations may therefore be purchased from large dealers at prices which are less than the cost of the raw material if bought through the usual channels of trade.

The dangerous properties of methyl alcohol when taken internally caused the Committee of Revision of the U. S. P. to introduce a test for determining the presence or absence of methyl alcohol, which is sometimes used as an adulterant for alcohol. See *Methanol,* Part II, also *U. S. D.,* 19th ed., p. 105.

Alcohol is capable of dissolving a great number of substances as, for example, sulphur and phosphorus in small quantity, iodine and ammonia freely, and the hydroxides of potassium, sodium, and lithium, but not the carbonates of these metals. Among organic substances, it is a solvent of most of the vegetable alkaloids, urea, tannic, citric, and tartaric acids, sugar, mannite, camphor, resins, balsams, volatile oils, and soap. It dissolves the fixed oils sparingly, except castor oil which is abundantly soluble in it. It reacts chemically with some acids, forming the ethyl esters, but with others acts only as a solvent. All deliquescent salts are soluble in alcohol, except potassium carbonate; while the efflorescent salts, and those either insoluble or sparingly soluble in water, are mostly insoluble in it. It dissolves ammonium chloride, and most of the chlorides readily soluble in water; also some nitrates, but none of the metallic sulphates.

A method of detecting alcohol in small proportions has been proposed by Carstanjin. The liquid supposed to contain it, having been mixed with platinum black in a small flask, is heated to 51.1° C., well shaken, and filtered. To the filtrate a few drops of solution of potassium hydroxide are added, and the liquor evaporated to dryness on a water bath. The residue is then heated with a little arsenic trioxide, when, if alcohol be present, a garlicky odor will be perceived, owing to the production of cacodyl. According to Nickles, however, propylic alcohol will produce the same result. (*A. J. P.,* 1865, p. 334.) A very delicate test for small quantities of alcohol is that of Lieben as modified by Hager. (*Zeit. An. Chem.,* ix, 492.) It depends on the fact that alcohol under the influence of iodine and an alkali yields iodoform, CHI_3, the properties of which are very characteristic. To 10 cc. of the clear suspected liquid five or six drops of a 10 per cent. solution of potassium or sodium hydroxide are added, and the liquid is warmed to about 50° C. A solution of potassium iodide fully saturated with free iodine is next added drop by drop, with agitation, until the liquid becomes permanently yellowish-brown, when it is carefully decolorized by a further cautious addition of the caustic alkali solution. If alcohol be present, iodoform is gradually deposited at the bottom of the tube in yellow crystals of the flat hexagonal type seen in snowflake crystals, which, after standing, may be transferred to a microscope-slide and examined with a lens. Spirit diluted with 2000 parts of water, when treated as above and allowed to stand twelve hours, gives a distinct dust-like deposit of iodoform. Unfortunately, the above delicate reaction is not peculiar to alcohol, being produced by acetone, aldehyde, propylic and butylic alcohols, various ethers, etc. On the other hand, it is not given by pure methyl or amyl alcohol, chloroform, chloral, glycerin, or ether, nor by acetic, formic, or oxalic acids. (Allen, *Com. Org. Anal.*)

A specific reaction for alcohol, which is not interfered with by impurities nor by methyl alcohol or acetone, has been proposed by A. Toninelli (*P. J.,* xciii, 47), as follows: The reagents required are (1) 1.5 Gm. of pure crystal dinitritoluol, dissolved in 200 cc. of a mixture of 1 part of carbon disulphide and 2 parts of ether; (2) 12 Gm. of iodine, dissolved in 100 cc. of ether; (3) 40 Gm. of potassium hydroxide, dissolved in 100 cc. of distilled water.

Into a 10 cc. graduated glass-stoppered tube are introduced 2 cc. of the liquid to be tested, 2 cc. of the iodine solution, and after shaking and allowing to stand for two minutes, 4 cc. of potassium hydroxide solution is added and the mixture shaken until decolorized. Finally, 2 cc. of the dinitritoluol reagent is added with vigorous shaking, the graduated tube is placed upon a white surface and the upper layer closely observed. If ethyl alcohol is present in quantity sufficient to react, an orange-yellow color is developed which passes through various shades, terminating in intense garnet red. With as little as 3 per cent. alcohol the color is a light rose. Some of the higher alcohols give somewhat similar effects, but are readily removed by salting out and shaking with petroleum benzin.

Alcohol tables will be found in Part III, which will give the specific gravities of the various strengths of alcoholic liquids. The temperature at which the specific gravities of these liquids is taken was not changed to 25° C. in the U. S. P. X, as it was for most liquids, because the temperature 15.6° C. was the one adopted by the U. S. government and still retained by it, for all of the national legal requirements.

ALCOHOL DEHYDRATUM. *Absolute Alcohol, Anhydrous Alcohol, Ethylic Alcohol.*—No process is given in the U. S. Pharmacopœia for the preparation of dehydrated alcohol; the definition given, however, is "A liquid containing not less than 99 per cent. by weight of $C_2H_5.OH$." *U. S.* The following is the process of the Br. Pharmacopœia (1885): "Rectified Spirit, 1 pint [Imp. meas.]; Carbonate of Potassium, anhydrous, 2 ounces [av.]; Chloride of Calcium, fused, a sufficiency. Add the carbonate of potassium to the spirit in a stoppered bottle, and macerate for twenty-four hours with frequent agitation. Put the chloride of calcium into a covered crucible, and subject it to a red heat for half an hour; then pour the fused salt on to a clean stone slab, cover it quickly with an inverted porcelain dish, and when it has congealed, break it up into small fragments and enclose in a dry stoppered bottle. Put one pound [av.] of this fused chloride of calcium into a flask, pour over it the spirit decanted from the carbonate of potassium, and, closing the mouth of the flask with a cork, shake them together and allow them to stand for twenty-four hours with repeated agitation. Then attaching a dry condenser closely connected with a receiver from which free access of air is excluded, and applying the flame of a lamp to the flask, distil about two fluidounces [Imp. meas.], which should be returned to the flask, after which the distillation is to be continued until fifteen fluidounces [Imp. meas.] have been recovered." *Br.*, 1885. By the term absolute alcohol is meant pure alcohol, entirely free from water. In this state it cannot be obtained by ordinary distillation; even with a column still the purest alcohol obtainable contains 5 per cent. of water. To separate this it is customary to have recourse to substances having a very strong affinity for water, sufficient not only to abstract it from the alcohol, but to retain it at a temperature at which alcohol will distil over.

In all cases, before decanting or distilling, the alcohol must be digested for two or three days with lime, at a temperature between 35° and 37.7° C. Lime will not answer as a substance to be distilled from, unless it be in sufficient excess; for otherwise, towards the end of the distillation, the calcium hydroxide formed will yield up its water to the alcohol, and weaken the distilled product. J. Lawrence Smith procures an alcohol of 98 to 100 per cent. by macerating 3 pints of alcohol, 94 per cent., in a four-pint bottle with about six troy ounces of well burned lime; well corked and agitated at intervals for ten days, the strengthened alcohol, at the end of this time, is drawn off by a siphon, and may be freed, if desired, of the small trace of lime by redistillation. Yvon prepares absolute alcohol by treating strong alcohol with powdered calcium carbide. L. W. Winkler recommends metallic calcium for dehydrating alcohol. About 20 Gm. of calcium are required for one liter of alcohol.

Properties.—Dehydrated alcohol is a colorless, volatile liquid, of an agreeable odor and burning taste. It boils at 78.4° C., and is congealed at –130.5° C. Its sp. gr. is 0.7978 at 68° C., according to Regnault; 0.79381 at 60° C., according to Drinkwater; 0.794 (equivalent to 99.95 per cent. of ethyl hydroxide by volume and by weight) to 0.7969 (equivalent to 99.4 per cent. of ethyl hydroxide by volume or 99 per cent. by weight), by the British Pharmacopœia; while E. R. Squibb has shown that pure alcohol is obtainable of as low a density as 0.7935, and possibly lower. (*Ephem.*, ii, p. 522.) The sp. gr. of its vapor is 1.59.

Description and Physical Properties.—"A transparent, colorless, mobile, and volatile liquid, having a characteristic odor, and a burning taste. It is very hygroscopic. Specific gravity: not above 0.798 at 15.56° C. (the U. S. Government standard temperature for alcohol). Shake 10 cc. of Dehydrated Alcohol in a stoppered tube with about 0.5 Gm. of powdered anhydrous cupric sulphate: the latter does not become blue (*water*). In other respects Dehydrated Alcohol has the properties of and complies with the tests for purity under *Alcohol.*

"Preserve in well-closed containers, in a cool place, remote from fire." *U. S.*

"Specific gravity from 0.794 (equivalent to 99.95 per cent. of ethyl hydroxide by volume and by weight) to 0.7969 (equivalent to 99.4 per cent. of ethyl hydroxide by volume or 99 per cent. by weight). Very volatile and hygroscopic at ordinary temperatures. Anhydrous *copper sulphate* shaken occasionally during two or three hours in a well-closed vessel with about fifty times its weight of Absolute Alcohol does not assume a decidedly blue color (absence of excess of water). Free from the impurities indicated under 'Spiritus Rectificatus,' and resembling it in other general characters." *Br.*

The tests usually given to prove the absence of water by dropping into the absolute alcohol anhydrous barium oxide or anhydrous copper sulphate are not reliable, as Squibb has demonstrated that when half of one per cent. of water was added to absolute alcohol no change in either the barium oxide or the anhydrous copper sulphate took place. Görgeu's test of forming a clear solution when mixed with an equal bulk of pure benzene is more delicate, but a test for determining the presence of as little as one per cent. of water is needed. Dehydrated alcohol should be free from fusel oil. Dehydrated alcohol burns with a pale flame without residue, the products being carbon dioxide and water. Its vapor, passed through a porcelain tube filled with pumice stone and heated to redness, yields carbon, gaseous hydrocarbons, aldehyde, naphthalene, benzene, phenol, and various other substances. (Berthelot.) It unites in all proportions with ether and water. Its union with water is attended by condensation and a rise of temperature. When 54 volumes of alcohol are mixed with 46 of water, the decrease of volume is at the maximum, amounting to 3.6 per cent. For further details see paper by H. C. Wood, Jr., *J. A. Ph. A.*, 1919, viii, 730.

ALCOHOL. *U. S. Alcohol,* sp. gr. 0.816 at 15.6° C.—This is the so-called "95 per cent. alcohol" of commerce (or 94.9 per cent. by volume); it was an official preparation of the Dublin College, which gave a formula for its preparation, and stated its sp. gr. at 0.818. The British Pharmacopœia (1914), under the title "Spiritus Rectificatus," recognizes alcohol of 90 per cent. by volume or 85.68 by weight, slightly weaker than U. S. P. alcohol.

It is described as follows:

Description and Physical Properties.—" A transparent, colorless, mobile, and volatile liquid. It has a slight, characteristic odor, and a burning taste. It is inflammable. Alcohol is miscible with water without any trace of cloudiness; also miscible with ether and with chloroform.

" Specific gravity: not above 0.816 at 15.56° C. (the U. S. Government standard temperature for Alcohol). Alcohol is readily volatilized even at low temperatures and boils at about 78° C. Alcohol diluted with an equal volume of distilled water does not affect the color of blue or red litmus paper previously moistened with water. Evaporate 40 cc. of Alcohol in a platinum or porcelain dish on a water bath, and dry at 100° C.: the residue does not exceed 0.001 Gm. Mix 10 cc. of Alcohol with 5 cc. of distilled water and 1 cc. of glycerin, and allow the mixture to evaporate spontaneously from clean, odorless blotting paper: no foreign odor is perceptible when the last traces of the Alcohol leave the paper (*fusel oil constituents*). Allow 25 cc. of Alcohol to evaporate spontaneously in a porcelain dish carefully protected from dust, until the surface of the dish is barely moist: no red or brown color is produced upon the addition of a few drops of sulphuric acid (*amyl alcohol or non-volatile, carbonizable organic impurities, etc.*). On mixing 10 cc. of Alcohol in a test tube with 5 cc. of potassium hydroxide T.S., the liquid does not at once assume a yellow color (*aldehyde or oak tannin*). Shake 20 cc. of Alcohol in a clean, glass-stoppered bottle with 1 cc. of silver nitrate T.S., and allow the mixture to stand in diffused daylight for 6 hours: the mixture does not become more than faintly opalescent, or acquire more than a faint brownish tint (*organic impurities, aldehyde, etc.*). Dilute the Alcohol with water to contain about 5 per cent. by volume of ethyl alcohol. To 5 cc. of this dilute alcohol contained in a test tube of 20 cc. capacity, add 0.5 cc. of phosphoric acid and 2 cc. of a 3 per cent. aqueous solution of potassium permanganate, and allow the mixture to stand for ten minutes. Add 1 cc. of an aqueous 10 per cent. solution of oxalic acid, and allow to stand until the liquid is a transparent brown. Now add 5 cc. of a diluted and cooled sulphuric acid, prepared by mixing 3 volumes of distilled water and 1 volume of sulphuric acid, add 5 cc. of freshly prepared fuchsin-sulphurous acid T.S., mix well, and allow to stand for ten minutes. At the end of this time the solution, when observed against a white background, may have a reddish or pale green tint, but not a distinct blue or violet color (*methanol*). A mixture of 5 cc. of Alcohol, 2 cc. of sodium hydroxide T.S., and 5 drops of a freshly prepared aqueous solution of sodium nitroprusside (1 in 50), rendered slightly acid with acetic acid, shows no violet tint within one minute (*acetone*). Alcohol, diluted with an equal volume of water, does not respond to the tests for *alkaloids, diethylphthalate, formaldehyde, isopropyl alcohol,* and *phenols* described under *Spiritus Frumenti.*

" Preserve in well-closed containers, in a cool place, remote from fire." *U. S.*

" Specific gravity 0.8337. It contains 85.68 per cent. by weight of ethyl hydroxide, C_2H_5-OH, and 14.32 per cent. by weight of water. Burns with a blue smokeless flame. Leaves no residue on evaporation (absence of non-volatile matter). Remains clear when mixed with *water* (absence of oily or resinous substances). A little exposed on clean white filter paper leaves no unpleasant smell after the alcohol has evaporated (absence of fusel oil and allied impurities). 100 cc., with 2 cc. of *N/10 solution of silver nitrate,* exposed for twenty-four hours to bright light and then decanted from the black powder which has formed, undergo no further change when again exposed to light with more *N/10 solution of silver nitrate* (absence of more than traces of amylic alcohol and of other organic impurities). When mixed with half its volume of an aqueous solution (1 in 5) of *sodium hydroxide,* the mixture does not immediately darken in color (absence of more than traces of aldehyde). No immediate darkening in color is caused by the addition of *solution of ammonia* (absence of tannic acid, excess of aldehyde, and other organic impurities)." *Br.*

On a large scale, alcohol of this strength is now prepared in the United States, very abundantly, by simple distillation by means of a modified distillatory apparatus known as a " still and column." The modification consists in substituting for a single refrigerated receiver a series of receivers, kept at such temperatures that, in the first of them, the aqueous vapor shall condense with comparatively little of the alcoholic, which, as it passes through the successive condensers, is more and more deprived of water, until, when condensed in the last, it yields a spirit at least as strong as the official Alcohol of the sp. gr. 0.816. At the same time that the spirit is thus strengthened, it becomes, through the principle of fractionation which the process introduces, more and more freed from fusel oil, until almost wholly deprived of it.

Commercial alcohol, though of standard strength, may still be impregnated with sufficient fusel oil to modify the characteristic odor.

The present *alcohol* of the U. S. P. corresponds to that formerly recognized as *Alcohol Deodoratum* (*Deodorized Alcohol*), U. S., 1890, and may be used for many purposes for which ordinary commercial alcohol would be unsuited, such as the solution of volatile oils and essences having delicate odors, the manufacture of compound spirits, etc.

Deodorized alcohol is manufactured under Atwood's process, in which manganic acid or potassium or sodium permanganate is used to destroy fusel oil and other foreign substances. This alcohol withstands the tests of silver nitrate and sulphuric acid remarkably well. Pure fused sodium acetate has been proposed as a substance particularly adapted to retain fusel oil, and has been used by adding it to the alcohol to be rectified in the proportion of about 10 pounds to the barrel of forty-five gallons, and redistilling. The purification of alcohol is accomplished, according to Schmitt, by taking crude alcohol containing 30 per cent. by volume, adding potassium carbonate (not enough to cause two layers to form), and agitating with pure petroleum benzin; this solvent removes completely the fusel oil from the alcohol. After separating the light layer, potassium carbonate is added to the alcohol in sufficient quantity to form two layers, the lower one consisting of a saturated solution of potassium carbonate, the upper one of 94 per cent. alcohol containing a small quantity of potassium carbonate. The alcohol layer is siphoned off and mixed with just sufficient strong sulphuric acid to precipitate the potassium salt as sulphate, which is insoluble in alcohol of 94 per cent., and which can then be removed. Alcohol purified in this manner, without distillation, it is stated, cannot be distinguished from that purified by the usual method. F. G. Earl recommends the following method, which has the advantage of requiring no special apparatus. "Rub four drachms of powdered unslaked lime with two drachms of powdered alum intimately; add one gallon (95 per cent.) alcohol, and shake well, then add one fluidrachm of spirit of nitrous ether, set aside for seven days, and filter through animal charcoal." (*C. D.*, 1895, 35.) *Perfumer's alcohol* can now be had, which is very much cleaner than *cologne spirit,* as the purest alcohol attainable was formerly called. It is termed perfumer's alcohol because it was found necessary to prepare a very high grade of alcohol for those who need a solvent for fine odors, on the score of economy and to insure greater excellence of product.

ALCOHOL DILUTUM. *U. S.*—Specific gravity from 0.935 to 0.937 at 15.6° C. and from 0.930 to 0.932 at 25° C.

Diluted alcohol is officially made by mixing equal measures of alcohol and water together.

"Alcohol 500 cc. Distilled Water 500 cc. Measure the alcohol and water at the same temperature, and mix them. If the two liquids are measured at the temperature of 25° C., the mixture when cooled to the same temperature will measure about 970 cc." *U. S.*

The British Pharmacopœia (1914) no longer uses the titles "Spiritus Tenuior" or "Proof Spirit" for diluted alcohol, but admits four official liquids under the name of diluted alcohol, as follows:

"1. **Alcohol (70 per cent.).**—With *one thousand millilitres* of Alcohol (90 per cent.) mix *three hundred and ten and a half* (310.5) *millilitres* of Distilled Water. Specific gravity 0.8899.

"2. **Alcohol (60 per cent.).**—With *one thousand millilitres* of Alcohol (90 per cent.) mix *five hundred and thirty-six and a half* (536.5) *millilitres* of Distilled Water. Specific gravity 0.9134.

"3. **Alcohol (45 per cent.).**—With *one thousand millilitres* of Alcohol (90 per cent.) mix *one thousand and fifty-three and a half* (more accurately 1053.4) *millilitres* of Distilled Water. Specific gravity 0.9435.

"4. **Alcohol (20 per cent.).**—With *one thousand millilitres* of Alcohol (90 per cent.) mix *three thousand five hundred and fifty-eight* (3558.0) *millilitres* of Distilled Water. Specific gravity 0.9760." *Br.*

This is a convenient pharmaceutical method of providing suitable menstrua for making tinctures, fluidextracts, and other galenical preparations, which have been adopted by the British Pharmacopœia.

"**Tests for Identity and Purity.**—Diluted Alcohol has a specific gravity of from 0.935 to 0.937 at 15.56° C. (the U. S. Government standard temperature for alcohol). It complies with the purity tests under *Alcohol,* allowance being made for the difference in strength and the presence of water, the boiling point being omitted.

"Preserve in well-closed containers, in a cool place, remote from fire." *U. S.*

Uses.—The local action of alcohol is mildly irritant, feebly anesthetic and distinctly germicidal. The most favorable concentration for the destructive action on bacteria is from 60 to 70 per cent.; either higher or lower concentrations are less efficient. This amount of alcohol is capable of destroying most of the pathogenic micro-organisms within a relatively short time, but some of the more resistant spore-bearing germs are not killed even by prolonged exposure.

Alcohol belongs, physiologically as well as chemically, to the group of aliphatic narcotics. In large doses it will produce a condition of coma which is precisely analogous to the anesthesia produced by ether. A number of authors, however, have maintained that in small quantity it acts as a cerebral excitant. There are arguments in favor of this view, and one may not speak too dogmatically on the subject, but the weight of evidence to-day indicates that any dose of alcohol sufficient to affect the system at all, lessens, rather than increases, intellectual activity.

Krapelin (*Ueber d. Beeinflussung einf. psychischer Vorgänge durch einige Arzneimittel,* Jena, 1892) found that doses of 30 cc. or more depressed all psychical processes, but with very small quantities there was a preliminary slight facilitation lasting 20 or 30 minutes and followed by a secondary depression, even after doses as small as 7.5 Gm. Dodge and Benedict (*Proc. Nat. Acid. Science,* 1915, 1) find that both the spinal and cerebral reactions are depressed by a single dose of 30 cc. (See also Benedict, *A. J. P.,* 1925, xcvii, 413.)

Small doses of alcohol seem to stimulate respiration (see Hooker, *J. P. Ex. T.,* 1919, x, 121), but large quantities are depressant. Scarborough (*J. P. Ex. T.,* 1921, xvii, 129) finds that the effect of alcohol upon muscle tissue is to cause a temporary increase of excitability which is followed by a period of lessened response.

The question of its effects on the circulation has been the subject of much study and dispute. When administered in moderate quantity, it usually does not produce any marked change in the blood pressure, although occasionally there may be some elevation. On the other hand, the rapidity of the flow of blood through the vessels is distinctly accelerated. This concordination of effects can be explained only by simultaneous increase in the cardiac action and dilatation of the blood vessels. While there is considerable difference of opinion on this subject we believe that the evidence is strong that quantities of alcohol equivalent to not over one-half an ounce for the ordinary man, increase the amplitude of the cardiac contractions. The experiments of Dixon (*J. P.*, 1907, xxxv) indicate that this effect is most marked when the heart is partially exhausted. The widening of the blood vessels is most noticeable in the vessels of the skin. Large quantities of alcohol produce a marked fall in the blood pressure which is due not only to paralysis of the vasomotor mechanism, but also to a depressant action upon the heart.

When a moderate quantity of alcohol is ingested, from 90 to 95 per cent. is completely oxidized in the system, only traces of the drug being recoverable from either the urine or breath. The oxidization of this amount of hydrocarbon material must of necessity yield energy. Some have, however, attempted to maintain that this energy was not utilizable by the animal economy. The experiments of Atwater and Benedict (*Memoirs of the National Academy of Science*, 1902, vii) and others, seem to demonstrate beyond cavil that small amounts of alcohol are entirely capable of replacing an equivalent portion of the hydrocarbon foodstuffs. But the amount of alcohol which the system is capable of oxidizing is rather limited, and if the administered dose be increased the drug begins to appear unchanged, or only partially oxidized, in the urine and in the exhalations. Whether the presence of unaltered alcohol in the bodily fluids hastens or retards metabolism is still an unsettled question. It seems, however, to be fairly well established that in some way it distorts metabolism, and that the oxidation, especially of purin-containing bodies, is not so complete as in the normal animal.

Alcohol has a marked influence upon gastric and probably also intestinal digestion. In small amounts it does not influence the activity of the peptic ferments, although concentrations of 10 per cent. or over greatly reduce or completely destroy the enzymic activity of pepsin. It has long been recognized that the swallowing of small quantities of alcoholic liquors increases the flow of gastric juice. While this is in part probably due to the local irritation of the mucous membrane of the stomach there is also some central mechanism involved, as an increase in the gastric and pancreatic secretions has been shown after the intravenous or rectal administration of alcohol. After section of the vagi or their paralysis by atropine this increase in the digestive secretions does not occur. (For review of literature on the effects of alcohol on digestion, see Salant, *A. J. Phys.*, 1907, xvii, p. 409.)

Alcohol is used locally as a mild counter irritant and as a germicide. Internally it is used (1) to excite the heart, (2) as a stimulant to digestion (3) as an accessory food and (4) for its narcotic effects.

As a circulatory stimulant there is no doubt that in the past too much confidence has been placed in alcohol. Nevertheless if used circumspectly it is often of great value. It is used especially when it is desired to tide the patient over for a limited period of time, as in cases of depressant *poisonings.* It must never be forgotten in this connection that large doses are depressant to the heart; while a small amount of alcohol may prove useful in cases of *snake bite,* it is no exaggeration to say that the injudicious exhibition of this drug has been responsible for as many deaths in rattlesnake bites as the venom itself. In the circulatory failure due to anesthetics it should be sedulously avoided; on account of its close chemical relation to both ether and chloroform it acts as a synergist rather than an antagonist to these poisons. The use of alcohol in *infectious fevers,* especially *typhoid fever,* involves a large number of factors concerning some of which we have at present no definite knowledge. While it seems to be well established that in large doses alcohol diminishes the resistance of the body to bacterial invasion the influence of small quantities upon the vital resistance is as yet a matter of dispute. The impairment of digestion, which is so universal an accompaniment of these diseases, suggests the use of alcohol both as a stimulant to gastric secretion and as an accessory food. While febrile patients are capable of burning up larger quantities of alcohol than normal individuals, if given too freely the unoxidized alcohol circulating in the blood may prove injurious. An alcoholic odor to the breath is generally a sign that the patient is receiving more than he can oxidize. Many believe that the mild narcotic action of alcohol is also of service in preserving the vitality in these adynamic states.

By dilating the vessels of the skin alcohol tends to increase the sweat and is frequently used as an aid to more powerful diaphoretic measures in the abortion of mild infections, such as *acute coryza.*

Locally it is of service for its disinfectant action not only in cleansing the hands of the surgeon but also as a dressing for local inflammations and *wounds.* Although not infrequently employed for the sterilization of surgical instruments the uncertainty of its effects against spore forming organisms makes it very unreliable for this purpose. Recently it has been widely employed for its local paralytic influence when injected into nerve tissue, as in *sciatica,* but especially in that most intractable disorder *tic douloureux.*

Raw alcohol is rarely used internally, preference being always shown for one of the alcoholic beverages, such as whiskey, brandy, or wine.

The purer forms of alcohol, whether strong or diluted, are employed almost exclusively in pharmacy; as in the preparation of medicines, such as ether, into the composition of which they enter; for the preservation of organic substances; in the extraction of the active principles of drugs, as in the tinctures; for dissolving bodies soluble in alcohol much more readily than in water, or insoluble in the latter fluid; and for other pharmaceutical purposes. Diluted alcohol is employed as an addition to some infusions and decoctions, and to some of the distilled waters; in order to preserve them from decomposition; as a menstruum for extracting the virtues of plants, preparatory to the formation of extracts and syrups; and in preparing many of the spirits, and a few of the medicated wines. But it is in forming the tinctures that diluted alcohol is chiefly used. Some of these are made with official alcohol (rectified spirit), but the majority with mixtures of alcohol and water of different percentages. As diluted alcohol contains more than half its weight of water, it is well fitted for acting on organic substances the virtues of which are partly soluble in water and partly in alcohol.

Toxicology.—The symptoms of acute alcohol poisoning are unfortunately so widely known that detailed description is unnecessary, but the striking similarity between the symptoms of alcoholic intoxication and ether anesthesia is worthy of note; in the more profound stages of alcoholism there is the complete loss of consciousness and of sensation, the muscular relaxation, and the slow respiration, which are characteristic of the ether narcosis. It should not be forgotten that acute alcohol poison may, and frequently does, end fatally. The treatment consists in the immediate evacuation of the stomach, the maintenance of the bodily temperature by the use of external heat, the use of respiratory stimulants, such as strychnine, cocaine and atropine, and of cardiac stimulants, as ammonia and digitalis.

The habitual use of alcoholic beverages may lead to profound degenerations of the various internal organs, especially the stomach, liver, and kidney. The changes may be either sclerotic or fatty. Besides these there are often marked symptoms of serious nervous diseases, but whether the latter are organic or toxic is as yet unsettled.

ALETRIS. N. F.

ALETRIS Aletr. [Star Grass, Unicorn Root]

"Aletris consists of the dried rhizome and roots of *Aletris farinosa* Linné (Fam. *Liliaceæ*). Aletris contains not more than 5 per cent. of foreign organic matter and yields not more than 10 per cent. of acid-insoluble ash." *N. F.*

Unicorn Root, Star Grass, Blazing Star, Mealy Starwort, Colic Root, Ague Root; Alétris farineux, *Fr.;* Mehlige Aletris, *G.*

Probably because of the fact that the English names "blazing star" and "starwort" have been applied to the aletris as well as to the chamælirium, this drug has commonly been confused with helonias. Both the plants and the roots of these two drugs are so different that they do not occur as intentional adulterants of each other but helonias is not infrequently substituted for aletris.

Aletris farinosa L. or *True Unicorn Root* is a perennial acaulescent herb indigenous to sandy and grassy woods of the Eastern United States and extending westward to Arkansas and Minnesota. It is characterized by possessing a horizontal to slightly oblique grayish-yellow to grayish-brown rhizome, from the sides and lower face of which emanate many tough, wiry, pale yellow or whitish, fibrous rootlets. From this rhizome there arises a spreading rosette of thin lanceolate foliage leaves and later, through the center of the rosette, a naked slender scape, bearing a spike-like raceme of small, white, tubular flowers. The fruit is an ovoid, beaked capsule inclosed in a roughened, mealy looking perianth.

The aerial portion of *Aletris* may be distinguished from the similar part of *Chamælirium* or *False Unicorn Root* (which yields the drug *Helonias*) by the following characters: The flowers of *Aletris* are perfect, whereas those of *Chamælirium* are dioecious; the perianth of *Aletris* is gamophyllous and distinctly roughened, whereas that of *Chamælirium* is composed of six distinct segments and smooth; the capsule of *Aletris* is ovoid and beaked and enclosed in the roughened perianth, whereas that of *Chamælirium* is ellipsoidal and devoid of a perianth investment; all of the foliage leaves of *Aletris* are grass-like and radical, whereas *Chamælirium* possesses radical foliage leaves which are spatulate and cauline foliage leaves which are lanceolate.

The rhizome systems of *Aletris* and *Chamælirium* show marked dissimilarities. Thus, the rhizomes of *Aletris* are generally horizontal and without annulations, while those of *Chamælirium* are generally vertical and annulate, the fracture of the former being strong, starchy and fibrous and of the latter horny and resinous; moreover, the rootlets of *Aletris* frequently have portions of their cortex abraded exposing a reddish-brown endodermis, whereas no such condition is evident in *Chamælirium.* The taste of *Aletris* is starchy, sweetish and bitter, whereas that of *Chamælirium* is strongly bitter.

Most of the aletris now on the market is collected in the Carolinas and Tennessee.

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Description and Physical Properties.—"*Unground Aletris.*—Rhizome horizontal or slightly oblique, nearly cylindrical or laterally compressed above, 2 to 4 cm. in length and 5 to 12 mm. in diameter; externally grayish-brown; upper portion with circular stem scars 3 to 7 mm. in diameter and with numerous leaf bases; the sides and lower portion with numerous tough, wiry, whitish roots which are reddish brown when the cortex is removed and are more or less flexuose and provided with short branches; fracture short; internally light brown, cortex 1 to 2 mm. in thickness, central cylinder with numerous twisted and branching fibrovascular bundles. Odor slight, acetous; taste sweetish, bitter.

"*Structure.*—Rhizome with epidermis bearing numerous glandular hairs with a short one-celled stalk and a rounded head; tissue composed chiefly of parenchyma cells filled with starch grains or raphides of calcium oxalate; numerous irregularly distributed and branching groups of tracheæ the latter with reticulate or simple pores and surrounded by several layers of lignified cells, these cells with thick walls and large oblique pores; endodermis usually absent except in the older portion of the rhizome where it occasionally occurs as an interrupted zone. Root with a distinct endodermis composed of one layer of cells with thick, deep yellow, closely lamellated walls; cortex composed chiefly of parenchyma and readily separated from the central stele, the latter containing numerous lignified fibers, a few tracheæ and sieve cells.

"*Powdered Aletris.*—Light gray to yellowish brown; numerous orange-yellow thick-walled fibers with tapering pointed ends and simple or branching pores; fragments of tracheæ with reticulate or simple pores and associated with lignified cells; numerous fragments of parenchyma containing starch grains, the latter spherical or ellipsoidal from 0.003 to 0.016 mm. in diameter, and numerous raphides of calcium oxalate in bundles or individual crystals, the latter from 0.025 to 0.50 mm. in length; fragments of epidermal tissue frequently bearing glandular hairs." *N. F.*

As far as we know, aletris has never been submitted to chemical examination.

Uses.—There is no reason to suspect that aletris possesses any therapeutic virtues other than those of a simple bitter. As suggested by its popular name of "colic root," it has, however, been used to considerable extent for the purpose of expelling *flatulence.* Probably because of its confusion with helonias it has been employed in the treatment of various uterine disorders but without clinical justification.

Dose, twenty to thirty grains (1.3–2.0 Gm.).

Off. Prep.—Fluidextractum Aletridis, *N. F.;* Elixir Viburni Opuli Compositum, *N. F.;* Elixir Aletridis Compositum, *N. F.*

ALLIUM. N. F.

GARLIC

"Garlic is the fresh bulb of *Allium sativum* Linné (Fam. *Liliaceæ*)." *N. F.*

Ail, *Fr.;* Knoblauch, *G.*

The genus *Allium* includes a large number of species, of which nearly seventy are indigenous in this country. Many, and perhaps all, of these species contain volatile oil upon which their activity depends. The cultivated garlic, of which the bulbs are official in the N. F., is *Allium sativum* L., for which, according to Griffith, *A. canadense* L., has been substituted and found efficient.

Allium sativum, L., or *English garlic,* is a perennial plant with numerous bulbs which have a common membranous covering, from the base of which the fibers that constitute the proper root descend. The stem is simple, and rises about two feet. The leaves are long, flat, keeled and grass-like, and sheathe the lower half of the stem. At the termination of the stem is a cluster of purple flowers and bulbels mingled together, and enclosed in a pointed spathe, which opens on one side and withers. The flowers make their appearance in July. This species of garlic is indigenous to Europe. It grows wild in Sicily, Italy, and the south of France. The bulbs, or so-called cloves, are usually six or eight in number, oblong or wedge-shaped, and covered with dry membranous scales with a pungent odor and a disagreeable and acrid taste.

Description and Physical Properties.—"*Whole Garlic.*—Bulb subglobular, 4 to 6 cm. in diameter, compound, with 8 to 15 bulbels surrounded by whitish, membranaceous scales and attached to a flattened circular base, the latter with numerous yellowish white roots; bulbels ovoid in transverse section 3- to 4-sided, the outer surface convex, apex acute and narrowed into a thread-like fibrous portion, base truncate; each bulbel covered by whitish, membranaceous, scale-like leaves, beneath which is a light brown or pinkish, thin and coriaceous layer of epidermis, cohering but easily separable from the solid portion of the bulbel. Odor when broken or bruised powerfully alliaceous, taste intensely pungent and persistent.

"*Structure.*—Bulbel with three distinct portions; (a) the large fleshy scale consisting chiefly of parenchyma enclosing scattered vascular bundles; epidermis in both ventral and dorsal surfaces of small tabular cells; (b) a middle layer nearly circular in outline, about 0.750 mm. in diameter, the tissues resembling those of the outer fleshy scale, but the cells containing numerous yellowish brown plastids; (c) an innermost bright green layer consisting of a single leaf folded lengthwise along the midrib so that the ventral surfaces lie close together. The membranaceous scales, dry leaf and root remains should be removed before Garlic is used for the manufacture of pharmaceutical preparations." *N. F.*

Constituents.—Such medicinal value as garlic may possess is undoubtedly due to its volatile oil.

The *oil of garlic* is of a dark brownish-yellow color, heavier than water, and decomposed at its boiling temperature. It may be purified by repeated distillation in a salt water bath, and is then lighter than water, of a pale yellow color, and not decomposed by boiling. Semmler obtained from garlic bulbs 0.09 per cent. of the volatile oil, sp. gr. at 14.5° C. 1.0525; it was yellow, having an intense odor and optically inactive. By fractional distillation he obtained four products, $C_6H_{12}S_2$, $C_6H_{10}S_2$, $C_6H_{10}S_3$, and $C_6H_{10}S_4$, which decomposed during distillation, and hence could only be obtained by distillation *in vacuo*. The oil, according to Semmler, is free from allyl sulphide, the latter having the sp. gr. 0.8991. (*A. Pharm.*, 1892, p. 434.) The impure oil has an exceedingly pungent odor and a strong acrid taste, and, when applied to the skin, produces much irritation and sometimes even blisters. The pure oil combines with silver nitrate, forming a precipitate soluble in heated alcohol and afterwards separating in crystals. Besides this oil, fresh garlic, according to Cadet de Gassicourt, contains, in 1406 parts, 520 of mucilage, 37 of albumen, 48 of fibrous matter, and 801 of water. Bouillon-Legrange mentions among its constituents sulphur, a saccharine matter, and a small quantity of starch. The fresh bulbs yield upon pressure nearly a fourth part of juice, which is highly viscid, and so tenacious as to require dilution with water before it can be easily filtered. When dried, it serves as a lute for porcelain. It has the medicinal properties of the bulbs. Water, alcohol, and vinegar extract the virtues of garlic. Protracted boiling renders it inert. According to Semmler (*A. Pharm.*, 1887, p. 927), *Allium ursinum* contains a volatile oil which consists mainly of *vinyl-sulphide*, C_4H_6S or $(C_2H_3)_2S$.

Uses.—Among the ancients garlic was credited with curative virtues in an extraordinarily large variety of diseases. At the present time its medical employment is limited chiefly to pulmonary conditions such as *chronic bronchitis*, especially with an asthmatic tendency, and sometimes *whooping-cough*. Minchin (*Pract.*, Feb., 1918) has revived the ancient idea of its value as an internal antiseptic and lauds it as a remedy for *diphtheria, tuberculosis* and other infectious diseases. Loeper and DeBray (*Bull. Soc. Hôp.*, 1921, xxxvii, 1032), from experiments upon both human beings and dogs, reach the conclusion that the tincture of garlic causes a fall in blood pressure which is most marked in cases of hypertension. They also find that it brings about a leucocytosis. There is no doubt that the oil of garlic is absorbed through the alimentary tract and eliminated partly through the lungs and partly through the urine. Garlic is also occasionally employed as an anthelmintic, especially in domestic practice.

Externally it is employed as a rubefacient and stimulant to the nervous system especially in cases of young children. In *catarrhal pneumonia* bruised garlic cloves are sometimes applied as a poultice to the lungs, partly because of their counterirritant effect and partly for endermic absorption.

The expressed juice of garlic is sometimes employed in doses of one-half fluidrachm (2 cc.) but the most popular preparation is the syrup, which is recognized by the N. F., and may be given in doses of one to two teaspoonfuls (4–8 cc.).

The fresh bulb is occasionally exhibited in substance in *doses* of from one-half to two drachms (2 to 8 Gm.).

Off. Prep.—Syrupus Allii, *N. F.*

ALOE. U. S. (Br.)

ALOE

"Aloe is the inspissated juice of the leaves of *Aloe Perryi* Baker, known in commerce as Socotrine Aloe; of *Aloe vera* Linné, known in commerce as Curaçao Aloe; or of *Aloe ferox* Miller, known in commerce as Cape Aloe (Fam. *Liliaceæ*). Aloe yields not more than 4 per cent. of ash, not more than 10 per cent. of moisture, and not less than 50 per cent. of water-soluble extractive." *U. S.* "Aloes is the juice that flows from the transversely cut leaves of Aloe chinensis, *Baker,* Aloe Perryi, *Baker,* and probably other species of Aloe, evaporated to dryness. Known in commerce as Curaçao aloes, Socotrine aloes, or Zanzibar aloes." *Br.*

Aloe Barbadensis; Aloe Socotrina; Aloès, *Fr.*; Socotora oder Socotrinische Aloe, *G.*; Barbados Aloe, *G.*; Musebber, *Ar.*; Acibar Sucotrino, *Sp.*

Most plants belonging to the genus *Aloe* are capable of yielding a bitter juice which is laxative and there is little doubt that in many cases a commercial aloe exported from one country is the product of several species.

1. *Aloe Perryi,* J. G. Baker, *Tr. Linn. Soc.*, xxviii. The true Socotrine aloe plant was first described from specimens sent to Kew Gardens by Wykeham Perry, and was subsequently found by Balfour, of Edinburgh, growing abundantly upon the island of Socotra, especially in the limestone tracts, from the sea level to an altitude of 3000 feet; along with it, but much less abundant, was a dwarf species with spotted leaves. It is a perennial herb indigenous to the island of Socotra. It has a trunk one foot high which bears on its summit a dense rosette of pale green or reddish, succulent, lanceolate leaves which are somewhat striate but not mottled. They are channeled above, convex below and show brown-tipped, marginal spines. From the center of the leaf rosette there extends a long raceme of tubular, reddish flowers which later turn yellow. The fruit is a membranous capsule.

The proper aloetic juice was formerly thought to exist in longitudinal vessels beneath the epidermis of the leaves, and readily flows out when these are cut transversely; but, according to E. Robiquet, who made elaborate researches in relation to this drug, these vessels are air ducts, and the juice flows in the intercellular passages between them. The liquid obtained by expression from the parenchyma is mucilaginous, and possessed of little medicinal virtue. After condensation by artificial or natural heat the aloe juice is poured into gourds, more commonly boxes, or into monkey skins, allowed to harden and sent into commerce.

2. *Aloe vera* L. (*A. barbadensis* Miel.).—This species, which is the source of Curaçao aloe, has a very short, woody stem, and lanceolate embracing leaves, which are first spreading, then ascending, of a glaucous green color, when young, irregularly mottled with white spots, flat on the upper surface, convex beneath, and armed with hard, pale spines, distant from each other, and perpendicular to the margin. It has bright yellow flowers arranged in a spicate inflorescence. *A. vera* is a native of Southeastern Europe, Northern Africa, and Madagascar. It is cultivated in Italy, Sicily, Malta, and especially in the West Indies, where it contributes largely to furnish the Barbados aloe.

3. *Aloe chinensis* Baker.—This species was introduced from China into the Dutch Colonies of Curaçao by W. Anderson, in 1817. It is Asiatic in origin and probably a variety of *A. vera* as shown by Haworth. The leaves of *A. chinensis* are not more than half the length of those in *A. vera,* and are more or less copiously spotted on the dorsal surface as in *A. abyssinica* Baker. The flowers have a strong and decidedly unpleasant odor; and occur in loose racemes, the stamens being much shorter than in *A. barbadensis.* Holmes suggests that *A. chinensis* may be a native of Africa, Arabia or India. Engler considers that *A. chinensis* is merely a form related to *A. vera.* (Baker, in *J. L. S.,* xviii, p. 161; Holmes, *P. J.,* xxi, p. 205.)

4. *A. ferox* Miller, one of the three species yielding Cape aloe, is one of the tallest species of the genus. It has a forked stem ten to fifteen feet long, four to six inches in diameter; furnished at the top with a dense rosette containing thirty to fifty leaves, which are lanceolate, one and one-half to two feet long, very rigid, with copious prickles on back and face, the purplish margin armed with reddish brown-tipped, deltoid or cuspidate prickles one-eighth to one-sixth of an inch long. Its inflorescence consists of a panicle of tubular, striped whitish flowers.

5. *Aloe africana* Mill. has a simple tall trunk which bears on its summit a few, triangular-oblong, glaucous, green leaves with large horny marginal teeth. Its flowers are tubular and yellow and are borne on a candelabra-like panicle. It is a native of the Cape Colony.

6. *Aloe spicata* Baker (*A. Eru* var. *cornuta* Berger) is a tall, branched aloe indigenous to tropical Africa. It possesses pale glossy, fleshy leaves with white blotches and a panicle of campanulate yellow flowers.

According to L. Pappe, Cape aloe of poor quality is obtained from *A. africana* and *A. plicatilis,* of Miller; while in Lindley's *Flora Medica, A. purpurascens* Haworth, *A. arborescens* Mill., *A. Commelyni* Willd., and *A. multiformis* are all said to contribute to commercial Cape aloes.

Commercial History and Varieties.—Three chief varieties of aloe have been known in comparatively recent commerce: Socotrine, Barbados or Curaçao, and Cape.

SOCOTRINE ALOE.—This variety appears to have been the original aloe, having been produced in the island of Socotra at least as early as the time of Alexander the Great, 333 B.C., who is said to have sent a commission to investigate its manufacture. This form of aloe under the title of "Aloes Socotrina" alone is official in the Spanish Pharmacopœia. It is said to be derived from *Aloe vera* Mill., *A. spicata* Thunb., *A. ferox* L., *A. arborescens* Mill., and *A. linguæformis* L., and other species of aloes.

It is stated that the production of aloe in Arabia was formerly a government monopoly, but that at present it is entirely free to the inhabitants. The leaves, which are cut at any time of year, are allowed to drain into a goat's or sheep's skin, and the gathered juice permitted to evaporate spontaneously. In the course of about one month, when it has become thick and viscid, it is known by the Arabic name of *Jâyef Gesheeshah;* several weeks subsequently when it has become hard, it is called *Jâyef Kasahul.* Due to its exposure throughout the long process of desiccation, all the varieties of Socotrine aloes contain much foreign matter, which, according to E. R. Squibb, amounts to from 7 to 22 per cent. of the bulk.

Socotrine aloe is brought from the island of Socotra, the east coast of Africa and from the Arabian coast by Arab traders to Bombay and exported in barrels, kegs, goats' skins, or tins to London whence it is shipped to the United States. It is usually very wet, containing up to 20 per cent. of moisture.

The best Socotrine aloe occurs in pieces verying from a dark ruby-red to a yellowish or reddish-brown, more or less semi-transparent, with a glossy surface and a smooth or ragged but not conchoidal fracture, and yielding a bright golden-yellow powder. Its odor is peculiar, almost fragrant, especially developed by breathing upon the aloe, and its bitter, disagreeable taste has a somewhat aromatic tang. The poorest variety of Socotrine aloe, *Mocha aloes* of the East, is soft, dark, and malodorous. Some of the drug supplied American dealers in recent years has consisted of this variety. Even the finest Socotrine aloe may consist of an orange or yellow colored distinctly fragrant, semi-liquid mass.

ZANZIBAR ALOE is a hepatic variety of

Socotrine aloe made by slow evaporation of the juice. It occurs in liver-brown masses, with a dull, waxy but nearly smooth and even fracture, a characteristic odor and a nauseous, bitter taste. It is poured into skins which are packed in cases for shipment. The variability of Socotrine aloe probably depends upon not only different methods of preparation but a different origin. Both Zanzibar and true Socotrine Aloes "are opaque even in small splinters, though they exhibit, when mounted in almond oil and examined under the microscope, numerous minute crystals embedded in a transparent, dark yellowish-brown mass, and impart to *nitric acid* a reddish- or yellowish-brown color." *Br.*, 1900.

CURAÇAO OR WEST INDIAN ALOE.—This aloe, which is produced in the Dutch West Indian Islands, chiefly in the islands of Aruba, Bonaire and Curaçao, appears not to have entered commerce extensively before the early part of the 19th century, but at present constitutes a very large proportion of commercial aloe. It occurs chiefly in three forms; first, an opaque, brittle aloe, showing abundant crystals under the microscope, and sold in gourds usually as Barbados aloe; second, aloes having an appearance like the first variety but sold in cases; third, glossy Curaçao or Capey Curaçao aloe, which occurs in cases and is glossy and transparent. This variety may become opaque upon long storage due to the gradual crystallization of the aloin. Small fragments show a garnet-red color.

Curaçao aloe is apparently produced by the following species: *A. vera* (L.) Webb, *A. vulgaris* Lam., *A. spicata* L., and *A. socatrina* Lam., all of which have been introduced into the island (see *P. J.*, Jan., Sept., 1890), although E. M. Holmes believes it to be at least in part the product of *A. chinensis* Baker.

Curaçao aloe is collected in the Dutch West Indies by workers during the early spring. The leaves are cut off at their bases and placed cut end downward in V-shaped troughs which are arranged on an incline. The juice, in trickling from the leaves, runs down the sides of the trough and through an aperture at its lower end into a receptacle beneath. As the receptacles are filled with the juice, their contents are poured into a cask and either evaporated spontaneously or by boiling in copper vessels. As soon as the juice has thickened to the proper consistency, it is poured into gourd shells or boxes and allowed to harden. This aloes is shipped direct to the United States from Aruba, Curaçao and Bonaire.

According to P. van der Wielden, shining Curaçao aloe dissolves completely in nitric acid with the production of a red color, while the dull Curaçao aloe, giving the same color reaction, fails to entirely dissolve. Kremel gives a method to distinguish Curaçao aloe from other kinds by adding to it a little cupric sulphate solution, then some saturated solution of common salt, which makes the color an intense carmine. The reaction is due to *cuproaloin.* (*C. D.*, 1895, 759.) Curaçao aloe is sometimes found in the markets which has been deprived of its aloin; this fraudulent product is then sold as Cape aloes; the odor of the Curaçao variety still remains.

CAPE ALOE.—This variety is from *Aloe ferox, Aloe africana* and *Aloe spicata.* The general method of collecting Cape aloe is to allow the excised leaves to drain into a sheep's skin, which has been so placed in a hole in the ground as to force the juice to collect in the center. Later this juice is poured into tins, subsequently boiled down over a fire in iron pans, and when sufficiently concentrated, poured into boxes or barrels and allowed to harden. In these containers it is shipped from Mossel Bay and Port Elizabeth to Cape Town, thence to Europe and America. Cape aloe differs from Socotrine aloe, especially in its brilliant conchoidal fracture and peculiar odor, which is strong, but neither nauseous nor aromatic. When freshly broken it has a very dark olive or greenish color approaching to black, presents a smooth, bright, almost glassy surface, and if held up to the light appears translucent at its edges. The small fragments also are semi-transparent, and have a tinge of yellow or red mixed with the deep olive of the opaque mass. The same tinge is sometimes observable in the larger pieces. The powder is of a fine greenish-yellow color, and, being generally more or less sprinkled over the surface of the pieces as they are kept in the shops, gives them a somewhat yellowish appearance. Cape aloe, when quite hard, is very brittle and readily powdered; but in very hot weather it is apt to become somewhat soft and tenacious, and the interior of the pieces is occasionally more or less so even in winter. This variety alone is official in the Swiss, German, and Austrian Pharmacopœias.

Uganda or *crown aloe* is a brand of Cape aloe formerly produced by manufacturers who bought the aloe juice from the collectors, allowed it to undergo a slight fermentation, and dried it in the sun in wooden troughs. It was sent into commerce in bags containing coarse or fine powder, or chips, and in bricks wrapped in red paper; it has a very bitter, aromatic taste and a strongly aromatic odor. The bricks are of a hepatic brown color, with a resinous fracture, which has a bronzy-gold luster by reflected light. Splinters are translucent, but not garnet-red. With nitric acid it forms a brown solution, gradually changing through dull brownish-yellow to a deep green color. Uganda aloe is now practically obsolete.

BARBADOS ALOE.—This aloe appears to have been brought to London as early as 1693, and to have reached its greatest commercial abundance in the year 1843, when 4227 gourds of it are said to have been exported from Barbados, a gourd containing from twenty to sixty pounds. Occasionally small quantities of Barbados aloe are on the American markets. Most of the Barbados aloe was produced from *A. vera,* although *A. socotrina, A. purpurascens,* and *A. arborescens* are said to have been cultivated.

The method of obtaining Barbados aloe seems to have varied at different periods of time, and possibly in different portions of the island. According to various authors the lower ends of the freshly cut leaves were put into wooden V-shaped troughs, and the exuding juice collected and dried in the sun or boiled in copper pans; again, a decoction of the chopped-up leaves was boiled to the proper consistency; in either case, when the liquor had become so thick that it hardened on cooling, it was poured into calabashes or gourds.

Barbados aloe, as formerly supplied, varied in color from very dark blackish-brown through reddish-brown and liver-colored to orange-brown. It yielded a dull olive-yellow powder, of a disagreeable, even nauseous odor, and it was described in the British Pharmacopœia as follows: "Fracture either dull and waxy, in which case small splinters are opaque; or smooth and glassy, in which case the splinters are transparent; the opaque variety examined under the microscope exhibits numerous minute crystals embedded in a transparent mass." *Br.,* 1898.

"Mixed with nitric acid, it acquires a red color. Barbados Aloes is not colored, or acquires only a light bluish-green tint, on being mixed with sulphuric acid and blowing the vapor of nitric acid over the mixture (difference from *Natal aloe*)." *U. S.,* 1890.

According to Marais, Barbados aloe could be distinguished by the fact that its solution in distilled water, 1 to 100,000 parts, yielded on the addition of gold chloride or of tincture of iodine a fine rose color, all other varieties of aloes producing with the reagents named either a feeble color of slow development, or no change of color whatever.

Unofficial Varieties.—Besides the official varieties of aloe several allied drugs have appeared from time to time in commerce.

Natal aloe is a variety coming from Natal on the southeast coast of Africa, the origin of which is not definitely ascertained but is possibly *A. succotrina,* Garsault. It occurs in irregular pieces, with a fracture much less shining than that of Cape aloe and a totally different color, having a greenish slate hue. It yields a greenish-brown powder, which has the odor of Cape aloe. It is less soluble than Cape aloe, and has a peculiar composition, which will be adverted to under the chemistry of the drug.

Besides the chief varieties of aloe, others are, or have been, known in the market. *Hepatic aloe,* as well as *fetid, caballine* or *horse aloe,* have no proper claim to be considered distinct varieties, being simply inferior aloe of various origins, the first liver-colored, the second blackish and fetid and full of impurities. *Jafferabad aloe,* supposed to be the same as *Mocha aloe* (*A. J. P.,* 1881, 175), has been shown to be the product of *A. abyssinica* Lam., and is said by Shenstone to contain *b*-barbaloin. (*A. J. P.,* 1883, 92.) Aloe made in India from the *A. vera* is known as *Musambra aloe.* It appears to be a very inferior variety, and rarely, if ever, reaches Europe. (*P. J.,* Aug., 1889.) Occasionally aloe is found on the market in which the aloin has been removed. Noyes has reported the presence of pea flour in the powdered drug.

It is evident that the labels under which aloe are largely sold often have little or no connection with the place of production, or with the variety of aloes in the package. This fact has probably come about through the indifference of retail druggists to the variety of the aloe which they are using, an indifference largely due to their common habit of buying aloe in powder. Wilbert (*A. J. P.,* 1903) proposed that aloes should be classified as follows:

Aloe A.—Containing barbaloin; responds to Bornträger's test for emodin, but does not give a distinct red color with nitric acid, or with Klunge's test.

Aloe B.—Containing isobarbaloin with barbaloin; responds to Bornträger's test for emodin, and also has a deep red color with strong nitric acid, or with Klunge's test.

The commercial aloes are sometimes divided into two groups: 1. Those which are shiny and amorphous, as Cape aloe, and 2. Those which are of a dull color and crystalline. To this latter group most of the other aloes belong. They are also grouped geographically as follows. 1. South African aloe, including Cape and Natal. 2. East African aloe, including Socotrine, the brown and black Zanzibar aloes and Madagascar aloe. 3. The West Indian aloe which includes the Curaçao, Barbados and Jamaica varieties. 4. The East Indian aloe which includes Jafferabad and Musumbra aloes. The official description is limited to the three principal varieties, viz., Socotrine, Curaçao and Cape aloes.

Description and Physical Properties.—"*Unground Socotrine Aloe.*—In yellowish-brown to blackish-brown, opaque, smooth and glistening masses; fractured surface somewhat conchoidal; odor characteristic.

"*Unground Curaçao Aloe.*—In orange to blackish-brown, opaque masses; fractured surface uneven, waxy, somewhat resinous; odor characteristic, disagreeable.

"*Unground Cape Aloe.*—In reddish-brown masses, usually covered with a yellowish powder, or in thin, transparent fragments, of a reddish-brown color; fracture smooth and glassy; odor characteristic, sour and disagreeable. The taste of each variety of Aloe is nauseous and very bitter.

"*Powdered Aloe.*—Yellowish-brown to dark reddish-brown; mounted in a bland, expressed oil, it appears as yellowish to reddish-brown angular or irregular fragments, the depth of color depending to some extent on the thickness of the fragments.

"Powdered Aloe dissolves in nitric acid with effervescence, Socotrine Aloe forming a yellowish to reddish-brown solution; Curaçao Aloe, a deep red solution; Cape Aloe a reddish-brown solution, changing to purplish-brown and finally to greenish. Intimately mix in a flask or bottle about 1 Gm. of powdered Aloe, accurately weighed, with 25 cc. of cold water, shake occasionally during two hours, transfer to a filter, tared after it has been dried over sulphuric acid, and wash with sufficient cold water to make the filtrate measure 100 cc.: the residue on the filter after drying over sulphuric acid should not exceed 50 per cent. of the weight of powdered Aloe taken. The color of the filtrate, viewed in the bulb of a 100 cc. volumetric flask, is light yellowish-brown with Socotrine Aloe, reddish-brown with Curaçao Aloe, and yellowish with Cape Aloe. The filtrate darkens upon standing. To 5 cc. of the filtrate mentioned above, add 2 cc. of nitric acid: the mixture is of a yellowish to yellowish-brown color with Socotrine Aloe; a deep red color with Curaçao Aloe; a reddish-brown color, changing to vivid green, with Cape Aloe. To 5 cc. of the filtrate mentioned above, add 45 cc. of water and 20 cc. of sodium borate solution (1 in 20): a greenish fluorescence results and, upon standing, the liquid acquires a brownish color. To 10 cc. of the filtrate mentioned above, add 90 cc. of water and shake with 10 cc. of benzene: upon separating the benzene layer, and adding to it 5 cc. of ammonia T.S., a permanent, deep rose color is produced in the lower layer.

"Add 1 Gm. of Aloe to 50 cc. of alcohol, gently heat the mixture and then cool it: a nearly clear solution is obtained (*gum or inorganic impurities*).

"**Assay.**—Process as directed under water-soluble extractive." *U. S.*

The 1914 British Pharmacopœia gives the following description: "In hard masses, varying in color from yellowish-brown to dark or chocolate-brown. Fractured surface dull, waxy and uniform (Curaçao and Zanzibar aloes), or uneven and somewhat porous (Socotrine aloes). Small splinters examined under the microscope exhibit minute crystals embedded in a transparent mass. Characteristic odor; taste nauseous and bitter. The solution obtained by dissolving 0.1 gramme of Aloes in 10 millilitres of boiling *water* and adding 0.5 gramme of *purified borax* acquires a green fluorescence. *Nitric acid* dropped on a little crushed Aloes acquires a reddish-brown color (Socotrine and Zanzibar aloes), or a crimson color (Curaçao aloes). Almost entirely soluble in *alcohol* (60 per cent.). Loss on drying at 100° C. not more than 10 per cent. Ash not more than 5 per cent." *Br.*

Constituents.—The purgative properties of the official varieties of aloe are chiefly due to the glucoside *barbaloin,* which according to Lèger has the formula $C_{21}H_{20}O_9$ (*P. J.,* 1902, 21), but the Br. 1898 assigned the formula $C_{16}H_{16}O_7.3H_2O$. This seems to be identical with the substances previously known as *socaloin* and *capaloin.* In Curaçao and Barbados aloes there is present also an isomeric compound, *isobarbaloin.* Both of these principles are crystalline. In Cape aloe there occurs also an amorphous, isomeric substance known as *beta-barbaloin.* Tschirch (*B. P. G.,* 1898, viii, Heft 6) has shown that when barbaloin is boiled with an alcoholic solution of hydrochloric acid it yields *emodin* $C_{15}H_{10}O_5$ or *trioxymethyl-anthraquinone* (see under *Rheum*). There is present also another anthraquinone derivative known as *aloe-emodin* and a bitter resin and various water soluble substances of which little is known. The resin of the Curaçao aloe consists of *barbaloresinotannol* combined with cinnamic acid; that of Cape and Socotrine aloes of *capaloresinotannol* combined with paracumaric acid.

The active principle of Natal aloe is different from that of the official varieties and is known as *nataloin.* It may be distinguished from the official aloin by Histed's reaction. A drop of nitric acid on a porcelain slab gives, with a few particles of barbaloin or nataloin, a vivid crimson (rapidly fading in the case of barbaloin, but permanent with nataloin unless heat be applied), but produces little effect with socaloin. To distinguish barbaloin from nataloin, test each by adding a minute quantity to a drop or two of sulphuric acid, then allowing the *vapor* from a rod touched with fuming nitric acid to pass over the surface. Barbaloin (and socaloin) will undergo no change, but nataloin will assume a fine blue. (*Pharmacographia,* 2d ed., p. 688.) The Curaçao aloe yields from 10 to 25 per cent. of glucosides of which about half is barbaloin and half isobarbaloin. Cape aloe and Socotrine aloe yield from 4 to 9 per cent. of barbaloin with only traces of isobarbaloin. Since barbaloin is found in almost all varieties, the significance of the prefix "barb" is misleading. The only aloe in which it does not occur is that of Natal.

The substance described by Robiquet under the name of *aloëtin* was probably an impure form of aloin.

Hugo Bornträger asserted that one part of aloe in 5000 can be detected in the following manner. A little of the suspected liquid is shaken with about twice its bulk of benzin, which is allowed to separate, decanted, and shaken with a few drops of stronger water of ammonia. On separation the ammonia will be of a clear red color. With solids a tincture should first be made. According to R. H. Groves (*P. J.,* 3d ser., xi, 1045), this test will never succeed with a less concentration than 1 part in 250, and with some aloes 1 in 100, and is due to the tannin-like substance of aloes; he also states that extreme care is necessary to have the benzin solution perfectly clear. (*P. J.,* 1885, p. 633.) No satisfactory method for assaying aloe for the aloin content has yet been devised. For that suggested by Hager, see *A. J. P.*, 1885, p. 237.

A color reaction delicate enough to detect Barbados aloe in the proportion of 1 part in 10,000 has been proposed by C. E. Staly. (*C. D.*, 1916, 68.) If a freshly prepared solution of potassium ferricyanide be added to a cold aqueous solution of the aloe a pink color is produced.

R. A. Cripps and T. S. Dymond have given the testing of aloes a lengthy investigation, and they recommend the following method. Place one grain of substance in a glass mortar standing on white paper, now add sixteen drops of strong sulphuric acid and triturate until dissolved, then add four drops of nitric acid, sp. gr. 1.42, and then one ounce of distilled water. If aloes be present, a color varying from deep orange to crimson will be produced, according to the kind of aloes that has been used; the color is deepened by the addition of ammonia. The table below is taken from the paper of Bainbridge and Morrow. (*P. J.*, Jan., 1890.) Under the heading of Kew Specimens are given the results obtained with juice of aloe plants grown in Kew Gardens.

Commercial Specimens.	HNO_3.	H_2SO_4 and Vapor of HNO_3.	Cripps and Dymond Test.	C. and D. Test with NH_4OH.	Bromine Test.	$FeCl_3$.
Hepatic aloe	Reddish-brown.	Nil.	Orange-red.	Intense brownish-red.	Nil.	All varieties of aloes give an olive-green coloration with the above reagent.
True Socotrine	Reddish-brown.	Nil.	Orange-red.	Intense brownish-red.	Nil.	
Commercial Socotrine	Faint crimson	Nil.	Crimson.	Deep claret.	Nil.	
Cape	Permanent green after standing a few minutes.	Nil.	Orange-red.	Pale claret.	Nil.	
Curaçao	Evanescent crimson.	Nil.	Crimson.	Intense claret.	Nil.	
Natal	Permanent crimson.	Deep blue.	Deep crimson.	Intense brownish-red.	Nil.	
Barbados	Crimson soon fading.	Slight bluish-green occasionally.	Crimson.	Deep claret.	Nil.	
KEW SPECIMENS.						
Aloe ferox	Evanescent crimson.	Green.	Pale yellow.	Red.	Violet.	
—*socotrina*	Permanent crimson.	Deep blue.	Crimson.	Intense brownish-red.	Deep purplish-red.	
—*vera*	Nil.	Slight green.			Nil.	
—*Perryi*	Nil.	Nil.			Nil.	
—*purpurascens*	Crimson fading to light red.	Nil.			Violet.	
—*platylepis*	Nil.	Nil.			Nil.	
—*arborescens*, var. *frutescens*	Nil.	Nil.			Nil.	
—*africana*	Evanescent red, changing after a few minutes to green.	Nil.	Orange-red.	Pale claret.	Nil.	
—*chinensis*	Nil.	Nil.			Nil.	

Aloe yields its active matter to cold water, and when good is almost wholly dissolved by boiling water; but the inert portion is deposited as the solution cools. It is also soluble in alcohol, rectified or diluted. Long boiling impairs its purgative properties by oxidizing the aloin and rendering it insoluble. The alkalies, their carbonates, and soap alter in some measure its chemical nature, and render it of easier solution. It is inflammable, swelling up and decrepitating when it burns, and giving out a thick smoke which has the odor of the drug.

A method for the detection of aloe in mixtures containing other cathartic drugs, such as rhubarb, cascara, etc., has been described by Mossley (*Chem. and Drug.*, 1913, 915). The method depends upon the precipitation of the oxymethyl anthraquinones, which usually interfere in such identification tests, and the subsequent detection of aloes by the addition of bromine T.S., which precipitates aloin, and the green fluorescence produced with aloes by borax.

E. M. Bailey (*A. J. P.*, 1915, 145) and Hubbard (*J. I. E. C.*, 1917, ix, 518) have devised other methods of distinguishing, by means of color reactions applied to the mixed anthraquinone derivatives, between a number of commonly used purgative drugs including chrysarobin, frangula, rhubarb, senna and aloes.

Uses.—Aloe was known to the ancients, being cultivated in the island of Socotra as far back as the time of Alexander the Great, and is mentioned in the works of Dioscorides and of Celsus. Its cathartic action is due to a stimulation of peristalsis, especially in the larger bowel, probably the result of a local irritant effect upon the mucous membrane, although there is some evidence that it exercises a specific stimulant effect upon unstriped muscles. As its action is largely limited to the colon it is not to be recommended in those conditions in which it is desirable to clean out the whole alimentary canal, and as its effect is largely the result of local irritation it should be avoided in inflammatory conditions of the intestine. In *chronic constipation*, however, especially when dependent upon an atonic condition of the lower bowel, it is one of the most useful laxatives that we possess. Many believe that it possesses a direct tonic action, not only evacuating the bowel of its contents but encouraging a restoration toward normal conditions. The presence of bile in the bowel seems in some way to be essential for the best effects of this drug, and in those cases in which this secretion is lacking it is well to exhibit some preparation of bile in conjunction with the aloes. Soap also appears to enhance the cathartic action of this drug. It was formerly almost universally believed that aloes possessed emmenagogue properties and it was accordingly largely used in the treatment of various forms of *amenorrhea.* It is, however, extremely doubtful whether it exercises any action upon the pelvic organs which is not attributable to its cathartic effects. Aloe was formerly regarded as a vulnerary but its use for this purpose has entirely disappeared except as an ingredient in compound tincture of benzoin.

Those substances only are incompatible with aloes which alter or precipitate the soluble matter, as the insoluble portion is without action upon the system. Among these is the infusion of galls, which we have found, probably through its tannic acid, to afford a copious precipitate with an aqueous solution of aloe. It is said that such a mixture will keep a long time, even for a period of several months, without mouldiness or putrescence, though it becomes ropy.

Crude aloes is rarely used in human medicine, but may be given in *doses* of from two to ten grains (0.13–0.65 Gm.).

Off. Prep.—Extractum Colocynthidis Compositum, *U. S.* (*Br.*); Pilulæ Aloes, *U. S.* (*Br.*); Pilulæ Rhei Compositæ, *N. F.* (*Br.*); Tinctura Aloes, *N. F.;* Tinctura Benzoini Composita, *U. S.* (*Br.*); Decoctum Aloes Compositum, *Br.;* Extractum Aloes, *Br.;* Pilulæ Aloes et Asafetidæ, *N. F., Br.;* Pilulæ Aloes et Ferri, *N. F., Br.;* Pilulæ Aloes et Myrrhæ, *N. F., Br.;* Pilulæ Colocynthidis Composita, *Br.;* Pilulæ Aloes et Podophylli Compositæ, *N. F.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Ferri, Quininæ, Aloes et Nucis Vomicæ, *N. F.;* Pulvis Aloes et Canellæ, *N. F.;* Tinctura Aloes et Myrrhæ, *N. F.;* Tinctura Antiperiodica (from Extract), *N. F.*

ALOINUM. U. S., Br.

ALOIN Aloin.

"A pentoside or mixture of pentosides obtained from aloe. It varies in chemical composition, and in physical and chemical properties according to the variety of aloe from which it is obtained." *U. S.* "Aloin is a crystalline principle obtained from aloes." *Br.*

This is a mixture of the glucosides known by the chemist as barbaloin and isobarbaloin (see under *Aloe*).

Preparation.—Aloin may be prepared by W. A. Tilden's process as follows: 1 part of aloes is dissolved in 10 parts of boiling water acidulated with hydrochloric acid, and allowed to cool. The liquid is then decanted from resinous matter, evaporated to about 2 parts, and set aside two weeks for crystals to form; the liquid portion is poured off, the crystals pressed, and the adherent resinous matter separated by shaking with acetic ether, which dissolves the resin. This process answers fairly well for obtaining aloin from Barbados or Curaçao aloe. Aloin from Socotrine aloe is best obtained by digesting it in 3 parts of alcohol for 24 hours, then transferring to a water bath, and boiling for 2 hours. After cooling, the liquid is filtered and set aside to crystallize. The crystals are washed with a little alcohol and dried. The yield is about 10 per cent. (H. C. Plenge, *A. J. P.,* 1884, p. 507.) According to Lewis Ough (*C. D.,* 1892, 837) Tilden's process, modified, affords the best results; Barbados aloe yielded 12 per cent. of aloin. Schäfer obtains from 15 to 30 per cent. of crystallized aloin from commercial aloe by the following process: 50 Gm. of aloe dissolved in 300 cc. of hot water is slightly acidulated with hydrochloric acid. The solution, after standing (for the resins to separate), is decanted, mixed with 50 cc. of 20 per cent. ammonia water, followed by a solution of 15 Gm. of calcium chloride in 30 cc. of water. The liquid is agitated and the aloin-calcium compound which separates is collected, drained, and mixed in a mortar with a slight excess of hydrochloric acid; the mixture of aloin and calcium chloride is dissolved in the smallest possible quantity of boiling water, filtered, and the filtrate cooled by means of ice; the aloin crystallizes. (*P. J.,* 1897, p. 287.) For further tests for aloin see under *Aloe.*

Description and Physical Properties.—"A lemon-yellow to dark yellow microcrystalline powder, or minute crystals. It is odorless, or has a slight odor of aloe. The taste is intensely bitter. Aloin darkens on exposure to light and air. Aloin is soluble in water, alcohol and acetone, the degree of solubility varying with its composition. It is also soluble in ammonia water and in solutions of alkali hydroxides, forming red solutions (or yellow solutions that soon become red) having a green fluorescence. It is slightly soluble in ether.

"A saturated aqueous solution of Aloin is yellow, changing to brown on standing. The solution is neutral or not more than faintly acid to litmus paper. Aloin is rapidly decomposed when added to alkaline solutions; when mixed with acid solutions, decomposition is slower. A drop of ferric chloride T.S. added to an alcoholic solution of Aloin produces a brownish-green color.

"Ash: not more than 0.5 per cent. Shake 1 Gm. of Aloin with 10 cc. of benzene for one minute and filter: the filtrate imparts not more than a faint, pink color to an equal volume of 5 per cent. ammonia water when shaken with it (*emodin*). Dissolve 1 Gm. of Aloin, accurately weighed, in 120 cc. of distilled water at 25° C. by shaking frequently during two hours. Collect the insoluble residue, if any, on a filter, or a Gooch crucible, tared after it has been dried at 100° C., and wash the residue with 25 cc. of distilled water: this residue when dried at 100° C. does not exceed 1.5 per cent.

"Preserve in well-closed containers, protected from light." *U. S.*

"A pale yellow, microcrystalline powder. Almost inodorous; taste intensely bitter. Almost entirely soluble in 130 parts of *water*, in 18 parts of *alcohol* (90 per cent.), and in 50 parts of *acetone;* very sparingly soluble in *ether, chloroform,* and *benzene;* readily soluble in dilute *solution of ammonia*, the liquid becoming red and acquiring a greenish-red fluorescence. 0.5 gramme of Aloin gently warmed with 25 millilitres of *water* forms an almost clear solution; the filtered liquid remains clear on cooling, but on long standing slowly deposits pale yellow crystals of Aloin. One drop of *solution of copper sulphate* added to 20 millilitres of an aqueous solution (1 in 1000) of Aloin produces a bright yellow coloration, which is changed to red by the addition of 0.5 millilitre of a saturated aqueous solution of *sodium chloride,* and to violet on the further addition of 1 millilitre of *alcohol* (90 per cent.). No appreciable ash." *Br.*

Aloin of commerce is frequently contaminated with resin, indicating want of care in manufacturing. According to Serre (*D. C.,* 1895, 8), this may be detected by finely powdering one grain of the sample, shaking it in a test tube with 20 cc. of water, and allowing it to stand one minute. The solution should be perfectly clear. See also paper by C. H. LaWall. (*Proc. Penn. Pharm. Assoc.,* 1895, 92.)

Uses.—The actions of aloin upon the system are precisely the same as that of aloe to which it is superior because of the variations of potency of the crude drug, as well as on account of the smaller dose of aloin. Moyer (*A. E. P. P.,* xxviii) has shown that when given hypodermically it is capable of producing purgative effects but it is never employed practically in this manner. There is a marked difference in the cathartic activity of the various kinds of aloin. Barbaloin is more powerful than socaloin and, according to Moyer, nataloin generally fails to purge in man, although acting energetically upon dogs. Aloin is one of the most frequently employed of laxatives in *chronic constipation,* especially in combination with belladonna and strychnine.

Dose, one-sixth to one grain (0.01–0.065 Gm.).

Off. Prep.—Pilulæ Aloini Compositæ, *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ, *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ, *N. F.;* Pilulæ Laxativæ Compositæ, *N. F.*

ALSTONIA. Br.

ALSTONIA

"Alstonia is the dried bark of Alstonia scholaris, *R. Br.,* and also of Alstonia constricta, *F. Muell.*" *Br.*

Dita Bark; Australian Fever Bark; Bitter Bark. Dita Rinde *G.;* Pali Mari, *Ind.*

Under Alstonia the British Pharmacopœia recognizes the dried barks of *Alstonia scholaris* (L.) R. Br. (*Echites scholaris* L.), of India and the Philippine Islands, and *Alstonia constricta* F. Muell., of Australia, two apocynaceous trees whose barks are quite dissimilar in appearance, and, as far as our present knowledge goes, contain different alkaloids. These barks are respectively described as follows:

"Bark of Alstonia scholaris usually in irregular fragments, three to twelve millimeters thick; texture somewhat spongy, fracture short and coarse; external layer unevenly rough and fissured, brownish-grey with occasional blackish spots; internal layer bright buff. Transverse section shows numerous small medullary rays in inner layer. Almost odorless; taste bitter. Bark of Alstonia constricta usually in curved pieces or quills about sixty millimeters wide, and twelve millimeters thick. Periderm from two and a half to six millimeters thick, rusty brown, strongly rugose, with large deeply fissured reticulations. Bark internally cinnamon-brown, with strong, coarse longitudinal striæ. Transverse section shows dark-brown periderm covering the inner orange-brown tissues, in which numerous small shining particles can be seen with a lens. Fracture short and granular in outer layers, fibrous in inner. Slight aromatic odor; taste very bitter." *Br.*

From the bark of *Alstonia scholaris* M. Gruppe extracted an uncrystallizable, hygroscopic, bitter principle, *ditaine.* (*P. J.,* Aug., 1875.) Harnack (*B. Chem. G.,* 1878) first obtained ditaine in pure crystallized form, and gave it the formula $C_{20}H_{30}O_4N_2$. O. Hesse (*P. J.,* Oct. 23, 1880) finds in dita the following principles: three alkaloids: *ditamine,* $C_{16}H_{19}O_2N$, the relative amount of which he estimates at 0.04 per cent.; *echitamine,* $C_{22}H_{28}O_4N_2 + H_2O$ (identical, according to Hesse, with Harnack's ditaine); and *echitenine,* $C_{20}H_{27}O_4N$. Of these, the second is the strongest base, and resembles ammonia in its chemical characters; Hesse considers it with one molecule of water to form the hydroxide of a strong basic radical, *echitammonium,* $C_{22}H_{29}O_4N_2$. The solutions of *echitammonium hydroxide* are so strongly basic that they precipitate the hydroxides of copper, iron, aluminum, and lead, and decompose sodium and potassium chlorides, liberating the corresponding hydroxides. Hesse considers echitammonium the most strongly basic of all the alkaloids. Hesse also obtained by extraction with petroleum benzin *echicaoutchin, echiretin, echicerin, echitin,* and *echitein,* of which the three last mentioned are crystalline.

From *Alstonia constricta,* F. V. Müller and A. Rummel obtained *alstonine.* Oberlin and Schlagdenhauffen found in 1879 another alkaloid, *alstonicine.* Hesse (*Ann. Ch. Ph.,* 1880, ccv) subsequently analyzed the bark and found alstonine, the *chlorogenine* of a former investigation, which has the composition $C_{21}H_{20}O_4N_2$, *porphyrine,* $C_{21}H_{25}O_2N_3$, and *alstonidine.* The alkaloids and their salts in acidulated solutions show decided blue fluorescence.

Uses.—This drug has been used for many years in Australia and the Philippine Islands in the treatment of *malarial* and other *fevers,* as well as a simple bitter. The alkaloid ditaine has been scientifically studied by Harnach (*A. E. P. P.,* 1877, xvii, p. 126), who finds that it has a paralyzing effect upon the endings of the motor nerve similar to that produced by curara. In large dose it also paralyzes the cardio-inhibitory nerves and lowers blood pressure. There is nothing in this study, which is, as far as we know, the only scientific investigation of the drug which has been made, to explain any action in malaria. Nevertheless some of the clinical reports, especially from the eclectic physicians, have been extremely laudatory, vaunting it even as a substitute for quinine.

Dose, two to four grains (0.13–0.25 Gm.).

Off. Prep.—Infusum Alstoniæ, *Br.;* Tinctura Alstoniæ, *Br.*

ALTHÆA. U. S.

ALTHEA [Marsh Mallow Root]

" Althea is the root of *Althæa officinalis* Linné (Fam. *Malvaceæ*) deprived of the brown, corky layer and small roots." *U. S.*

Radix Hibisci, Radix Bismalvæ; Wymote, White Mallow, Mortification root; Racine de Guimauve, Guimauve, *Fr.;* Radix Althææ, *P. G.;* Altheewurzel, Althee, Eibischwurzel; Eibisch, *G.;* Altea, Malvavischio, *It.;* Altea, Raiz de Malvavisco, *Sp.*

ALTHÆÆ FOLIA. N. F.

ALTHEA LEAVES Alth. Fol. [Marsh Mallow Leaves]

"Althea leaves consists of the dried leaves of *Althæa officinalis* Linné (Fam. *Malvaceæ*). Althea leaves contain not more than 5 per cent. of stems and fruits or other foreign organic matter." *N. F.*

" The dried leaves of the Althæa officinalis L. without the presence of more than 5 per cent. of stems or other foreign matter." *N. F.*

Feuilles de Guimauve, *Fr.;* Folia Altheæ, *P. G.*

Althæa officinalis is an herbaceous perennial, with a perpendicular branching root and erect woolly stems, from two to four feet or more in height, branched and leafy towards the summit. The leaves are alternate, ovate to slightly cordate, toothed, often 3-lobed and of velvety texture. The flowers are terminal and axillary, with short peduncles, each bearing one, two, or three flowers. The calyx is surrounded by a six to nine cleft involucel. The corolla has five spreading, obcordate petals, of a pale rose color. The fruit consists of numerous capsules united in a compact circular form, each containing a single seed. The plant is native to Europe, inhabiting salt marshes, the banks of rivers, and other moist places. It is found also in this country, from New England to New York and westward to Michigan and Arkansas. It is largely cultivated in Europe for medicinal use, particularly in Germany, Holland, Belgium and France. These countries supply most of the drug used in the United States.

The roots should be collected in autumn from plants at least two years old. They are usually prepared for the market by removing the outer layers. The commercial drug sometimes consists of the unpeeled root, which is sliced transversely and diagonally.

Description and Physical Properties.—The *root,* which is recognized by the U. S. P., is described as follows:

" *Unground Althea.*—Slenderly tapering, when entire up to 30 cm. in length and 2 cm. in thickness, usually cut into small pieces, about 5 mm. in diameter; externally whitish, longitudinally furrowed, frequently spirally twisted and covered with somewhat loosened bast-fibers; fracture of bark fibrous, of wood short and granular; internally yellowish-white; bark 1 to 2 mm. thick, porous, due to mucilage cells, and separated from the slightly radiating wood by a distinct grayish cambium zone; odor slight; taste sweetish, mucilaginous.

" *Powdered Althea.*—Starch grains numerous, up to 0.03 mm. in diameter, usually with a long central cleft; groups of fibers with thick, more or less lignified walls; tracheæ with scalariform thickenings or with bordered pores; calcium oxalate crystals few, in rosette aggregates, 0.020 to 0.035 mm. in diameter.

" Add 1 Gm. of Althea to 10 cc. of cold water allow it to stand with occasional stirring during thirty minutes, and filter through purified cotton: a pale yellow-colored mucilage is obtained, which is neutral to litmus paper and is colored a deep yellow on the addition of a few drops of sodium hydroxide T.S. The mucilage does not have a sour or ammoniacal odor." *U. S.*

The drug contains on the average 37 per cent. of starch, 35 per cent. of mucilage, 11 per cent. of pectin, 11 per cent. of sugar, 1.25 per cent. of fat and up to 2 per cent. of asparagin.

The abundant mucilage is situated chiefly in special cells, and can be seen to be in layers when alcohol is added. Kraemer (*A. J. P.,* 1898, p. 285) proposed the use of an alcoholic solution of methylene blue for the differentiation of the mucilage. It, with starch and saccharine matter, is taken out by boiling water. The gum may be extracted, without the starch, by cold water and forms a ropy mucilage.

The principle discovered in the root by Bacon, by him called *althein,* has been ascertained to be *asparagin.* This substance belongs to the group of amides and hence has been called *asparamide.* When decomposed it breaks up into ammonia and *aspartic acid,* $C_4H_7NO_4$, and one molecule of the resulting ammonium aspartate corresponds with one molecule of asparamide and one of water. (*J. P. C.,* xix, 208.) Asparagin, being now recognized as a derivative of succinic acid, is called *amido-succinamide,* and the aspartic acid is called *amido-succinic* acid. It is found in various other plants besides the marshmallow, as in the shoots of asparagus, in vetches grown in the dark, in all the varieties of the potato, and in the roots of the comfrey and licorice plant. According to Pira, asparagin has acid properties. It has no therapeutic value. Betaine has been obtained from althea by Orlow. (*Ph. Z. R.,* 1898.)

The roots of other *Malvaceæ* are sometimes substituted for that of marshmallow, without disadvantage, as they possess similar properties. Among these are *Althæa rosea* Cav., or *hollyhock,* and *Malva Alcea* L. The dark purple flowers of a variety of *A. rosea* have been proposed as a test for acids and alkalies . A strong infusion of these flowers imparts to slips of white filtering paper a permanent purplish-blue color, which is reddened by acids, and rendered bluish-green by alkalies.

ALTHÆA OR MARSHMALLOW LEAVES, under the title of *Althææ Folia,* are official in the National Formulary. They are collected in June or July, while the plant is in flower, and dried. They are described in the N. F. as follows:

Description and Physical Properties.—"*Unground Althea Leaves.*—Crumpled or matted; gray-green or yellowish-gray-green; densely and finely tomentose throughout; petioles 1 to 6 cm. long; blades 3 to 15 cm. long and 3 to 10 cm. wide, thin, cordate or rhomboidal-ovate in outline, rounded or nearly truncate at the base, acute at the apex; margin doubly serrate-dentate, the principal teeth from 1 to 3 pairs, the lowest almost large enough to be regarded as lobes, the secondary very irregular, triangulate, acute, broader than long, the sinuses acute; 2 to 6 principal veins originating with the midrib in the petiole, prominent underneath, terete; branches of midrib arising at a wide angle, nearly straight, each terminating in a marginal tooth. Odor slight, scarcely characteristic; taste mucilaginous.

"*Powdered Althea Leaf.*—Grayish to grayish-green; numerous unicellular, non-lignified, stellate clustered hairs, up to 0.600 mm. long, usually in clusters of 2 to 6; few, short stalked, multicellular glandular hairs; calcium oxalate in rosette aggregates up to 0.030 mm. in diameter; epidermal tissue with stomata, the latter up to 0.037 mm. in length; few lamellated mucilage cells; pollen grains, few, spherical, spiny, up to 0.125 mm. in diameter." *N. F.*

Marshmallow leaves, like the root, are used for their mucilage which is, however, less abundant than in the root.

Uses.—The virtues of marshmallow are exclusively those of a demulcent. The decoction of the root is much used in Europe in irritation and inflammation of the mucous membranes. A syrup of althæa is official in the German Pharmacopœia, and was introduced into the U. S. Pharmacopœias of 1880 and 1890 (see *U. S. D.,* 18th edition, p. 1327). Owing to its tendency to ferment rapidly it was not retained in the U. S. P., but is found in the N. F. V. (See *Syrupus Althææ.*) The roots themselves, as well as the leaves and flowers, boiled and bruised, are sometimes employed as a poultice. Its most important use is as an excipient for pills. It enters, as an ingredient, into one mass and two pills of the U. S. P.

Dose of the leaves one-half to one drachm (2–4 Gm.).

Off. Prep.—From the root: Syrupus Althææ, *N. F.* From the leaves: Species Emollientes, *N. F.*

ALUMEN. U. S. (Br.)

ALUM

"Alum contains not less than 99.5 per cent. of $AlNH_4(SO_4)_2.12H_2O$ or $AlK(SO_4)_2.12H_2O$. The label of the container must indicate whether the salt is Ammonium Alum or Potassium Alum." *U. S.* "Purified Alum is aluminum and potassium sulphate (Potassium Alum), $Al_2(SO_4)_3,K_2SO_4,24H_2O$, or aluminum and ammonium sulphate (Ammonium Alum), $Al_2(SO_4)_3, (NH_4)_2SO_4,24H_2O$, and is obtained by the combination of aluminium sulphate with potassium sulphate or with ammonium sulphate." *Br.*

Alumen Purificatum, *Br.;* Aluminum and Potassium Sulphate, *U. S. P. VIII.;* Aluminii et Potassii Sulphas, *U. S.* 1870, Potassa Alum; Sulphas Aluminico-potassicus; Alun de potassium, *Fr. Cod.;* Alun, Sulfate d'Alumine et de Potasse, *Fr.;* Alumen ,*P. G.;* Alaun, Kalialaun, *G.;* Solfato di allumino e di potassio, Allume, *It.;* Sulfato aluminicopotasico, Alumbre, *Sp.*

Aluminii et Ammonii Sulphas; Sulphas Aluminico-Ammonicus; Alun ammoniacal, *Fr.;* Ammoniak-Alaun, *G.*

The name alum has been applied indifferently to two salts, one consisting of *aluminum trisulphate* combined with ammonium sulphate, the other of the same salt of aluminum combined with potassium sulphate, and distinguished as *ammonium alum* and *potassium alum.* From time to time one or the other of these has been given the official preference but at present both are recognized under the common title *Alumen* in the United States and British Pharmacopœias.

The British authority (1914) added the word "Purificatum" to the title.

AMMONIUM ALUM. *Aluminum and Ammonium Sulphate.*—It is made by adding ammonium sulphate to the solution of aluminum sulphate. This kind of alum formerly came into very general use, owing to the comparative cheapness of ammonia, and during the World War, owing to the great advance in the cost of potassium salt, was almost exclusively used. *Scotch alum,* made near Paisley, generally contains both potassium and ammonium. Ammonium alum resembles potassium alum so exactly that it cannot be distinguished by simple inspection; and in composition it is perfectly analogous to the potassium salt. It may be distinguished by subjecting it to a strong calcining heat, after which alumina will be the sole residue; or by rubbing it with potassium hydroxide or lime and a little water, when the odor of ammonia will be perceived.

POTASSIUM ALUM. *Aluminum and Potassium Sulphate.*—Potassium alum is manufactured occasionally from earths which contain it ready formed, but most generally from minerals which, from the fact of their containing most or all of its constituents, are called *alum* *ores.* The principal alum ores are the *alum stone,* or *alunite,* which is a native mixture of aluminum sulphate and potassium sulphate, found in large quantities at Tolfa and Piombino in Italy; certain natural mixtures of iron disulphide with alumina, silica, and bituminous matter, called *aluminous schist* or *alum slate; bauxite,* a native aluminum hydroxide, and *cryolite.* (See *Sodii Carbonas.*)

At the Solfatara, and other places in Southern Italy, alum was formerly extracted from earths containing it ready formed. The ground being of volcanic origin, and having a temperature of about 40° C., an efflorescence of pure alum formed upon its surface. This was collected and lixiviated, and the solution crystallized by slow evaporation in leaden vessels sunk in the ground. The alum stone is manufactured into alum by calcination, and subsequent exposure to the air for three months, the mineral being frequently sprinkled with water, in order that it may be brought to a soft mass. This is lixiviated, and the solution obtained crystallized by evaporation. The alum stone may be considered as consisting of alum united with a certain quantity of aluminum hydroxide. The latter, by the calcination, loses its water, and becomes incapable of remaining united with the alum of the mineral, which is consequently set free. Alum of the greatest purity is obtained from this kind of ore.

Large amounts of alum are made from *alum shale,* a clay containing iron pyrites. On calcination the sulphur of the pyrites is in part converted into sulphuric acid, which unites with the alumina. The iron, in the meantime, is almost wholly converted into sesquioxide, and thus becomes insoluble. The matter is lixiviated, the solution concentrated and potassium chloride added and the resultant alum crystallized out. When alum slate is easily disintegrated, it is not calcined, but merely placed in heaps and occasionally sprinkled with water. The iron disulphide gradually absorbs oxygen, and passes into ferrous sulphate, which effloresces on the surface of the heap. Part of the sulphuric acid formed unites with the alumina, so that, after the chemical changes are completed, the heap contains both ferrous sulphate and aluminum sulphate. At the end of about a year, the matter is lixiviated, and the solution of the two sulphates produced is concentrated to the proper degree in leaden boilers. The ferrous sulphate crystallizes, while the aluminum sulphate, being of a more soluble nature, remains in the mother waters.

For an account of the manufacture of alum in India, see *C. D.,* 1892, 636. *Bauxite,* a hydrated oxide of aluminum, containing from 56 to 60 per cent. of aluminum oxide, has within recent years become one of the most important raw materials for the alum manufacture. It is found in very rich deposits in Georgia and Alabama. *Cryolite,* a double fluoride of sodium and aluminum, also serves as a source of supply, the aluminum hydroxide being produced as an intermediate product.

The elements *rubidium* and *cæsium* are found in *lepidolite,* and, as much of the alum in continental Europe is made from this mineral, Salzer found samples of commercial potassium alum which contained a considerable quantity of rubidium alum; this contaminated potassium alum is less soluble in water than ordinary alum. (*A. Pharm.,* 1887, p. 217.)

Description and Physical Properties.—"Large, colorless crystals, crystalline fragments, or a white powder. Alum is odorless, and has a sweetish, strongly astringent taste. One Gm. of Ammonium Alum is soluble in 5.2 cc. of water at 25° C., and in 0.3 cc. of boiling water. One Gm. of Potassium Alum is soluble in 7.2 cc. of water at 25° C., and in 0.3 cc. of boiling water. Alum is insoluble in alcohol but is freely soluble in glycerin. When heated, Alum fuses, and at about 200° C. loses all of its water of crystallization. When strongly heated, it loses sulphuric anhydride, becoming incompletely soluble in water.

"Sodium hydroxide T.S. added to an aqueous solution of Ammonium Alum (1 in 20) at first causes a precipitate which completely dissolves in an excess of the reagent, ammonia being evolved. Potassium Alum imparts a violet color to a non-luminous flame. The addition of 10 cc. of sodium bitartrate T.S. to 5 cc. of a saturated aqueous solution of Potassium Alum produces within thirty minutes a white, crystalline precipitate. Sodium hydroxide T.S. added to an aqueous solution of Potassium Alum (1 in 20) at first causes a precipitate, which completely dissolves in an excess of the reagent, but no ammonia is evolved. Unless otherwise indicated Ammonium Alum and Potassium Alum conform to the following tests: An aqueous solution of Alum (1 in 20) is acid to litmus paper. An aqueous solution of Alum (1 in 20) responds to the reactions for aluminum, and for sulphates.

"An aqueous solution of Alum meets the requirements of the test for *heavy metals.* An aqueous solution of Alum meets the requirements of the test for *arsenic.* Add 5 drops of potassium ferrocyanide T.S. to 20 cc. of an aqueous solution of Alum (1 in 150): no blue color is produced immediately (*iron*). Completely precipitate the aluminum from a boiling solution of 1 Gm. of Ammonium Alum in 100 cc. of distilled water by the addition of a slight excess of ammonia water, and filter: not more than 0.5 per cent. of residue remains on evaporating the filtrate to dryness and igniting (*alkali and earths*).

"**Assay.**—Dissolve about 1 Gm. of Alum, accurately weighed, and about 1 Gm. of ammonium chloride in 250 cc. of distilled water. Heat the solution to boiling, and add a slight excess of ammonia T.S. to precipitate aluminum hydroxide. Collect the precipitate on a filter, wash thoroughly with hot distilled water, dry, ignite strongly, and weigh. The weight of the aluminum oxide so obtained, multiplied by 8.889 indicates its equivalent in $AlNH_4(SO_4)_2.12H_2O$ and when multiplied by 9.302 indicates its equivalent in $AlK(SO_4)_2.12H_2O$. Each Gm. of aluminum oxide corresponds to 8.874 Gm. of $AlNH_4(SO_4)_2.12H_2O$ and to 9.286 Gm. of $AlK(SO_4)_2.12H_2O$." *U. S.*

"In colorless transparent crystalline masses; taste sweetish, astringent. Soluble in 10 parts of *water,* the solution being clear and having an acid reaction; freely soluble in *glycerin,* insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of aluminium, of potassium or ammonium, and of sulphates. Yields no characteristic *reactions* for copper, lead, zinc, calcium, or sodium, and not more than very slight *reactions* for iron. *Arsenic limit* 5 parts per million." *Br.*

Its sp. gr. is 1.71. It reddens litmus, but changes the blue tinctures of the petals of plants to green. When heated a little above 100° C., it undergoes the aqueous fusion; and, if the heat be continued, it loses its water, swells up, becomes a white, opaque, porous mass, and is converted into the official *exsiccated alum.* (See *Alumen Exsiccatum.*) Exposed to a red heat, it gives off oxygen, together with sulphurous and sulphuric oxides, and the residue consists of aluminum oxide and potassium sulphate. When calcined with finely divided charcoal, it forms a spontaneously inflammable substance, called *Homberg's pyrophorus,* which consists of a mixture of potassium sulphide, alumina, and charcoal.

Several varieties of alum are known in commerce. *Roche alum,* so called from its having come originally from Rocca, in Syria, is a sort which occurs in fragments about the size of an almond, and of a pale rose color, which is given to it, according to Pereira, by bole or rose-pink. *Roman alum,* which is another variety found in commerce, also occurs in small fragments, covered with a reddish-brown powder, resembling ochre, which is put on by the manufacturers. It has been supposed that the powder contains iron, but this is probably a mistake. Roman alum crystallizes in cubes, from the fact that the crystals are deposited from a solution always containing an excess of alumina, which decomposes any iron salt that may be present. This crystalline form of alum is, therefore, an index of its freedom from much contamination with iron.

All the alums of commerce contain more or less ferrous sulphate, varying from five to seven parts in the thousand. The iron is readily detected by adding to a solution of the suspected alum a few drops of potassium ferrocyanide, which will cause a greenish-blue tint, if iron be present. It may be detected also by precipitating the alumina as a subsulphate with a solution of potassium hydroxide, and afterwards adding the alkali in excess. This will redissolve the precipitate, with the exception of any iron, which will be left in the state of sesquioxide. The proportion of iron usually present, though small, is injurious when the salt is used in dyeing. Alum may, however, be purified, either by dissolving it in the smallest quantity of boiling water, and stirring the solution as it cools, or by repeated solution and crystallization.

ALUMINUM.—The existence of the metal aluminum (formerly known as *aluminium*) was rendered probable by Sir H. Davy in 1808; but it was not fairly obtained until 1828, when Wöhler procured it in an impure state, in globules of the size of a pin's head, by the action of potassium on aluminum chloride. In 1854, Deville succeeded in obtaining the pure metal in ingots by decomposing the same chloride with sodium. The process of Deville remained the only practical process for its manufacture until 1886, when the Messrs. Cowles of Cleveland, Ohio, succeeded in effecting the reduction of corundum, the native oxide, by charcoal with the aid of a powerful electric current from a Brush dynamo-electric machine, using large carbon electrodes. They manufactured the pure aluminum and the alloys of copper known as aluminum bronzes. This process in turn has been practically displaced by the Hall process, as operated by the Pittsburg Reduction Company at Niagara Falls and elsewhere. This is to electrolyze pure *alumina* (*aluminum trioxide*) dissolved in a bath of melted cryolite. The cryolite (a double fluoride of sodium and aluminum) is continuously regenerated, so that by feeding in the pure alumina the process can be made continuous. A German process, that of Graetzel, for electrolyzing the fused chloride, is also in successful use.

Aluminum is silver-white, sonorous, unalterable in the air, and lighter than glass, having the low sp. gr. of 2.56. Its fusing point is somewhat lower than that of silver. It is not attacked by sulphuric or nitric acid, nor tarnished by hydrogen sulphide. It is acted upon slightly by acetic acid and is attacked readily by alkaline solutions. Its best solvent is hydrochloric acid. After silver, gold, and platinum, it is the least alterable of the metals.

Uses.—Alum is absorbed from the intestinal tract only in relatively small quantities, although Gies (*J. A. M. A.*, 1911, lvii, p. 57) has shown that the former view that it was completely excreted, unabsorbed, with the feces is incorrect. The germicidal power of alum is lower than many of the other salts of aluminum. According to Miquel it will inhibit the multiplication of bacteria in the proportion of about one part in two hundred.

Alum is a powerful astringent with very decided irritant qualities, and when taken internally in sufficient quantities is emetic and purgative, and may even cause gastro-intestinal inflammation. It is widely employed in various conditions in which an astringent or styptic is desired, as for instance, *serous diarrheas,* *pharyngitis,* local *hemorrhages,* and the like. It has also been used internally in the treatment of *colica pictonum* in which disease it seems to do more than act as a chemical precipitant of any lead in the intestinal tract and to exercise some beneficial action upon the intestines directly. As an emetic it was formerly used to a considerable extent in the treatment of *laryngeal diphtheria,* but has in modern times been largely replaced by various operative procedures. It is occasionally employed to empty the stomach in cases of poisoning, but is inferior for this purpose to zinc sulphate. As a gargle in various *anginas* it has been a favorite remedy, but because of its acidity exercises a destructive influence upon the teeth and is inferior to aluminum acetate.

The most important use of alum to-day is as a local styptic in external *hemorrhages,* in *epistaxis,* and other bleeding from mucous membranes to which it can be directly applied. It is also employed as an astringent in *leucorrhea,* unhealthy *ulcers,* and similar conditions. As an astringent it is usually employed in strengths ranging from 1 to 5 per cent., according to the location to which it is applied. Occasionally powdered alum may be thinly dusted over the area. As a styptic if the bleeding point is easily accessible it may be touched with the alum stick or the powdered alum directly applied. In *epistaxis* it is usually employed by plugging the nares with pledgets of cotton soaked in a saturated solution. When used as an astringent on the more delicate mucous membranes, as in *conjunctivitis,* it is often desirable to modify its action by combining it with albuminous matter as in the form of the *alum curd.* This is made by boiling two drachms of alum in a pint of milk and straining off the whey.

When taken in large dose alum acts as an irritant poison causing burning in the mouth and throat followed by vomiting, purging, collapse, and other symptoms of toxic gastroenteritis. Ricquet records a fatal case from an ounce of alum. (*J. P. C.,* Oct., 1873, p. 333.) When small quantities of the soluble salts of aluminum are introduced into the circulation they produce a slow form of poisoning characterized by motor palsies and areas of local anesthesia with fatty degeneration in the kidney and liver. The nervous symptoms have been shown by Doellken (*A. E. P. P.,* 1897, xl) to be due to anatomical changes in the nerve centers. There are also often symptoms of gastro-intestinal inflammation which is presumably the result of the effort of the glands of the intestinal tract to eliminate the poisoning.

The question of the toxic effects of repeated small doses of alum has become a matter of some importance because of the widespread use of the salt in baking powder. It has been held by some that under these conditions the aluminum is converted into a form which is non-absorbable and therefore harmless. The experiments of Gies appear to demonstrate that bread stuffs made from alum baking powder yield their alum to absorption, at least partially. The wider question of whether the relatively minute doses of aluminum which enter the system under these conditions is deleterious or not, is still a matter of dispute.

Alum is incompatible with the alkali hydroxides, carbonates and bicarbonate, potassium bitartrate and lead acetate.

Dose, as an astringent, five to twenty grains (0.32–1.3 Gm.); as an emetic, one drachm (3.9 Gm.).

Off. Prep.—Alumen Exsiccatum, *U. S.;* Glycerinum Aluminis, *Br.;* Alumen Exsiccatum, *Br.*

ALUMEN EXSICCATUM. U. S., Br.

EXSICCATED ALUM Alum. Exsic. [Dried Alum, Burnt Alum]

"Exsiccated Alum, when recently dried to constant weight at 200° C., contains not less than 96.5 per cent. of anhydrous $AlNH_4(SO_4)_2$ or of anhydrous $AlK(SO_4)_2$. The label of the container indicating whether it is made from Ammonium Alum or from Potassium Alum." *U. S.*

Alun calciné, desséché, brûlé, *Fr.;* **Alumen ustum,** *P. G.;* **Gebrannter Alaun, Gebrannter Kalialaun,** *G.;* **Solfato di allumino e di potassio usto, Allume usto,** *It.;* **Solfato aluminico-potasico anhidro, Alumbre calcinado,** *Sp.*

"Alum, in small pieces, 100 Gm. To make about 55 Gm. Place a thin layer of alum in a tared, shallow, porcelain dish, and heat it cautiously on a sand bath until liquefied. Continue the application of heat, at a temperature not exceeding 200° C. and stir constantly, until aqueous vapors cease to evolve and a dry, white, porous mass is obtained. When cold, reduce the product to a fine powder." *U. S.*

"Potassium Alum, 100 grammes. Heat the Potassium Alum in a porcelain dish or other suitable vessel till it liquefies, then increase and continue the application of heat until aqueous vapor ceases to be disengaged, and the salt has lost from 45 to 46 per cent. of its weight." *Br.*

The object of these processes is to obtain the alum free from its water of crystallization, without otherwise in the least decomposing it. For this purpose a certain degree of heat is necessary; and yet if the heat be too great the salt itself is decomposed, and the desired end is not obtained. If the alum employed be the potassium alum, the old indefinite directions will generally be sufficient to secure the requisite result, as this salt will resist a heat short of redness; but this is not the case with the ammonium salt. To guard against failure from this cause, the Pharmacopœias formerly directed 205° C. as the highest heat to be used, and the checking of the operation when nearly all the water has been driven off, as indicated by the weight of the residue. John M. Maisch satisfactorily determined by experiment that, whichever alum may be used, this temperature is quite high enough, and the direction of the Pharmacopœias, as to the weight of the residue, insures that a sufficient heat will be employed. By the official process there is left behind about one and one-fourth per cent. of the water of crystallization, when potassium alum is used.

Description and Physical Properties.—"A white, odorless powder. It has a sweetish astringent taste, and absorbs moisture on exposure to air. One Gm. of Exsiccated Alum is very slowly and usually incompletely soluble in about 20 cc. of water at 25° C. One Gm. is soluble in about 1.5 cc. of boiling water. It is insoluble in alcohol. Exsiccated Alum responds to the reactions, respectively, for Ammonium Alum or Potassium Alum described under *Alumen.*

"Add 2 Gm. of Exsiccated Alum to 40 cc. of distilled water, and allow it to stand with occasional agitation for twenty-four hours. Collect the insoluble residue on previously dried, counterbalanced filter papers, or a Gooch crucible, wash with 50 cc. of distilled water, and finally dry to constant weight at 100° C.: the residue weighs not more than 0.05 Gm. Dry about 1 Gm. of Exsiccated Alum to constant weight at 200° C. in an air bath: the loss does not exceed 10 per cent. An aqueous solution of Exsiccated Alum meets the requirements for *arsenic, heavy metals, iron,* and Exsiccated Ammonium Alum meets the test for limit of *alkali and earths,* under *Alumen,* allowance being made for the difference in strength.

"**Assay.**—Dry about 0.5 Gm. of Exsiccated Alum to constant weight at 200° C., weigh accurately, and dissolve in 100 cc. of distilled water. Filter, if necessary, thoroughly wash the insoluble residue with distilled water, dilute the filtrate and washings to about 250 cc. with distilled water, and add 1 Gm. of ammonium chloride. Proceed with the assay as directed under *Alumen,* beginning with the words 'Heat the solution,' second line of the assay. The weight of the aluminum oxide so obtained multiplied by 4.650 indicates its equivalent in $AlNH_4(SO_4)_2$, and multiplied by 5.063 indicates its equivalent in $AlK(SO_4)_2$. Each Gm. of aluminum oxide corresponds to 4.643 Gm. of $AlNH_4(SO_4)_2$ and to 5.055 Gm. of $AlK(SO_4)_2$.

"Preserve in well-closed containers and do not dispense if it contains more than 10 per cent. of moisture." *U. S.*

"A white powder slowly and completely soluble in 20 parts of *water.* Absorbs moisture on exposure to air. Yields the reactions and is free from the impurities indicated under 'Alumen Purificatum." *Br.*

Before pulverization, it is a light, white, opaque, porous mass. During the exsiccation, alum loses 45 per cent. of its weight in dissipated water. Exsiccated alum resists the action of cold water for a long time, showing its altered aggregation. In composition it differs from crystallized alum merely in the absence of water.

Uses.—Exsiccated alum has the same medicinal properties as ordinary alum, but it is much more powerful and irritant and must be employed in correspondingly dilute solutions. It is used as a mild escharotic to destroy *exuberant granulations,* on which it may be freely dusted.

ALUMINI CHLORIDUM. N. F.

ALUMINUM CHLORIDE Alum. Chlor.

"Aluminum Chloride contains $AlCl_3.6H_2O$ (241.58) corresponding to not less than 20.5 per cent. of aluminum oxide (Al_2O_3)." *N. F.*

Description and Physical Properties.—"Aluminum Chloride occurs as a white, or yellowish-white deliquescent, crystalline powder; nearly odorless; taste sweetish and very astringent. One Gm. dissolves in about 0.5 cc. of water and in about 4 cc. of alcohol at 25° C., also soluble in glycerin.

"An aqueous solution of the salt (1 in 10) is clear and is acid to litmus. Separate portions of an aqueous solution of the salt (1 in 10) yield with silver nitrate T.S. a white curdy precipitate insoluble in nitric acid, with ammonia water a white gelatinous precipitate almost insoluble in an excess of ammonia water, and with sodium hydroxide T.S. a white gelatinous precipitate completely soluble in an excess of the reagent.

"Ten cc. of an aqueous solution of the salt (1 in 100) after the addition of 0.2 cc. of barium chloride T.S. does not become cloudy within one minute (*sulphate*). The addition of 0.3 cc. of potassium ferrocyanide T.S. to 20 cc. of an aqueous solution of the salt (1 in 150) does not produce a blue coloration within one minute (*iron*). An aqueous solution of the salt does not respond to the Test for heavy metals. An aqueous solution of the salt meets the requirements of the Test for arsenic.

"**Assay.**—Dissolve about 0.5 Gm. of the salt, previously dried over sulphuric acid and accurately weighed, in 100 cc. of distilled water, add 1 Gm. of ammonium chloride, boil and then precipitate the aluminum hydroxide by the addition of a slight excess of ammonia water to the boiling solution. Collect the precipitate on a filter, wash it with distilled water, dry, ignite thoroughly and weigh. The weight of the aluminum oxide so obtained is not less than 20.5 per cent. of the weight of the Aluminum Chloride taken for the assay.

"Preserve it in well-closed containers." *N. F.*

Uses.—Externally it is used as an astringent and antiseptic, especially in *hyperidrosis.* It is an ingredient in some of the proprietary preparations for diminishing the odor of perspiration; some of these solutions containing over 30 per cent. of aluminum chloride. Internally it has been employed in *locomotor ataxia* in *doses* of five grains (0.3 Gm.).

Off. Prep.—Liquor Hydrastini Compositus, *N. F.*

ALUMINI SULPHAS. N. F.

ALUMINUM SULPHATE Alum. Sulph.

"Aluminum sulphate contains not less than 99.5 per cent. of $Al_2(SO_4)_3.18H_2O$ (666.47)." *N. F.*

Concentrated Alum; Sulfas Aluminicus; Sulphate d'Aluminium, *Fr.;* Aluminium Sulfuricum, *P. G.;* Schwefelsaüre Thonerde, *G.*

This salt may be manufactured by various methods (see U. S. D., 19th ed., p. 124), but is now obtained chiefly as one of the by-products in the manufacture of soda from cryolite or from bauxite.

Description and Physical Properties.—"Aluminum Sulphate occurs as a white crystalline powder, shining plates, or crystalline fragments; without odor, having a sweetish and afterwards an astringent taste; permanent in the air. One Gm. dissolves in 1 cc. of water at 25° C.; it is more soluble in boiling water, but insoluble in alcohol.

"When gradually heated to about 200° C., it loses its water of crystallization (about 48.6 per cent. of its weight). An aqueous solution of the salt (1 in 20) is acid to litmus. Separate portions of an aqueous solution of the salt (1 in 20) yield with barium chloride T.S. a white precipitate insoluble in hydrochloric acid, and with sodium hydroxide T.S. a white gelatinous precipitate which is soluble in an excess of the alkali, but which is again separated on the addition of a sufficient amount of ammonium chloride T.S.

"Gently heat 1 Gm. of Aluminum Sulphate with 10 cc. of sodium hydroxide T.S.; the liquid does not evolve the odor of ammonia. A filtered aqueous solution of the salt (1 in 10) does not become more than faintly opalescent within five minutes after the addition of an equal volume of tenth-normal sodium thiosulphate (*free acid*). The addition of 5 drops of potassium ferrocyanide T.S. to 20 cc. of an aqueous solution of the salt (1 in 150) does not produce at once a blue coloration (*iron*). An aqueous solution of the salt does not respond to the Test for heavy metals. An aqueous solution of the salt meets the requirements of the Test for arsenic.

"**Assay.**—Dissolve about 0.5 Gm. of Aluminum Sulphate, accurately weighed, in 100 cc. of distilled water, add 1 Gm. of ammonium chloride, boil and then precipitate the aluminum hydroxide by the addition of a slight excess of ammonia water to the boiling solution. Collect the precipitate on a filter, wash it with distilled water, dry, ignite thoroughly and weigh. The weight of the aluminum oxide so obtained is not less than 15.23 per cent. of the weight of the Aluminum Sulphate taken for the assay, corresponding to not less than 99.5 per cent. of $Al_2(SO_4)_3.18H_2O$." *N. F.*

Uses.—Aluminum sulphate has medicinal properties very similar to those of alum. It has been employed in aqueous solution (20 grains in a fluidounce or stronger) as an antiseptic, detergent application to *foul ulcers,* and as an injection in *fetid discharges from the vagina.* Solution of aluminum sulphate is capable of dissolving a considerable quantity of recently precipitated gelatinous alumina. Such a solution, impregnated with benzoin, has been proposed by Mentel as a hemostatic, under the name of *benzoinated solution of alumina.* It resembles the *styptic liquid of Pagliari.* It is prepared by saturating with gelatinous alumina a solution made of eight ounces of aluminum sulphate dissolved in a pint of water. To the saturated solution six drachms of bruised benzoin are added, and the whole is kept at a temperature of about 65.5° C. for six hours, with occasional agitation, so that the liquid, after filtration, may have about the density 1.26. This liquid, put in a cool place for several days, so as to deposit some crystals of alum, forms the benzoinated solution, remarkable for its very sweet odor and astringent balsamic taste. Benzoinated solution of alumina, diluted in the proportion of from two to five fluidrachms to the pint of water, has been found useful as an injection in *leucorrhea.*

Off. Prep.—Liquor Alumini Acetatis, *N. F.;* Liquor Alumini Subacetatis, *N. F.*

AMIDOPYRINA. U. S.

AMIDOPYRINE Amidopyrin.

"Dimethylamino-antipyrine $[C_3ON_3(CH_3)_4.C_6H_5]$." U. S.

Pyramidonum, *Fr. Cod.;* Pyramidon, *P. G.;* Dimethylamino Antipyrinum.

This compound may be regarded as a derivative of antipyrine in which an hydrogen atom of the pyrazolon group is replaced by $N(CH_3)_2$. It is manufactured by the reduction of isonitroso-antipyrine with zinc and subsequent methylation by means of methyl iodide.

It occurs as a colorless crystalline powder, practically tasteless, and moderately soluble in water. From antipyrine it may be distinguished by the facts that it gives a fugitive violet color with ferric chloride instead of red; with nitrous acid it gives a temporary purplish instead of a more permanent green reaction; with nitric acid it yields an amethyst instead of a yellow color.

Description and Physical Properties.—"Colorless or white, small crystals, or a white, crystalline powder. It is odorless, and is stable in the air. One Gm. of Amidopyrine is soluble in 18 cc. of water, 1.5 cc. of alcohol, 12 cc. of benzene, 1 cc. of chloroform, and in 13 cc. of ether, at 25° C.

"Amidopyrine melts between 107° and 109° C. An aqueous solution of Amidopyrine (1 in 25) is slightly alkaline to litmus paper. To 5 cc. of an aqueous solution of Amidopyrine (1 in 25) add 3 drops of diluted hydrochloric acid and 1 cc. of ferric chloride T.S.: a bluish-violet color is produced. On the subsequent addition of a few cc. of diluted sulphuric acid, the color changes to violet-red. The addition of 5 drops of silver nitrate T.S. to 5 cc. of an aqueous solution of Amidopyrine (1 in 25) produces an intensely violet color (other oxidizing substances yield the same color). On allowing the mixture to stand, a grayish-black precipitate of metallic silver is deposited. To a solution of about 0.02 Gm. of Amidopyrine in 5 cc. of distilled water, add 2 drops of sulphuric acid and 2 drops of a 10 per cent. solution of sodium nitrite: a transient blue color is produced which disappears quickly, the liquid remaining colorless (the appearance of a green color indicates *antipyrine*). An aqueous solution of Amidopyrine (1 in 25) added to a freshly prepared solution of potassium ferricyanide, containing a little ferric chloride, produces at once a dark blue color or precipitate (difference from *antipyrine*).

"Ash: not more than 0.1 per cent. A solution of 0.1 Gm. of Amidopyrine in 1 cc. of sulphuric acid is colorless (*readily carbonizable substances*). Its aqueous solution (1 in 25) meets the requirements of the test for *heavy metals*. The addition of a few drops of silver nitrate T.S. to 5 cc. of an aqueous solution of Amidopyrine (1 in 25), previously acidulated with a few drops of diluted nitric acid, produces no turbidity at once (*chloride*)." *U. S.*

Uses.—Amidopyrine resembles antipyrine in its general effects upon the system. It is, however, somewhat slower and more persistent in its action and is also asserted to be more powerful in its analgesic properties. Although the details of its fate in the body are not definitely understood, it is eliminated in the urine in part as a compound which yields an amethyst color with ferric chloride and is probably antipyrylurea. At times, after its administration, the urine acquires a pinkish hue which was at one time attributed to the formation of hematoporphyrin, but is probably due to decomposition products of the drug itself, perhaps rubaronic acid. It is also asserted that it increases the nitrogenous metabolism and must, therefore, be used with much caution in diabetic patients.

While unquestionably it is capable of reducing the body temperature in various *fevers*, its use as an antipyretic is probably open to the same objections as other drugs of this class. Its most important field of usefulness is for the purpose of relieving *pain* in *migraine, neuralgia, dysmenorrhea, locomotor ataxia*, and similar conditions. Like antipyrine it very greatly enhances the anodyne properties of the opiates, even in those forms of pain in which it is not highly efficacious by itself. Bardet (*B. G. T.*, March 30th, 1903) has found it useful in the treatment of *asthma*.

Dose, from two to eight grains (0.12–0.5 Gm.).

AMMONIA

AMMONIA

All the compounds of ammonium owe their distinctive properties to the presence of a gas, composed of nitrogen and hydrogen (NH_3) called *ammonia*. This is easily obtained by the action of lime on ammonium chloride,—when the calcium unites with the hydrochloric acid, so as to form calcium chloride and water, and the ammonia is liberated. It is transparent and colorless, but possesses an acrid taste and an exceedingly pungent odor. It has a powerful alkaline reaction, and, from this property and its gaseous nature, was called the *volatile alkali* by the earlier chemists. Its sp. gr. is 0.56 compared with air. It is irrespirable, the glottis closing spasmodically when the attempt is made to breathe it. The sources of ammonia will be mentioned elsewhere (see *Ammonii Chloridum*), but a synthesis of ammonia from simple elements may be noted here. Hydrogen, nitrogen, and aqueous vapor in the presence of porous contact substances like pumice, charcoal, etc., unite to form ammonia, and this, in the presence of CO and CO_2, gives rise to ammonium formate or carbonate. These elements in the presence of moisture, as in damp atmosphere, under the influence of an electric discharge, produce ammonium nitrate directly as follows: $N_2 + O + 2H_2O = NO_3NH_4$. (See also nitrogen fixation under *Acidum Nitricum.*)

As the gas ammonia exists in the free state, the molecule NH_3 is a definite saturated compound under ordinary conditions. When, however, ammonia gas is mixed with hydrochloric acid gas or its aqueous solution with hydrochloric acid in solution, the two unite to form a new compound, NH_4Cl, which proves to be a definite compound, analogous to potassium or sodium chlorides. Berzelius, therefore, proposed to call this ammonium chloride, assuming that the monad group (NH_4) acted like the monad metal K in forming compounds, and in fact it is found that when sulphuric, nitric, carbonic, and other acids are neutralized by *ammonia* gas or solution, crystallizable salts like $(NH_4)_2SO_4$, NH_4NO_3, and $(NH_4)_2CO_3$ are formed, which are termed ammonium sulphate, nitrate, and carbonate respectively. *Ammonium* is believed to exist, although it has not been isolated in a pure state. *Ammonium amalgam* is a compound of ammonium with mercury.

Ozone oxidizes the elements of ammonia, producing water and nitric acid; the latter, uniting with undecomposed ammonia, generates ammonium nitrate. Ordinary oxygen, under the influence of platinum-black, or finely-divided copper, likewise oxidizes the elements of ammonia, the nitrogen to the extent only of forming nitrous acid, with the result of producing ammonium nitrite.

AMMONIACUM. Br.

AMMONIACUM

"Ammoniacum is a gum-resin exuded from the flowering and fruiting stem of Dorema Ammoniacum, *D. Don,* and possibly other species of Dorema." *Br.*

Gum Ammoniac, Gummi-resina Ammoniacum; Ammoniaque, Gomme-résine ammoniaque, Gomme ammoniaque, *Fr.;* Ammoniacum, *P. G.;* Ammoniak, Ammoniak-gummi, *G.;* Gomma ammoniaco, *It.;* Gomo-resina amoniaco, Goma amoniaco, *Sp.;* Ushek, *Ar.;* Semugh belsheren, *Pers.*

This gum-resin was dropped in the Eighth Revision of the U. S. Pharmacopœia on account of its having fallen, at least in America, almost into desuetude. It is, however, official in the British as well as the Swiss and German Pharmacopœias.

The ammoniac plant (*Dorema Ammoniacum*) is an erect, fleshy stemmed, perennial herb with a stem having a few pinnately decompound leaves near the base and bracts above, and woolly umbels of small white flowers; grows spontaneously in Farsistan, Irak, Khorassan, and other Persian provinces extending into Southern Siberia. It attains the height of six or seven feet, and in the spring and early part of summer abounds in a milky juice, which flows out upon the slightest puncture. From the accounts of travellers, it appears that in the month of May the plant is pierced in innumerable places by beetles. A milky juice contained within reservoirs of the cortex is thus induced to exude. Part of this juice, exuding through the punctures, concretes upon the stem, a part falls to the ground and becomes mixed with impurities and when quite dry is collected by the natives. Fontanier states that the juice exudes spontaneously, and that the harvest is about the middle of June. The gum-resin occurs in special reservoirs near the phloem tissues of the stems, roots, and petioles of the leaves. According to Grant, the drug is collected in Sygham, like asafetida, from the root of the plant. The gum-resin is sent to Bushire, whence it is transmitted to India, chiefly to Bombay. A small portion is said to be taken to the ports of the Levant, and thence distributed. The name of the drug is thought to have been derived from the temple of Jupiter Ammon in the Libyan desert, where the ammoniac of the ancients is said to have been collected; but Don considers it a corruption of *Armeniacum,* originating in the circumstance that the gum-resin was formerly imported into Europe through Armenia. The drug is now collected mainly in the central provinces of Persia and exported from Persian Gulf ports.

The *African Ammoniac* is said by Holmes (*P. J.,* 1907, lxxix, p. 570) to be derived from the *Ferula communis* L., var. *brevifolia.* It has been described by Daniel Hanbury as follows: "In large, compact, dark, heavy masses, formed of agglutinated tears of a gum-resin of hard, waxy consistence. The tears are opaque, white or of a pale greenish-yellow, mixed with others of a blackish-brown, which, with vegetable and earthy impurities, constitute a large portion of the mass." The odor of the drug is feeble, and quite different from that of the Persian gum-resin; its taste slightly acrid and very persistent. Examined by John Moss, it was found to consist of 67.76 per cent. of resin, 9.1 of gum, 4.29 of water and volatile oil, and 18.85 of bassorin and insoluble matters. (*P. J.,* 1873, p. 742.) It is used chiefly for incense in Mohammedan countries, and is sent eastward by the caravans, or in vessels from the ports of Morocco to Alexandria.

Properties.—Ammoniac comes either in the state of tears, or in aggregated masses, and in both forms is frequently mixed with impurities. That of the tears, however, is preferable, as the purest may be conveniently picked out and kept for use. These are of an irregular shape, usually more or less globular, from 5 to 25 mm. in diameter, opaque, yellowish on the outside, whitish within, compact, homogeneous, brittle when cold, and breaking with a conchoidal, shining, waxy fracture. The masses are often of a darker color and less uniform structure, appearing, when broken, as if composed of numerous white or whitish tears, embedded in a dirty-gray or brownish substance, and frequently mingled with foreign matters, such as seeds, fragments of vegetables, and sand or earth. According to the 1890 U. S. Pharmacopœia, only such masses should be considered up to the standard as are composed entirely of tears "without any intervening dark-colored substance."

The odor of ammoniac is peculiar, and stronger in the mass than in the tears The taste is slightly sweetish, bitter, and somewhat acrid. The sp. gr. is 1.207. When heated, the gum-resin softens and becomes adhesive, but does not melt. It burns with a white flame, swelling up, and emitting a smoke of a strong, resinous, slightly alliaceous odor. It is partly soluble in water, alcohol, ether, acetic acid, and alkaline solutions. The alcoholic solution is transparent, but is rendered milky by the addition of water.

"In small dull white, yellowish-white, or brownish-white tears or in nodular masses varying from about five to twenty-five millimetres in diameter. Hard and brittle when cold, the freshly fractured surface having a waxy lustre; softens when warmed. Internally opaque and varying in color from milky-white to pale brownish-yellow. Faint characteristic but not alliaceous odor; taste bitter, acrid. Triturated with *water* forms a white emulsion. Freshly fractured surface colored yellow by *solution of sodium hydroxide* and dark-red or orange by *solution of chlorinated soda.* The solution obtained by boiling 1 gramme of the powdered gum-resin with 10 millilitres of *water,* filtering, and adding *alcohol* (90 per cent.) till clear, assumes a reddish-violet coloration on the addition of one drop of *T. Sol. of ferric chloride.*

The solution obtained by boiling 1 gramme of the coarsely powdered gum-resin for a few minutes with 10 millilitres of *hydrochloric acid* diluted with an equal volume of *water* does not exhibit a blue fluorescence when filtered and made alkaline with *solution of ammonia* (absence of asafetida and African ammoniacum). Ash not more than 7 per cent." *Br.*

For list of its physical constants see Dieterich. (*Ph. Ztg.*, xcvi, 401, and *P. J.*, 1900, 647.)

Tschirch and Luz (*A. Pharm.*, 1895, p. 571) have made an elaborate research of the chemistry of ammoniac, and state the following conclusions. Ammoniac contains resin, gum, and volatile oil, together with about 3.5 per cent. of a residue insoluble in water and alcohol. The portion soluble in alcohol and ether is a mixture of a so-called acid resin and a neutral resin, and amounts to 69 per cent. Both resins are free from sulphur, despite the statement of Preiszewski, who considered the latter of them to contain sulphur. The saponification of the so-called acid resin yielded salicylic acid of the formulas $C_6H_4OHCOOH$ and $C_6H_4OHCOOH + \frac{1}{2}H_2O$. Along with this were volatile acids, consisting of valeric and butyric acids, and an alcohol which belongs to the class of *resinotannols,* and has the same formula as galbaresinotannol, $C_{18}H_{30}O_3$. The resin is, therefore, a salicylic ester of resinotannol. From this resinotannol both the acetyl and the benzoyl derivatives were made, and the formula $C_{18}H_{30}O_3$ thus established. On oxidizing the resinotannol with nitric acid, *styphnic acid* was obtained, and on fusing it with potassium hydroxide, resorcinol was yielded. Volatile oil was found in small amount only. It contains no umbelliferone, and is free from sulphur. The crude ammoniac showed traces of a free acid which was recognized as salicylic both by its fusing point and the ferric chloride reaction. The gum contained 3.5 per cent. of ash, of which 1.2 per cent. was calcium oxide, so that the gum is probably related to gum arabic, and is an acid calcium arabinate.

Plugge's analysis (*A. Pharm.*, 1883) gave 1.27 per cent. of volatile oil, 65.53 per cent. of resin, and 26.10 of gum. Semmler and Roenish (*J. Chem. S.*, 1918, cxiv, p. 118) obtained 0.3 per cent. of volatile oil containing linalyl acetate, citronellyl acetate, ferulene doremone, a ketone and cetyl alcohol, which has not hitherto been reported in plants. This oil has a disagreeable odor. It contains no sulphur nor umbelliferone.

Uses.—This gum-resin is stimulant and expectorant, in large doses cathartic, and, like many other stimulants, may be so given as occasionally to prove diaphoretic, diuretic, or emmenagogue. It has been employed in medicine from the highest antiquity, being mentioned in the writings of Hippocrates, but is now seldom administered. The complaints in which it was most frequently used were *chronic catarrh, asthma,* and other *pectoral affections* attended with deficient expectoration without acute inflammation, or with a too copious secretion from the bronchial mucous membrane, dependent upon debility of the vessels. It is usually administered in combination with other expectorants, with tonics, or with emmenagogues. Externally applied, in the shape of a plaster, it is thought to be useful as a discutient or resolvent in white swellings of the joints, and other indolent tumors. (See *Emplastrum Ammoniaci cum Hydrargyri, U. S. Dispensatory,* 19th edition, p. 437.) It is given in substance, in pill or emulsion. The latter form, however, is preferable. (See *Mistura Ammoniaci,* Br., 1914.)

Dose, from five to twenty grains (0.3–1.3 Gm.).

Off. Prep.—Mistura Ammoniaci, *Br.;* Pilula Ipecacuanhæ cum Scilla, *Br.;* Pilula Scillæ Composita, *Br.;* Pilula Ipecacuanhæ cum Urginea, *Br.;* Pilula Urgineæ Composita, *Br.*

AMMONII BENZOAS. U. S., Br.

AMMONIUM BENZOATE Ammon. Benz.

"Ammonium Benzoate, when dried for twenty-four hours over sulphuric acid, contains not less than 98 per cent. of $C_6H_5.COONH_4$." *U. S.* "Ammonium Benzoate, $NH_4C_7H_5O_2$, may be obtained by neutralising benzoic acid with solution of ammonia." *Br.*

Ammoniæ Benzoas; Ammonium Benzoicum; Benzoas Ammonicus; Benzoate of Ammonia; Benzoate d'Ammoniaque, *Fr. Cod.;* Benzöesaures Ammonium, Ammonium benzoat, *G.;* Benzoato amonico, *Sp.*

The process for the preparation of this salt was omitted in the latter editions of the U. S. P. The process of U. S., 1870, is appended. "Take of Benzoic Acid *two troyounces;* Water of Ammonia *three fluidounces and a half,* or a *sufficient quantity;* Distilled Water *four fluidounces.* Dissolve the Acid in three fluidounces and a half of the Water of Ammonia, previously mixed with Distilled Water; evaporate with a gentle heat, occasionally adding Water of Ammonia, if necessary, to maintain a slight excess of the alkali; then set aside to crystallize, and dry the crystals without heat." *U. S.*, 1870.

Although the quantity of ammonia ordered in the formula is in excess, yet, from the feeble action between the constituents, and the consequent escape of ammonia during the evaporation, a portion of the acid benzoate would be formed, if it were not that a little solution of ammonia is from time to time added during or near the close of the evaporation, so as to maintain the alkali in slight excess. The crystals, for the same reason, should be dried without heat. If slightly evaporated, and then allowed to cool, the solution becomes a mass of crystals, retaining so much water as to render it necessary to dry them by means of bibulous paper.

Description and Physical Properties.—"Thin, white, laminar crystals or a crystalline powder, gradually losing ammonia on exposure to air.

It is odorless, or has a slight odor of benzoic acid. One Gm. of Ammonium Benzoate is soluble in 10 cc. of water, 35.5 cc. of alcohol, and in 8 cc. of glycerin, at 25° C.

"When Ammonium Benzoate is heated to about 200° C., ammonia and benzoic acid are given off. An aqueous solution of Ammonium Benzoate (1 in 10) responds to the reactions for ammonium, and for benzoates. An aqueous solution of the salt (1 in 20) is neutral or not more than slightly acid to litmus paper. Ash: not more than 0.05 per cent. Acidulate 10 cc. of an aqueous solution of the salt (1 in 50) with hydrochloric acid, and filter: the filtrate meets the requirements of the test for *heavy metals.*

"**Assay.**—Dry about 0.5 Gm. of Ammonium Benzoate for twenty-four hours over sulphuric acid, weigh accurately, and dissolve in 10 cc. of distilled water in a separator. Add to the solution 5 cc. of diluted sulphuric acid, and extract the liberated benzoic acid by shaking out with three successive portions of 25, 15 and 10 cc., respectively, of chloroform, passing the chloroform solution through a filter previously moistened with chloroform, and removing any benzoic acid adhering to the stem of the funnel and filter paper with a few cc. of chloroform. Evaporate the chloroform solution at a temperature not above 40° C. to about 5 cc., add 25 cc. of a mixture of equal volumes of neutralized alcohol and distilled water, and titrate this solution with tenth-normal barium hydroxide, using phenolphthalein T.S. as indicator. Each cc. of tenth-normal barium hydroxide corresponds to 0.01391 Gm. of $NH_4C_7H_5O_2$.

"Preserve in well-closed containers, in a cool place." *U. S.*

"Colorless lamellar crystals. Taste saline, slightly acrid. Soluble in 6 parts of *water,* and in 30 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of ammonium salts. An aqueous solution yields a pale reddish precipitate on the addition of *T. Sol. of ferric chloride.* A strong aqueous solution, to which a little *hydrochloric acid* is added, yields a crystalline precipitate of benzoic acid. Completely volatilised by heat. If 1 gramme is dissolved in 20 millilitres of *water* and excess of *nitric acid* added, a crystalline precipitate of benzoic acid separates, the filtrate from which remains clear on the addition of *solution of barium chloride,* and does not become more than slightly opalescent on the addition of *solution of silver nitrate. Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million." *Br.*

Gmelin states that by boiling its solution the salt is converted into the acid benzoate, which crystallizes in feathery tufts of needles. (*Handbook,* xii, 38.)

Uses.—Ammonium benzoate owes its virtues chiefly to the benzoic acid radical. (See *Acidum Benzoicum.*) Like the other benzoates it is of service in the treatment of various forms of *rheumatism,* but is especially prized as an urinary antiseptic in fermentative *cystitis.* It has the great advantage in this condition that not only is the benzoic acid directly antiseptic but, because the ammonium radical is destroyed in the body, the salt also tends to increase the acidity of the urine, thereby aiding in the antibacterial effects of other agents.

Dose, from ten to thirty grains (0.65–2.0 Gm.).

AMMONII BROMIDUM. U. S., Br.

AMMONIUM BROMIDE Ammon. Brom.

"Ammonium Bromide, when dried for twenty-four hours over sulphuric acid, contains not less than 98.5 per cent. of NH_4Br." *U. S.* "Ammonium Bromide may be obtained by neutralising hydrobromic acid with solution of ammonia. When dried at 100° C. it contains not less than 98 per cent. of pure ammonium bromide, NH_4Br." *Br.*

Ammonium Bromatum; Bromhydrate d'Ammoniaque, *Fr. Cod.;* Bromure d'Ammonium, *Fr.;* Ammonium bromatum, *P. G.;* Ammonium bromid, Brom-Ammonium, *G.;* Bromuro di ammonio, *It.;* Bromuro amonico, *Sp.*

Ammonium bromide may be made by dissolving bromine in ammonia water; but the U. S. Pharm., 1870, preferred the method of first forming solution of ferrous bromide, precipitating with ammonia water, separating by filtration the ferric oxide, and obtaining by evaporation the ammonium bromide from the solution. This process is similar to that by which potassium bromide is prepared. Charles Rice (*A. J. P.,* 1873, p. 249) recommends making ammonium bromide by double decomposition between hot solutions of potassium bromide and ammonium sulphate, assisting the precipitation of potassium sulphate by alcohol. W. H. Pile (*Proc. A. Ph. A.,* 1874, p. 434) published a simple process for this salt. Pour the bromine (one pound) carefully into four times its weight of distilled water in a stone jar, add *very gradually* about one quart of solution of ammonia, cover the top of the jar with a glass plate when vapors arise, and when all the ammonia has been added, and the solution is free from the odor of bromine, it is evaporated and the salt granulated; the yield is about twenty ounces.

Properties.—Ammonium bromide may be obtained in colorless crystals; on exposure to the air it gradually becomes yellowish, in consequence of a partial decomposition, by which hydrobromic acid appears to be liberated, as it now changes litmus red. The salt has a saline, pungent taste. Exposed to heat, it sublimes unchanged.

It is officially described as follows:

Description and Physical Properties.—"Colorless crystals, or a white, crystalline or granular powder, having no odor. It is somewhat hygroscopic. One Gm. of Ammonium Bromide is soluble in 1.3 cc. of water and in 12 cc. of alcohol, at 25° C. One Gm. is soluble in 0.9 cc. of boiling water and in 1.2 cc. of boiling alcohol. When heated, Ammonium Bromide volatilizes without fusing. An aqueous solution of the salt (1 in 10) responds to the reactions for ammonium, and for bromides.

"An aqueous solution of the salt (1 in 20) is neutral or not more than slightly acid to litmus paper. Add 2 cc. of nitric acid to about 2 Gm. of Ammonium Bromide, evaporate the mixture to dryness in a porcelain dish on a water bath, and ignite: not more than 0.05 per cent. of residue remains. Add a few drops of ferric chloride T.S. and 1 cc. of chloroform to 10 cc. of an aqueous solution of the salt (1 in 20), and shake the mixture: the chloroform does not acquire a violet tint (*iodide*). Drop 1 cc. of diluted sulphuric acid upon about 1 Gm. of the powdered salt: no yellow color appears at once (*bromate*). A blue color is not immediately produced on adding potassium ferrocyanide T.S. to 20 cc. of an aqueous solution of the salt (1 in 250) (*iron*). Add 1 cc. of potassium sulphate T.S. to 10 cc. of an aqueous solution of Ammonium Bromide (1 in 20) acidulated with hydrochloric acid: no turbidity is produced immediately (*barium*). The addition of barium chloride T.S. to a similar solution of the salt acidulated with hydrochloric acid produces no turbidity (*sulphate*). An aqueous solution of the salt meets the requirements of the test for *heavy metals*.

"**Assay.**—Proceed as directed under the assay for bromides, using about 0.4 Gm. of Ammonium Bromide, previously dried for twenty-four hours over sulphuric acid, and accurately weighed. Each cc. of tenth-normal silver nitrate corresponds to 0.009796 Gm. of NH_4Br. Each Gm. of Ammonium Bromide, previously dried, corresponds to not less than 100.5 cc. and not more than 103.4 cc. of tenth-normal silver nitrate.

"Preserve in well-closed containers." *U. S.*

"Small colorless crystals. Taste somewhat pungent, saline. Soluble in 1.5 parts of *water*, and in 13 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of ammonium salts and of bromides. Loses not more than 1 per cent. of its weight when dried at 100° C. 0.5 gramme of this dried salt dissolved in *water* requires for complete precipitation not less than 50.5 and not more than 51.5 millilitres of *N/10 solution of silver nitrate* (limit of impurities). Completely volatilised by heat. Yields no characteristic *reactions* for iron, bromates, iodides, or nitrates, and not more than the slightest *reaction* for sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

The incompatibilities are those of the bromides (see *Potassii Bromidum*), or of ammonium salts in general (see *Ammonii Chloridum*).

Uses.—Ammonium bromide is useful chiefly for the action of its bromic ion. (See under *Potassii Bromidum.*) By some it is believed to be less prone to cause disturbances of the digestion than is potassium bromide Theoretically the ammonium ion should impart to this salt a stimulant action upon the circulation and upon the spinal cord, but for reasons pointed out elsewhere (see *Ammonii Carbonas*) it is doubtful whether this is of any practical importance.

Dose, ten to thirty grains (0.6–1.9 Gm.) well diluted.

Off. Prep.—Elixir Ammonii Bromidi, *N. F.;* Elixir Bromidorum Trium, *N. F.;* Elixir Bromidorum Quinque, *N. F.;* Syrupus Bromidorum, *N. F.;* Syrupus Thymi Compositus, *N. F.*

AMMONII CARBONAS. U. S., Br.

AMMONIUM CARBONATE Ammon. Carb.

"Ammonium Carbonate consists of acid ammonium carbonate (NH_4HCO_3) and ammonium carbamate ($NH_4NH_2CO_2$) in varying proportions, and yields not less than 30 per cent. and not more than 32 per cent. of NH_3." *U. S.* "Ammonium Carbonate is a variable mixture of ammonium hydrogen carbonate, NH_4HCO_3, with ammonium carbamate, $NH_4NH_2CO_2$. It may be obtained by heating ammonium sulphate or chloride with calcium carbonate." *Br.*

Ammoniæ Carbonas, *Br.* 1867; Ammoniæ sesquicarbonas; Carbonas Ammonicus; Alkali Volatile Concretum; Volatile Salt, Sal Volatile; Carbonate d'Ammoniaque, *Fr. Cod.;* Alcoli volatil concret, Sel volatil d'Angleterre, *Fr.;* Ammonium carbonicum, *P. G.;* Ammonium-carbonat, Kohlensaures Ammonium, Flüchtiges Laugensalz, Reines Hirschhornsalz, *G.;* Carbonato di ammonio, *It.;* Carbonato amonico, *Sp.*

There have been many methods of obtaining ammonium carbonate, in all of which the ammonia originated in organic decomposition. It was probably originally prepared from putrid urine, and it is sometimes made in Scotland now from this source. A patent was taken out in England for manufacturing it from guano, and another for making it by the direct combination of its constituents, the carbon dioxide and ammoniacal gases being introduced simultaneously into leaden chambers. (*Chem. News,* Dec. 29, 1865.) At present the salt is manufactured by subliming a mixture of either ammonium chloride or sulphate with chalk. Ammonium chloride and chalk (calcium carbonate) are heated together in iron pots or retorts, and sublimed into large earthen or leaden receivers. By the reciprocal action of the salts employed, the carbon dioxide of the chalk unites with the ammonia of the chloride, generating ammonium carbonate, and the hydrochloric acid with the lime, forming water and calcium chloride. The carbonate and water sublime together as hydrated ammonium carbonate, and the residue is calcium chloride,

$$\begin{aligned} 4NH_4Cl + 2CaCO_3 = {} & \\ & NH_4HCO_3NH_4NH_2CO_2 + NH_3 \\ & + 2CaCl_2 + H_2O. \end{aligned}$$

The relative quantities of chalk and ammonium chloride, for mutual decomposition, are 50 of the former and 53.5 of the latter, or one molecule of each. But a great excess of chalk is usually taken, in order to insure the perfect decomposition of the ammonium chloride, any redundancy of which would sublime with the carbonate and render it impure. Barium carbonate is sometimes used in place of calcium carbonate, barium chloride, the by-product, having a greater commercial value than calcium chloride.

Ammonium sulphate may be substituted for the chloride with much economy, as was shown by Payen. This double decomposition between ammonium sulphate and calcium carbonate takes place in the dry way only—that is, by sublimation. In the wet way, the double decomposition is reversed, ammonium carbonate and calcium sulphate reacting so as to form ammonium sulphate and calcium carbonate. Large quantities of this carbonate are manufactured indirectly from *coal gas liquor* and *bone spirit,* the ammoniacal products in these liquors being converted successively into ammonium sulphate, chloride, and carbonate. (See *Ammonii Chloridum.*) The salt as first obtained has a slight odor of tar, and leaves a blackish carbonaceous matter when dissolved in acids. Hence it requires to be purified, which is effected in iron pots surmounted with leaden heads. The American carbonate has almost supplanted the English article, which was formerly used exclusively.

Description and Physical Properties.—"White, hard, translucent, columnar masses, having a strong odor of ammonia, without empyreuma, and a sharp, ammoniacal taste. On exposure to the air, the salt loses both ammonia and carbon dioxide, becoming opaque, and is finally converted into friable, porous lumps, or a white powder. For medicinal purposes, use only the translucent portions. One Gm. of Ammonium Carbonate is very slowly soluble in 4 cc. of water at 25° C. It is decomposed by hot water, with the evolution of carbon dioxide and ammonia. By prolonged boiling with water, the salt is completely decomposed and volatilized. Alcohol dissolves the carbamate, leaving the acid carbonate.

"When heated, Ammonium Carbonate is volatilized without charring, the vapor being strongly alkaline to moistened litmus paper. An aqueous solution of the salt (1 in 20) effervesces with acids, and is alkaline to litmus paper.

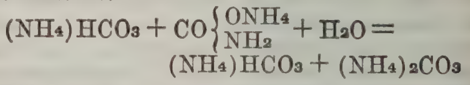
"When heated until volatilized, not more than 0.05 per cent. of residue remains. An aqueous solution of the salt (1 in 50) to which a slight excess of hydrochloric acid has been added meets the requirements of the test for *heavy metals,* A 10 cc. portion of an aqueous solution of the salt (1 in 20) on the addition of a slight excess of silver nitrate T.S., followed by a slight excess of nitric acid does not assume a brown color (*thiosulphate*). A 2 Gm. portion of the salt shows no more *chloride* than corresponds to 0.1 cc. of fiftieth-normal hydrochloric acid, and no more *sulphate* than corresponds to 0.1 cc. of fiftieth-normal sulphuric acid. Add a slight excess of nitric acid to an aqueous solution containing 1 Gm. of the salt, and evaporate to dryness on a water bath: a colorless, odorless residue is obtained (*empyreumatic matter*).

"**Assay.**—Place in a weighing bottle about 10 cc. of distilled water, tare the bottle and its contents, add about 2 Gm. of unaltered, translucent Ammonium Carbonate, and weigh accurately. Transfer the contents of the bottle to a 200 cc. flask, add 50 cc. of normal sulphuric acid, and, when solution is effected, titrate the excess of acid with normal sodium hydroxide, using methyl orange T.S. as indicator. Each cc. of normal sulphuric acid corresponds to 0.01703 Gm. of NH_3.

"Preserve in well-closed containers, in a cool place." *U. S.*

"Translucent, crystalline masses. Ammoniacal odor; taste pungent, ammoniacal. Alkaline to *litmus.* Soluble in 4 parts of *water.* Exposed to the air it becomes covered with a white efflorescence which is only superficial; this efflorescence should be scraped off before the salt is used for dispensing. Yields the *reactions* characteristic of ammonium salts and of carbonates. 1 gramme dissolved in 40 millilitres of *water* requires for neutralisation not less than 18.0 millilitres of *N/1 solution of sulphuric acid.* Completely volatilised by heat. Yields not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million. When its aqueous solution is neutralised with a mineral acid and evaporated to dryness, the residue is colorless and odorless (absence of tarry matters)." *Br.*

If commercial ammonium carbonate be treated with 90 or 91 per cent. alcohol, it is decomposed into the two salts of which it is composed, ammonium carbamate going into solution while the acid ammonium carbonate remains undissolved. This latter compound also remains undissolved when the commercial carbonate is treated with an amount of water insufficient for complete solution. The result of the complete solution of the commercial salt in water is a mixture of acid and neutral carbonates, the carbamate having been decomposed according to the reaction:



$$(NH_4)HCO_3 + CO\left\{\begin{matrix}ONH_4\\NH_2\end{matrix}\right. + H_2O = (NH_4)HCO_3 + (NH_4)_2CO_3$$

When long or insecurely kept, it gradually passes into a bicarbonate, becoming opaque and friable, and falling into powder. When heated in a porcelain dish the commercial carbonate should evaporate without residue, and, if turmeric paper held over it undergoes no change, it has passed into bicarbonate. As prepared from coal gas liquor, it sometimes contains traces of tarry matter, which give a dark color to its solution in acids, but a refined carbonate, made by resubliming the commercial article, is now in the market. For papers on testing commercial ammonium carbonate, see *A. J. P.,* 1890, p. 500, by G. M. Beringer; also *Ph. Era,* 1889, p. 417, by Charles C. Abbey.

Uses.—Locally ammonium carbonate is an active irritant and capable in overdose of causing gastritis. Systemically its action is purely that of its ammonium radical. When injected into the circulation in proper dose ammonium acts as a rapid but fugacious stimulant to both the circulation and nervous system. The blood pressure is elevated partly from an effect on the cardiac muscles and probably also in part from a stimulation of the vasomotor center in the medulla. After toxic doses the rise in blood pressure may be followed by a fall to a point below the norm. There is also an increase in the rapidity of breathing due to an action upon the respiratory center. The action upon the spinal cord is shown by increased activity of reflexes and in sufficient doses it is capable of causing in the lower animals tetanic convulsions. These effects are caused only when it is introduced fairly rapidly into the circulation and do not occur, at least to any practical degree, when the drug is exhibited by the mouth, because the ammonium is so rapidly destroyed in the system that it is scarcely possible for a sufficient quantity to be absorbed through the mucous membrane of the alimentary tract to obtain the necessary concentration in the blood for its physiological effect. It is oxidized in the liver appearing in the urine chiefly as urea, although a small amount seems to be excreted as nitric acid. The irritant salts of ammonium, however, by virtue of their local effects on mucous membranes reflexly, may excite the medullary centers. To this action is due the improvement in circulation and respiration seen in cases of syncope as the result of smelling or swallowing such salts as the carbonate or hydroxide.

Ammonium carbonate is used as an antacid in the treatment of various forms of *gastric disturbances,* especially when associated with *headache.* It is also employed for its expectorant effect. It is probably largely converted in the stomach into the chloride and exercises the same type of action in *bronchitis* as that salt. As a rapid stimulant in cases of *circulatory failure,* as in adynamic *pneumonias, snake-bite,* and other conditions it may prove of great value if administered hypodermically.

Coarsely bruised with the addition of half its bulk of stronger ammonia water, and scented with oil of lavender, it constitutes the common *smelling-salts,* so much used as a nasal stimulant in *syncope* and *hysteria.* It should never be given in powder or in pill, on account of its volatile nature and its irritant action on the mucous membrane.

Ammonium carbonate is sometimes employed in making effervescing draughts, 20 grains of the salt requiring for this purpose 6 fluidrachms of lemon juice, 24 grains of citric acid, or 25½ grains of tartaric acid. It is sometimes used as a leavening agent, replacing sodium bicarbonate in culinary operations and is then usually called *baker's ammonia.*

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Spiritus Ammoniæ Aromaticus, *U. S., Br.;* Mistura Pectoralis, Stokes, *N. F.*

AMMONII CHLORIDUM. U. S., Br.

AMMONIUM CHLORIDE Ammon. Chlor.

"Ammonium Chloride, when dried for twenty-four hours over sulphuric acid, contains not less than 99.5 per cent. of NH_4Cl." *U. S.* "Ammonium Chloride, NH_4Cl, may be obtained by neutralising crude solution of ammonia or ammonium carbonate with hydrochloric acid, and purifying the product." *Br.*

Ammonium Muriaticum, Chlorhydras Ammoniæ; Chloretum Ammonicum, Sal Ammoniacum, Ammoniæ Hydrochloras, s. Murias; Sal Ammoniac, Hydrochlorate of Ammonia; Chlorure d'Ammonium, *Fr. Cod.;* Chlorhydrate d'Ammoniaque, Sel Ammoniac, *Fr.;* Ammonium Chloratum, *P. G.;* Ammoniumchlorid, Salmiak, Chlorammonium, Reiner (gereinigter) Salmiak, *G.;* Chlorurio d'ammonio, Sale ammoniaco, *It.;* Cloruro amonico, Sal amoniaco, *Sp.*

In the U. S. Pharmacopœia of 1870 both the crude and the purified ammonium chloride were official, under the names *Ammonii Chloridum* and *Ammonii Chloridum Purificatum.* The U. S. P. VIII recognized but one, *Ammonii Chloridum,* but it transferred this title, which formerly was given to the crude sal ammoniac, to the purified salt, without giving a process for preparing it. The U. S. P. X has retained this plan. The U. S. P., 1870, process is as follows: "Take of Chloride of Ammonium, in small pieces, *twenty troyounces;* Water of Ammonia *five fluidrachms;* Water *two pints.* Dissolve the Chloride of Ammonium in the water, in a porcelain dish, with the aid of heat; add the Water of Ammonium, and continue the heat for a short time; filter the solution while hot, and evaporate to dryness, with constant stirring at a moderate heat, until it granulates." *U. S.,* 1870.

This process is used to free the salt from ferric chloride, a frequent impurity of the crude product, derived from the subliming vessels.

Ammonium chloride originally came from Egypt, where it was obtained by sublimation from the soot resulting from the burning of camels' dung, which is used in that country for fuel, and it is still to be found in the Indian bazaars in an impure state as it has been obtained from the unburnt residue in the interior of brick-kilns in which camel's manure is used for fuel. The name amonia is derived from the fact that it was largely thus obtained in the Libyan desert near the temple of Jupiter Ammon. It has long been known in China, where it is obtained from the water of certain volcanic springs, and exists in commerce in various states of purity. It is found in the fumaroles of Vesuvius, Etna, Hecla, and other volcanoes, and in the cracks and fissures in recent lava streams.

Preparation.—At present ammonium chloride is derived from the ammonia liquor, called *gas liquor,* found in the condensing vessels of coal gas works. It is obtained in lesser amount from the brown, fetid ammonia liquor, known under the name of *bone spirit,* which is a secondary product, obtained from the destructive distillation of bones, in the manufacture of bone black. These two liquors are the chief sources of ammonia compounds, for they are both used to procure ammonium sulphate, and this salt is employed directly or indirectly for obtaining all the other salts of ammonium. A third source of increasing importance is its production as a by-product in ovens for coking coal. Other sources in the past were stale urine, coal soot, guano, peat, and bituminous schist.

Gas liquor contains ammonium carbonate, cyanide, sulphide, and sulphate, but principally the carbonate. It is saturated with sulphuric acid, and the solution obtained, after due evaporation, furnishes brown crystals of ammonium sulphate. These are then sublimed with sodium chloride in iron pots lined with clay and furnished with an iron dome or head. By the mutual action of the sulphate and chloride, there are formed ammonium chloride which sublimes, and sodium sulphate which remains behind. Thus:

$$(NH_4)_2SO_4 + 2NaCl = 2NH_4Cl + Na_2SO_4$$

Gas liquor is usually distilled with lime with the aid of column stills, whereby a relatively pure and strong solution of ammonia is obtained.

This may be further purified, however, from empyreumatic matter by treatment with potassium permanganate and then driven over by heat and absorbed in hydrochloric acid. In this way, as the solution becomes concentrated, the sal ammoniac crystallizes out in the bottom of the leaden tanks in which the absorption takes place. Impure sal ammoniac may be purified either by crystallization or by sublimation. In the latter case the sal ammoniac is placed in an iron subliming pot coated with a composition of clay, sand, and charcoal and covered with a dome of lead, iron, earthenware, or glass. These pots are sometimes sufficiently large to hold 500 pounds. A gentle fire is kept up under the subliming pot for seven or eight days, when, the dome having cooled down, and the sal ammoniac somewhat contracted, so as to loosen from the sides, the dome is thrown off from the iron pot, and about two or three hundred-weight of white, semi-transparent sal ammoniac is obtained.

In the destructive distillation of bones for making bone black, the distilled products are the bone spirit already mentioned, being chiefly an aqueous solution of ammonium carbonate, and an empyreumatic oil, called animal oil. Ammonium chloride may be obtained from the bone spirit in the manner just described for procuring it from gas liquor. Sometimes, however, the ammonium sulphate is not made by direct combination, but by digesting the bone spirit with ground plaster of Paris. By double decomposition, ammonium sulphate and calcium carbonate are formed. The ammonium sulphate is then converted into the chloride by sublimation with common salt.

Properties.—Commercial ammonium chloride is a white, transparent, tough, fibrous salt, occurring in large cakes about two inches thick, convex on one side and concave on the other, due to the shape of the dome of the subliming apparatus; the pieces are frequently tinged on the surface with iron stains, from the iron dome which is used for crude sal ammoniac. It has a pungent, saline taste, but no odor. Its sp. gr. is 1.45. This salt is very difficult to powder in the ordinary way. Its pulverization, however, may be readily effected by making a boiling saturated solution of the salt and stirring it as it cools. The salt is thus made to granulate, and in this state, after draining from the remaining solution and drying, may be easily powdered. At a red heat it sublimes without decomposition or residue. Exposed to a damp atmosphere it becomes slightly moist. It has the property of increasing the solubility of corrosive sublimate in water. It is decomposed by the strong mineral acids, and by the alkalies and alkaline earths—the former disengaging hydrochloric acid, the latter ammonia, both sensible to the smell. Ammonium chloride is usually employed for obtaining gaseous ammonia, which is conveniently disengaged by lime.

Description and Physical Properties.—" A white, crystalline or granular powder, without odor, and having a cooling, saline taste. It is somewhat hygroscopic. One Gm. of Ammonium Chloride is soluble in 2.6 cc. of water, 100 cc. of alcohol, and in 8 cc. of glycerin, at 25° C. One Gm. is soluble in 1.4 cc. of boiling water.

" Ammonium Chloride on ignition is volatilized without fusing. An aqueous solution of the salt (1 in 10) responds to the reactions for ammonium, and for chlorides. An aqueous solution of the salt (1 in 20) does not show an immediate acid reaction with 1 drop of methyl orange T.S. An aqueous solution of Ammonium Chloride meets the requirements of the test for *heavy metals.* Acidulate 10 cc. of an aqueous solution of the salt (1 in 10) with hydrochloric acid and add a few drops of ferric chloride T.S.: no red color should be produced (*thiocyanate*). Add 2 cc. of nitric acid to 2 Gm. of the salt, and evaporate the mixture to dryness in a porcelain dish on a water bath: a white residue is obtained which, when ignited, yields not more than 0.1 per cent. of *non-volatile substances.*

" **Assay.**—Proceed as directed under the assay for chlorides, using about 0.2 Gm. of Ammonium Chloride, previously dried for twenty-four hours over sulphuric acid and accurately weighed. Each cc. of tenth-normal silver nitrate corresponds to 0.005350 Gm. of NH_4Cl." *U. S.*

" Colorless, inodorous crystals. Taste saline, cooling. Soluble in 3 parts of *water,* and in 60 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of ammonium salts and of chlorides. Completely volatilised by heat. Yields no characteristic *reactions* for copper, carbonates, or nitrates, and not more than the slightest *reactions* for iron, or for sulphates. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million." *Br.*

It is incompatible with lead acetate and silver nitrate, producing precipitates respectively of lead and silver chlorides.

It is also incompatible with all alkali and alkali earth hydroxides and carbonates which gradually decompose it by liberating NH_3. This incompatibility is shared by all salts of ammonium.

Uses.—Ammonium chloride possesses the stimulant properties of its basic ion and probably differs but little in its physiological action from the carbonate, although it is believed by some to be less powerful and less fugacious. Clinically it is employed chiefly in the treatment of various types of *bronchitis* for the purpose of increasing the secretions. Its effect in these conditions is probably owing chiefly to its "salt action," a property common to most of the nontoxic salts. Some believe, however, that it exercises a specific stimulant effect upon mucous membranes not only of the lungs but also of the digestive organs. It has been used, therefore, in the treatment of *acute hepatitis, catarrhal jaundice,* and *gastric catarrh,* and with asserted good results. For its old use in *sciatica, dysmenorrhea,* and *glandular enlargements* there is little scientific support, and it has been almost entirely abandoned for these purposes.

Hermann Beigel, of London, strongly recommends its inhalation in the nascent state, resulting from a mixture of the two gases composing it. Three bottles are used, one containing ammonia water, the second an equivalent quantity of liquid hydrochloric acid, and the third half filled with water, connected with the first two by tubes, and supplied itself with a tube for inhalation. By inhalation the patient draws the two gases from their respective bottles into the third, where they combine to form ammonium chloride, which is freed from any excess of either gas by the water. Another mode of inhaling ammonium chloride is in *spray,* by means of the atomizer; ten to twenty grains are dissolved for the purpose in a fluidounce of water. Ammonium chloride has been used in some European countries in place of sodium chloride for salting food before eating it.

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Trochisci Ammonii Chloridi, *U. S.*

AMMONII HYPOPHOSPHIS. N. F.

AMMONIUM HYPOPHOSPHITE Ammon. Hypophos.

"Ammonium hypophosphite contains, when dried over sulphuric acid for twenty-four hours, not less than 97.5 per cent. of $NH_4PH_2O_2$ (83.10)." *N. F.*

Description and Physical Properties.—"Ammonium Hypophosphite occurs in deliquescent, colorless, hexagonal plates, or as a granular powder, odorless and having a saline and bitter taste. One gram dissolves in about 1 cc. of water, and in about 20 cc. of alcohol at 25° C.; very soluble in boiling water or boiling alcohol.

"When heated, the salt is decomposed with the evolution of hydrogen phosphide, which is spontaneously inflammable. An aqueous solution of the salt (1 in 20) is neutral or slightly acid to litmus and when heated with sodium hydroxide T.S. gives off ammonia. An aqueous solution of the salt (1 in 20) slightly acidulated with sulphuric acid, yields with silver nitrate T.S. a white precipitate, which rapidly turns brown or black through the separation of metallic silver. A similar portion of the solution, slightly acidulated with sulphuric acid, yields, on heating with copper sulphate T.S. a reddish brown precipitate.

"Ten cc. of an aqueous solution of the salt (1 in 20) remains clear for five minutes after the addition of 5 cc. of ammonium oxalate T.S. and a few drops of ammonia water (*calcium salt*). Add 1 cc. of calcium chloride T.S. to 10 cc. of the aqueous solution of the salt (1 in 20) previously acidulated with 1 cc. of acetic acid; no turbidity is produced (*oxalate*). An aqueous solution of salt does not respond to the Test for heavy metals. Boil 5 cc. of an aqueous solution of the salt (1 in 25) with 3 cc. of sodium hydroxide solution until the ammonia is expelled, add 5 cc. of nitric acid, and evaporate to dryness on a water bath; the residue meets the requirements of the Test for arsenic.

"**Assay.**—Dissolve about 0.2 Gm. of Ammonium Hypophosphite, previously dried over sulphuric acid for twenty-four hours and accurately weighed in 10 cc. of distilled water, add 3 cc. of sodium hydroxide T.S. and boil until the ammonia is expelled. Then add 5 cc. of nitric acid and evaporate the solution to dryness on a water bath. Add 1 cc. of nitric acid and again evaporate it to dryness on a water bath. Dissolve the residue in 20 cc. of distilled water, transfer it to a 200 cc. graduated flask, add a drop of phenolphthalein T.S. and sufficient sodium hydroxide T.S. (free from chloride) to produce a pink color, and then add 100 cc. of tenth-normal silver nitrate and agitate well. Now gradually add zinc oxide (free from chloride) in small portions until the liquid is neutral to litmus, and then sufficient distilled water to make the mixture measure 200 cc. Agitate the mixture thoroughly, filter it through a dry filter and collect 100 cc. of the filtrate (representing one-half of the Ammonium Hypophosphite taken). Add to this 2 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S. and titrate with tenth-normal potassium thiocyanate to the production of a permanent red color. Each cc. of tenth-normal silver nitrate used corresponds to 0.00277 Gm. of $NH_4PH_2O_2$. Each Gm. of Ammonium Hypophosphite corresponds to not less than 352.0 cc. of tenth-normal silver nitrate.

"Preserve it in well-closed containers." *N. F.*

Uses.—The peculiar advantages of this salt are not evident. It is recommended particularly in the latter stages of *bronchitis* and *laryngitis.*

Dose, two to five grains (0.13–0.3 Gm.) every two or three hours.

Off. Prep.—Syrupus Ammonii Hypophosphitis, *N. F.*

AMMONII PHOSPHAS. N. F.

AMMONIUM PHOSPHATE Ammon. Phos.

"Ammonium phosphate contains diammonium hydrogen phosphate [$(NH_4)_2HPO_4 = 132.13$] and ammonium dihydrogen phosphate ($NH_4H_2PO_4 = 115.09$), corresponding to not less than 22 per cent. of combined ammonia ($NH_3 = 17.03$)." *N. F.*

Ammoniæ Phosphas; Phosphate of Ammonia; Phosphas Ammonicus; Phosphate d'Ammoniaque, *Fr.;* Ammonium Phosphoricum; Phosphorsaures Ammoniak, *G.*

The *diammonium hydrogen phosphate* was formerly official, under the name of ammonium phosphate, in both the United States and British Pharmacopœias. The preparation recognized at present, by the N. F., is a mixture of this salt with the more acid ammonium di-hydrogen phosphate.

The process formerly given in the British Pharmacopœia involved treating diluted phosphoric acid with stronger ammonia water until the solution was slightly alkaline, then evaporating until crystals formed on cooling, ammonia being added from time to time in order to maintain constantly a slight excess of this base. Without such a precaution a portion of the more acid phosphate will be formed owing to the escape of the ammonia during the process of evaporation. "Neutral" ammonium phosphate prepared in this way is a white salt, crystallizing in six-sided tables, efflorescent, insoluble in alcohol, and soluble in four parts of cold water. The solution has an alkaline, somewhat saline taste, and an alkaline reaction, and gives off ammonia when heated.

The acid phosphate, $NH_4H_2PO_4$, is obtained by boiling a solution of the neutral phosphate so long as ammonia escapes, and then crystallizing. Its crystals are four-sided prisms, permanent in the air, of an acid taste and reaction, and soluble in 5 parts of cold water.

The ammonium phosphate of commerce is a mixture of these two phosphates and hence corresponds more closely with the N. F. definition.

Description and Physical Properties.—"Ammonium Phosphate occurs in colorless crystals, or as a white crystalline powder, losing ammonia on exposure to the air. One Gm. dissolves in about 4 cc. of water; it is insoluble in alcohol. The aqueous solution (1 in 20) is neutral or alkaline to litmus.

"Separate portions of an aqueous solution of the salt (1 in 20) yield with magnesia mixture T.S. a white precipitate, with silver nitrate T.S. a yellow precipitate, and, upon warming with ammonium molybdate T.S., a yellow precipitate.

"Dissolve 1 Gm. of Ammonium Phosphate in 20 cc. of distilled water; the resulting solution is not more than slightly turbid (*calcium, aluminum*). Ten cc. of an aqueous solution of the salt (1 in 100) acidulated with nitric acid, is not rendered more than slightly opalescent by silver nitrate T.S. (*chloride*). Ten cc. of an aqueous solution of Ammonium Phosphate (1 in 100), mixed with 2 cc. of hydrochloric acid is not rendered turbid at once by the addition of a few drops of barium chloride T.S. (*sulphate*). An aqueous solution of the salt does not respond to the Test for heavy metals. Five cc. of a solution of Ammonium Phosphate in diluted nitric acid (1 in 25) heated with 1 cc. of sulphuric acid until fumes of sulphur trioxide appear, meets the requirements of the Test for arsenic.

"**Assay.**—Transfer about 1 Gm. of Ammonium Phosphate, accurately weighed, to a distilling flask, dissolve it in 200 cc. of distilled water and add 25 cc. of an aqueous solution of sodium hydroxide (1 in 4). Connect the flask with a small glass condenser, the lower outlet tube of which is inserted beneath the surface of 50 cc. of half-normal sulphuric acid, contained in a flask of about 500 cc. capacity, and distil the liberated ammonia into the acid. Titrate the excess of acid with half-normal sodium hydroxide, using methyl orange T.S. as an indicator, and calculate the percentage of ammonia in the salt. Each cc. of half-normal sulphuric acid corresponds to 0.008515 Gm. of NH_3. Each Gm. of Ammonium Phosphate corresponds to not less than 23.5 cc. of half-normal sulphuric acid.

"Preserve it in well-closed containers in a cool place." *N. F.*

Uses.—Many years ago this salt was introduced as a remedy for *gout* and *rheumatism* on the supposition that it increased the solubility of uric acid in the urine, a hypothesis which as far as we know has not been established. The salt is retained in the National Formulary chiefly because it is an ingredient in the compound syrup of phosphates known popularly as "chemical food."

Dose, from five to thirty grains (0.32–1.9 Gm.), three or four times a day, dissolved in a tablespoonful of water.

Off. Prep.—Liquor Phosphatum Compositus, *N. F.*

AMMONII SALICYLAS. U. S.

AMMONIUM SALICYLATE Ammon. Salicyl.

"Ammonium Salicylate, when dried for twenty-four hours over sulphuric acid, contains not less than 98 per cent. of $NH_4C_7H_5O_3$." *U. S.*

Ammonium Salicylicum; Salicylate d'Ammoniaque, *Fr.;* Ammoniumsalicylat, Salicylsaüres Ammonium, *G.*

This salt may be made by adding salicylic acid to ammonia water until the acid is in slight excess, then evaporating the solution (which should be slightly acid to litmus paper) and crystallizing. Care should be used to prevent contamination with iron, which would give the product a pinkish or reddish tinge, and overheating, which would cause decomposition, evidenced by a phenol-like odor.

Description and Physical Properties.—"Colorless, lustrous, monoclinic prisms, or plates, or a white, crystalline powder. It is odorless, and has at first a slightly saline, bitter taste, with a sweetish after-taste. It is stable in dry air. One Gm. of Ammonium Salicylate is soluble in 1 cc. of water and in 3 cc. of alcohol, at 25° C.

"When heated, Ammonium Salicylate fuses with decomposition, giving off inflammable vapors and the odor of phenol, and is finally volatilized. Ammonium Salicylate responds to the reactions for ammonium, and for salicylates. An aqueous solution of the salt (1 in 10) is colorless and neutral or slightly acid to litmus paper. Ash: not more than 0.1 per cent. Acidulate 10 cc. of an aqueous solution of Ammonium Salicylate (1 in 50) with hydrochloric acid, and filter: the filtrate meets the requirements of the test for *heavy metals.*

"**Assay.**—Dry about 0.5 Gm. of Ammonium Salicylate over sulphuric acid, weigh accurately, and dissolve in 10 cc. of distilled water in a separatory funnel. Add to the solution 5 cc. of diluted sulphuric acid, and extract the liberated salicylic acid by shaking out with three successive portions of 25, 15 and 10 cc., respectively, of chloroform, passing the chloroform solutions through a filter previously moistened with chloroform, and removing any salicylic acid adhering to the stem of the funnel and filter paper with a few cc. of chloroform. Evaporate the chloroform solution to about 5 cc., add 25 cc. of a mixture of equal volumes of neutralized alcohol and distilled water, phenolphthalein T.S. being used as indicator, and titrate this solution with tenth-normal barium hydroxide. Each cc. of tenth-normal barium hydroxide corresponds to 0.01551 Gm. of $NH_4C_7H_5O_3$.

"Preserve in well-closed containers, protected from heat and light." *U. S.*

Uses.—Ammonium Salicylate is one of the best forms of administering salicylic acid. For consideration of its uses, see under *Acidum Salicylicum.*

Dose, ten to twenty grains (0.65–1.3 Gm.).

AMMONII VALERAS. N. F.

AMMONIUM VALERATE Ammon. Valer.

[Ammonium Valerianate]

"Ammonium valerate is a compound of ammonia with valeric acid having a somewhat varying composition." *N. F.*

Valerianas Ammonicus; Ammonium Valerianicum, *Fr. Cod.;* Valérianate d'Ammoniaque, *Fr.;* Baldriansaures (Valeriansaures) Ammonium, Ammoniumvalerianat, *G.;* Valerianato amonico, *Sp.*

A process for preparing this salt is no longer official; that of the United States Pharmacopœia of 1870 will be found in the *United States Dispensatory,* 18th ed., p. 163.

The official, as well as the commercial, salt is not the normal valerate but is an acid salt with an approximate formula of $NH_4C_5H_9O_2 + 2C_5H_{10}O_2$; the neutral salt is obtained only with difficulty, is in prismatic crystals, and is easily liquefied by moderate temperatures.

Description and Physical Properties.—"Ammonium Valerate occurs in colorless, or white, quadrangular plates, emitting the odor of valeric acid; it is deliquescent in moist air, and has a sharp and sweetish taste. One Gm. of Ammonium Valerate dissolves in 0.3 cc. of water and in 0.6 cc. of alcohol at 25° C.; soluble in ether.

"An aqueous solution of the salt (1 in 20) is acid to litmus and when heated with potassium hydroxide T.S. evolves ammonia. Supersaturate slightly a concentrated aqueous solution of Ammonium Valerate with sulphuric acid; an oily layer of valeric acid rises to the surface.

"Precipitate completely 10 cc. of an aqueous solution of the salt (1 in 20) with ferric chloride T.S.; the filtrate does not possess a deep red color (*acetate*). When heated, the salt fuses, gives off vapors of ammonia and valeric acid, and is finally volatilized, leaving not more than 0.05 per cent. of residue. An aqueous solution of the salt (1 in 50), when slightly acidulated with hydrochloric acid and filtered through a small, wetted filter, does not respond to the Test for heavy metals.

"Preserve it in well-closed containers." *N. F.*

Uses.—On the theory that valerian owed its activity to valeric acid the ammonium valerate was brought forward many years ago as a nerve sedative in *hysteria, epilepsy, neuralgia,* and other nervous affections. Physiologically, however, it is practically inert and any beneficial result which may have followed its administration in these conditions may more reasonably be attributed to the psychic effect than to any direct action upon the nervous system. *Pierlot's solution* should be made by dissolving a drachm of valeric acid and thirty-two drachms of distilled water, saturating the solution with ammonium carbonate, and adding to the salt formed forty grains of the alcoholic extract of valerian. The solution of Pierlot is neutral, color brown, odor of valerian strong. It contains one twenty-fifth of its weight of the pure salt. The dose is six to thirty minims (0.4–1.8 cc.), given in water or on a lump of sugar.

Dose, of ammonium valerate, two to ten grains (0.13–0.6 Gm.).

Off. Prep.—Elixir Ammonii Valeratis, *N. F.*

AMYGDALA AMARA. Br.

BITTER ALMOND

"Bitter Almond is the ripe seed of Prunus Amygdalus, *Stokes, var.* amara, *Baill.*" *Br.*

Semen Amygdali Amarum; Amandes amères, *Fr. Cod.;* Amygdalæ, Amaræ, *P. G.;* Bittere Mandeln, *G.;* Mandorle amare, *It.;* Almendra amarga, *Sp.*

The almond tree resembles the cherry. The leaves are elliptical, petiolate, minutely serrated, and are of a bright green color. The flowers are large, of a pink color varying to white, with very short peduncles, and petals longer than the calyx, and usually stand in pairs upon the branches. The fruit is a drupe with the outer covering thin, tough, dry, downy, and marked with a longitudinal furrow, where it opens when fully ripe. Within this covering is a rough shell, containing the kernel or almond.

There are several varieties of this species of *Amygdalus,* differing chiefly in the size and shape of the fruit, the thickness of the shell, and the taste of the kernel. The two most important are the var. *dulcis* and the var. *amara,* the former bearing sweet, the latter bitter almonds. Both of these varieties have been known since ancient times. The var. *dulcis* yields the hard and paper-shelled variety. The latter, owing to the thin endocarp, is particularly suitable for table use. Another variety grows wild in Turkestan and has a nearly smooth endocarp or "stone." The almond tree is a native of sub-tropical China, Persia, Syria, Asia Minor and probably also Turkestan. It is now cultivated not only in the Orient, but in the Mediterranean countries of southern Europe and northern Africa, and also in southern England, Scandinavia and California. Bitter almonds are chiefly imported from Morocco and Sicily.

Bitter Almond.—This seed is smaller than the sweet almonds, and "resembles the Sweet Almond in general appearance, but is distinguished by being shorter and proportionally broader, by its bitter taste, and by the characteristic odor resembling that of prussic acid given off by its aqueous emulsion." *Br.*

They have the bitter taste of the peach kernel, and, though when dry, inodorous or nearly so, have, when triturated with water, the fragrance of the peach blossom. They contain nearly the same ingredients as sweet almonds, and like them form a milky emulsion with water. It was formerly supposed that they also contained hydrocyanic acid and volatile oil, to which their peculiar taste and odor and their peculiar operation upon the system were ascribed. These principles do not pre-exist in the almond, but result from the decomposition of a glucoside denominated *amygdalin,* $C_{20}H_{27}O_{11}N$, which is the characteristic constituent of bitter almonds. This substance, which was discovered by Robiquet and Boutron in 1830, is white, crystallizable, inodorous, of a sweetish bitter taste, unalterable in the air, freely soluble in water and hot alcohol, very slightly soluble in cold alcohol, and insoluble in ether. It is decomposed by the action of diluted acids or, in the presence of water, by the nitrogenous ferments, like *emulsin,* which accompany it in the bitter almond. Liebig and Wöhler give the following process for obtaining amygdalin, in which the object of the fermentation is to destroy the sugar with which it is associated: Bitter almonds, previously deprived of their fixed oil by pressure, are boiled in successive portions of alcohol till exhausted. From the liquors thus obtained all the alcohol is drawn off by distilation, care being taken, near the end of the process, not to expose the syrupy residue to too great a heat. This residue is then to be diluted with water, mixed with good yeast, and placed in a warm situation. After the fermentation which ensues has ceased, the liquor is filtered, evaporated to the consistence of syrup, and mixed with alcohol. The amygdalin is thus precipitated in connection with a portion of gum, from which it may be separated by solution in boiling alcohol, which will deposit it upon cooling. If pure, it will form a perfectly transparent solution with water. Any oil which it may contain may be separated by washing with ether. One pound of almonds yields approximately 120 grains of amygdalin. (*Ann. Pharm.,* xxii, 329.)

Amygdalin, or cyanogenetic glucosides, of similar composition and effect, appear to be extensively diffused in plants, having been noticed not only in the different genera of the *Rosaceæ,* as *Amygdalus, Cerasus,* and *Prunus,* but also by Wicke in various *Pomaceæ,* as *Pyrus Malus, Sorbus Aucuparia, Sorbus hybrida, Sorbus torminalis, Amelanchier vulgaris, Cotoneaster vulgaris,* and *Cratægus Oxyacantha.* (*Ann. Ch. Ph.,* lxxix, 79.) The cyanogenetic glucosides are a related group of compounds which eventually hydrolyze to prussic acid, benzaldehyde and glucose. Their relationship may be illustrated by the products of hydrolysis of amygdalin.

$$C_{20}H_{27}NO_{11} + H_2O = C_6H_{12}O_6 + C_{14}H_{17}O_6N$$

This last, *mandelonitrile glucoside,* forms glucose, benzaldehyde, and hydrocyanic acid.

$$C_{14}H_{17}O_6N + H_2O = C_6H_{12}O_6 + C_7H_6O + CNH$$

Mandelonitrile glucoside occurs in three isomeric forms, *sambunigrin* found in elder flowers; *prulaurasin* found in cherry laurel; and *l-mandelonitrile* (also known as *amygdinitrile,* or *Fischer's glucoside*) found in wild cherry bark. All of these are optically active, being laevo-rotary, but vary in the degree of rotation. According to Power and Moore (*Tr. Chem. Soc.,* 1909, p. 243) they are combinations of dextro-, racemic and laevo-mandelonitrile respectively. According to the researches of Johannen, the emulsin is contained in the radicle and plumule, and in the vascular bundles of the cotyledons, while the parenchyma of the cotyledons contains the amygdalin. (*P. J.,* March, 1888.) Sweet almonds contain the ferment emulsin but not the glucoside amygdalin.

Certain substances have the effect of preventing the reaction between amygdalin and emulsin among which are alcohol and acetic acid. It is asserted that emulsin procured from other seeds, as those of the poppy, hemp, and mustard, is capable of producing the same reaction between water and amygdalin, though in a less degree. (*Ann. Pharm.*, xxviii, 290.) Amygdalin appears not to be poisonous when taken pure in the stomach, unless there be emulsin in the food in the stomach.

Bitter almonds yield their fixed oil by pressure, and at the present time this oil is an article of commerce, and is frequently sold as expressed oil of almond, this being now officially permitted. It is usually produced from North African bitter almonds; the volatile oil, impregnated with hydrocyanic acid, may be obtained from the residue by distillation with water. (See *Oleum Amygdalæ Amaræ.*)

Uses.—Bitter almonds are used solely for their flavoring powers. For medicinal purposes the oil is preferable. (See *Oleum Amygdalæ Amaræ.*) It has been ascertained that bitter almond paste, and other substances which yield the same volatile oil, such as bruised cherry-laurel leaves, peach leaves, etc., have the property of destroying the odor of musk, camphor, most of the volatile oils, creosote, cod liver oil, the balsams, etc.; and Mahier, a French pharmacist, has employed them successfully to free mortars and bottles from the odor of asafetida and other substances of disagreeable odor. All that is necessary is first to remove any oily substance by means of an alkali, and then to apply the paste or bruised leaves.

Bitter almonds, on account of the hydrocyanic acid developed in them, are poisonous.

AMYGDALA DULCIS. Br.

SWEET ALMOND Amygd. Dulc.

"Sweet Almond is the ripe seed of Prunus Amygdalus, *Stokes, var.* dulcis, *Baill.* Known in commerce as the Jordan almond." *Br.*

Semen Amygdali Dulce; Amandes douces, *Fr. Cod.*; Amygdalæ Dulces, *P. G.*; Süsse Mandeln, *G.*; Mandorle dolci, *It.*; Almendra dulce, *Sp.*

For description of the almond tree see *Amygdala Amara.*

We are supplied with sweet almonds chiefly from Spain, Italy, France, and Southern California. They are separated into the soft-shelled and hard-shelled, the former of which come from Marseilles and Bordeaux, the latter from Malaga. From the latter port they are sometimes brought to us without the shell. In British commerce, the two chief varieties are the *Jordan* and *Valencia* almonds, the former imported from Malaga, the latter from Valencia. The former are longer, narrower, more pointed, and more highly esteemed than the latter.

Properties.—Each kernel consists of two white cotyledons, enclosed in a thin, yellowish-brown, bitter skin, which is easily separable after immersion in boiling water. Deprived of this covering they are called *blanched almonds.* On exposure to the air they are apt to become rancid; but, if thoroughly dried and kept in well-closed glass vessels, they may be preserved unaltered for many years.

Sweet almonds, when blanched, are without odor, and have a sweet, very pleasant taste, which has rendered them a favorite article of diet in all countries where they are readily attainable.

"About two and a half centimeters or somewhat more in length, nearly oblong in outline, more or less compressed, pointed at one extremity and rounded at the other. Testa cinnamon-brown, thin and scaly. Seed exalbuminous, containing two large planoconvex oily cotyledons. Taste bland; when triturated with *water* forms a white emulsion with no marked odor." *Br.*

The U. S. IX gave the following description of the microscopic appearance. "The powder is creamy-white, exhibiting numerous very small oil globules, 0.001 mm. or less in diameter, and larger oil globules and crystalloids, the latter sometimes with adhering globoids; fragments of parenchyma of endosperm, containing oil globules and aleurone grains; also occasional fragments of seed-coat with characteristic, more or less scattered, large, elliptical, thin-walled, strongly lignified epidermal cells and narrow, closely spiral tracheæ. Starch grains are absent." *U. S. IX.*

Shelled Almonds are sometimes substituted by the kernels of the peach, plum and apricot. The stone cells in the epidermal layer of the almond are much larger than in the kernels of the substitutes. For microscopic distinctions see Winton and Moeller, *"The Microscopy of Vegetable Foods."* Almond cake, a by-product in the manufacture of almond oil, is largely used in the preparation of a class of detergent powders known as "almond meal." It is also used as a diabetic food and sometimes as an adulterant of ground spices and powdered drugs. By the analysis of Boullay, it appears that almonds contain 54 parts of fixed oil, 24 of protein, 6 of uncrystallizable sugar, 3 of gum, 9 of fibrous matter, 3.5 of water, and 0.5 of acetic acid, comprising loss. The protein is somewhat peculiar, consisting of *amandin* and *emulsin,* the latter being an enzyme. It may be obtained separate by treating the emulsion of almonds with ether, allowing the mixture, after frequent agitation, to stand until a clear fluid separates at the bottom of the vessel, drawing this off by a siphon, adding alcohol to it so as to precipitate the emulsin, then washing the precipitate with fresh alcohol, and drying it under the receiver of an air pump. In this state it is a white powder, inodorous and tasteless, soluble in water, and insoluble in ether and alcohol. Its solution has an acid reaction, and, if heated to 100° C., becomes opaque and milky, and gradually deposits a snow-white precipitate, amounting to about 10 per cent. of the protein employed. The distinguishing characteristic of the emulsin is that of producing certain changes noticed previously in amygdalin, which property it loses when its solution is boiled, although not by exposure in the solid state to a heat of 100° C. It consists of nitrogen, carbon, hydrogen, and oxygen, with a minute proportion of sulphur, and is probably identical with the *synaptase* of Robiquet. L. Portes has reported asparagin in sweet almonds. (*N. R.*, January, 1877.) The fixed oil is described under the head of *Oleum Amygdalæ Expressum,* to which the reader is referred. Sweet almonds, when rubbed with water, form a milky emulsion, free from the odor of hydrocyanic acid, the insoluble matters being suspended by the agency of the albuminous, mucilaginous, and saccharine principles.

Uses.—Sweet almonds have no other influence on the system than that of a nutrient and demulcent. The emulsion formed by triturating them with water is a pleasant vehicle. From their nutritive properties, and the absence of starch in their composition, they are valuable used in the diet of *diabetics.* Care must be taken when almond meal is directed to be taken as a food product, as in diabetes, that neither bitter almond meal, which is poisonous, or the factitious product, which contains soap and is inedible, is supplied. *Almond meal* or almond press cake is used for cosmetic purposes as an addition to the bath or to the water used in washing the face and hands. Much of the so-called almond meal used for this purpose is factitious or adulterated.

Off. Prep.—Mistura Amygdalæ, *Br.;* Pulvis Amygdalæ Compositus, *Br.*

AMYLIS NITRIS. U. S. (Br.)

AMYL NITRITE Amyl. Nitris

"Amyl Nitrite contains not less than 80 per cent. of $C_5H_{11}NO_2$." *U. S.* "Amyl Nitrite is a liquid obtained by the interaction of amylic alcohol [which has been distilled between 128° and 132° C.] and nitrous acid. It consists chiefly of iso-amyl nitrite, $C_5H_{11}NO_2$, but contains also other nitrites of the homologous series. It should be kept in small, stoppered bottles in a cool, dark place." *Br.*

Amyl Nitris, *Br., U. S.,* 1890; Nitris Amylicus; Amylonitrous Ether, Amylæther Nitrosus; Ether amylnitreux, Ether amylazoteux, Azotite d'Amyl, *Fr.;* Amylium Nitrosum, *P. G.;* Amynitrit, *G.;* Etere isoamilnitroso, *It.;* Nitrito de amilo, *Sp.*

This substance, which was discovered by Balard in 1844, should not be confounded with *amyl nitrate,* $C_5H_{11}NO_3$, which is not used as a medicine.

Preparation.—Amyl nitrite may be prepared by passing a stream of nitrous acid (hyponitric acid) gas through purified amyl alcohol at a temperature of 132° C., or by acting upon amyl alcohol with nitric acid, as originally suggested by Balard. The amyl alcohol should always first be purified by agitating it with an equal bulk of strong solution of common salt, then distilling in a retort with a thermometer, collecting what comes over between 125° C. and 140° C., and redistilling this until it has a boiling point near 132° C. The purified alcohol should be mixed with about an equal bulk of nitric acid in a capacious glass retort, being gradually heated until it approaches boiling, when the fire is to be removed. As soon as a thermometer inserted into the tubulures rises above 100° C. the receiver is changed, because both ethyl-amylic ether and amyl nitrate at such temperatures come over freely and would contaminate the product. The distillate obtained below 100° C. is agitated with a solution of potassium carbonate, and the oily liquid which separates is very slowly heated in a clean retort to 96° C., then the receiver is changed and the distillate collected as before, until the thermometer reaches 100° C. That which comes over between the two temperatures is pure amyl nitrite. It is essential to this process that in every case the heating be very gradual.

Amyl nitrite is also manufactured by distilling a mixture of amylic alcohol, sodium nitrite, and diluted sulphuric acid,

$$2C_5H_{11}OH + 2NaNO_2 + H_2SO_4 = 2C_5H_{11}NO_2 + Na_2SO_4 + 2H_2O.$$

Other methods of preparation will be found in the *U. S. D.*, 20th edition, page 140. W. H. Greene (*A. J. P.*, 1879, p. 65) shows that *nitropentane* (an isomer of amyl nitrite) is almost invariably a constituent of amyl nitrite, and he believes that commercial amyl nitrite is frequently put upon the market unrectified, specimens examined having boiling points varying from 70° C. to 180° C. J. M. Francis examined amyl nitrite of commerce in 1905 and found many samples of inferior grade. He stated that 80 per cent. of the total volume should distil between 90° C. and 100° C.

Dustan and W. Lloyd Williams (*P. J.*, 1888, p. 487) have shown that the supposed pure amyl nitrite is a mixture of α-amyl nitrite and β-amyl nitrite, arising from the fact that the amyl alcohol used is always a mixture of α-amyl alcohol and β-amyl alcohol in varying proportions. They find the α-amyl nitrite to be optically inactive and to boil at 97° C., while β-amyl nitrite has dextro-rotatory power and boils at about 94° C. Much of the commercial amyl nitrite also contains isobutyl nitrite, boiling at 67° C. It is a question whether the physiological action of commercial amyl nitrite is really due to the amyl nitrite or to impurities, especially to the isobutyl nitrite, but the experiments of Brunton and Bokenham (*P. J.*, xix, 490) indicated that the commercial, impure nitrite is stronger than either pure α- or β-amyl nitrite. According to Bals and Broglio, the *tertiary amyl nitrite* differs from amyl nitrite in not giving rise to toxic symptoms, and in being slightly hypnotic.

Description and Physical Properties.—"A clear, yellowish liquid, having a peculiar, ethereal, fruity odor, and a pungent, aromatic taste. It is volatile even at low temperatures, and is inflammable. Amyl Nitrite is almost insoluble in water, but is miscible with alcohol and with ether.

"Specific gravity: 0.865 to 0.875 at 25° C. Add 2 cc. of sulphuric acid to a mixture of 2 drops of Amyl Nitrite and 2 drops of water: amyl valerate is produced, recognized by its odor on dilution with water. Add a few drops of Amyl Nitrite to a mixture of 1 cc. of ferrous sulphate T.S. and 5 cc. of diluted hydrochloric acid: a greenish-brown is produced.

"Mix 1 cc. of normal sodium hydroxide and 10 cc. of distilled water with a drop of phenolphthalein T.S. in a glass-stoppered cylinder, and add 5 cc. of Amyl Nitrite. After inverting the cylinder a few times, the red tint of the aqueous layer is still perceptible (*free acid*). To a mixture of 1.5 cc. of silver nitrate T.S. and 1.5 cc. of alcohol, add a few drops of ammonia T.S. until the precipitate first formed is redissolved. Then add 1 cc. of Amyl Nitrite, and gently heat for one minute: the mixture does not become brown or black (*aldehyde*).

"Preserve in hermetically-sealed glass bulbs, or in tightly-stoppered vials, in a cool place, protected from light." *U. S.*

"A volatile liquid of a yellowish color, fragrant odor, and not more than the faintest acid reaction. Almost insoluble in *water;* soluble in *alcohol* (90 per cent.) in all proportions. Specific gravity 0.870 to 0.880. Not less than 90 per cent. distils below 100° C. A mixture of 5 volumes with sufficient *alcohol* (90 per cent.) to form 100 volumes yields a liquid of which a portion tested in a nitrometer as described under 'Spiritus Ætheris Nitrosi' yields not less than 7.9 times its volume of nitric oxide gas. On shaking with an equal volume of *solution of sodium hydroxide* the aqueous portion acquires not more than a pale yellow color (limit of aldehyde). Remains transparent when cooled to 0° C. (absence of water)." *Br.*

Assay.—"Transfer about 3 cc. of Amyl Nitrite, which has been previously shaken with 0.5 Gm. of potassium bicarbonate and carefully decanted, to a 100 cc. flask, tared with about 20 cc. of alcohol, and weigh accurately. Add sufficient alcohol to bring the volume to exactly 100 cc., and mix thoroughly. Introduce into a nitrometer, page 437, exactly 10 cc. of the alcoholic solution, wash any adhering Amyl Nitrite into the nitrometer with 5 cc. of alcohol, followed by 10 cc. of potassium iodide T.S., and afterwards by 5 cc. of diluted sulphuric acid. When the volume of gas has become constant (in about thirty to sixty minutes), note the amount collected, multiply this volume in cc. by 4.8, and divide the product by the weight of the Amyl Nitrite taken. At standard temperature and pressure, the quotient represents the percentage of Amyl Nitrite in the liquid. The temperature correction is 1/273 of the total percentage just found for each degree, additive if the temperature is below 25° C., and subtractive if it is above 25° C. The barometric correction is 1/760 of the total percentage just found for each millimeter, additive if it is above 760 mm., and subtractive if it is below 760 mm." *U. S.*

Uses.—Physiologically, amyl nitrite acts precisely like sodium nitrite (see *Sodii Nitris*), except that it is much quicker and more evanescent. Amyl nitrite is used in medicine for three purposes: To relax spasms in the arteries, to control convulsions, and for the relief of the asthmatic paroxysm. In all its usages it is to be borne in mind that its action while extremely rapid is very fleeting and it is therefore of service only where an immediate effect is desired. In the circulatory conditions in which it is of service the most important is *angina pectoris.* This disease is probably associated with spasms of the coronary arteries, but whatever be its pathology, clinical experience has demonstrated the extreme value of inhalations of amyl nitrite. In convulsive disorders, amyl nitrite is of service only when it is necessary to cause immediate relaxation; thus in *tetanus,* because of the duration of the convulsive tendency, the fugaciousness of its action renders it of relatively small service; on the other hand, in *strychnine poisoning,* by restraining the convulsions long enough for more durable motor depressants to act, it may prove a life-saving remedy. In ordinary *epilepsy* it is of little service, but in that condition known as *status epilepticus* in which the patient passes from one convulsion to another, the drug may be of great benefit. Again, in those occasional cases of epilepsy in which the seizure is preceded by an aura of sufficient length, if the patient carry in the pocket pearls of amyl nitrite and inhale the vapor as soon as the aura commences the paroxysm may usually be aborted. In many cases of *asthma* it will cause an immediate, if only temporary, cessation of the paroxysm. Whether this effect is due to the action of the nitrite radical upon the circulation or whether it is the result of some narcotic effect of the amyl group is at present uncertain.

The claim of Hare that amyl nitrite is of great value for the relief of *hemoptysis* has been confirmed by a number of observers. (See *B. M. J.*, July 15, 1911.) Its action in this condition is probably the result of dilatation of the splanchnic and contraction of the pulmonary blood-vessels.

Amyl nitrite is generally administered by inhalation, usually in doses of from three to five drops, although much larger quantities have been given without bad results. The rule is to commence with three drops on a handkerchief held close to the nose, and then gradually to increase *pro re nata.* The handkerchief should always be withdrawn so soon as the face flushes or the heart begins to become excited, as the effects always increase for some time, even if no more be inhaled. The best method, however, of administering the very volatile liquid is by the use of glass pearls—small flask-shaped vessels containing two, five, or ten minims of the nitrite; these are crushed in a handkerchief or towel when wanted for inhalation, the thin and fragile glass causing no inconvenience. The drug may also be given by the mouth.

When inhaled in doses of from five to ten drops, amyl nitrite produces in man violent flushing of the face, accompanied with a feeling as though the head would burst, and a very excessive action of the heart. Along with these symptoms, after a larger quantity, there is a sense of suffocation, and more or less marked muscular weakness. We know of no case of serious poisoning from amyl nitrite in man.

Dose, from three to five minims (0.2–0.3 cc.), if given by mouth it may be dissolved in alcohol.

AMYLUM. U. S., Br.

STARCH Amyl. [Corn Starch]

"Starch consists of the granules separated from the grain of *Zea mays* Linné (Fam. *Gramineæ*). Starch contains but a trace of organic foreign matter and yields not more than 0.5 per cent. of ash, and not more than 14 per cent. of moisture." *U. S.* "Starch is procured from the grains of (1) common wheat, Triticum sativum, *Lam.;* (2) maize, Zea Mays, *Linn.;* and (3) rice, Oryza sativa, *Linn.*" *Br.*

Amylum, *P. G.;* Amylum Zeæ, Wheat Starch; Amidon, Fécule, Empois, *Fr.;* Stärkmehl, Stärkes, Kraftmehl, Maisstärke, Weizenstärke, *G.;* Amido, *It.;* Almidon, *Sp.*

Starch is a proximate vegetable principle contained in most plants and especially abundant in the various grains, such as corn, wheat, rye, and barley; in seeds, as peas, beans, chestnuts, acorns, etc.; and in numerous rhizomes and tuberous roots, as those of the potato, the sweet potato, the arrow-root, canna, cassava, sago, yam, curcuma and erythronium. The starch is always in the form of grains, which are contained within the parenchymatous cells, and is procured by reducing the substances in which it exists to a state of minute division, agitating or washing them with cold water, straining or pouring off the liquid, and allowing it to stand till the fine grains which are held in suspension have subsided. This, when dried, is starch, more or less pure, according to the care taken in conducting the process. In the U. S. P. of 1880 the official starch was that derived from wheat, but in the revision of 1890 corn starch was recognized, and has been since. In most of the European Pharmacopœias the official starch is derived from wheat. In some of them rice is also recognized. The starch of European commerce is largely obtained from the potato, while in the United States corn starch is almost exclusively in use, wheat and rice starch coming next in importance. For a description of the differences, see page 132.

Properties.—Starch is white, inodorous and tasteless, pulverulent, opaque, and, as found in commerce, is usually in columnar or irregular angular masses (wheat starch), which are easily reduced to powder, which produces a peculiar sound when pressed between the fingers. Its specific gravity is 1.505 at 19.4° C. (Payen.) It is composed of minute microscopic granules, in starch from the same plant nearly uniform in size, more or less plainly striate, and having a distinct hilum or point of origin of growth. In the different species of plants the starch granules differ in their characteristic forms. When exposed to a moist air, it absorbs a considerable quantity of water, which may be driven off by a gentle heat. It is insoluble in alcohol, ether, and cold water, but unites with boiling water, which, on cooling, forms with it a soft, semi-transparent paste or a gelatinous, opaline solution according to the proportion of starch employed. The paste placed on folds of blotting-paper, renewed as they become wet, loses water, contracts, and assumes the appearance of horn. If the proportion of starch be very small, the solution, after slowly depositing a very minute quantity of insoluble matter, continues permanent, and upon being evaporated yields a semi-transparent mass, which is partially soluble in cold water. The starch has, therefore, been modified by the combined agency of water and heat; nor can it be restored to its original condition. Heating with glacial acetic acid to 100° C., or with glycerin to 190° C., will also make starch soluble.

Corn starch is officially described as:

"In irregular, angular white masses or in fine powder; consisting chiefly of polygonal, rounded or spheroidal starch grains from 0.003 to 0.035 mm. in diameter and usually with a lenticular or 3- to several-rayed central cleft; inodorous; taste characteristic, slight. Starch is insoluble in cold water and in alcohol. The individual grains of Starch are colored a deep blue by iodine T.S. Boil 1 Gm. of Starch with 15 cc. of water: upon cooling, a translucent, whitish jelly forms. Triturate about 0.5 Gm. of Starch with 5 cc. of distilled water: the mixture is neutral to litmus paper. Add 10 cc. of distilled water to 1 Gm. of Starch, and acidify with 0.5 cc. of hydrochloric acid: the mixture should show no blue color within five minutes on the addition of 3 drops of potassium ferrocyanide T.S. (*iron*)." *U. S.*

"In fine powder or in irregular angular or columnar masses, which are readily reduced to powder; white, inodorous. Cold *water* mixed with an equal weight of Starch does not become more than faintly acid or alkaline to *litmus.* Boiled with *water* and cooled, it gives a deep blue color with *N/10 solution of iodine.* Under the microscope the several varieties of Starch present the following characters:—1. Wheat Starch: A mixture of large and small granules, the former lenticular in shape, and marked with faint concentric striæ surrounding a nearly central hilum. 2. Maize Starch: Granules more uniform in size, frequently polygonal, somewhat smaller than the large granules of wheat starch, and having a very distinct hilum, but without evident concentric striæ. 3. Rice Starch: Granules extremely minute, nearly uniform in size, polygonal, without evident hilum or striæ. Starch is free from granules other than those described." *Br.*

At a temperature of 160° C. for air-dried starch, and 200° C. for starch previously dried at 100° C., it is changed into dextrin, and at 200° C. to 215° C. forms a transparent fused mass, which consists exclusively of dextrin (Payen); at 220° C. to 230° C. it undergoes further change and yields chiefly *pyrodextrin,* a brown, tasteless, and odorless compound, readily soluble in water, insoluble in alcohol and ether. (Gelis, *Ann. Ch. Phys.,* (3) lii, 388.)

Composition and Nature.—The formula of starch is generally taken as $C_6H_{10}O_5$, or a multiple of this. This formula does not give us a clear idea of the nature of the starch grain. It consists of at least two or three substances. The wall or membrane is very distinct and clearly differentiated from the rest of the grain. The inner portion consists of two substances which are distributed in alternate layers. The one is colloidal, taking up aniline stains, and the other is made up of soluble starch. (See Kraemer, *A. J. P.,* 1907, pp. 217 and 412; 1914, p. 81.)

Recent determinations of its molecular weight by Brown and Morris make it as high as $5(C_{12}H_{20}O_{10})_{20}$. Iodine forms with starch, whether in its original state or in solution, a blue compound; and a solution of iodine is the most delicate test for its presence. The color varies somewhat according to the proportions employed. When the two substances are about equal, the compound is of a beautiful indigo blue; if the iodine be in excess, it is blackish-blue; if the starch, violet blue. This reaction is not altogether characteristic of starch; Barger and Starling (*P. J.,* 1912, xcii, 146) have compiled a list of over sixty organic substances which give a blue color with iodine. A singular property of starch iodide is that its solution becomes colorless if heated to about 93.5° C., and afterwards recovers its blue color upon cooling. By boiling, the color is permanently lost, while Puchot states that certain nitrogenized organic bodies, as albumin, prevent the reaction of iodine on starch or destroy it. Alkalies unite with starch, forming soluble compounds, which are decomposed by acids, the starch being precipitated. It is thrown down from its solution by lime water and baryta water, forming insoluble compounds with these earths. The solution of lead subacetate precipitates it in combination with the oxide of the metal. Starch may be made to unite with tannin by boiling their solutions together; and a compound results, which, though retained by the water while hot, is deposited when it cools. By long boiling with diluted sulphuric, hydrochloric, or oxalic acid, it is converted into dextrin and dextrose. A similar conversion into dextrin and glucose is effected by means of diastase, which change can be represented as taking place in several stages:

$$3C_6H_{10}O_5 + H_2O = \underset{\text{Dextrin}}{C_{12}H_{20}O_{10}} + \underset{\text{Dextrose}}{C_6H_{12}O_6}$$

$$C_{12}H_{20}O_{10} + H_2O = \underset{\text{Maltose}}{C_{12}H_{22}O_{11}}$$

$$C_{12}H_{22}O_{11} + H_2O = \underset{\text{Dextrose}}{2C_6H_{12}O_6}$$

Many observers claim to recognize the production of other intermediate substances, as *amylodextrin* (soluble starch), *erythrodextrin, achroodextrin, maltodextrin,* none of which reduce Fehling's solution, followed by *maltose,* which does reduce Fehling's solution. Strong hydrochloric and nitric acids dissolve starch; and the latter acid, by the aid of heat, converts it into oxalic and malic acids. By the action of strong nitric, sulphuric, or crystallizable acetic acid, used with certain precautions, the starch is rendered soluble, and may be obtained in this state by separating the acid by means of alcohol. By the continued action of concentrated sulphuric acid it is decomposed. When it is dissolved in strong nitric acid, and precipitated by water, a white powder is thrown down, called *xyloidin,* $C_6H_9(NO_2)O_5$ (Braconnot), in which one atom of the hydrogen of the starch is replaced by one group, NO_2, furnished by the nitric acid. Leulier (*J. P. C.,* 1918, xviii, 291) makes soluble starch by boiling together for fifteen minutes a mixture of 100 Gm. of 95 per cent. alcohol, 5 Gm. of sulphuric acid and 25 Gm. of starch. It is then transferred to a filter and washed with cold water or alcohol until free from acid. The product thus obtained is a white powder, insoluble in cold water but readily soluble in warm water. Mixed with hot water and exposed to a temperature of 27° C., starch undergoes chemical changes, which result in the formation of several distinct principles, among which are sugar, a gummy substance (perhaps dextrin), and a soluble modification of starch. With yeast, starch undergoes the vinous fermentation, being, however, first converted into sugar. All plants which contain chlorophyll have the power of using the chemical rays of sunlight in producing from carbon dioxide and water a substance which is organic. There is first formed in the center of the chlorophyll granule a minute speck, which is believed to be starch; this new starch granule is incapable of solution, but by conversion into sugar or dextrin is rendered soluble, and in this form is carried in the juices of the plant. One of two destinies there awaits it. It may be converted into the permanent compound cellulose which constitutes the woody tissue, or it may be reconverted to its original form and be deposited in the buds, seeds, barks, roots or rhizomes of the plant. These stores of starch are usually accumulated for future growth, and are especially seen in plants which flower in the spring before the leaves are put forth, or which reproduce the species without seeding.

The structure and nature of the starch granule has been the subject of much investigation and discussion. Its microscopic appearance supports, but of course does not prove, the original theory advanced by Schleiden, that it is composed of concentric layers of similar chemical composition, in which the outer layer has been the first formed while the inner layers have been successively deposited in its interior. The microscopic characters, however, are just as readily explained on the theory that the central layer was the first formed and that the peripheral layers have been deposited around the point of the hilum. This view, originally advanced by Fritsche in 1834, has been widely supported by various observers. Other authorities have come to the conclusion that the starch grains grow as do ordinary vegetable cells, but the theory brought forward in 1880 by Schimper, that all starch grains develop within plastids, *i.e.*, in protoplasmic masses or cells, and that in starch which is stored, the leucoplastids finally disappear, is the theory which has been of recent times most widely believed and is probably correct. In stating his views, Schimper further came to the conclusion that the outer portion of the grain is the part most recently produced. That there is a marked difference in the layers of the starch grains is shown by the varying effects of staining reagents, certain parts of the grains being much more affected by safranin and gentian-violet than others. It would further appear that though the starch layers each contain colloidal substances besides crystalloidal cellulose, the proportion of their constituents varies so much that the alternate layers are different, one set being colloidal and others crystalloidal, in their general nature. For details see Kraemer, *Botan. Gaz.*, xxiv, Nov., 1902; also *Proc. Am. Philosoph. Soc.*, xli.

Varieties.—Starch, as obtained from different substances, is somewhat different in its characters. *Wheat starch,* when examined with a microscope, is found to consist of more or less rounded or biscuit-shaped grains, from 0.005 to 0.035 mm. in diameter, the smaller being spheroidal, the larger rounded and flattened, and are without distinct markings, except when heated with chemical solutions. The granules are mixed with loose integuments, resulting from the process of grinding. This variety of starch has a certain degree of hardness and adhesiveness, owing, according to Guibourt, to the escape of a portion of the interior substance of the broken granules, which attracts some moisture from the air, and, thus becoming glutinous, acts as a bond between those which remain unbroken. Another opinion attributes this peculiar consistence to the retention of a portion of the gluten of the wheat flour, which causes the granules to cohere. The granules of *maize starch* are very small, with a diameter not exceeding, according to Payen, one-sixth of that of the potato, and little more than one-half of that of the wheat granules. They have a very distinct hilum which is either circular or in the form of a 3- to 5-rayed cleft, but no evident concentric striæ. *Rice starch* has extremely minute granules, nearly uniform in size, polygonal, without evident hilum or striæ. *Potato starch* is employed in various forms, being prepared so as to imitate more costly amylaceous substances, such as arrowroot and sago. In its ordinary state it is more pulverulent than is wheat starch, has a somewhat glistening appearance, and may be distinguished with the aid of the microscope, by the size of its granules, which are larger than those of any other known fecula except canna, or *tous les mois.* They are exceedingly diversified in size and shape, though their regular form is said to be ovate or shell-shaped, the grains varying from 0.005 to 0.125 mm. in long diameter. The characters of other kinds of starch will be given under the heads of the several official substances of which they constitute the whole or a part. According to Chevallier, starch is sometimes adulterated with calcium carbonate and calcium sulphate; and the fraud is also practised of saturating it with moisture, of which it will absorb 12 per cent. without any obvious change.

Several authors have reported upon the value of the micro-polariscope in the examination of commercial starches. (See Ewers, *Zeitschr. f. öffentl. Chem.*, 1908, pp. 8 and 150; Herman, *Bull. Soc. Chim. Belg.*, 1908, p. 340.) For a report on the ultra-microscopic structure of the starches, their constituents and a method of separating the latter, see *C. R. A. S.*, 1908, pp. 285, 599 and 978.

Uses.—Starch is demulcent and, when cooked, nutritive; in the raw state it is scarcely affected by human digestive secretions. Powdered and dusted upon the skin, it is sometimes used to absorb irritating secretions and prevent excoriation. Mixed with water it forms the basis of several pastes used in dermatological practice. Dissolved in hot water, and allowed to cool, it is often employed in enemata, either as a vehicle, or as a demulcent application in irritated states of the rectum; this liquid may also be used as an antidote in iodine poisoning, and given freely in other cases where amylaceous or mucilaginous drinks are indicated. It is also used officially as a diluent for powdered extracts.

Off. Prep.—Glyceritum Amyli, *U. S.* (*Br.*); Pulvis Tragacanthæ Compositus, *Br.*

ANETHOL. N. F.

ANETHOL

"The methyl ether of para-propenyl phenol [$C_6H_4.C_3H_5.OCH_3 = 148.15$]. It is the main constituent in the oils of anise, star anise, and fennel, and is usually obtained from these by fractionating, chilling and crystallizing." *N. F.*

This principle is recognized by the N. F., as it is used in a number of preparations to impart the anise flavor.

Description and Physical Properties.—"Anethol is a colorless or faintly yellow, highly refractive liquid at a temperature of 23° C. or above, having a sweet taste and the aromatic odor of anise. At from 20° to 21° C. it solidifies to a white glistening, crystalline mass which remelts at from 22° to 23° C.

"Anethol is almost insoluble in water, readily soluble in ether or chloroform, and forms a clear solution with two volumes of alcohol. Specific gravity: 0.984 to 0.986 at 25° C. Boiling point: 235° to 236° C. Refractive index: 1.558 to 1.561 at 25° C.

"It is optically inactive or shows a deviation of not more than 0.08° in a 100 mm. tube at 25° C., due to a slight trace of the oil from which the Anethol has been prepared (if prepared from oil of anise this deviation will be lævorotatory, if from oil of fennel, dextrorotatory). Shake 10 cc. of Anethol with 50 cc. of a saturated aqueous solution of sodium bisulphite in a graduated cylinder and allow the mixture to stand for six hours. No appreciable diminution in the volume of Anethol will be observed nor does a crystalline deposit separate (*aldehydes*).

"Preserve it in well-stoppered, amber-colored bottles protected from light and air." *U. S.*

For further description, see under *Oleum Anisi.*

Dose, from one to five minims (0.06–0.3 cc.).

Off. Prep.—Elixir Anisi, *N. F.;* Pulvis Rhei et Magnesiæ Anisatus, *N. F.;* Spiritus Ammoniæ Anisatus, *N. F.*

ANETHI FRUCTUS. Br.

DILL FRUIT

"Dill Fruit is the dried ripe fruit of Peucedanum graveolens, *Benth. and Hook. f.*" *Br.*

Garden Dill, Dilly, Anet; Aneth, *Fr. Cod.;* Fenouil puant, *Fr.;* Dill, *G.;* Eneldo, *Sp.*

Peucedanum graveolens (*Anethum graveolens* L.), or garden dill, resembles the fennel plant, but is smaller. It is an annual plant, three or four feet high, with a long spindle-shaped root; an erect, striated, jointed, branching stem; and bipinnate or tripinnate, glaucous leaves, which stand on sheathing footstalks and have linear and pointed leaflets. The flowers are yellow, and in large, flat, terminal umbels, destitute of involucre. The plant is a native of Mediterranean countries and Southern Russia, and is found growing wild in various parts of Africa and Asia. It is cultivated in Germany, Roumania and England and has been introduced into our gardens. The whole plant is aromatic, the leaves are used as a flavor for soups, sauces and pickles. For a paper by J. C. Umney describing the commercial varieties, see *Year Book of Pharmacy,* 1898, 374. The seeds, as the fruit is commonly called, are the only part used. They are "composed of two mericarps usually separate and freed from the pedicel; each broadly oval, about four millimetres long, and two to three millimetres broad; brown; very strongly compressed dorsally; dorsal ridges inconspicuous, but the lateral ridges prolonged into paler brown wings. In transverse section, six vittæ in each mericarp. Odor and taste agreeably aromatic." *Br.* The latter property depends on a volatile oil, which is present in the fruits to the extent of 2.8 to 4 per cent. (See *Oleum Anethi.*) The bruised fruits impart their virtues to alcohol and to boiling water.

Indian dill fruit (*P. Sowa* Kurz) has recently appeared on the European market as a substitute for the genuine article. It may be distinguished from true dill fruit by being narrower and more convex, by the mericarps being usually coherent and by the pale color of the dorsal ridges of the mericarps.

Uses.—Dill seeds have the properties common to the aromatics, but are very seldom used in this country. They may be given in powder or infusion.

Dose, of the fruit, from fifteen grains to a drachm (1–3.9 Gm.).

Off. Prep.—Aqua Anethi, *Br.*

ANGELICÆ FRUCTUS. N. F.

ANGELICA FRUIT Angel. Fruct.
[Angelica Seed]

"Angelica Fruit is the dried ripe fruit of *Angelica Archangelica* Linné and of other species of *Angelica.* (Fam. *Umbelliferæ.*) Angelica Fruit contains not more than 3 per cent. of foreign fruits, seeds or other foreign organic matter." *N. F.*

Off. Prep.—Pilula Antiperiodica, *N. F.;* Pilula Antiperiodica sine Aloe, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.*

ANGELICÆ RADIX. N. F.

ANGELICA ROOT Angel. Rad.

"Angelica Root consists of the dried rhizome and roots of *Angelica Archangelica* Linné and of other species of *Angelica.* (Fam. *Umbelliferæ.*) Angelica Root contains not more than 5 per cent. of its stem basis or other foreign organic matter and yields not more than 4 per cent. of acid-insoluble ash." *N. F.*

Angelique, *Fr. Cod.;* Racine d'Angelique, *Fr.;* Radix Angelicae, *P. G.;* Engelwurzel, *G.*

Two species of this genus are used in medicine, the *Angelica Archangelica* L. (*Garden Angelica*), a native of Europe, and the *A. atropurpurea* (*Masterwort*), which grows throughout the eastern United States. *Garden angelica* has a long, thick, fleshy, biennial root, furnished with many rootlets, and sending up annually a hollow, jointed, round, channelled, smooth, purplish stem, which rises five feet or more in height, and divides into numerous branches. The leaves are twice pinnate, and the flowers, which are greenish-white, are borne in compound umbels. The plant is a native of Europe and Asia and is commonly found in the high mountainous regions in the southern section of Europe, as in Switzerland and among the Pyrenees. It is often cultivated. The whole plant is aromatic, but the root only is official in the Swiss, Austrian, and German Pharmacopœias, while the fruit is official in the N. F. Angelica root is imported chiefly from Hamburg and London. The root should be dug up in the autumn of the first year, as it is then least liable to become mouldy and worm eaten. It is spindle-shaped, 4 to 6 cm. thick at the crown, and beset with long descending rootlets. The fresh root has a yellowish-gray epidermis, a freshly yellow parenchyma, and when wounded yields a honey-colored juice, having all the aromatic properties of the plant. The dried root is grayish-brown and much wrinkled externally, whitish and spongy within, and breaks with a starchy fracture, exhibiting shining resinous masses. It is very apt to be attacked by insects, and should be conserved by the addition of a few drops of chloroform or carbon tetrachloride.

Description and Physical Properties.—"*Unground Angelica Root.*—Rhizomes short and thick, 5 to 10 cm. long, sometimes split, frequently crowned with leaf and stem bases; roots numerous, 10 to 20 cm. long, 5 to 7 mm. thick at the base and gradually tapering to about 1 mm., frequently twisted or braided together; externally dark gray-brown to reddish or purplish brown; with deep furrows; fracture smooth and short. Odor aromatic; taste sweetish, pungent, aromatic, and bitter.

"*Structure.*—Bark, spongy, nearly as wide as the wood zone and with radial rows of brownish oleoresin canals; parenchyma of cortex with numerous starch grains; wood rays finely porous and more narrow than the medullary rays; pith distinct in the rhizome, absent in the root.

"*Powdered Angelica Root.*—Yellowish-brown; numerous, mostly simple, irregularly rounded starch grains up to 0.008 mm. in diameter, sometimes with a cleft at the center and occasionally two or more compound; tracheæ or fragments of tracheæ up to 0.075 mm. in width, with reticulate markings or large simple pores; brownish oil canals or fragments thereof, up to 0.250 mm. in width, sometimes with adjoining epithelial cells; fragments of parenchyma tissue with some of the cells filled with starch; fragments of large brownish cork cells; wood-fibers with thin walls and often with oblique markings; yellowish oil globules." *N. F.*

It has a strong odor and a warm aromatic taste. The juice of the recent root is acrid, and is said to be poisonous; but the acridity is dissipated by drying.

The constituents of the root are *angelic acid,* $C_5H_8O_2$, a monatomic acid of the acrylic series, valeric acid, $C_5H_{10}O_2$, resin, bitter principle, tannin, pectin, malic acid, sugar, starch and a volatile oil consisting largely of phellandrene. For further information concerning the constituents of this drug, see *U. S. D.,* 19th ed., p. 1386. *Schim. Rep.,* 1902, 15; 1911, 21; 1913, 26.

The *fruit* is officially described as follows: "*Unground Angelica Fruit.*—Cremocarps oval, externally pale yellowish brown, 4 to 8 mm. long, 3 to 6 mm. broad, 1 to 2 mm. thick; the base faintly notched; apex bearing 5 minute calyx-teeth and remains of the style; mericarps joined, or separate; each mericarp nearly flat on one surface, the latter bearing a central longitudinal groove, margins sharp, slightly upturned, convex upon the other surface and with 3 strong longitudinal ribs, the latter separated from one another by narrow grooves and from the margin by broader grooves; pericarp soft, tough and spongy; single-seeded. Odor characteristic and agreeable; taste aromatic, pungent, and sweetish.

"*Structure.*—Transverse sections of the mericarp pentangular in outline, the angles formed by the ribs which project outward, often 0.500 mm. or more; four of the sides of the mericarp being almost equal in length, the fifth or commissural surface being about three times as long as one of the dorsal sides and concave near the middle; a distinct fibrovascular bundle at each angle; epidermis composed of cells with the outer walls slightly thickened and rarely modified into short one-celled hairs; pericarp composed chiefly of soft spongy parenchyma and 10 to 30 oil-tubes, the latter situated close to the inner epidermis; seed coat thin with a yellowish brown pigment and enclosing an endosperm made up of parenchyma containing numerous fixed oil globules and aleurone grains, the latter containing rosettes of calcium oxalate.

"*Powdered Angelica Fruit.*—Light-brown; exhibiting numerous fragments of the characteristic spongy parenchyma with cells having many large simple pores; yellowish-brown pieces of the oil-tubes; fibro-vascular bundles and endosperm parenchyma containing fixed oil, and aleurone grains, the latter with rosettes, up to 0.011 mm. in diameter." *N. F.*

Angelica Fruit comes to the United States from Belgium, France and England. Most of it is used by essential oil firms.

Uses.—Angelica is one of those survivals of ancient superstition which attributed medicinal properties to so many aromatic herbs. The potency of the drug may be estimated by the fact that in Europe the root and stem are candied and eaten as a conserve.

There is probably no essential difference in the therapeutic value of the European and American species nor, indeed, is there any sufficient reason for believing that either drug possesses any therapeutic virtues beyond that of the mild aromatics.

Angelica root has been used as an aromatic in *flatulent colic* and also as a domestic diaphoretic and diuretic, and, occasionally externally as a counterirritant. The seeds were at one time supposed to possess *antimalarial* properties and are an ingredient of the *Tinctura Antiperiodica. N. F. From the fruit;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloe, *N. F.;* Tinctura Antiperiodicæ, *N. F.;* Tinctura Antiperiodicæ sine Aloe, *N. F.*

Dose, of either root or seeds, from fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Fluidextractum Angelicæ Radicis, *N. F.*

ANISUM. N. F. (Br.)

ANISE Anis. [Anise Seed]

"Anise is the dried ripe fruit of *Pimpinella Anisum* Linné (Fam. *Umbelliferæ*). Anise contains not more than 3 per cent. of other fruits, seeds or foreign organic matter and yields not more than 1.5 per cent. of acid insoluble ash." *N. F.* "Anise Fruit is the dried ripe fruit of Pimpinella Anisum, *Linn.*" *Br.*

Anisi Fructus, *Br.;* Fructus (Semen) Anisi, s. Anisi vulgaris; Aniseed, Anny, Aneys, Annyle; Anis, Anis vert, Graines d'Anis, *Fr.;* Fructus Anisi, *P. G.;* Anissame, Anis, *G.;* Anice, Anace, Semi d'Aniso, *It.;* Anis (Fruto de), Simiente de Anis, *Sp.;* Anison, *Ar.*

Pimpinella Anisum is an annual plant, about a foot in height, with an erect, smooth and branching stem. The leaves are petiolate, the lower roundish-cordate, lobed, incised-serrate, the middle pinnate-lobed with cuneate or lanceolate lobes, the upper trifid, or undivided, linear. The flowers are small white, and in terminal compound unbels, destitute of involucres. The fruit is a mouse-shaped cremocarp.

The anise plant is a native of Egypt and the Levant, but has been introduced into Southern Europe and is cultivated in all warm climates, especially Germany, Russia, Italy, Spain, France, Turkey, India, Japan and Chili. It is also cultivated occasionally in the gardens of this country. The Spanish, or Alicante, anise is smaller than the German or French, and is usually preferred; the Russian fruit is very short. It is said also to be extensively cultivated in India and South America, although we are not aware that the product ever comes into American commerce. Over a million pounds of anise enter the United States annually, most of it coming from Malaga, Spain. Smaller quantities were imported from Barcelona and London. That from London represented the Russian variety.

It is one of the oldest aromatics, having been used by the ancient Egyptians, and is spoken of by Theophrastus and cultivated in the imperial German farms of Charlemagne. In 1305 Edward I granted a patent giving the right to levy tolls upon it at the Bridge of London for the purpose of repairing the bridge.

Description and Physical Properties.—"*Unground Anise.*—Cremocarp broadly oval, laterally compressed; 3 to 6 mm. long and 2 to 3 mm. wide; mericarps usually cohering and attached to a slender pedicel 2 to 12 mm. long; apex with a ring-like disc and two projecting, diverging styles; externally grayish or greenish-gray, seldom grayish-brown, slightly pubescent; each mericarp with 5 light-brown, filiform ridges. Odor and taste agreeable and aromatic.

"*Structure.*—Epidermal layer with numerous papillæ and short, one-celled, non-glandular hairs having very thick papillose walls; primary ribs each with a small vascular bundle, surrounded by a few fibers; from 15 to 45 oil tubes extending as a more or less interrupted circle in the tissues of the mesocarp on the dorsal side of each mericarp and 2 large oil tubes on the commissural side; inner epidermis of pericarp consisting of a layer of narrow, tangentially elongated thin-walled cells except near the middle line of the commissural side where the cells may have thick porous or reticulate walls and some adjacent cells in the mesocarp may be thick-walled and porous, resembling stone cells; the seed coat of one layer of cells with thickened, yellowish-brown, inner walls, closely unites with the epidermis of the pericarp except where separated by a large cavity along the commissural side; endosperm chiefly of polygonal, thick-walled cells filled with spherical or ellipsoidal aleurone grains.

"*Powdered Anise.*—Yellowish-brown; numerous irregular fragments of pericarp showing portions of the yellowish oil tubes; fragments with tracheæ and fibers of carpophore; cells of endosperm filled with aleurone grains, the latter about 0.006 mm. in diameter and usually enclosing a rosette aggregate of calcium oxalate about 0.004 mm. in diameter; non-glandular hairs 1-celled, 0.025 to 0.200 mm. long, either straight or curved and with numerous, slight, centrifugal projections on the outer surface.

"Heat 1 Gm. of anise with 10 cc. of potassium hydroxide T.S.; no mouse-like odor develops (absence of fruits of *Conium maculatum*)." *N. F.*

"Ovoid, somewhat compressed laterally; about five millimetres long and two millimetres broad. Mericarps usually united and attached to the pedicel. Rough from the presence of short, bristly hairs. Greenish-grey or greyish-brown; primary ridges pale, slender and entire. In transverse section, numerous vittæ in each mericarp; commissural surface of the endosperm not deeply grooved. Agreeably aromatic odor; taste aromatic and sweet. Ash not more than 11 per cent." *Br.*

Their odor and taste, which depend upon a peculiar volatile oil existing to the extent of from 1.5 to 3.5 per cent., are imparted sparingly to boiling water, but freely to alcohol. (See *Oleum Anisi.*) The endosperm of the fruit contains a bland fixed oil. By expression, a greenish oil is obtained, which is a mixture of the two. The fruits are sometimes adulterated with fine gravel and small fragments of an argillaceous earth which resembles them in color. This accounts for the fact that the amount of ash may run as high as 30 per cent., greatly exceeding the official requirements. Their aromatic qualities are occasionally impaired by a slight fermentation, which they are apt to undergo in the mass, when collected before maturity. Russian anise is sometimes admixed with as much as 30 per cent. of coriander. Anise is also contaminated with weed seeds and stems of the anise plant. Occasional shipments of anise are found adulterated with exhausted fruits.

The Italian anise not infrequently is admixed with from 2 to 10 per cent. or even 50 per cent. of the fruits of conium. A case of poisoning is on record from the accidental admixture of the fruits of *Conium maculatum,* which latter may be distinguished by their crenate or notched ridges and the absence of oil tubes; by their mericarps being smooth, grooved upon the face, and having crenate or notched ridges with wrinkles between them. The conium fruits are, moreover, broader in proportion to their length, and are generally separated into half fruits (or single mericarps), while those of anise are whole (double mericarps).

Star aniseed, the *Cardamomum Siberiense* or *Annis de Sibérie* of the seventeenth century and the *badiane* of the French writers, is the product of *Illicium verum* Hook. f., Gaertn., and is fully described under the heading *Illicium,* Part II. They contain about 4 per cent. of a volatile oil very closely resembling that of anise. There are no known chemical differences between these oils, although dealers distinguish them by their odor and taste.

Ruschenberger has shown that oil of anise has a remarkable power of masking the odor of potassium sulphide; a drop of the oil having entirely deprived of offensive odor a drachm of lard with which five grains of the sulphide had been incorporated. (*Am. J. M. S.,* N. S., xlviii, 419.)

Uses.—Anise is a grateful aromatic carminative and may be used in flatulent *colic.* The oil is usually preferred, in this country.

Dose, eight to fifteen grains (0.5–1.0 Gm.).

Off. Prep.—Aqua Anisi, *Br.;* Species Laxativæ, *N. F.;* Species Pectorales, *N. F.;* Tinctura Rhei Dulcis, *N. F.*

ANTHEMIDIS FLORES. Br.

CHAMOMILE FLOWERS [Chamomile, English Chamomile, Roman Chamomile]

"Chamomile Flowers are the expanded flowerheads of Anthemis nobilis, *Linn.,* collected from cultivated plants, and dried." *Br.*

Anthemis, *U. S. VIII;* Flores Chamomillæ Romanæ, Roman, Low, Garden, White or English Chamomile, Chamomile Flowers, Camil, Camovyne, Whig-plant; Camomille Romaine, *Fr.;* Flos Chamomillae, *P. G.;* Römische Kamille, *G.;* Camomilla Romana, Camomilla Ingleses, *It.;* Manzanilla (Flor de), Manzanilla Romana, *Sp.*

The term "Chamomile" has been applied to several aromatic plants and it is therefore important always to distinguish by adjectives which variety of chamomile is desired or, better yet, avoid the use of the English name altogether. In this country the only chamomile at present officially recognized is the so-called German chamomile (see *Matricaria*); in Europe the Roman chamomile seems to be more popular.

Several species of anthemis have been employed in medicine. (See below.)

Anthemis nobilis is an herbaceous plant with a perennial root. This plant is a native of Europe, and grows wild in all the temperate parts of that continent. It is also largely cultivated for medicinal purposes. In France, Germany, and Italy, it is generally known by the name of *Roman chamomile.* The stems are from six inches to a foot long, round, slender, downy, trailing, and divided into branches, which turn upward at their extremities. The leaves are bipinnate, the leaflets small, thread-like, somewhat pubescent, acute, and generally divided into three segments. The flowers are solitary, with a yellow convex disk, and white rays. The involucre is of a hemispherical form, and composed of several small imbricated hairy scales. The receptacle is convex, prominent, and furnished with rigid bristle-like paleæ. The ray florets are numerous, narrow and terminated with three small teeth. The whole herb has a peculiar fragrant odor, and a bitter aromatic taste.

By cultivation the yellow disk florets are often converted into the white ray florets. Thus altered, the flowers are said to be *double,* while those which remain unchanged are called *single;* but, as the conversion may be more or less complete, it generally happens that with each of the varieties there are intermingled some flowers of the other kind, or in different stages of the change. The double flowers are generally preferred; though, as the sensible properties are found in the greatest degree in the disc florets, the single flower heads are the more powerful. It is rather, however, in aromatic flavor than in bitterness that the radical florets are surpassed by those of the disk. If not well and quickly dried, the flowers lose their beautiful white color, and are less efficient. The flowers which are largest, most double, and whitest should be preferred.

They are officially described as: "Flowerheads hemispherical, from about twelve to twenty millimetres in diameter, white or pale buff in color. Involucre composed of several rows of oblong bracts with membranous margins; receptacle solid, conical, and densely covered with concave, blunt, narrow, scaly bracts; florets mostly ligulate and white, the ligula possessing four veins and terminating in three teeth. Strong aromatic odor; taste bitter." *Br.*

C. W. Ballard states that this drug is offered as "chamomile" and "Spanish chamomile," and that the U. S. P. IX gives "chamomile" and "wild chamomile" as synonyms of matricaria. He tabulates the chief differences and similarities in wild anthemis, cultivated anthemis and matricaria. (See *J. A. Ph. A.,* 1918, vii, 952.)

The seeds yield by expression a fixed oil, which is said to be applied in Europe to various economical uses.

Though not a native of America, chamomile grows wild in some parts of this country, and is occasionally cultivated in our gardens for family use, the whole herb being employed. The medicine, as found in commerce, consists chiefly of the double flowers, and is imported from Germany and England. From the former country the flowers of *Matricaria Chamomilla* are also occasionally imported, under the name of chamomile. (See *Matricaria.*) In Europe the flowers of *A. arvensis* L. (*corn chamomile*) are sometimes substituted for the official drug.

A. Tinctoria L. has been used as a vermifuge in Europe.

The chief adulterant at present for Roman chamomile is the flower heads of *Anthemis Cotula* L. (*Dog chamomile, Mayweed*), an annual, glabrous herb with a disagreeable odor, indigenous to Europe but widely naturalized in the United States. These flower-heads differ from the genuine article in possessing a more elongated-conical receptacle, neutral, ligulate floret, fimbriate, obovate bracts and rough, 10-ribbed achenes. It was formerly recognized by the U. S. (1870) under the title *Cotula.*

Properties.—Chamomile flowers, as usually found in commerce, are large, almost spherical, of a dull white color, a fragrant odor, and a warmish, bitter, aromatic taste. When fresh, their odor is much stronger, and was fancied by the ancients to resemble that of the apple. Hence the name *chamæmelum* (χαμαί, on the ground, and μῆλον, an apple); and it is somewhat singular that the Spanish name *manzanilla* (a little apple) has a similar derivation. The flowers impart their odor and taste to water and alcohol, the former of which, at the boiling temperature, extracts only one-fourth of their weight.

The sensible, and probably the medicinal properties are due to a volatile oil, which when fresh is blue in color but as commonly seen is greenish or even brown. The investigations of several chemists made in 1878–1879, in Fittig's laboratory at Strassburg, have shown the *oil of chamomile* to contain the following constituents: a fraction distilling at 147° to 148° C. consisting of isobutylic esters and hydrocarbons; *isobutyl angelicate* at 177° C.; *isoamyl angelicate* at 200° to 201° C.; *isoamyl tiglinate* at 204° to 205° C. (both of these esters answering to the formula $C_5H_{11},C_5H_7O_2$). In the residual portion, hexylic alcohol, C_6H_{13}, OH, and an alcohol of the formula $C_{10}H_{16}O$ isomeric with camphor, to which the name of *anthemol* has been given (see *Chem. Cb.*, 1903 (1), 1226), are met with, both probably occurring in the form of esters. By decomposing the angelicates and the tiglinate with potassium hydroxide, angelic acid, $C_5H_8O_2$, and *tiglic acid* (or *methyl-crotonic*), isomeric with the former, are obtained to the extent of about 30 or more per cent. of the crude oil. In the oil examined by Fittig, angelic acid prevailed; from another specimen E. Schmidt (1879) obtained but very little of it, tiglic acid prevailing. Naudin (*Bull. Soc. Chim.*, 1884, 41, 483) extracted also a solid paraffin, $C_{18}H_{36}$, to which the name of *anthemene* was given; Klopp obtained another body, *anthesterin,* from chamomile. (*P. J.*, 1903, 458.) Umney states that pure oil of chamomile has the sp. gr. 0.905 to 0.912 at 15° C. (*P. J.*, 1895, p. 949).

The oil from *Anthemis Cotula* closely resembles that from *A. nobilis,* see *A. J. P.*, 1885, pp. 376, 381. E. Amerman (*A. J. P.*, 1889, p. 69) obtained a wax which was nearly white, bitter, and crystalline, melting at about 130° C., and a crystalline substance distinctly acid and of a glucosidal nature. There was no evidence of the presence of an alkaloid. (See *Oleum Anthemidis.*)

Uses.—Chamomile is an aromatic bitter, in small doses acceptable and corroborant to the stomach, in large doses capable of acting as an emetic. In cold infusion it is often advantageously used in cases of *enfeebled digestion* in convalescence of *general debility,* with languid appetite, which often attends convalescence from infectious fevers. The flowers are sometimes applied externally in the form of fomentation, in cases of irritation or inflammation of the abdominal viscera, and as a gentle incitant in flabby, ill-conditioned *ulcers.* The infusion is usually preferred. The decoction or extract cannot exert the full influence of the medicine, as the volatile oil is driven off.

Dose, from half a drachm to a drachm (2.0–3.9 Gm.).

ANTIMONII ET POTASSII TARTRAS.
U. S. (Br.)

ANTIMONY AND POTASSIUM TARTRATE Antim. et Pot. Tart. [Tartar Emetic; Tartarated Antimony; Antimonyl Potassium Tartrate]

"Antimony and Potassium Tartrate contains not less than 98.5 per cent. of $K(SbO)C_4H_4O_6.\frac{1}{2}H_2O$." *U. S.*

"Tartarated Antimony may be obtained by setting aside a mixture of antimonious oxide and acid potassium tartrate, made into a paste with a little water, until combination has taken place, and then purifying by crystallisation from water. Contains not less than 99 per cent. of antimonium potasso-tartrate, $(KSbOC_4H_4O_6)_2,H_2O$." *Br.*

Antimonium Tartaratum, *Br.;* Tartrated Antimony; Emetic Tartar; Potassium antimonyl tartrate; Antimonium Tartarizatum; Potassio-Tartrate of Antimony; Antimonii Potassio-Tartras, Tartarus Emeticus; Tartras Stibii et Kalii; Stibio-Kali Tartaricum, *Fr. Cod.;* Antimoniotartrate Acide de Potassium; Tartrate d'Antimoine et de Potasse, Emétique, Tartre stibié, *Fr.;* Tartarus Stibiatus, *P. G.;* Brechweinstein, *G.;* Tartrato di antimonico e di potassio, *It.;* Tartrato antimonico potasico, *Sp.*

A process for Tartar Emetic not now being given in the U. S. Pharmacopœia, that of 1870 follows: "Take of Oxide of Antimony, in very fine powder, *two troyounces;* Bitartrate of Potassium, in very fine powder, *two troyounces and a half;* Distilled Water, *eighteen fluid-*

ounces. To the Water, heated to the boiling point in a glass vessel, add the powders, previously mixed, and boil for an hour; then filter the liquid while hot, and set aside that crystals may form. Lastly, dry the crystals, and keep them in a well-stoppered bottle. By further evaporation the mother-water may be made to yield more crystals, which should be purified by a second crystallization." *U. S.*, 1870.

Tartar emetic is not usually prepared by the apothecary, but made on a large scale by the manufacturing chemist. Different processes are pursued in different manufactories; it is not material what plan is adopted, provided the crystals of the antimonial salt be carefully purified. For other methods and comments on its preparation see *U. S. D.*, 17th edition, p. 175 and *U. S. D.*, 20th edition, p. 149.

The theoretical structure of this salt is a matter of some difference of opinion; some regard it as a derivative of the neutral potassium tartrate in which one of the elements of potassium is replaced by the basic radical SbO. Fargher and Gray (*J. P. Ex. T.*, 1921, xviii, p. 341) favor the view, however, that it is a derivative of ortho-antimonious acid $Sb(OH)_3$, in which two of the hydroxyl groups are replaced by the divalent tartaric acid and the remaining hydrogen atom by potassium.

Description and Physical Properties.—"Colorless, odorless, transparent crystals of the rhombic system, or a white granular powder. The crystals effloresce upon exposure to air. One Gm. of Antimony and Potassium Tartrate is soluble in 12 cc. of water and in 15 cc. of glycerin, at 25° C. One Gm. is soluble in 3 cc. of boiling water. It is insoluble in alcohol.

"An aqueous solution of Antimony and Potassium Tartrate (1 in 20) is slightly acid to litmus paper. When heated to redness, it chars, emits an odor resembling that of burning sugar, and leaves a blackened residue. This residue has an alkaline reaction, and when a small fragment of it is held in a non-luminous flame, a violet tint is produced. In an aqueous solution of Antimony and Potassium Tartrate (1 in 20), acidulated with hydrochloric acid, hydrogen sulphide T.S. produces an orange-red precipitate, which is soluble in ammonium sulphide T.S. or potassium hydroxide T.S.

"A 10 cc. portion of an aqueous solution of the salt (1 in 100) acidulated with acetic acid does not at once assume a blue color on the addition of 5 drops of potassium ferrocyanide T.S. (*iron*). Dissolve 0.1 Gm. of Antimony and Potassium Tartrate in 5 cc. of concentrated hydrochloric acid: the solution meets the requirements of Bettendorf's Test for *arsenic*.

"**Assay.**—Dissolve about 0.5 Gm. of Antimony and Potassium Tartrate, accurately weighed, in 30 cc. of distilled water, add 25 cc. of a cold, saturated solution of sodium bicarbonate and a few drops of starch T.S., and immediately titrate with tenth-normal iodine to the production of a permanent blue color. Each cc. of tenth-normal iodine corresponds to 0.01662 Gm. of $K(SbO)C_4H_4O_6 . \frac{1}{2} H_2O$.

"Preserve in well-closed containers." *U. S.*

"Soluble in 17 parts of *water*, forming a slightly acid solution; almost insoluble in *alcohol* (90 per cent.), moderately soluble in weak alcoholic liquids. Taste sweet and metallic. Precipitated from its solutions by *solution of tannic acid.* Yields the *reactions* characteristic of antimony, of potassium, and of tartrates. The solution obtained by dissolving 0.5 gramme in 25 millilitres of *water*, and adding 5 grammes of *sodium potassium tartrate* and 1.5 grammes of *sodium bicarbonate*, discharges the color of not less than 29.8 or more than 30.2 millilitres of *N/10 solution of iodine.* Yields no characteristic *reactions* for lead, copper, iron, sodium, ammonium, chlorides, or sulphates. Does not effervesce with an aqueous solution of *sodium bicarbonate* (absence of acid potassium tartrate)." *Br.*

It is incompatibile with acids, hydroxides, carbonates, some of the earths and metals, calcium chloride, and lead acetate and subacetate. It is incompatible also with astringent infusions and decoctions, as of rhubarb, cinchona, catechu, galls, etc.; but these substances, unless galls be an exception, do not render it inert, though they lessen its activity to a greater or less extent. Hydrochloric and sulphuric acids, added to a solution of the antimonial salt, not too dilute, throw down a white precipitate of antimony trichloride or subsulphate, mixed with cream of tartar, which is redissolved by an excess of the precipitant. Nitric acid throws down a subnitrate, which is taken up by an excess of acid. When solution of potassium hydroxide is added to a concentrated solution, it produces at first no effect, and then a precipitate of trioxide, which is redissolved on the continued addition of the alkali. Lime water acts in a weaker solution, and throws down a white precipitate, consisting of the mixed calcium and antimony tartrates. Potassium carbonate affects still weaker solutions, throwing down a white precipitate of trioxide; but this test does not act in solutions containing less than a quarter of a grain to the fluidounce. Ammonia, both pure and carbonated, precipitates a solution of tartar emetic, throwing down the pure trioxide. To these reagents may be added infusion of galls, which when fresh and strong, causes a dirty-yellowish-white precipitate of antimony tannate.

Uses.—When tartar emetic is given in minute doses (gr. 1/12, or 0.005 Gm.) to a healthy man it produces only a slight lessening of the force of the pulse and a tendency to increased secretion from the skin. After somewhat larger amounts these symptoms are more pronounced, and have nausea added to them. If a grain be ingested, the nausea and vomiting will be severe and persistent, and accompanied by severe purging and marked prostration, both of the circulation and of the muscular strength. In the lower animals antimony causes symptoms similar to those which it produces in man. It has been experimentally proved that the fall of the arterial pressure is produced, at least in part, by a direct action upon the heart. The loss of muscular power, of reflex activity, and of sensibility is believed to be due to depression of the spinal centers, and the disturbance of respiration to a direct influence upon the nerve-centers which preside over that function. The purging and vomiting are connected with an effort at elimination, the poison escaping through the gastro-intestinal mucous membrane, as well as through the kidneys. After death from antimony, fatty degeneration of the liver, kidneys, and other organs has been found, indicating that the poison has a powerful influence upon nutrition. It is evident that in small doses tartar emetic is powerfully depressant to the circulation and stimulant to the secretion of the skin. Weiss and Hatcher (*J. Ex. M.*, 1923, xxxvii, 97) conclude that the emesis after oral exhibition of antimony is due chiefly to irritation of the stomach; the nausea following its intravenous injection they believe is a reflex from the heart.

Tartar emetic is employed occasionally as a diaphoretic and expectorant, but has been largely supplanted by other less dangerous remedies as a circulatory depressant. In the first stage of a *bronchitis* in a sthenic subject it is often of great service. Its emetic action is very certain, powerful, prolonged, but accompanied with much depression. It is very badly borne by children. Tartar emetic is occasionally used as a counter-irritant in the form of an ointment or plaster, whose application produces sooner or later a burning sensation accompanied by a very painful pustular eruption with ulcerations.

Like its related element arsenic, antimony is poisonous to various of the lower forms of life, notably protozoa. Within recent years it has achieved a considerable importance in the treatment of various tropical infections. Its use in these conditions dates from the discovery of Plimmer and Thompson in 1908 (*Proc. Roy. Soc.*, Series B, lxxx, 1) of its effect in *trypanosomiasis*. Although Voegtlin and Smith (*J. P. Ex. T.*, 1920, xv, p. 453), in studies on rats find that the ratio between the toxic and curative dose of antimony tartrate is narrower than that of arsphenamine, it has been found to be clinically useful in the treatment of human infections by trypanosomes. McWalter (*B. M. J.*, Oct. 10, 1914) has also found it exercises beneficial effects in *syphilis* although by itself not completely curative. The most favorable results have been obtained in *schistosomiasis* (*bilharziasis*) (see Christopherson, *L. L.*, 1919, ii, 1021) and *kala-azar* (see Kerr, *L. L.*, July 13, 1918, and Rogers, *Indian Med. Gaz.*, 1917, lii, p. 265). It is also recommended by Rogers (*B. M. J.*, Jan. 6, 1917) for the destruction of the crescents in the treatment of *tertian malarial fever*. It has been recommended by MacFie (*Annals of Tropical Med. and Parasitology*, 1920, xiv, p. 145) in infestation by the *Guinea-worm*. It is also employed in the treatment of *granuloma inguinalis* (see Lynch, *J. A. M. A.*, 1921, lxxvii, 925).

For the destruction of various blood parasites antimony must be given intravenously. Various preparations have been employed but it is not yet demonstrated that any of them are superior in value to the tartar emetic. For this purpose it is used in doses of from one-half to two grains (0.03 to 0.12 Gm.) every alternate day. Klemperer (*D. M. W.*, 1911) also reports favorable results from the use of tartar emetic in *pernicious anemia*. He gave hypodermically one sixty-fourth of a grain (1 mgm.) daily. The drug has also been employed in veterinary medicine as a vermifuge.

Poisoning.—Symptoms of acute poisoning by the drug are an austere metallic taste, excessive nausea, copious vomiting, frequent hiccough, burning pain in the stomach, colic, frequent stools and tenesmus, fainting, rapid and feeble pulse, coldness of the skin, and even of the internal organs, difficult and irregular respiration, cutaneous anesthesia, convulsive movements, painful cramps in the legs, prostration, and death. Ten grains (0.65 Gm.) is the smallest dose reported to have proved fatal. In rare cases vomiting and purging do not take place, and when they are absent, the other symptoms are aggravated. Sometimes a pustular eruption is produced, like that caused by the external application of the antimonial.

When given in repeated small doses, tartar emetic produces both in man and in the lower animals a chronic poisoning, in which the chief symptoms are nausea, vomiting, watery purging, often followed by constipation, failing circulation, and a general asthenia, deepening into death from exhaustion. After death from antimonial preparations, decided evidences of gastro-intestinal irritation are apt to be present, but they have been in some cases wanting. The blood is often markedly fluid. Intense venous congestion, especially of the lungs, is usually present, and in some cases pulmonary apoplexy, atelectasis, or other structural lesion of the lungs has been found. A wide-spread fatty degeneration has been noted as constant in chronic poisoning in animals, and probably occurs also in man.

The treatment of tartar emetic poisoning consists, first, in washing out the stomach with a solution of tannic acid; second, in meeting the symptoms as they arise, especially by the use of opiates, which should be administered hypodermically and by rectal suppositories; external warmth, stimulants, etc., should be used *pro re nata*. Rosenthal and Severn (*A. E. P. P.*, 1912, lxvii, p. 275) assert that potassium hexatantalate is a valuable antidote in poisoning by antimony, being capable of following the drug after its absorption and producing a non-toxic compound in the system. In all cases of suspected poisoning, the vomit, the passages from the bowels, and especially the urine should be saved. The metal has been found in all the tissues of the body, but in the experiments of B. W. Richardson it was most abundant in the liver.

Dose, as a diaphoretic or expectorant, one-thirtieth to one-tenth of a grain (0.002–0.006 Gm.); as an emetic, half a grain (0.032 Gm.).

Off. Prep.—Mistura Glycyrrhizæ Composita, *U. S.;* Syrupus Scillæ Compositus, *U. S.;* Tinctura Antimonii, *N. F.* (*Br.*)

ANTIMONII OXIDUM. N. F., Br.

ANTIMONY OXIDE Antim. Oxid.

"Antimony Oxide contains not less than 97 per cent. of antimonous oxide (Sb_2O_3 = 288.4)." *N. F.*

"Antimonious Oxide, Sb_2O_3, may be obtained by pouring solution of antimonious chloride into water, and decomposing the precipitated antimony oxychloride with sodium carbonate." *Br.*

Antimonious Oxide; Antimonious Anhydride; Antimony Trioxide; Oxide of Antimony; Stibium Oxydatum, Oxydum Antimonicum s. Stibicum; Oxyde d'Antimoine, *Fr.;* Antimonoxyd, *G.;* Oxido de antimonio, *Sp.*

This compound is no longer official in the U. S. Pharmacopœia, but has been introduced into the N. F. The process of the U. S. P. 1870, with comments will be found in the *U. S. D.,* 20th edition, p. 151.

Description and Physical Properties.—"Antimony Oxide is a white or grayish-white powder, odorless and tasteless, It is insoluble in water, alcohol or nitric acid; readily dissolved by hydrochloric acid without effervescence, and also by a warm aqueous solution of tartaric acid or by a boiling aqueous solution of potassium bitartrate. When heated Antimony Oxide turns yellow but it again becomes white on cooling. At a dull red heat it fuses to a yellowish liquid and at a higher temperature it volatilizes.

"Dissolve Antimony Oxide in a slight excess of hydrochloric acid and dilute the solution with a large volume of distilled water; a white precipitate is produced which is changed to orange by hydrogen sulphide.

"A solution of 0.1 Gm. of the Oxide in 3 cc. of hydrochloric acid and 5 cc. of distilled water is not rendered turbid at once by a few drops of barium chloride T.S. (*sulphate*). A solution of 0.1 Gm. of the Oxide in 10 cc. of distilled water and 1 Gm. of tartaric acid does not become more than slightly opalescent on the addition of 0.2 cc. of nitric acid and 0.2 cc. of silver nitrate T.S. (*chloride*). Dissolve 0.5 Gm. of the Oxide in 10 cc. of hydrochloric acid, dilute the solution with distilled water until it begins to become permanently turbid and then precipitate with hydrogen sulphide. This precipitate when thoroughly washed with distilled water dissolves in ammonium sulphide T.S. or sodium sulphide T.S., without leaving a black insoluble residue (*copper* or *lead*). A solution of 0.1 Gm. of Antimony Oxide in 5 cc. of hydrochloric acid does not respond to Bettendorf's test for arsenic.

"**Assay.**—Dissolve about 0.2 Gm., of Antimony Oxide, accurately weighed, by warming it in a solution of 1 Gm. of tartaric acid in 10 cc. of distilled water (adding a few drops of hydrochloric acid to aid the solution). Nearly neutralize the solution with sodium carbonate, then add 40 cc. of a cold saturated solution of sodium bicarbonate and titrate at once with tenth-normal iodine, using starch as indicator. Each cc. of tenth-normal iodine corresponds to 0.00721 Gm. of Sb_2O_3. One Gm. of Antimony Oxide corresponds to not less than 134.5 cc. of tenth-normal iodine." *N. F.*

"A greyish-white powder, fusible at a low red heat. Insoluble in *water.* Readily soluble in *hydrochloric* acid, the solution yielding the *reactions* characteristic of antimony. The solution obtained by dissolving 0.25 gramme in *diluted hydrochloric acid,* adding 5 grammes of *sodium potassium tartrate* and then a slight excess of *sodium bicarbonate,* discharges the color of 34.5 millilitres of *N/10 solution of iodine.* Yields no characteristic *reactions* for lead, copper, arsenium, calcium, sodium, or potassium, not more than slight *reactions* for iron, and not more than the slightest *reactions* for chlorides or sulphates. Dissolves entirely when boiled with an excess of an aqueous solution of *acid potassium tartrate.*" *Br.*

It is frequently impure from the presence of the before-mentioned antimony antimonate, in which case it is not *entirely* soluble in hydrochloric acid. If it contain oxychloride, which it is apt to do from the imperfect action of the alkaline solutions employed in its purification, its solution in tartaric acid will be precipitated by silver nitrate. When antimony antimonate is substituted for it, the fraud may be detected by the spurious preparation being entirely insoluble in hydrochloric acid.

Uses.—This oxide, which must not be confounded with the powder of Algaroth or antimony oxychloride (see Part II), has the general therapeutic properties of the antimonials. It is not suited for administration by the mouth because of the uncertainty of its effects by this channel, on account of the variations in acidity of the stomach.

Antimony trioxide has been recently recommended in the place of tartar emetic for the treatment of protozoal infections. It has the advantage over tartar emetic that being less locally irritant it may be administered subcutaneously or intramuscularly.

Dose, one to two grains (0.06–0.12 Gm.).

Off. Prep.—Pulvis Antimonialis, *Br., N. F.*

ANTIMONIUM

ANTIMONY

Stibium, *Lat.;* Antimoine, *Fr.;* Antimon, Spiessglanz Metall, *G.;* Antimonia, *It.;* Antimonio, *Sp.*

Metallic antimony, sometimes called *regulus of antimony,* is not official in the British or United States Pharmacopœia, but, as it enters into the composition of a number of important pharmaceutical preparations, we have thought it proper to notice it under a distinct head.

Antimony exists in nature: (1) uncombined; (2) as an oxide; (3) as antimonous sulphide (tersulphide), and (4) as an oxysulphide. It is found in France, Japan, and Hungary, but most largely in China which it is stated yields 85 per cent. of the world's production, and has been discovered also in Ontario, Alaska, and in smaller amounts in California and Nevada.

Extraction.—Much of the antimony of commerce is extracted from the native sulphide called *stibnite* (see *Antimony sulphide,* Part II). The ore is first separated from its gangue by fusion. It is then reduced to powder, and placed on the floor of a reverberatory furnace, where it is subjected to a gentle heat, being constantly stirred with an iron rake. This process of roasting is known to be completed when the matter is brought to the state of a dull, grayish-white powder called *antimony ash.* By this treatment the antimony is partly trioxidized, and partly converted into antimonous acid, while nearly all the sulphur is dissipated in the form of sulphurous acid gas; a portion of trisulphide, however, remains undecomposed. The matter is then mixed with charcoal impregnated with a concentrated solution of sodium carbonate, and the mixture heated in crucibles, in a melting-furnace. The charcoal reduces the antimony trioxide, while the alkali unites with the undecomposed trisulphide, and forms melted scoriæ, which cover the reduced metal and diminish its loss from volatilization. Antimony is also frequently obtained by the reduction by iron of the native sulphide. The reduction of the antimony sulphide by iron takes place at a red heat, but as iron sulphide needs a higher temperature for its fusion, and its specific gravity is not much less than that of the metallic antimony, the mass must be heated to a white heat to effect a perfect separation, and this occasions a loss of antimony. In order to avoid this, sodium sulphide is added in practice, which unites with the iron sulphide to form a more fusible and lighter slag of double sodium and iron sulphide. For 100 parts of antimony sulphide are taken 42 parts of iron, 10 parts of anhydrous sodium sulphate, and 2½ to 3½ parts of carbon.

The purest commercial antimony is not entirely free from foreign metals, chiefly iron, lead, and arsenic. Lefort purifies it for the purposes of pharmacy by gradually adding twenty-five parts of the metal, in fine powder, to fifty parts of nitric acid, by the action of which the antimony is precipitated as antimonous acid, while the foreign metals remain in solution. The precipitate is then thoroughly washed with water containing a hundredth part of nitric acid, drained completely, mixed with three or four parts of powdered sugar, and reduced to the metallic state by being heated to redness in a Hessian crucible. Antimony is imported into the United States in the form of antimony sulphide, as antimony regulus or metal, and most largely as *"hard lead"* or *antimonial lead* obtained as a by-product in smelting lead or silver ores which contain from 3 to 10 per cent. of antimony.

Properties.—The time of the discovery of antimony is not known, but Basil Valentine was the first to describe the method of obtaining it, in his work entitled *"Currus Triumphalis Antimonii,"* published towards the end of the fifteen century. It is a brittle, brilliant metal, ordinarily of a lamellated texture, of a silver-white color when pure, but bluish white as it occurs in commerce. Its atomic weight is 120.2, Symbol Sb, sp. gr. 6.7, and fusing point 630° C. On cooling, after fusion, antimony assumes an appearance on the surface bearing some resemblance to a fern leaf. When strongly heated, it burns with the emission of white vapors, consisting of teroxide, formerly called *argentine flowers of antimony.* A small portion being fused and then thrown upon a flat surface divides into numerous globules, which burn rapidly as they move along. It forms three combinations with oxygen, *antimony trioxide* (antimonous oxide), Sb_2O_3, *antimony tetroxide,* Sb_2O_4 (by some considered to be an antimonate of the radical *antimonyl,* $SbO.SbO_3$), and *antimony pentoxide* (antimonic oxide), Sb_2O_5. The first of these unites with water to form antimonous acid, the salts of which are called *antimonites,* the third unites with water to form antimonic acid, the salts of which are called *antimonates.* The trioxide was noticed under the head of *Antimonii Oxidum.* The tetroxide is a white powder, yellowish when hot, and difficultly soluble in acids. It forms when either of the other two oxides is strongly heated in air. *Antimony ash,* described above, is also an impure tetroxide. *Antimonic acid* is a lemon-colored powder, which may be prepared by oxidizing the metal by digestion in nitric acid, and then driving off the excess of the acid by a heat not exceeding 315.5° C. When exposed to a red heat, it parts with oxygen, and is converted into the *antimony tetroxide* just described. This, though medicinally inert, frequently was found in former days in a large proportion of the preparation called antimonial powder. (See *Pulvis Antimonialis.*)

The activity of antimonials is proportional not merely to their solubility in the gastric juices but, according to the researches of Brunner (*A. E. P. P.*, 1912, lxviii, p. 186), especially depends upon whether the metal is in the trivalent or pentavalent condition, the latter being comparatively innocuous.

ANTIMONIUM SULPHURATUM. Br.

SULPHURATED ANTIMONY [Kermes Mineral]

"Sulphurated Antimony is a mixture containing antimony sulphides and oxides, and sulphur." *Br.*

Antimonium Oxysulphuratum, Antimonii Oxysulphuretum, Antimonii Sulphuretum Aureum; Precipitated Sulphide of Antimony; Antimony Pentasulphide; Sulphur Auratum Antimonii; Golden Sulphuret of Antimony, Golden Sulphur; Pentasulfure d'Antimoine, *Fr. Cod.;* Soufre doré d'Antimoine, *Fr.;* Stibium Sulfuratum Aurantiacum, *P. G.;* Goldschwefel, Gefälltes Schwefelantimon, *G.;* Kermes minerale, *It.;* Quermes mineral, Oxisulfuro de antimonio hidratado, *Sp.*

Sulphurated antimony was not introduced into the U. S. P. or N. F.

The process of the British Pharmacopœia (1914) is as follows: "Antimonious sulphide ('black antimony') of commerce, 200 grammes; Sublimed Sulphur, 200 grammes; Caustic soda of commerce, 100 grammes; Diluted Sulphuric Acid, Distilled Water, of each a sufficient quantity. Dissolve the caustic soda in two thousand millilitres of the Distilled Water; with this solution mix the antimonious sulphide and the Sublimed Sulphur; boil for two hours with frequent stirring, adding Distilled Water occasionally to maintain the same volume; then, while the mixture is still hot, add three thousand six hundred millilitres of boiling Distilled Water; strain the product through calico; before the strained liquid cools add to it by degrees Diluted Sulphuric acid till the latter is in slight excess; collect the precipitate on a calico filter; wash with Distilled Water till the washings are free from sulphates; dry at a temperature not exceeding 100° C." *Br.*

For description of the native antimonous sulphide (black antimony) see *Antimony Sulphide,* Part II. When this is boiled with sodium hydroxide there is formed *sodium dihydrogen orthoantimonite* and *sodium sulphantimonite* according to the following reaction:

$$Sb_2S_3 + 4NaOH = NaH_2SbO_3 + Na_3SbS_3 + H_2O.$$

This was the substance recognized by the U. S. 1890 as *Antimonium Sulphuratum.* In the process of the British Pharmacopœia a part of the free sulphur combines with the sodium hydroxide to form sodium sulphide and the latter reacts with the antimony sulphide to form *sodium sulphantimonate,* sometimes called *Schlippe's salt.* The latter reaction may be represented thus:

$$Sb_2S_3 + 3Na_2S + S_2 = 2Na_2SbS_4.$$

The sodium sulphantimonate when decomposed by a mineral acid yields *antimony pentasulphide* according to the reaction:

$$2(SbS_4Na_3 + 9H_2O) + 3H_2SO_4 = 3Na_2SO_4 + Sb_2S_5 + 3H_2S + 18H_2O.$$

Ten parts of Schlippe's salt yield in theory 4.17 parts of antimony pentasulphide. In actual practice, however, there is present variable amounts of antimony oxides and free sulphur. A purer form of antimony pentasulphide may be obtained, according to the suggestion of E. G. Eberhardt, by treating the native sulphide with hydrochloric acid and precipitating the solution with hydrogen sulphide. The objection that arsenic might be found in the product was met by an examination which showed that traces of arsenic present were not more than when the then official process had been employed. *A. J. J.,* 1886, p. 229.) The color of sulphurated antimony or Kermes mineral is influenced by porphyrization, with the admixture of a little sugar or gum; if hastily porphyrized, the mixture has a violet tint; if carefully and slowly, it has a russet color.

Properties.—"An orange-red powder, readily dissolved by hot *hydrochloric acid,* with evolution of hydrogen sulphide and separation of sulphur. 1 gramme digested with 20 millilitres of hot *water* yields a filtrate which, after acidification with *diluted nitric acid,* becomes not more than slightly cloudy on the addition of *solution of barium chloride* (limit of sulphates). *Arsenic limit* 1000 parts per million. 3 grammes moistened with *diluted nitric acid,* warmed with successive portions of *fuming nitric acid* until red fumes cease to be evolved, and then dried and carefully heated to redness, leave a whitish residue weighing not less than 1.6 or more than 1.8 grammes." *Br.*

The former U. S. preparation was "an amorphous, reddish-brown powder, becoming lighter in color on exposure to light, and having neither odor nor taste. Insoluble in water or alcohol, but soluble in hydrochloric acid with the evolution of hydrogen sulphide.

"When heated in a dry test-tube, it emits moisture and leaves a black residue.

"If 1 Gm. of Sulphurated Antominy be gently heated with 10 cc. of hydrochloric acid, it should dissolve, with the exception of a slight residue, which, when washed and dried, should burn on the application of a flame with the characteristic odor of sulphur, leaving not more than a scanty ash. The acid solution, completely deprived of hydrogen sulphide by boiling yields, when added to water, a white precipitate, which, after being washed and dried should weigh not less than 85 per cent. of the original weight of the sulphide. The liquid filtered from this precipitate yields an orange-red precipitate with hydrogen sulphide T.S.

"If 1 Gm. of Sulphurated Antimony be shaken with 20 cc. of hot water, the filtrate should be neutral to test paper, should not be rendered more than slightly opalescent by barium chloride T.S. (limit of *sulphate*), or silver nitrate T.S. (limit of *chloride*), and should not be affected by ammonium oxalate T.S. (absence of *calcium*)." *U. S.,* 1890.

Uses.—Precipitated antimony sulphide (*sulphurated antimony*) is alterative, diaphoretic, and emetic. It is, however, an uncertain medicine, and is very little used. In combination with calomel and guaiac (*Plummer's pill*), it was formerly employed in *secondary syphilis* and *cutaneous eruptions.* (See *Pilulæ Antimonii Compositæ,* U. S. P. 1890.) During its use the patient should abstain from acidulous drinks.

Dose, as an alterative, from one to two grains (0.065–0.13 Gm.).

Off. Prep.—Pilulæ Hydrargyri Subschloridi Composita, *Br.*

ANTIPYRINA. U. S. (Br.)

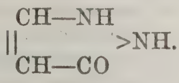
ANTIPYRINE Antipyr. [Phenazone]

"Phenyldimethyl pyrazolon [$C_3HON_2(CH_3)_2.C_6H_5$]." *U. S.* "Phenazone, or phenyl-dimethyl-iso-pyrazolone, $C_{11}H_{12}N_2O$, may be obtained from phenyl-hydrazine by interaction with aceto-acetic ether, and the subsequent interaction of the resulting phenyl-methyl-iso-pyrazolone with methyl iodide." *Br.*

Phenazonum, *Br.;* Phenazone; Phenyldimethylisopyrazolone, Methozine, Dehydrodimethylphenylpyrazine; Analgésine, Parodyne, Anodynine, *Fr.;* Pyrazolonum phenyldimethylicum, *P. G.;* Phenyldimethylpyrazolon, Antipyrin, *G.;* Antipirina, *It., Sp.*

Dose, three to fifteen grains (0.2–1.0 Gm.).

Preparation.—This compound is one of the first important synthetical remedies introduced into medicine; it is now generally conceded to be a derivative of *pyrrol,* C_4H_5N, a base found in coal tar and in bone oil. From this base is derived *pyrazole* (see Part II) and from the latter *pyrazolon.* This in turn by molecular rearrangement yields *isopyrazolon,*



$$\begin{array}{l} CH—NH \\ || \qquad\qquad >NH. \\ CH—CO \end{array}$$

Phenyldimethylisopyrazolon is a substitution product from this. Practically it is made by Knorr's patented process of acting upon phenylhydrazine, $C_6H_5.NH.NH_2$, with ethyl acetoacetate, $(CH_3.CO)CH_2.CO.C_2H_5$, when phenylmethyl-pyrazolon is formed. This is then methylated by treatment with methyl iodide, when the hydriodide of the finished base results. It has also been made by condensing molecular proportions of ethyl aceto-acetate and methylphenyl-hydrazine. Another process consists in combining phenyl-hydrazine with β-chlorozopropionic acid to form phenyl-dihydro-pyrazolone, which is later oxidized to phenyl pyrazolone, which upon methylation is converted into antipyrine. Another reaction product—viz., that of halogen butyrate acting upon phenyl-hydrazine with the subsequent oxidation and methylation of the compound so obtained, which is also a phenyldimethylpyrazolon—is only an isomer of true antipyrine; not identical with it.

Description and Physical Properties.—"Colorless crystals, or a white, crystalline powder. It is odorless, and has a slightly bitter taste. One Gm. of Antipyrine is soluble in less than 1 cc. of water, 1.3 cc. of alcohol, 1 cc. of chloroform, and in 43 cc. of ether, at 25° C.

"Antipyrine melts between 111° and 113° C. The addition of tannic acid T.S. to an aqueous solution of Antipyrine produces an abundant white precipitate. Mix 0.1 Gm. of sodium nitrite and 12 cc. of an aqueous solution of Antipyrine (1 in 100): a nearly colorless liquid is obtained, which, upon the addition of 1 cc. of diluted sulphuric acid, develops a deep green color. One drop of ferric chloride T.S. added to 2 cc. of a dilute aqueous solution of Antipyrine (1 in 1000) produces a deep red color, which, upon the addition of 10 drops of sulphuric acid, is changed to light yellow.

"Its aqueous solution (1 in 20) is neutral to litmus paper. Ash: not more than 0.1 per cent. Antipyrine is completely soluble in its own weight of cold distilled water, the solution being colorless or not more than slightly yellow when viewed transversely in a tube having a diameter of about 20 mm. An aqueous solution of Antipyrine meets the requirements of the test for *heavy metals.*" *U. S.*

It is described in the British Pharmacopœia as "small, colorless, scaly crystals. No odor; taste bitter. Soluble in 1.2 parts of *water,* in 1.3 parts of *alcohol* (90 per cent.), and in 1.3 parts of *chloroform.* Melting point from 111° to 113° C. Aqueous solution neutral to *litmus.* An aqueous solution (1 in 100) responds to the following tests:—Mixed with an equal volume of *nitric acid* it assumes a yellow color passing to crimson on warming; 2 millilitres are colored green by 2 drops of *fuming nitric acid,* and the color is changed to red by boiling with an additional 3 or 4 drops of the *fuming nitric acid;* 12 millilitres remain nearly colorless on the addition of 0.1 gramme of *sodium nitrite,* but turn deep green on the further addition of 1 millilitre of *diluted sulphuric acid;* 1 millilitre, diluted with 9 millilitres of *water,* is colored deep red by *T. Sol. of ferric chloride,* the color being nearly discharged by excess of *diluted sulphuric acid.* An aqueous solution (1 to 20) gives with *T. Sol. of mercuric chloride* a white precipitate which disappears on boiling, but reappears on cooling. Aqueous solution not affected by *hydrogen sulphide.* No appreciable ash." *Br.*

Antipyrine may be quantitatively determined by taking advantage of its power, of combining with iodine, and several methods have been devised for its estimation. (*J. P. C.,* 1917, xv, 93–337.)

Antipyrine is incompatible with hexamethyleneamine, formaldehyde, nitrites and ferric salts, the latter producing marked color reactions. It forms eutectic mixtures which liquefy when it is triturated with many other organic compounds like salol, etc.

Uses.—Locally antipyrine exercises an anesthetic effect upon the nerve endings and causes constriction of the superficial blood vessels. When taken into the stomach it is absorbed rapidly and eliminated unchanged chiefly through the kidneys, although it has been demonstrated in various other secretions. In appropriate dose it causes in the lower animals increased activity of reflexes through an action upon the spinal cord, a rise in the blood pressure through an influence upon the cardiac and vascular muscles, and a slight stimulation of the respiratory center. These actions, however, are of little importance from a standpoint of the clinical use of the drug. The medicinal value of antipyrine, aside from its local uses, is based on its effects on the pain-perceiving mechanism and upon the thermoregulator apparatus, similar to that described under acetanilid. As far as at present known, these effects are precisely analogous to that of the anilin derivatives, but it is somewhat more prompt in its action and some believe also more prone to produce collapse than either acetanilid or acetphenetidin.

Antipyrine is useful in medicine most largely for the relief of pain, especially of nervous origin, as *neuralgias, migraine,* crises of *locomotor ataxia,* and similar conditions. In so-called *muscular rheumatism* many believe that it is not merely of value as a symptomatic drug, but that it possesses some curative effect. As an antipyretic it is employed in the same class of cases as the aniline derivatives. It is also used in certain spasmodic disorders, especially *whooping-cough* and *epilepsy.* In the latter disease it usually fails when given alone, but appears to enhance the action of the bromides.

It is a valuable local remedy in the treatment of various inflammatory conditions of the mucous membranes, as *rhinitis* and *laryngitis,* both for its local anesthetic and vasoconstricting effects. For this purpose it is usually employed in strengths of from 5 to 15 per cent. It is occasionally used as a styptic in *nasal hemorrhage.*

Toxicology.—Antipyrine, like the other coal-tar derivatives, is prone to produce unpleasant and sometimes alarming symptoms, even after doses which would scarcely be regarded as excessive. The most common type of antipyrine poisoning is characterized by giddiness, tremor, free sweating with more or less collapse, a peculiar lividity with, in many cases, eruption of the skin most commonly morbilliform, but sometimes erythematous or urticarial. After very large doses there may be drowsiness deepening into coma with dilatation of the pupil and epileptiform convulsions. Various irregular symptoms have been noted, such as amaurosis, pseudo-membranous stomatitis, swelling of the lips and tongue, laryngeal interference with the respiration. In some cases fever with nervous unrest and epileptiform convulsions have been reported.

The treatment of antipyrine poisoning is purely symptomatic. Circulatory stimulants, as ammonia, strychnine and atropine, should be given and the bodily temperature maintained by the external application of heat.

Dose, from five to fifteen grains (0.3–1.0 Gm.)

ANTITOXINUM DIPHTHERICUM

DIPHTHERIA ANTITOXIN

ANTITOX. DIPH. [Serum Antidiphthericum Purificatum, U. S. P. IX, Concentrated Diphtheria Antitoxin, Refined Diphtheria Antitoxin, Antidiphtheric Globulins.]

"Diphtheria Antitoxin is an aqueous solution of certain antitoxic substances obtained from the blood serum or plasma of an animal of the genus *Equus,* which has been properly immunized against diphtheria toxin. After the serum or plasma from the immunized animal has been collected, the antitoxin-bearing globulins are separated from the other constituents of the serum or plasma and dissolved in water. Sodium chloride and a preservative are then added and the solution is filtered through a bacteria-excluding filter. It has a potency of not less than 350 antitoxin units per cc." *U. S.*

Serum Antidiphthericum, *P. G.;* Diphtherie-Heilserum, *G.;* Sérum antidiphtérique, *Fr.;* Siero antidifterico, *It.;* Suero antidifterico, *Sp.*

Formerly the U. S. Pharmacopœia recognized three forms of diphtheria antitoxin under the names respectively of *Serum Antidiphthericum, Serum Antidiphthericum Purificatum,* and *Serum Antidiphthericum Siccum.* At the tenth revision the first and last of these was dropped because of the rarity of their employment. The substance formerly official as purified antidiphtheric serum is now recognized under the name of diphtheria antitoxin. For the natural or unpurified serum of the former pharmacopœia there is no place in medicine today. For the dried serum, however, there is a limited field of usefulness which is based upon the fact that it does not deteriorate so rapidly as the liquid and is occasionally useful for transportation far from centers of manufacture.

The antitoxic property of the blood serum of animals immunized by the inoculation of bacterial toxins was discovered in 1890 by Behring and Kitasato (*D. M. W.,* 1890, Nos. 49, 50). The great practical therapeutic value of diphtheria antitoxin was demonstrated independently by Behring and by Roux and announced in papers read before the International Congress of Hygiene and Demography which met in Budapest in 1894.

Only the serum of the blood is used in medicine for prophylactic or curative purposes, although other body juices contain the active principle. The antitoxin has never been isolated in pure form. It is precipitated with the globulins and is believed to be allied to the enzymes. The antitoxin globulin retains its properties more persistently than the allied globulins with which it is associated. That is, it is more resistant to deleterious influences, more stable and more soluble than the other globulins found in blood serum. As we lack definite knowledge of the true chemical nature of the active principle contained in antitoxic serums, the antitoxin is variously spoken of as *antikörper* (G.) or *antibodies,* free receptors (Ehrlich), *cytases*

(Metchnikoff), etc. Of the several antitoxins known, diphtheria and tetanus antitoxins are the only ones recognized by the U. S. Pharmacopœia. These are the only ordinary diseases caused solely by a soluble toxin; in other words, in these two diseases, not the bacteria themselves, but the poison which they excrete, produce the severe symptoms and frequent fatalities. And these two toxins, in the animal body, each give rise to an antitoxin which may be therapeutically or prophylactically efficient. Each antitoxin is specific; that is, neutralizes the poison of the particular infection which was inoculated into a susceptible animal to produce it. While diphtheria antitoxin is used for other diseases, it is specific only in neutralizing the poisons produced by the diphtheria bacillus. Diphtheria antitoxin is sometimes normally present in small amounts in the blood serum of horses, man and other animals.

Preparation.—Diphtheria antitoxin is made by injecting the diphtheria poison (toxin) into horses. The horses are injected either subcutaneously or intravenously; usually the former method is preferred. Horses are selected because, on account of their size, a large amount of blood may readily be obtained, and because the serum of the horse is more easily borne by the human organism in large quantities than that of most other animals. Behring originally employed dogs and sheep with success; Aronson preferred the goat; Roux was the first to use the horse.

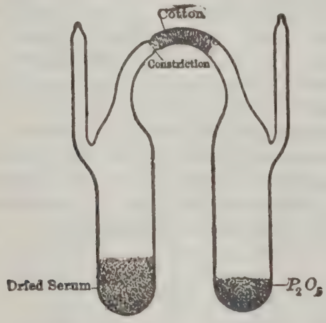
The antitoxin is produced by a vital reaction of the cells of the body caused by the stimulation of the toxin. Just which cells of the body take most active part in the production of the antitoxin is not exactly clear. Metchnikoff believed this power lies almost solely with the phagocytes, while Ehrlich believed that any of the body cells, but especially the connective tissue cells, play the most important rôle. The followers of Ehrlich and Metchnikoff have built up two divergent schools of thought to account for antitoxin immunity. It is interesting to note that both schools place the nutrition and metabolism of the cell at the ground work of antitoxin production.

The toxin is made by growing a virulent culture of the diphtheria bacillus in an alkaline nutrient bouillon at about 37° C. This culture, when five to seven days old, is filtered through unglazed porcelain or diatomaceous earth in order to remove the bacterial cells. The clear filtrate, containing the soluble poisons elaborated by the growth and multiplication of the bacilli, is the *diphtheria toxin.* The horse is inoculated with increasing amounts of the toxin. At first very small amounts are used, but even these usually cause a local and constitutional reaction, swelling and edema at the site of inoculation, fever, and derangement of appetite. These symptoms pass away in a few days, when a larger quantity of toxin is then inoculated, and this process is continued until within a few months the horse is able to withstand the subcutaneous inoculation of as much as a liter of a strong toxin with perhaps less local and general disturbance than is caused by the first treatment with a very small fraction of this amount.

As the doses of toxin given to the horse increase, the amount of antitoxin in the blood gradually increases until, after three to six months of treatment, the horse's blood usually contains from 300 to 800 units of antitoxin to the milliliter. The production of stronger antitoxic serums depends upon the horse and not upon the treatment. Some horses react actively and produce very high potency serums for long times; others cannot be induced to give a serum containing more than 150 to 200 units per milliliter. After a variable period (from several months to years) the horse loses the power of reaction, so that despite active treatment the immunizing power of the blood serum steadily diminishes. The horse is bled from the external jugular vein by means of a trocar and cannula. The blood is drawn into long sterile cylindrical tubes or other vessels containing sodium citrate or calcium oxalate solution and allowed to sediment. In about 24 hours the clear supernatant plasma is siphoned off and a preservative is added. The plasma so obtained from a number of horses is mixed and the antitoxic bearing globulins are separated by precipitation with ammonium sulphate, followed by dialysis to remove the sulphate. The remaining globulins bearing the antitoxin have sodium chloride and a preservative added and the solution is then passed through a sterile filter stone. The antitoxin is then tested for potency, for freedom from toxins and for sterility. After these tests are completed it is ready to be filled into the final container.

Preservatives.—The antitoxin in the blood serum neutralizes the toxin when the two are brought into contact, but the antitoxic serum does not prevent the growth of the bacteria themselves. Diphtheria bacilli grow and multiply well in diphtheria antitoxic serum. In other words, diphtheria antitoxin is a good culture medium for bacteria of all kinds. The greatest care must therefore be taken to prevent contamination. The serum may be kept sterile indefinitely only by means of the most exacting bacteriological precautions. It is sometimes marketed without the addition of an antiseptic substance, but this practice has been largely discontinued for the following reasons: (1) The technic required to prevent slight accidental contamination during the process of preparation and bottling is arduous; (2) there is danger of the introduction of serious contamination by unskilled persons who use the serum; (3) the addition of a small amount of certain preservatives is harmless. The serums made by the American manufacturers generally contain cresol (0.4 per cent.), phenol (0.5 per cent.), or chloroform (to saturation).

The preparation and preservation of the standard antitoxin is encompassed by many technical difficulties. A high-grade serum is selected. This is given a preliminary test to determine its potency. The serum is now reduced to dryness by evaporation *in vacuo*. Special apparatus is used to accomplish this evaporation quickly and at the same time to prevent contamination. The dried antitoxic serum must be kept guarded under special conditions to prevent deterioration. The oxygen of the air must be excluded in order to retard the process of oxidation, which rapidly alters the antibodies, especially under the influence of light; the standard antitoxin is, therefore, always kept under a vacuum and in absolute darkness in the Hygienic Laboratory of the U. S. Public Health Service. The serum must be perfectly dry; it is therefore kept under the influence of phosphoric anhydride, P_2O_5. Further, it is kept in a specially built ice-box maintained at the constant temperature of 5° C. by means of circulating brine. The dried serum is preserved in a small glass apparatus consisting of two parts connected by means of a glass tube, as shown in the accompanying illustration. The dried serum is placed in one portion of the apparatus and phosphoric anhydride, which is a very powerful dehydrating substance, in the other. The air is exhausted as much as possible by means of a high vacuum and the apparatus hermetically sealed. Several hundred such tubes are prepared, each one containing a weighed quantity of the powdered serum. From this arrangement, it will be seen that the antitoxin is kept dry, free from contact with the oxygen of the air, guarded against the action of light, and preserved at a constant low temperature. Once every two or three months, or whenever it is desired to prepare the standard solution, one of these bulbs is broken and 1 gramme of the dried serum carefully weighed and dissolved in a solution made by mixing physiological saline solution (0.85 per cent.) one part, and pure glycerin two parts.



U-shaped tubes used for preserving the standard serum. Half size.

Testing the Standard Antitoxin.—This glycerinated solution of blood serum is now accurately compared with previous standard solutions in terms of the immunity unit. This comparison is made by means of the test (L +) dose of toxin. The L + dose of a toxin is that quantity which when mixed with one immunity unit of serum is just able to kill a 250-gramme guinea pig on the fourth day (about 96 hours). In the commercial testing of antitoxin in order to have a coefficient of safety it is better to require the pig to live.

Testing the Toxin.—The toxin is a complex substance composed, according to Ehrlich, of several poisons, *e.g., toxin, toxoid, toxone* and *epitoxonoid*. The diphtheria toxin is first investigated biologically by adding varying quantities of the poison to the immunity unit and inoculating the mixtures into a series of guinea pigs. In this way, it is very evident, as Ehrlich has shown, that two limits, boundaries or zones are always shown, which are of the greatest importance in determining the nature and composition of the poison. Each of these limits is designated by the letter L, from *limes*, a boundary or zone. These limits are known respectively as L_0 (O = nil) and L + (+ = death).

By L_0 is meant that quantity of poison which just neutralizes or saturates one immunity unit as shown at the necropsy done forty-eight hours after the subcutaneous injection of the mixture into the guinea pig. The reaction at the site of inoculation at this examination must be hardly noticeable. Theoretically the L dose of toxin must unite with and neutralize just 200 "combining units" of antitoxin. A "combining unit" of antitoxin is in theory one two-hundredth of an immunity unit, and is supposed to contain enough antitoxin to just neutralize one fatal guinea pig dose of a pure toxin which is all poison without the comparatively inert (but antitoxin-neutralizing) toxoids and toxones. The L_0 dose, therefore, contains just 200 minimal lethal doses of a theoretically pure poison.

By L + is meant the smallest quantity of toxin of which when mixed with one immunity unit of antitoxin there is left unneutralized a quantity to kill the animal on the fourth day. As defined by Ehrlich the L + dose is that quantity of poison which, despite the antibodies contained in one immunity unit of serum, contains a sufficient excess of poison to cause the death of the guinea pig within the course of four days.

In studying the constitution of the diphtheria poison it is also necessary to determine its absolute toxicity with the greatest possible precision. The absolute toxicity of the diphtheria poison is expressed as the minimal lethal dose (MLD), sometimes spoken of as the minimal fatal dose (MFD); and occasionally simply as the lethal dose. The minimal lethal dose may be readily defined as the smallest quantiy of toxin which will surely kill every guinea pig weighing 250 grammes in the course of four days, or at the latest, five days. As Ehrlich has pointed out, such a quantity may kill some of the animals sooner, that is, within thirty-six to forty-eight hours. A quantity of diphtheria poison that will kill every guinea pig, without exception, acutely within thirty-six to forty-eight hours contains more than the minimal lethal dose. The L + dose is a much more definite and constant measure than the MLD. It does not show the irregularities or present the difficulties met with in determining the absolute toxicity of the poison. On account of the importance of the L + and the L_0 doses the following simplified tables taken from actual experiments are given to show just how the two are made:

Test to determine the L + dose of a toxin.

	Result.
1 immunity unit + 0.19 cc. toxin	Invariably causes late paralysis, never acute death.
1 immunity unit + 0.20 cc. toxin	Sometimes causes late paralysis and sometimes acute death.
1 immunity unit + 0.21 cc. toxin	Always causes acute death about the fourth day.
I immunity unit + 0.22 cc. toxin	Always causes acute death, usually on the second or third day.

The L + dose of this toxin is, therefore, just 0.21 cc.

Tests to determine the L_0 dose of a toxin.

	Result at autopsy 48 hours after inoculation.
1 immunity unit + 0.14 cc. toxin	No visible reaction.
1 immunity unit + 0.15 cc. toxin	No visible reaction.
1 immunity unit + 0.16 cc. toxin	Slightest possible congestion about carbon particles or no reaction.
1 immunity unit + 0.17 cc. toxin	Apparent reaction at site of inoculation.
1 immunity unit + 0.18 cc. toxin	Injection and edema at site.
1 immunity unit + 0.19 cc. toxin	Injection and edema at site.

The L_0 dose of this toxin, therefore, is 0.16 cc.

Description and Physical Properties.—"A transparent or slightly opalescent liquid, with sometimes a slight granular deposit, of a faint brownish, yellowish or greenish color, nearly odorless, or having an odor due to the presence of the antiseptic used as a preservative. Diphtheria Antitoxin must come from healthy animals, must be sterile, free from toxins, and must not contain an excessive amount of preservative (not more than 0.5 per cent. of phenol or 0.4 per cent. of cresol, when either of these is used) and the total solids must not exceed 20 per cent.

"Diptheria Antitoxin must be prepared in an establishment licensed by the Secretary of the Treasury of the United States. The requirements for labeling are that the outside label must bear the name *Diphtheria Antitoxin* and the minimum number of units in the package, the lot number of the antitoxin, the name, address and license number of the manufacturer, and a statement of the date beyond which the minimum potency may not be maintained. This date is one year from date of issue from the manufacturing establishment if an excess of 20 per cent. over the minimum potency has been placed in the container, two years for a 30 per cent. excess, three years for a 40 per cent. excess, or four years for a 50 per cent. excess.

"The strength shall be expressed in units of antitoxic power, and the unit shall be that of the standard Diphtheria Antitoxin distributed by the Hygienic Laboratory of the United States Public Health Service. Diphtheria Antitoxin must be dispensed in the unopened glass containers in which it was placed by the manufacturing establishment, and it should be *preserved* at a temperature between 4.5° and 20° C., preferably at the lower limit." *U. S.*

Legal Requirements.—All diphtheria antitoxin and other biologic products sold in interstate commerce in this country must comply with the regulations made in accordance with the Law approved July 1, 1902, entitled "An Act to regulate the sale of viruses, serums, toxins, and analogous products in the District of Columbia, to regulate interstate traffic in said articles, and for other purposes." It is illegal to sell, barter, or exchange diphtheria antitoxin made in one State or Territory or the District of Columbia in another State or Territory or the District of Columbia unless the following salient points of the law have been complied with: 1. The product must be plainly marked with the proper name of the article contained therein: 2. The label on the package must plainly state the name and address of the manufacturer. 3. The package must be plainly labelled with the license number issued by the Secretary of the Treasury. 4. The date beyond which the contents cannot be expected, beyond reasonable doubt, to yield specific results, must be given on the label or package. The execution of the law rests with the Surgeon-General of the U. S. Public Health Service. Annual inspections of all licensed manufacturers are made by officers of the above named service. From time to time products of each licensed manufacturer are bought on the open market and examined in the hygienic Laboratory of the Public Health Service at Washington for purity and potency.

DIPHTHERIA TOXIN-ANTITOXIN MIXTURE for the immunization of susceptible persons against diphtheria. Because of the shortness of the duration of passive immunity, within recent years there has been introduced a method of producing active immunity by the injection of a mixture of the diphtheria toxin and antitoxin.

The protection against diphtheria afforded by injections of diphtheria antitoxin alone is passive and continues not more than three or four weeks. Active immunity such as that capable of being produced through the use of diphtheria toxin, on the contrary, usually lasts three years or longer.

Following the experimental work of Behring, Park and his associates succeeded in developing a modification by combining in a single product, diphtheria toxin and diphtheria antitoxin, to which they gave the name *Diphtheria T. A. Mixture.* The antitoxin is added to the diphtheria toxin solely for the purpose of robbing it of its irritant action on the tissues at the point of injection and thus allowing a large dose of the modified toxin to be injected.

Park and his assistants have employed active immunization with toxin-antitoxin mixture in a large number of susceptibles, including 1000 infants under one week old, without the subsequent occurrence of a single case of diphtheria. Park summarizes his observations as to the value of active immunization as follows:

"The procedure is absolutely harmless. No reaction develops in infants, while in older children and adults a moderate swelling of the arm may appear and last for from one to three days.

"One injection gives immunity to 80 per cent. of those previously susceptible, two injections give immunity to 90 per cent., and three injections to 97 per cent.

"The immunity conferred lasts for three years, and probably much longer.

"No diphtheria has occurred in those so far immunized."

The Toxin-Antitoxin Mixture originally used by Park and colleagues was made so that each cubic centimeter contained 3 L + doses of toxin properly neutralized by antitoxin. This preparation, while efficient, sometimes produced marked protein reactions in older children and adults. More recent work has shown that a formula containing 0.1 L + dose of toxin per cubic centimeter has the same immunizing effect as the old formula preparation with the objectionable features of the older preparation removed.

Preparation.—Diphtheria toxin-antitoxin is prepared by combining the required amount of an aged, accurately standardized diphtheria toxin and diphtheria antitoxin (for method of preparation of both, see under diphtheria antitoxin). The mixture is made in such proportions that it contains one-tenth of an L + dose of toxin and sufficient amount of antitoxin to have enough unneutralized toxin that one cc. will not cause the death of a 250-gramme guinea pig, but 5-cc. doses will cause acute death of most of the animals injected. The mixture must conform to all of the requirements of the Treasury Department for biologic products sold in interstate commerce.

Dose, 1 cc. injected subcutaneously for three doses given at intervals of 7 days.

DIPHTHERIA TOXIN FOR THE SCHICK TEST.—What is known as the *Schick Test* for the determination of immunity to diphtheria is widely employed for that purpose, especially in children of school age. The test consists in the intracutaneous injection of one-fiftieth the minimal lethal dose of diphtheria toxin for guinea pigs. If the individual injected is immune to the disease no reaction will occur, but if susceptible, a local reaction will develop on 24 to 48 hours. The test is of particular value in institutions, in localized outbreaks of diphtheria and for the detection of susceptibles with a view to their later immunization with toxin-antitoxin mixture. The test material consists of accurately standardized diphtheria toxin with sterile normal salt solution as a diluent. The formula generally used is one in which one-fiftieth of a minimal lethal dose of toxin for a guinea pig is contained in 0.2 cc. of the final dilution. The diluted toxin quickly loses in potency and must always be freshly prepared. The injection must be made intracutaneously—that is into, not beneath, the skin, and preferably on the flexor surface of the forearm. In Schick Tests of children over six years of age, it is advisable to make a control test by the injection of a similar amount of the same dilution which has been heated to 75° C. for 10 minutes The control test enables the observer to eliminate reactions due to the protein in the toxin and blood of the person tested.

The percentage of positive reactions varies greatly at different ages, the highest percentage of positive reactions occurring in children between six months and four years of age.

Uses.—Diphtheria antitoxin is a true specific for diphtheria if it is given in sufficient quantity and sufficiently early in the disease. The very unfavorable results obtained in England in 1895 in the treatment of *diphtheria* with serum were due, according to the report of the Lancet Commission (*L. L.,* July 19, 1896), in a great majority of cases, to the uses of serum too weak to produce therapeutic results. Experimental researches, for example, the very careful work of Madsen in Copenhagen in 1896, showed that for therapeutic purposes weak serum is of very little value. Equally disappointing results will be obtained if the antitoxin is administered after the toxine has damaged the cells. The early use of the remedy is of the greatest importance. No time should be lost, not even delay in waiting for bacteriological confirmation. As soon as diphtheria is suspected, 10,000 units of antitoxin should at once be injected into the subcutaneous or intramuscular tissue.

The following figures, from the Philadelphia Hospital for Contagious Diseases, show even more convincingly the great value of the early administration of antitoxin as well as general average reduction of mortality by antitoxin.

Mortality of Diphtheria According to Day on which Antitoxin was first injected in 8591 consecutive cases.

Day of illness	Number of patients	Deaths	Per cent. mortality
First	329	5	1.52
Second	2269	77	3.39
Third	2407	165	6.85
Fourth	1612	176	10.91
Fifth	911	136	14.92
Sixth	416	54	12.98
Seventh	320	53	16.56
Unknown	327	50	15.29
Totals	8591	716	8.33

In Boston, a city which has suffered severely from diphtheria and where the antitoxin treatment has been particularly thorough, the reduction in the death rate has been striking. In the Boston City Hospital the death rate between 1888 and 1894 was only once below 40 per cent.; since 1895, when antitoxin was introduced, it has not once reached 15 per cent. (J. H. McCallum). Numerous statistics from all parts of the world upon the effect of the antitoxin treatment of diphtheria are practically unanimous in showing the good results of this remedy. The great value of diphtheria antitoxin is perhaps most strikingly seen in the laryngeal cases (*"membranous croup"*).

The standard curative dose is 10,000 units administered at once, though mild cases require less and severe ones more—particularly if not seen at the early stage The entire amount needed should be given at one dose, intravenously if the case is urgent. A vein at the bend of the elbow may be punctured with the injection needle under aseptic precautions, and the antitoxin slowly introduced. Fortunately the serum is usually harmless even when injected in large quantities. The remedy should always be given by the hypodermic, intramuscular, or intravenous method. Strict asepsis must be observed. The liquid may be injected under the skin of any part of the body where the subcutaneous tissue is loose. The back, near the angle of the scapula, is a favorite site for inoculation; sometimes the flank or abdominal walls are chosen. The intramuscular route is more rapid and hence more effective than the subcutaneous; the heavy musculature of the buttocks is usually chosen for this method. If improvement is not manifest after a few hours more antitoxin should be given, though this implies that the first dose was too small. It is the early administration rather than the large quantity which is most efficient. The exhibition of the remedy by the mouth or per rectum is practically valueless.

Diphtheria antitoxin is just as valuable for prophylaxis as for curative purposes. The passive immunity produced by the inoculation of the antitoxic serum does not last very long. The transitory nature of the immunity afforded by prophylactic injections is probably dependent upon the fact that the antitoxin-bearing horse serum, being a foreign protein, is broken down in the human body and excreted by the kidneys. The usual prophylactic dose is 1000 units. If the exposure to the infection continues, the dose should be repeated in two weeks, or, preferably, use the toxin-antitoxin mixture described above. The antitoxin in the blood neutralizes the toxin elaborated by the bacilli growing on the mucous membrane of the throat, but has no deleterious effect upon the bacteria themselves. The microorganisms in this situation may continue to grow and remain virulent for months. This is the explanation of occasional failures of the antitoxin to prevent a subsequent attack of the disease.

Although the injection of the serum is usually harmless, there are certain individuals who are abnormally sensitive to horse serum in which the injection may cause unpleasant reactions or even, in rare instances, death. Two types of reactions of this kind have been reported, one characterized by urticaria and sometimes pains in the joints, which usually passes away in a few days without further ill-consequences. In the other type there occurs asthmatic paroxysms of greater or lesser severity which, in some instances, has lead to complete obstruction of respiration and consequent death. In patients who are subject to asthma, especially of the so-called "horse asthma," the treatment is fraught with considerable danger. MacKenzie (*J. A. M. A.*, 1921, lxxvi, p. 1563) recommends in all cases of doubt the intracutaneous injection of 0.002 cc. (${}^1/_3$ minim) of horse serum. In sensitive individuals there occurs within a half hour a reaction shown by the appearance of a wheal surrounded by a zone of erythema. The method of desensitizing such individuals suggested by Besredka, which is often although not universally successful, consists in the intravenous injection at intervals of from five to ten minutes of increasing doses of the serum beginning with very little quantities. These unpleasant reactions are much less frequent since the use of the purified antitoxin; they are also less likely to occur when the antitoxin is given subcutaneously than when administered intravenously. Leyton (*L. L.*, June 10, 1916) recommends scopolamine, especially if combined with morphine to prevent the anaphylactic reactions. In any case, however, the danger from diphtheria is greater than the danger from serum reaction (anaphylaxis), and the antitoxin should not be withheld.

Diphtheric antitoxin gradually loses its strength, especially when kept under unfavorable conditions of light, temperature, etc. The loss in one year is usually from 10 to 30 per cent.; however, a serum will retain considerable antitoxic potency after years. Except for its diminished potency an old serum is quite as good as one freshly prepared; so that in an emergency or in order to save time an old serum may be administered, provided it remains uncontaminated.

Dose, prophylactic, 1000 units; curative, 10,000 units or more.

ANTITOXINUM TETANICUM. U. S.

TETANUS ANTITOXIN

ANTITOX. TET. [Serum Antitetanicum Purificatum, U. S. P. IX, Concentrated Tetanus Antitoxin, Refined Tetanus Antitoxin, Antitetanic Globulins.]

"Tetanus Antitoxin is an aqueous solution of certain antitoxic substances obtained from the blood serum or plasma of an animal of the genus *Equus,* which has been properly immunized against tetanus toxin. After the serum or plasma from the immunized animal has been collected, the antitoxin-bearing globulins are separated from the other constituents of the serum or plasma and dissolved in water. Sodium chloride and a preservative are then added and the solution is filtered through a bacteria-excluding filter. It has a potency of not less than 300 units per cc." *U S.*

Tetanus-Heilserum, *G.;* Serum Antitetanique *Fr.;* Siero Antitetanico, *It.;* Suero Antitetanico, *Sp.*

This antitoxin takes the place of the formerly official *Serum Antitetanicum Purificatum.*

The discovery of tetanus and diphtheria antitoxins was simultaneous, Behring, who worked principally on diphtheria, and Kitasato who worked on tetanus publishing their results together (*D. M. W.,* 1890, Nos. 49, 50) from the Hygienic Institute in Berlin under Robert Koch. In general the method of preparation is the same as that described under *Serum Antidiphthericum.* The purified and dried tetanus toxin is the most powerful poison known, the fatal dose for mice being as low as 0.000,000,05 gramme. There are at least two toxins produced by the tetanus bacillus—*tetano-spasmin,* which causes the muscular contractions typical of the disease, and *tetano-lysin,* which destroys the red corpuscles of the blood. The former is by far the more important, giving the symptoms of rigidity (*e.g.,* lockjaw), and tonic convulsions by which the disease is recognized in man and animals, and causing the high mortality. This poison is absorbed by the end-plates of the nerves in muscle, and travels up these motor nerves to the ganglion cells of the central nervous system. It is the passage along the nerves which occupies the greater part of the time of the incubation period.

Preparation.—The chief difference in method of preparation from that used in the case of diphtheria antitoxin lies in the fact that the tetanus bacillus belongs to the group of bacteria known as obligatory anaerobes, that is, those which thrive only in the absence of oxygen—and in the further fact that the poison formed by the tetanus bacillus is very unstable and rapidly loses in strength under ordinary conditions. The former difficulty is overcome by growing in deep vessels containing specially prepared broth which has been freshly heated to drive off the oxygen; and the latter by using the toxin soon after preparation or by storing it under special conditions.

Description and Physical Properties.—"A transparent or slightly opalescent liquid, with sometimes a slight granular deposit, of a faint brownish, yellowish or greenish color, nearly odorless, or having an odor due to the presence of the antiseptic used as a preservative. Tetanus Antitoxin must come from healthy animals, must be sterile, free from toxins, and must not contain an excessive amount of preservative (not more than 0.5 per cent. of phenol or 0.4 per cent. of cresol, when either of these is used) and the total solids must not exceed 20 per cent.

"Tetanus Antitoxin must be prepared in an establishment licensed by the Secretary of the Treasury of the United States. The requirements for labeling are that the outside label must bear the name *Tetanus Antitoxin* and the minimum number of units in the package, the lot number of the antitoxin, the name, address and license number of the manufacturer, and a statement of the date beyond which the minimum potency may not be maintained. This date is one year from date of issue from the manufacturing establishment if an excess of 20 per cent. over the minimum potency has been placed in the container, two years for a 30 per cent. excess, three years for a 40 per cent. excess, or four years for a 50 per cent. excess.

"The strength shall be expressed in units of antitoxic power, and the unit shall be that of the standard Tetanus Antitoxin distributed by the Hygienic Laboratory of the United States Public Health Service. Tetanus Antitoxin must be dispensed in the unopened glass containers in which it was placed by the manufacturing establishment, and it should be *preserved* at a temperature between 4.5° and 20° C., preferably at the lower limit." *U. S.*

The standard for tetanus antitoxin is the result of research done in the hygienic laboratory in conection with the governmental control of biologic products. (The Standardization of Tetanus Antitoxin, by M. J. Rosenau and John F. Anderson, *Hyg. Lab. Bull.,* No. 43, U. S. P. H. S., March, 1908.) This method of standardization is distinct from any previously in use, but, since its adoption in this country, has come to be used to a large extent outside the United States as well. As with diphtheria antitoxin, the ultimate standard unit is a definite amount of dried serum kept under special condition at Washington. The technic of the preparation, storage, weighing, and solution of this antitoxin is the same as in the case of the diphtheria standard. The medium of measurement, however, is a standardized toxin which is likewise dried and preserved in vacuum tubes in the absence of moisture, and sent out to the establishments in various parts of the world manufacturing tetanus antitoxin. On account of the hygroscopic quality of this dried poison and its extreme instability in the presence of moisture, it is necessary that the tubes be kept after opening in a vacuum desiccating chamber at a low temperature and protected from light. For each use the powder must be weighed quickly on delicate balances and computation made for gain in weight due to absorption of moisture. Any deterioration in the toxin may be detected by testing with the standard antitoxin or by ascertaining the minimal lethal dose (MLD), which is stated for each tube of toxin when sent out.

The animal used for testing tetanus antitoxin by the American standard is the guinea pig. The standard weight is 350 grammes, and the test dose of the toxin when mixed with one-tenth unit of antitoxin, should kill the guinea pig in about ninety-six hours.

Tetanus antitoxin, as well as all similar products, is tested for sterility by planting in suitable culture media and incubating for a number of days, and for presence of toxin, excess of preservative, or other deleterious content, by animal inoculation.

For other legal requirements, see *Serum Antidiphthericum,* U. S.

Uses.—Tetanus antitoxin has achieved its great success as a preventive rather than as a curative measure. Though in times of peace *tetanus* is not a common disease, the tetanus bacillus is ubiquitous and in its spore form, very long lived; its relative infrequence as a cause of sickness and death is due to the excellence of the bodily defenses against it. As explained above, the tetanus bacillus requires an absence of oxygen to thrive; this is not obtained unless the organism is introduced deep below the surface of the skin or under a tight covering, is accompanied by other organisms which absorb the oxygen, or has necrotic tissue as a nutrient. Even if so introduced, the natural antagonism of the body fluids or the wandering cells of the blood may render the invasion harmless. There is abundant evidence, however, that when the above conditions are favorable to its development, the tetanus bacillus produces a high mortality among wounded, and that this mortality is due to the toxin alone. Aside from the occasional tetanus infection when an ordinary wound is contaminated with dirt, and the cases of *tetanus neonatorum* now fortunately obsolete with the advent of asepsis in labor and in treatment of the umbilical cord, there are three large causes of tetanus: Fourth of July wounds—the laceration from explosion at short range driving contaminated material deep into the tissues; operation and wounds of horses—since horse manure is one of the most prolific sources of the tetanus bacillus; the wounds of warfare, particularly on cultivated terrain. In each of these three classes we have evidence of the value of tetanus antitoxin as a preservative.

In St. Louis, where tetanus had been common following Independence Day, the institution of serum treatment in 1904 was followed by entire absence of tetanus among those so treated. For the whole United States, where the growing use of tetanus antitoxin has been parallelled with decreasingly violent celebrations, the reduction in fatality is striking, the deaths from tetanus having fallen from 406 in 1903 to 1 in 1915, while the ratio of deaths from tetanus to total deaths from fireworks has fallen from 1 in 1.15 (406 out of 466) to 1 in 30, thus indicating that the tetanus prophylaxis has outstripped the general measures of safety.

The veterinary use of tetanus antitoxin in this country has repeatedly eliminated the disease among horses where it had previously been endemic. In France tetanus following operations on horses had been extremely common until the use of antitoxin was instituted, when the tetanus ceased except in the practice of those veterinarians who did not use the antitoxin.

All observers in the European war hospitals agree that when tetanus antitoxin was difficult to procure, in the early part of the war, the mortality from tetanus was high; but when properly standardized potent serum became available and was thoroughly administered, tetanus was rare. From official statistics of this military experience it seems clear that in all wounds, except the slight ones which heal quickly, the prophylactic injection of tetanus antitoxin should be repeated at weekly intervals until the wound is healed, and wounded soldiers should receive a prophylactic dose when operated upon, even though the original wound be closed.

The results with tetanus antitoxin as a curative agent in the presence of the developed disease have not been as satisfactory as is the case with diphtheria antitoxin in the treatment of diphtheria. Nevertheless, there seems to be a general agreement with American surgeons, as well as those abroad, that the mortality is reduced at least 20 per cent. as a result of the use of tetanus antitoxin. As is the case with diphtheria, the mortality is greater the longer the interval elapsing between the onset of symptoms and the time treatment is begun. It also appears that the previous administration of a prophylactic dose of antitoxin has some influence on the outcome of the disease which may later develop. According to some of the British Army reports in the recent war, the mortality was about 35 per cent. among those who developed the disease after the prophylactic injection of antitoxin, and 71 per cent. among those who had not a prophylactic treatment. Intensive treatment, however, particularly intraspinal injection, apparently gives a lower death rate than is usual with tetanus treated without antitoxin. The technic for intraspinal medication is described under *antimeningococcus serum* in Part II.

For prophylaxis 1500 units should be injected subcutaneously in case of any wound contaminated with dirt, caused by an explosive, or accompanied by severe mutilation of tissue. This injection should be repeated at weekly intervals until the wound has healed. It is also important that all such wounds receive thorough surgical attention, with wide opening and cleansing, removal of tissue likely to necrose, and repeated antiseptic dressings. For treatment, about 5000 units should be given intraspinally as promptly as possible, and 10,000 units intravenously at the same time; unless the serum is of low viscosity, it may well be diluted with sterile salt solution for intraspinous injection. The intraspinal dose may be repeated daily and the larger dose repeated subcutaneously a few days later to keep the blood saturated with antitoxin. The powdered antitoxin is sometimes used as a dusting powder on wounds, but absorption in this method is uncertain; chief reliance in prophylaxis must be placed in subcutaneous injection.

Hypersusceptibility to horse serum should be guarded against in the use of tetanus antitoxin as in the case of diphtheria antitoxin. The deterioration of the two serums is also similar.

Dose, as a prophylactic, 1000 to 2000 units; as a curative, 10,000 to 20,000 units.

ANTITOXINUM TETANICUM CRUDUM. U. S.

CRUDE TETANUS ANTITOXIN Antitox. Tet. Crud.

[Serum Antitetanicum, U. S. P. IX. Crude Antitetanic Serum, Unconcentrated Tetanus Antitoxin, Unrefined Tetanus Antitoxin.]

Crude tetanus antitoxin is a fluid, having a potency of not less than 150 units per cc., separated from the coagulated blood of an animal of the genus *Equus,* which has been properly immunized against tetanus toxin.

Description and Physical Properties.—" A yellowish, or yellowish-brown, transparent, or slightly turbid liquid with sometimes a slight granular deposit, having the faint odor of horse serum or having an odor due to the presence of the antiseptic used as a preservative. Crude Tetanus Antitoxin must come from healthy animals, must be sterile, free from toxins, and must not contain an excessive amount of preservative (not more than 0.5 per cent. of phenol or 0.4 per cent. of cresol, when either of these is used) and the total solids must not exceed 20 per cent.

" Crude Tetanus Antitoxin must be prepared in an establishment licensed by the Secretary of the Treasury of the United States. The requirements for labeling are that the outside label must bear the name *Crude Tetanus Antitoxin* and the minimum number of units in the package, the lot number of the antitoxin, the name, address and license number of the manufacturer and a statement of the date beyond which the minimum potency may not be maintained. This date is one year from the date of issue from the manufacturing establishment if an excess of 20 per cent. over the minimum potency has been placed in the container, two years for a 30 per cent. excess, three years for a 40 per cent. excess, or four years for a 50 per cent. excess.

" The strength shall be expressed in units of antitoxic power, and the unit shall be that of the standard Tetanus Antitoxin distributed by the Hygienic Laboratory of the United States Public Health Service. Crude Tetanus Antitoxin must be dispensed in the unopened glass containers in which it was placed by the manufacturing establishment, and it should be *preserved* at a temperature between 4.5° and 20° C., preferably at the lower limit." *U. S.*

For preparation, preservatives, tests and uses, see *Antitoxinum Tetanicum.*

Dose, curative 10,000 units, protective 1500 units.

APII FRUCTUS. N. F.

CELERY FRUIT Apii. Fruct. [Celery Seed]

" Celery Fruit is the dried ripe fruit of *Apium graveolens* Linné (Fam. *Umbelliferæ*). Celery Fruit contains not more than 5 per cent. of unsound or foreign fruits or other foreign organic matter and yields not more than 3 per cent. of acid-insoluble ash." *N. F.*

Smallage; Marsh Parsley; Ache, Céleri, *Fr.;* Eppich, Cellerie, *G.;* Apio, *Sp.*

Description and Physical Properties.—" *Unground Celery Fruit.*—Mericarps united or separate, ovoid, slightly curved, 1 to 2 mm. long and about half as broad and half as thick; dark brown; inner surface flat; outer surface convex, smooth except for 5 very slender light-colored ribs, 2 of which are marginal. Odor characteristic, agreeable; taste aromatic, warm and somewhat pungent.

" *Structure.*—Mericarp nearly equilaterally pentagonal in transverse section; with 6 to 165 oil-tubes in the pericarp, the latter closely surrounding a somewhat pentagonal seed; epidermis of pericarp with tangentially elongated cells, the latter with a thick cuticle and occasionally developed into short, smooth papillæ; a fibro-vascular bundle in each of the ribs, composed of a few tracheæ and strongly lignified fibers; inner tissue of pericarp of tangentially elongated parenchyma with brownish walls; seed chiefly of endosperm parenchyma; seed-coat of several layers of yellowish more or less collapsed cells; endosperm of thick-walled polygonal cells containing fixed oil and aleurone grains, the latter each with a small rosette of calcium oxalate.

" *Powdered Celery Fruit.*—Brown and oily; fragments of the pericarp with yellowish oil-tubes, brown secretion cells and few epidermal papillæ; tracheæ and fibers; parenchyma cells of endosperm with aleurone grains, the latter usually containing rosettes of calcium oxalate, 0.002 to 0.008 mm. in diameter." *N. F.*

The celery plant is a hardy biennial native to Great Britain but cultivated in all parts of the temperate zone. In the wild state it has a rank disagreeable taste but by cultivation the leaves have lost their coarse taste and afford the familiar vegetable. The plant has a glabrous stem 1 to 3 feet high; the leaves are pinnate, the basal and lower being long-petioled and the upper short-stemmed. The small flowers are borne in umbels opposite the leaves.

Celery seed yields a volatile oil possessing the characteristic odor of the drug. This volatile oil consists chiefly of terpenes, but its odor appears to be due to two anhydrides: *sedanolid* $C_{12}H_{18}O_2$, the lactone of sedanolic acid, and *sedanonic anhydride* $C_{12}H_{18}O_3$.

Apium nodiflorum (L.) B. et H. (*Sium nodiflorum* L.) *Water parsnip.*—This is a perennial, umbelliferous, aquatic, European plant, growing also in the southern section of the United States. It is commonly considered poisonous; but the fresh juice has been used by Withering and others, in the *dose* of three to four ounces every morning, for scrofulous *lymphadenitis* and obstinate *skin diseases.*

Uses.—There is a popular superstition among the uneducated that celery seed has a sedative and tonic effect upon the central nervous system and it is sometimes added to mixtures intended for nerve tonics. There is, however, not the slightest reason to ascribe any therapeutic virtue to the drug.

Dose, from twenty to sixty grains (1.3–4 Gm.).

Off. Prep.—Fluidextractum Apii Fructus, *N. F.;* Elixir Guaranæ et Apii, *N. F.*

APOCYNUM. N. F.

APOCYNUM Apocyn. [Canadian Hemp]

"Apocynum consists of the dried rhizome and roots of *Apocynum cannabinum* Linné (Fam. *Apocynaceæ*). Apocynum contains not more than 5 per cent. of its stems or other foreign organic matter." *N. F.*

Canadian Hemp; Black Indian Hemp; Amy Root; Chanvre du Canada, *Fr.;* Canadische Hanfwurzel, *G.*

There are several indigenous species of this genus of very similar general aspect, the rhizome and roots of two of them being collected, viz.: *Apocynum cannabinum* L., and *A. androsæmifolium* L. Both plants abound in a milky juice, which is present in simple latex cells that occur in the cortex and pith of the stems and mesophyll of the leaves, and have a tough, fibrous bark, which, by maceration, affords a substitute for hemp; hence the common name. It was used by the Indians of California for making cordage and for weaving. Both species are indigenous to North America and widely distributed.

In *A. cannabinum* the stems and branches are upright or ascending, terminated by erect and close, many-flowered cymes, which are usually shorter than the nearly sessile leaves, and the corolla has nearly erect lobes, with the tube not longer than the lanceolate divisions of the calyx. In *A. androsæmifolium* or *dogbane* the branches are divergently forked, the leaves are slender petioled, the cymes loose and spreading, the open bell-shaped corolla with revolute lobes and a tube much longer than the ovate-pointed divisions of the calyx. *A. cannabinum,* of which there are several well recognized varieties, grows in gravelly or sandy soil mostly near streams, while *A. androsæmifolium* grows in dry thickets and open woods. According to E. A. Manheimer, the root of the latter is distinguished from *A. cannabinum* by the thick-walled stone cells, which are arranged in an interrupted circle near the middle of the bark. (*A. J. P.,* Nov., 1881. See also *A. J. P.,* 1888.) Holm has contributed an article on the structure of *A. cannabinum.* (*Merck's Rep.,* 1910, p. 277.)

Description and Physical Properties.—"*Unground Apocynum.*—Cylindrical, somewhat branched, of varying length, 3 to 10 mm. thick, externally reddish brown to grayish brown; longitudinally wrinkled, occasionally with transverse fissures having vertical sides extending through the bark; fracture short; internal bark light brown, 1.5 to 3 mm. thick; wood radiate and with large tracheæ; pith small, in rhizome pieces only. Almost inodorous; taste starchy, afterwards becoming bitter and somewhat acrid.

"*Structure.*—Numerous laticiferous vessels in the bark and pith; cortex chiefly parenchyma cells, the latter filled with starch grains; wood with medullary rays, 1 to 2 cells in width and separating numerous narrow wedges of tracheæ and wood fibers; pith of thin-walled parenchyma, absent in the root. Stem portion with thin fibrous bark, a light brown porous wood and a large pith.

"*Powdered Apocynum.*—Light brown; numerous starch grains 0.003 to 0.020 mm. in diameter, spherical, ellipsoidal, ovate, pyriform or irregular, sometimes altered, swollen and with a hyaline central cleft; numerous fragments of strongly lignified wood fibers, the latter associated with tracheæ having bordered pores or spiral thickenings; few fragments of cork cells with reddish brown walls; occasional fragments with laticiferous tissues; stone cells few or absent." *N. F.*

The fresh root, when wounded, emits a milky juice, which concretes into a substance resembling caoutchouc.

The nature of the active principle of apocynum is as yet somewhat uncertain. Finnemore, in 1908, obtained from the *A. cannabinum* a crystalline substance to which the name of *cynotoxin* was applied. The following year Moore (*J. Chem. Soc.,* 1909, xcv) separated from the *A. androsæmifolium* a glucoside having the formula $C_{14}H_{18}O_3$, to which he applied the name of *apocynamarin.* These two principles, which appear to be identical, possess the characteristic physiological effects of the crude drug.

Taub and Fickewirth (*A. G. P.*, cliii, p. 239) believe that neither of these principles is chemically pure and that the activity of the plant is due to an intensely bitter principle which is not of glucosidal nature and to which they apply the name of *cymarin.* According to Windaus and Hermauns (*Ap. Ztg.*, 1915, 337) anhydrous cymarin has the formula $C_{30}H_{44}O_9$. Puckner (*J. A. M. A.*, 1914, lxiii, 1393) says it is not a glucoside although sensitive to acids. Cymarin has been studied pharmacologically by Impens and found to exert the characteristic effects of the drug.

Von Oefele (*Journ. Pharm. Elsass-Lothr.*, 1891, 325) described *apocynteine,* an alkaloid obtained from *A. venetum;* it is said to be a cardiac sedative.

Uses.—Apocynum was first called to the attention of the medical profession by M. L. Knapp in 1826, although its virtues seem to have been known to the aborigines. Subsequent to this date a number of clinicians employed it in the treatment of various dropsies and presented evidence that it was related to the digitalis group in its therapeutic effects. H. C. Wood, Jr. (*J. A. M. A.*, Dec. 24, 1904) has shown that, like digitalis, apocynum in moderate dose causes a slowing of the pulse and increase in the amplitude of the cardiac contractions and in toxic dose it causes marked increase in the systolic tone of the heart with great irregularity of its beat. In his experiments on the intact animal Wood found that the blood pressure was usually lowered because of the marked effect on cardiac inhibition, but that when the pneumogastric nerves had previously been divided there was a notable increase in the blood pressure, which he attributed chiefly to stimulation of the heart. Dale and Laidlaw (*Proc. Roy. Soc. of Med.*, Dec., 1909) have shown, however, that apocynum has a very marked stimulant action upon the vasomotor system. It appears to be more irritant to mucous membranes than either digitalis or strophanthus, and therefore is prone to cause nausea and catharsis. Perhaps this local stimulant effect is also the explanation of its very powerful diuretic action, although Dale and Laidlaw believe that the effect upon the kidneys is due chiefly to a relative dilatation of the renal arteries.

Although there is scarcely room for doubt that apocynum may be used as a substitute for digitalis in the treatment of chronic heart disease the careful studies of Marvin and White (*J. A. M. A.*, 1921, lxxvii, p. 1865) on patients suffering with auricular fibrillation show that it is ordinarily inferior in its action to digitalis. These authors found that doses large enough to control the cardiac irregularity produced almost uniformly nausea and vomiting and in several cases in which digitalis was afterwards used successfully, they were unable to obtain distinct benefit from apocynum. The older writers believe that it has a stronger effect upon the kidney and is especially of service in the treatment of *dropsies* both of those due to failure of the heart and the *ascites of hepatic cirrhosis.*

Cymarin has been used clinically by Bounsmann (*Med. Klin.*, 1921, xvii, 1522) and others as a cardiac stimulant and tonic in daily doses of one one-hundred-and-twentieth to one-sixtieth of a grain (0.5–1.0 milligramme) hypodermically.

Its irritant action upon the intestinal tract and irregularity of absorption militate strongly against its clinical usefulness; many patients are quite unable to take the drug because of the occurrence of emesis or purgation.

Dose, five to fifteen grains (0.32–1.0 Gm.).

Off. Prep.—Fluidextractum Apocyni, *N. F.*

"CAUTION.—It has been stated that the absorption of Apocynum in the gastro-intestinal tract is uncertain and irregular. To avoid possible toxic or cumulative action of the drug the physician should determine in each case the tolerance of the patient and regulate the dosage accordingly." *N. F.*

APOMORPHINÆ HYDROCHLORIDUM.
U. S., Br.

APOMORPHINE HYDROCHLORIDE

Apomorph. Hydrochl.

"The hydrochloride [$C_{17}H_{17}O_2NHCl.\frac{1}{2}H_2O$] of an alkaloid prepared from morphine by the abstraction of one molecule of water. *Caution.—Apomorphine Hydrochloride must be rejected if it at once imparts an emerald-green color to 100 parts of distilled water when shaken with it in a test tube.*" *U. S.* "Apomorphine Hydrochloride, $(C_{17}H_{17}NO_2,HCl)_2,H_2O$, is the hydrochloride of an alkaloid which may be obtained from morphine by the abstraction of the elements of a molecule of water." *Br.*

Hydrochlorate of Apomorphine; Chlorhydrate d'Apomorphine, *Fr. Cod.;* Apomorphinum Hydrochloricum, *P. G.;* Apomorphinhydrochlorid, *G.;* Cloridrato di apomorfina, *It.;* Cloruro de apomorfina, *Sp.*

Apomorphine was discovered by Matthiessen and C. A. Wright. It is prepared by heating morphine in a closed tube with a great excess of hydrochloric acid for two or three hours to the temperature of 140° to 150° C. The contents of the tube are then dissolved in water, an excess of sodium bicarbonate added, and the precipitate exhausted with ether or chloroform. On the addition to the solution of a very small quantity of hydrochloric acid, crystals of apomorphine hydrochloride form. The process is one of dehydration; the morphine parting with one molecule of water, the formula of apomorphine being $C_{17}H_{17}O_2N$. Apomorphine may also be made by the action of hydrochloric acid upon codeine, and it is affirmed that the best method in practice is that of E. Mayer, in which morphine is treated with a solution of zinc chloride, at 120° C. (*B. Chem. G.*, 1871, iv, 121.) Codeine, $C_{18}H_{21}O_3N$, when treated with hydrochloric acid, yields first $C_{18}H_{20}ClNO_2$, and then splits off methyl chloride, CH_3Cl, and leaves apomorphine, $C_{17}H_{17}O_2N$. Pschorr (*B. Chem. G.*, 1902, 4377) believes that apomorphine is a derivative of phenanthrenequinoline.

Description and Physical Properties.—"Minute, white or grayish-white glistening crystals, acquiring a greenish tint upon exposure to light and air. It is odorless. One Gm. of Apomorphine Hydrochloride is soluble in 50 cc. of water and in 50 cc. of alcohol, at 25° C. One Gm. is soluble in 17 cc. of water at 80° C. and is very slightly soluble in chloroform and in ether.

"The addition of a solution of sodium bicarbonate to an aqueous solution of the salt (1 in 100) produces a white, or pale greenish-white precipitate, which rapidly becomes green on exposure to air and when dissolved in ether, produces a violet color; in chloroform, a violet-blue color. Apomorphine Hydrochloride dissolves in nitric acid, producing a dark purple solution. Silver nitrate T.S. added to an aqueous solution of the salt produces a white precipitate, insoluble in nitric acid. This precipitate soon turns black by reduction to metallic silver, and is instantly reduced by the addition of ammonia water.

"A saturated aqueous solution of Apomorphine Hydrochloride is neutral to litmus paper. The ash from 0.2 Gm. is negligible. Shake 0.1 Gm. of the salt with 5 cc. of ether: the latter acquires not more than a pale reddish color (*decomposition products*).

"Preserve in small, dark amber-colored, well-stoppered vials, which have been previously rinsed with diluted hydrochloric acid and dried." *U. S.*

"Small grayish-white, shining, acicular crystals, turning green on exposure to air and light. Soluble in 60 parts of *water* and in 50 parts of *alcohol* (90 per cent.). The solutions decompose on boiling or keeping, with production of a green color; but remain unchanged for a considerable time if acidified with a trace of *hydrochloric acid.* Yields the *reactions* characteristic of chlorides. Gives a deep red color with dilute *T. Sol. of ferric chloride.* The addition of an aqueous solution of *sodium bicarbonate* to an aqueous solution (1 in 100) of Apomorphine Hydrochloride produces a white precipitate rapidly changing to green; this precipitate forms a purple solution with *ether,* a bluish solution with *chloroform,* and a green solution with *alcohol* (90 per cent.)." *Br.*

The alkaloid is colored dark red by nitric acid and rose red by ferric chloride, changing to violet, and finally black, on exposure. The aqueous and alcoholic solutions are at first colorless, if heated becoming pinkish, but change rapidly to greenish, finally becoming deep emerald green in color. This change in color has been attributed to oxidation, and it has been noticed that the solution on standing loses its power; for this reason it is best not to keep the solution, but to make it as wanted. C. Bernbeck affirms that the change in the solution to a green color may be prevented by the addition of a small quantity of hydrochloric acid, the decomposition being due to ammonia. (*Ph. Ztg.*, 1885.)

According to Max Quehl and H. Koehler, apomorphine is precipitated from its solutions, greenish by tannic acid, lemon yellow by picric acid, bluish-white—turning to sap-green—by copper sulphate on boiling, purplish by gold chloride, white—turning to blackish-violet—by potassium ferricyanide on boiling, blood-red by iodine in solution of potassium iodide, the precipitate disappearing on boiling, white and curdy by potassium sulphocyanate. (*A. J. P.*, 1873, p. 166.) With potassium dichromate and concentrated sulphuric acid it turns a dark red; with the potassium salt alone, a deep yellow-orange; with neutral iron chloride, an amethyst color.

A delicate test proposed for the detection of apomorphine is as follows: To 5 cc. of apomorphine solution add 5 drops of a saturated solution of mercuric chloride followed by 5 drops of a 10 per cent. sodium acetate solution. Boil for a minute and when cool add 1 cc. of amyl alcohol and shake. The amyl alcohol acquires a blue coloration in solutions of as little as 2 parts to the million of apomorphine.

According to Harnack and Hildebrand (*A. E. P. P.*, 1911, lxv, p. 38) apomorphine hydrochloride is sometimes contaminated with *chloromorphine,* whose action is very similar to that of acetyl-morphine. Frerichs (*P. J.*, lxxxiv, p. 293) reports having examined two samples of apomorphine hydrochloride which consisted almost entirely of *trimorphine hydrochloride.*

Uses.—Apomorphine hydrochloride was first brought forward by Gee as a prompt and efficient emetic. According to the researches of Eggleston and Hatcher (*J. P. Ex. T.*, 1912, iii, p. 551) the vomiting is due solely to an action on the vomiting center. Aside from its emetic effects, therapeutic doses of apomorphine ordinarily have very little influence upon the system. Rosenwasser (*N. Y. M. R.*, July, 1907), however, and some other writers maintain that it has narcotic properties, but it is not impossible that the effects they have observed have been due to impurities in the drug. It has the great advantages of smallness of dose and freedom from irritating properties, so that it can be used hypodermically. When from one-fifteenth to one-tenth of a grain (0.004–0.006 Gm.) of it is injected under the skin of a man, free emesis usually occurs in from 5 to 20 minutes. The effects upon the general system are usually not marked; but in some cases very alarming syncopal symptoms have been produced, and death is said to have resulted from one-sixteenth of a grain (0.004 Gm.) in a feeble adult worn out with chronic bronchitis and emphysema. (*Med. Rec.*, 1877, p. 664; see also Seuffer, *M. M. W.*, 1921, xix, p. 584.) Apomorphine hydrochloride is a very useful emetic in cases of *poisoning* or *acute gastritis* or any other condition where it is desired to promptly evacuate the stomach. Its advantages are, first, lack of irritation of the gastric mucosa, secondly, the smallness of dose which makes it possible to carry it in the form of a hypodermic tablet, and thirdly, the promptness of its effect. In cases of *narcotic poisoning,* however, it frequently fails to act, because of the depression of the vomiting centers. Given in doses too small to act as an emetic it is a valuable nauseating expectorant in the early stages of *acute bronchitis.* One drawback to its wider use for this purpose is its instability when in solution. The green substance formed does not seem to be toxic, but it does not possess the peculiar therapeutic properties of the drug. Under no circumstances should more than one-fourth of a grain (0.016 Gm.) by mouth, or one-eighth of a grain (0.008 Gm.) hypodermically, be given at a dose.

Dose, as an expectorant, one-thirtieth to one-twentieth of a grain (0.002–0.003 Gm.); as an emetic, one-fifteenth to one-eighth of a grain (0.004–0.008 Gm.).

Off. Prep.—Injectio Apomorphinæ Hypodermica, *Br.*

AQUA. U. S.

WATER

"Natural water (H_2O), conforming to the following description and tests." *U. S.*

Eau, *Fr.;* Wasser, *G.;* Acqua, *It.;* Agua, *Sp.*

Water has always been included in the U. S. Pharmacopœia, on account of its great importance as a medicinal and pharmaceutical agent. It is more or less concerned in almost all the changes which take place in inorganic matter, and is essential to the growth and existence of living beings, whether animal or vegetable. In treating of a substance of such diversified agency, our limits will allow of a sketch only of its properties and modifications. We shall speak of it under the several heads of *pure water, common water,* and *mineral waters.* For description of distilled water, see under *Aqua Destillata.*

Pure Water.—Water, in a pure state, is a transparent liquid, without color, taste, or odor. Its sp. gr. is assumed to be unity, and forms the term of comparison for that of solids and liquids. A cubic inch of it, at the temperature of 15.5° C., weighs very nearly 252.5 grains; when weighed in air with brass weights at 25° C. it weighs 251.91 grains. In the metric system the weight of 1 cc. of distilled water taken at 4° C. is made equal to 1 gramme, the unit of weight in this system. Water is compressible to a small extent, as was proved first by Canton, and afterwards, in an incontestable manner, by Perkins. Reduced in temperature to 0° C., it becomes a solid or ice, with the sp. gr. 0.9175; and raised to 100° C. an elastic gas called steam. In the latter state its bulk is increased nearly 1700-fold, and its sp. gr. so far lessened as to be not much more than half that of atmospheric air. At the temperature of 4° C., its density is at the maximum; and consequently, setting out from that point, it is increased in bulk by being either heated or cooled. It has the power of dissolving all gases, to a greater or lesser extent, including the constituents of common air, which are always present in natural water in variable proportions. It invariably exists in the atmosphere, in the form of invisible vapor.

Common Water.—By reason of its extensive solvent powers, water, in its natural state, must be more or less contaminated with foreign matter. Thus, it becomes variously impregnated, according to the nature of the strata through which it percolates. When the foreign substances present are in so small an amount as not materially to alter its taste and other sensible qualities, it constitutes the different varieties of *common water.*

There are almost innumerable shades of difference in common water, as obtained from different localities and sources; but all its varieties may be conveniently arranged under the two heads of soft and hard. A *soft water* is one which contains but little dissolved matter, particularly compounds of calcium and magnesium, and which, when used in washing, readily forms a lather with soap. By a *hard water* is understood a variety of water which contains calcium or magnesium salts, through which it curdles soap by forming insoluble compounds with the fatty acids, and is often unfit for domestic purposes. Solution of soap is a good test liquid for ascertaining the hardness of water. In distilled water it produces a very slight opalescence, due to the hydrolysis of the soap; in soft water, only a slight opalescence; but in hard water, a milky appearance or a curdy precipitate which is due to the formation of an insoluble compound between the fatty acids of the soap and the calcium or magnesium compounds. The hardness may be classed as temporary or permanent. Temporary hardness is observed in waters which contain much free carbon dioxide; the hardness is removed or diminished by boiling, which causes a loss of the gas and a deposition of the calcium and magnesium salts which produce the hardness and which have been held in solution as bicarbonates. Permanent hardness is caused by the presence of calcium sulphate or by calcium or magnesium chlorides which are not removed by boiling and filtering. The hardness may be estimated by means of a volumetric soap solution which is added in small quantities to a measured quantity of the water, shaking after each addition and noting the volume of the soap solution which is required to produce a lather which will remain on the surface for five minutes. The hardness is usually expressed in parts of calcium carbonate per 100,000 in the water.

The most usual foreign substances in solution in common water, besides oxygen and nitrogen, and matters held in a state of mechanical suspension, are carbon dioxide, calcium sulphate, calcium and magnesium carbonate, and sodium chloride. Carbon dioxide is detected by lime water, which produces a precipitate before the water is boiled, but not afterwards, as ebullition drives off the carbon dioxide. The presence of calcium sulphate is shown by precipitates being produced by barium chloride, and, after ebullition, by ammonium oxalate. The former test shows the presence of sulphate, and the latter, after boiling the water, indicates lime not held in solution by carbon dioxide. Calcium carbonate when held in solution by an excess of carbon dioxide, may be detected by boiling the water, which causes it to precipitate; but even after ebullition and filtration the water will retain enough calcium carbonate to give a precipitate with lead acetate, calcium carbonate being itself to a minute extent soluble in water. Silver nitrate will produce a precipitate if any soluble chloride be present; and, ordinarily, the one present may be assumed to be common salt. Small amounts of iron and aluminum salts and silica are almost always found in potable waters.

Clark has proposed to purify hard water, when the hardness arises from calcium bicarbonate, by a process which he calls *liming*. This consists in adding to the water sufficient lime water to convert the bicarbonate into the very sparingly soluble carbonate. This procedure renders the water soft, and gets rid of all the lime, except that in the minute portion of carbonate dissolved. The merit of this process consists chiefly, not in the removal of lime, but in preventing the formation of organic growths, principally confervæ, the decomposition of which renders the water offensive and unwholesome. River water containing the usual amount of calcareous matter, if allowed to stagnate in open reservoirs, in the summer, will become contaminated with myriads of microscopic plants and animals. This change is prevented, according to Clark, by his peculiar treatment, which deprives the living organisms of the nutriment derived from loosely combined carbon dioxide. A more modern method of softening water is to pass it through a filter composed of certain alkaline silicates, either natural or artificial, called *zeolites*. After the filter has lost its power of water softening it may be quickly and easily regenerated by passing through it a solution of sodium chloride.

The oxygen and nitrogen present in neutral waters are not usually in the same proportion as in atmospheric air; the oxygen in atmospheric air amounts to about 20 per cent. in volume, while the usual gaseous mixture expelled from fresh water by boiling contains over 30 per cent. (See table on page 161.) The important discovery has been made by Moore and Kellerman of the U. S. Department of Agriculture, that copper sulphate, if present in amounts such as 1 in 4,000,000 will be toxic to algæ, destroying them and preventing their reappearance; this statement has been confirmed by Gildersleeve (*Am. J. M. S.*, 1905, 129, p. 757), Stewart (*Am. J. M. S.*, 1905, p. 761), Kraemer (*A. J. P.*, 1906, 140), and others. They state that one part of copper sulphate in 100,000 of water will destroy typhoid and cholera germs in from three to four hours, and it appears to be established that waters not containing too large amounts of organic matter, exposed to the action of copper foil, kept in copper vessels, or treated with small amounts of copper sulphate (1 to 500,000), will destroy all typhoid bacilli and many other organisms in from 3 to 6 hours. On the other hand as shown by Doty (*N. Y. M. R.*, cxvii, p. 90), and Fowler (*Jour. Roy. Army Med. Corps,* 1905, v, 391), in the presence of even moderate quantities of organic matter the bactericidal power of copper is much reduced, while in foul waters it is almost nil. See Henry Kraemer. (*A. J. P.*, 1905, p. 265.)

Common water is also divided into varieties according to its source. Thus, we have rain, snow, spring, river, well, lake, and marsh water.

Rain (*aqua pluvialis*) and *snow water* (*aqua nivalis*) are the purest kinds of natural water. Rain water, to be obtained as pure as possible, must be collected in large vessels in the open fields, at a distance from houses, and some time after the rain has commenced falling; otherwise it will be contaminated with the dust which floats in the atmosphere, and with other impurities derived from roofs. The rain water of large cities contains nitrogenized organic matter, as shown by the odor produced by burning the residue left after the water has been evaporated. In districts near the sea coast rain water usually contains appreciable quantities of chlorides.

Rain water ordinarily contains atmospheric air, and, according to Liebig, a little nitric acid, the amount of which is increased when the rain descends during a thunder storm. Chabrier states as the result of his observations that rain water contains either nitrous or nitric acid, the one or the other predominating according to the condition of the weather, the nitrous acid being relatively in excess in mild weather, but the nitric when the rain is attended with tempestuous winds. According to an analysis, made by Martin, of rain water which fell at Marseilles during a violent storm, 1000 parts by weight contained 0.004 of chlorine and 0.003 of ammonia. Not a trace of iodine or of nitric acid was discovered. Boussingault has ascertained that the rain which falls in towns contains considerably more ammonia than that which falls in the country. Thus the rain of Paris was found by him to contain three or four parts of ammonia per million, while that collected in a mountainous region contained about four-fifths of one part only in a million. The average results of J. B. Lawes and J. H. Gilbert give one part of ammonia to the million of rain water. Snow water has a peculiar taste, which was supposed to depend on the presence of air more oxygenated than that of the atmosphere; but in point of fact it contains no air, and this accounts for its vapid taste. Rain and snow water are sufficiently pure for most chemical operations.

Spring water (*aqua fontana*) depends entirely for its quality on the strata through which it flows, being purest when it passes through silicious sand or gravel, or where the prevailing rock formation is granitic. On the contrary, where the formation is limestone, the water will, because of the carbon dioxide dissolved in it, take up calcium carbonate, convert it into a bicarbonate, and become what is called a *hard water.* It almost always contains a trace of common salt, and generally other impurities, which vary according to the locality of the spring.

River water (*aqua fluvialis*) is, generally speaking, less impregnated with saline matter than spring water, because made up in considerable part of rains, while its volume bears a larger proportion to the surface of its bed. It is, however, much more apt to have mechanically suspended in it insoluble matters, of an earthy nature, like clay and silt, which impair its transparency. It is frequently rendered more sightly by being run through porous stone, carbon, or sand filters. The coarse particles are removed by this filtration; but sewage or injurious products resulting from decomposition which are dissolved in the water are not removed, so that such clean filtered water may be deleterious to health. Water may be purified for manufacturing purposes by what is termed the alum process,—*i.e.,* by adding 2 grains of alum to a gallon of water, and permitting the impurities to subside for 48 hours. (*Chem. News,* July 23, 1886.) River water is purified now at many cities on the large scale by filtration through sand. (See *U. S. D.,* 19th ed., p. 163.)

Well water, like that from springs, is liable to contain various impurities. As a rule, the purity of the water of a well will be in proportion to its depth and the constancy with which it is used. Well water in large cities always contains a large amount of impurity, both organic and inorganic, the result of sewage contamination. The presence of nitrates in water is destructive to many forms of organic life. *Artesian Wells,* from their great depth, generally afford a pure water, although on analysis they frequently show a larger proportion of solid constituents on evaporation than do waters from rivers.

Lake water cannot be characterized as having any invariable qualities. The water of most of the lakes in the United States is pure and wholesome except where it is near large centers of population, when it is usually contaminated by sewage.

Marsh water is generally stagnant, and contains vegetable matter undergoing decomposition. It is unwholesome, and ought never to be used internally.

All water which is exposed to the air dissolves a quantity of oxygen, nitrogen, and carbon dioxide, in obedience to the laws of gaseous absorption. It is indeed upon this dissolved oxygen that the life of water-breathing animals depends. In every pure water the proportion between the dissolved nitrogen and oxygen is found to be constant, and it is represented by the following numbers:—oxygen 34.91, and nitrogen 65.09 per cent.; 1000 parts of pure water, such as rain water, when saturated dissolves 17.95 parts of air. If the water be rendered impure by the introduction of organic matter undergoing oxidation, the proportion between the dissolved oxygen and nitrogen becomes different, owing to the oxygen having been partly or wholly used for the oxidation of this material.

The measurement of this condition is accomplished by determining what is known as its oxygen consuming power which depends upon the amount of potassium permanganate which is reduced under specified conditions.

The second class of dissolved impurities consists of inorganic salts, even rain water washing some of these out of the atmosphere. It invariably contains ammonium salts, sodium chloride, and particles of organic matter, living and dead. In towns the rain water also contains a larger proportion of nitrates than that falling in the country. It is, however, the spring waters especially which contain the largest amount of mineral matter in solution. The salts which most commonly occur in solution in spring water are: (1) Calcium, magnesium, iron, and manganese carbonates, dissolved in an excess of carbon dioxide. (2) Calcium and magnesium sulphates. (3) Alkaline carbonates, chlorides, sulphates, nitrates, or silicates.

Spring waters which issue from considerable depths, or which originate in volcanic districts, are always hotter than the mean annual temperature of the locality where they come to the surface.

Properties.—The term *Aqua,* in the United States Pharmacopœia, may be considered as designating any natural water of good quality which answers well for cooking and does not curdle soap.

Description and Physical Properties.—"A colorless, limpid liquid, practically tasteless and odorless.

"Water is neutral to litmus paper. When heated nearly to the boiling point and agitated, no disagreeable odor is evolved. The residue obtained upon evaporating 100 cc. of Water in a platinum dish does not exceed 0.03 Gm. (*solids*), and this residue, when carefully heated to redness, evolves no visible fumes and shows no appreciable charring (*organic impurities*). Add 1 cc. of hydrochloric acid to 100 cc. of Water and then add 50 cc. of hydrogen sulphide T.S.: no darkening occurs after standing for fifteen minutes (*lead or copper*). Add 1 cc. of hydrochloric acid to 100 cc. of Water and then add 1 cc. of potassium ferrocyanide T.S.: no blue coloration is produced immediately (*iron*). Add 0.5 cc. of tenth-normal silver nitrate to 200 cc. of Water, heat to boiling, filter, and add to the filtrate 3 drops of potassium chromate T.S.: a red precipitate is produced (*limit of chloride*). Add successively 1 drop of acetic acid, 1 cc. of sulphanilic acid T.S., and 1 cc. of naphthylamine acetate T.S. to 100 cc. of Water in a Nessler tube, stirring with a glass rod after each addition. Closely cover the tube with a glass plate, place it upon a white surface, and view it from above: no pink coloration appears within five minutes (*nitrite*). Add 1 cc. of sodium carbonate T.S. to 100 cc. of Water, and evaporate the liquid in a small porcelain dish just to dryness. Moisten the residue thoroughly with 2 cc. of phenoldisulphonic acid T.S., gently warm the dish, add 20 cc. of ammonia T.S. and sufficient distilled water to measure 100 cc. Any yellow color produced is not greater than that obtained by evaporating 0.0021 Gm. of potassium nitrate, dissolved in 3 cc. of distilled water and 1 cc. of sodium carbonate T.S., to dryness and treating the residue in the same manner as the residue from the Water. The comparison of colors must be made in Nessler tubes of the same diameter and size (*nitrate*). Add 2 cc. of alkaline mercuric potassium iodide T.S. to 100 cc. of Water in a Nessler tube, and mix thoroughly. Place the tube on a white surface, and view the contents from above: the water does not at once assume a deep yellow or orange color (*ammonium salts and nitrogenous impurities*). Mix 100 cc. of Water with 10 cc. of diluted sulphuric acid in a clean porcelain dish, and heat it rapidly to boiling, then add 0.4 cc. of tenth-normal potassium permanganate, and boil the liquid for ten minutes: the color of the liquid is not completely destroyed (*oxidizable substances*)." *U. S.*

The British Pharmacopœia no longer includes *"Aqua"*; it recognizes *"Aqua Destillata,"* and gives appropriate tests.

Water should never be allowed to stand in contact with leaden pipes, etc., on account of the risk of its dissolving a small portion of lead. This risk is greater in proportion to the softness and purity of the water; for it is found that the presence of a minute proportion of saline matter, as for example of calcium sulphate, protects the water from the slightest metallic impregnation. This result is produced by the formation of a thin film of insoluble lead sulphate upon the surface of the metal, thus preventing further action. The chlorides are not protective, as they give rise to lead chloride, which is slightly soluble. Upon this principle is based a plan of protection by Schwartz of Breslau, who proposes to fill leaden pipes through which water is conducted, with a strong solution of an alkaline sulphide, which forms a perfectly insoluble coating of lead sulphide (*sulphuret*), said to be quite impermeable by the water afterwards introduced. Galvanized iron (zinc coated) does not corrode as readily as iron which is unprotected, because as the zinc has the greater solution tension it protects the iron, which remains unacted upon; galvanized iron pipes are, however, attacked by water containing much free CO_2. On the other hand, tinned iron (tinplate) corrodes more readily than iron alone if the iron is exposed at any point; the iron being the anode end is at once attacked. The action of water upon various metals has been exhaustively studied by Jorissen (*Internat. Pharm. Cong.*, 1914, 696) who found that aluminum was but slightly affected by distilled water; ordinary water acted upon it decidedly, producing crater-shaped corrosions. Magnalium (an alloy of magnesium and aluminum) is less liable to corrosion. Copper is only slightly affected by distilled water; sea water, free from air, does not act upon copper, but in the presence of air, corrosion readily occurs with formation of carbonates and chlorides. Lead is affected by water which is free from CO_2, especially when dissolved oxygen is present. The presence of CO_2 considerably lowers the percentage of dissolved lead. Nickel is not corroded even by sea water; over 35 per cent. of nickel will prevent iron from rusting. Tin is proof against the action of distilled water. Ordinary water acts upon it slightly. Sea water containing air acts upon it at first, but it is soon protected by a layer of basic salts. Zinc in distilled water free from CO_2 and oxygen preserves its shining surface for years. When oxygen is present zinc hydroxide is produced, which is slightly soluble, and when CO_2 is present, a slightly soluble carbonate is also formed.

A very important class of dissolved impurities is made up of organic compounds. This organic matter may be derived from a vegetable source, such as leaf-mould and the decomposition products of wood, in which case it is practically harmless, or it may be derived from animal sources, in which case it almost always proves a serious impurity.

The careful observations of students of public health leave no doubt that a number of epidemic diseases, especially cholera and typhoid fever, are often contracted and spread by means of drinking water contaminated with germs of disease from excreta and general sewage. This impure water may be clear and may have filtered through considerable distances of soil, and yet may contain these poisonous germs. Now, nitrogen is one of the characteristic constituents of animal matter as contrasted with vegetable matter, relatively few forms of which contain it, and those are of a character not likely to be found in natural waters. Hence, if water should be impregnated with animal matter, this would be indicated by the presence of nitrogen in solution, either in the form of albumin or albuminous matter, if the animal matter in the water is still unchanged, or, if the animal matter has undergone oxidation, in the form of ammonia or nitrous or nitric acid.

There are, therefore, to be determined in this presence of organic nitrogenous matter, (1) the examination of a water with reference to the free ammonia, (2) the unchanged albuminous matter, which, as it is changed into and determined as ammonia, is called "albuminoid ammonia," and (3) the nitrates and nitrites present.

The free ammonia is first determined by distilling the water made alkaline with sodium carbonate as long as the distillate carries enough ammonia to be recognized by *Nessler's solution.* (See Part III.) For this purpose the distillate is collected successively in volumes of 50 cc. and the amount of ammonia in each of these separate distillates determined. The smallest quantity of ammonia will produce a yellow color, the tint of which is to be compared with that obtained from the Nessler solution treated with a standard ammonium chloride solution.

After the free ammonia has been distilled off, a solution of sodium hydroxide and potassium permanganate is added and the distillation is continued. Another portion of ammonia now comes off, owing to the action of the permanganate on the nitrogenous organic matter. The amount of ammonia thus obtained is determined, and is tabulated as "albuminoid ammonia," because albumin is one of the bodies which is decomposed in this way. L. de Konnick found that the Nessler test in ammonia liquids does not produce the usual yellowish-brown precipitate, nor even a coloration, in the presence of alcohol. (*Am. Drug.,* 1893, p. 386.)

Instead of this method proposed by Wanklyn and Chapman, another process, described by Frankland and Armstrong, is often used. In this case, the water having been evaporated, the dry residue is submitted to an organic combustion analysis, which gives the "organic nitrogen" and the "organic carbon," and the ratio of these gives an indication as to the presence of albuminous matter rich in nitrogen. If the amount of albuminoid nitrogen indicated by either of these processes exceeds 0.15 part for one million of water, the latter should be rejected as a drinking water. In some large towns, however, the surface well waters have shown albuminoid nitrogen to the amount of 0.3 to 0.8 part per million. Such waters are little better than sewage. The free ammonia, moreover, should not exceed 0.08 part per million, or the water must be considered as containing sewage contamination.

Nitrates may be estimated by the following process. A measured volume (15–25 cc.) of the water is evaporated just to dryness in a flat-bottomed porcelain dish, 1 cc. of phenoldisulphonic acid (made by heating 37 grammes of strong sulphuric acid with 3 grammes of pure phenol for 6 hours in a water bath) is added and thoroughly mixed with the residue by means of a glass rod. It is then diluted with about 25 cc. of water, solution of ammonium hydroxide added in excess and the volume of the solution made up to 50 cc. The nitrates present in the residue convert the phenoldisulphonic acid into picric acid, which, by the action of ammonium hydroxide forms ammonium picrate; this imparts to the solution a yellow color which is proportional in its intensity to the amount of nitrates present in the water, and by carrying out a similar test with a standard solution of potassium nitrate similarly evaporated, the amount may be accurately estimated. Nitrites may be estimated by the sulphanilic acid and naphthylamine hydrochloride test given for the qualitative detection of nitrites by the U. S. Pharmacopœia, by carrying out a similar test with a standard solution of sodium nitrite and making a comparison of the relative intensity of the color which is produced in each.

The determination of chlorides is also frequently of great importance, for although mineral waters may be rich in chlorides, ordinary well waters or river waters, which are the chief sources of supply, will not contain much chlorine unless they have been contaminated. Both urine and sewage may contribute this chlorine, as they are highly charged with sodium chloride. As a rule, it may be said that water containing more than two grains of chlorine per gallon must be looked upon with suspicion, unless some good reason for the presence of sodium chloride can be assigned. According to some authorities the amount of chlorine should not be over 10 per cent. of the total solids found in the water by evaporation.

MINERAL WATERS.—When natural spring waters are so far impregnated with foreign substances as to have a decided taste, and to operate in a peculiar manner upon the human economy, they are called *mineral waters.* There has been an enormous amount of fraud perpetrated in connection with the mineral waters. The so-called natural "lithium waters" contain only traces of that element and a number of them have been proven misbranded within the meaning of the Food and Drugs Act. Mineral waters are conveniently arranged under the heads of *carbonated, alkaline, sulphuretted, saline* (including *magnesian, chalybeate,* and *chlorinated*), and *siliceous.* For a more comprehensive and detailed classification of this class of waters see *Mineral Waters of the United States,* U. S. Department of Agriculture, Bulletin No. 91.

1.—*Carbonated waters* are always cold, as they issue naturally from the earth and are characterized by containing an excess of carbon dioxide, which gives them a sparkling appearance, and the power of reddening litmus paper. These waters frequently contain calcium, magnesium, and iron, which are held in solution by the excess of carbon dioxide as bicarbonates. The waters of Seltzer, Spa, Apollinaris, and Pyrmont in Europe, and of the sweet springs in Virginia, belong to this class. For Artificial Carbonic Acid Water, see page 162.

2.—*Alkaline waters* contain a large quantity of sodium bicarbonate or carbonate, as well as common salt and Glauber's salt. These are sometimes warm, such as the springs at Ems and Vichy, but generally cold. Gettysburg spring water is of this class.

3.—*Sulphuretted waters* are such as contain hydrogen sulphide, and are distinguished by the peculiar fetid odor of that gas, and by yielding a brown precipitate with the salts of lead or silver. Examples of this kind are the waters of Aix-la-Chapelle and Harrogate in Europe, and those of the White, Red, and Salt sulphur springs in Virginia. Sulphuretted waters are not marketable without deterioration as the gas is very fugitive and easily oxidizable in dilute solutions.

4.—*Saline waters* are those the predominant properties of which depend upon saline impregnation. The salts most usually present are sodium, calcium, and magnesium sulphates and carbonates, in which latter case the name *magnesian* is given to them, the presence of the chlorides of these alkalies making the class *chlorinated waters,* which reach their maximum concentration in sea waters; while the presence of ferrous salts makes another class, the *chalybeate.* Among magnesium waters may be mentioned those of Friedrichshall, Hunyádi Janos, and Epsom; among chalybeate waters, those of Tunbridge and Brighton in England, of Pyrmont, Wiesbaden, and Spa on the Continent, and of Bedford, Pittsburg, and Brandywine in the United States. Potassium sulphate is occasionally present, and lithium has been detected by Berzelius in Carlsbad and other salt springs of Germany, and is also found in some American spring waters. Boric acid, usually in the form of an alkaline borate, is of frequent occurrence in mineral waters of certain portions of the United States. Cæsium and rubidium have also been detected in certain mineral waters, such as the Dürkheim and Baden-Baden waters, in the former of which these elements were first discovered by Bunsen. Bromine is found in the saline at Theodorshalle, in Germany, as also in the salt wells of western Pennsylvania, Ohio, Michigan, and West Virginia. The mineral springs at Saratoga contain a small proportion of iodine and bromine . The principle saline waters are those of Seidlitz in Bohemia, Cheltenham and Bath in England, and Harrodsburg and Saratoga in the United States.

Arsenic in minute quantity has been found in some waters used as drink. At Whitbeck, in Cumberland, England, the inhabitants employ, both as drink and for culinary purposes, a water holding enough arsenic in solution to be quite sensible to tests, without any known injurious consequences.

5.—*Siliceous waters* are those in which the contents consist chiefly of alkaline silicates, such as the hot spring waters of Iceland and the geysers of Fire-hole Basin and Gardiner's River, Yellowstone National Park, U. S.

6.—*Sea Water:* The water of the oceans differs from most inland waters chiefly in containing a larger amount of dissolved salts, especially sodium chloride. The composition of ocean water differs in various parts of the world. Generally spaking, it is less concentrated near the shores because of the influence of fresh water rivers. The following is an analysis of the water in the English Channel ten miles from the coast of France (*J. P. C.,* 1865, i, p. 381) which had a specific gravity of 1.026 at 15° C.

Gaseous Contents.	*In one kilo.* *Liters.*	*In one liter.* *Liters.*
Atmospheric air	0.0120	0.0123
Free carbonic acid	traces	traces
" hydrogen sulphide	traces	traces
Solid Contents.	*Gm.*	*Gm.*
Potassium Chloride	0.09763	0.10019
Sodium "	26.09300	26.78913
Lithium "	0.00042	0.00043
Ammonium "	0.00178	0.00183
Magnesium "	3.19300	3.27700
Sodium iodide	0.00920	0.00944
" bromide	0.10605	0.10882
Magnesium bromide	0.03084	0.03163
Calcium sulphate	0.09017	0.92540
Potassium "	0.00919	0.00943
Sodium "	2.57250	2.64012
Magnesium sulphate	0.32736	0.33597
" phosphate	0.00046	0.00047
(Ammonio-magnesian) phosphate	signs	signs
Calcium carbonate	0.13600	0.13959
Magnesium "	traces	traces
Iron "	0.00021	0.00021
Manganese "	signs	signs
Silicic acid	0.01420	0.01457
Organic matter	signs	signs
Pure water	966.50646	991.91577
Total	1000.00000	1026.30000

Further out from shore the proportion of sodium chloride may rise to 36 or 37 parts per thousand.

In inland seas the proportion of salt is often very much greater than that of the ocean, thus the amount of solids in the water of the Great Salt Lake of Utah has varied between 15 and 20 per cent. while in the Dead Sea of Palestine there is 27 per cent. of solids. Besides these ingredients, others are alleged to exist in minute proportion in sea water, as fluorine by G. Wilson; lead, copper, and silver by Malaguti, Durocher, and Sarzeau; and iron and manganese by Uziglio. Gold in very minute quantities has been found in sea water. Prior to Wilson's researches, Middleton and Silliman, Jr., had inferred the existence of fluorine in sea water, from its presence in marine animals. The lead and copper above mentioned were found in certain fuci only, the silver in the sea water itself. The presence of silver in sea water has been demonstrated by F. Field, by a comparative analysis of the same copper sheathing, when new, and after having been on a vessel for many years. Schweitzer's analysis gives a small proportion of calcium carbonate, but Bibra could not detect any. John Davy's examinations of sea water show that calcium carbonate does not exist at a great distance from land, except in very minute proportion, but becomes quite evident at a distance of from fifty to a hundred miles from coasts. Boric acid has been found by Veatch in the sea water on the coast of California. (See *A. J. P.*, 1860, p. 330.)

Sea water, filtered, and charged with five times it volume of carbon dioxide, forms, according to Pasquier, a gentle purgative, which keeps very well, and is not disagreeable to take. The dose is from half a pint to a pint.

By freezing, sea water is almost entirely freed from saline matter, the ice being nearly pure water. It is obvious that the unfrozen water contains much more than its ordinary proportion of salts; and this is one of the methods of concentrating this and other saline solutions.

Medicinal Properties of Water.—Water is a remedy of great value in a large number of complaints either internally or externally. When taken internally, cold water, below 10° C., inhibits the secretion of the digestive juices and therefore delays digestion. If at a temperature of from 15° to 21° C. it is almost without effect; the elaborate studies of Hawk (*J. Am. C. S.*, 1911, xxiii, and 1912, xxxiv) have completely dissipated the old superstition that water lowered digestive activity by diluting the ferment in the stomach. At tepid temperatures, 26° to 32° C., it is likely to nauseate, and if taken in large quantities may even produce emesis. After its absorption water has a profound influence in increasing all the bodily secretions, notably those of the kidney and sweat glands. It is therefore frequently used as a diuretic when it is desired either to wash out toxic substances from the system or, by dilution, to make an irritating urine more bland. Carr (*J. P. Ex. T.*, 1921, xviii, 221) has found that the drinking of large amounts of water tends to increase the elimination of urea and sulphates and to decrease the acidity of the urine but that the excretion of creatinin and phosphates is not affected. In conjunction with external heat, or diaphoretic drugs, it is also of much service to increase the perspiration in various morbid conditions. When the systemic effects of water are desired quickly it may frequently be given advantageously in the form of salt solution, either hypodermically or intravenously. (See *Liquor Sodii Chloridi Physiologicus.*) Although a very potent agent for good in proper cases it should not be forgotten that the too free drinking of water may prove harmful, especially in patients with feeble heart muscle.

Externally, although occasionally useful for the purpose of softening the skin, water is mostly applied as a means of conveying other medicinal forces either chemical, thermal or mechanical. Over small areas it may be applied either very hot, 49° to 60° C., or ice cold, for its counter-irritant effect in various internal inflammations. The use of hot and cold baths has become one of the most important methods of treatment, and for consideration of the subject the reader is referred to text-books on hydrotherapy.

Frequently various chemicals are added to increase the effects of the bath. Of these forms of saline baths the most important is the so-called *Nauheim* or *carbonated baths.* For this purpose a naturally effervescent springs, Bad Nauheim in the Grand Duchy of Hesse, was originally used. *Artificial Nauheim baths,* however, have been widely employed. For this purpose the following formula may be used: In one package a mixture of sodium carbonate 1½ pounds, sodium bicarbonate ½ pound, calcium chloride 3 pounds, sodium chloride 2 pounds. This is dissolved in the bath of about 50 gallons, and then afterward 1 pound of sodium bisulphate is added slowly. This bath is used chiefly in the treatment of certain forms of *heart disease.* Another and very old bath which is used both as a diaphoretic and as a stimulant in various forms of *shock,* especially in young children, is the *mustard bath,* which is made by adding ground mustard in the proportions of 1 or 2 ounces for each gallon of water.

AQUA ACIDI CARBONICI, *Carbonic Acid Water,* or *Soda Water* (so called), (*Eau gazeuse simple,* Fr.; *Kohlensaurewasser,* G.), which was formerly official in the U. S. Pharmacopœia, consists of water highly charged with carbonic acid.

Preparation.—Water is found to take up its own volume of this gas under the pressure of the atmosphere; and Henry ascertained that precisely the same *volume* of the compressed gas is absorbed under a higher pressure. From this law, the bulk taken up is constant, the quantity being different in proportion as there is more or less driven into a given space. As the space occupied by a gas is inversely as the compressing force, it follows that the quantity of the acid forced into the water will be directly as the pressure. From the principles above laid down it follows that, to saturate water with five times its volume of carbon dioxide, it must be subjected to a pressure of five atmospheres. Carbonic acid gas compressed into the liquid state is now manufactured on an immense scale and supplied in 20-pound and 50-pound steel cylinders. This allows of convenient transportation, and the purity of the gas is usually excellent.

Carbonic acid water is familiarly called in this country *"mineral water," "plain soda,"* and *"soda water"*; the latter names originally applied to the preparation when it contained sodium carbonate, being from habit continued since the alkali has been omitted.

Carbonic acid water is dispensed in most of the pharmacies in this country. The reservoir, called the "fountain," is sometimes placed in the cellar, and the tube proceeding from the fountain is made to pass through the floor and counter of the store, and to terminate in a draught tube, by means of which the carbonic acid water may be drawn off at pleasure. In other and more modern devices the cylinder of compressed carbon dioxide is attached in such a manner to the reservoir that the water is continuously and automatically carbonated until the cylinder is exhausted. In order to have the liquid cool, the tube from the carbonating device or the "fountain" generally terminates in a strong metallic vessel of convenient shape, or a series of block tin pipes called coolers, placed inside the counter apparatus, and surrounded with ice.

Properties.—Carbonic acid water is a sparkling liquid, possessing an agreeable, pungent, acidulous taste. It reddens litmus and produces a precipitate with lime water. Being impregnated with a large quantity of the acid gas under the influence of pressure, it effervesces strongly when the pressure is released by drawing it into an open vessel. Hence, to preserve its sparkling qualities, it should be kept in strong vessels or in strong, well-corked bottles placed inverted in a cool place. Several natural waters contain an excess of carbonic acid, such as those of Seltzer, Spa, Pyrmont, Apollinaris, etc., but the artificial water has the advantage of a stronger impregnation with the acid gas. Carbonic acid water should be made with every precaution to avoid metallic impurity. Hence the necessity of having the reservoir and tubes well protected on the inner surface. Iron fountains lined with a hard enamel are preferred to those of copper, but the best fountains are made of cast steel, lined with block tin. When leaden tubes are employed to convey the water, it is liable to be contaminated with this metal, which renders it deleterious. Tubes of pure tin are free from objection, and are now almost exclusively used.

Copper fountains, well tinned, are liable to the objections that the tin lining wears away by use, and that there is no convenient means of inspecting the interior, owing to the solder joint which permanently unites the two sections of the fountain. There can be no doubt that carbonic acid water is sometimes rendered poisonous by metallic impregnation. R. O. Doremus has proved by a chemical examination that lead and copper are sometimes present. Lead is detected by hydrogen sulphide, which gives with it a black precipitate, and copper by potassium ferrocyanide, which causes a brown precipitate. In testing for copper, a few drops of the reagent should be added to a glass of the suspected water, placed on a sheet of white paper, when, if even a minute proportion of copper be present, a brownish discoloration will be seen, upon looking down through the liquid. Fortunately copper fountains have largely gone out of use, having been supplanted by those made of steel.

Uses.—Carbonic acid water is a grateful drink to *febrile patients,* allaying thirst, lessening *nausea* and *gastric distress,* and promoting the secretion of urine. The quantity taken need only be regulated by the reasonable wishes of the patient. It also forms a very convenient vehicle for the administration of magnesia, the carbonated alkalies, magnesium sulphate, and the saline cathartics generally, rendering these medicines less unpleasant to the palate, and, in irritable states of the stomach, increasing the chances of their being retained. When used for this purpose, six or eight fluidounces (180–240 cc.) will be sufficient.

AQUA AMMONIÆ. U. S. (Br.)

AMMONIA WATER Aq. Ammon. [Solution of Ammonium Hydroxide]

"Ammonia Water is an aqueous solution of ammonia (NH_3) containing not less than 9.5 per cent. nor more than 10.5 per cent. by weight of NH_3. This solution deteriorates rapidly, and must be assayed frequently." *U. S.* "Solution of Ammonia is an aqueous solution containing 10 per cent. by weight of ammonia, NH_3." *Br.*

Liquor Ammoniæ, *Br.;* Solution of Ammonia; Water of Ammonia; Spiritus Salis Ammoniaci Causticus; Ammonium Hydroxide Solution; Ammonium Causticum; Alkali Volatile; Ammoniaque officinale, *Fr. Cod.;* Eau (Liqueur) d'Ammoniaque, *Fr.;* Liquor Ammonii Caustici, *P. G.;* Salmiakgeist, Aetzammoniak, Ammoniak-Flüssigkeit, *G.;* Ammoniaca, *It.;* Amoniaco, Amoniaco liquido, *Sp.*

The U. S. Pharmacopœia X gives no process for preparing Ammonia Water. The U. S. P., 1870, contained an excellent process, which is as follows: "Take of Chloride of Ammonium, in small pieces, Lime, each, *twelve troyounces;* Water, *six pints;* Distilled Water, *a sufficient quantity.* Pour a pint of the Water upon the Lime, in a convenient vessel; and, after it has slaked, stir the mixture so as to bring it to the consistence of a smooth paste. Then add the remainder of the Water, and mix the whole thoroughly together. Decant the milky liquid from the gritty sediment into a glass retort, of the capacity of sixteen pints, and add the Chloride of Ammonium. Place the retort on a sand-bath, and adapt to it a receiver purposely connected with a two-pint bottle, by means of a glass tube, reaching nearly to the bottom of the bottle, and containing a pint of Distilled Water. Surround the bottle with ice-cold water; and apply heat, gradually increased, until ammonia ceases to come over. Remove the liquid from the bottle, and add to it sufficient Distilled Water to raise its specific gravity to 0.960. Lastly, keep the liquid in small bottles, well-stoppered."

"Strong Solution of Ammonia, 500 millilitres; Distilled Water, 1000 millilitres. Mix." *Br.*

In the U. S. P., 1870, process the ammonium chloride is decomposed by the superior affinity of the calcium for the chlorine, ammonia is disengaged, and calcium chloride and water are formed.

$$2NH_4Cl + Ca(OH)_2 = CaCl_2 + 2H_2O + 2NH_3$$

The British Pharmacopœia gives directions for diluting *Liquor Ammoniæ Fortis* so as to reduce it to the strength of *Liquor Ammoniæ.* This is effected by mixing one measure of their stronger preparation with two measures of distilled water. The ammonia water of commerce is sometimes known as 'Aqua Ammoniæ F. F. F.," or "20° ammonia"; corresponding to about 16 per cent. of NH_3; it may be diluted by adding 2 volumes of water to 4 volumes of 20° ammonia water to make official ammonia water. Ammonia water of other strengths may be diluted by consulting the table given in Part III, and applying the rules given in Remington's *Practice of Pharmacy.*

Ammonia water of the various commercial strengths is one of the few substances which continue to be designated by strength in terms of the specific gravity expressed in degrees Baumé. Thus *"16° ammonia"* is equivalent to 10 per cent., and *"26° ammonia"* is equivalent to 28 per cent.

Description and Physical Properties.—"A colorless, transparent liquid, having a very pungent, characteristic odor. Specific gravity: about 0.958 at 25° C. Ammonia Water is strongly alkaline to litmus paper. Dense, white fumes are produced on bringing a glass rod dipped into hydrochloric acid near the surface of the Ammonia Water.

"A 25 cc. portion of Ammonia Water, evaporated to dryness in a platinum or porcelain dish and dried to constant weight at 120° C., leaves not more than 0.005 Gm. of residue. Add 0.1 cc. of tenth-normal potassium permanganate to 10 cc. of Ammonia Water to which a slight excess of diluted sulphuric acid has been added: the pink color is not completely destroyed within ten minutes (*oxidizable substances*). When neutralized and then made slightly acid with hydrochloric acid, a 10 cc. portion of the Water meets the requirements of the test for *heavy metals,* page 439.

"**Assay.**—Pour into a weighing bottle about 10 cc. of distilled water, tare the bottle and its contents, add about 5 cc. of Ammonia Water, and weigh accurately. Then titrate with normal sulphuric acid, using methyl orange T.S. as indicator. Each cc. of normal sulphuric acid corresponds to 0.01703 Gm. of NH_3.

"Preserve in a cool place in glass-stoppered or rubber-stoppered bottles made of hard glass, free from lead." *U. S.*

"Specific gravity 0.959. 3 grammes require for neutralisation 17.6 millilitres of *N/1 solution of sulphuric acid.* Responds in other respects to the tests and possesses the general characters described under 'Liquor Ammoniæ Fortis.'" *Br.*

Commercial solution of ammonia sometimes contains pyrrol, naphthalene, aniline, and pyridine. These may be detected by the solution being reddened by nitric acid, and, after having been supersaturated with hydrochloric acid, by its tingeing a slip of fir wood a rich purple color, characteristic of pyrrol. (Maclagan.) The source of these impurities is coal gas liquor, from which the ammonia compounds are largely obtained. Donath (*Dingler's Polytechnisches Journal,* vol. iv, p. 229) tested some ammonia prepared from gas liquor, by neutralizing with diluted sulphuric acid, when the liquid assumed a rose color, and a solution of the sulphate emitted the characteristic odor of naphthalene.

According to Eber (*Ph. Centralb.,* 1892, 238) the well-known test for ammonia of exposing a glass rod dipped into hydrochloric acid to the fumes, is rendered more sensitive by using a mixture of hydrochloric acid 1 part, alcohol 3 parts, and ether 1 part, shaken together.

Composition.—Water is capable of absorbing 670 times its volume of ammonia gas at 10° C., and increases in bulk about two-thirds. But the official solution of ammonia is by no means a saturated one. Thus, the ammonia contained in the strongest U. S. preparation is about 28 per cent. The official table in Part III gives the percentage of ammonia gas in aqueous solutions of different densities at the temperatures of 25° C. and 15° C.

Ammonia Water is incompatible with acids, and with acidulous and many earthy and metallic salts; but it does not decompose the salts of lime, barium, or strontium, and only partially decomposes those of magnesium.

Uses.—When brought into contact with living tissue ammonium hydroxide acts as a stimulant, irritant, or caustic according to the strength of its solution. The official water of ammonia if applied for a short time to the skin produces burning pain and redness, but if contact be maintained is capable of destroying the whole dermal tissue. The irritant effects of ammonia water are due to the hydroxyl ion, not to the ammonium. When injected into the circulation the water of ammonia produces the characteristic effects of the ammonium salts but for reasons pointed out (see under *Ammonii Carbonas*) it cannot be absorbed from the stomach in sufficient quantity to exercise any direct influence upon the general system. It is, however, often of service in sudden *syncope,* especially of nervous origin, even when given by the mouth. Its effects under these circumstances are due to the reflex stimulation of the vasomotor center from the irritation of the gastric mucous membrane. Still more marked action of the same nature may be elicited by smelling the fumes which arise from the ammonia water. When injected hypodermically, however, it is a powerful direct stimulant to the heart and vasomotor system, although somewhat fleeting in its effects. It was at one time brought forward as an antidote for *snake-venom,* but the only value it has in this condition is due to its stimulant effect upon the circulation. It is widely employed to correct *hyperacidity of the stomach,* especially where a local stimulant as well as an antacid effect is required.

In serious *collapse,* as pointed out above, it is necessary to inject the ammonia hypodermically, or better, intravenously. Half a drachm to a drachm diluted with half an ounce to an ounce of water may be slowly thrown directly into a vein. In some cases the drug has been simply used hypodermically, but is almost certain to cause severe local symptoms. On account of its cheapness, ammonia water is much used as an ingredient in stimulating liniments, especially when combined with olive or other oil.

Toxicology.—The symptoms of poisoning by ammonia are solely those of local irritation: pain in the mouth, throat, and epigastrium; vomiting and collapse from the severity of the gastritis. In some cases the irritation of the throat is so severe as to produce an acute edema of the glottis which may mechanically obstruct respiration, and rapid death from asphyxia has occurred. In the treatment of the condition, diluted acetic acid in the form of vinegar may be used as an antidote; olive oil or other fatty substance is useful not only because it combines with the caustic alkali to form a comparatively non-irritant soap, but also by virtue of its local soothing action upon the inflamed mucosa. In case of edema of the larynx, tracheotomy is indicated; it should not be forgotten that this accident may be postponed for an hour or two after the ingestion of the poison and the physician should remain ready for immediate operation if necessary. The subsequent treatment is purely symptomatic.

Dose, ten to thirty minims (0.6–1.8 cc.), largely diluted.

Off. Prep.—Linimentum Ammoniæ, *N. F., Br.;* Linimentum Hydrargyri, *Br.;* Lotio Ammoniacalis Camphorata, *N. F.;* Spiritus Ammonii Aromaticus, *U. S.;* Linimentum Opii Compositum, *N. F.;* Linimentum Saponato-Camphoratum, *N. F.;* Spiritus Ammonii Anisatus, *N. F.*

AQUA AMMONIÆ FORTIOR. U. S. (Br.)

STRONGER AMMONIA WATER Aq. Ammon. Fort.

"Stronger Ammonia Water is an aqueous solution of ammonia (NH_3), containing not less than 27 per cent. and not more than 29 per cent. by weight of NH_3. This solution deteriorates rapidly and must be assayed frequently. *Caution—Great care should be used in handling the liquid because of its caustic and irritating properties.*" *U. S.* "Strong Solution of Ammonia is an aqueous solution containing 32.5 per cent. by weight of ammonia, NH_3. It may be obtained by heating a mixture of ammonium chloride and slaked lime, and passing the resulting ammonia into distilled water." *Br.*

Liquor Ammoniæ Fortis, *Br.;* Strong Solution of Ammonia; Eau d'Ammoniaque forte, *Fr.;* Stärker Salmiakgeist, *G.*

This preparation is too strong for internal exhibition, but forms a convenient ammonia solution for reduction, by dilution, to the strength of ordinary Ammonia Water, or for preparing strong rubefacient liniments.

Stronger Ammonia Water is prepared on a large scale, from one of the products of the coal gas manufacture, by the process of distilling *gas liquor;* the distillate, which is principally ammonium sulphide, is then converted into ammonium sulphate by sulphuric acid. The sulphate is gently distilled with milk of lime, the still being connected with a series of glass carboys, arranged like Woulff's bottles, and three-fourths filled with distilled water. In this way solution of ammonia may be obtained of maximum strength. It is also made by diluting the concentrated liquid ammonia.

Anhydrous liquefied ammonia is now an article of commerce, being used on a large scale in the manufacture of artificial ice and in refrigerating plants, where the cold produced by its rapid evaporation under a partial vacuum is utilized to furnish the necessary lowering of temperature. The apparatus used for its production is almost identical with that employed in the manufacture of liquid carbon dioxide, and consists of a combination of vacuum and condensing pumps. The gas is obtained from the strongest ammonia water by heating, with application of a partial vacuum, and must be well dried before the compression. To obtain a pure product, it has been found best to allow the liquefied ammonia to expand several times in a gasometer, in which case, the larger part of the impurities are left behind in liquid form. These consist of water, alcohol, acetone, traces of the lubricating oil from the compressing pumps, and a little ammonium carbonate. In ammonias made from the distillation of bones, pyridine is also found to occur as an impurity. Liquefied ammonia comes into commerce in steel cylinders which have been tested to stand 100 atmospheres internal pressure, and are provided with well fitting screw valves. Anhydrous ammonia is said to dissolve metallic sodium, and the solution is intensely blue.

Stronger ammonia water of the U. S. is somewhat weaker than the corresponding strong solution of ammonia of the Br.

Description and Physical Properties.—"A colorless, transparent liquid, having an excessively pungent, characteristic odor, and a very caustic and alkaline taste. *Stronger Ammonia Water must never be tasted nor smelled unless greatly diluted.* Specific gravity: about 0.897 at 25° C. Stronger Ammonia Water is strongly alkaline to litmus paper. Stronger Ammonia Water diluted with twice its volume of distilled water conforms to the tests for identity and purity under *Aqua Ammoniæ.*

"**Assay.**—Pour into a weighing bottle about 25 cc. of distilled water, tare the bottle and its contents, add about 2 cc. of Stronger Ammonia Water, and weigh accurately. Then titrate with normal sulphuric acid, using methyl orange T.S. as indicator. Each cc. of normal sulphuric acid corresponds to 0.01703 Gm. of NH_3.

"Preserve in a cool place in partly filled, strong, glass-stoppered bottles made of hard glass, free from lead." *U. S.*

"A colorless liquid, with a characteristic, very pungent odor. Strongly alkaline. Specific gravity 0.888. 1 gramme requires for neutralisation 19.1 millilitres of *N/1 solution of sulphuric acid.* When mixed with an equal volume of *water* and a slight excess of *sulphuric acid* no color or odor is developed (absence of tarry matters). Yields no characteristic *reactions* for aluminium, zinc, calcium, magnesium, potassium, sodium, carbonates, sulphates, or sulphides, and only the slightest *reactions* for chlorides. 0.5 millilitre of *solution of sodium sulphide* added to 50 millilitres of Strong Solution of Ammonia contained in a Nessler glass produces no change of color (absence of copper, iron, and lead). *Arsenic limit* 0.5 part per million. Leaves no appreciable residue on evaporation." *Br.*

Great care should be exercised in opening bottles containing stronger ammonia water. It is safer, if the ammonia water has been kept in a warm room, to cool it with ice before attempting to withdraw the stopper, as the liberated gas, when warm, frequently is forced out with extreme violence, and accidents which have resulted in injury to the sight of the operator are recorded.

Uses.—This solution is too strong for medicinal use in its unmixed state. Sufficiently diluted with spirit of camphor and rosemary, it was formerly much employed as a prompt and powerful rubefacient, vesicatory, or escharotic, in various *neuralgic, gouty, rheumatic, spasmodic,* and *inflammatory affections* in which strong and speedy counter-irritation is indicated. When mere rubefaction is desired five parts of the stronger ammonia water may be mixed with eight parts of the diluent. This will answer even for blistering or cauterizing, unless a very prompt effect be necessary. In the latter case a lotion may be resorted to consisting of five measures of the ammonia to three of the diluent liquid. These mixtures are applied by means of linen folded several times, or a thick piece of flannel saturated with the liniment. A convenient mode of applying is to fill the wooden cover of a pill or ointment box, an inch or two in diameter, with purified cotton, saturate this with the liquid, and press it upon the part. The ammonia is thus prevented from escaping, and a definite boundary given to the inflammation. The application will generally produce rubefaction in from one to eight minutes, vesication in from three to ten minutes, and a caustic effect in a somewhat longer time.

When a solution of ammonia of 25° C. (sp. gr. 0.905) is mixed with fatty matter, the mixture forms the *vesicating ammoniacal ointment* of Gondret. The revised formula of this ointment is as follows: Take of lard 32 parts, oil of sweet almond 2 parts. Melt them together by a *gentle* heat, and pour the melted mixture into a bottle with a wide mouth. Then add 17 parts of solution of ammonia of 25° C., and mix with continued agitation until the whole is cold. The ointment must be preserved in a bottle with a ground stopper, and kept in a cool place. When well prepared, it vesicates in ten minutes.

There may be danger of excessive irritation and inflammation of the nostrils, mouth, and air passages, from the inadvertent inhalation of the gas escaping from a bottle of the stronger ammonia water, when freshly opened; and serious consequences have occurred from this cause, or from the accidental breaking of the bottle. The best antidote, under these circumstances, is the inhalation of the vapors of vinegar or acetic acid.

Dose, three to six minims (0.2–0.4 cc.), largely diluted.

Off. Prep.—Linimentum Camphoræ Ammoniatum, *Br.;* Liquor Ammoniæ, *Br.;* Spiritus Ammoniæ Aromaticus, *Br.;* Spiritus Ammoniæ Fetidus, *Br.*

AQUA ANETHI. Br.

DILL WATER

Eau d'Aneth, *Fr.*, Dillwasser, *G.*

"Dill Fruit, 100 *grammes;* Water, 2000 *millilitres.* Distil one thousand millilitres. In preparing this and other similar aqueous liquids by distillation, only good natural potable water must be employed, as directed for 'Distilled Water.'" *Br.*

"This Water may be prepared by triturating the oil of dill with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

This water, which is frequently prescribed in Great Britain, is occasionally used here; it closely resembles fennel or anise water, over which it has no advantages. It is used only as a vehicle.

AQUA ANISI. U. S., Br.

ANISE WATER Aq. Anisi

"A saturated solution of oil of anise in distilled water, prepared by one of the processes for aromatic waters." *U. S.*

Eau d'Anis, *Fr.;* Aniswasser, *G.;* Acqua distillata di anice, *It.;* Agua destilada de anis, *Sp.*

"Anise Fruit, 100 *grammes;* Water, 2000 *millilitres.* Distil one thousand millilitres." *Br.*

"This water may be prepared by triturating the oil of anise with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

Anise water is rarely made by distillation, although the product thus secured has a more delicate flavor than the U. S. preparation. It is used solely as a vehicle.

AQUA AURANTII FLORUM. U. S. (Br.)

ORANGE FLOWER WATER Aq. Aurant. Flor.

[Aqua Aurantii Florum Fortior, U. S. P. IX.]

"A saturated solution of the odoriferous principles of the flowers of *Citrus Aurantium* (var. *amara*) Linné (Fam. *Rutaceæ*), prepared by distilling the fresh flowers with water and separating the clear, saturated portion of the distillate. Its odor is best preserved by allowing a limited access of fresh air to the container." *U. S.*

"Orange-flower Water is the orange-flower water of commerce, prepared by distillation from the flowers of the Bitter Orange tree, Citrus Aurantium, var. Bigaradia, *Hook., f.*, diluted, immediately before use, with twice its volume of distilled Water." *Br.*

Aqua Aurantii Floris, *Br.;* Aqua Florum Naphæ; Aqua Aurantii Florum Fortior *U. S. IX;* Stronger Orange-flower Water; Triple Orange-flower Water; Hydrolatum Floris Citri Vulgaris; Eau distillée (Hydrolat) de Fleurs d'Oranger, *Fr. Cod.;* Eau de Naphe, *Fr.;* Orangenblüthenwasser, *G.;* Acqua distillata di arancio, *It.;* Agua destilada de azahar, *Sp.*

The U. S. P. IX recognized two grades of orange flower water, one of them known as *Aqua Aurantii Florum Fortior,* corresponding in strength to the distillate commercially known as "orange flower water," and the other a dilution of this with distilled water. In the U. S. P. X that latter has been omitted and only the stronger recognized. The British Pharmacopœia recognizes only the more dilute water which is made by diluting the "orange flower water of commerce" with two parts of distilled water. The British orange flower water has therefore about one-third the strength of the American.

The advantage of the stronger orange flower water is that it retains its fragrance longer than the dilute solution. Its odor, however, is too strong for most pharmaceutical processes and it should be diluted with one to two parts of distilled water when used as a vehicle.

Orange flower water is manufactured chiefly in Italy and France although small quantities have been distilled in this country. The flowers of the bitter orange are preferred as yielding the most fragrant product.

L. Malenfant observed that fresh orange flowers, mixed with cold water, yield, on distillation over the naked fire, a milky water, possessing a somewhat empyreumatic odor and a strong, somewhat acrid taste. Kept for twelve or eighteen months in glass vessels covered with parchment, it loses its empyreuma, and after filtering has an agreeable odor and taste. If the flowers be mixed with boiling water and immediately distilled, the water is limpid, and gradually separates some thick oil of a brownish color; the water has the odor and taste of the flowers, but complicated with an odor of the still, which it loses after long keeping; it seems to alter less rapidly than that obtained by the former process. Distilled by steam, limpid water of a pure odor and taste is at once obtained, free from empyreuma; it may be at once used, and keeps better in the light than when obtained by the two former processes. (*A. J. P.,* June, 1874.) Hesse and Zeitschel (*J. Pr. Chem.,* 1901, 525) found by exhausting with ether the orange flower water obtained in the distillation of the orange blossoms that the quantity of oil dissolved in the water represented about one-third of the total amount of oil from the blossoms. A distilled water of the leaves is also prepared, and sometimes a mixture of the leaves and flowers is employed. But this is a fraud, as the distilled water of the leaves never has the sweet perfume of that of the flowers. (*J. P. C.,* 4e sér., iii, 249.)

Orange flower water is stored in large glass vessels of carboys in cool cellars by the manufacturers in Grasse, France, care being taken not to stopper them tightly, but simply cover the orifice with a piece of paper or coarse cloth.

Nitric, sulphuric, or hydrochloric acid produces a red coloration with orange flower water, particularly if the water be shaken with ether to take up the oil, and the acid added to the ethereal solution.

Description and Physical Properties.—"Nearly colorless and clear or only faintly opalescent, possessing a strong, pleasant odor and taste of orange blossoms. It must be free from empyreuma, mustiness, or fungoid growths.

"Orange Flower Water is neutral or only slightly acid to litmus paper. Evaporate 100 cc. of the Water on a water bath, and dry the residue to constant weight at 100° C.: not more than 0.001 Gm. of residue remains. Orange Flower Water shows no reaction with hydrogen sulphide T.S. or with sodium sulphide T.S. (*metallic impurities*)." *U. S.*

"Colorless or with a slight yellowish tint; odor vary fragrant. Yields no *reactions* for lead or copper. The orange-flower water of commerce is a saturated solution of the volatile oil of the fresh flowers." *Br.*

From being kept in tinned copper cans, it sometimes contains metallic impurity, which is said to be chiefly lead carbonate, derived from the lead used as a solder in making the cans. The means of detecting metallic impurity is also mentioned under the general observations on distilled water. Much color, offensive odor, or mouldiness indicates impurity derived from the flowers in distillation.

Uses.—Orange flower water is used solely for its pleasant odor to perfume external lotions or to flavor internal medicines.

Off. Prep.—Syrupus Aurantii Florum, *U. S.;* Syrupus Aurantii Floris, *Br.;* Elixir Amygdalæ Compositum, *N. F.;* Elixir Aurantii Amari, *N. F.;* Elixir Glycyrrhizæ Aquosum, *N. F.*

AQUA CAMPHORÆ. U. S. (Br.)

CAMPHOR WATER Aq. Camph.

"A saturated solution of camphor in distilled water, prepared by one of the processes for aromatic waters, using 2 Gm. of powdered camphor in each 1000 cc." *U. S.*

Aqua Camphorata; Eau camphrée *Fr.;* Kampher-wasser, *G.;* Agua alcanforada, *Sp.*

"Camphor, 1 *gramme;* Alcohol (90 per cent.), 2 *millilitres;* Distilled Water, 1000 *millilitres.* Dissolve the Camphor in the Alcohol; add the solution in successive portions to the Distilled Water, shaking after each addition; finally shake occasionally until all the Camphor is dissolved." *Br.*

In this process the sole object is to effect a solution; water is capable of dissolving but a very small proportion of camphor, but the quantity varies with the method employed. The present British process is more efficient than the old formula, a definite quantity of camphor being dissolved in a small quantity of alcohol and this solution gradually added to the proper quantity of water; it is questionable, however, whether it would not be advantageous to use an insoluble powder to aid in the solution and thus obtain quickly a clear liquid, as the water made by the British process is sometimes cloudy. In the former British process no trouble was taken even to comminute the camphor, or to shake it with the water, which was thus allowed to take up what it might be disposed to do by contact with the camphor contained in a bag. The solution thus affected was extremely feeble, containing probably less than one part in a thousand; this proportion, according to Berzelius, is taken up by water when triturated with camphor. It was, besides, of uncertain strength, varying with the size of the fragments of camphor. Wm. B. Addington proposed to add to the camphor just enough alcohol to dissolve it, and triturate the liquor with magnesia, during which process he affirmed that the alcohol evaporated (*A. J. P.*, xlv, 209); and F. T. Hartzell substituted ether for alcohol, a few drops of which enabled him to bring the camphor to an impalpable powder. John K. Thum states that in the U. S. process part of the camphor remains with the talc on the filter and proposes to make camphor water by using eight grammes of camphor in small pieces and adding it to 1000 cc. of distilled water, shaking the bottle until the solution is saturated and filtering through sterilized gauze. (*Proc. Pennsylvania P. A.*, 1913, 364.) Camphor is separated from its aqueous solution by a solution of pure potassium hydroxide, and, according to Paris, by magnesium sulphate and several other salts. J. Murray proposes a solution of camphor and magnesium bicarbonate, which contains three grains of the former and six grains of the latter in each fluidounce.

Camphor water has this advantage over camphor in substance, that the latter is with difficulty dissolved by the liquors of the stomach; but it is too feeble a preparation for use when a decided effect is desired; it is, however, an excellent vehicle for the administration of more active substances.

Dose, half to one fluidounce (15–30 cc.), repeated every one or two hours.

Off. Prep.—Mistura Camphoræ Acida, *N. F.;* Mistura Camphoræ Aromatica, *N. F.*

AQUA CARUI. Br.

CARAWAY WATER

Aqua Carvi; Eau Distillée de Carvi, *Fr.;* Kümmelwasser, *G.*

"This Water may be prepared by triturating the oil of caraway with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

"Caraway Fruit, 100 *grammes;* Water, 2000 *millilitres.* Distil one thousand *millilitres.*" *Br.*

Distilled Caraway Water has the flavor of the fruit or seeds, but is seldom used in the United States. The water made from the volatile oil (16 minims in a pint), in the same manner as is cinnamon water, is largely employed. It is used only as a vehicle.

AQUA CHLOROFORMI. U. S., Br.

CHLOROFORM WATER Aq. Chlorof.

Eau Chloroformée, *Fr.;* Chloroformwasser *G.;* Agua Cloroformada, *Sp.*

"Chloroform, Distilled Water, each, a sufficient quantity. To a convenient quantity of distilled water contained in a dark amber-colored bottle, add enough chloroform to maintain a slight excess after the contents have been repeatedly and thoroughly shaken. When Chloroform Water is required for use, pour off the needed quantity, refill the bottle with distilled water, and saturate it by thorough agitation, taking care that there is always an excess of chloroform present.

"Preserve in well-stoppered, amber-colored bottles." *U. S.*

"Chloroform, 2.5 *millilitres;* Distilled Water sufficient to produce 1000.0 *millilitres.* Dissolve." *Br.*

The water should be fully saturated, in which case it should contain one-half per cent. of chloroform. Chloroform water has been proved to be an excellent vehicle for administering active remedies, and, owing to its antiseptic properties, mixtures having it for a basis resist decomposition longer than those made with ordinary water.

Dose, one-half to two fluidounces (15–60 cc.).

AQUA CINNAMOMI. U. S., Br.

CINNAMON WATER Aq. Cinnam.

"A saturated solution of oil of cinnamon in distilled water, prepared by one of the processes for aromatic waters." *U. S.*

Hydrolatum Cinnamomi, Eau distillée de Cannelle, *Fr. Cod.;* Aqua Cinnamomi, *P. G.;* Zimmtwasser, *G.;* Acqua distillata di canella, *It.;* Agua destilada de canela, *Sp.*

"Cinnamon Bark, bruised, 100 *grammes;* Water, 2000 *millilitres.* Distil *one thousand millilitres.*" *Br.* "This Water may be prepared by triturating the oil of cinnamon with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

On standing, cinnamon water, made from oil of Ceylon cinnamon, is apt to precipitate, owing to the gradual oxidation and formation of cinnamic acid, which is comparatively insoluble in water: this can be prevented, according to E. Backhaus, by passing a stream of carbon dioxide through the fresh water for a few minutes. We have never seen the precipitation successfully prevented, notwithstanding the application of numerous so-called preventives; these usually delay the precipitation, but in a few weeks' time the cloudiness due to the formation of minute crystals of cinnamic acid invariably appears. When oil of cassia cinnamon is used as directed in the U. S. process precipitation rarely occurs. E. Holmes recommends glycerin as an excellent intermedium between the oil of cinnamon and water. Ten drops of glycerin will effect the solution of a drop of the oil in a fluidounce of water.

Cinnamon water is much used as a vehicle for other less agreeable medicines, but should be given cautiously in inflammatory affections. For ordinary purposes the U. S. preparation is sufficiently strong when diluted with an equal measure of water.

Off. Prep.—Cinnamon water is used to flavor several official preparations besides the following vehicles: Mistura Spiritus Vini Gallici, *Br.;* Syrupus Aromaticus, *Br.;* Syrupus Cinnamomi, *N. F.*

AQUA DESTILLATA. U. S., Br.

DISTILLED WATER Aq. Dest.

"Water (H_2O) purified by distillation." *U. S.* "Distilled Water is prepared by distillation from good natural potable water." *Br.*

Eau distillée, *Fr. Cod.;* Aqua distillata, *P. G.;* Destillirtes Wasser, *G.;* Acqua distillata, *It.;* Agua destilada, *Sp.*

No natural water is sufficiently pure for certain pharmaceutical purposes; and hence the necessity of the above process for its distillation. It is best to reject the first portion which comes over, as this may contain carbon dioxide and other volatile impurities; and the last portion of the water ought not to be distilled, lest it should pass over with an empyreumatic taste. The distillation is usually performed with the ordinary still and worm; but, to avoid any impurity from the worm or the receiver, the condenser is directed in the U. S. Pharmacopœia to be of block tin or glass. The large stills for making distilled water commercially are not run upon the principle of the rejection of the first and the last portions, as they are continuous in their operation. They are all provided with a vent at the highest portion of the condensing system where a small amount of steam escapes, carrying with it the gases which ordinarily would contaminate the condensed distillate. Commercial distilled waters are frequently passed through charcoal filters to aerate the water and remove the flat insipidity of taste. Brande states that distilled water often derives from the still a foreign flavor, which it is difficult to avoid. He therefore recommends that a still and condenser be kept exclusively for distilling water; or, where this cannot be done, that steam be driven through the worm for half an hour, for the purpose of steaming it out, before it is used, the worm-tub having been previously emptied. J. N. Hurty prefers well water as the source of distilled water, and that it be boiled before collecting the distillate, to get rid of ammonia, and, to prevent access and growth of spores, that the water be heated to boiling before introducing it into the container, and that it be drawn off by a siphon tube reaching to the bottom of the vessel, the mouth of which is loosely stoppered with cotton. (*West. Drug.,* 1887, p. 4.) Even the use of pure tin, which is generally considered unexceptionable, does not give perfect security against impurity, as water distilled from metallic alembics with the head and worm of this metal has a peculiar odor which it retains for some time. Ordinary distilled water often contains ammonia, as may be proved by adding a few drops of Nessler's reagent. (See Part III.) In order to free distilled water from volatile nitrogenous bodies, it is necessary to redistil it after it has been placed in contact with potassium permanganate and potassium hydroxide. After about one-twentieth of the water has come over, the distillate is usually free from ammonia, and leaves no residue on evaporation. If traces of ammonia remain, acid potassium sulphate is added, and it is redistilled. (Stas.) Distilled water when kept long in glass vessels dissolves a minute quantity of the glass and the official test permitting 0.075 Gm. of residue in 1000 cc. after evaporation to dryness, was inserted to avoid unnecessary severity in the test for a solvent used for pharmaceutical purposes. Williams and Swett (*J. A. M. A.,* 1922, lxxviii, 1024) have shown that distilled water tends to become acid in reaction on standing.

Properties.—Distilled water, as usually obtained, has an insipid taste, which is very different from that of ordinary potable water. Inasmuch as distilled water has a solvent action upon glass the purest distilled water is distilled in silver vessels. The properties of pure water have already been given under the head of *Aqua.*

Description and Physical Properties.—"A colorless, limpid liquid, without odor or taste, and neutral to phenolphthalein T.S. and to methyl orange T.S.

"Evaporate 100 cc. of Distilled Water to dryness on a water bath, and subsequently dry the residue in an oven to constant weight at 100° C.: not more than 0.001 Gm. of residue remains. Separate portions of 100 cc. each of

Distilled Water are not affected by the addition of barium chloride T.S. (*sulphate*); silver nitrate T.S. (*chloride*); ammonium oxalate T.S. (*calcium*); hydrogen sulphide T.S. (*metals*). Distilled Water shows no deep yellow, orange or brown coloration when 1 cc. of alkaline mercuric potassium iodide T.S. is added to a 100 cc. portion (*ammonia*). Add 50 cc. of calcium hydroxide T.S. to 25 cc. of Distilled Water: the mixture remains clear and transparent (*carbon dioxide*). Heat 100 cc. of Distilled Water to boiling, acidulate with 10 cc. of diluted sulphuric acid, and subsequently add 0.1 cc. of tenth-normal potassium permanganate: the color of the liquid is not completely destroyed by boiling for ten minutes (*oxidizable substances*)." *U. S.*

The British Pharmacopœia requires distilled water to be "colorless, odorless, and tasteless. Yields no *reactions* for sulphates, chlorides, or nitrates. 100 millilitres evaporated to dryness on a water-bath leave not more than 0.005 gramme of solid residue. 50 millilitres with one drop of *solution of sodium sulphide* remain colorless when viewed in a Nessler glass standing on a white tile (absence of lead, copper, and iron). 250 millilitres with a mixture of 3 millilitres of *sulphuric acid* and 0.1 millilitre of *N/10 solution of potassium permanganate,* after standing for three hours at about 15.5° C., are colored blue on the addition of a crystal of *potassium iodide* and 1 millilitre of *mucilage of starch* (absence of more than traces of organic matter). 50 millilitres mixed with 2 millilitres of *alkaline solution of potassio-mecuric iodide* when viewed in a Nessler glass standing on a white tile do not, after five minutes, yield a more intense color than that yielded by 50 millilitres of ammonia-free water with 0.5 millilitre of *dilute solution of ammonium chloride* (*Nessler's*) when tested under similar conditions (limit of ammonia)." *Br.*

It is needlessly employed in some formulas, but is essential in others. As a rule, when small quantities of active medicines are to be given in solution, and in the preparation of collyria, distilled water should be directed. The following list contains the chief substances which require distilled water as a solvent: tartar emetic, corrosive sublimate, silver nitrate, barium and calcium chlorides, lead acetate and subacetate, potassium permanganate, iron and zinc sulphates, quinine sulphate, morphine sulphate, hydrochloride, and acetate, and, in general terms, all the alkaloids and their salts. Distilled water is used in preparing the official diluted acids, for absorbing gaseous ammonia, and for forming nearly all the official aqueous solutions.

AQUA DESTILLATA STERILISATA. U. S.

STERILIZED DISTILLED WATER Aq. Dest. Steril.

"Water, freshly distilled, a sufficient quantity. Place freshly distilled water, neutral to litmus paper, in sterilized containers of insoluble glass, having a capacity of not over 1000 cc. each. Stopper the containers with plugs of purified absorbent cotton, wrapped in gauze. Fasten stout, non-absorbent paper or tinfoil over the top of the plug and the lip of the flask, and sterilize in an autoclave, under steam pressure giving a temperature of 115° C., for thirty minutes. If an autoclave is not available, close the mouth of the flask containing the freshly distilled water with a plug of purified absorbent cotton wrapped in gauze, boil the contents actively for one hour and allow the water to cool without removing the cotton plug. Until ready for use, protect the mouth of the flask and the plug from infection through dust by wrapping the top of the flask tightly with paper.

"Sterilized Distilled Water should be used within twenty-four hours after its distillation if it is to be employed for intravenous injection. For other uses, it is preferable that the Water be resterilized after each opening and that it be used within a mouth after its preparation." *U. S.*

Distilled water is ordinarily not sterile, due to the contamination of the vessels in which it is collected or by air-borne organisms. For the preparation of hypodermic injections, therefore, and for some other purposes it is necessary to re-sterilize the distilled water, hence the admission of this sterilized water into the Pharmacopœia.

It is of the utmost importance that the water to be sterilized shall be freshly distilled, since distilled water which has stood even for a short time will contain many bacteria which, if present, would be killed by the sterilization process, but subsequently form a bacterin (a suspension of dead bacteria), and this if used for dissolving salts for hypodermic injection is apt to cause febrile and other systemic disturbances. If the U. S. method is followed the flask must be of so-called insoluble glass, such as Jena glass, or the solution will contain silicates which are likely to separate as needle-like spicula. Sterilized distilled water may to advantage be prepared in an autoclave. The container should be sterilized before filling and then both water and container re-sterilized.

AQUA FŒNICULI. U. S., Br.

FENNEL WATER Aq. Fœnic.

"A saturated solution of oil of fennel in distilled water, prepared by one of the processes for aromatic water." *U. S.*

Eau de Fenouil, *Fr.;* Aqua Fœniculi, *P. G.;* Fenchelwasser, *G.;* Acqua distillata di finocchio, *It.;* Agua de hinojo, *Sp.*

"Fennel Fruit, 100 *grammes;* Water, 2000 *millilitres.* Distil one thousand *millilitres.*" *Br.*

"This Water may be prepared by triturating the oil of fennel fruit with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

Uses.—Fennel water is a pleasant vehicle for other medicines, and useful when a mild aromatic is indicated. The distillation process of the British Pharmacopœia, although more troublesome, furnishes a more delicate and agreeable water than does that of the U. S. Pharmacopœia.

AQUA LAUROCERASI. Br.

CHERRY-LAUREL WATER

Hydrolatum Laurocerasi, Eau distillée de Laurier-cerise, *Fr. Cod.;* Kirschlorbeerwasser, *G.;* Agua destilada de laurel-cerezo, *Sp.*

"Cherry-Laurel Leaves, crushed, 800 *grammes;* Water, 2500 *millilitres.* Distil one thousand *millilitres;* shake the product; filter, if necessary; adjust the strength of the finished product either by adding hydrocyanic acid or Distilled Water, so that, when tested as described under 'Acidum Hydrocyanicum Dilutum,' it contains 0.1 per cent. by weight of hydrocyanic acid, HCN." *Br.*

The International Protocol (1906) fixed the strength of Cherry-Laurel Water at 0.1 per cent. of hydrocyanic acid which corresponds with the strength of the Br. Pharm, 1898 and 1914.

It is greatly to be regretted that this uncertain, dangerous, and troublesome preparation should retain a place in European pharmacopœias, inasmuch as it could easily be replaced by a flavored water containing a definite amount of a soluble cyanide. See *S. W. P.,* 1909, No. 10, 147, and 1909, No. 36, 542.

As the cherry-laurel is little cultivated in the United States, the water is not official; but from several experiments by William Procter there is little or no room to doubt that a preparation identical in its effects might be made from the leaves of our common wild cherry, *Prunus serotina.* The imported cherry-laurel water, as found in commerce, is generally impaired by age, and not to be relied on.

Cherry-laurel leaves contain 65 per cent. of water, sufficient to provoke the reaction which results in the formation of a volatile oil and hydrocyanic acid. Water is very prone to hasten the conversion of the benzaldehyde, contained in the volatile oil, into benzoic acid by oxidation, and it has been found by C. Umney (*P. J.,* x, 467) and by Moore (*Ibid.,* 604) that the water distilled without previous maceration is somewhat stronger in hydrocyanic acid and decidedly stronger in oil (Umney) than the official product. The strength of cherry-laurel water was formerly very variable, but the British Pharmacopœia requires 0.1 per cent. of hydrocyanic acid. The proportion of hydrocyanic acid in the water diminishes with time. It has been ascertained by Deschamps that if a drop of sulphuric acid be added to a pint of the preparation it will keep unchanged for at least a year. It is best preserved by the entire exclusion of air and light. Lepage found that, preserved in full and perfectly air-tight bottles, both this and bitter almond water remained unchanged at the end of a year; while if freely exposed to the air, they lost all their hydrocyanic acid and essential oil in two or three months. (*J. P. C.,* xvi, 346.) For Denigés' method of assaying the water, see *Proc. A. Ph. A.,* 1894, 556.

Uses.—Cherry-laurel water is employed in Europe as a sedative narcotic, identical in its properties with a diluted solution of hydrocyanic acid; but it is of uncertain strength, and should not be allowed to supersede the preparation of the acid now in use.

Dose, twenty minims to a fluidrachm (1.3–3.75 cc.).

AQUA MENTHÆ PIPERITÆ. U. S., Br.

PEPPERMINT WATER Aq. Menth. Pip.

"A saturated solution of oil of peppermint in distilled water, prepared by one of the processes for aromatic waters." *U. S.*

Hydrolatum Menthæ Piperitæ, Eau distillée de Menthe poivrée, *Fr. Cod.;* Aqua Menthæ Piperitæ, *P. G.;* Pfefferminzwasser, *G.;* Acqua distillata di menta piperita, *It.;* Agua destilada de menta piperita, *Sp.*

"Oil of Peppermint, 1 *millilitre;* Water, 1500 *millilitres.* Distil one thousand *millilitres.*" *Br.*

"This Water may be prepared by triturating the oil of peppermint with twice its weight of calcium phosphate and five hundred times its volume of distilled water, and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

Uses.—Peppermint water is one of the most popular of the aqueous vehicles. It is especially useful as an ingredient in mouth washes because the menthol content produces a pleasant and cool sensation on mucous membranes.

Off. Prep.—Liquor Sodæ et Menthæ (Alternative with Spearmint), *N. F.*

AQUA MENTHÆ VIRIDIS. U. S., Br.

SPEARMINT WATER Aq. Menth. Vir.

"A saturated solution of oil of spearmint in distilled water, prepared by one of the processes for aromatic waters." *U. S.*

Eau de Menthe verte, *Fr.;* Römisch-Minzwasser, *G.;* Agua de yerba buena, *Sp.*

"Oil of Spearmint, 1 *millilitre;* Water, 1500 *millilitres.* Distil one thousand *millilitres.*" *Br.*

"This Water may be prepared by triturating oil of spearmint with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

There would seem to be no good reason for distilling the mint waters from their respective volatile oils, as directed in the British processes. If the fresh plants were available, a good source for a distilled water could be provided; but if a volatile oil must be used with its uncertainty of freshness always present, the quicker process of the U. S. P. is greatly preferable.

Uses.—Spearmint water is used solely as a vehicle. Its flavor to most persons is inferior to that of peppermint, and it lacks the characteristic cooling effect of the menthol which is found in peppermint.

Off. Prep.—Liquor Sodæ et Menthæ, *N. F.*

AQUA ROSÆ. U. S. (Br.)

ROSE WATER Aq. Ros.

Hydrolatum Rosæ, Eau distillée de Rose, *Fr. Cod.;* Aqua Rosæ, *P. G.;* Rosenwasser, *G.;* Acqua distillata di Rose, *It.;* Agua destilada de rosas, *Sp.*

"Stronger Rose Water, Distilled Water, each, 1 volume. Mix them immediately before use.

"Rose Water complies with the description and tests under *Aqua Rosæ Fortior.*" *U. S.*

The British Pharmacopœia of 1898 abandoned the former process of distilling the petals and followed the method adopted by the U. S. Pharmacopœia of diluting the so-called triple rose water of commerce with distilled water. This, however, does not make rose water identical in strength in these authorities, the U. S. preparation being the stronger.

Although domestic rose water of fair quality may be made by distilling fresh rose petals, it does not possess the strength or delicacy of the by-product obtained from abroad, as officially described under *Aqua Rosæ Fortior;* hence the above process of diluting this stronger rose water. The process of distilling the fresh petals of the hundred-leaved rose is sometimes practised. These are usually preferred in the recent state; but it is said that, when preserved by being incorporated with one-third of their weight of common salt, they retain their odor, and afford a water equally fragrant with that prepared from the fresh flowers. Indeed, Haselden prefers the salted roses, believing that the water prepared from them is less mucilaginous, less apt to become sour, and keeps its odor better than that prepared from the fresh flowers. (*P. J.*, xvi, 15.) It is not uncommon to employ the whole flower, including the calyx; but the product is less fragrant than when the petals only are used, as officially directed. A. Monthus states that the petals of the hundred-leaved rose are more odorous the nearer they are to the center of the flower, and, contrary to what is said in the text, thinks that the calyx should not be rejected in preparing the distilled water. He maintains that so far from injuring the product it in fact contributes to its preservation, and that the water obtained from the whole flower is less liable to that mucosity which is the commencement of decomposition. This effect he ascribes to the astringent matter of the calyx, coagulating the mucilaginous matter of the petals, and preventing it from passing over in the distillation. (*J. P. C.*, 1863, p. 497.) Rose water is sometimes made by distilling together water and the oil of rose. This is best performed by dropping 10 drops of oil of rose on a sponge and adjusting it in the upper part of a still in the body of which a gallon of water is placed; the steam from the boiling water will carry over portions of the oil, and the distillate will thus be impregnated. Alpers (*Am. Drug.*, 1896, 384) prepares rose water by dropping 10 drops of oil of rose into a liter of hot distilled water, agitating and filtering. Rauschenberger improves the flavor by adding a trace of oil of cloves; 2.5 Gm. of oil of rose, 0.25 Gm. of oil of cloves are added to sufficient alcohol to make 100 cc.; then 10 cc. of this solution is added to 1000 cc. of boiling water and the liquid cooled and filtered.

Rose water, when properly prepared, has the perfume of the rose in great perfection. It is most successfully made on a large scale. Like the other distilled waters, it is liable to spoil when kept; and the alcohol which is sometimes added to preserve it is incompatible with some of the purposes to which the water is applied, and is even said to render it sour through acetous fermentation. It is best, therefore, to avoid this addition, and to substitute a second distillation. It may be kept in a bottle stoppered with a plug of absorbent cotton. This distilled water is chiefly employed, on account of its agreeable odor, in collyria and other lotions. It is wholly destitute of irritating properties, unless it contain alcohol, although it is not suitable for dissolving silver nitrate on account of the reducing power of the small amount of volatile oil present.

Off. Prep.—Mistura Ferri Composita, *Br.;* Linimentum Terebinthinæ Aceticum, *N. F.;* Mistura Ferri Composita, *N. F.;* Unguentum Aqua Rosæ, *Br.*

AQUA ROSÆ FORTIOR. U. S.

STRONGER ROSE WATER Aq. Ros. Fort.

"A saturated solution of the odoriferous principles of the flowers of *Rosa centifolia* Linné (Fam. *Rosaceæ*), prepared by distilling the fresh flowers with water and separating the clear saturated portion of the distillate. Its odor is best preserved by allowing a limited access of fresh air to the container." *U. S.*

Rose Water of Commerce, *Br.*, [Triple Rose Water] Aqua Rosæ, *U. S.* 1880; Stärkeres Rosenwasser, *G.*

This has been introduced for the purpose of making rose water. (See the preceding article.)

Description and Physical Properties.—"Rose Water is nearly colorless and clear, possessing a strong, pleasant odor and taste of fresh rose blossoms. It must be free from empyreuma, mustiness, or fungoid growths. It is neutral or only slightly acid to litmus paper. Evaporate 100 cc. of the Water on a water bath, and dry the residue to constant weight in an oven at 100° C.: not more than 0.001 Gm. of residue remains. Stronger Rose Water shows no reaction with hydrogen sulphide T.S. or with sodium sulphide T.S. (*metallic impurities*)." *U. S.*

Off. Prep.—Aqua Rosæ, *U. S., Br.;* Unguentum Aquæ Rosæ, *U. S., Br.;* Confectio Rosæ, *N. F.*

AQUÆ AROMATICÆ

AROMATIC WATERS

"Aromatic Waters are saturated solutions (unless otherwise specified) of volatile oils or other aromatic or volatile substances in distilled water. They are clear and free from solid impurities. They possess an odor similar to the plant or volatile substance from which they are made, and are free from empyreumatic or foreign odors. Aromatic Waters should be protected from strong light and preferably stored in containers which are stoppered with purified cotton to allow access of some air but to exclude dust.

"Aromatic Waters are prepared by one of the following general processes:" *U. S.*

Medicated Waters; Aquæ stillatitiæ; Aquæ Olei Volatili; Distilled Waters; Hydrolati; Eaux Medicinales, Eaux distillées, Hydrolats, *Fr.;* Aquæ Destillatæ, *P. G.;* Destillirte Wässer, *G.;* Acque distillate, *It.;* Aguas Destiladas, *Sp.*

"(*a*) *Distillation.*—Place the odoriferous portion of the plant or drug from which the Aromatic Water is to be prepared in a suitable still with sufficient water, and distil most of the water, carefully avoiding the development of empyreumatic odors through the burning of the substances. Separate any excess of oil, and preserve or use the clear aqueous portion, which should be saturated with the flavoring or aromatic principles of the plant.

"(*b*) *Solution.*—The Volatile Oil, or Other Specified Volatile Substance, 2 cc. or 2 Gm.; Distilled Water, a sufficient quantity, to make 1000 cc. Shake the volatile substance with 1000 cc. of distilled water in a capacious bottle, and repeat the shaking several times during a period of about fifteen minutes. Set the mixture aside for twelve hours or over night, filter through paper, and pass enough distilled water through the filter to obtain 1000 cc.

"If preferred, the Aromatic Water may be prepared by the above formula but with the addition of about 15 Gm. of purified talc, or a sufficient quantity of purified siliceous earth, or pulped filter paper, with which the volatile substance is thoroughly incorporated. Agitate the mixture well, and filter, returning the first portions of the filtrate until it comes through clear." *U. S.*

The Distilled Waters hold a much more prominent position in the pharmacy of Europe, particularly of continental Europe, than in that of the United States; and a great deal of thought and elaborate investigation has been bestowed there upon the various conditions calculated to furnish the best products by the most convenient method. The British Pharmacopœia (1914) directs the distillation process for the waters, but provides for certain medicated waters the alternative process as follows:

"**Aquæ Olei Anethi, Anisi, Carui, Cinnamomi, Fœniculi, Menthæ Piperitæ, Menthæ Viridis.**—Each of these Waters may be prepared by triturating the corresponding Oil with twice its weight of Calcium Phosphate and five hundred times its volume of Distilled Water and filtering the mixture. In tropical and subtropical parts of the Empire these Aquæ Olei may be used in place of the corresponding Aquæ of the Text of the Pharmacopœia." *Br.*

Many vegetable substances impart their peculiar flavor to water distilled from them, and more or less of their medicinal properties. The Distilled Waters chiefly used are those prepared from aromatic plants, the volatile oils of which rise with the aqueous vapor and are condensed with it in the receiver. But as water is capable of holding but a small proportion of the oil in solution, these preparations are generally feeble, and are employed chiefly as pleasant vehicles or corrigents of other medicines.

In the preparation of the Distilled Waters, dried plants are sometimes used, because fresh plants are not to be had at all seasons; but the latter, at least in the instance of herbs and flowers, should be preferred if attainable. Flowers which lose their odor by desiccation may be preserved by incorporating them intimately with one-third of their weight of common salt, and in this state afford Distilled Waters of delicate flavor. Some pharmacists prefer to employ the salted flowers in certain instances, believing that the waters distilled from them keep better than when prepared from the fresh flowers. C. R. Tichborne proposed the method of simply immersing the fresh flowers in glycerin, which preserves them with all their aromatic properties wholly unimpaired.

It is necessary to observe certain practical rules in conducting the process of distillation. When the substance employed is dry, hard, and fibrous, it should be mechanically divided, and macerated in water for a short time previous to the operation. The quantity of materials should not bear too large a proportion to the capacity of the still, as the water might otherwise boil over into the receiver. The water should be brought quickly to the state of ebullition, and continued in that state until the end of the process. Care should be taken to leave sufficient water undistilled to cover the whole of the solid matter, lest a portion of the latter, coming in contact with the sides of the vessel, be decomposed by the heat, and yield empyreumatic products. Besides, when the operation is urged too vigorously, or carried too far, a slimy matter is apt to form, which adheres to the sides of the still above the water, and is thus exposed to igneous decomposition. To obviate these disadvantages, the heat may be applied by means of an oil bath, regulated by a thermometer, or of a bath of solution of calcium chloride, by which any temperature may be obtained between 100° C. and 132.2° C., according to the strength of the solution; or, when the process is conducted a large scale, by means of steam introduced under pressure into a space around the still termed a "jacketed body." To prevent the disagreeable effects of charring and the excessive empyreumatic odor frequently noticed in Distilled Waters, caused by the solid contents of the still coming into direct contact with the heated bottom, Remington devised an expedient which prevents the herb from touching the bottom and yet permits the water and steam to have free access to all parts of it. (See Pharmaceutical Still, under *Extracta.*) A hemispherical No. 12 copper sieve with a handle and loosely fitting lid is filled with the herb and placed in the water in the still. If the bottom of the still be flat or nearly so, the rounded bottom of the cage will have only a very slight point of contact, and thus charring will be prevented. A convenient mode of applying heat by steam is by means of a coil of metal tubing placed in the bottom of the still, having one end connected with a boiler, and the other passing out beneath or at the side, and furnished with a steam-cock, by which the pressure may be increased or the condensed water drawn off at will.

The best mode of applying heat is generally conceded today to be the direct application of steam, because the Distilled Waters prepared by means of it have a freshness of aroma that is wanting in the others, are always free from the odor of the still, are much more limpid, are less apt to deposit mucilaginous matter, and keep better.

But, however carefully the process may be conducted, the Distilled Waters prepared from plants always have at first an unpleasant smoky odor. They may be freed from this by exposure for a short time to the air before being enclosed in well-stoppered bottles, in which they should be preserved. When long kept, a viscid ropy matter is apt to form in them from the growth of micro-organisms and they lose their characteristic flavor and odor. To prevent this decomposition, a little alcohol is sometimes added to the water employed in its distillation. But this addition is inadequate, and is in fact injurious, as the alcohol by long exposure to the air undergoes the acetous fermentation. A better plan is to redistil the Waters. When thus purified, it is said that they may be kept for several years unchanged.

Another mode of preparing the Distilled Waters is to substitute the volatile oil, previously separated from the plant, for the plant itself in the process. This mode is directed in the British Pharmacopœia in several instances. It is said to afford a more permanent product than the preceding, but does not always preserve the flavor of the plant.

The U. S. Pharmacopœia X recognizes for the making of Aromatic Waters only the process of dissolving the separated volatile oil. In former editions the oil was directed to be triturated with some insoluble powder, which aids in the solution of the oil by causing its division into very small particles; the powder impregnated with the oil was then shaken with water and filtered. Magnesium carbonate was at one time used for the dispersing substance, but although it produces a water that has a fine flavor and appearance, the alkalinity imparted makes it unsuitable for many purposes. Among the various other substances that have been suggested for this purpose may be mentioned calcium phosphate (*U. S.* 1980), talcum (*N. F.*, 1888), kieselguhr (LaWall, *Proc. N. J. Ph. A.*, 1908) and absorbent cotton (*U. S.* 1880). Thum (*Proc. Pa. Ph. A.*, 1916, p. 225) showed that for the use of these an intervening filtering agent was unnecessary and the U. S. P. X recommends simple agitation with cold water, a period of maceration and subsequent filtration.

As alternative processes, purified talc, purified siliceous earth or pulped filter paper are permitted as distributing media. A very good way to make medicated waters when a volatile oil is directed, is that proposed by Percival, which is to heat the water required, pour it into a bottle and add the oil, cork tightly, shake occasionally until cool, then pour off and filter; this secures a medicated water free from foreign substances, and a saturated solution, most oils being more soluble in hot than in cold water. The Dublin College prepared its Waters by agitating an alcoholic solution of the oil with distilled water, and filtering. They consequently contained alcohol, and were liable to objection in this account. In the preparation of the aromatic waters by these processes, it is very important that distilled water should be used, for tap water frequently contains constituents which have a deteriorating effect upon the aroma of the water.

The Distilled Waters are liable to contain various metallic impurities, derived from the vessels in which they are prepared or preserved. The metallic salts which have been found in them are those of iron, zinc, copper, and lead. With potassium ferrocyanide, iron will give a blue color, zinc and lead white precipitates, and copper a rose color followed by a chestnut brown precipitate. Sodium sulphide causes with salts of iron, copper, or lead, a brown discoloration more or less deep, followed by precipitates varying from brown to black; with those of zinc a white precipitate.

ARALIA. N. F.

ARALIA [American Spikenard, Spignet]

"Aralia consists of the dried rhizome and roots of *Aralia racemosa* Linné (Fam. *Araliaceæ*). Aralia contains not more than 5 per cent. of its stem bases or other organic matter." *N. F.*

Indian Root, Pettymorrel; Nard-Americain, *Fr.;* Amerikanische Nard, *G.*

American Spikenard is a perennial herb with several widely branched, unarmed, aerial stems which arise to the height of 1 to 1.8 meters and bear ternately to quinately compound leaves, each with broadly ovate leaflets having acuminate apices, cordate bases and doubly serrate margins. The flowers are small greenish-yellow and borne on panicles of umbels. The fruits are sub-globular, dark purplish to reddish-brown berries. It is indigenous to Eastern North America west to Minnesota and Missouri. The rhizomes and roots are collected in summer and autumn, cut into segments, the thicker rhizomes cut lengthwise and all carefully dried. Most of the commercial drug comes from Indiana, Missouri, North Carolina, Virginia, Washington and Illinois.

Description and Physical Properties.—"*Unground Aralia.*—Rhizome, oblique, about 12 cm. long and 5 cm. thick, somewhat flattened, tortuous, externally pale brown, and often scaly, somewhat annulately roughened, frequently cut longitudinally, whitish internally; nodes approximate, each with a prominent stem scar about 3 cm. in width; fracture fibrous; roots numerous, of varying length, 5 to 25 mm. thick, furrowed, sometimes with transverse ridges and corky patches, usually cut longitudinally, light-brown or purplish-brown externally, whitish and spongy internally, fracture of the cortex short, of the wood short and fibrous. Odor aromatic; taste mucilaginous, pungent and slightly acrid.

"*Structure.*—Root with a thick bark composed of several zones of secretion reservoirs containing oil, and surrounded by parenchyma, a well developed cork with one or more hypodermal layers of lignified cells; wood more or less distinctly radiate.

"*Powdered Aralia.*—Starch grains spherical or angular, single or 2- or more compound, 0.005 to 0.025 mm. in diameter; rosettes of calcium oxalate, 0.030 to 0.070 mm. in diameter, tracheæ with scalariform or reticulate thickenings and simple or bordered pores; characteristic lignified cells from the hypodermis 0.040 to 0.100 mm. in length and about one-half as broad, their walls showing simple pores (distinction from *Aralia nudicaulis*)." *N. F.*

Closely allied to the official species, both botanically and therapeutically, are the *A. nudicaulis* L. (*American, False* or *Wild Sarsaparilla* or *Shot-bush*) and the *A. spinosa* L. (*Angelica Tree, Hercules Club* or *Prickly Elder*). The latter has sometimes been referred to, improperly, as "prickly ash" and has occurred as an adulterant of the true prickly ash, *Xanthoxylum Americanum.*

As far as we know *A. racemosa* has never been submitted to a chemical examination but Holden (*A. J. P.*, 1880) found in the *A. spinosa* a glucosidal saponin to which he gave the name of *araliin.* It is probable that the official species owes whatever medicinal virtue it may possess to a similar principle.

Uses.—Aralia has been used, especially in domestic practice as an alterative similar to sarsaparilla, in the treatment of rheumatic, syphilitic and cutaneous affections. In medical practice it is employed chiefly in the treatment of pectoral complaints. Its therapeutic value is extremely questionable.

Dose, twenty to thirty grains (1.2–2 Gm.).

Off. Prep.—Fluidextractum Araliæ, *N. F.;* Syrupus Pini Albæ Compositus, *N. F.;* Syrupus Pini Albæ Compositus cum Morphina, *N. F.*

ARAROBA. Br.

ARAROBA [Goa Powder; Crude Chrysarobin]

"Araroba is a substance found in cavities in the trunk of Andira Araroba, *Aguiar,* freed as much as possible from fragments of wood, dried and powdered." *Br.*

Crude Chrysarobin, Goa Powder, Poh di Bahia; Poudre de Goa, *Fr.;* Goa-Pulver, *G.*

Under the name of Chrysarobin, or Araroba, a medicine has long been used in Brazil; it is exported in considerable quantities to Portugal, whence it found its way through the Portuguese colonies into Eastern commerce. It is officially recognized, after being purified, in the British, Swiss and German Pharmacopœias.

It was at one time supposed to be yielded by certain lichens, but was shown by R. A. Monteiro to be obtained from a leguminous tree abundant in the forests of the Brazilian province of Bahia, which was referred by E. M. Holmes to the genus *Cæsalpinia,* but which was determined by studies made in its native forests by J. M. de Aguiar to be a species of *Andira.*

Andira Araroba is a large leguminous tree, attaining a height of 100 feet, with a smooth trunk, common in the province of Bahia, Brazil. The wood is yellowish, with numerous vessels, besides abundant irregular interspaces of lacunæ, in which the chrysarobin is deposited. (See *P. J.*, ix, 755; x, 42, 814.) It is now known that chrysarobin is a result of the breaking down of the walls of the wood elements but the exact nature of the change or the influences that induce it remain to be determined. It is collected by felling the trees, sawing the trunks into segments and splitting them lengthwise. The yellowish araroba powder is then scraped out with the ax and with it splinter and other foreign matter. In this crude condition it is exported, and later it is freed of wood, etc., by sifting, drying and powdering it. The oldest trees yield the largest amount of the powder. The workmen who procure it often suffer severely from irritation of the eyes and face. As first obtained, chrysarobin is stated to be of a pale primrose yellow, but it rapidly darkens with age, so that in commerce it varies from a dull ochre to a dark chocolate or maroon-brown. It is sometimes a rather fine powder, but is usually more or less agglomerated, and not rarely contains fragments of woody tissue.

"The powder varies in color from brownish-yellow to umber-brown. Yields to hot *benzene* not less than 50 per cent. of a substance which, on evaporating the filtrate, drying and powdering the residue, has the character described under ' Chrysarobinum.' " *Br.*

Its taste is bitter. It is insoluble in water and most menstrua, but yields as much as 80 per cent. of its weight to solutions of caustic alkalies and to benzene. Attfield analyzed Goa powder, and found, along with 2 per cent. of resin, 5.5 per cent. of woody fiber, 7 per cent. of bitter extractive, and from 80 to 84 per cent. of what he considered to be chrysophanic acid; but Liebermann and Siedler showed that this was not chrysophanic acid, but a substance easily convertible into the acid, which substance they called *chrysarobin,* and gave to it the formula $C_{30}H_{26}O_7$. (See *Chrysarobinum.*)

For consideration of the therapeutic uses of Araroba, see *Chrysarobin.*

ARGENTI NITRAS. U. S., Br.

SILVER NITRATE Arg. Nit.

" Silver Nitrate when finely powdered and dried to constant weight in the dark over sulphuric acid contains not less than 99.8 per cent. of $AgNO_3$." *U. S.*

" Silver Nitrate, $AgNO_3$, may be obtained by the interaction of nitric acid and silver." *Br.*

Nitrate of Silver, Lunar Caustic; Azotas (Nitras) Argenticus; Azotate d'Argent, *Fr. Cod.;* Nitre lunaire, *Fr.;* Argentum Nitricum Crystallisatum, *P. G.;* Salpetersäures Silberoxyd Silbersalpeter, Silbernitrat, *G.;* Nitrato di argento cristallizzato, *It.:* Nitrato argentico cristalizado, Nitrato de plata, *Sp.*

The U. S. and Br. Pharmacopœias do not give processes for making this salt. The U. S. Pharmacopœia, 1870, gave the following: " Take of Silver, in small pieces, *two troyounces;* Nitric Acid, *two troyounces and a half;* Distilled Water, *a sufficient quantity.* Mix the Acid with a fluidounce of Distilled Water in a porcelain capsule, add the Silver to the mixture, cover it with an inverted glass funnel, resting within the edge of the capsule, and apply a gentle heat until the metal is dissolved and red vapors cease to be produced; then remove the funnel, and, increasing the heat, evaporate the solution to dryness. Melt the dry mass, and continue the heat, stirring constantly with a glass rod, until free nitric acid is entirely dissipated. Dissolve the melted salt, when cold, in six fluidounces of Distilled Water, allow the insoluble matter to subside, and decant the clear solution. Mix the residue with a fluidounce of Distilled Water, filter through paper, and, having added the filtrate to the decanted solution, evaporate the liquid until a pellicle begins to form, and set it aside in a warm place to crystallize. Lastly, drain the crystals in a glass funnel until dry, and preserve them in a well-stoppered bottle. By evaporating the mother-water, more crystals may be obtained." *U. S.*, 1870.

In the above process two details deserve notice. One of these is the direction to cover the materials in the evaporating dish, during the continuance of the reaction, with a glass funnel. This is in order to prevent the escape of fumes and to economize the nitric acid, a portion of which rises in vapor, and, being condensed on the inner surface of the funnel, falls again into the dish. The second detail is the fusion of the salt before being dissolved; the effect is to decompose any copper nitrate that might have been derived from the silver, which, if coin be employed, always contains copper. The heat decomposes the copper nitrate, and the comparatively insoluble oxide is formed, which remains on the filter when the mass is subsequently dissolved in water and filtered, the silver nitrate not being decomposed by the heat used.

A practical method used in Calcutta for separating the copper nitrate depends upon the fact that strong nitric acid only slightly dissolves silver nitrate in the presence of copper nitrate. The silver nitrate is crystallized out from the first solution as long as it can be obtained pure, and the bluish-green mother liquor is evaporated to dryness; the powdered salt, placed in a funnel stopped with asbestos, is percolated with nitric acid (sp. gr. 1.42). This washes out all of the copper nitrate, and the silver nitrate can be freed from the adhering nitric acid by heat. (*P. J.*, 1897, 61.)

During the solution of silver in nitric acid, part of the acid is decomposed and nitric oxide is given off, which becomes red by contact with the atmosphere, and the oxygen oxidizes the silver. This is taken up by the remainder of the acid, and produces silver nitrate in solution, which, by due evaporation, furnishes crystals of the salt. The silver should be pure, and the acid diluted for the purpose of promoting its action. If the silver contain copper, the solution will have a greenish tint, not disappearing on the application of heat; and if a minute portion of gold be present, it will be left undissolved as a black powder. The acid also should be pure. The commercial nitric acid, as it frequently contains both hydrochloric and sulphuric acids, should never be used. The hydrochloric acid gives rise to an insoluble chloride, and the sulphuric, to the sparingly soluble silver sulphate. It is desirable that pure silver, free from copper, should be used in this process. As silver coin always contains copper, it should be purified before being employed. For this purpose, according to the method of Lienau, it should be dissolved in nitric acid, and the solution precipitated by chlorine water, which throws down the silver only in the form of chloride. The precipitate is to be well washed with chlorine water, then dissolved in solution of ammonia, and precipitated by clean copper wire. The silver is deposited as a black powder, which, when washed with solution of ammonia, is perfectly pure. For an account of the manufacture of silver nitrate, see *D. C.*, 1887, p. 3.

Description and Physical Properties.— " Colorless, odorless, transparent, tabular, rhombic crystals, becoming gray or grayish-black on exposure to light in the presence of organic matter. One Gm. of Silver Nitrate is soluble in 0.4 cc. of water and in 30 cc. of alcohol, at 25° C. One Gm. is soluble in slightly more than 0.1 cc. of boiling water and in 6.5 cc. of boiling alcohol. It is slightly soluble in ether. When heated in a porcelain crucible to about 200° C., Silver Nitrate melts, forming a faintly yellow liquid, which on cooling, congeals to a pure white, crystalline mass. At a higher temperature it gradually decomposes with the evolution of nitrogen oxides.

"An aqueous solution of the salt (1 in 50) responds to the reactions for silver, page 444. Mix an aqueous solution of the salt (1 in 10) in a test tube with a drop of diphenylamine T.S., and then carefully superimpose it upon sulphuric acid: a deep blue color appears at the line of contact. An aqueous solution of the salt (1 in 10) is clear and colorless, and is neutral to litmus paper. An aqueous solution of the salt (1 in 10) is not colored even faintly blue by the addition of an excess of ammonia T.S. (*copper*).

"**Assay.**—Dissolve about 0.8 Gm. of finely powdered Silver Nitrate, previously dried in the dark over sulphuric acid and accurately weighed, in 50 cc. of distilled water. Add 2 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate. Each cc. of tenth-normal potassium thiocyanate corresponds to 0.01699 Gm. of $AgNO_3$. Silver Nitrate may also be assayed by the electrolytic method.

"Preserve in dark amber-colored, glass-stoppered vials, protected from light." *U. S.*

"In colorless tabular crystals. Taste bitter, metallic. Soluble in less than its own weight of *water*, slightly soluble in *alcohol* (90 per cent.); soluble in *ether*, and in *glycerin*. Yields the *reactions* characteristic of silver and of nitrates. 1 gramme dissolved in 15 millilitres of *water* yields with *hydrochloric acid* a precipitate, which, when washed and dried, weighs 0.843 gramme. The filtrate, when evaporated to dryness on a water bath, leaves no appreciable residue. Yields no characteristic *reactions* for lead, copper, iron, or sulphates." *Br.*

The solution stains the skin an indelible black color, and is itself discolored by the most minute portion of organic matter, for which it forms a delicate test. The affinity of this salt for animal matter is evinced by its forming definite compounds with albumin and fibrin. The solution also stains linen and muslin in a similar manner, and hence its use in making the so-called indelible ink. To remove these stains, W. B. Herapath advises to let fall on the moistened spots a few drops of tincture of iodine, which converts the silver into silver iodide. The iodide is then dissolved by a solution of sodium thiosulphate, made with from half a drachm to a fluidounce of water, or by a moderately diluted solution of potassium hydroxide, and the spots are washed out with warm water. Silver stains may also be taken out by a solution of two and a half drachms of potassium cyanide, and fifteen grains of iodine, in three fluidounces of water. H. Kraetzer recommends, instead of potassium cyanide, a solution of 10 parts ammonium chloride and 10 parts corrosive sublimate in 100 parts of water, with which the stains are said to be removed readily from the hands, and from linen, wool, and cotton without injuring the fabric. (*A. Pharm.*, 1880, 52.) Solutions of calcium or sodium hypochlorite are also useful to remove these stains.

Uses.—When silver nitrate in a pure state is brought in contact with a living tissue, it acts as an escharotic. Owing to the formation of a dense film of coagulated albumin, the depth of its action is very limited; the albuminous coating is at first white, but soon becomes black, owing to the reduction of the silver. Silver nitrate is among the most powerful of the chemical germicides. According to Boer, one part in four thousand is sufficient to destroy the viability of the typhoid bacillus in two hours, and Behring (*D. M. W.*, 1887) found that as dilute as 1 part in 10,000 it was capable of destroying the higher resistant anthrax spores if the exposure was sufficiently long (48 hours). It is antiseptic in proportions of 1 part in 30,000. Despite the fact that it is so easily precipitated it retains a considerable degree of germicidal power even in the presence of large quantities of albuminous material. When applied to the human tissues in dilute solution it is an active astringent; in concentrated form it is mildly caustic, but the depth of its action is very limited because the dense film of silver albuminate which is rapidly formed prevents further penetration.

Although silver nitrate, because of it affinity for proteins, cannot exist unchanged in the blood, when taken into the stomach the silver is absorbed in some form, perhaps as a proteinate. When a non-precipitable salt of silver is introduced into the blood in sufficient quantities it causes convulsions followed by paralysis through its effect upon the spinal cord, weakening of the circulation with pulmonary edema, and respiratory embarrassment. There is, however, no known physiological action which lends any support to its use as a systemic drug.

The most important use of silver is locally as an astringent and germicide, especially in infections of the mucous membranes. The strength employed varies greatly according to the location and nature of the infection, thus in *diphtheria* or *tonsillitis* it may be used as concentrated as 4 or 5 per cent., while in *urethritis* at times it cannot be borne in higher concentrations than one part in ten thousand. In *ophthalmia neonatorum* it is useful either as a prophylactic or a curative. As a preventive the instillation of one or two drops of a 2 per cent.

solution is advised in all cases of suspicious birth. In sluggish *ulcers* its astringent and stimulating effect is often of great value. It has been widely employed as an astringent in treatment of various types of *gastritis,* especially in *ulcer of the stomach.* Colonic injections of silver nitrate in strengths of ten to twenty grains to the quart have been highly lauded not only in *chronic colitis* but also in *dysentery.*

Internally silver nitrate was formerly used to some extent in the treatment of various chronic diseases of the nervous system, as *epilepsy, locomotor ataxia,* etc., but has largely passed out of vogue. The prolonged use internally of silver leads to a peculiar slate blue discoloration of the skin known as *argyria.* This discoloration may also appear on the mucous membrane and is probably due to a deposit of metallic silver. When once produced it is usually permanent, although Yandel has reported its disappearance under a course of potassium iodide. (*N. R.,* July, 1873.) It is possible that methenamine as suggested by Olson (*J. A. M. A.,* 1917, lxix, p. 87) may be of service.

Silver nitrate should always be given in pill, as the solution is decomposed by the liquids of the mouth. It should not be made up into pill with crumb of bread, as this contains common salt, but with kaolin and petrolatum, cacao butter, or other media not readily oxidizable. But, as all organic substances decompose it more or less, Vée proposes the use of inorganic matter, such as potassium nitrate, or preferably pure silica obtained by precipitating one of the silicates by an acid, and washing it. The least possible proportion of tragacanth may be used to give adhesiveness to the mass.

When ingested in sufficient dose, silver nitrate is a violent poison, and upon several occasions caused death. The symptoms are those of toxic gastro-enteritis, with marked constitutional disturbances, especially coma, convulsions, paralysis, and profound alterations of the respiration. The treatment of the poisoning resolves itself into the use of the ordinary antidotes (common salt, soap, alkalies, etc.), and the use of stimulants to maintain the circulation if needed.

Silver nitrate is incompatible with most natural waters, on account of the chlorides usually contained in them; with soluble chlorides; with hydrogen sulphide, sulphuric, hydrochloric, and tartaric acids, and their salts; with the alkalies and their carbonates; with lime water, and with astringent infusions. It is sometimes improperly prescribed in pills with tannic acid, by which it is decomposed.

Dose, one-fourth to one-half grain (0.016–0.032 Gm.).

Off. Prep.—Argenti Nitras Fusus, *U. S.* (*Br.*); Argenti Nitras Induratus, *Br.;* Argenti Nitras Mitigatus, *Br.*

ARGENTI NITRAS FUSUS. U. S. (Br.)

FUSED SILVER NITRATE Arg. Nit. Fus. [Moulded Silver Nitrate, Lunar Caustic]

"Fused Silver Nitrate contains not less than 94.5 per cent. of $AgNO_3$." *U. S.*

Argenti Nitras Induratus, *Br.;* Fused Nitrate of Silver; Lapis Infernalis, Argentum Nitricum Fusum; Styli Argenti Nitrici, Crayons d'Azotate d'Argent, *Fr. Cod.;* Azotas (Nitras) Argenticus Fusus, Azotate d'Argent fondu, Pierre Infernale, *Fr.;* Gehärteter Höllenstein, Geschmolzenes Salpetersaures Silberoxyd, Silbernitrat, *G.;* Nitrato di argento fuso, *It.;* Nitrato argentico fundido, Piedra infernal, *Sp.*

"Silver Nitrate, 95 grammes; Potassium Nitrate, 5 grammes. Fuse together, mix and pour into suitable moulds." *Br.*

The U. S. no longer recognizes a method for this preparation; that of the U. S. 1890 was as follows: "Silver Nitrate, 100 grammes; Hydrochloric Acid, 4 grammes. Add the hydrochloric acid to the silver nitrate, contained in a porcelain dish, and melt the mixture at as low a temperature as possible. Stir it well, and pour the melted mass into suitable moulds. Preserve it in dark amber-colored vials, protected from light." *U. S.* 1890. This can be achieved by the addition of various salts as sodium chloride, potassium nitrate, etc. The former method of the U. S. IX followed the suggestion of E. R. Squibb of adding hydrochloric acid whereby silver chloride with formed. In order to keep the stick from becoming discolored during the casting process, it is advisable to add a diluted nitric acid (1 in 5) occasionally to the melted nitrate, and carefully prevent the mass from becoming overheated. Edward J. Hughes (*Proc. Penna. Pharm. Assoc.,* 1922, p. 208) finds it advantageous to replace the hydrochloric acid by sodium chloride, using 1.4 grammes of sodium chloride to each 100 grammes of silver nitrate. The fusion takes place quietly without the disagreeable fuming produced by former methods, the moulded product is tough and answers the assay requirements for an official product. In the British process the "toughening" is effected by the addition of 5 per cent. of potassium nitrate. In our opinion, this is not as efficient as is the use of hydrochloric acid.

As the molten salt is capable of penetrating a common crucible, the fusion is performed in a porcelain dish or preferably a casserole, the size of which should be sufficient to hold five or six times the quantity of the salt operated on, in order to prevent its boiling over. Sometimes small portions of the liquid are spurted out, and the operator should be on his guard against this occurrence. When the mass flows like oil, it is completely fused, and ready to be poured into the moulds. These should not be greased, as the organic matter would partially decompose the fused salt. Stein (*S. W. P.,* 1877) recommends a plan for obtaining sticks of lunar caustic of special diameter or length by taking a glass tube or rod of the required outside diameter and wrapping around it moistened parchment paper, pasting the edges, tying the lower end, and drying. The melted lunar caustic is poured into the paper mould, held upright in a test tube, and allowed to cool by standing. *Elastic crayons* of silver nitrate may be made by taking a laminaria tent one-tenth of an inch (0.002 mm.) in diameter, dipping it into thick mucilage, rolling it in finely powdered lunar caustic, and drying it. (Pajot.)

Moulded silver nitrate, as prepared by the above process is in the form of hard, brittle sticks of the size of a goose quill, at first translucent, but quickly becoming gray or more or less dark under the influence of light, owing to the reduction of the silver, through organic matter or conversion through hydrogen sulphide contained in the atmosphere. That the change does not depend on the sole action of light has been proved by Scanlon, who finds that silver nitrate in a clean glass tube hermetically sealed undergoes no change by exposure to light. The sticks often become dark colored and nearly black on the surface, and when broken across, exhibit a crystalline fracture with a radiated surface. Entirely black lunar caustic is sometimes seen in France, which contains about 2 per cent. of potassium nitrate and the same quantity of black manganese oxide. *Heller's caustic pencils* look like ordinary lead pencils, and consist of long, thin sticks of lunar caustic, encased in wood; they may be sharpened like lead pencils, and the point protected by a cap to prevent injury when not in use.

Description and Physical Properties.—"A white, hard, odorless solid, generally in the form of pencils or cones, showing a fibrous fracture and becoming gray or grayish-black on exposure to light. Fused Silver Nitrate, with the exception of about 5 per cent. which is silver chloride, possesses the solubility described under *Argenti Nitras.* A filtered, aqueous solution of Fused Silver Nitrate (1 in 10) is neutral to litmus paper, and conforms to the tests for identity and purity under *Argenti Nitras.*

"**Assay.**—Add about 0.8 Gm. of Fused Silver Nitrate, accurately weighed, to 50 cc. of distilled water, and, when the silver nitrate has dissolved, filter the solution. Thoroughly wash the filter and sediment with distilled water, add 2 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S. to the mixed filtrate and washings, and titrate with tenth-normal potassium thiocyanate. Each cc. of tenth-normal potassium thiocyanate corresponds to 0.01699 Gm. of $AgNO_3$. Fused Silver Nitrate may also be assayed by the electrolytic method.

"Preserve in dark, amber-colored, glass-stoppered vials, protected from light." *U. S.*

"White or grayish-white cylindrical rods or cones. Freely soluble in *water,* but only sparingly in *alcohol* (90 per cent.). Yields the *reactions* characteristic of silver, of potassium, and of nitrates. 1 gramme, dissolved in 15 millilitres of *water,* yields with *hydrochloric acid* a precipitate which, when washed and dried, weighs 0.8 gramme, and the filtrate when evaporated leaves a white residue." *Br.*

Uses.—Lunar caustic affords a convenient method for applying silver nitrate locally in the concentrated form, especially where combined escharotic and germicidal action is desired. It is of special service in *aphthous stomatitis, exuberant granulations, chancroids,* and various other *ulcers.* The mode of application consists in dipping the stick into distilled water and applying to the part for a greater or less period of time according to the degree of action which is desired.

The moulded silver nitrate has also been used as a counter-irritant. If it be rubbed gently back and forth over the moistened skin until the latter assumes a grayish color, it generally vesicates, usually with less pain than is produced by cantharides. As a counter-irritant it has been employed in the treatment of violent inflammations of the subcellular tissue and it is asserted that it will sometimes avert a felon or an *epididymitis.*

ARGENTI NITRAS MITIGATUS. Br.

MITIGATED CAUSTIC

Mitigated Silver Nitrate [Argenti Nitras Dilutus, U. S. 1890, Diluted Silver Nitrate, Mitigated Caustic] Silver and Potassium Nitrate; Lapis infernalis nitratus; Crayons d'Azotate d'Argent Mitigé, Pierre Infernale diluée, *Fr.;* Argentum Nitricum cum Kalio nitrico, *P. G.;* Salpeterhaltiges Silbernitrat, Salpeterhaltiger Höllenstein, *G.;* Nitrato di argento fuso con nitrato di potassio, *It.;* Nitrato argentico mitigado, Piedra infernal mitigada, *Sp.*

"Silver Nitrate, 20 *grammes;* Potassium Nitrate, 40 *grammes.* Fuse together, mix and pour into suitable moulds." *Br.*

The introduction of this preparation grew out of the frequent demand for a fused silver nitrate which would not be so severe in its action as the pure article. The diluted nitrate of the U. S. P. VIII was the same as the British preparation, 33 per cent.

Properties.—"White or greyish-white cylindrical rods or cones. Freely soluble in *water,* but only sparingly in *alcohol* (90 per cent.). Yields the *reactions* characteristic of silver, of potassium, and of nitrates. 3 grammes, dissolved in 15 millilitres of *water,* yield with *hydrochloric acid* a precipitate which, after washing with hot *water* and drying, weighs 0.843 gramme." *Br.*

Uses.—This preparation is used only externally. It is similar in its action to the fused nitrate, but less energetic.

ARGENTO-PROTEINUM FORTE. U. S.

STRONG SILVER-PROTEIN

Arg.-Prot. Fort. [Strong Protargin]

"A compound of silver and protein, containing not less than 7.5 and not more than 8.5 per cent. of silver (Ag)." *U. S.*

Silver Proteinate; Strong Protein Silver.

In the attempt to produce a substance which would have the desirable disinfectant properties of the silver salts but be free from the objectionable irritant action of the nitrate, chemists have produced a large number of compounds containing silver—or some salt of it—at least partly in colloid suspension with more or less protein matter. These compounds are all of them much weaker germicides than the nitrate, but some possess considerable disinfectant power. They are also less actively astringent or irritant and have a distinct field of usefulness. They differ very widely among themselves both in their physical and biological properties. As shown by Pilcher and Sollmann (*J. Lab. Clin. Med.*, 1923, viii, p. 301 and 1924, x, p. 38) there seems to be a rather sharply defined separation of these compounds into several groups; one of these, containing smaller amounts of total silver and having relatively low specific gravities, constitutes the *Argento-Proteinum Fortius* of the U. S. P.; another group, containing from 20 per cent. of silver upwards, darker in color and more viscid, is the *Argento-Proteinum Mite.* There are also corresponding biological differences, the first type being more actively germicidal and more irritant. Pilcher and Sollmann believe that the differences in biological properties depend upon the relative proportion of ionic silver present, but Giesy (*J. A. Ph. A.*, 1925, xiv, p. 8) has pointed out that they have confused the difference between ionic and ionizable silver. However, the classification corresponds fairly accurately with clinical experience.

There has been considerable discussion as to the state of the silver in these compounds; some believe that they are colloidal suspensions of silver oxide, others that the silver is largely in a metallic state, while still others believe it chemically combined with the protein.

Smith and Giesy (*J. A. Ph. A.*, 1925, xiv, p. 10) find that the difference between these two groups is not so much in the proportion of ionic silver present, but is better measured by the proportion of silver more ionizable than silver chloride (see also Kolthoff, *J. A. Ph. A.*, xiv, p. 183). In the first group some 75 per cent. of the silver can be changed, according to Giesy, into a less ionizable form by sodium chloride. In the second group, the mild proteinates, practically none of the silver ions are removed by the chlorides, although they are by the iodides.

Kolthoff (*J. A. Ph. A.*, 1925, xiv, p. 183) from a potentiometric study of silver protein concludes that the reason that hydrochloric acid does not cause a visible precipitate, is not on account of the failure to form silver chloride, but because the silver chloride formed remains in colloidal solution.

The U. S. P. test on yeast fermentation is not intended as an evidence of antibacterial power but merely as a biological differentiation between allied drugs.

The definition given in the Pharmacopœia of silver protein has purposely been made broad enough to admit several proprietary preparations. It represents a group of compounds rather than any individual drug. In a way this may seem unfortunate, because there is not to be expected an absolute uniformity in their effects, but the present evidence indicates that there may be as wide differences between different samples of the same brand as among the various members of a group.

Description and Physical Properties.—" A brown, odorless powder, usually somewhat hygroscopic. Strong Silver-Protein is freely soluble in water, but almost insoluble in alcohol, chloroform, and ether.

" Heat about 0.2 Gm. of Strong Silver-Protein in a porcelain crucible until all carbonaceous matter is burned off, warm the residue with 1 cc. of nitric acid, dilute with 10 cc. of distilled water, and add hydrochloric acid: a white precipitate is produced which dissolves in ammonia T.S. The addition of 2 cc. of a 1 per cent. aqueous solution of sodium chloride to 10 cc. of an aqueous solution of Strong Silver-Protein (1 in 100) causes no turbidity. Ferric chloride T.S. added to its aqueous solution (1 in 100) discharges the dark color, and a precipitate is gradually produced. With mercuric chloride T.S. a white precipitate is formed, and the supernatant liquid becomes colorless or nearly so.

" When tested by the method described below, Strong Silver-Protein permits abundant gas formation when 0.6 cc. of its aqueous solution (1 in 200) is added to 20 cc. of the yeast-sugar mixture, and at most only one bubble of gas is formed when 1.5 cc. of the same strength solution is added to 20 cc. of the yeast-sugar mixture. If the yeast is more active, as determined by the control with silver nitrate described below, a proportionately larger volume of the Strong Silver-Protein solution is required, or if the yeast is less active, a proportionately smaller volume of the Strong Silver-Protein solution is required. Triturate an aqueous solution of sucrose (1 in 10) with 4 per cent. of its weight of compressed yeast. Place four 20 cc. portions of this mixture in test tubes. To one test tube add 0.6 cc. of an aqueous solution of Strong Silver-Protein (1 in 200), mix well, immediately fill a small test tube with this mixture and invert it into the larger test tube, being careful that no air bubbles rise into the small test tube. To the second test tube add 1.5 cc. of an aqueous solution of Strong Silver-Protein of the same concentration; to the third tube add 0.6 cc. of an aqueous solution of silver nitrate (1 in 2000), and to the fourth tube add 1 cc. of the same silver nitrate solution. Fill smaller test tubes with each solution and proceed as directed for the first tube. Place all four of the test tubes in a bath at 38° C. and maintain this temperature for one hour. At the end of this period, the first and third of the smaller tubes should show abundant gas formation, the second smaller tube should show not more than a bubble of gas, and the fourth tube should show not more than about 1 cc. of gas. If the third tube shows no gas, repeat the tests reducing the concentration of all of the silver solutions to one-half, and if there should still be no gas formation in the third tube, again repeat the tests, reducing the concentration of all of the silver solutions by one-third. If the fourth tube in the first series of tests contains more than about 1 cc. of gas, repeat the tests, but increase the concentration of all of the silver solutions by one-third, and if this also produces more than 1 cc. of gas in the fourth tube, again repeat the tests, increasing the concentration of all of the silver solutions by one-half (distinction from *Mild Silver-Protein*).

" **Assay.**—Ignite about 2 Gm. of Strong Silver-Protein, accurately weighed in a porcelain crucible until all of the carbon is burned off. Transfer as much as possible of the residue to a beaker, add to the crucible 5 cc. of nitric acid, warm to dissolve any adhering silver, and transfer the solution to the beaker with the aid of a little distilled water. Cover the beaker, and heat on a water bath until all of the metallic silver is dissolved, adding a little more nitric acid, if necessary. Filter into a flask, wash the insoluble residue thoroughly with distilled water, cool, and dilute with distilled water, if necessary, to about 50 to 75 cc. Add 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate. Each cc. of tenth-normal potassium thiocyanate corresponds to 0.01079 Gm. of silver.

" Preserve in well-closed containers, protected from light. *Caution.—Solutions of Strong Silver-Protein should be freshly prepared and dispensed in amber-colored bottles.*" *U. S.*

Uses.—The stronger silver protein has a very pronounced germicidal effect. In a general way it would probably be approximately correct to say that this group of drugs had a bactericidal power of about one-half or one-third that of phenol. This seems insignificant when we consider the extraordinary disinfectant power of silver nitrate. Even when we consider the degree of dilution necessary to avoid local irritation, it must be conceded that the silver nitrate still exceeds silver protein in germicidal power, but there is reason to believe that the silver protein solution retains its antibacterial powers better in the face of the bodily secretions than the nitrate. Clinical experience indicates that a higher degree of germicidal effect without undue irritation is obtainable over mucous membranes with silver protein than is possible from silver nitrate.

Silver proteins are used in medicine solely for their local disinfectant powers, especially of infections of mucous membranes, such as *acute coryza, tonsillitis, conjunctivitis, urethritis* and the like. In acute urethritis it is employed in strengths of from 1 to 2 per cent. In tonsillitis it is commonly applied as a 10 per cent. solution and occasionally even stronger.

This silver protein, if used in strong solution—10 per cent. or upwards,—has a slight irritating action suggestive of silver nitrate, but differs from silver nitrate even when in strong solution, in lacking astringent properties.

Several cases of local argyria, especially of the eyelids, have been reported from the topical use of silver protein. Olson (*J. A. M. A.*, 1917, lxix, p. 87) has made a literary and experimental study of this condition and presents evidence suggesting the value of methenamine for removing these discolorations.

ARGENTO-PROTEINUM MITE. U. S.

MILD SILVER-PROTEIN

Arg.-Prot. Mit. [Mild Protargin]

" Silver rendered colloidal by the presence of or combination with protein. It contains not less than 19 per cent. and not more than 25 per cent. of silver (Ag)." *U. S.*

See remarks under *Argento-proteinum Fortius.*

Description and Physical Properties.—" Dark brown or almost black shining scales or granules. It is odorless, and is frequently hygroscopic. Mild Silver-Protein is freely soluble in water, but almost insoluble in alcohol, chloroform, and ether.

" Heat about 0.1 Gm. of Mild Silver-Protein in a porcelain crucible until all carbonaceous matter is burned off, warm the residue with 1 cc. of nitric acid, dilute with 10 cc. of distilled water, and add hydrochloric acid: a white precipitate is produced which dissolves in ammonia T.S. The addition of 2 cc. of an aqueous solution of sodium chloride (1 in 100) to 10 cc. of an aqueous solution of Mild Silver-Protein (1 in 100) causes no turbidity. Ferric chloride T.S. added to its aqueous solution (1 in 100) discharges the dark color and a precipitate is gradually produced. With mercuric chloride T.S. a white precipitate is formed and the supernatant liquid becomes colorless or nearly so. When tested by the method described under *Argento-Proteinum Fortius,* 0.8 cc. of an aqueous solution of Mild Silver-Protein (1 in 20) permits abundant gas formation (distinction from *Strong Silver-Protein*).

" **Assay.**—Proceed as directed under *Argento-Proteinum Fortius,* using about 1 Gm. of Mild Silver-Protein.

" Preserve in well-closed containers, protected from light. *Caution.—Solutions of Mild Silver-Protein should be freshly prepared and dispensed in amber-colored bottles.*" *U. S.*

Uses.—As remarked under *Argento-proteinum Fortius* the Pharmacopœial definition represents a group rather than an individual compound. The various individuals that belong to the type of mild silver proteins—the term " mild " applies both to their lack of irritant qualities and their antibacterial powers—differ even more widely among themselves than the stronger type. Indeed different specimens of the same brand seem to differ very widely in their germicidal properties. It is not obvious, however, that there is any very material difference in their therapeutic value. Their chief therapeutic importance is not as germicides—that is, to destroy bacteria—but as antiseptics, to inhibit the growth of bacteria. Some writers go so far as to maintain that the therapeutic effect of this group of silver compounds is largely, if not chiefly, due to mechanical factors. Their peculiar colloidal state makes them of great value as mechanical cleansers of mucous membranes. They differ materially from the stronger proteins, in that even in concentrated solution they are practically non-irritant.

They are used in the same diseases as the stronger silver proteins, but preferred in those very acute types of catarrh in which it is important to sedulously avoid any irritation of the mucous membrane. Ordinarily they are applied in strengths of from 10 to 25 per cent., or sometimes up to 50 per cent.

For information concerning the individual brands of silver protein see under *Silver Compounds,* Part II.

ARGENTUM

SILVER

Argentum purificatum; Argent raffiné, Argent, *Fr.;* Argentum Foliatum, *Fr. Cod., P. G.:* Silber, Raffinirtes Silber, *G.;* Argento, *It.;* Plata, *Sp.*

Silver is found at times in the metallic state, usually crystallized, also associated with gold, antimony, arsenic, or mercury; but usually it occurs as a sulphide, pure or mixed with other sulphides, as those of copper, lead, and antimony. It is sometimes found as a chloride.

The most productive mines of silver are found on this continent, being those of Mexico and Peru and our own Rocky Mountain States and Territories; the richest in Europe are those of Norway, Hungary, and Transylvania. Mines have been opened and profitably worked in California and Nevada but at present it is chiefly Colorado and Montana which furnish the great bulk of the American silver production. Idaho, Utah, and Arizona also contain very rich silver deposits. The principal ore is the sulphide. The mineral containing silver which is most disseminated is argentiferous *galena,* which is lead sulphide containing a little silver sulphide. Argentiferous galena exists in several localities in the United States. Native silver is associated, in small quantities, with the native copper of the Lake Superior region, and a little of it has come into the market. The two metals, though more or less mixed, are yet quite distinct, never being alloyed to any considerable extent, showing conclusively that the deposits have not undergone igneous fusion at any time, but that the metals have deposited from solution.

Extraction.—Silver is extracted from its ores by two principal processes, *amalgamation* and *cupellation.* When the ore is principally silver sulphide, it is mixed with a tenth of sodium chloride and roasted in reverberatory furnaces. As fast as the sulphide is oxidized to sulphate, this reacts with the sodium chloride, forming silver chloride and sodium sulphate. The roasted mass is then reduced to very fine powder, mixed with half its weight of mercury, one-third of its weight of water, and about one-seventeenth of iron in flat pieces, and subjected for sixteen or eighteen hours to constant agitation in barrels turned by machinery. The chlorine combines with the iron, and remains in solution as iron chloride, while the reduced silver forms an amalgam with the mercury. The amalgam is then subjected to pressure in leather bags, through the pores of which the excess of mercury passes, a solid amalgam being left behind. This is then subjected to heat in a distillatory apparatus, by means of which the mercury is separated from the silver, which is left in a porous mass. In Peru and Mexico the process is similar to that above given, common salt and mercury being used; but slaked lime and iron sulphide are also employed, with little effect.

When argentiferous galenas are worked for the silver they contain, they are at first reduced, and the argentiferous lead obtained is fused on a large, oval, shallow vessel called a test, and exposed to the blast of a bellows, whereby the lead is oxidized, half vitrified, and driven off the test in scales, in the form of litharge. The operation being continued on successive portions of argentiferous lead, the whole of the lead is separated, and the silver, not being oxidizable, accumulates on the test as a brilliant fused mass, until its amount is sufficient to be removed. The time required for the separation is much abridged by the process of Pattinson. This consists in allowing the melted alloy to cool slowly, and separating the crystals which first form, consisting mainly of lead, by means of a perforated ladle. The residue is a very fusible alloy of lead and silver, in which the latter metal is in large proportion, and from which it can be easily separated by cupellation or other means. In recent years much gold and silver have been extracted from tailings and so-called "slimes" by the cyanide process and most recently by the "oil flotation" process.

Properties.—Silver is a white metal, very brilliant, tenacious, melleable, and ductile. In malleability and ductility it is inferior only to gold. It is harder than gold, but softer than copper. Its atomic weight is 107.88, symbol Ag, and sp. gr. from 10.4 to 10.5. What is termed "molecular silver" is obtained as a very fine powder, by reducing freshly precipitated silver chloride with formaldehyde in the presence of potassium carbonate. *"Colloidal silver"* is obtained by heating to 100° C. silver citrate in a stream of hydrogen or by passing an electric current between silver electrodes in water. It dissolves in water to a red solution which does not dialyze. Both these allotropic forms are converted into ordinary silver by fusion. (For further description, see Part II.) Silver forms but one well-characterized oxide. Exposed to a full red heat, it enters into fusion, melting at 954° C., and exhibits a brilliant appearance. It is not oxidized in the air, but contracts a superficial tarnish of silver sulphide by the action of hydrogen sulphide in the atmosphere, from which it may be freed by washing it with a strong solution of potassium cyanide, and, as soon as it becomes bright, washing it with water and drying it. It is entirely soluble in diluted nitric acid. If any gold be present, it will remain undissolved as a dark-colored powder. From the nitric solution the whole of the silver may be thrown down by sodium chloride, as a white precipitate of silver chloride, characterized by being completely soluble in ammonia. If the remaining solution contain copper or lead, it will be affected by hydrogen sulphide. "The solution, deprived of silver by means of sodium chloride, and filtered, is not colored, *or but slightly so,* and is not precipitated by hydrosulphuric acid." *U. S.* 1870. "If ammonia be added in excess to a solution of the metal in nitric acid, the resulting fluid exhibits neither color nor turbidity" (*Br.* 1885); proving the absence of copper, lead, and other metals. "10 grains dissolved in a little nitric acid, the solution diluted with water, and diluted hydrochloric acid added in slight excess, yields a white precipitate which, when thoroughly washed, dried, and heated, weighs 13.25 grains." *Br.* 1885.

ARMORACIÆ RADIX. Br.

HORSERADISH ROOT

"Horseradish Root is the fresh root of Cochleria Armoracia, *Linn.*, collected from cultivated plants." *Br.*

Armoracia, *Br.* 1864; Radix Raphani Rusticani Raifort *Fr. Cod.*; Moutarde des Moines, Radis de Cheval, Cran de Bretagne, *Fr.*; Meerrettig, *G.*; Rabano rusticano (Raiz de), *Sp.*

Cochlearia Armoracia L. (also known as *Roripa Armoracia* L., Hitch. and *Radicula Armoracia* L., Robinson) a member of the *Cruciferæ,* is a native of the marshy districts of Eastern Europe. It is cultivated very largely for its roots which are used as a condiment, being considered stimulating to the digestive organs. It has escaped from our gardens, growing in moist grounds, especially along streams. The root of this plant is perennial, sending up numerous very large radical leaves from the midst of which a round, smooth, erect, branching stem rises two or three feet in height. The radical leaves are lance-shaped, wavy, scalloped on the edges, sometimes pinnatifid, and stand upon strong footstalks; those of the stem are much smaller, oblong or lanceolate, sessile, sometimes divided at the edges, sometimes almost entire. The flowers are white, and arranged in terminal and axillary panicles of racemes. The fruit is a silicle.

The root, which is most active in early spring and autumn, is long, conical at top, then nearly cylindrical for some inches, at last tapering, of a strong, pungent, odor when scraped or bruised, and of a hot, biting, somewhat sweetish, and sometimes bitterish taste. "Nearly cylindrical, except at the crown, where it is somewhat enlarged, and marked with closely approximated semi-amplexicaul leaf-scars. Diameter from twelve to twenty-five millimetres, length commonly thirty centimetres or more; pale yellowish-white or brownish-white externally, whitish within. Inodorous when unbroken, but yielding a characteristic pungent odor when scraped or bruised; taste very pungent." *Br.*

Its virtues depend upon a *volatile oil,* which is dissipated by drying, the root becoming at first sweetish, and ultimately insipid and quite inert. Its acrimony is also destroyed by boiling. The oil may be obtained by distillation with water. It is colorless or pale yellow, heavier than water, very volatile, excessively pungent, acrid, and corrosive, exciting inflammation and even vesication when applied to the skin. Hubatka considers it as identical with the volatile oil of mustard. He combined it with ammonia and obtained crystals of *thiosinamin.* $NH_2.CS.N(C_3H_5)H$, which agreed with that produced from mustard oil. (*J. P. C.,* 3e sér., v, 42.) According to Gutret, only six parts of it are obtained from 10,000 of the root. Besides this principle, the fresh root contains, according to the same chemist, a little resin in minute quantity, sugar, extractive, gum, starch, albumen, acetic acid, calcium sulphate and acetate, water and lignin. From observations made by F. L. Winckler, it may be inferred that like mustard it contains *potassium myronate* which in the presence of water is decomposed by an enzyme, also existing in the root, and water, to produce the volatile oil. (See *Sinapis.*) Horseradish when distilled with alcohol yields none of the oil. Buried in cool sand the root may be kept for some time without material deterioration.

It is said that if to the powder of the dried root which has become apparently inert, the emulsion of white mustard seed containing myrosin be added, it re-acquires its original irritant properties; so that it is the ferment myrosin and not the potassium myronate which is injured by drying. Hence the powdered root may be added with advantage to mustard in preparing cataplasms, pediluvia, etc. (*J. P. C.,* xxvii, 268.)

The French Codex contains a formula for *compound syrup of horseradish* under the name of *Sirop de Raifort Composé.* It was formerly called *Sirop Antiscorbutique.*

Uses.—Horseradish is highly stimulant, exciting the stomach when swallowed, and promoting the secretions, especially that of urine. Externally it is rubefacient. Its chief use is as a condiment to promote appetite and invigorate digestion.

Dose, fifteen to thirty grains (1–2 Gm.) or more, grated or cut into small pieces.

Off. Prep.—Spiritus Armoraciæ Compositus, *Br.*

ARNICA. N. F. (Br.)

ARNICA Arnic. [Arnica Flowers]

"Arnica is the dried flower-head of *Arnica montana* Linné (Fam. *Compositæ*). Arnica contains not more than 3 per cent. of foreign organic matter." *N. F.*

"Arnica Flowers are the dried flower-heads of Arnica montana, *Linn.*" *Br.*

Arnicæ Flores, *Br.;* Leopard's Bane, Wolf's Bane, Mountain Tobacco; Fleurs d'Arnique, *Fr.;* Flores Arnicæ, *P. G;* Wohlverleihblüthen, Arnicablüthen, Arnika, Blutblume, Gemsblume, Fallkraut, *G.;* Fiori di arnica, *It.;* Flor de arnica, *Sp.*

Arnica montana is a perennial herbaceous plant, having a woody, brownish, horizontal rhizome, from 2 to 10 cm. long, and 0.5 to 5 mm. thick, ending abruptly, and sending forth numerous slender fibers of the same color. The stem is about 3 dm. high, cylindrical, striated, hairy, and terminating in one, two, or three peduncles, each bearing a flower. The radical leaves are ovate, entire, ciliated, and obtuse; those of the stem, which usually consist of two opposite pairs, are lance-shaped. Both are bright green, and somewhat pubescent on their upper surface. The flower-heads are yellow.

This plant is a native of the mountainous districts of western and central Europe, and is found, according to Nuttall, in the northern regions of this country, west of the Mississippi. It has been introduced into England, and might no doubt be cultivated in the United States. The flowers, leaves and root are employed; but the flowers only are official. In the Swiss and German Pharmacopœias the definition of arnica flowers is restricted to the flowers separated from the receptacles, this being done as the latter contain the larvæ of *Trypeta arnicivora.* On the other hand the Austrian Pharmacopœia permits the use of the entire flower heads, but the receptacles containing larvæ must be removed.

Description and Physical Properties.—"*Unground Arnica.*—Consisting chiefly of the tubular and ligulate flowers, usually with the involucre and receptacle present; involucral bracts narrowly lanceolate, about 1 cm. long, dark green and pubescent; receptacle slightly convex, deeply pitted and densely short hairy; ray flowers yellow, the ligulate portion up to 2 cm. long, more or less folded lengthwise, 3-toothed, 7- to 12-veined, pistillate; tubular flowers perfect, reddish yellow, stamens without a tail-like appendage; the achenes spindle shaped, 5 to 7 mm. long, dark brown, finely striate; glandular pubescent and surmounted by a pappus a little longer than the achene and composed of a single circle of nearly white barbellate bristles. Odor characteristic and agreeable, taste bitter and acrid.

"*Powdered Arnica.*—Yellowish brown; pollen grains numerous, 0.025 to 0.035 mm. in diameter, spherical triangular in section and spinose; non-glandular hairs of three kinds, either unicellular, 4- to 6-celled, or consisting of a pair of unicellular hairs with numerous pores on the dividing wall; glandular hairs of three kinds, either with a large unicellular stalk and a unicellular glandular head, or with a 4-celled stalk and a unicellular glandular head, or a stalk of a double row of 5 cells which may be more or less broken and a 2-celled, glandular head; pappus consisting of a multicellular axis with unicellular branches." *N. F.*

"Receptacle nearly flat, bristly, with two rows of dark-green, linear-lanceolate, acute, hairy bracts. Each ray-floret possesses a much shrivelled dark yellow ligulate corolla which, after expansion in water, exhibits from eight to twelve veins and three terminal teeth. Disc-florets numerous, yellow. Fruits slender, shrivelled, with numerous appressed hairs, and crowned with a single row of stiff, whitish, barbed bristles. Slight aromatic odor; taste bitter and acrid." *Br.*

Arnica flowers of commerce are not infrequently admixed with and substituted by other composite flowers. Farwell states that the heads of *Lapachis columnaris* T. et G., a western composite, have been offered in large quantities for arnica. Hartwich has recently found a sample of arnica adulterated with the flowers of the common dandelion. Beilstein reported having found in one lot approximately 90 per cent. of the flowers of *Inula.* The following flowers also have been used: *Anthemis tinctoria* L., *Calendula officinalis* L., *Doronicum Pardalianches* L., *Inula britannica* L., *Scorzonera humilis* L., *Heterotheca inuloides.* The first three of these are distinguished by the fact that the achenes do not have any pappus. In *Inula britannica* the receptacle is naked and the ligulate flowers are four-nerved. In *Scorzonera* the flowers are all ligulate and the pappus is feather-shaped. In *Heterotheca inuloides* the florets have an inner long pappus and an outer short pappus.

The rhizome was formerly official in both the British and U. S. Pharmacopœias and was described by the latter as follows:

"Rhizome about 5 Cm. long and 3 or 4 Mm. thick; externally brown, rough from leaf-scars; internally whitish, with a rather thick bark, containing a circle of resin-cells, surrounding the short, yellowish wood-wedges, and large, spongy pith. The roots numerous, thin, fragile, grayish-brown, with a thick bark containing a circle of resin-cells. Odor somewhat aromatic; taste pungently aromatic and bitter." *U. S.,* 1890.

It appears to contain the same active constituents as the flowers.

The *arnicin* of Walz (*N. Jahrb. Pharm.,* xiii), extracted from both the root and the flowers, is an amorphous yellow mass of acrid taste, slightly soluble in water, freely in alcohol or ether, and dissolving also in alkaline solutions. It is precipitable from its alcoholic solution by tannic acid or by water. Walz assigns to arnicin the formula $C_{20}H_{30}O_4$; other chemists that of $C_{35}H_{54}O_7$. Arnicin has not been proved to be a glucoside, although it is decomposed by diluted acids. Sigel (1873) obtained from dried arnica root about ½ per cent. of essential oil, and 1 per cent. from the fresh; the oil of the latter had a sp. gr. of 0.999 at 18° C. The oil was found to be a mixture of various bodies, the principal being the *dimethyl ether of thymohydroquinone,* $C_{10}H_{12}(OCH_3)_2$, boiling at about 235° C., and with this, *phloryl isobutyrate* to the extent of one-fifth of the oil, and the methyl ether of a phlorol. (*Pflanzenstoffe,* 2d ed., p. 1530.) Kondakow confirmed the results of Sigel's investigations. (*J. P. C.,* 1910, ii, 79.) (See also Gildemeister and Hoffmann, *Die Aetherische Oele,* p. 900.) The water from which the oil separates contains isobutyric acid, probably also a little angelic and formic acids, but neither capronic nor caprylic acid, which had been pointed out by Walz. Arnica root contains about 10 per cent. of inulin. (*Pharmacographia,* 2d edition, p. 391.) Klobb reported the presence in arnica flowers of a colorless, crystalline body which he at first named *arnisterin,* but in 1905 he changed its name to *arnidiol.* (*Ph. Ztg.,* 1905, xl, p. 846.)

Uses.—Arnica is an active irritant, which is capable, when taken in overdose, of producing symptoms of violent toxic gastro-enteritis, with great nervous disturbance, reduction or increase of the pulse rate, and collapse. In a number of cases of severe or even fatal poisoning by it, the symptoms have been burning pains in the stomach, vomiting, choleraic diarrhea, giddiness, intense muscular weakness, dilated pupils, finally complete insensibility and collapse. In some cases the disturbances of the gastro-intestinal canal have been absent, and the symptoms have chiefly been of cerebral origin. An ounce of the tincture has produced serious although not fatal, symptoms.

Arnica has been used in Germany in the treatment of *palsies* and various other diseases, but we have very little positive knowledge concerning its action upon the system, and there is no sufficient reason for believing that it is valuable in the treatment of internal diseases. It is largely employed externally in the treatment of *bruises* and *sprains,* generally in the form of the tincture.

The powdered flowers and leaves are sternutatory; and the inhabitants of Savoy and the Vosges are said to substitute them for tobacco. A tincture of the root was official in the British Pharmacopœia, 1898.

Dose, of the flowers, one to two grains (0.6–1.2 Gm.).

Off. Prep.—Tinctura Arnicæ, *N. F.* (*Br.*) (from flowers); Fluidextractum Arnicæ, *N. F.*

ARSENI IODIDUM. U. S. (Br.)

ARSENOUS IODIDE Arsen. Iod. [Arsenic Tri-iodide]

"Arsenous Iodide, when dried to constant weight over sulphuric acid, contains not less than 99 per cent. of AsI_3." *U. S.* "Arsenious Iodide, AsI_3, may be obtained by the direct combination of iodine and arsenium, and purification of the product by crystallization." *Br.*

Arsenii Iodidum, *Br.;* Arsenici Iodidum, *U. S.* 1870; Iodide of Arsenic, Arsenious Iodide; Iodure d'Arsenic, *Fr.;* Arsenicum jodatum, Arsenik Jodür, Arsentrijodid, *G.*

This iodide was introduced into the U. S. Pharmacopœia for the purpose of preparing the solution of arsenous and mercuric iodides. It may be made by the direct combination of its constituents, with the aid of a gentle heat, but this form readily decomposes, the iodine subliming and condensing in crystals upon the upper portion of the bottle, containing it. The orange red crystalline powder, now official, is much more permanent.

Nickle's process enables the operator to obtain the salt in a crystalline condition. Arsenic and iodine in equivalent proportions are heated together with carbon disulphide in a flask, to which an upright condenser is attached, until the iodine color disappears. The solution is then evaporated to the crystallizing point.

In the *B. Chem. G.,* 1881, 2643, may be found a process for obtaining this salt chemically pure, by making a hot solution of arsenic trioxide in hydrochloric acid, and mixing it with a concentrated solution of potassium iodide, whereupon the triiodide separates as a crystalline powder; this may be washed with hydrochloric acid, sp. gr. 1.120, until a portion of the washings on evaporation ceases to leave a residue of potassium chloride.

Description and Physical Properties.—"An orange-red, inodorous, crystalline powder, stable when protected from direct sunlight and kept in a cool place. *Caution.—Arsenous Iodide is extremely poisonous.*

"One Gm. of Arsenous Iodide is soluble in about 12 cc. of water at 25° C., with partial decomposition. It is soluble in alcohol, chloroform, ether, and carbon disulphide. A freshly prepared aqueous solution of the salt is colorless, but upon standing it gradually decomposes with the formation of arsenous and hydriodic acids and becomes yellow due to the liberation of iodine. No loss of iodine occurs when dry Arsenous Iodide is heated on a water bath, but at higher temperatures it volatilizes.

"An aqueous solution of Arsenous Iodide (1 in 50) responds to the reactions for arsenous compounds, and for iodides. When volatilized, Arsenous Iodide leaves not more than 0.5 per cent. of residue.

"**Assay.**—Proceed as directed under the assay for iodides, using about 0.5 Gm. of Arsenous Iodide, previously dried to constant weight over sulphuric acid and accurately weighed. Each cc. of tenth-normal silver nitrate corresponds to 0.01519 Gm. of AsI_3.

"Preserve in amber-colored, glass-stoppered vials, in a cool place, protected from light." *U. S.*

"Small orange-colored crystals. Soluble in *water,* and in *alcohol* (90 per cent.). The aqueous solution is acid to *litmus,* and yields the *reactions* characteristic of arsenic and of iodides.

Heated in a test-tube it entirely volatilises, violet vapors of iodine being set free." *Br.*

It has a tendency to decompose even at ordinary temperatures, iodine separating and volatilizing, oxygen being absorbed and arsenic trioxide formed.

Uses.—Following the suggestion of Biett, arsenous iodide has been somewhat extensively used in the treatment of *lupus* and other skin conditions in which a powerful stimulant is desired; Biett employed the ointment of the strength of three grains to the ounce. The iodide has also been given internally as an alterative, in *cancer,* in *scrofula, lepra,* etc., and probably does not differ in its action from other preparations of arsenic. In large doses it acts as a violent gastro-intestinal irritant and poison.

Dose, one-twentieth to one-fifth grain (0.003–0.012 Gm.).

Off. Prep.—Liquor Arseni et Hydrargyri Iodidi, *U. S.* (*Br.*).

ARSENI TRIOXIDUM. U. S. (Br.)

ARSENIC TRIOXIDE Arsen. Triox. [Arsenous Oxide, White Arsenic]

"Arsenic Trioxide, when dried to constant weight at 100° C., contains not less than 99.8 per cent. of As_2O_3. *Note.—Powdered Arsenic Trioxide when administered in solid form, as in powders, tablets, and pills, must consist of particles not greater than* 0.0125 *mm. in diameter.*" *U. S.*

"Arsenious Anhydride may be obtained by roasting certain arsenical ores, and contains not less than 99.8 per cent. of arsenious oxide, As_4O_6." *Br.*

Acidum Arseniosum, *Br.;* Acidium Arsenosum, Arsenous Acid; Arsenous Anhydride; Arsenicum Album, *Ed.;* Anhydride arsénieux, *Fr. Cod.;* Arsenic blanc, Fleurs d'Arsenic, *Fr.;* Acidum Arsenicosum, *P. G.;* Arsenigesäure, Arsenichte Säure, Weisser Arsenik, *G.;* Anidride arseniosa, Acido arsenioso, Arsenico bianco, *It.;* Anhidrido arsenioso, Arsenico blanco, *Sp.;* Arsenik, Dan., *Swed.*, *Pol.*

Arsenic trioxide is found native in octahedral crystals, called *arsenalite,* or as monoclinic crystals, called *clandetite.* It is always formed when arsenic or arsenical minerals are heated or roasted in the presence of air, and is a by-product in a number of metallurgic operations.

Arsenic trioxide is prepared in Bohemia and Saxony, where it is procured on a large scale as a collateral product during the smelting of cobalt ores which are almost invariably accompanied by arsenic, and in England from the mineral *arsenopyrite,* also called *mispickel* or *arsenical iron,* which is associated with the ores of tin and copper. Most of the arsenous oxide produced in the United States is from this latter mineral and much of it comes from Ontario from the residues left after treating gold ores. The German process is that usually quoted as the older and better known. According to this the ores are roasted in reverberatory furnaces with long horizontal flues. The arsenic is converted by combustion into arsenic trioxide, which rises in vapor and condenses on the sides of the flues. In this state it is impure, and requires a second sublimation, which is performed in cast iron vessels, fitted with conical heads of the same material, having an opening at the summit. The vessels are placed over a furnace, and brought to a red heat, when a portion of the impure arsenic trioxide is thrown in through the opening, which is immediately stopped. This portion being sublimed, a second portion is introduced in a similar manner. Finally, the vessels are allowed to cool; and upon removing the heads the purified oxide is found attached to them, in vitreous layers, at first as transparent as glass, but gradually becoming, by contact with the air, opaque at their surface. These are broken into fragments of a convenient size, and thus enter commerce. The arsenic trioxide so obtained is generally packed in casks, containing from two to five hundred pounds and is shipped principally from the ports of Hamburg and Bremen. The English process differs somewhat in its details, and essentially in its final product, which is fine and crystalline rather than amorphous. In this process the crude arsenic of the first sublimation is refined by introducing it into another furnace or series of furnaces, where it is again volatilized by the heat. When it condenses in the long series of chambers through which the vapors are carried, it is, if the process be fully successful, in the form of a perfectly white crystalline solid, which needs only to be ground and packed into kegs to be made ready for the market. The unground arsenic is, as stated, all in the *crystalline* condition, the temperature of the chambers being too low to permit the formation of the glassy variety.

The German arsenic occurs in commerce, in masses, with a vitreous fracture, and of a milk-white color externally, but, internally, often perfectly transparent. As first sublimed, the whole mass is transparent; but it gradually becomes white and opaque, the change proceeding progressively from the surface inwards. This change has not been well explained, but probably depends upon the absorption of moisture, causing a gradual passage of the acid from the amorphous to the crystalline state.

Description and Physical Properties.—"A white powder, or irregular masses of two varieties, one amorphous, transparent, and colorless, like glass; the other, crystalline, opaque and white, resembling porcelain. Frequently the same piece has an opaque, white, outer crust enclosing the glassy variety. Contact with moist air gradually changes the glassy into the white, opaque variety. All varieties are odorless. *Caution.—Arsenic Trioxide is extremely poisonous.*

"Arsenic Trioxide is slowly soluble in water, the amorphous or glassy variety being somewhat more soluble than the crystalline. It is slightly soluble in alcohol and in ether, and freely soluble in glycerin. It is dissolved by hydrochloric acid and by solutions of alkali hydroxides and carbonates. An aqueous solution of Arsenic Trioxide is faintly acid to litmus paper. When slowly heated in a dry test tube of hard glass, Arsenic Trioxide yields a sublimate of minute crystals. When heated rapidly to about 200° C., the amorphous variety fuses, then sublimes, while the crystalline variety sublimes without fusing. When Arsenic Trioxide is covered with charcoal in an ignition tube and strongly heated, it is reduced to metallic arsenic which is deposited on the cooler portion of the tube as a mirror, having a metallic luster. This mirror is rapidly soluble in solution of chlorinated lime or chlorinated soda. Hydrogen sulphide T.S. colors an aqueous solution of Arsenic Trioxide (1 in 100) yellow. Upon the addition of a few drops of hydrochloric acid to the colored solution, a lemon-yellow precipitate of arsenic trisulphide is produced.

"Not more than 0.1 per cent. of residue remains upon the ignition of 1 Gm. of Arsenic Trioxide. Dissolve 1 Gm. of Arsenic Trioxide in 10 cc. of ammonia T.S. with the aid of gentle heat: a clear, colorless solution results. Dissolve about 0.2 Gm. of Arsenic Trioxide in 50 cc. of distilled water with the aid of 2 cc. of hydrochloric acid and completely precipitate by hydrogen sulphide. Allow the precipitate to subside, and pour off the clear liquid: the precipitate dissolves completely upon the addition of an excess of ammonium carbonate T.S. (*antimony, tin, or cadmium*).

"**Assay.**—Dissolve about 0.2 Gm. of Arsenic Trioxide previously dried to constant weight at 100° C., and accurately weighed, in 20 cc. of boiling distilled water, and gradually add sodium hydroxide T.S. until complete solution results. Neutralize this solution with diluted sulphuric acid, using phenolphthalein T.S. as indicator, cool, dissolve in it 2 Gm. of sodium bicarbonate, and titrate the mixture with tenth-normal iodine, using starch T.S. as indicator. Each cc. of tenth-normal iodine corresponds to 0.004948 Gm. of As_2O_3." *U. S.*

"A heavy white powder, or broken white lumps which have a vitreous fracture and usually appear stratified. Very slowly soluble in 65 parts of *water*. Slowly heated in a test-tube it yields a sublimate of minute, brilliant, transparent, octahedral crystals. Its aqueous solution, which is odorless, tasteless, and faintly acid to *litmus*, gives with *solution of silver ammonio-nitrate*, a canary-yellow precipitate readily dissolved by *solution of ammonia* and by *nitric acid*. Sprinkled on ignited charcoal, it emits an alliaceous odor. Entirely volatilised by heat. 0.1 gramme, dissolved in boiling *water* with the aid of a little *solution of sodium hydroxide*, the cooled solution being slightly acidified with *hydrochloric acid* and then made alkaline with excess of *sodium bicarbonate*, decolorises not less than 20.1 millilitres of *N/10 solution of iodine*. Dissolves completely in *solution of ammonia*, and the resulting liquid, when diluted with an equal volume of *water* and acidified with *hydrochloric acid*, is not yellow (absence of arsenious sulphide)." *Br.*

The English make of arsenic is always powdered, and, under a lens, is seen to consist of small crystals perfect in form, or of small fragments of larger crystals. As it occurs in commerce for medicinal use, it is often in the form of a white powder, almost as fine as flour. It has no odor, even in vapor; but when thrown on ignited charcoal it emits a garlicky odor, in consequence of its deoxidation, and the volatilization of the reduced metal. Its point of sublimation, according to Berzelius, is at an incipient red heat; but, according to Mitchell and Durand, it is lower than that of metallic arsenic, being only 218° C. In the British Pharmacopœia, 1898, it is said to be volatilized at a temperature not exceeding 204.4° C. When slowly sublimed it condenses in regular octahedral crystals of a sparkling luster. It may also be obtained crystallized in fine octahedral crystals by the slow-cooling of a solution of the oxide in boiling diluted hydrochloric acid.

Uses.—The official preparations of arsenic are all of them, when in sufficient concentration, violent irritants or escharotics. Taken internally in sufficient dose they are exceedingly poisonous to both man and the lower animals.

Although in large doses arsenous oxide depresses the central nervous system and also the vasomotor center, these effects have no connection with its therapeutic uses. The properties for which it is employed in practical medicine, so far as they are at all explicable, may be ascribed to its influence on the nutritive processes and the blood making organs, or to its toxic action on certain lower forms of life. Arsenic in sufficient strength is capable of destroying the vitality of all forms of living matter but appears to be especially poisonous to certain pathogenic micro-organisms. While because of its general protoplasmic toxicity it has a certain degree of power as an antibacterial, it is too poisonous to man for use as a medical germicide.

The most important physiological action of arsenic is its power of inhibiting chemical actively of the bodily cells; in other words, it lessens nitrogenous metabolism. Because of the diminished metabolism there is a tendency for the body to take on weight. This effect is especially marked in growing animals. Gies found that newly born rabbits after four weeks of arsenical treatment averaged 30 per cent. heavier than normal and that the bones were longer and thicker, and there was a proportional increase in the muscular tissue. Van den Eckhout (*C. R. S. B.*, 1921, lxxxv, 740) although he failed to obtain evidence of increased growth found that the bones become denser and stronger. Especially marked in the human being have been the nutritive changes in the skin. The mode of action of arsenic in dermatological conditions is not well understood, but in cases of chronic arsenic poisoning one of the most remarkable symptoms has been the overgrowth of the horny layer and appendages, such as the nails. After small doses of arsenic there has been demonstrated, in the lower animals, hyperemia of the bone marrow and an increase in the number of white blood corpuscles. We have, however, no knowledge of any physiological action which would explain its beneficial influence in *anemia;* the proof of its value in this condition rests entirely on clinical evidence.

The therapeutic uses of arsenic may be divided into six categories: (1) to stimulate nutrition, (2) for its effect on the blood, (3) in the treatment of certain skin diseases, (4) for its effect upon the bronchial mucous membrane, (5) for the destruction of certain pathogenic micro-organisms, and (6) as a local remedy.

In chronic wasting diseases, as in *tuberculosis* or in certain types of *neurasthenia* with malnutrition, arsenic is one of the most powerful drugs that we possess. It is one of the very few substances which really deserves the name of a general tonic since it increases both the weight and strength of the patient. It is perhaps due to its effect on nutrition that it owes its value in certain obscure nervous diseases, especially *chorea* and *migraine.* It is also sometimes a powerful remedy in various chronic types of *arthritis.*

In *chlorosis,* as shown by Seiler (*D. M. W.,* 1911, xxxvii, 1340), arsenic by itself has little if any beneficial power, but in some way greatly enhances the action of iron. In other types of *anemia,* in which iron is of little value, especially the so-called *pernicious anemia,* arsenic often produces marked amelioration. In the various types of *leukemia* it frequently produces marked temporary improvement but rarely permanent cures. It is possible that its value in these latter dyscrasias of the blood, as well as in *malarial anemia,* is due to an action upon some causative parasite. In skin diseases its use should be avoided in the acute inflammatory forms, reserving it for the more sluggish lesions, such as certain types of chronic *eczema* or *psoriasis.*

While the inorganic forms of arsenic are highly toxic to many of the hematozoa they are usually less successful in the treatment of parasitic infections of the blood than the organic forms, because the latter can be given in so much larger doses without danger to the human host. (See *Atoxyl* and *Arsphenamine.*) To what action arsenic owes its value in pulmonary diseases is entirely unknown, but there is strong clinical evidence that in chronic *bronchitis,* especially of the aged, and in *asthma* it is often of much service.

Locally arsenic is a valuable caustic for the destruction of *malignant growths.* While a universal poison, the cells of unhealthy tissue are more readily affected by it than normal structure and it is therefore used widely for the destruction of *cancers,* especially of the skin. It is an ingredient of nearly all the proprietary and semi-proprietary cancer pastes. *Plunket's caustic* consists of *Ranunculus acris* and *Ranunculus flammula,* each one ounce, bruised and mixed with sixty grains of arsenic trioxide and one hundred grains of sulphur; beaten into a paste and dried in the sun. *Arsenical paste of Frére Côme* was made by mixing water with a powder consisting of ten grains of arsenic trioxide, forty grains of red mercuric sulphide, and ten grains of powdered animal charcoal.

Febure's remedy for cancer consisted of ten grains of arsenic trioxide, dissolved in a pint of distilled water, to which were added an ounce of extract of conium, three fluidounces of solution of lead subacetate, and a fluidrachm of tincture of opium. With this the cancer was washed every morning. Febure's formula for internal exhibition was, arsenic trioxide two grains, rhubarb half an ounce, syrup of chicory q. s., distilled water sufficient to make a pint. Of this mixture, a tablespoonful, containing about the sixteenth of a grain of the oxide, was given every night and morning. The dose was gradually increased to six tablespoonfuls a day.

The *Asiatic pills,* so called, consist of arsenic trioxide and black pepper, in the proportion of 1 part of the former to 80 parts of the latter. A preparation much used on the continent of Europe is *Boudin's solution,* which is simply an aqueous solution of arsenic trioxide with the addition of wine, and is made by boiling one gramme (15.4 grains) of the oxide with one liter (2.1 pints) of distilled water till entirely dissolved, then cooling, filtering, adding enough distilled water to supply the loss, and finally mixing with one liter of white wine. Of this solution a fluidounce contains about one-quarter of a grain of arsenic trioxide.

In certain portions of Styria the peasants are in the habit of taking routinely considerable quantities of a native arsenical earth. The quantities of arsenic ingested by these so-called *arsenic eaters* is extraordinarily large; it is well established that they will imbibe amounts of more than half a grain at a dose. It has been commonly believed that lack of toxic action was due to tolerance formed through the long-continued use of the metal. Recent investigators, however, especially Schwartz (*J. P. Ex. T.,* 1922, xx, p. 181), have thrown considerable doubt on this theory and explain the lack of toxic symptoms on the ground of non-absorbability of solid arsenic. Schwartz has found that the pure arsenous oxide varies enormously in its toxicity according to the fineness of its pulverization. Cloetta (*A. E. P. P.,* 1906, liv) showed that the tolerance which can be induced in dogs is due to an irritation of the intestinal tract which impedes absorption, and Sollmann (*J. P. Ex. T.,* 1921, xviii, p. 43) was unable to produce in rats any increased resistance to arsenic. While the question can not yet be considered as fully settled, the present evidence throws grave doubt on the possibility of an acquired immunity towards this poison.

Toxicology.—Arsenic is one of the most commonly used poisons for criminal purposes. The symptoms, which generally do not appear for a period of from one-half to one hour after the ingestion of the poison, are somewhat varied in different cases. The most frequent symptoms are pain in the epigastrium, vomiting, the vomitus being occasionally bloody, more commonly not, profuse serous purging, great thirst, rapid, weak pulse, prostration and weakness, and restlessness, sometimes with delirium and convulsions. Any or all of these symptoms, however, may be lacking, death occasionally taking place with no prodromal symptoms except heart failure or stupor. Death usually occurs in the fatal cases after about twenty-four hours but may occur within an hour, or may be delayed for more than a week. At post-mortem examination there will be found evidence of inflammation of the alimentary canal and of the kidney and frequently fatty degeneration in various of the internal organs.

There can be no doubt that, when applied to any ulcerated surface, arsenic may be absorbed with fatal result; death has indeed occurred in a number of cases from the use of arsenic as an escharotic to tumors, cancerous ulcers, etc. As indicated by Blackader, absorption is less likely to follow the use of large than of small quantities, the larger amount probably killing the part to which it is applied, and thereby preventing absorption. If this dangerous caustic be used at all, it should be in accordance with these facts. Harles's observations also seem to show that when the surface is that of a chronic ulcer, either simple or malignant, absorption is less prone to occur than from a fresh wound.

The diagnosis of acute arsenical poisoning is sometimes impossible without chemical examination. For the methods of detecting arsenic in the human body, see *U. S. D.*, 19th edition, p. 202. It should be remembered that even after the post-mortem injection of arsenic, as in the use of embalming fluids, the poison may be diffused throughout the entire body.

In the *treatment* of poisoning by arsenic, it is of the utmost importance to prevent the absorption of the drug, because after the poison has once entered the system, there is probably nothing that can be done to mollify its baneful effects. The most important method of preventing absorption is the mechanical evacuation of the stomach—unless nature has already done so by vomiting—either by use of the stomach tube or a promptly acting emetic such as zinc sulphate. It is to be remembered that, especially if the arsenic has been taken in solid form, the poison may remain in the stomach for long periods, and therefore even if the patient is not seen immediately after the ingestion of the poison, the cleaning of the stomach is still advisable. The removal of the gastric contents should be folowed by evacuation of the intestines by a saline purgative such as magnesium sulphate. Chemical antidotes may be of adjuvant service and useful to prevent absorption temporarily when emetics are not immediately available, but they ought never be allowed to exclude the mechanical washing of the stomach. Among the chemical antidotes we believe the most useful is ferric hydroxide or preferably ferric hydroxide with magnesium oxide, in the moist or pulpy state. The official *Ferri Oxidum Hydratum cum Magnesii Oxido* is the best form and may be given in doses of one-half to one tumblerful. Its efficacy is, of course, greater the sooner it is administered after the ingestion of the poison; but even after delay its use will prove advantageous, so long as any portion of the poison still remains in the stomach. Ferric hydroxide acts by producing with the poison, by a transfer of oxygen from the oxide to the acid, an insoluble, and therefore inert, ferrous arsenate: $4Fe(OH)_3 + As_2O_3 = Fe_3(AsO_4)_2 + 5H_2O + Fe(OH)_2$.

It should always be freshly prepared immediately before use. (See *Ferri Hydroxidum cum Magnesii Oxido.*) Dialyzed iron and saccharated oxide of iron have been suggested as an antidote but are less efficient. The light magnesium oxide has also shown itself possessed of antidotal properties, and the U. S. has authorized the use of magnesia to precipitate the ferrous hydroxide. For the full precipitation of arsenic trioxide eighteen parts of weight of the anhydrous magnesia are required.

If the official antidote be not directly at hand, a substitute can be extemporized by adding to a solution of any soluble ferric salt some form of alkaline hydroxide.

As the result of studies on dogs, McGuigan, Atkinson and Brough (*J. A. Ph. A.*, 1923, xii, 327) have called in question the antidotal value of ferric hydroxide. Although the interpretation of their experimental results has been criticized (see Wood, *J. A. Ph. A.*, xii, 482) they have at least emphasized the importance of the evacuation of the stomach in the treatment of poisoning by arsenic.

The subsequent treatment consists in the administration of mucilaginous drinks, and the treatment of symptoms as they arise. Convalescence is generally long and distressing; usually dyspeptic symptoms mark the presence of gastro-intestinal inflammation or even ulceration, while not rarely violent neuralgic pains, with loss of power, wasting of the muscle, and other trophic changes, show that a peripheral neuritis has been produced.

Chronic arsenical poisoning has occurred either as a result of the inhalation or the swallowing of the poison. Wall paper which is colored with arsenical dyes has been shown to be capable of giving off a fine poisonous dust. Chronic arsenic poisoning has also occurred from various foodstuffs colored with arsenic—containing dyes, and a large epidemic which occurred in Manchester in the year 1900 was traced to glucose used in the manufacture of beer, originating in this case in the arsenic contaminating sulphuric acid used in making the glucose. The symptoms are so protean as to defy detailed description. The most important are *peripheral neuritis,* inflammation or overgrowth of the skin and dermal appendages, and irritation of the alimentary canal; when the poison has been inhaled to these are often added the signs of laryngitis and bronchitis.

When preparations of arsenic are given for their tonic effect only, they should be used in doses so small as not to cause any general symptoms; but when a specific action, as in *chorea,* is desired, it is proper to begin with small doses and rapidly increase them until the limit of tolerance is reached. Not rarely, such doses produce gastro-intestinal irritation, especially pain and diarrhea. To avoid this as much as possible, the remedy should be given after meals. When either gastro-intestinal irritation, puffiness under the eyes, or other of the peculiar effects of arsenic are caused, the drug should be, at least temporarily, withdrawn. The specific symptoms of *arsenicalism* are a general disposition to edema, especially of the face and eyelids, a feeling of stiffness in these parts, itching of the skin, tenderness of the mouth, loss of appetite, and uneasiness and sickness of the stomach, usually with diarrhea. The peculiar swelling produced is called *œdema arsenicalis.* When used continuously over long period of time even in doses too small to cause the customary symptoms of arsenicalism the drug may give rise to alterations in the skin. The most important of these are peculiar dryness and a tendency to the overgrowth of the keratin as shown by the formation of warts. These skin lesions may be accompanied with evidence of peripheral neuritis. (See under *Chronic arsenical poisoning.*) In some instances the internal use of arsenic causes a rash not unlike that of measles, and, as in that affection, attended with catarrhal symptoms. Sometimes salivation is produced, and occasionally the hair and nails fall off.

Dose, of arsenic trioxide, one-fortieth to one-twentieth of a grain (0.0016–0.003 Gm.).

"*Note.—The fine degree of subdivision of the powdered form of this arsenic trioxide renders it more soluble and therefore more effective than the powder previously official. This should be borne in mind in adjusting the dosage.*" *U. S.*

Off. Prep.—Liquor Acidi Arsenosi, *U. S.* (*Br.*); Liquor Potassii Arsenitis, *U. S.* (*Br.*); Liquor Auri et Arseni Bromidi, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arseni Fortiores, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arseni Mites, *N. F.*

ARSENUM.

ARSENIC

As = 74.96.

Arsenicum, *U. S.* 1870; Arsenium; Arsenic, *Fr.;* Arsen; Arsenik, *G.;* Arsenico, *It.;* *Sp.*

For a method of preparing metallic arsenium from the oxide see *U. S. D.,* 20th ed., p. 196.

Arsenium is a brittle, crystalline metal, of a steel-gray color, and possessing much brilliancy when recently broken or sublimed. Exposed to the air, its surface becomes dull and blackish. Its texture is granular, and sometimes a little scaly. Rubbed on the hands, it communicates a peculiar odor, but it is devoid of taste. Its sp. gr. is about 5.73 (5.88). When heated to about 180° C. it sublimes, giving rise to white vapors having a garlicky odor. The statement that arsenic on being heated sufficiently, passes at once into the state of vapor without fusing was disproved by experiments of Dunnington and Odger, made under direction of Mallet. They succeeded in fusing arsenic without great difficulty. An amorphous modification results from the decomposition of hydrogen arsenide by heat, the arsenic appearing as a dark brown deposit. There is also a yellow modification which is formed when arsenic vapor is strongly cooled; it resembles yellow phosphorus, as it is soluble in carbon disulphide and oxidizes in the air with luminosity.

The atomic weight of arsenium is 74.96. It forms two combinations with oxygen, arsenous and arsenic oxides, As_2O_3 and As_2O_5 respectively, to each of which the corresponding acid is known, and three with sulphur, namely, the disulphide, or realgar, As_2S_2; the trisulphide, or orpiment, As_2S_3, corresponding in composition to arsenous oxide; and the pentasulphide, As_2S_5, corresponding to arsenic oxide. (See *Arseni Trioxidum;* also *Realgar* and *Orpiment* in Part II of this work.) *Arsenic oxide* is obtained by distilling off a mixture of twelve parts of nitric and one of hydrochloric acid from four parts of arsenic trioxide, until the whole acquires the consistence of a thin syrup. The liquid is then poured into a porcelain dish, and evaporated at a moderate heat. Suddenly the arsenic oxide concretes into an opaque white mass, which should be transferred, while warm, to a well-stoppered bottle. Arsenic oxide is white, solid, deliquescent, and soluble in six parts of cold and two of boiling water. It forms several acids, corresponding to the several varieties of phosphoric acid, to which it bears a close analogy. With silver nitrate it gives a brick-red precipitate of silver arsenate.

The world's supply of arsenic and arsenic compounds at the present time is obtained chiefly from Germany, Spain, England and Canada, although in Montana and Washington considerable quantities of arsenic are being produced as a by-product in the smelting of copper ores.

The detection of arsenic in toxicological procedures is accomplished by means of the method known as Marsh's test for arsenic which depends upon the liberation of H_3As (*arsene*) and its subsequent reduction to metallic arsenic in a hard glass tube or upon a cold porcelain surface. The Marsh test has largely been replaced by the modified Gutzeit test which requires much less elaborate apparatus and may be made accurately quantitative. This is the test which is described in the U. S. P. (See *Arsenic Test*, Part III.)

Arsenic is much diffused. Besides being present in a great many minerals, it has been detected, in minute proportion, in certain soils and mineral waters; in the ashes of various plants by Stein; also in various mineral coals. Recently it has been found in minute quantities in many plants and even in the tissues of the human body.

ARSPHENAMINA

ARSPHENAMINE Arsphen. [Diaminodihydroxyarsenobenzene Hydrochloride]

"Arsphenamine [$HCl.NH_2.OH.C_6H_3As:As\text{-}C_6H_3.OH.NH_2HCl.2H_2O$] contains not less than 30 per cent. of arsenic (As), and complies with the requirements of the United States Public Health Service." *U. S.*

Salvarsan, 606, Arsaminol, Arsenobenzol, Diarsenobenzol, Arsenobillion, Arsen-phenol-amine Hydrochloride, Kharsivan, Dioxydiamidoarsenobenzol, 3.3-diamino-4.4-dihydroxy-arsenobenzene.

Arsphenamine is prepared commercially by reduction of 3-nitro-4-hydroxy-phenyl-arsenic acid, generally with sodium hydrosulphite. There are a number of modifications of the method of manufacture, the modifications usually having to do with the method of obtaining the 3-nitro-4-hydroxy-phenyl-arsenic acid.

According to Raiziss and Proskonriakoff (*Arch. of Derm. and Syph.*, 1920, ii, p. 280), the theoretical percentage of arsenic in arsphenamine is 31.6 and of nitrogen 5.89; but neither the percentage of arsenic, nor of nitrogen, nor the ratio between the two, nor the amount of oxygen absorbed by the preparation affords any criterion of the toxicity of a sample. In the twelve samples examined by them the percentage of arsenic varied from 29.3 to 31.8, and of nitrogen from 5.40 to 5.95.

H. Cousin (*J. P. C.*, 1920, xxii, 390) points out that the toxic compound which develops in arsenobenzol is an oxidation product, *amino-oxyphenyl arsenous-oxide*. This compound was stated by Ehrlich to be twenty times more toxic than fresh arsphenamine, and an assay has been suggested which will determine the preparation of water soluble arsenous oxide, which should not be more than 0.8 per cent. Administration of arsphenamine requires very careful manipulation on the part of the pharmacist or physician who prepares it for hypodermic use.

As arsphenamine appears upon the market it is a hydrochloride. Upon the addition of a very small amount of sodium hydroxide, the base itself is liberated in the form of an insoluble yellow precipitate which is not suitable for intravenous administration. The addition of a slightly larger amount of sodium hydroxide solution produces the mono-sodium salt of arsphenamine which, while entirely soluble, is still not a proper form for intravenous administration. The only proper form is the disodium salt which is produced by the addition of the amount of sodium hydroxide necessary to produce this definite compound. The United States Public Health Service has issued a circular concerning the outline and rate of administration of arsphenamine solution in which the subject is discussed from the standpoint of errors which may occur in the preparation and administration of this remedy.

Arsphenamine may vary considerably in toxicity in consequence of the presence of certain impurities derived during its manufacture. The presence of some inorganic arsenic, even when carefully made, as well as organic arsenic compounds having a greater toxicity than arsphenamine makes a biologic test imperative before the product may be placed upon the market. Sulphur compounds of arsenic are also stated to cause some of the toxic effects of certain specimens of arsphenamine. Christensen (*J. Am. C. S.*, 1921, xliii, 2202) states that the most important factor in the preparation of arsphenamine of low toxicity, is to use pure 3-amino-4-hydroxy-phenylarsonic acid as the starting point.

Arsphenamine may be conveniently identified by Gaebel's reaction in which it gives a positive diazo reaction with *alpha-naphthylamine* but no reaction with the *beta* compound.

It may be distinguished from neo-arsphenamine by adding picric acid T.S. Arsphenamine produces an immediate yellow precipitate, while neo-salvarsan produces only a slight opalescence even after long standing.

Kober (*J. P. Ex. T.*, 1925, xxv, p. 154) states that the commercial arsphenamines differ from the compound originally described by Ehrlich, in being soluble in methyl alcohol and that they are also therapeutically less efficient. He states that the reprecipitation of these commercial products by hydrochloric acid increases their potency and reduces their toxicity. He further asserts that manufacturers in their effort to produce arsphenamine or especially neo-arsphenamine of low toxicity are sacrificing curative power.

Description and Physical Properties.—"A light yellow powder. It is odorless or has a slight odor, and is hygroscopic. In the dry state or in solution it is oxidized by exposure to the air, becoming darker and more toxic. Arsphenamine is soluble in water, alcohol, and glycerin, but only very slightly soluble in chloroform and in ether.

"An aqueous solution of Arsphenamine (1 in 100) is acid to litmus paper (difference from *neoarsphenamine*). Add sodium hydroxide T.S., drop by drop, to an aqueous solution of Arsphenamine (1 in 100). A precipitate is formed (difference from *neoarsphenamine*), which readily dissolves in an excess of the sodium hydroxide. Sodium carbonate T.S. or solution of sodium bicarbonate also produces a precipitate, but this is insoluble in an excess of the reagent. An aqueous solution of Arsphenamine (1 in 100) is precipitated by mercuric potassium iodide T.S. (difference from *neoarsphenamine*). An aqueous solution of Arsphenamine (1 in 100) is unaffected by the addition of diluted hydrochloric acid, diluted nitric acid, or by acetic acid even after heating (difference from *neoarsphenamine*). With an excess of hydrochloric acid a precipitate is formed. Diluted sulphuric acid or solutions of alkali sulphates immediately produce a precipitate. The addition of 2 drops of freshly prepared ferric chloride T.S. to 5 cc. of an aqueous solution of Arsphenamine (1 in 1000) produces a brownish, violet tinted color, rapidly changing to deep red. Add 3 cc. of silver nitrate T.S. to 5 cc. of an aqueous solution of Arsphenamine (1 in 100). A red color is produced, but no precipitate is formed even after standing at ordinary room temperature for ten minutes (difference from *neoarsphenamine*). When a 6 cc. portion of silver nitrate T.S. is added to the same volume of solution, a precipitate is immediately formed which blackens on heating. On now adding 5 cc. of nitric acid, and again heating, the precipitate becomes white and dissolves in ammonia water. The solution resulting from the following assay yields with hydrogen sulphide a yellow precipitate, soluble in ammonium carbonate T.S.

"**Assay.**—Place about 0.2 Gm. of Arsphenamine, accurately weighed, in a glass-stoppered, 200 to 300 cc., flask. Add 1 Gm. of finely powdered potassium permanganate and 5 cc. of diluted sulphuric acid, and allow to stand for ten minutes, rotating the contents of the flask during this time to insure thorough mixing. Add 10 cc. of concentrated sulphuric acid in portions of about 2 cc., rotating the flask after each addition. When the reaction has ceased, add sufficient hydrogen dioxide T.S. to dissolve completely the brown precipitate (about 5 to 7 cc.). Toward the end of the reaction the hydrogen dioxide is to be added drop by drop to avoid any great excess. Dilute with 25 cc. of distilled water, and boil gently over an asbestos wire gauze for from fifteen to twenty minutes, or until the excess of hydrogen dioxide is expelled. Dilute with 50 cc. of distilled water, and add tenth-normal potassium permanganate until the liquid is faintly pink, then discharge the pink color by the addition of a drop of tenth-normal oxalic acid. Cool the solution, add 2.5 Gm. of potassium iodide, stopper the flask tightly, and allow it to stand in a cool, dark place for one hour. Then titrate the liberated iodine with tenth-normal sodium thiosulphate without the use of starch indicator. Make a blank test with the same quantities of the reagents, and correct the assay for the volume of tenth-normal sodium thiosulphate used in the blank. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.003748 Gm. of As.

"Preserve in sealed containers of colorless glass, from which the air has been excluded either by the production of a vacuum or by displacement with a non-oxidizing gas." *U. S.*

Uses.—This compound was introduced into medicine in 1910 as the result of a long series of experiments by Ehrlich, undertaken with the idea of preparing a substance which should be non-toxic for higher animals, especially man, but poisonous to certain infective parasites.

Arsenic, when in the pentavalent state, is relatively non-poisonous to either unicellular or more highly developed micro-organisms. Therefore, while pentavalent arsenicals are not injurious to human beings, they are likewise not destructive to pathogenic micro-organisms. The destructive effect of arsenic upon infecting parasites—*i.e.*, its therapeutic activity—depends upon the decomposition of the molecule, probably by oxidation, with the liberation of the arsenic in a trivalent, or active, state. Unfortunately, the human tissues have this same power of oxidizing arsphenamine so that it is toxic to man as well as micro-organisms. Certain types of organisms, however, appear to decompose this compound more rapidly; to them it is, therefore, more poisonous than to their human host and for this reason can be used to destroy these parasites in the body. The only group of micro-organisms which have been definitely shown to be peculiarly susceptible to arsphenamine are the protozoa which are today grouped together under the genus *Spirochæta*. To this genus belong the germs giving rise to relapsing fever, syphilis, yaws, rat-bite fever, Vincent's angina, yellow fever, etc. By far the most important of this group of infections is *syphilis*.

Although arsphenamine has failed to realize the hopes of its inventor, who had dreams of a compound so innocuous to man that a single dose might be given large enough to destroy all the parasites in the body and thus cure at once the infection, there can be no doubt of its value in syphilitic disease. It is probable that if used during the primary stage of the infection a considerable proportion of cases can be rapidly and permanently cured. In the secondary stage its effects are less certain and most modern syphilographers not only recommend repeated doses of arsphenamine but also the use of mercury as a succedaneum. One great benefit from arsphenamine in this stage is that it causes a rapid disappearance of the gross lesions of the infection thereby not only lessening the liability of permanent sequela of the diseased person, but also rendering him less liable to spread the infection. If the patient is not seen until the establishment of the tertiary lesions, while arsphenamine should usually be employed in the hope of preventing further progress of the disease, it must be remembered that it cannot exercise any beneficial action on the sclerotic degenerations which have been the result of the syphilitic fires and, therefore, it may fail to produce any great amelioration of symptoms.

Arsphenamine has been used in an experimental way, at least, in practically all protozoal infections and even in a number of bacterial diseases. An excellent résumé of its effects in non-syphilitic diseases, with numerous references to the literature, has been made by Reasoner and Nichols (*J. A. M. A.*, 1920, lxxv, p. 645). In *relapsing fever* its effects are very striking; according to Manson and Thornton (*Journal of the Royal Army Medical Corps,* August, 1919), the most satisfactory results are obtained from it if it is given during the febrile period. A number of authors have reported very favorable results in *Vincent's angina;* Reckford (*J. A. M. A.*, 1920) recommends the local application of a 10 per cent. solution of arsphenamine, in glycerin, directly to the lesions, by means of a cotton swab, twice daily. This solution should be well rubbed in. If the lesions have become very extensive it may be advisable to also give the drug intravenously. In the tropical disease known as *yaws* or *frambesia,* arsphenamine seems to realize the ideal of Ehrlich of a *therapia sterilisans magna,* an immediate cure from a single dose. Noguchi (*J. Ex. M.*, 1919, xxix, and xxx) has shown that *yellow fever* is due to an organism belonging to the group of spirochetes. While some authors have reported favorably on the use of arsphenamine in this infection, its value is not firmly established. All of the foregoing are spirochete infections, but the use of arsphenamine has not been limited to this group of diseases. Allied to the spirochetes are the trypanosomes, one of which gives rise to the almost universally fatal *African sleeping sickness,* and others to various diseases of lower animals. While laboratory trypanosomiasis can be almost absolutely controlled by arsphenamine, the results of its use in human infection have been far from satisfactory. In many cases it has exercised an apparently beneficial action but its effects do not seem to be superior to other arsenicals, such as atoxyl. In *malarial fevers* it is apparently of some value in quartan and tertian fevers, which have been proved refractory to quinine, but here again it is very questionable whether it is superior to older arsenicals. Carr and Chandler (*J. A. M. A.*, 1920, lxxiv, May 22) have reported beneficial effects in amebic *dysentery* and the allied condition known as *trench-diarrhea* or *giardiasis.* Allison (*J. M. R.*, 1918, xxviii, p. 55) states that arsphenamine has a powerful germicidal effect on streptococci and has achieved favorable results from its use in experimental *septicemia.* Evidence of its clinical use in this disease is as yet lacking. Perrin (*Paris Med.*, Dec. 10, 1921) and Molnar (*W. K. W.*, 1921, xxxiv, p. 255) both report good results from it in the treatment of *gangrene of the lungs.*

Toxic Effects.—Arsphenamine has produced, in a large number of cases, unpleasant and even alarming symptoms and in a few, fatal results. It is difficult to determine accurately the number of deaths attributed to the drug. Guy (*J. A. M. A.,* 1919, lxxiii, p. 901) in 25,000 injections, done under careful technic, had two deaths. Corlett (*J. A. M. A.*, 1913, lxi,) from a careful review of the literature during the first three years after the introduction of this remedy, estimated the mortality from its use as one death in 18,000 injections. The toxic manifestations may be divided into five groups: (1) those due to acute poisonous effects of arsphenamine itself; (2) those resembling arsenic poisoning and probably due to too rapid oxidation of the compound in the body; (3) those due to idiosyncrasies, either inherent or acquired, of the patient; (4) those due to impurities in commercial samples of the drug; (5) those due to errors of technique of its administration.

Smith (*J. P. Ex. T.*, 1920, xv, p. 279) has shown that when rapidly injected into a vein, arsphenamine causes a violent contraction of the pulmonary arteries with an accompanying rise in the pulmonary and fall in the general blood pressure. If the dose has been large enough, this is followed by dilation of the right heart and death from circulatory collapse. These effects are produced only when the drug is injected too rapidly or in too concentrated solution. Accidents of this type from the clinical use of the drug are comparatively rare.

Two types of toxic cases have been reported which suggest arsenical poisoning; these have shown either neuritis, especially of the optic nerve, or signs of degeneration of the liver. Lynch and Hoge (*J. A. M. A.*, 1919, lxxiii, p. 1687) reported three cases of toxic jaundice, one of which ended fatally, the symptoms of which suggested acute yellow atrophy of the liver. Several similar cases have been reported by Stümpke (*Med. Klin.*, 1922, xviii, 295) and others. It has been suggested that both these neuritic and hepatitic accidents are the result of the syphilis rather than of the arsphenamine, but it seems impossible to explain all of them on that basis. They are, however, comparatively infrequent. The most common type of unpleasant reaction is characterized by chill followed with fever, associated with nausea and sometimes severe vomiting, the whole lasting from two hours to two days and often followed by herpetic eruptions. Another type of reaction, which is commonly called "nitritoid crisis" consists of sensation of choking, redness of the face and cardio-respiratory embarrassment. These groups of reactions have been variously attributed to imperfect technic, impurities in the drug, improperly distilled water, etc. The observations of Busman (*J. A. M. A.*, 1921, lxxvi, p. 1302) indicate very strongly, however, that in many instances at least they are to be classed among the anaphylactoid reactions and are more likely to occur after repeated than after the first injection. Milian (*Paris Med.*, Feb. 2, 1918) has found epinephrine of great value both as a preventive and curative of the nitritoid crisis.

Administration.—Arsphenamine has been employed by intravenous, intramuscular and intrarectal injection. Most authorities, however, give preference to the intravenous route. The following important points in the technic of this injection must be carefully observed: The ampules of the drug should be floated in alcohol for the purpose of detecting any flaw in the containers. The contents are then dissolved in sterile, *freshly distilled* water and a 15 per cent. solution of sodium hydroxide added drop by drop until the precipitate which at first forms, is redissolved and one or two drops of the soda solution are added in excess. This solution is then diluted with further portions of the freshly distilled water. The concentration of solution which is to be recommended is a matter of considerable difference of opinion. In general, the tendency seems to be, for intravenous injection, to employ the drug in strengths of about 0.5 per cent. The solution, which should be at body temperature, must be injected very slowly.

Dose, of asphenamine, is from three to nine grains (0.2–0.6 Gm.) which may be cautiously increased, usually given at intervals of a week.

ASAFŒTIDA. U. S. (Br.)

ASAFETIDA Asafœt. [Gum Asafetida]

"Asafetida is gum-resin obtained by incising the living rhizomes and roots of *Ferula Asafœtida* Linné and *Ferula fœtida* Regel and of other species of *Ferula* (Fam. *Umbelliferæ*). Asafetida yields not less than 50 per cent. of alcohol-soluble extractive and not more than 15 per cent. of acid insoluble ash." *U. S.* "Asafetida is an oleo-gum-resin obtained by incision from the root of Ferula fœtida, *Regel,* and probably other species of Ferula." *Br.*

Asafetida, *Br.*; Stercus Diaboli, Cibus Deorum; Gummiresina Asafœtida; Asa fœtida, Asse-fétide, Assafœtida, *Fr.*; Asa fœtida, *P. G.*; Asant, Stinkasant, Teufelsdreck, *G.*; Assa fetida, *It.*; Asafetida, *Sp.*; Ungoozeh, *Pers.*; Hilteet, *Arab.*; Hing, *India;* Angusa-kema, *Afgh.*

Ferula Asafœtida was first described from actual observation by H. Falconer, who found it near Kashmir, and it has long been successfully cultivated in the Edinburgh Botanical Gardens. It is distinguished from allied plants by the greater height of the stem (6 to 10 feet), and by the numerous stem leaves furnished with wide sheathing petioles. The flowers are pale yellow, and the oval fruit thin, flat, foliaceous, and reddish brown, with pronounced vittæ. It yields a milky juice having a powerful odor of asafetida.

Ferula fœtida is a coarse umbelliferous plant, growing from five to seven feet high, with a large fleshy root, the crown of which is covered with coarse bristly fibers, and gives origin to large bipinnate radical leaves and a nearly naked stem which has only a few bipinnate leaves without wide sheathing petioles, and ends at the top in very numerous umbels. The flat-winged fruits have the vittæ almost obsolete. This plant was first discovered in the sandy desert near the sea of Aral, by Lehmann, in 1844. Bunge found it in Persia about twenty years later. It would seem to be native all through Afghanistan.

It is possible that asafetida is obtained from other species of *Ferula,* yet the bulk of the drug probably comes from the official plants. Among the other plants yielding asafetida is *Ferula Narthex* Boiss. While this is disputed by Aitchison yet it appears that it is the source of the gum-resin obtained from certain portions of Afghanistan. Tschirch describes this plant with illustrations in *S. W. P.,* 1910, p. 289. E. M. Holmes's discussion of the asafetida plants (*P. J.,* ser. iii, xix, 1888–1889) still remains one of our chief sources of information on the subject. (See also article on the sources of the fetid gum-resins by James Small, *P. J.,* 1913, vol. xc, p. 287.) *Ferula Jæschkeana* Vatke, which has been believed to be the source of asafetida, according to E. M. Holmes, has, at least in its dried state, not the slightest odor of asafetida, and yields a strongly celery-scented juice. (*P. J.,* 1894, xxv.)

The asafetida plants are indigenous to Western Afghanistan and Eastern Persia. In 1687 the collection of asafetida was witnessed by Kaempfer, whose description of the method is very similar to that given by J. E. T. Aitchison in 1884. According to Aitchison, the high plains of Afghanistan, two to four thousand feet above the sea, are arid and bare in winter, but in the early summer are covered with a thick growth of *Ferula fœtida, Dorema ammoniacum,* and *Ferula galbaniflua.* The great cabbage-like heads of the asafetida plant, representing the primary stage of the flower heads covered over by the stipules of its leaves, are eaten raw by the natives as a sort of green. In June the asafetida is obtained. The root-stock is first laid bare to the depth of a couple of inches, those plants only which have not reached their flower-bearing stage being selected. A slice is then taken from the top of the root-stock, which is immediately covered with twigs and clay, forming a sort of dome, with an opening towards the north, so that the sun cannot get at the exposed root. About five or six weeks later, a thick, gummy, not milky, reddish substance found upon the exposed surface of the root in more or less irregular lumps is scraped off with a piece of iron hoop or removed with a slice of the root and at once placed in a leather bag. The product of many plants is mixed and permitted to harden in the sun. Most of the drug is now gathered in Eastern Persia and Western Afghanistan. It is conveyed to Herat and Kandahar from whence it enters commerce. The present supply of this drug to America comes from London. It sometimes comes in mats, but more frequently in cases, the former containing eighty or ninety pounds, the latter from two hundred to four hundred pounds. Asafetida is sometimes also imported in casks.

The fruit of the asafetida is said to be sent to India, where it is highly esteemed as a medicine.

Properties.—As usually found in commerce, asafetida is in irregular masses, soft when not long exposed, of a yellowish or reddish-brown color externally, exhibiting when broken an irregular, whitish, somewhat shining surface, which soon becomes red on exposure, and ultimately passes into a dull yellowish-brown. This change of color is characteristic of asafetida, and is ascribed to the influence of air and light upon its resinous ingredient. The masses appear as if composed of distinct portions agglutinated together, sometimes of white, almost pearly tears, embedded in a darker, softer, and more fetid paste. Occasionally the tears are separate, though rarely in the commerce of this country. They are roundish, oval, or irregular, and generally flattened, from the size of a pea to that of a large almond, sometimes larger, yellowish or brownish externally and white within, and not unlike ammoniac tears, for which they might be mistaken except for their odor, which, however, is weaker than that of the masses.

The effect of time and exposure is to render it more hard and brittle, and to diminish the intensity of its odor and taste, particularly the former. Asafetida softens by heat without melting, and is difficult of pulverization. Its sp. gr. is 1.327. (Berzelius.) It is inflammable, burning with a clear, lively flame.

Description and Physical Properties.—"A soft mass, sometimes almost semi-liquid, or irregular, more or less pliable masses composed of agglutinated tears imbedded in a yellowish-brown or dark brown matrix, or loose ovoid tears, from 1 to 4 cm. in diameter, the surface sometimes containing streaks of violet, yellowish-red or brownish-red and with a few vegetable fragments; becoming hard and occasionally brittle on drying; surface of the freshly fractured tears milky-white and opaque, changing gradually on exposure to air or light to a pinkish or reddish-purple or even reddish-brown; on moistening with water the tears become milky-white; odor persistent, alliaceous; taste bitter alliaceous and acrid.

"Asafetida, triturated with water, yields a milk-white emulsion, which becomes yellowish on the addition of alkalies. A reddish-brown solution is formed when a fragment of Asafetida is heated with sulphuric acid. Greatly dilute this solution with water, filter, and render alkaline: the solution acquires a blue fluorescence. A few drops of phloroglucinol T.S. and of hydrochloric acid added to 10 cc. of the alcoholic filtrate obtained in the assay, produces a cherry-red color.

"A few drops of ferric chloride T.S., added to 5 cc. of the alcoholic filtrate, obtained in the assay, produces an olive-green color (*most foreign resins*). Hydrochloric acid, added to 10 cc. of the alcoholic filtrate from the assay until a faint turbidity results, produces a bluish-green color which fades on standing (*galbanum*). Asafetida does not show the presence of rosin, page 457. Mix 2 cc. of an emulsion, prepared as directed under *Emulsum Asafœtidæ,* with 5 cc. of water and add 5 cc. of sodium hypobromite T.S. to form a separate layer: a red color is not produced (*ammoniac*).

"**Assay.**—Place about 10 Gm. of Asafetida in a tared, 250 cc. Erlenmeyer flask, weigh accurately, add 100 cc. of alcohol, and having connected the flask with an upright condenser, boil the mixture in the flask during one hour or until the drug is completely disintegrated. Filter and wash the flask and filter with several small portions of boiling alcohol until the washings no longer produce a cloudiness when dropped into water. Collect the mixed alcoholic solutions, using an aliquot part (50 per cent.) for the completion of the assay, and reserve the remainder for the tests given above. Evaporate the aliquot part in a suitable tared container and dry to constant weight. The anhydrous alcohol-soluble extractive of the aliquot portion equals not less than 25 per cent. of the weight of Asafetida taken." *U. S.*

"Rounded or flattened tears from twelve to twenty-five millimetres in diameter, or masses containing tears, greyish-white to dull yellow, darkening on keeping. Fresh tears usually tough at ordinary temperatures, hard when cold. Internally yellowish and translucent, or milk-white and opaque; freshly exposed surfaces often slowly become pink, then red, and finally reddish-brown. Odor strong, alliaceous and persistent; taste bitter, acrid and alliaceous. When triturated with *water* Asafetida forms a white emulsion. When the freshly fractured surface of a tear is touched with *sulphuric acid,* a bright red or brownish-red color is produced. The tincture obtained by macerating 0.5 gramme of Asafetida with 10 millilitres of *alcohol* (90 per cent.), filtered, made alkaline with *strong solution of ammonia,* and then largely diluted with *alcohol* (90 per cent.), does not exhibit a blue fluorescence (distinction from and absence of galbanum). Contains not more than 50 per cent. of matter insoluble in *alcohol* (90 per cent.). Ash not more than 15 per cent." *Br.*

Much commercial asafetida of prime appearance fails to come up to the requirements of the U. S. Pharmacopœia. Large quantities are said to be returned from the United States ports to Europe on account of their failure to contain the proper percentage of material soluble in alcohol. Macerated in water it produces a turbid red solution, and triturated with that fluid it gives a white or pinkish, milky emulsion of considerable permanence. Touched with nitric acid (sp. gr. 1.2) the tear becomes of a evanescent green color. O. Tunmann gives the following micro-chemical test for asafetida; sublime 0.05 gramme of powdered asafetida to obtain ferulic acid. The latter is identified by the development of a vanillin odor when warmed with a few drops of potassium permanganate solution.

Constituents.—Asafetida consists of 40 to 65 per cent. of resin, 20 to 30 of gum, 10 to 17 of volatile oil, and 2 to 15 of ash. Tschirch (*Harze und Harzebehälter,* 1900, p. 234) states that the resin is the *ferulaic ester of asaresinotannol* containing some free *ferulic acid,* and some vanilein, which latter is a produce of the oxidation of the ferulic acid. J. Polásek (*A. Pharm.,* 1897, ccxxxv, 125) found in the pure tears 61.40 per cent. of resin soluble in ether, which is regarded by him to be the ferulaic acid ester of asaresino-tannol; 0.60 per cent. of resin insoluble in ether, regarded to be free asaresinotannol; 25.10 per cent. of gum; 6.70 per cent. of volatile oil; 0.06 per cent. of vanillin; 1.28 per cent. of free *ferulaic* (*ferulic*) *acid;* 2.36 per cent. moisture; 2.50 per cent. impurities. *Asaresino-tannol* has the composition corresponding to the formula $C_{24}H_{35}O_5$. Umbelliferone was obtained as a secondary product of hydrolysis with sulphuric acid from asaresinotannol, and was also obtained from ferulic acid synthetically, guaiacol being produced at the same time. By nitrification of asaresino-tannol, picric acid is produced. (*A. Pharm.,* 1897, ccxxxv, 125, 132.) Hlasiwetz, 1866, and Barth (*Ann. Ch. Ph.,* cxxviii, 61), obtained *ferulic acid,* $C_{10}H_{10}O_4$, crystallizing in iridescent needles, by precipitating the alcoholic solution with lead acetate, washing the precipitate, and decomposing it with diluted sulphuric acid. Fused with potassium hydroxide, ferulic acid yields oxalic acid and carbon dioxide, several acids of the fatty series, and protocatechuic acids of the fatty series, and protocatechuic acid. The resin itself treated in like manner, after it has been freed from gum, yields resorcinol.

The odor of the gum-resin depends on the *volatile oil,* which may be procured by distillation with water or alcohol. It is lighter than water, colorless when first distilled, but becomes yellow with age, of an exceedingly offensive odor, and of a taste at first flat, but afterwards bitter and acrid. Hlasiwetz (*Ann. Ch. Ph.,* lxxi, 23) considers it a mixture, in variable proportions, of the sulphide and disulphide of a compound radical consisting of carbon and hydrogen (C_6H_{11}). Allyl persulphide, which is sublimed when oil of mustard is heated with potassium persulphide, is said by Wertheim to have an extremely intense odor of asafetida, a fact which justifies the supposition that it may be identical with the oil of that gum-resin. Semmler, in a later study (*B. Chem. G.,* xxiii, p. 3530, and xxiv, p. 78), states that it contains pinene and a second terpene in smaller amount, and in the higher boiling fractions, a disulphide, $C_7H_{14}S_2$; a disulphide, $C_{11}H_{20}S_2$; a body $(C_{10}H_{16}O)_n$; a disulphide, $C_8H_{18}S_2$; and $C_{10}H_{18}S_2$. Although the presence of umbelliferone has been reported by some authorities, it probably does not occur, naturally, in the drug but is easily formed by the action of hydrochloric or sulphuric acids on the ferulic acid of the resin.

Impurities and Adulterations.—Asafetida is often purposely adulterated; it frequently comes of inferior quality, and mixed with various impurities, such as sand and stones. It is generally conceded to be the worst adulterated drug upon the market. A factitious substance, made of garlic juice and white pitch with a little asafetida, has occurred in commerce. It is said to be sometimes mixed with wheat or barley flour or with earthy matters at the place of its production, the impurities sometimes exceeding 30 per cent. The gum-resin imported from the Persian Gulf and Bombay is largely adulterated with sand and other gum-resins. Patch (*Proc. A. Ph. A.,* 1905, p. 183) has found asafetida on the market which yielded 62, 62.5 and 73.3, respectively, of material insoluble in alcohol. The Belgian inspectors reported in 1905 finding as high as 75 per cent. of ash in some commercial samples. In spite of these figures Gehe & Co. report that the quality of the available asafetida has materially improved.

J. U. Lloyd, after examining a large number of samples of commercial asafetida, was convinced that it is impracticable to obtain the crude drug of the official standard, gypsum, carbonates, and other insoluble matters being present in large amounts. He did not find white turpentine or rosin in any of the samples; exhausting asafetida with alcohol and evaporating the alcohol carefully, he obtained an extract for which he proposed the name of *Purified Asafetida.* (*Ph. Rev.,* 1896.) H. William Jones (*Y. B. P.,* 1900, 503) purifies asafetida by pouring a concentrated alcoholic solution into water slightly acidulated with hydrochloric acid, collecting the precipitate, washing and drying it.

A few years ago a new method was proposed for the detection of adulteration in asafetida which depended upon the combining power of the purified resins with the lead in a standard solution of lead acetate. This method, the details of which will be found in *J. A. C.,* vol. ii, p. 86, is called the lead number. The method has not been found sufficiently reliable to warrant its inclusion among the official tests; Rippetoe (*A. J. P.,* 1913, p. 199) finds it to be subject to fluctuations as yet unexplained. Harrison and Self (*Ph. J.,* 1912, 205) present what they term a preliminary report on the investigation of this drug for the purpose of suggesting an improved method of standardization. They claim that there is good reason to believe that the virtues of asafetida are due not only to the volatile oil, but to the sulphur containing constituents of the volatile oil. They give abundant analytical data in support of their views and as showing how adulterations with other gum-resins may be readily detected. They state that if a gum-resin contains not less than 1.5 per cent. of sulphur it may unhesitatingly be pronounced as genuine asafetida. Bernegau and E'we propose a method for estimating asafetida in commercial tablets, pills, etc., depending upon extractions with hot chloroform under specified conditions. (*Proc. P. Ph. A.*, 1912, p. 305.)

Asafetida is sometimes kept in a powdered state, but this is objectionable, as the drug is thus necessarily weakened by the loss of volatile oil, and is more liable to adulteration. Powdered asafetida is best prepared by drying the crude drug over freshly burnt lime and then comminuting it at a low temperature.

Uses.—Asafetida appears to have been used in the East from the earliest times of which we have any record and notwithstanding its repulsive odor is at present much used in India and Persia as a condiment. In small amounts it gives the distinctive aroma to the type of sauce known as "Worcestershire." It is by some believed to have been imported into Europe as far back as the second century, but the earliest undoubted reference to it in European medical literature is in the twelfth century. Although it is without doubt capable of being absorbed from the intestinal tract in greater or lesser quantities there is no convincing evidence that after its absorption it exercises any distinct effect upon the system. Pidoux took a half an ounce at one dose without perceptible effects not ascribable to its local action. It has in the past been supposed to exercise a stimulant action upon the cerebral centers. The evidence in favor of this view is based upon the beneficial effects which have followed its administration in *hysteria* and conditions of *nervous exhaustion.* Its effects in these conditions, however, are entirely explicable on the grounds of the psychical impression made by taking a drug of so powerful odor and taste. On the other hand as a local stimulant to the mucous membranes, especially of the alimentary tract, it is a remedy of much value, thus it is a favorite carminative in the treatment of *flatulent colic;* it is often useful as an addition to laxative drugs in various types of *constipation.* There is evidence that after its absorption the volatile oil of asafetida is eliminated through the lungs and consequently it has been used as a stimulating expectorant in various forms of *bronchitis,* in *whooping cough,* and in *asthma.*

When used internally in adults it is generally preferable to administer it in the form of a pill on account of its disagreeable taste. In *colic,* especially in infants, it is often administered per rectum. For this purpose the emulsion of asafetida in the proportion of from one-half to one fluidounce to a pint of water may be employed.

J. W. Wood prepared *syrup of asafetida* by dissolving 256 grains of asafetida in two fluidounces of glycerin by the aid of a gentle heat and straining. He then dissolved 15 drops of oil of wintergreen, 5 drops of oil of cinnamon and 1 drop of oil of bitter almond in 3 fluidrachms of 95 per cent. alcohol, and added to it the above, together with enough syrup to make one pint. Each teaspoonful represents two grains of asafetida. (*A. J. P.*, 1874.)

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Emulsum Asafœtidæ, *U. S.;* Pilula Aloes et Asafœtidæ, *Br., N. F.;* Pilulæ Asafœtidæ, *U. S.;* Spiritus Ammoniæ Fetidus, *Br.;* Tinctura Asafœtidæ, *U. S., Br.*

ASARUM. N. F.

ASARUM Asar. [Canada Snake-root, Wild Ginger]

"Asarum consists of the dried rhizome of and roots of *Asarum canadense* Linné (Fam. *Aristolochiaceæ*). Asarum contains not more than 5 per cent. of foreign organic matter." *N. F.*

Radix Asari; Asaret de Canade, *Fr.;* Canadische Haselwurzel; Schlangenwurzel, *G.*

This plant is a low, perennial herb having an underground aromatic-bitter rhizome and root system. The rhizome bears several long petioled, radical, reniform leaves and also bell-shaped flowers that have a brownish-purple calyx.

Description and Physical Properties.—"*Unground Asarum.*—Rhizome horizontal, 5 to 17 cm. long, 2 to 4 mm. thick, occasionally branched, two edged when young, quadrangular when older, finely striate, more or less twisted; nodes enlarged with irregular scars from petioles and remains of pedicels; internodes with annular scars from scales; dark purplish brown externally; fracture short, internally whitish, starchy or resinous; roots few, 5 to 7 cm. long up to 1 mm. thick. Odor ginger-like or recalling serpentaria, non-irritating upon heating; taste pungent and slightly bitter.

"*Structure.*—Rhizome with thick bark of parenchyma and numerous oil cells; wood with about 12 fibrovascular bundles separated by broad medullary rays, and a large pith; parenchyma cells more or less filled with starch grains. Root with from four to six radial fibrovascular bundles.

"*Powdered Asarum.*—Starch grains simple or 2- to 4-compound, the individual grains 0.003 to 0.020 mm. in diameter; tracheæ with scalariform or reticulate thickenings, a few spiral; brownish fragments of epidermal tissue, parenchyma and numerous oil cells." *N. F.*

Asarum owes its activity to an acrid bitter resin and a volatile oil. According to Petersen, the chief ingredient of the latter is the methyl ether of eugenol, a compound which has been made synthetically but was not previously found in nature. According to the researches of Power and Lees (*Tr. Chem. Soc.*, 1902), the oil of *Asarum canadense* contains the following substances: a phenol, $C_9H_{12}O_2$; pinene, apparently a mixture of the d- and l- forms; d-linalool, l-borneol, l-terpineol, geraniol, eugenol-methyl-ether, a blue oil, of undetermined composition, consisting of oxygenated substances of alcoholic nature; a lactone, $C_{14}H_{20}O_2$, palmitic acid, acetic acid, and a mixture of fatty acids intermediate between acetic and palmitic acids.

Under the name of *asaron,* or *asarin,* a stereopten from the *A. Europeum* has been recommended as an antiseptic and tonic. *A.*

arifolium Michx. contains a volatile oil having a sassafras odor, sp. gr. 1.0585; see also *Schim. Rep.*, 1902, p. 12; also *Proc. Alabama Pharm. Assoc.*, 1910, 56–58.

Uses.—The medicinal properties of this drug are those of a feeble aromatic. From a half to one drachm (2–3.9 Gm.) may be used. It is employed as an aromatic adjuvant to tonic mixtures and infusions.

The *Asarum Europæum,* known popularly as *asarabacca* or *wild nard,* was formerly used for its local irritant action especially as an errhine and as a sialogogue. In doses of one-half to one drachm it acts as an emetic.

Off. Prep.—Syrupus Asari Compositus, *N. F.*

ASCLEPIAS. N. F.

ASCLEPIAS Asclep. [Pleurisy Root]

" Asclepias is the dried root of the *Asclepias tuberosa* Linné (Fam. *Asclepiadaceæ*). Asclepias contains not more than 5 per cent. of foreign organic matter." *N. F.*

Orange Milkweed Root; Butterfly Weed Root; Pleurisy Root; Wind Root; Orange Swallowwort; Racine d'Asclepiade tubereuse, *Fr.;* Knollige Schwalbenwurzel, *G.*

Asclepias tuberosa is a perennial herb with roughish-hairy stems branching at a summit and bearing umbels of orange flowers in a terminal corymb or scattered in racemes along the branches. The fruit consists of acuminate follicles, each containing numerous comose seeds. It grows from Ontario and Minnesota southward and southwestward. It is the only species of asclepias that is devoid of milk juice.

Besides the official species, various other members of this genus have been used in medicine. The *Asclepias Syriaca* L. (*A. Cornuti* Decaisne)—*milkweed* or *silkweed*—and the *A. incarnata* L. were formerly recognized by the U. S. Pharmacopœia (1840). The *A. Galoides* has been reported as the cause of death of horses and sheep by Marsh (*A. J. P.*, 1921, p. 274).

For microscopical differentiation for the various species of Asclepias see article by Fanchon Hart, *Year Book of American Pharm. Assoc.*, 1916, vol. v. For further description of unofficial species see *U. S. D.*, 19th edition, p. 1400.

Description and Physical Properties.—"*Unground Asclepias.* Irregularly fusiform; when entire 10 to 20 cm. long, 0.5 to 5 cm. thick, occasionally branched, usually cut or in broken pieces of variable size; externally pale orange-brown, or grayish brown; annulate above, the surface roughened by numerous intersecting fine intersecting grooves; bark thin; fracture tough, the broken surface granular and white, with pale yellow wood bundles and white medullary rays. Odor slight; taste bitterish and disagreeable, somewhat acrid.

"*Powdered Asclepias.* — Yellowish - brown; starch grains numerous, simple or 2- to 4-compound, individual grains up to 0.015 mm. in diameter, somewhat spherical or truncate and often with a cleft at center; calcium oxalate in rosettes up to 0.050 mm. in diameter parenchyma abundant, many of the cells with starch grains; stone cells up to 0.075 mm. in diameter, with strongly lignified thick walls, the latter with simple or branching pores; tracheæ with reticulate markings, occasionally bordered pores; fibers few, lignified and mostly with simple pores." *N. F.*

It contains a glucosidal principle, *asclepiadin,* which occurs as an amorphous body, is soluble in ether, alcohol and hot water. It also contains several resins and a trace of volatile oil.

Quackenbush (*A. J. P.*, 1889) isolated from both *A. tuberosa* and *A. Syriaca* a crystalline principle which he believed to be glucosidal. Whether this is the same substance as *asclepiadin,* previously found in *A. incarnata* by Gram (*A. E. P. P.*, 1884, xix, 319) is uncertain.

Uses.—In full doses asclepias is emetic and cathartic. Probably through its nauseating action in smaller doses it acts as a diaphoretic and expectorant. With the group of physicians who call themselves eclectics it was a popular remedy in the treatment of *pneumonia, bronchitis* and other pulmonary complaints. It was also employed in catarrhal *diarrheas,* in acute *rheumatism* and to promote the eruption in exanthematous *fevers.* It is probable that such therapeutic virtues as it may possess depends very largely upon its nauseating effect.

Dose, twenty to sixty grains (1.3–4 Gm.).

Off. Prep.—Fluidextractum Asclepiadis, *N. F.*

ASPIDIUM. U. S. (Br.)

ASPIDIUM [Male Fern]

" Aspidium consists of the rhizome and stipes of *Dryopteris Filix-mas* (Linné), Schott (Fam. *Dryopteris Filix-mas* (Linné), Schott (Fam. *Polypodiaceæ*). Aspidium yields not less than 6.5 per cent. of oleoresin, and not more than 3 per cent. of acid-insoluble ash. Only such portions as have retained their internal green color should be used." *U. S.* " Male Fern is the rhizome of Dryopteris Filix-mas, *Schott.* Collected late in the autumn, divested of its roots, leaves, and dead portions, and carefully dried. Should not be kept more than a year." *Br.*

Filix Mas, *Br.*, and *U. S.*, 1870; Stipites aspidii, Filicis Rhizoma, Male Shield Fern, Knotty or Sweet Brake, Basket Fern, Bear's-paw Root; Fougère Mâle, *Fr.;* Rhizoma Filicis Maris, *P. G.;* Wurmfarnwurzel, Waldfarnwurzel, Johanniswurzel, Farnwurzel, *G.;* Felce Maschio, *It.;* Helecho macho (Rhizoma de), *Sp.*

As the term Dryopteris was first used by Amman in 1739, and applied in 1763 by Adamson, as the name of the genus to which the Aspidium was applied in 1800 by Swartz, the use of the generic term Dryopteris would seem to be necessitated by the ordinary laws of botanic nomenclature. The synonyms for the male fern are extraordinarily numerous. We append some of them: *Aspidium Filix-mas,* of many authors; *Polypolium Filix-mas* Linn.; *Polystichum Filix-mas* Roth.; *Nephrodium Filix-mas* Rich.; *Lastrea Filix-mas* Presl.; *Tectarea Filix-mas* Cavan.; *Dryopteris Filix-mas* (L.) Schott; *Lophodium Filix-mas* Newm.; *Polypodium nemorale* Salisb.; *Polystichum durum et indur-*

atum Schur.; *Polystichum abbreviatum* De Candolle; *Aspidium wildeanum* Göppert; *Dryopteris affinis; Polypodium heleopteris.*

The Male Fern is of very wide distribution occurring in Greenland, Europe, Asia, Northern Africa and in some of the Polynesian Islands; in the Western Hemisphere it is found in the Rocky Mountains in North America and the Andes Mountains in South America.

The U. S. IX also recognized the *marginal fern, Dryopteris marginalis* (L.) Asa Gray (*Aspidium marginale* Sw.; *Polypodium marginale* L.) but it was dropped at the last revision. This fern is differentiated from the preceding by having the sori (fruit bodies) on the margin of the leaves instead of near the midrib. It is found in rocky woods and on banks in eastern North America from Nova Scotia to Alabama.

The male fern has a perennial, oblique rhizome, from which numerous annual fronds or leaves arise, forming tufts from a foot to four feet in height. The stipe, or footstalk, and midrib are thickly beset with brown, tough, transparent scales; the frond itself is ovate-oblong in outline, the pinnæ being linear-lanceolate, tapering from base to apex. The fructification is in small dots on the back of each lobe, occurring close to the midvein.

Dryopteris Filix-mas yields the commercial variety of drug known as *European Aspidium.* Little of this variety has been imported since the outbreak of the war and none is arriving at the present writing. The oleoresin, however, is being imported from Europe. *Dryopteris marginale* yields the commercial variety known as *American Aspidium.* This variety is collected sparingly in scattered sections of the eastern and central United States but is no longer official.

It is probable that all of the species of this genus possess more or less anthelmintic properties. The activity of the *D. marginalis* is supported by the observations of Cressler (*A. J. P.*, 1878). According to Rosendahl (*P. J.*, 1911, lxxxvii, p. 35) the *Dryopteris dilatata* is indeed four times as active a poison to the tapeworm as the true aspidium. According to V. Penndorf (*Ap. Ztg.*, 1903), in Germany the rhizomes of *D. spinulosum* and *Athyrium Filix-fœmina* are frequently found mixed with those of the true male fern, in quantities varying from five to ninety per cent. The rhizomes of *D. Filix-fœmina* are readily recognized by having only two large dumb-bell-shaped steles. The rhizomes of *D. spinulosum* closely resemble those of the genuine drug, but it is stated that they can be distinguished by the numerous small glands found on the margin of their scales, the scales of *D. Filix-mas* having only two upon each. On account of this substitution, many of the German extracts of the male fern are said to contain *aspidin,* a yellow crystalline substance having a melting point of 124° to 125° C., which is found only in *D. spinulosum.* (*Ap. Ztg.*, 1903.) Lauren of Helsingsfors states that the extract of *D. spinulosum* is a very active tenicide, and is less apt to produce disagreeable sensations in the patient than is the official drug. He gives the dose as sixty grains (3.9 Gm.), followed by a laxative, and states that some Finnish apothecaries are especially noted for their fern extracts, because they use only the rhizome of *D. spinulosum.* (*Ap. Ztg.*, 1903.) Under the name of *filicone* there is used what is asserted to be the active principle of *D. spinulosum.* The dose is thirty grains.

On the Pacific slope the indigneous *D. rigida* Underw. is locally used against the tapeworm, and W. J. Bowman has found in it filicic acid and resin. Popular belief has long ascribed tenicidal virtues to our native *Asplenium Filix-femina,* commonly known as *Lady Fern.* It occurs in conical pieces from 8 to 13 cm. long, 2 to 5 cm. in diameter, of a reddish-brown color, covered with root fibers and leaf scars. According to R. Kürsten (*P. J.*, xxii, 1891), its active principle, *pannic acid,* is closely allied to filicic acid, differing in being especially soluble in strong alcohol, in subliming at 80° C., and is not yielding isobutyric acid when heated in a sealed tube with water. Pannic acid crystallizes is thin, shining, light yellow, rectangular prisms, melting at 187° C.

Under the name of *inkomankomo* or *uncomocomo,* the rhizome of *Aspidium athamanticum* (Hook.) Kuntze, has long been used by the South African Kaffirs, and has entered European commerce as *pannum.* In it Heffter (*A. E. P. P.*, 1897, 458) finds three well characterized and crystallized principles: *flavopannin, albopannin* and *pannol* (*pannic acid* of Kürsten). Heffter compares these three compounds with the three obtained from *D. Filix-mas* by Boehm. According to the experiments of A. Heffter, both *flavopannin* and *albopannin* are powerful muscle poisons, directly affecting the heart. (*A. E. P. P.*, Bd. xxxviii.)

The rhizomes of other species of fern are frequently substituted for the official, and in the dried state it is difficult to distinguish them. The varying results reported by physicians, when using this drug, can undoubtedly be ascribed to the employment of spurious male fern, or old brownish rhizomes which should have been thrown away.

The rhizome of aspidium apparently loses its therapeutic activity very rapidly when kept although Sollmann (*J. P. Ex. T.*, 1918, xii, p. 129) has shown that the oleoresin may retain its activity for many years.

As taken from the ground, the rhizome consists of a long cylindrical caudex, around which are closely arranged, overlapping each other like the shingles of a roof, the remains of the leafstalks or stipes, which are 2 to 5 cm. in length, from 3 to 8 mm. thick, somewhat curved and directed upwards, angular, brown, shining, and surrounded near their origin from the rhizome with thin silky scales of a light brown color. From near the bases of these remains

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of the footstalks emerge numerous small rootlets. The whole rhizome, thus constituted, presents a somewhat flexible, cylindrical mass, 2.5 to 5 cm. thick, and from 7 cm. to 4 dm. in length. In this form, however, it is not usually found in commerce. The whole is ordinarily broken up into fragments, consisting of the separated remains of the leafstalks before described, with a small portion of the substance of the rhizome attached to their base, where they are surrounded by the silky scales. These fragments, as seen in commerce, often appear as if long kept, and are probably, in general, much deteriorated by time.

Description and Physical Properties.—"*Unground Aspidium.*—Rhizome, 1 to 3 cm. in thickness, cylindraceous and nearly straight, or curved and tapering toward one end, usually split longitudinally, roughly scarred with remains of the stripe bases, or bearing several coarse, longitudinal ridges and grooves. Stipes, nearly cylindrical, but tapering toward one end, nearly straight or somewhat curved, 3 to 5 cm. in length, about 8 mm. in thickness; externally brownish-black, or if peeled, light brown; fracture short; internally pale green, spongy and exhibiting an interrupted circle of from 6 to 12 small vascular bundles; odor slight; taste sweetish, astringent, bitter and acrid.

"*Structure.*—An outer row of epidermal cells and several rows of brown, thick-walled hypodermal cells; parenchyma with intercellular spaces into which project characteristic glandular hairs; vascular bundles bicollateral, each surrounded by an endodermis, the tracheæ large, scalariform or reticulate; starch abundant, ellipsoidal or irregular, 0.002 to 0.025 mm. in length.

"**Assay.**—Aspidium yields not less than 6.5 per cent. of greenish oleoresin when prepared as directed under *Oleoresina Aspidii.*" *U. S.*

"From seven to fifteen centimetres or more in length; the rhizome itself about two centimetres in diameter. Entirely covered with the hard, persistent, curved, angular, dark brown bases of the petioles, which bear numerous brown membranous scales. Petioles green internally and exhibiting in transverse section about eight pale yellow fibrovascular bundles arranged in a diffuse circle (distinction from the petioles of Athyrium Filix fœmina, *Roth.*). Rhizomes brown externally, green internally. In transverse section, stalked secreting glands in intercellular spaces. Margins of the membranous scales with two-celled projections but no glands; at the base two minute glands (distinction from the rhizomes of certain other ferns). Feeble but disagreeable odor; taste sweetish and astringent at first, but subsequently bitter and nauseous." *Br.*

In collecting male fern, all the black, discolored portions should be cut away, the fibers and scales separated, and only the sound green parts preserved. These should be immediately, but carefully, dried and then pulverized; and the powder should be kept in small well-stoppered glass bottles. Powdered althæa leaves are sometimes used as an adulterant of powdered aspidium, giving the desirable light-green tint indicative of a good quality of drug. At other times the powder is said to consist entirely of the chaff and other inert material which the Pharmacopœia directs should be rejected.

Kraemer has reported that much of the aspidium in the American market consists of the large rhizomes of *Osmunda Claytoniana.* For distinction see *Proc. A. Ph. A.*, 1906, p. 345. Capelle discusses the characteristics of genuine aspidium and the differentiation of related species. (*Ap. Ztg.*, 1907, p. 433.)

Microscopic examination of the rhizome shows the following structural peculiarities, passing from periphery toward the center: (1) epidermis composed of brown polyhedral cells, some of which bear scaly hairs; (2) outer cortex (hypodermis) of several layers of thick walled, lignified cells, separating the epidermis from the inner cortex beneath; (3) inner cortex of several layers of isodiametric cells containing starch and separated from each other by intercellular air-spaces, many of which contain internal glandular-hairs; (4) fundamental parenchyma, resembling the last and forming the central matrix. Imbedded in this region are 6–12 fibrovascular bundles of concentric type arranged in an interrupted circle. Each bundle in cross section shows a central xylem consisting mainly of scalariform tracheids that are completely enveloped by a phloem of sieve tubes and phloem cells. Surrounding each bundle as a 1-to 3-layered pericambium and around this an endodermis or bundle sheath.

Microscopic examination of the stipe shows a similar arrangement of the tissues as found in the rhizome, but the bundles range in number from 6 to 10.

Constituents.—The activity of aspidium resides in its oleoresin. This contains as its most important anthelmintic principle an amorphous acid discovered by Kraft (*Ph. Ztg.*, 1903, p. 275) and called *filmaron.* Previous to this research various other principles had been separated. *Filicic acid* was discovered by Luck and later shown by Poulson (*A. E. P. P.*, 1891) to occur in a crystalline and amorphous condition; the former, which he believed to be the lactone of the latter, he found to be inactive and suggested that it be called *filicin.* Boehm, in addition, found *flavaspidic acid, albaspidin* and *aspidinol.* These substances are derivatives of phloroglucinol. By some they are believed to be decomposition products of filmaron.

Filmaron, $C_{47}H_{54}O_{16}$, is a bright, yellowish-brown, amorphous powder, insoluble in water, difficulty soluble in cold alcohol but readily so in most of the organic solvents and, with partial decomposition, in alkaline solutions. It shows a marked tendency to fuse together into masses and hence, is very difficult to pulverize. There is present also a peculiar tannin known as *filicitannic acid.* The rhizome contains about 5 per cent. of *filmaron.*

Aspidium may be assayed by first preparing the oleoresin, then dissolving 5 Gm. of this in ether and shaking out with 100 Gm. of 3 per cent. barium hydroxide solution after allowing to stand until clear, 86 Gm. of the barium hydroxide solution is decanted, acidulated with 3 Gm. of hydrochloric acid and shaken out with 25, 15 and 10 cc. portions of petroleum ether. The residue of filicic acid is dried at 100° C to constant weight. The final weight is multiplied by 25 to obtain the percentage. (See also *Am. Drug.,* 1897, p. 73.)

For further details of composition and assay see under *Oleoresina Aspidii.*

Uses.—Male fern was used by the ancients, and is mentioned as a vermifuge in the works of Dioscorides, Theophrastus, Galen and Pliny, and by some of the earlier modern writers. But it does not appear to have been generally known till about the year 1775, when the King of France purchased from Madame Nouffer, the widow of a Swiss surgeon, a secret remedy for tapeworm, which proved to be the powdered root of the male fern. As was first demonstrated by Straub (*A. E. P. P.,* 1902, xlviii, p. 1) the principles of aspidium paralyze the voluntary muscles of the higher animals as well as the analogous contractile tissue of the invertebrates. In smaller quantities these principles are stimulant to the central nervous system and may cause even tetanic convulsions.

Aspidium is used in medicine almost solely for the purpose of getting rid of various intestinal parasites, especially the *tapeworm.* As to its value in other forms of *helminthiasis* there is difference of opinion. Schultz (*J. A. M. A.,* 1911, lvii) reports 75 per cent. of cures in cases of *hookworm* infection, but Patterson (*T. G.,* 1908, xxxii), on the other hand, states that it has been found absolutely without value in this infection. Its action appears not to be so much to kill the parasite as to paralyze it so that it can be washed out of the alimentary canal with an active purge. For the latter purpose castor oil is often employed, but there is little doubt that its use increases the absorbability of the drug and hence adds to the danger of poisoning. For this reason calomel is generally to be preferred.

Besides its use as a vermifuge, aspidium has been recommended by La Nara (*J. des Pract.,* 1910) as a local application in *eczema* and *acne.*

Aspidium is a violent poison, the relative rarity of serious symptoms from its use being due to its non-absorbability. Under certain conditions, probably when there is a large amount of fatty matter in the bowel, it may be absorbed with unexpected readiness and give rise to serious and even fatal poisoning. Six drachms of it have caused death. (*L. L.,* 1882.) The common symptoms have been vomiting, diarrhea, vertigo, headache, tremors, cold sweats, dyspnea, cyanosis, convulsions and mental disturbances. In nearly half of the cases there was disturbance of vision and even blindness, which in a few instances remained permanently. According to Harnack (*M. M. W.,* 1912, lix, 1941), the blindness is due to spasm of the retinal vessels and subsequent optic atrophy. Prevost and Binet have found that in the lower animals, given hypodermically, the oleoresin produces violent dyspnea and death from arrest of the heart in systole, and Fröhner has found parenchymatous nephritis in animals fatally poisoned by it. The crude drug is to-day rarely used, preference always being given to the oleo-resin.

Filmaron has been used as a clinical vermifuge. Because of difficulties in pharmaceutical manipulation it is marketed in the form of a 10 per cent. solution in castor oil. The dose of filmaron is from eight to twelve grains (0.5 to 0.75 Gm.).

Dose, of aspidium rhizome in powder, sixty to one hundred and twenty grains (3.0–7.7 Gm.).

Off. Prep.—Oleoresina Aspidii, *U. S.* (*Br.*).

ATROPINA. U. S., Br.

ATROPINE Atrop.

"An alkaloid [$C_{17}H_{23}O_3N$] chiefly obtained from belladonna." *U. S.*

"Atropine, $C_{17}H_{23}NO_3$, is an alkaloid obtained from Atropa Belladonna, *Linn.,* and other plants of the natural order Solanaceæ." *Br.*

Atropia; Atropine, *Fr. Cod.;* Atropinum, *P. G.;* Atropin *G.;* Atropina, *It., Sp.*

Atropine is the optically inactive mixture of dextro- and laevo-hyoscyamine. Dextro-hyoscyamine does not occur in nature. Laevo-hyoscyamine occurs in the several species of *Solanaceæ* (see *Belladonnæ Radix*), the most abundant source being the Egyptian *Hyoscyamus muticus,* which also contains atropine. Atropine is manufactured, on the commercial scale, mainly from *Datura Stramonium.*

Description and Physical Properties.—"White, odorless crystals. *Caution.—Atropine is extremely poisonous.* One Gm. of Atropine is soluble in 455 cc. of water, 2 cc. of alcohol, about 27 cc. of glycerin, 1 cc. of chloroform, and in 25 cc. of ether, at 25° C. One Gm. is soluble in 90 cc. of water at 80° C., and in 1.2 cc. of alcohol at 60° C.

"Atropine melts between 114° and 116° C. Atropine is optically inactive. Its saturated aqueous solution is alkaline to litmus paper and to phenolphthalein T.S. Add a few drops of nitric acid to about 0.01 Gm. of Atropine contained in a porcelain dish, and evaporate the mixture to dryness on a water bath: a yellow residue is obtained. Add to the cooled residue a few drops of alcoholic potassium hydroxide T.S. and a fragment of potassium hydroxide: an intensely violet color is produced. (*Hyoscyamine* and *hyoscine* produce the same color as Atropine, but the presence of *other alkaloids masks* the reaction.) Gold chloride T.S. produces in a solution of Atropine (1 in 50) in diluted hydrochloric acid, a lusterless precipitate. (*Hyoscyamine* yields a lustrous precipitate.)

"Five cc. portions of a solution made by dissolving 0.2 Gm. of Atropine in 1 cc. of normal sulphuric acid and 14 cc. of distilled water, do not respond to the platinic chloride test for *most other alkaloids* or the test for *apoatropine* or *belodonnine* described under *Atropinæ Sulphas.* Atropine complies with the tests for *ash* and *readily carbonizable substances* under *Atropinæ Sulphas.*" *U. S.*

"Colorless acicular crystals. Soluble in about 500 parts of *water,* readily soluble in *alcohol* (90 per cent.), in *chloroform,* and in *ether.* Melting point 114.5° to 115.5° C. Its aqueous solution has an alkaline reaction and powerfully dilates the pupil of the eye. 0.05 gramme dissolved in 5 millilitres of *water* acidified with *hydrochloric acid* yields with *solution of auric chloride* a lemon-yellow precipitate which, after recrystallization from boiling *water* acidified with *hydrochloric acid,* has a minutely crystalline character, is dull and pulverulent when dry, and melts at 137° to 139° C. (distinction from hyoscyamine). 0.01 gramme with 5 drops of *nitric acid* yields, when evaporated to dryness on a water bath, a residue scarcely yellow in color which, after cooling, assumes a violet color on moistening with freshly prepared *alcoholic solution of potassium hydroxide.* 0.05 gramme dissolves in 1 millilitre of *sulphuric acid* without coloration, and the solution remains colorless on the addition of 1 drop of *nitric acid.* 10 millilitres of a solution containing 1 part of Atropine in 80 parts of *water* slightly acidified with *hydrochloric acid* does not at once become cloudy on the addition of 4 millilitres of *solution of ammonia* (absence of apoatropine)." *Br.*

It is inflammable, giving off an odor like that of benzoic acid, and, when burned in the open air, leaves no residue. Kraut in 1864 demonstrated that atropine could be broken up by heating with hydrochloric acid or with baryta water in a closed vessel into a base, tropine, and an acid, tropic acid. Ladenburg (*B. Chem. G.,* 1880, xiii) succeeded in effecting the synthesis of atropine from these two constituents, which, when heated over a water bath in the presence of diluted hydrochloric acid, unite to form the alkaloid; later (*Ph. Ztg.,* 1902, 355), he produced tropine by the direct action of hydrobromic acid on tropidine. Willstätter produced tropidine synthetically and the following synthetic chain was completed: Glycerin, glutaric acid, suberone, tropidine, tropine, tropic acid, and atropine.

Tropic acid, $C_9H_{10}O_3$, crystallizes in prisms with a melting point of 117° C. According to King (*Tr. Chem. Soc.,* 1919, cxv, p. 490), it is a mixture of two optical isomers, dextro- and laevo-tropic acid. *Tropine,* $C_8H_{15}ON$, is a strongly basic substance crystallizing in rhombic tablets with a melting point of 63° C., soluble in water and several of the organic solvents. It is optically inert.

Ladenburg and others (see Pyman, *Tr. Chem. Soc.,* 1917, cxi, p. 1104) have formed a large number of esters of tropine to which the general name of *tropeines* has been given. Some of these have pronounced toxic effects, and one (homatropine) has found use as a valuable substitute for atropine.

Hinterberger states that an alcoholic solution of atropine, when cyanogen is passed through it, assumes a blood-red color, and, on spontaneous evaporation, deposits a red, syrupy liquid insoluble in water. The detection of atropine in small quantity is a matter of great difficulty; the best test is the physiological, which consists in placing the suspected liquid in the eye of a cat, or other animal, when, if the alkaloid be present, dilatation of the pupil will occur. According to Brunner, the best chemical test is the aromatic odor which is produced by adding the alkaloid and a little water to a hot mixture of sulphuric acid and potassium dichromate or ammonium molybdate. (*P. J.,* iv, 385.) Fabris believes that strychnine in the presence of atropine interferes with the toxicological identification of the latter by chemical tests, but a physiological test reveals the presence of both alkaloids. (*B. S. Ph. Br.,* 1894.) Wormley made comparative examinations of various tests for atropine, hyoscyamine, and hyoscine. (*A. J. P.,* 1894, 513.)

Uses.—The effects of atropine upon the system are due chiefly to two actions, namely, a stimulation of certain higher nerve centers and a paralysis of the peripheral endings of the nerves known as the autonomic (or parasympathetic) system. The autonomic nerves carry impulses to certain organs of unconscious life; among them are the secretory nerves for salivary, sweat, gastric, and probably all other glands except the kidney and mammæ; the vagus which carries inhibitory impulses to the heart, motor fibers to the bronchi and to a part of the intestines; the oculo-motor nerve which supplies the sphincter pupillæ and ciliary muscle. As atropine affects all of these nerves it is evident that it will produce a large number of changes in the bodily functions.

The earliest symptom of atropine poisoning is usually dryness of the throat. This is due to a paralytic action of the drug not only upon the chorda tympani nerve which supplies the salivary gland, but also probably to an action upon the mucous glands throughout the oral cavity. There is a corresponding decrease—although ordinarily only after somewhat larger dose—in the secretion of the sweat glands, of the digestive glands, and of the lachrymals; neither the kidney nor liver are affected. Concerning the mammary glands there is still some difference of opinion; pharmacologists have failed to demonstrate any effect upon these organs but clinicians continue to believe that the drug will cause a diminution in the secretion of milk. A little later in the action of atropine the pulse rate is increased through a paralysis of the cardio-inhibitory mechanism. [McGuigan (*J. A. M. A.*, 1921, lxvi, 1338) and Platz (*Zeitsch. f. Ges. Exper. Med.*, June 7, 1922) have both found that in man small doses of atropine cause a primary slowing of the pulse.] As a result of the more rapid heart action, but also largely from the effects upon the vasomotor center in the medulla, there is an increase in the blood pressure. The question of whether atropine has a direct stimulant influence upon the heart muscle is as yet undecided, but if it possesses any such action it is a feeble one. Its stimulant action upon the medullary center is also shown in the increased rapidity of breathing while that it possesses an action upon the cerebral centers is manifest by the delirium which follows toxic doses. The action upon intestinal peristalsis is probably a combination of various factors; through its paralytic action upon the branch of the pneumogastric nerve supplying the intestinal muscles it tends to counteract various spasmodic influences. At the same time, as has been shown by Magnus (*A. G. P.*, 1905, cviii, p. 1), it possesses an action upon the so-called Auerbach plexus by virtue of which it increases the size of the peristaltic wave and also tends to restore their rhythmicity. When directly applied in sufficient concentration it is capable of paralyzing the unstriped muscle. The dilatation of the pupil which may be caused by the systemic action of toxic doses of atropine, but is more commonly the result of its local application, is due to an action upon the peripheral endings of the oculomotor nerve. At the same time there is paralysis of accommodation through an effect upon the branches of this nerve which run to the ciliary muscle.

In the lower animals very large doses of atropine may cause increased reflexes, and even convulsions, through its effect upon the motor centers of the spinal cord, but this action is rarely seen in human poisoning. When brought in direct contact with either motor or sensory nerve endings it produces more or less complete abolition of their function.

Atropine is used in medicine for five purposes, namely, to check secretion, stimulate circulation, stimulate respiration, to overcome spasm of the involuntary muscles, locally for its effect upon the eye and externally as a local anodyne.

In the various forms of *colliquative sweating*, such as seen, for example, in *phthisis*, in *salivation*, as for instance, in mercurial poisoning, in *hyperchlorhydria*, atropine ranks as one of our most useful remedies. It is also of service to check the nasal secretions, as for instance in *acute coryza* or *hay fever*. In *galactorrhea* and threatened *mammary abscesses* belladonna plasters are routinely applied with the idea that the atropine in them may diminish the lacteal secretions, but as pointed out above, it is doubtful whether the drug possesses any such power.

As a circulatory stimulant atropine is of great value in severe emergencies, such as *surgical shock* or *collapse*. Its value in these conditions is due in part to the stimulating action on the vasomotor center and also in part to the effect upon the nerves of the skin which tend to check the excessive sweating which is characteristic of these states and thereby prevent the loss of animal heat. In the milder forms of circulatory failure it is ordinarily not to be recommended because the drying up of the secretion is often a source of great discomfort to the patient. As a respiratory stimulant it is of service, especially in the treatment of *poisoning* by various depressants, such as opium, chloral, and the like. It should be borne in mind that large doses of atropine are depressant and the physician should never give more than one-fiftieth of a grain when used either as a circulatory or respiratory stimulant.

In spasmodic affections involving the unstriped muscles, such as the *colica pictonum* and the *asthmatic paroxysm*, atropine is perhaps the most certain symptom remedy which we possess. In the latter affection it is usually best administered by inhalation; for this purpose it may be volatilized by burning one of the plants containing it. (See *Stramonium*.) In *whooping cough* and *dysmenorrhea* it is sometimes of value, but its action is much less certain. Certain cases of nocturnal *enuresis* appear to be due to a hyper-irritability of the muscle in the walls of the bladder and in these patients full doses of atropine are of the greatest service. The injection of atropine into the substance of the trapezius muscle in cases of *wry-neck*, for the purpose of paralyzing the motor nerve supplying it, while commonly recommended in text-books, generally does not prove of avail. Allied to its antispasmodic action is the power of atropine to regulate as well as increase the movements of the bowel. For this purpose it is habitually added to laxative mixtures for the purpose of preventing griping as well as to enhance the aperient effect. Massive doses (as high as one-twentieth grain) have also been used with apparent favorable results in the treatment of *ileus*. Wolf believes that atropine has an effect on the labyrinthine nerves of the ear and therefore recommends it in *sea-sickness*.

In ophthalmology atropine is a remedy of extreme service. It is used both for the purpose of dilating the pupil and of paralyzing the muscles of accommodation. Its action is so slow and persistent that in cases where only temporary effects are desired, as, for example, the fitting of glasses, it has been largely abandoned for more rapidly acting drugs, but in inflammatory conditions of the eye, as in *iritis*, *keratitis*, etc., the very persistency of its effect makes it of extreme usefulness. For this purpose one or two drops of a 1 per cent. solution may be instilled into the eye at such intervals as may be deemed necessary. The same purpose may be accomplished by inserting beneath the eyelid small gelatin disks containing atropine. (See *Lamellæ Atropinæ.*)

Locally atropine in the form of an ointment and the plaster of belladonna is largely used in various painful conditions, but its use does not seem highly rational for this purpose.

Toxicology.—Atropine poisoning may occur from the ingestion of any of the numerous plants of which it is the active principle, most frequently, however, from either belladonna or the widespread stramonium. It should be remembered that severe poisoning may follow the external application either of the ointment or plaster of belladonna. The symptoms are dryness of the throat, dilatation of the pupil, rapid, hard pulse, hurried respirations, the skin warm and dry, the face flushed and frequently there is an erythematous rash somewhat resembling that of scarlet fever. (For description and literature of atropine eruptions see Knowles, *A. J. M. S.,* July, 1911.) The most striking of the symptoms, however, is the peculiar delirium. In the earlier stages this manifests itself simply by profuse and somewhat incoherent talkativeness, but later there is complete obfuscation often with hallucinations, sometimes more or less maniacal in character. After large doses a stage of depression may develop with stupor, weakening of the pulse, and respiratory failure. The condition, though alarming, usually ends in recovery. In case of doubt as to the cause of the condition a presumptive diagnosis can be made by instilling a drop or two of the urine from the patient into the eye of a cat. In most cases of atropine poisoning sufficient of the drug is eliminated through the kidneys to cause dilatation of the pupil.

In the *treatment* after emptying the stomach with the stomach tube or suitable emetics, twenty minims of the compound solution of iodine should be given as the best chemical antidote. Morphine may be used cautiously for the purpose of quieting the delirium, but as the real danger in the case is from respiratory failure it should not be given in large dose. Physostigmine is almost a complete physiological antagonist of atropine and would probably prove useful in cases of poisoning. Symptoms of respiratory and circulatory failure may best be met by the use of strychnine and caffeine.

The hypodermic *dose* of atropine may be set down as one one-hundred-and-fiftieth of a grain (0.0004 Gm.), the dose by the mouth as one one-hundredth of a grain (0.0006 Gm.), although in serious cases these amounts may be much exceeded. Thus in *ileus* German clinicians have given as high as the one-twentieth of a grain (0.003 Gm.) at a dose. On the other hand in susceptible persons, one-hundredth of a grain (0.0006 Gm.) will produce decided dryness of the throat, and one-fiftieth of a grain (0.0013 Gm.) is alleged to have caused toxic symptoms. As atropine itself is nearly insoluble, the sulphate should always be preferred. For application to the sound skin, the form of ointment or oleate is most convenient. The ointment may be made by rubbing a grain of the alkaloid first with four minims of alcohol, and then with a drachm of lard. The ointment of belladonna, is, however, usually preferred.

When solution of atropine sulphate is used for dilating the pupil, it may be either dropped into the eye within the lower lid, or introduced on small slips of paper previously saturated with the solution and dried, or, what is still more convenient, by means of minute circular disks of gelatin, made by mixing the solution with gelatin and evaporating so as to produce a thin film, which is to be cut into circular pieces. (See *Lamellæ Atropinæ.*) These have the advantage over paper that they do not require to be subsequently removed from the eye.

The solution of atropine or its salts is very prone to have developed in it a fungous growth with consequent decomposition of the alkaloid. Simon (*J. A. M. A.,* 1915, lxiv, 705) has shown that a solution of atropine may become entirely inert in three days.

Dose, of atropine, one two-hundredth to one-fiftieth of a grain (0.0003–0.0013 Gm.).

Off. Prep.—Oleatum Atropinæ, *N. F.;* Unguentum Atropinæ, *Br.*

ATROPINÆ SULPHAS. U. S., Br.

ATROPINE SULPHATE Atrop. Sulph.

"$(C_{17}H_{23}O_3N)_2H_2SO_4.H_2O$." *U. S.*

"Atropine Sulphate, $(C_{17}H_{23}NO_3)_2,H_2SO_4$, is the sulphate of the alkaloid Atropine." *Br.*

Sulphate of Atropia; Sulfate d'Atropine, *Fr. Cod.;* Atropinum Sulfuricum, *P. G.;* Schwefelsaures Atropin, Atropinsulfat, *G.;* Solfato di atropina, *It.;* Sulfato de atropina, *Sp.*

Atropine sulphate may be prepared by the interaction between a solution of atropine in ether and of sulphuric acid in strong alcohol, and a formula for its manufacture was official in the U. S., 1870. Considerable care is necessary in the preparation of the salts of this alkaloid because of the great facility with which atropine is decomposed. For details of the formerly official method see *U. S. D.,* 20th ed., p. 208.

Description and Physical Properties.—"A white, odorless, crystalline powder. It is efflorescent in dry air. *Caution.—Atropine Sulphate is extremely poisonous.* One Gm. of Atropine Sulphate is soluble in 0.4 cc. of water, 5 cc. of alcohol, 2.5 cc. of glycerin, 420 cc. of chloroform, and in 3000 cc. of ether, at 25° C. One Gm. is soluble in 2.5 cc. of boiling alcohol.

"Melting point: not below 188° C. Add a few drops of nitric acid to about 0.01 Gm. of Atropine Sulphate, contained in a porcelain dish, and evaporate the mixture to dryness on a water bath: a yellow residue is obtained. Add to the cooled residue a few drops of alcoholic potassium hydroxide T.S. and a fragment of potassium hydroxide: an intensely violet color is produced. (*Hyoscyamine* and *hyoscine* produce the same color as Atropine, but the presence of *other alkaloids* masks the reaction.) Gold chloride T.S. produces in an aqueous solution of Atropine Sulphate (1 in 50) a lusterless precipitate. (*Hyoscyamine* yields a lustrous precipitate.) Barium chloride T.S. produces in an aqueous solution of Atropine Sulphate a white precipitate which is insoluble in hydrochloric acid.

"An aqueous solution of Atropine Sulphate (1 in 20) is neutral to litmus paper. The ash from 0.1 Gm. is negligible. One-tenth Gm. of Atropine Sulphate dissolves in 2 cc. of concentrated sulphuric acid without producing more than a slightly yellow coloration (*readily carbonizable substances*), and the solution becomes only light yellow upon the addition of 0.1 cc. of nitric acid (*many other alkaloids*). In an aqueous solution of Atropine Sulphate (1 in 50), mixed with a few drops of hydrochloric acid, platinic chloride T.S. produces no precipitate (*most other alkaloids*). An aqueous solution of the salt (1 in 60) is rendered turbid by sodium hydroxide, but no turbidity is produced immediately upon the addition of 2 cc. of ammonia T.S. to 5 cc. of the solution (*apoatropine or belladonnine*)." *U. S.*

"Nearly colorless, crystalline, somewhat hygroscopic. Soluble in less than 1 part of *water*, and in 4 parts of *alcohol* (90 per cent.), the solutions being neutral to *litmus* and, even when largely diluted, dilating the pupil of the eye. Melting point from 189° to 190° C. 0.05 gramme dissolves in 1 millilitre of *sulphuric acid* without coloration, and the solution remains colorless on the addition of 1 drop of *nitric acid.* 10 millilitres of an aqueous solution (1 in 60) do not at once become cloudy on the addition of 4 millilitres of *solution of ammonia* (absence of appoatropine). An aqueous solution, not too dilute, yields with *solution of sodium hydroxide* a white precipitate which, when washed and dried, responds to the tests described under 'Atropina.' Yields the *reaction* characteristic of sulphates. Loses not more than 2 per cent. of moisture when dried at 105° C." *Br.*

Uses.—The effects of the salt on the system are precisely the same as those of atropine, and it may be used in the same dose. Its great advantage over the alkaloid is its solubility in water.

Dose, one two-hundredth to one one-hundredth of a grain (0.0003–0.0006 Gm.).

Off. Prep.—Lamellæ Atropinæ, *Br.;* Liquor Atropinæ Sulphatis, *Br.*

AURANTII AMARI CORTEX. U. S. (Br.)

BITTER ORANGE PEEL Aur. Amar. Cort.

"Bitter Orange Peel is the dried rind of the unripe fruit of *Citrus Aurantium* Linné (Fam. *Rutaceæ*)." *U. S.* "Dried Bitter Orange Peel is the dried outer part of the pericarp of Citrus Aurantium, var. Bigaradia, *Hook. f.*" *Br.*

Aurantii Cortex Siccatus, *Br.;* Aurantii Pericarpium; Cortex Aurantiorum, Cortex Pomorum Aurantii; Curaçao Orange Peel, Wild Orange Peel; Ecorce (Zestes) d'Oranges amères, Ecorce de Bigarade, *Fr.;* Cortex Aurantii Fructus, *P. G.;* Pomeranzenschale, *G.;* Corteccia di arancio amaro, *It.;* Corteza de maranja amarga, *Sp.*

Bitter Orange Peel of the U. S. P. X is the dried rind. In the Br. Pharm., 1914, both the dried and fresh rind are official, while under the name of *Aurantii Cortex Indicus,* Indian Orange Peel, the British Pharmacopœia, 1914, recognizes the bitter orange peel obtained from varieties of the *Citrus Aurantium,* grown in India and Ceylon. For description and properties, see under *Aurantii Dulcis Cortex.*

Off. Prep.—Infusum Aurantii, *Br.;* Infusum Aurantii Compositum, *Br.;* Tinctura Aurantii Amari, *U. S.* (*Br.*); Syrupus Aurantii (from Tincture), *Br.*

AURANTII CORTEX INDICUS. Br.

INDIAN ORANGE PEEL

"Indian Orange Peel is the fresh and the dried outer part of the pericarp of varieties of Citrus Aurantium, *Linn.,* grown in India and Ceylon." *Br.*

It is thus described: "Possesses the pleasant aromatic odor and bitter taste characteristic of Bitter Orange Peel derived from Citrus Aurantium, var. Bigaradia, *Hook, f.* Inner surface retains not more than a very small amount of the white spongy part of the pericarp." *Br.*

In India and the Eastern divisions of the Empire, Indian Orange Peel, fresh or dried, may be employed in making the official preparations for which Fresh or Dried Bitter Orange Peel is directed to be used.

AURANTII CORTEX RECENS. Br.

FRESH BITTER-ORANGE PEEL

"Fresh Bitter-Orange Peel is the fresh outer part of the pericarp of Citrus Aurantium, var. Bigaradia, *Hook. f.*" *Br.*

It is thus described: "Outer surface red or deep orange-red in color, and generally rough. Inner surface retains not more than a very small amount of the white spongy part of the pericarp; in transverse section numerous large oil-glands below the epidermis. Pleasant aromatic odor; taste aromatic, bitter." *Br.*

AURANTII DULCIS CORTEX. U. S.

SWEET ORANGE PEEL Aurant. Dulc. Cort.

"Sweet Orange Peel is the fresh, outer rind of the ripe fruit of *Citrus Aurantium* var. *sinensis* Linné (Fam. *Rutaceæ*)." *U. S.*

Cortex Aurantiorum Dulcium; Oranger Vrai, *Fr. Cod.;* Ecorce (Zestes) d'Oranges douces, *Fr.;* Apfelsinenschalen, *G.;* Scorze del frutto dell' aranioc, *It.;* Corteza de naranja dulce, *Sp.*

The citrus trees, lemon and orange, appear to have been cultivated in ancient India as far back as history goes, the names of the fruits being of Sanskrit etymology. There is considerable difficulty in classifying the species of this genus, partly because of similarities and partly because of tendency to hybridization; some regard the different fruits as distinct species, while others consider them as merely varieties. Engler (*Die naturlichen Pflanzenfamilien,* 1897) divides the species *Citrus Aurantium* L. into a number of sub-species, some of which have been considered by others as distinct species, as follows:

C. aurantium amara L. (*C. Bigaradia* Duhamel; *C. aurantium* var. *Bigaradia* Hook. f.) known as the *bitter* or *Seville orange,* or *Bigarade; C. aurantium sinensis* Gallesi (*C. aurantium* var, *dulcis* L.), *sweet orange* or *Malta orange; C. aurantium Bergamia* (Risso et Poyteau) Wight et Arnott which is the *Bergamot;* and several other varieties which are not of medicinal importance.

In all its varieties the orange tree is a beautiful evergreen growing to the height of about 30 feet and having the fruit mingled in every stage of its growth with blossoms and foliage. It is a native of China and India, was introduced into Europe by the Arabians about the ninth century and is now cultivated in subtropical lands all over the world. The American supply is grown chiefly in California, Florida and the West Indies. The stem of the tree is rounded, much branched, and covered with a smooth, shining, greenish-brown bark. In the wild state, and before inoculation, it is often furnished with axillary spines. The leaves are ovate, pointed, entire, smooth, and of a shining pale green color. When held between the eye and the light, they exhibit numerous small transparent vesicles, filled with volatile oil, and when rubbed between the fingers, are highly fragrant. Their footstalks are about an inch long, and have wings or lateral appendages. The flowers, which have a delightful odor, are large, white, and attached by short peduncles, singly or in clusters, to the smallest branches. The calyx is saucer-shaped, with pointed teeth. The petals are oblong, concave, white, and beset with numerous small glands. The filaments are united at their base in three or more distinct groups, and support yellow anthers. The ovary is roundish, and bears a cylindrical style, terminated by a globular stigma. The fruit is a hesperidium, often somewhat flattened at its base and apex, rough, of a yellow or orange color, and divided internally into a number of vertical loculi, each containing from two to four seeds, surrounded by a pulp. The rind of the fruit consists of a thin exterior layer, abounding in schizo-lysigenous cavities filled with a fragrant volatile oil, and of an interior one, which is thick, white, spongy, bitterish, and inodorous.

The fruit of the bitter orange is smaller than that of the sweet orange and of a deeper color, more acid and slightly bitterish in taste. It is round but flattened above and below, and has a smooth, thin, delicate rind. The commercial supplies come chiefly from the south of Spain and Sicily, but it is also cultivated in Florida. The flowers of this tree yield a very fragrant oil (see *Oleum Aurantii Florum*). They were formerly recognized by the U. S. P. (1880) and were described as follows: "about half an inch (12 mm.) long; calyx small, cup-shaped, five-toothed; petals five, oblong, obtuse, rather fleshy, white and glandular-punctate; stamens numerous, in three or more sets; ovary globular, upon a small disk, with a cylindrical style, and a globular stigma; odor very fragrant; taste aromatic and somewhat bitter." *U. S.,* 1880. The dried flowers were formerly used on the continent of Europe as a gentle nervous stimulant. The fresh flowers may be kept for some time by mixing them well with half their weight of sodium chloride, pressing the mixture in a suitable jar, and keeping it well closed in a cool place.

The leaves, which are bitter and aromatic, also yield a volatile oil which is often mixed with the oil of the blossoms.

The fruit of the sweet orange is larger and of a lighter color, and the pulp is less acid and free from bitterness. Because of its superior flavor this orange is usually given the preference for eating, and several variations have been produced. Among these are the seedless variety called the *navel orange,* so popular in this country, and the *blood orange,* the pulp of which has a red instead of yellow color.

The fruit is applied to several purposes. Small unripe oranges, about the size of a cherry or less, previously dried, and rendered smooth by a turning-lathe, are sometimes found in commerce under the name of *orange berries.* They are sub-globular, 5 to 20 mm. in diameter, of a grayish or greenish-brown color, fragrant odor, and bitter taste, and are said to be used for flavoring cordials. A volatile oil is obtained from them by distillation, known to the French by the name of *essence de petit grain,* and employed for similar purposes with that of the flowers. The oil, however, which now goes by this name is said to be distilled from the leaves, and those of the bitter orange yield the best. The oils from the unripe and the ripe fruit have a rotating power to the right, the latter much greater than the former; and this property might serve to distinguish them from the oil of the leaves. Several of the oils from the *Rutaceæ* deposit a crystalline substance, differing from camphor.

The best mode of separating the outer rind, when its desiccation and preservation are desired, is to pare it from the orange in narrow strips with a sharp knife, as one pares an apple. When the object is to use the fresh rind for certain pharmaceutical purposes, as for the preparation of the *confection of orange peel,* it is best separated by a grater, carefully avoiding the grating of the white portion which contains the bitter principle. The dried peel sold in the shops is usually that of the Seville orange, and is brought chiefly from countries adjacent to the Mediterranean.

Bitter orange peel has a grateful aromatic odor, which depends upon the volatile oil contained in its schizo-lysigenous cavities, and a warm, bitter taste.

Description and Physical Properties.—"*Unground Bitter Orange Peel.*—Thin, irregular bands (ribbons) or quarters; outer surface yellowish- or reddish- or greenish-brown with numerous, minute pits and fine reticulate ridges; inner surface whitish with many slight conical projections and fine anastomosing lines formed by the vascular bundles; fracture hard, short; odor fragrant and aromatic; taste aromatic and bitter.

"*Structure.*—An epidermis of small, angular cells; an outer parenchyma of thick-walled cells containing chloroplasts or chromoplasts and occasionally calcium oxalate prisms, and bearing the large oil reservoirs, arranged mostly in two irregular rows; an inner spongy parenchyma of branched cells surrounding large intercellular spaces, and bearing delicate, anastomosing vascular bundles.

"*Powdered Bitter Orange Peel.*—Yellowish-gray or light brown; fragments of parenchyma abundant, the cells walls from 0.004 to 0.012 mm. thick; tracheæ very small with close spiral markings or simple pores; calcium oxalate prisms from 0.020 to 0.045 mm. long.

"Powdered Bitter Orange Peel is colored yellow upon the addition of sodium hydroxide T.S." *U. S.*

"In thin strips. Outer surface deep orange-red and rough. Inner surface retains not more than a very small amount of the white spongy part of the pericarp; in transverse section numerous large oil-glands below the epidermis. Pleasant aromatic odor; taste aromatic, bitter." *Br.*

The Br. Pharmacopœia requires that the other surface both of the fresh and of the dried bitter orange peel shall be of a deep orange-red color, and rough and glandular.

The *sweet orange peel* is described officially as follows:

"*Unground Sweet Orange Peel.*—The outer, orange-yellow layer recently separated by grating or paring and consisting of epidermal cells, parenchyma and oil reservoirs with globules of volatile oil; odor highly fragrant; taste pungently aromatic. The inner, white portion of the rind should not be used." *U. S.*

For the preparation of powdered bitter orange peel the German Pharmacopœia directs that the drug should be previously dried over freshly burnt lime. Bitter orange peel is sometimes adulterated with sweet orange peel. The latter is distinguished by the pieces being thinner and of a more orange-red color. They are less aromatic and less bitter. The following test which is distinctive for bitter orange peel is recognized by the Netherland Pharmacopœia: the section of the fruit is mounted in a solution of potassium bichromate slightly heated when the tissues become colored brown. This reaction does not take place with sweet orange peel. A distinctive test for the latter is the use of fuming nitric acid (containing 55 per cent. N_2O_5) which gives a dark green color distinguishing it from bitter orange peel which is colored brown.

Constituents.—Tanret found in the rind of the bitter orange, (1) a crystalline acid, $C_{44}H_{28}O_{14}$; (2) a non-crystalline resinous body; (3) the glucoside *hesperidin;* (4) *isohesperidin,* a crystalline glucoside isomeric with hesperidin; (5) *aurantiamarin,* another glucoside to which, in part, the bitterness of the peel is due. (*P. J.*, 1886, 839.) *Hesperidin,* $C_{22}H_{26}O_{12}$, was discovered by Lebreton in 1828. Treated with diluted acids it yields *hesperetin,* $C_{16}H_{14}O_6$, and glucose. Hesperidin has a fusing point 250° to 251° C., and may be prepared by Paterno and Briosi's process, as follows: The cut and bruised oranges are covered with diluted alcohol, solution of potassium hydroxide added in excess, the liquor filtered after two days, and impure hesperidin precipitated by hydrochloric acid; the precipitate is boiled with acetic acid for ten minutes, and, after cooling, filtered from the resinous mass left. The hesperidin gradually separates from the filtrate upon standing, in white fine needles. From 4000 oranges about 6 ounces av. of the principle were obtained. (*B. Chem. G.*, 1876, 250.)

Orange peel contains also albumen, pectin, resin, a trace of fixed oil, volatile oil, and a principle resembling tannin in its action on salts of iron and notable amounts of certain vitamins, according to recent investigations. Fresh orange peel, the waste material from the orange oil industry, has become one of the sources of commercial pectin. The bitter principles are much more abundant in the white spongy inner portion of the peel than in the outer yellowish layer. For description of the volatile oil see *Oleum Aurantii.*

Uses.—Bitter orange peel is a mild tonic, carminative, and stomachic; the sweet is simply aromatic; but neither is much used alone. They are chiefly employed to communicate a pleasant flavor to other medicines, to correct their nauseating properties, and to assist their stimulant impression upon the stomach. They are a frequent and useful addition to bitter infusions and decoctions, such as those of gentian, quassia, calumba, and Peruvian bark. It is obviously improper to subject orange peel to the action of heat, as the volatile oil is thus driven off. Violent colics, convulsions, and even death have been caused in children by eating large quantities of the rind. When orange peel is used simply for its agreeable flavor, the rind of the sweet orange is preferable; as a tonic, that of the Seville orange.

Dose, from half a drachm to a drachm (2.0–3.9 Gm.).

Off. Prep.—Syrupus Aurantii, *U. S., Br.* (from Tincture); Tinctura Aurantii Dulcis, *U. S.;* Vinum Aurantii (from Fresh Peel), *Br.*

AVENA SATIVA. N. F.

OAT Even. Sat.

"Oat is the grain of *Avena Sativa* Linné (Fam. *Graminæ*). Oat contains not more than 5 per cent. of other seeds or of foreign organic matter." *N. F.*

Oatmeal; Avenæ Farina; Oatmeal; Avoine, Farine d'Avoine *Fr.*; Hafermehl, *G.*; Farina dell' Avena, *It.*; Harina de Avena, *Sp.*

Avena sativa L., or the common cultivated oat (Fam. *Gramineæ*), is so well known that a minute description would be superfluous. It is an annual, specifically distinguished by its loose panicle of spikelets and its elongated hairy grain, firmly enveloped by a "hull" consisting of a lemma and palet. It was known to the ancients, and is now cultivated in all civilized countries; but its original locality has not been satisfactorily ascertained. It grows wild in Sicily, and is said to have been seen by Anson in the island of Juan Fernandez, off the coast of Chili. The seeds deprived of their husks are sometimes known as *groats.* As a human food coarsely ground oatmeal is usually preferred to the fine meal, and the grain grown in a northern climate is superior to that produced further south. The market preparations at present are hardly to be called meals for instead of being ground the grain is crushed between heavy rollers sometimes with heat and moisture as accompaniments of the process.

Description and Physical Properties.—"*Unground Oat.*—Pale yellow or pale yellowish-green; up to 1.5 cm. in length and about 3 mm. in diameter, tapering toward each end, the base somewhat contracted, slightly protruding and with an elliptical scar, the apex pointed, showing the more or less broken upper part of the lemma and palet, the former surrounding the grain except on the ventral side where there is a distinct longitudinal groove, the latter usually exhibiting a minute stalk at the base; outer surface of the lemma glabrous with five or more longitudinal veins on the dorsal surface; above the center, a scar or, rarely, remains of a straight or slightly twisted awn (presence of strongly twisted awn indicates *Wild Oat*); within the groove a narrow, thinly-membranous, two-veined palet or scale; fruit or naked grain tapering toward either end, a distinct longitudinal groove on the ventral side, at the micropylar end of which occurs a wart-like excrescence or caruncle, at the opposite end a dense mass of long slender hairs which also occur less abundantly over the surface of the fruit. Odor slight; taste starchy.

"*Structure.*—Lemma; outer epidermis chiefly of elongated cells with beaded and heavily salicified and lignified walls and rounded ends, between the elongated cells a few crescent-shaped or circular cells, the latter fitting into the concave side of the former and each with heavily salicified walls, a few elliptical stomata and near the margin straight or slightly curved unicellular non-glandular hairs with thick lignified walls; hypodermis composed of about five layers of fibers with thick, partially beaded, lignified walls, the cells with taper-pointed ends and up to about 1 mm. in length and spongy parenchyma composed of irregularly shaped cells with large intercellular spaces. Palet; margins with numerous sharp pointed, straight or slightly curved, unicellular hairs with lignified walls; elliptical stomata up to about 0.040 mm. in length and in rows parallel to the keel; hypodermis of about three layers of cells otherwise resembling the glume but with thinner, less heavily developed tissue. Fruit: epicarp of longitudinally elongated cells, some of which give rise to unicellular, lignified-walled, pointed hairs, other layers of tissue of pericarp and seed coat of more or less collapsed cells, outer layer of endosperm usually one cell thick, the cells filled with protein, remaining tissue of endosperm composed of parenchyma chiefly filled with starch grains; broad spindle-shaped embryo about 2 mm. in length embedded in the endosperm near the micropylar end.

"*Powdered Oat.*—Whitish; fragments of epicarp with thin-walled cells up to about 0.400 mm. in length, from some of the latter arising slender pointed hairs up to 2 mm. in length, 0.020 mm. in diameter at the base, larger at the middle and with lumina up to 0.009 mm. in diameter and walls up to 0.008 mm. in thickness; fragments of glume with characteristic tissues; occasional fragments of palet with coarse unicellular hairs up to 0.250 mm. in length; irregular portions of endosperm tissue with cells containing rounded or ellipsoidal, many-compound starch grains, the compound grains up to 0.060 mm. in diameter with individual grains polygonal or spindle-shaped up to 0.010 mm. in diameter." *N. F.*

Constituents.—A very elaborate report on the composition of American cereals by Clifford Richardson (*Department of Agriculture, Bulletin* No. 9) gives as the average ratio in oats from all parts of the country 70 per cent. of kernel to 30 per cent. of husk. According to the same authority, the composition of the kernel (average of 179 analyses) is as follows: Water, 6.93 per cent.; ash, 2.15; oil, 8.14; carbohydrates, 67.09; fiber, 1.38; albuminoids, 14.31; corresponding to nitrogen per cent. 2.28. The nitrogenous principle has been called *avenin,* and somewhat resembles legumin. Ritthausen (*Die Eiweisskörper, Bonn,* 1872, 135) considers Nortin's avenin to have been a mixture of legumin or vegetable casein and a vegetable gluten containing sulphur, to which he gives the name *gliadin,* the legumin, however, predominating.

Uses.—Gruel made with fine oatmeal affords a nutritious, bland aliment, which, from its somewhat laxative tendency, is often preferable to other amylaceous preparations. *Oatmeal gruel* may be prepared by boiling an ounce of the meal with three pints of water, to a quart, straining the decoction, allowing it to stand until it cools, and then pouring off the clear liquor from the sediment. Sugar, lemon juice, or wine may be added to improve its flavor.

Diuretic properties have been attributed to the oatmeal, but probably incorrectly. It probably has no therapeutic properties not possessed by all cereal grains.

The N. F. gives the *dose* as sixty grains (4 Gm.) but indefinite amounts may be used.

Off. Prep.—Elixir Hydrastis Compositum, *N. F.;* Fluidextractum Avenæ Satival, *N. F.*

BALSAMUM PERUVIANUM. U. S., Br.

BALSAM OF PERU Bals. Peruv. [Peru Balsam]

"Balsam of Peru is obtained from *Toluifera Pereiræ* (Royle) Baillon (Fam. *Leguminosæ*)." *U. S.* "Balsam of Peru is a viscid balsam exuded from the trunk of Myroxylon Pereiræ *Klotzsch,* after the bark has been beaten and scorched." *Br.*

Balsamum Peruvianum Nigrum; Balsamum Indicum; Baume du Pérou *Fr. Cod.*; Baume de Sonsonate, *Fr.*; Balsamum peruvianium, *P. G.*; Peruvianischer Balsam, Perubalsam, *G.*; Balsamo peruviano, Balsamo del Peru, *It.*; Bálsamo del Peru liquido, Bálsamo de San Salvador, Bálsamo Peruviano negro, *Sp.*

The name "*Toluifera Pereiræ*" assigned to the tree yielding Balsam of Peru by Baillon seems inappropriate in respect to its generic part, since it means Tolu bearing. We are, accordingly, inclined to prefer the name for this plant as given in the British Pharmacopœia, *Myroxylon Pereiræ* Klotzsch. There is a difference of opinion as to the classification of this plant. Baillon and also Hartwich and Jama (*Schweiz. Woch. Chem. Pharm.*, 1909, xlvii, 641) consider that it is a variety of the *M. Balsamum.*

The term Balsam of Peru is a survival of the times when the products of the Spanish colonial coast were assembled at Callao, Peru, for shipment to Europe. This fact has caused Gane and Webster to assert that Balsam of Peru is misbranded under the Foods and Drugs Act in that it does not come from Peru. (*Drug Topics,* 1910, p. 4.)

Myroxylon Pereiræ is a tall tree with ash-colored bark which attains the height of 50 feet. At about 5 feet above ground the trunk divides into horizontal or slightly obliquely ascending branches which combine to form an egg-shaped crown. These bear alternate, imparipinnate leaves with the usually 5, at least 4, less frequently 6, coupled leaflets and an extra terminal one. The leaflets almost always are alternate along the midrib, oblong to oval-oblong in shape, acute at apex and rounded at the base. The blooming axillary twigs are marked by a scattering of point-shaped bright lenticels. Each of these terminates in a loose raceme of nodding flowers. Each of the flowers possesses a green cup-shaped slightly toothed calyx, a bluish-white, papilionaceous corolla, 10 stamens with white filaments and red anthers (the latter constituting the most showy portion of the flower) and a green pistil. The fruit is a yellowish-brown legume. This tree grows in Central America, in the State of San Salvador, upon the Pacific coast. It is found in the wild forests, singly or in groups, but the trees are owned by individuals. Charles Dorat states that it is never found at a greater height on the mountains than one thousand feet, that it begins to be productive after five years, and continues to yield for thirty years or more, and that the aroma of its flower is perceived at the distance of one hundred yards. The tree has been introduced into the island of Ceylon.

The balsam is collected within a small district denominated the Balsam Coast, extending from Acajutla to La Libertad. Early in November or December the bark is beaten on four sides of the trunk, so as to separate it from the wood without breaking it, intermediate strips being left sound, in order not to destroy the life of the tree. The bruised bark soon splits, or cuts are made in it. Five or six days after the beating the injured surface is set on fire, and about a week later the bark, if it has not fallen off spontaneously, is removed. The juice now begins to exude freely from the exposed wood, which the natives cover with rags. The latter, when saturated, are boiled in water in large jars, and the liquid allowed to stand, whereupon the water rises to the top, and is poured off, leaving the balsam, which is put into calabashes or bladders. Seven to ten days later a second flow of balsam occurs, and is secured as before. Subsequently the exposed parts are scraped or otherwise wounded, and a third balsam is obtained. These three grades of balsam are said to be known respectively as *Tagauzonte, balsamo de trapo, balsamo de contrapique.* The balsam is then taken for sale to the neighboring towns, where it is purified by subsidence and straining and put into jars or metallic drums for exportation. The destroyed bark is said to renew itself in two years, so that by care a tree can be worked for a long time; two pounds is stated to be the average yearly yield.

It is exported to the United States from San Julian, San Salvador, usually in tin canisters, and shows a whitish scum on the surface with more or less deposit which may be dissolved with the aid of heat.

A substance called *white balsam* (*Bálsamo blanco*) is procured from the fruit. This has been confounded with the balsam of Tolu, but is wholly distinct. It is of a semi-fluid or soft-fluid consistence, somewhat granular, and, on standing, separates into a white, resinous crystalline deposit, and a superior, transulcent more fluid portion. The odor, though quite distinct from that of the balsams of Tolu and Peru, is not disagreeable. Stenhouse in 1850 obtained from it a crystallizable resin, which he denominated *myroxocarpin.* (*P. J.*, x, 290.) Tschirch (*Harze und Harzbehälter,* 1900, p. 166) gives the compound the name *myroxoresene,* and the formula, $C_7H_{10}O$. Another substance obtained from the same tree, and much used in Central America, is a tincture of the fruit made by digesting it in rum. It is called *balsamito* by the inhabitants, and is used by them both internally and externally. Neither this nor the white balsam reaches the markets of this country.

Besides the official species, there are several allied trees which furnish products possessing more or less similar properties. The *M. peruiferum* L. fil. yields an oleoresin sometimes known as *Brazilian balsam.* It resembles Peru balsam but is harder and redder in color. A balsam is also derived from the *M. punctatum* Klotzsch. This tree is by some considered as identical with the *M. Toluiferum* which yields the Tolu balsam. The bark of this species has been used in Paraguay under the name of *quinoquino* as a remedy for wounds and ulcers.

From the pods of the related *Myrospermum frutescens* Jacq. which grows in Trinidad is prepared a tincture used as a lotion in rheumatic pains, and also from the incisions in the stem a balsam very similar to that of Tolu balsam. In bulk it is of a dark brown color, but in thin layers it is dark red. Its odor is smoky, feebly fragrant; its taste slightly pungent, leaving a choking, disagreeable, persistent feeling. It is entirely soluble in ether and in rectified spirits. It also mixes with castor oil in all proportions, and forms with carbon disulphide a clear, light brown solution with residue, also a deposit, in its chloroform solution, which becomes a powdery precipitate upon standing. At 17° C. its specific gravity is 1.031. Its general constitution is very similar to that of balsam of Peru, containing volatile oil, myroxylin, cinnamic and tannic acids, and resin. It is especially to be distinguished from Peru balsam by its behavior with sulphuric acid. When Peru balsam is treated with sulphuric acid, and cold water poured upon it, a beautiful violet color is imparted to the surface, and the whole mass has a bright shade. The same procedure yields with the oleo-balsam a gray mass. For further information, see *P. J.*, xv, 771.

Description and Physical Properties.—"A dark brown, viscid liquid, transparent, and appearing reddish-brown in thin layers. It has an agreeable, vanilla-like odor, and a bitter, acrid taste, with a persistent after-taste, and is free from stringiness or stickiness. It does not harden on exposure to air. The Balsam is nearly insoluble in water, but is soluble in alcohol, chloroform, and glacial acetic acid, with not more than an opalescence. It is only partly soluble in ether and in petroleum benzin.

"Specific gravity: 1.130 to 1.160 at 25° C. Water becomes acid to litmus paper when agitated with the Balsam. One Gm. of the Balsam forms a clear solution when shaken with a solution of 3 Gm. of chloral hydrate in 2 cc. of distilled water (*fixed oils*). Shake about 1 Gm. of the Balsam with 5 cc. of purified petroleum benzin, and warm the mixture on a water bath for ten minutes, adding a sufficient quantity of the solvent to replace the loss by evaporation. On evaporating 2 cc. of the benzin solution, no odor of oil of turpentine is noticeable (*turpentine*). Balsam of Peru does not show the presence of *rosin.* Dissolve about 1 Gm. of the Balsam, accurately weighed, in 100 cc. of neutral alcohol, add 1 cc. of phenolphthalein T.S., and titrate the solution with half-normal sodium hydroxide: the acid number thus obtained is not less than 56 and not more than 84. Mix about 3 Gm. of the Balsam, accurately weighed, with 30 cc. of sodium hydroxide T.S. in a separator, shake the mixture for a few minutes with 60 cc. of ether, and allow to stand until complete separation into two layers has taken place. Draw off the lower, aqueous layer and quickly filter the ethereal layer into a flask. Transfer 50 cc. of the ether filtrate (representing five-sixths of the weight of the Balsam taken) to a tared, conical flask, evaporate the ether, and dry the residue at 100° C. for thirty minutes. The weight of the residue of cinnamein so obtained corresponds to not less than 50 per cent. and not more than 60 per cent. of the weight of the Balsam represented by the 50 cc. of ethereal solution taken. Dissolve this residue in 25 cc. of alcohol, add 25 cc. of half-normal alcoholic potassium hydroxide, and heat the mixture carefully on a water bath for one-half hour, in a flask provided with a reflux condenser. Then add 1 cc. of phenolphthalein T.S., and titrate the excess of alkali with half-normal hydrochloric acid. The amount of half-normal alcoholic potassium hydroxide consumed corresponds to a saponification value for the cinnamein of not less than 235 and not more than 238." *U. S.*

"A viscid liquid, in bulk nearly black but in thin layers deep orange-brown or reddish-brown and transparent. Agreeable balsamic odor; taste acrid, leaving when swallowed a burning sensation in the throat. Insoluble in *water;* soluble in *chloroform.* 1 volume is soluble in 1 volume of *alcohol* (90 per cent.), but on the further addition of 2 or more volumes of the *alcohol* the mixture becomes turbid. Specific gravity between 1.140 and 1.158. Does not diminish in volume when shaken with an equal bulk of *water* (absence of ethylic alcohol). When tested by the following method it yields not less than 57 per cent. of cinnamein, the saponification value of which is not less than 235:—Dissolve 1 gramme of the Balsam in 30 millilitres of *ether* and shake in a separating funnel with two successive quantities of 20 and 10 millilitres of *N/2 solution of sodium hydroxide.* Separate the alkaline solution, mix and shake with 10 millilitres of *ether.* Draw off and reject the alkaline solution. Add the second ethereal solution to that previously obtained. Wash the mixed ethereal solution with two successive quantities of 5 millilitres of *water.* Transfer the ethereal solution thus washed to a tared wide-mouthed flask, evaporate at a gentle heat until the odor of ether has disappeared, add 1 millilitre of *absolute alcohol,* dry at 100° C. for half an hour, and weigh. The weight of the cinnamein thus obtained is not less than 0.57 gramme. To this residue add 20 millilitres of *N/2 alcoholic solution of potassium hydroxide* and 20 millilitres of *alcohol* (90 per cent.). Attach a reflux condenser, boil for half an hour, and tirate back with *N/2 solution of sulphuric acid, solution of phenolphthalein* being used as indicator. Each gramme of the residue thus treated requires not less than 8.4 millilitres of the alkaline solution for complete saponification (corresponding to a saponification value of not less than 235)." *Br.*

Constituents.—Balsam of Peru is a very complex mixture, and the composition is doubtless somewhat variable. Parry (*Chemistry of Essential Oils and Artificial Perfumes,* 1919) states that the principal constituents are *benzyl cinnamate,* $C_9H_2O_2.C_7H_7$ (*cinnamein*), *benzyl benzoate, benzyl alcohol, cinnamyl cinnamate* (*styracin*) and esters of an alcohol called *peruresinotannol.*

Thoms discovered a constituent called by him *peruviol* ($C_{13}H_{22}O$), which Parry believes to be identical with *nerolidol.* Tschirch states that in the sample of Peru balsam investigated by him benzyl benzoate was the main constituent, but small amounts of benzyl cinnamate were also present, and he considers that the relative proportions of the two esters may vary greatly in different samples of the balsam. The odor of the balsam Tschirch considers to be due to the *peruviol.*

The volatile oil from Balsam of Peru, according to Parry, has the following characteristics: Sp. gr. 1.10 to 1.125; optical rotation, +0 to +3; refractive index, 1.5710 to 1.5800; acid number, 25 to 48; ester number, 200 to 254. This oil is said to contain free benzoic and cinnamic acids, benzyl cinnamate, and benzyl benzoate, farnesol, dihydrobenzoic acid, and vanillin. The resinous constituent of Peru balsam, which is precipitated by hydrochloric acid from the alkaline solution of the balsam, was found by Tschirch to be the peruresinotannol referred to above, combined with cinnamic acid.

Formerly Peru balsam was much adulterated with castor oil, copaiba, turpentine, gurjun balsam, etc., but during recent years the rigid inspection has excluded most of the grossly adulterated samples from importation. Dodge and Sherndal (*J. A. Ph. A.,* 1915, p. 1222) assert that the assay for peruviol is the most reliable means for determining the authenticity of the balsam and give a method therefore. Heiduschka and Rheinberger (*Ph. Centralh.,* 220) give a method for determining the bromine value and state that a pure balsam shows a value of 17 while the adulterated samples show considerably higher values.

A synthetic substitute known as *synthetic balsam of Peru,* or *Perugen,* made by mixing benzyl benzoate with storax, benzoic and Tolu balsams so closely resembles the genuine that Enz (1913) states that the only constants useful for its detection are the acid number, iodine number, isolated cinnamein nitric acid reaction, and behavior in contact with benzin; the other pharmacopœial constants are of no value. Cæsar and Soretz state that the characteristic odor and taste of the natural balsam are absent in the substitute.

A color test to distinguish true Peru balsam from the factitious variety is as follows: One drop of Peru balsam is shaken with 5 cc. of petroleum benzin, and to 2.5 cc. of this liquid 5 cc. of ether is added. Sulphuric acid is then added, drop by drop, until from 10 to 15 drops have been added. Genuine Peru balsam gives beautiful violet to cornflower blue color in the lower layer, while the artificial products give either no color or very different shades.

For additional tests of purity of Peru balsam, see van Itallie, *Ph. Wb.,* 1920, lvii, 1383; also *Proc. A. Ph. A.,* 1894, 903; and 1895, 866; *D. C.,* 1898, 60.

Grote's test consists in shaking 3 drops of balsam with 2 cc. of official ammonia water; if, after standing, the mixture solidifies, rosin or other adulterant is present; benzoin, storax, and certain other substances cannot be detected by this test. (*A. J. P.,* 1881, 302, 361.)

Cocking and Kettle (*P. J.,* 1918, p. 90) propose an assay for the valuation of Peru balsam and give figures obtained upon various samples.

Uses.—Balsam of Peru is useful internally as a stimulating expectorant in *asthma* and *chronic bronchitis,* especially when of tuberculous origin. Although not so agreeable as balsam of Tolu it is much more active. Externally it affords a valuable stimulating dressing in indolent *ulcers* and local *tuberculosis* of the skin, bone, larynx, etc. It has also been highly lauded by Malannik (*M. M. W.,* 1912) as a first dressing for military *wounds.* He asserts that it is not only bactericidal of itself but that it stimulates the local resistance of the tissues and and that it exercises a valuable protective action. Extensive erythema has followed its local application. (Hazen, *J. A. M. A.,* 1910, liv.) Internally it is best administered in emulsion.

Dose, five to fifteen minims (0.3–1 cc.).

Off. Prep.—Mistura Oleo-balsamica, *N. F.;* Solutio Mastiches Chloroformica Compositura, *N. F.*

BAPTISIA. N. F.

BAPTISIA Baptis. [Wild Indigo]

"Baptisia is the dried root of *Baptisia tinctoria* (Linné) R. Brown (Fam. *Leguminosæ*). Baptisia contains not more than 10 per cent. of its stem bases, overground parts or foreign organic matter." *N. F.*

Wild Indigo; *N. F.* Indigo sauvage, *Fr.;* Baptisie, *G.*

This is an indigenous, perennial herb, abundant throughout the Eastern United States, in woods and dry, barren uplands. Its leaves are trifoliate with cuneate-obovate leaflets. Its inflorescence is a short raceme of yellow flowers. Its fruit is a subcylindric, many seeded legume.

Description and Physical Properties.—"*Unground Baptisia.*—Fleshy, 0.5 to 4 cm. thick, usually cut into elongated cylindrical pieces, the crown 5 to 8 cm. thick, more or less warty and marked by stem scars; outer surface dark brown; usually longitudinally wrinkled, the thicker pieces covered with a soft friable corky layer, bearing few branching rootlets; fracture tough the fractured surface whitish; bark section radially striate, wood section inconspicuously radiate, porous. Nearly odorless, the bark bitter and acrid, the wood nearly tasteless.

"*Powdered Baptisia.*—Light grayish; starch grains numerous, rounded, simple or 2- to 4-compound, up to 0.016 mm. in diameter, the larger grains sometimes with a cleft through the center; tracheæ up to 0.090 mm. in diameter and with bordered pores; numerous fibers, long, thick-walled, non-porous, more or less lignified and up to 0.024 mm. in width; fragments of medullary ray tissue composed of cell with lignified walls and numerous simple pores; groups of parenchyma, many of the cells filled with starch; few epidermal and cork cells with brownish walls." *N. F.*

Baptisia contains, according to Gorter (*A. Pharm.*, 1897, ccxxxv, p. 321), a non-toxic glucoside *baptisin,* and an alkaloid *baptitoxine;* the latter appears to be identical with cytisine (see *Cytisus,* Part II). There is present also a blue dye which has been used as a substitute for indigo, to which it is, however, greatly inferior.

Uses.—Baptisia is used both locally and internally in the treatment of various septic conditions. Thus, it has been recommended as a gargle in ulcerative *pharyngitis,* as an application to foul *ulcers* and internally in the treatment of various infectious *fevers.* Its value, however, is open to question. In over-doses it acts as an emetic and cathartic.

Dose, from five to twenty grains (0.3–1.3 Gm.).

Off. Prep.—Dentifricium, *N. F.;* Fluidextractum Baptisiæ, *N. F.*

BARBITALUM. U. S. (Br.)

BARBITAL Barbital. [Diethylbarbituric Acid, Barbitone]

"Diethylmalonylurea [$CO(HN.CO)_2C(C_2H_5)_2$]." *U. S.*

"Barbitone, $C_8H_{12}N_2O_3$, may be obtained by the interaction of the diethyl ester of malonic acid, and carbamide." *Br.*

Barbitonum, *Br.;* Acidum Diaethyl-barbituricum, Diethyl Malonyl-urea, Malonurea; Veronal; Veronalum, *Fr. Cod.;* Malourea.

This compound is chemically related to urea. It is prepared by the condensation of diethylmalonic ester and urea in the presence of sodium. The sodium salt is first produced and the acid is then set free by the hydrochloric acid. In another method diethyl cyano-acetic ester is heated with sodium and urea in absolute alcohol solution. This produces iminodiethylmalonylurea which is heated with hydrochloric acid in weak solution which hydrolizes it to barbitone. In a third method diethyl malonyl chloride and urea are heated together to form barbitone by direct combination, hydrochloric acid being evolved.

Description and Physical Properties.—"Colorless or white crystals, or a white crystalline powder. It is odorless, has a slightly bitter taste, and is stable in the air. One Gm. of Barbital is soluble in 130 cc. of water, 14 cc. of alcohol, 75 cc. of chloroform, and in 35 cc. of ether, at 25° C. One Gm. is soluble in 13 cc. of boiling water. It is also soluble in acetone, and in ethyl acetate.

"Barbital melts between 187° and 190° C. A saturated aqueous solution of Barbital is acid to litmus paper. A saturated aqueous solution of Barbital yields with mercuric nitrate T.S. a white precipitate which is soluble in an excess of the reagent. When Barbital is boiled with an excess of sodium carbonate T.S. for thirty minutes, or when fused with sodium hydroxide, it is decomposed with the evolution of ammonia.

"The ash from 0.5 Gm. is negligible. A solution of 0.2 Gm. of Barbital in 2 cc. of sulphuric acid is colorless (*readily carbonizable substances*). Another portion of 0.2 Gm. of Barbital is not colored by shaking with 2 cc. of nitric acid." *U. S.*

It is described by the British Pharmacopœia as: "A white crystalline powder. Inodorous; taste faintly bitter. Slightly soluble in cold *water,* the solution being neutral to *litmus;* more soluble in hot *water,* and in *alcohol* (90 per cent.); freely soluble in aqueous solutions of the alkalies. Melting point 191° C. When fused with a caustic alkali, ammonia is evolved; and, when the cooled residue is dissolved in *water* and the solution acidified with *diluted sulphuric acid,* carbon dioxide is liberated, and a characteristic odor resembling that of fatty acids is developed. A few drops of *solution of mercury nitrate* added to 25 millilitres of a saturated aqueous solution acidified with *nitric acid,* produces a gelatinous precipitate. No appreciable ash." *Br.*

Barbital may be detected in the urine of persons taking it, by treating the urine with lead acetate solution, filtering and shaking out with ethyl acetate.

Barbitone unites with various bases to form salts, many of which are soluble. One of these, the sodium salt, is official.

Uses.—Barbital is absorbed with moderate rapidity through the intestinal mucous membrane, its effects generally being manifest in about thirty minutes after its ingestion. It is eliminated solely through the kidneys, although Bachem (*A. E. P. P.*, 1910, lxiii, p. 228) believes that a considerable proportion is destroyed in the system. After small doses it is practically all eliminated within twelve hours, but when large quantities have been taken it may be retained in the system for long periods of time and when used repeatedly tends to accumulate in the body. In small doses it produces in the lower animals usually no symptoms but sleep, although after even moderate quantities the blood pressure may be reduced. In large doses it causes decided fall in the blood pressure through dilatation of the abdominal blood vessels, muscular weakness in the posterior extremities without loss of reflex, muscular fibrillation which may be sufficiently violent to simulate convulsions, diminution of respiration, and fall of bodily temperature. After very large poisonous doses there is loss of pain perception and diminution of reflex. (Roemer, *J. P. Ex. T.*, 1911, vi, p. 241.)

Barbital is a powerful somnifacient useful in many forms of *agrypnia* when not due to pain. Its effects are generally manifest in from a half to one hour and last over the greater portion of the night. Generally the patients awake without showing any symptoms of veronal action, but House (*T. G.*, May, 1913) reports that occasionally patients complain of slight vertigo in the morning, which he attributes to the reduction in blood pressure.

Diethylbarbituric acid has also been used as a general sedative in *hysteria, chorea,* and especially in *sea-sickness.* Hildebrandt (*Zeitschrift für ärztliche Fortbildung,* 1913, No. 12, p. 366) recommends it for the relief of *night sweats* in pulmonary tuberculosis.

While in the proper doses barbital is usually a satisfactory somnifacient it is by no means the harmless drug that it has been sometimes considered. A considerable number of fatal cases of poisoning have been reported (see *P. J.*, 1911, lxxxvi, p. 235, and Boenheim, *Med. Klin.*, 1921, xvii, p. 1263). While in most of these cases the dose has been very large—more than 5 Gm. (75 grains), Wilcox (*B. M. J.*, 1913, ii, p. 663) states that fifteen grains has proven fatal. On the other hand, according to Gautier (*R. M. S. R.*, 1918, xxxviii, 641), recoveries are known after doses of 10 Gm. There have also been reported a number of cases of veronal addiction.

There are apparently a considerable number of people who have marked idiosyncrasy against the drug, in whom even doses as small as 0.3 Gm. (5 grains) produce violent eruptions of the skin, usually scarlatinaform in character, often accompanied with considerable fever and followed by desquamation.

In ordinary cases of *barbital poisoning* the most striking symptom is profoundly stuporous sleep from which, in severe cases, no external excitation can arouse the patient. The pupils are neither dilated nor contracted, the respiration is usualy quiet and, although somewhat slower than normal, not much slower than is often seen in natural sleep. In many cases there is marked fever. There is frequently also a manifest tendency towards pneumonia or pulmonary edema. The treatment, after washing out of the stomach, is purely symptomatic.

The *dose* is from five to ten grains (0.32–0.65 Gm.), stirred up in water or enclosed in a gelatin capsule. It should not be given in pill form.

BARBITALUM SOLUBILE. U. S.

SOLUBLE BARBITAL Barbital Sol.

BARBITAL SODIUM. [Sodium Diethylbarbiturate, [Sodium Diethylmalonylurea Barbitone Sodium]

"Soluble Barbital, when dried to constant weight at 100° C., contains not less than 98.5 per cent. of $CO(NaN.CO)(HN.CO)C(C_2H_5)_2$." *U. S.*

Veronal Sodium; Veronal Soluble; Medinal; Sodii Diæthyl barbituras; Barbital Sodium.

This compound is the mono-sodium salt of diethyl-barbituric acid and represents 89.3 per cent. of barbital. Its chief advantage is its solubility in water.

Barbital sodium is officially described as follows:

Description and Physical Properties.—"A white powder. It is odorless, has a bitter taste, and is stable in the air. One Gm. of Soluble Barbital is soluble in about 5 cc. of water at 25° C., and in 2.5 cc. of boiling water. It is slightly soluble in alcohol and is insoluble in ether.

The barbital obtained in the assay melts between 187° and 190° C., and responds to the other identity tests given under *Barbitalum.* An aqueous solution of Soluble Barbital is alkaline to litmus paper. The addition of diluted hydrochloric or sulphuric acid to an aqueous solution of the salt (1 in 20) produces a precipitate of barbital.

"A solution of 0.2 Gm. of the salt in 2 cc. of sulphuric acid is colorless (*readily carbonizable substances*). Ten cc. portions of an aqueous solution of Soluble Barbital (1 in 100) acidulated with a few drops of nitric acid yield no opalescence at once on the addition of a few drops of silver nitrate T.S. (*chloride*), and no turbidity within one minute on the addition of 1 cc. of barium chloride T.S. (*sulphate*). An aqueous solution of the salt meets the requirements of the test for *heavy metals.* When dried to constant weight at 100° C., it loses not more than 1 per cent. (*water*). Shake 0.5 Gm. of Soluble Barbital with 20 cc. of dehydrated ether for ten minutes, filter, evaporate the ether, and dry at 100° C.: the weight of the residue does not exceed 0.003 Gm. (*uncombined barbital*).

"**Assay**—Dissolve about 1 Gm. of Soluble Barbital, previously dried at 100° C. and accurately weighed, in 10 cc. of distilled water in a separator, add to the solution 15 cc. of diluted hydrochloric acid, and extract the liberated barbital by shaking successively with eight portions of 25 cc. each of ether. Evaporate the combined ether solutions at as low a temperature as possible, and dry at 100° C. The weight of the barbital so obtained is not less than 88 per cent. and not more than 90 per cent. of the dried Soluble Barbital. About 0.2 Gm. of the barbital, obtained in the assay, leaves a negligible residue upon ignition." *U. S.*

Because of its freer solubility, this drug acts more promptly than barbital. It may be used for the same purposes as veronal. Munk (*Med. Klin.*, iv, p. 1834) has also employed it hypodermically in the form of a ten per cent. solution. The injections are somewhat painful, because of the large volume of the injection.

Dose, from five to fifteen grains (0.3–1.0 Gm.).

BARII SULPHAS. U. S.

BARIUM SULPHATE

"Barium Sulphate [$BaSO_4$], freed from soluble barium salts. *Caution.—In prescribing Barium Sulphate the title should never be abbreviated, to avoid confusion with the poisonous barium sulphide or sulphite.*" *U. S.*

Sulphate of Barytes, Synthetic Barytes, Precipitated Barium Sulphate, Artificial Heavy Spar, Permanent White, Baroselenite, Terra Alba, Constant White, Terra Ponderosa, Baric Sulphate, New White, Mineral White, Snow White; Baryte Sulfate, Baryte Sulphurique, Blanc Fixé, *Fr.*; Barytspath Schwefelsaurer Baryt, *G.*; Baryum Sulfuricum.

A native barium sulphate, known as *barytes* or *heavy spar,* is the most abundant of the natural salts of barium and is mined extensively in the United States. The medicinal salt, however, is usually produced by precipitation in order to provide a purer article. The native variety of barium sulphate is a heavy, lamellar, brittle mineral, usually translucent, sometimes transparent or even opaque; color white or pale pink. It sometimes occurs in flat rhombic prisms. Artificial barium sulphate, obtained as a by-product in many chemical manufactures, is much used in the arts as a pigment, and as a weighting and filling material in paper manufacturing, etc. When prepared with especial care and subsequently purified it forms one of the most insoluble and inert substances known to chemistry, and is especially valuable in the outlining of the alimentary tract for X-ray work.

Description and Physical Properties.—"A fine, white, odorless, tasteless and bulky powder, free from grittiness. Barium Sulphate is insoluble in water, in organic solvents, and in aqueous solution of acids and alkalies.

"Mix 0.5 Gm. of Barium Sulphate with 2 Gm. each of anhydrous sodium carbonate and anhydrous potassium carbonate, heat the mixture in a crucible until fusion is complete, treat the resulting fused mass with hot water, and filter. Acidulate a portion of the filtrate with hydrochloric acid, and add 1 cc. of barium chloride T.S.: a white precipitate forms. Dissolve in acetic acid a portion of the well-washed precipitate, obtained in the preceding test: the solution responds to the reactions for barium.

"Boil 10 Gm. of Barium Sulphate with a mixture of 10 cc. of diluted hydrochloric acid and 90 cc. of distilled water for ten minutes, and add sufficient distilled water to restore the original volume. During boiling there should be no evolution of hydrogen sulphide, recognizable by the darkening of lead acetate paper exposed to the vapor (*sulphide*). Cool the mixture, and filter through paper which has been previously washed with a solution of 10 cc. of diluted hydrochloric acid and 90 cc. of distilled water, returning the first portions if necessary until a perfectly clear filtrate is obtained. Evaporate 50 cc. of the filtrate to dryness on a water bath, add two drops of hydrochloric acid and 10 cc. of hot distilled water. Filter through acid-washed paper, wash with 10 cc. of hot distilled water, and evaporate the combined filtrate and washings to dryness in a tared dish on a water bath. The residue, when dried to constant weight at from 100° to 110° C., should not be fine, white, odorles, tasteless and bulky powder, more than 0.3 per cent. (*limit of acid-soluble substances*). Treat this residue with 10 cc. of distilled water, filter the solution through a filter previously washed with a mixture of 10 cc. of diluted hydrochloric acid and 90 cc. of distilled water, and add 0.5 cc. of diluted sulphuric acid: no turbidity should develop within one-half hour (*soluble barium salts*). Boil 1 Gm. of Barium Sulphate with a mixture of 3 cc. of nitric acid and 5 cc. of distilled water during five minutes. Filter, and add to the warm filtrate an equal volume of ammonium molybdate T.S.: no yellow precipitate is formed (*phosphate*). Digest 1 Gm. of Barium Sulphate with 20 cc. of distilled water during five minutes: the latter remains neutral to litmus paper (*free acid or alkali*). Boil 5 Gm. of Barium Sulphate with 50 cc. of diluted acetic acid, and filter while hot: the filtrate meets the requirements of the test for *heavy metals.* Triturate 2 Gm. of Barium Sulphate with 5 cc. of concentrated hydrochloric acid, and add 10 cc. of a freshly made, saturated solution of stannous chloride: no dark coloration occurs with one-half hour (*arsenic*)." *U. S.*

Uses.—Barium sulphate is used in medicine solely because of its opacity to the X-ray. Because of this property and its insolubility it is of great value in making roentgenograms of internal cavities, especially the alimentary canal. The advantages claimed for it over the bismuth salts, which are used for similar purposes, are its relative inexpensiveness and that slightly smaller quantities are required. For X-ray examination of the alimentary canal it is usually given suspended in water by some mucilaginous substance. The following formula for this purpose has been suggested: barium sulphate 50 Gm., corn flour 5 Gm., sugar 5 Gm., cocoa 7 Gm., water 150 cc. (*A. J. P.*, 1918, xc, 284).

Toxicology.—It should be remembered that the soluble barium salts are actively poisonous. The safety of barium sulphate in such large doses is due to its insolubility. Karaoglanow (*Pharm. Weekblad.*, 1918, lv, 47) has found that from 2.5 milligrammes to 4.3 milligrammes of barium sulphate dissolve in a liter of water, according to the degree of fineness of the powder. The same author has also shown that the solubility is decreased by the presence of the sulphuric ion and increased by nitric or hydrochloric acid. The exact lethal dose of barium is not definitely known but Aloy and Kournet (*J. P. C.*, 1918, xvii, p. 76) have found that the barium chloride is fatal to dogs in doses by mouth of from 0.025 to 0.09 Gm. per kilo of body weight which would correspond to approximately 27 to 98 gr. for the ordinary adult man (1.7 to 6.3 Gm.). A number of fatal cases of poisoning by other salts, especially the sulphide, of barium, which have been mistakenly used for X-ray work have been recorded. In a case reported by Bensaude and Antoine (*B. Hôp. Par.*, 1919, xliii, 369), the patient was seized immediately after drinking the suspension of barium and was dead in 10 minutes. In other cases the appearance of symptoms has been delayed as much as an hour and death until the following day. The characteristic symptoms are; burning pain in the stomach, nausea and vomiting, the latter often bilious followed by diarrhea with violent abdominal cramps. Post-mortem examination shows intense congestion of the alimentary canal, with sometimes minute hemorrhages, also congestion of the liver and kidney.

The proper *treatment* consists in the immediate administration of large quantities of magnesium sulphate followed by repeated washings of the stomach. Unfortunately, however, many of these cases occur where medical attention is not to be had immediately and the progress of the poisoning is so rapid that the patient is dead before proper aid can reach him.

In view of the considerable number of fatalities that have been recorded from the substitution of barium sulphide for the sulphate we would urge—upon the medical profession: 1. That no abbreviation be used in prescribing the drug; the official name should be written out in full, *Barii Sulphatis.* 2. The addition of sulphuric acid to the suspension which would tend to increase the insolubility of the drug—and on the pharmacist: 3. That in labelling all stock bottles he avoid the use of the abbreviation so common as Bar. Sulph.; like the physician's prescription his label should bear the official name written out in full. 4. That he never dispense large amounts of barium sulphide without definite information of the purpose for which it is to be used. 5. If he carries barium sulphide in stock it be kept on the poison shelf. 6. That barium sulphide, which may be called for as a depilatory, be labeled "Poison."

BELÆ FRUCTUS. Br.

BAEL FRUIT

"Bael Fruit is the fresh half-ripe fruit of Ægle Marmelos, *Correa.*" *Br.*

Fructus Baël, Béla; Bael fruit, Indian Bael, Bhel, Bengal Quince; Marmelos de Benguala, Cirifole, Beli; Indische Quitten, Marmelosbeeren, Marmelosfrüchte, *G.*

The so-called *Bengal quince* is a rather large tree (Fam. *Rutaceæ*), extensively cultivated in India, with an erect stem, few and irregular branches, an ash-colored bark, strong, very sharp, axillary thorns, single or in pairs, trifoliate leaves and large white flowers. The fruit is a berry of delicious flavor, of about the size of a large orange, with a hard, smooth, greenish shell, and from ten to fifteen loculi containing besides the compressed, wooly seeds a large quantity of exceedingly tenacious mucilage, which when dried is hard and transparent. "Fruit about 7 or 8 cm. in diameter, globular, ovoid or pyriform, grayish or yellowish-brown. Outer surface hard, nearly smooth. Rind about three millilitres in diameter, and adherent to a pale-reddish juicy pulp in which are ten to fifteen cells, each containing several woolly seeds. Faint aromatic odor; taste mucilaginous, acidulous, and slightly astringent." *Br.* The mucilage about the seeds is applied to various purposes in the arts, on account of its viscid properties. The rind is used in dyeing. The flowers are deemed refrigerant by the native physicians. The fresh leaves yield by expression a bitterish and somewhat pungent juice, which, diluted with water, is occasionally used in the early stage of catarrhal and other *fevers.* The bark of the stem and root is thought to possess febrifuge properties.

The difficulty of obtaining bael in England is said to have led to the substitution for it of *mangosteen,* the fruit of *Garcinia Mangostana* L. (Fam. *Guttiferæ*). This is in irregular fragments of the rind, without adhering pulp. The pieces are convex, three or four lines or more in thickness, externally covered with a smooth, deep reddish-brown, easily separable coating, and internally pale reddish-brown or reddish-yellow, smooth, with projecting vertical lines. Another substitute which has appeared is the wood apple, *Feronia Elephantum* Correa (Fam. *Rutaceæ*).

The most important constituent of bael fruit appears to be its mucilage. It also contains pectin, sugar and traces of tannic acid and of an essential oil (see Badakow, *Ap. Ztg.*, 1894, p. 773).

Uses.—Bael fruit has been used in India in the treatment of *diarrhea* and *dysentery* for many years. It is also asserted to have laxative properties. Whether it has any real therapeutic activity is, at present, very doubtful. The *decoction,* two ounces of dried fruit in a pint of water boiled down to four fluidounces, is used in *doses* of one to two fluidounces (30–60 cc.) every two to six hours.

Off. Prep.—Extractum Belæ Liquidum, *Br.*

BELLADONNÆ FOLIA. U. S., Br.

BELLADONNA LEAVES Bellad. Fol. [Belladonnæ folium P. I.]

"Belladonna Leaves consist of the dried leaves and tops of *Atropa Belladonna* Linné (Fam. *Solanaceæ*). Belladonna Leaves yield not less than 0.3 per cent. of the alkaloids of Belladonna Leaves, and contain not more than 3 per cent. of their stems over 10 mm. in diameter, and yield not more than 3 per cent. of acid-insoluble ash." *U. S.*

"Belladonna Leaves are the leaves of Atropa Belladonna, *Linn.*, collected when the plant is in flower, and dried." *Br.*

Folia (s. Herba) Belladonnæ, Black Cherry, Poison black cherry, Deadly Nightshade, Doft-berry, Dwayberry, Devale (Dwale), Mad, Great Morel, Mekilwort; Feuilles de Belladone, *Fr.*; Folia Belladonnæ, *P. G.*; Belladonnablätter, Tollkirschen-Blätter, Wolfskirschen-Blätter, Tollkraut, *G.*; Foglie di belladonna, *It.*; Hoja de belladonna, *Sp.*

Off. Prep.—Emplastrum Belladonnæ, *U. S.* (from extract); Extractum Belladonnæ, *U. S.*; Extractum Belladonnæ Siccum *Br.*; Fluidextractum Belladonnæ Foliorum, *U. S.*; Tinctura Belladonnæ, *U. S.* (*Br.*); Unguentum Belladonnæ, *U. S.* (from extract); Pilulæ Aloes et Podophylli Compositæ (from Pilular Extract), *N. F.*; Pilulæ Aloini Compositæ (from Pilular Extract), *N. F.*; Pilulæ Aloini, Strychninæ et Belladonnæ (from Pilular Extract), *N. F.*; Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ (from Pilular Extract), *N. F.*; Pilulæ Antidyspepticæ (from Pilular Extract), *N. F.*; Pilulæ Laxativæ Compositæ (from Pilular Extract), *N. F.*

BELLADONNÆ RADIX. U. S., Br.

BELLADONNA ROOT Bellad. Rad.

"Belladonna Root is the dried root of *Atropa Belladonna* Linné (Fam. *Solanaceæ*). Belladonna Root yields not less than 0.45 per cent. of the total alkaloids of Belladonna Root, and contains not more than 10 per cent. of its stem bases and woody crowns, and not more than 2 per cent. of other foreign organic matter, and yields not more than 4 per cent. of acid-insoluble ash." *U. S.* "Belladonna Root is the root of Atropa Belladonna, *Linn.*, collected in the autumn and dried." *Br.*

Racine de Belladone, Belladone, *Fr.*; Gemeine Tollkirsche, Wolfskirschen-Wurzel, *G.*; Radice di Belladonna, *It.*; Raiz de Belladona, Belladama, *Sp.*

The belladonna, or *deadly night-shade* (*Atropa Belladonna*) is an herbaceous perennial, with a fleshy, creeping root, from which rise several erect, round, purplish, branching stems, to the height of about three feet. The leaves, which are attached by short footstalks to the stem, are in pairs of unequal size, oval, pointed, entire, of a dusky green on their upper surface, and paler beneath. The flowers are large, bell-shaped, pendant, of a brownish-purple color, with solitary peduncles, rising from the axils of the leaves. The fruit is a roundish berry with a longitudinal furrow on each side, at first green, afterwards red, ultimately deep purple and containing, in two loculi, numerous seeds and a sweetish violet-colored juice. The calyx adheres to the base of the fruit.

The plant is a native of Central and Southern Europe, where it grows in shady places, along walls, and amidst rubbish, flowering in June and July, and ripening its fruit in September. It grows vigorously under cultivation in England, France and the United States. During the past few years there has been very great interest in the cultivation of belladonna in the United States. The results of all experiments show that a high grade of belladonna can be grown in this country. (Consult Borneman, *A. J. P.*, 1909, p. 1; Miller, *A. J. P.*, 1913, p. 291; Carr, *Ibid.*, 1913, p. 487; Sievers, *A. J. P.*, 1914, p. 483, also 1917, lxxxix, 203; Newcomb, *A. J. P.*, 1915, p. 1; Kock, *J. A. Ph. A.*, 1919, p. 390.) Plants cultivated in California are very rich in active constituents. The yield per acre of stems and leaves is somewhat less than one ton. The experiments in California seemed to show that the alkaloidal contents of belladonna stems is equal to that of the leaves, ranging from 0.51 to 0.82 per cent. of total alkaloids. (*Pacific Pharmacist*, 1909; 1910, p. 295.) Belladonna leaves grown in the shade are uniformly larger, though somewhat thinner. It is quite likely that the percentage of alkaloids can be increased through selection. (*A. J. P.*, 1914, p. 483, and 1917, lxxxix, 254.) All parts of it are active. The leaves and roots are directed by the United States and British Pharmacopœias, the latter including the branches, which, if young, are probably not less efficient. The leaves should be collected in June or July, when the plant is in flower, the roots in the autumn or early in the spring, and from plants three to four years old. Leaves which have been kept long should not be used, as they undergo change through absorption of atmospheric moisture, emitting ammonia, and probably losing a portion of their active nitrogenous matter. Sievers (*A. J. P.*, 1916, lxxxviii, 193) has found that no relation exists between the appearance of the leaves and the percentage of alkaloid. He found the amount of alkaloid in leaves of cultivated plants varied from 0.30 to 0.76 per cent. Specimens which contain much stem or are musty should always be rejected, as weak in active principle. Holmes has found in the English market the root of *Medicago sativa* used as an adulterant. (*P. J.*, 1882.)

Both herb and root drugs are obtained for the most part from plants cultivated in the United States, Central Europe and England.

Description and Physical Properties.—"*Unground Belladonna Leaves.*—Usually matted together, crumpled or broken; leaves mostly light green, from 5 to 20 cm. in length, and from 4 to 12 cm. in width, broadly ovate, apex acute, margin entire, narrowed into the petiole, with few hairs, the latter more abundant along the veins, and numerous whitish dots (crystal cells) visible with a lens; stems more or less hollow and flattened, finely hairy when young; flowers with campanulate corolla, yellowish-purple, becoming faded, usually subtended by the calyx; fruits nearly globular, green to brown or purplish-black with numerous, flattened somewhat reniform seeds, up to 2 mm. in width; odor slight, somewhat tobacco-like when moistened; taste somewhat bitter and acrid.

"*Structure.*—Leaves of simple structure; epidermis with wavy vertical walls and distinctly striated cuticle; stomata more numerous on the lower surface and usually with 3 neighboring cells; non-glandular hairs 2- to 6-celled; glandular hairs, short-stalked with 1- to many-celled heads; crystal cells large, filled with microcrystalline calcium oxalate, numerous in the mesophyll. Stem with long, thin-walled, slightly lignified bast, crystal cells and a few hairs. Pollen grains narrow ellipsoidal, with three meridional furrows. Seed epidermis with convolute, thickened cell walls.

"*Powdered Belladonna Leaves.*—Green to brownish-green in color. The following are among the elements of identification: the separate microcrystals, the dark gray crystal cells, the cuticular striping of the epidermal cells, the tracheæ with bordered pores, the bast- and wood-fibers of the stem, and, rarely, the hairs and pollen grains.

"In Belladonna Leaves rosette aggregates of calcium oxalate are absent (*stramonium leaves*). In Belladonna Leaves raphides are absent (*phytolacca leaves*).

"**Assay.**—Proceed by Type Process B, using 10 Gm. of Belladonna Leaves in fine powder, ether-chloroform mixture for percolating the drug, and chloroform as the immiscible solvent for extracting the alkaloid from the aqueous liquid. Determine the alkaloids volumetrically. Each cc. of tenth-normal sulphuric acid corresponds to 0.02893 Gm. of the alkaloids of Belladonna Leaves (Proximate Assays)." *U. S.*

"Eight to twenty centimetres long, broadly ovate, acute, entire, glabrous or nearly so. Transverse section exhibits bi-collateral vascular bundles; mesophyll contains numerous cells filled with very minute crystals of calcium oxalate; epidermal cells of both surfaces possess a delicately striated cuticle. Yields not less than 0.30 per cent. of alkaloids when assayed as directed below." *Br.*

The roots are described as follows:

"*Unground Belladonna Root.*—Cylindrical or tapering, sparingly branched, often split longitudinally or broken transversely; from 0.5 to 4 cm. in thickness; light grayish-brown externally, nearly white internally; somewhat wrinkled longitudinally and the soft periderm frequently abraded; fracture short, mealy and emitting a puff of dust consisting chiefly of starch grains; nearly odorless when dry, but characteristic when moistened; taste sweetish, then bitterish and acrid.

"*Structure.*—Cork, a few layers of thin-walled cells; large crystal cells, filled with microcrystalline calcium oxalate, and relatively numerous in the younger roots, scattered through the abundant, starch-bearing parenchyma of the bark and wood; large porous or reticulate tracheæ in scattered groups and, in the older roots, associated with wood-fibers; cambium layer conspicuous; the medullary rays 1 to 5 cells wide.

"*Powdered Belladonna Root.*—Ash-gray to light brown; starch grains numerous, simple and compound, the single grains up to 0.030 mm. in diameter and with a distinct somewhat excentric hilum, the polarizing bands increasing in distinctness in direct ratio to the size of the grains; numerous sphenoidal microcrystals from 0.003 to 0.010 mm. in length; fragments of tracheæ and wood-fibers few; long, thin-walled, slightly lignified bast-fibers from belladonna stem very few. Old fibrous roots contain an excess of lignified tissue.

"**Assay.**—Proceed by Type Process B, using 10 Gm. of Belladonna Root in fine powder, ether-chloroform mixture for percolating the drug, and chloroform as the immiscible solvent for extracting the alkaloids from the aqueous liquid. Determine the alkaloids volumetrically. Each cc. of tenth-normal sulphuric acid corresponds to 0.02893 Gm. of the alkaloids of Belladonna Root (Proximate Assays)." *U. S.*

"Nearly cylindrical pieces, entire or longitudinally split, usually ten to twenty millimetres in diameter, and fifteen to thirty centimetres or more in length. Externally pale greyish-brown, and finely wrinkled longitudinally. Transverse fracture short. Internally whitish and starchy. Within and mostly near to the cambium ring are numerous scattered groups of vessels and fibers which do not exhibit a prominently radiate arrangement. Most of the parenchymatous cells contain small compound starch grains; some are filled with numerous very minute, crystals of calcium oxalate. Taste slightly bitter." *Br.*

The British assay process is as follows:

"Into a small, stoppered, glass percolator provided with a glass tap and suitably plugged with cotton wool introduce 10 grammes of Belladonna Leaves in No. 60 powder and 50 millilitres of a mixture of *chloroform* 1 volume and *ether* 4 volumes. Shake; set aside for ten minutes; then add 2 millilitres of *solution of ammonia* diluted with 3 millilitres of *water,* and set aside for one hour, shaking frequently, Then allow percolation to proceed slowly, receiving the percolate in a separator containing 6 millilitres of *N/1 solution of sulphuric acid* diluted with 20 millilitres of *water.* When the liquid ceases to pass continue the percolation with a further 50 millilitres or more of the ether-chloroform mixture, added in small quantities, until the Leaves are exhausted. Shake the separator well and, after separation, draw off the acid liquid into a second separator. Repeat the extraction of the ether-chloroform solution with two successive portions, each of 10 millilitres, of the diluted acid. Make the mixed acid solutions alkaline with *solution of ammonia,* and shake out with three successive portions of 15, 15, and 5 millilitres of *chloroform.* Evaporate the mixed chloroformic solutions to dryness, dissolve the residue in 3 millilitres of *ether,* and again evaporate to dryness. Dissolve the residue in 10 millilitres of *N/20 solution of sulphuric acid,* and titrate with *N/20 solution of sodium hydroxide, tincture of cochineal* being used as indicator. Deduct the number of millilitres of the alkaline solution required from 10, multiply the difference by 0.1446; the product will be the percentage of alkaloids in the Leaves." *Br.*

For other assays of belladonna leaves and root, and comments, see Keller (*Ph. Ztg.,* 1894, 345); Moerk (*A. J. P.,* 1899, 105); LaWall and Pursell (*A. J. P.,* 1899, 394); Puckner (*Ph. Rev.,* 1902, 457); Bird (*P. J.,* 1900, 195); Kebler (*Am. Drug.,* 1902, 215); Schmidt (*Ap. Ztg.,* 1900, 13).

The usual adulterants of belladonna leaves are the leaves of *Phytolacca* and *Ailanthus* and the leaves and tops of *Solanum nigrum* and *Scopola carniolica.* Phytolacca leaves may be detected by the presence of numerous raphides as well as crystal sand. Scopola leaves and tops show characteristic barrel-shaped reticulate tracheæ as well as short calyx tubes, each having a contained pyxis. Solanum nigrum or black nightshade has ovate, wavy-toothed leaves and a white rotate corolla. For distinction between belladonna and scopola leaves see article by Kraemer. (*Proc. A. Ph. A.,* 1908, p. 819.) Guérin and Guillaume describe the anatomical difference in the leaves of belladonna, phytolacca and ailanthus. (*Bull. Soc. Pharmacol.,* 1908, p. 213.)

Belladonna root is not infrequently of inferior quality because of the presence of large quantities of the stem-bases of the plant. Reports still come in that the root is adulterated with phytolacca and replaced by 15 to 20 per cent. of scopola. Rusby has reported the presence of 25 per cent. of some inert root, apparently wild althæa, or a relative of that plant. Youngken reports the main adulterants of belladonna root as roots of *Phytolacca decandra,* unpeeled roots of *Althæa officinalis* and rhizomes of *Scopola carniolica.* Phytolacca roots possess a tough fibrous fracture and exhibit in transverse sections series of concentric circles of open collateral fibrovascular bundles; the diagnostic tracheæ have diamond-shaped bordered pores; as in the case of the leaves, raphides and crystal sand are present. Althæa roots show numerous mucilage sacs, sclerenchyma fibers, ellipsoidal starch grains and a few rosettes of calcium oxalate. Scopola rhizomes possess characteristic reticulate tracheæ.

Scopola rhizome has been largely used by manufacturers of belladonna plasters in the place of belladonna root.

Constituents.—Belladonna contains volatile bases both of an alkaloidal and a non-alkaloidal type. They are pyridines, pyrrols and diamines. It is generally recognized that the following mydriatic alkaloids are found in the solanaceous plants; *atropine, hyoscyamine, scopolamine, atroscine, apoatropine, tropacocaine, meteloidine* and *belladonine.* The first two of these, atropine and hyoscyamine, are isomeric, having the formula $C_{17}H_{23}O_3N$, and yield the same decomposition products. They differ, however, in their physical constants, especially in their relation to polarized light; whereas hyoscyamine is strongly lævo-rotatory, atropine is optically inert. Will (*B. Chem. G.,* 1888, p. 1717) has shown that hyoscyamine is readily changed into atropine and that varying proportions of the two alkaloids may be obtained from the same specimen of belladonna, according to the method of extracting from the crude drug. His conclusions have been confirmed by Gorio and Coty (*Bull. d. Sciences Pharmacol.,* 1921, xxviii, 545). The studies of the latter as well as those of Schutte (*A. Pharm.,* 1891, ccxxix, No. 7) demonstrate that atropine, if it occur at all in belladonna, is in much smaller amount than hyoscyamine. Atropine appears to be a mixture of lævo-rotatory and dextro-rotatory hyoscyamines. The dextro-hyoscyamine does not appear to occur in nature, but has been prepared artificially. Of these, atropine occurs in the *Atropa Belladonna* and in *Datura Stramonium,* hyoscyamine in these plants and also in *Hyoscyamus niger, Hyoscyamus muticus* and *Duboisia myoporoides;* scopolamine is found in *Hyoscyamus niger* and in *Scopola carniolica,* and belladonine in belladonna root alone.

For differentiation between atropine and hyoscyamine see under *Atropina.*

Apoatropine, $C_{17}H_{21}O_2N$, or *atropamine,* was discovered by Pesci in 1881 (see also Hesse, *An. Chem.,* 1893, cclxxvii, p. 290). It crystallizes in prisms and has a melting point of 60° C. It decomposes into tropine and *atropic acid,* the latter being related to tropic acid. *Belladonine* discovered by Hübschmann in 1858 is isomeric with apoatropine. According to Hesse, the latter changes into belladonine when heated with hydrochloric acid in sealed tubes. It is an uncrystallizable resinous base whose chemical individuality is questioned by some authorities.

Uses.—All parts of the belladonna plant are poisonous. It is not uncommon in countries where it grows wild, for children to pick and eat the berries, allured by their fine color and sweet taste. The symptoms of belladonna poisoning are precisely the same as those of atropine poisoning.

The conclusion of chemists that the active principle of belladonna is hyoscyamine rather than atropine, harmonizes with clinical experience because practical experience has shown that, although qualitatively indistinguishable in its action from atropine, belladonna is efficacious in doses considerably smaller than might be expected from its content of alkaloid if the latter were atropine. For description of the physiological and therapeutic properties of belladonna, see under *Atropine.*

The various preparations are much used locally. Rubbed upon the areola of the breast, it has been believed to arrest the *secretion of milk* and is frequently employed in *mastitis.*

The decoction or extract, applied to the neck of the uterus, is asserted to have hastened *tedious labor* dependent on rigidity of the os cervicis; and spasmodic *stricture of the urethra, neck of the bladder,* and *anal fissures* and *painful uterine affections* have been relieved by the local use of the extract, either smeared upon bougies or administered by injection. It is asserted also to be useful in *paraphimosis.* The inhalation of the vapor from a decoction of the leaves or extract has been recommended in *spasmodic asthma.* For this purpose, two drachms of the leaves, or fifteen grains of the aqueous extract, are employed to the pint of water. A much better plan is to smoke the dried leaves in the form of a cigarette or in a pipe.

Belladonna should never be given in substance, but in the form of extract or tincture, or, when accuracy or quickness of action is desired, of atropine. (See *Atropina.*)

Dose, one grain (0.065 Gm.).

Off. Prep.—Emplastrum Belladonnæ, *Br.* (from liquid extract); Fluidextractum Belladonnæ Radicis, *U. S.* (*Br.*); Linimentum Belladonnæ, *U. S., Br.* (from liquid extract); Suppositoria Belladonnæ, *Br.* (from alcoholic extract); Unguentum Belladonnæ, *Br.* (from liquid extract).

BENZALDEHYDUM. U. S.

BENZALDEHYDE Benzaldehyd.

"Benzaldehyde contains not less than 85 per cent. of $C_6H_5.CHO$." *U. S.*

Benzoic aldehyde; Oleum Amygdalarum Æthereum Artificiale; Aldéhyde Benzoique, *Fr.;* Benzaldehyd, Künstliches Bittermandelöl, *G.*

Preparation.—Benzaldehyde is the first in the series of aromatic aldehydes, being the first oxidation product of benzyl alcohol, $C_6H_5.CH_2OH$, and going in turn into the fuller oxidation product, benzoic acid, $C_6H_5.COOH$. It is mainly produced artificially from toluene by the following reactions:

$$C_6H_5.CH_3 + 2Cl_2 = C_6H_5.CHCl_2 + 2HCl$$
$$C_6H_5.CHCl_2 + HOH = C_6H_5.COH + 2HCl$$

By the action of chlorine upon the hot hydrocarbon, benzyl chloride, $C_6H_5CH_2Cl$, results, and this yields benzoic aldehyde on distillation with lead nitrate and water in an atmosphere of carbon dioxide gas. More generally, however, *benzal chloride,* $C_6H_5CHCl_2$, is taken, as this, when heated under pressure with water or sulphuric acid, readily yields the benzaldehyde. The product is purified by conversion into the acid sulphite compound.

It may be obtained pure by agitating it strongly with calcium hydroxide and a solution of ferrous chloride, submitting the mixture to distillation, and drying the oil which comes over by digestion with calcium chloride. Whipple (*A. J. P.,* xxvi) obtained benzaldehyde by treating the oil of bitter almond with a solution of silver nitrate—thus precipitating silver cyanide—and distillation.

Exposed to the air, benzaldehyde tends to pass by oxidation into benzoic acid, which latter is therefore liable to be found as a contamination of the sample of benzaldehyde if not freshly rectified.

Description and Physical Properties.—"A colorless or yellowish, strongly refractive liquid, having an odor resembling that of oil of bitter almond, and a burning aromatic taste. Benzaldehyde is soluble in about 350 volumes of water, and is miscible with alcohol, ether, and with fixed or volatile oils.

"Specific gravity: about 1.045 at 25° C. Shake 0.5 cc. of Benzaldehyde with 5 cc. of distilled water, add 0.5 cc. of sodium hydroxide T.S. and 0.1 cc. of ferrous sulphate T.S., and warm the mixture gently. Upon the addition to the mixture of a slight excess of hydrochloric acid, no greenish-blue color or blue precipitate is produced within fifteen minutes (*hydrocyanic acid*). Wind the end of a copper wire into a spiral about 6 mm. in diameter and 6 mm. in length, and hold it in a non-luminous flame until it glows without coloring the flame green. Cool the wire, dip the spiral in the Benzaldehyde, ignite, allow it to burn outside of the flame, and then bring the spiral into contact with the lower, outer edge of the non-luminous flame: not even a transient green color is imparted to the flame (*chlorinated compounds*). Dissolve 1 cc. of Benzaldehyde in 20 cc. of alcohol, and add distilled water until a slight turbidity is produced. Add zinc and diluted sulphuric acid, maintaining a brisk evolution of hydrogen for one hour. Filter, evaporate the liquid to about 20 cc., and boil 10 cc. of the evaporated liquid with 1 drop of potassium dichromate T.S.: no violet color is produced (*nitrobenzene*).

"**Assay.**—Dissolve about 3 cc. of freshly redistilled phenylhydrazine in 60 cc. of alcohol, and titrate 25 cc. of the solution (this solution must always be freshly prepared) with half-normal hydrochloric acid, using 1 or 2 drops of methyl orange T.S. as indicator. To about 1 Gm. of the Benzaldehyde, accurately weighed, add 25 cc. of the phenylhydrazine solution, and allow the mixture to stand for thirty minutes. Add 1 or 2 drops of methyl orange T.S., acidify with a measured excess of half-normal hydrochloric acid, and add 20 cc. of distilled water. Filter, and wash the precipitate with small portions of distilled water until the washings cease to redden blue litmus paper. Titrate the excess of hydrochloric acid in the filtrate with half-normal sodium hydroxide. Subtract the number of cc. of half-normal hydrochloric acid consumed from the number of cc. of half-normal hydrochloric acid used in titrating the 25 cc. of phenylhydrazine solution. The difference, multiplied by 0.05304, indicates the weight of $C_6H_5.CHO$ present.

"Preserve in small, well-stoppered bottles, protected from light." *U. S.*

Uses.—Benzaldehyde is used as a flavoring agent, in place of the oil of bitter almond, from which it differs in containing no hydrocyanic acid; it is often called *artificial* or *synthetic oil of bitter almond.* (See *Oleum Amygdalæ Amaræ.*) It is much less poisonous than the true oil of bitter almonds.

Dose, one-half to one minim (0.03–0.06 cc.).

BENZAMINÆ LACTAS. Br.

BENZAMINE LACTATE

"Benzamine Lactate, $C_{15}H_{21}NO_2,C_3H_6O_3$, is the lactate of benzoyl-vinyl-diaceton-alkamine, from which it may be obtained by neutralising with lactic acid." *Br.*

Betaeucaine Lactate; Eucaine Lactate.

"A white crystalline powder. Taste slightly bitter followed by a sensation of numbness. Soluble in 5 parts of *water,* and in 8 parts of *alcohol* (90 per cent.). Its aqueous solution yields with an aqueous solution of *salicylic acid* a white precipitate, and with *solution of ammonia* a white precipitate readily soluble in excess of the reagent. Treated with *nitric acid* and *alcoholic solution of potassium hydroxide* as rescribed under 'Cocainæ Hydrochloridum' a characteristic odor is evolved, recalling peppermint. Does not darken in color when moistened with *alcohol* (90 per cent.) and triturated with *mercurous chloride* (distinction from cocaine and α-eucaine). An aqueous solution (1 in 100) gives no precipitate with *solution of potassium iodide* (distinction from α-eucaine). Dissolves in *sulphuric acid* and in *nitric acid* without coloration. No appreciable ash." *Br.*

For further information concerning the chemistry and uses of this salt see *Eucainæ Hydrochloridum.*

BENZENUM. Br.

BENZENE

"Benzene, C_6H_6, is a liquid hydrocarbon obtained from light coal-tar oil." *Br.*

Benzene, Benzole, Phenyl Hydride, Benzen; Benzenum-Medicinale, *N.N.R.;* Benzinum, *Fr. Cod.;* Benzine, *Fr.;* Benzol *P. G.;* Phenylwasserstoff, Steinkohlenbenzin, *G.;* Benzolo, *It.*

It is to be regretted that the British Pharmacopœia (1914) has abandoned the name "Benzol" and adopted the name "benzene" for this product, and that the French Codex uses the word "Benzine" for crystallizable benzene. Benzol (Benzene, Br. Pharm. and U. S. P. reagent) must not be confounded with the commercial article *benzin,* which is a mixture of various hydrocarbons of light specific gravity, obtained in the distillation of petroleum. (See *Benzinum Purificatum.*) Originally the two names benzol and benzin were applied to the same substance, but after the discovery of petroleum it was found that the liquid obtained by distillation from coal tar was quite different from that obtained from petroleum. In the United States it has become the custom to call the liquid obtained by the fractional distillation of petroleum, having the specific gravity 0.638 to 0.660 at 25° C., *benzin.* It is unfortunate that in Europe, and on the Continent especially, the term benzin was used for both liquids. The two substances are essentially different although resembling each other somewhat in their solvent powers. Benzol is a definite hydrocarbon of fixed constitution, petroleum benzin a complex body of varying constitution. Benzol can be frozen; petroleum benzin has never yet been congealed. Petroleum benzin boils at from 45° to 60° C., while benzol boils at 79° to 80° C. Benzol can be converted into nitrobenzol, and by further treatment into aniline colors; petroleum benzin cannot. The term *benzene* is gradually becoming limited to the pure hydrocarbon, C_6H_6, while *benzol* is applied to the mixture of benzene with its homologues *toluene, paraxylene, metaxylene, mesitylene, pseudocumene,* etc. This view was probably in the minds of the revisers of the British Pharmacopœia (1914) and caused them to abandon the name "Benzol" and adopt "Benzene," thus signifying the purified product.

Benzene was discovered by Faraday in 1825 in the liquid obtained upon compressing illuminating gas. Hoffmann afterwards found a more abundant source in coal tar. For many years coal tar furnished the major portion of the benzene of commerce, but during the war the scarcity of the substance led to a search for new sources of supply. One of these, which furnishes much of the commercial product, is the by-product from coke ovens in which the volatile products of destructive distillation are collected and fractionated. Still another source is petroleum benzine. The aliphatic compounds in petroleum benzine are converted into cyclic compounds by heating the vapors under pressure. In this way benzene, toluene and other similar cyclic hydrocarbons are produced. Commercial benzol is found of varying degrees of purity on the market, as for many industrial purposes it is not necessary to free it from volatile impurities. The purest benzene, such as is used for reagent purposes, is obtained by the dry distillation of benzoic acid with lime. Benzene finds many uses in the industries for its solvent effect, and also has been employed as one of the immiscible solvents in the manufacture of alkaloids.

Benzol may be distinguished from benzin by the use of dracorubinresin which is dissolved by the former with a deep red color but is completely insoluble in the latter. When petroleum benzin is shaken in the cold with one-third of its volume of fused crystals of absolute phenol, the latter remains undissolved, while benzol is miscible with absolute phenol in all proportions. (Allen.) According to Pusch, benzol can be distinguished from petroleum benzin by the fact that benzol forms a violet-red and petroleum benzin a raspberry-colored solution with iodine.

Commercial benzol is always contaminated with more or less toluene and xylene. It is graded by such terms as "90 per cent. benzol" or "50 per cent. benzol." (See *Ph. Era,* 1918, p. 280.)

In consequence of the great volatility and extreme inflammability of benzol and its attendant hydrocarbons, much care is necessary both in their preparation and in their subsequent use in order to avoid any possible exposure to flame. Very serious accidents have taken place from want of the proper caution in this respect. Benzene vapor and air when mixed produce a highly explosive combination. The limit of maximum explosibility is from about 3 to 6 per cent. of benzene vapor in the air.

Properties.—The British Pharmacopœia describes benzene as "a colorless, mobile, inflammable liquid. Insoluble in *water,* but miscible with *absolute alcohol* or *ether.* Specific gravity 0.880 to 0.887. 95 per cent. distils between 79° and 82° C. It solidifies when cooled to 0° C., and if the temperature be allowed to rise, does not entirely re-melt below 4° C." *Br.*

"A colorless, transparent, liquid. Boiling point, 79° to 81° C. Congealing point, about 5° C. Specific gravity, about 0.876 at 25° C. Insoluble in water, miscible with alcohol, ether, and with fixed or volatile oils. When equal volumes of benzene and sulphuric acid are shaken together in a glass cylinder during fifteen minutes, the acid upon separation is not colored. Add a few mgm. of isatin, shake well, and allow to stand for thirty minutes. The acid does not acquire a blue or green color (*thiophene*). Non-volatile residue at 100° C., not over 0.01 per cent." *U. S.* (*Reagents.*)

Its powers as a solvent are very extensive. Among the substances soluble in it are sulphur, phosphorus, and iodine, and most resins and fats. It dissolves quinine, but not cinchonine, with which it forms a bulky gelatinous mass. Morphine and strychnine are sparingly soluble. Its solvent power over some of the organic alkaloids led John Williams, of London, to employ it in extracting them. Dragendorff has corroborated and extended this use of benzol for obtaining the alkaloids, whose salts are, however, not usually soluble in the menstruum. Benzol is also a solvent of many of the resins, of mastic, camphor, wax, fatty and oily substances, essential oils, caoutchouc, and gutta-percha. It often becomes a matter of great importance commercially to test the purity of commercial benzol, and a very thorough method of assay based on fractional distillation is found in Allen's commercial organic analysis. The following method, originating with Schorlemmer, is based on the conversion of this hydrocarbon into aniline, and of that into one of the characteristic colors derived from it. That part of the mixture which volatilizes at 150° C. is operated on. This is treated with fuming nitric acid, which, if benzol be present, gives rise to a nitrobenzol with its bitter-almond odor. The nitrobenzol is then converted by the action of granulated tin and hydrochloric acid into aniline, which is isolated by distilling the product with potassium hydroxide. The aniline floats on the top of the liquid that passes. A little of this gives with sodium hypochlorite a fine purple color; and a drop of it, if heated with a little corrosive sublimate, will yield the beautiful color of rosaniline. (*J. P. C.,* 4e sér., ii, 177.) According to Balls, magnesium ribbon, with the addition of a few drops of solution of platinic chloride, rapidly and completely reduces nitrobenzene in alcoholic solution to aniline, giving a solution which can be at once decanted and tested with bleaching powder. (Allen.)

Uses.—Benzol has been shown by Chassevant (*Archiv. de Pharmacodyn,* 1896, ii) to be depressant to the central nervous system and to the vasomotor system. It was experimented with as an anesthetic by Simpson, but was found scarcely capable of producing unconsciousness. In 1897 Guyot reported that habitual exposure to the fumes of benzol during its manufacture produced a chronic poisoning characterized by uncertainty of gait, mental disturbance, loss of sexual power, and epileptiform convulsions. Sanlessen found that, in lower animals, after death from benzol poison, there were hemorrhages into the lungs and the stomach, with various fatty degeneration, and a plastic bone-marrow. Selling (*J. H. H. B.,* 1910, xxi) reported fatal cases of human poisoning, showing the same lesions. His studies of these cases led Von Koranyi (B. K. W., 1912, xlix) to the use of benzol in the treatment of *leukemia.* Since this a large number of authors have reported favorable results in this intractable disease. Ravenna (*Rif. Med.,* 1920, xxxvi, 86) concludes, however, that its effects are only palliative, not curative. Barker has also reported favorable effects (*J. H. H. B.,* 1913) in *Hodgkin's disease* and McLester (*J. A. M. A.,* 1914, lxii) in *polycythemia.* It is best administered by mixing with equal parts of olive oil and emulsifying with mucilage of acacia. Bordarampé (*Rivista d. l. Assoc. Med. Argentina,* 1919, xxx, 237) has used it locally with asserted excellent results in inoperable *cancer.*

The remedy is evidently not harmless. Neumann (*Ther. Geg.,* 1913, p. 56) reports a case of leukemia in which benzol was given for thirty-six days with great reduction in the number of leukocytes, but after the drug was stopped the action continued, the leukocytes fell to 200, the patient developed fever, weakness, diarrhea and epistaxis, and died thirty-nine days after the last dose. A number of cases of serious poisoning, some of them fatal, have been reported by Ronchetti (*Giorn. di Clin. Med.,* Sept. 20, 1922) and by Hamilton (*J. A. M. A.,* 1922, lxxviii, 628) among workers in rubber factories where benzene was used as a solvent. Pappenheim (*W. K. W.,* 1913, p. 48) from experiments upon the lower animals finds that benzol is injurious to both the liver and kidney. Koranyi, however (*W. K. W.,* 1913), insists that in quantities of not over 3 Gm. per day benzol is perfectly safe, but generally smaller quantities are sufficient for therapeutic purposes. It should be noted that commercial benzol often contains toxic impurities, especially nitrobenzol and aniline. A crystallizable benzol is described in the N. N. R., under the name of *Benzenum medicinale;* it is liquid at ordinary temperatures.

The beginning *dose* is generally fifteen minims (0.9 cc.) cautiously increased to forty-five minims (2.8 cc.).

BENZINUM PURIFICATUM. U. S.

PURIFIED PETROLEUM BENZIN Benzin. Purif. [Petroleum Ether]

"Purified Petroleum Benzin is a purified distillate from American petroleum consisting of hydrocarbons, chiefly of the Methane series." *U. S.*

Benzin, Petroleum Ether; Æther Petrolei; Esprit (naphte, Ether) de Pétrole, *Fr.;* Benzinum Petrolei, *P. G.;* Petroleumbenzin, Petroläther, *G.;* Benzina del petrolio, *It.*

Purified petroleum benzin was introduced into the U. S. Pharmacopœia VIII and IX, and is used mainly as a solvent. The process of purification was not introduced into the U. S. IX, as the liquid is very inflammable and not suited for purification on the small scale by the pharmacist. The U. S. VIII process was as follows: "Potassium Permanganate, *ten grammes;* Sodium Hydroxide, *two grammes;* Sulphuric Acid, *sixty cc.;* Petroleum Benzin, *one thousand cc.;* Water, *a sufficient quantity.*

"Add the Acid to *five hundred and fifty cc.* of Water, and when the mixture has become cold, pour it into a bottle having the capacity of about two liters. Add *eight grammes* of Potassium Permanganate and agitate until it is dissolved, then add the Petroleum Benzin, in four portions, shaking the liquid after each addition. Allow the liquids to remain in contact for twenty-four hours, shaking the bottle at frequent intervals; then decant the Petroleum Benzin into another bottle of the same capacity, and having dissolved *two grammes* of Potassium Permanganate in *two hundred and forty cc.* of Water, in which the Sodium Hydroxide has previously been dissolved, mix the liquids and agitate the mixture frequently during several hours, then decant, repeat the washing with Water, and again decant the Purified Petroleum Benzin." *U. S. VIII.*

Description and Physical Properties.—"A clear, colorless, non-fluorescent, volatile liquid, having an ethereal or faint, petroleum-like odor, and a neutral reaction. *Caution.—It is highly inflammable, and its vapor, when mixed with air and ignited, explodes violently.* Purified Petroleum Benzin is practically insoluble in water. It is freely soluble in alcohol, and is miscible with ether, chloroform, benzene, and with fixed or volatile oils, with the exception of castor oil.

"Specific gravity: 0.634 to 0.660 at 25° C. Purified Petroleum Benzin distils completely between 35° and 80° C., when determined by method II, page 433. Pour 10 cc. of Purified Petroleum Benzin in portions upon clean, odorless filter paper laid on a warm glass plate: no disagreeable or notably sulphureted odor becomes apparent as the last portions disappear from the paper, and no greasy stain remains. Not more than 0.001 Gm. of residue remains on evaporating 50 cc. of Purified Petroleum Benzin at a temperature not exceeding 40° C. Boil 10 cc. of Purified Petroleum Benzin for a few minutes with one-fourth its volume of alcoholic ammonia T.S. and a few drops of silver nitrate T.S.: the liquid does not turn brown (*pyrogenous products or sulphur compounds*). Add 5 drops of Purified Petroleum Benzin to a mixture of 40 drops of sulphuric acid and 10 drops of nitric acid in a test tube, warm the liquid for about ten minutes, set it aside for half an hour, and dilute it with water in a shallow dish: no odor of nitrobenzene is evolved (*benzene*).

"Preserve in well-closed containers, in a cool place, remote from fire." *U. S.*

Benzin is a very inflammable liquid. This inflammability may be somewhat reduced by the addition of carbon tetrachloride, but it has been found that even as high an admixture as 70 per cent. of carbon tetrachloride will not make benzin entirely uninflammable. When benzin vapor is mixed with air it becomes highly explosive.

This useful product of petroleum was first introduced into the U. S. Pharmacopœia (1880); it is obtained in the process of purifying petroleum by fractional distillation. (See *Petroleum,* Part II.) Petroleum benzin must be carefully distinguished from benzene (official in the British Pharmacopœia under the name of *Benzenum* and a reagent in the U. S. P.), a product derived from coal tar. Although the U. S. Pharm. gives a test to distinguish an admixture with benzene, this adulteration of petroleum benzin is hardly likely to take place here in the near future, because of the great difference in price. The principal consumption of petroleum benzin at present is in the arts as a solvent, especially as a substitute for oil of turpentine, which it resembles very much in its solvent properties. In pharmacy it has been used to deprive powdered drugs of their fixed oil by percolation; to obtain volatile oils by percolating the oily drug with the benzin and subsequently evaporating the mixture spontaneously; as a substitute for ether in making oleoresins; and for many other purposes to which it is adapted on account of its powers as a solvent. Petroleum benzin is a good solvent for fats, resins, rubber, and some of the alkaloids.

Dragendorff recommends the rectification of benzin by fractional distillation from lard, collecting the portion which distils below 45° C. Petrolatum has also been found to be efficient in retaining the impurities in the still.

Uses.—Not only benzin, but various other commercial mixtures derived from petroleum, such as gasoline and naphtha, have been used by depraved humanity for the purpose of producing intoxication. (See *Petroleum,* Part II.)

Jaffé (*M. M. W.,* 1914, lxi) concludes from an experimental investigation, as well as from the study of cases of human poisoning, that the most marked effect of benzin is extensive hemorrhage in the lungs, which he believes is due to an effort at elimination. It has been largely used as a solvent for iodine in the disinfection of the skin, but if evaporation is prevented it has a marked irritant effect and even a caustic action, indeed Sehrwald (*D. M. W.,* 1913, p. 318) has recommended it clinically as a counter-irritant.

Purified benzin is official in the Pharmacopœia purely for pharmaceutical properties. It is not used in medicine. It was at one time suggested by Schleich as a diluent for chloroform in producing surgical anesthesia, but H. C. Wood, Jr. (*P. M. J.,* April 15, 1899), showed that it was a direct depressant to both the heart and vasomotor system far beyond its power as a narcotic, and the method practically yielded such unfavorable results that it was soon abandoned.

A number of cases of benzin poisoning, both acute and chronic, have been reported. In the acute cases the most constant symptom has been disturbance of intellection, or unconsciousness, with slowing of the respirations. The pulse is generally somewhat slower than normal, pupils dilated, the surface cold, and frequently there has been cyanosis and occasionally convulsions. In most of the cases whether the poison has been swallowed or inhaled, the benzin odor can be peceived upon the breath. (For report of cases see Wichern, *M. M. W.,* lvi, p. 11.) In the chronic cases the symptoms have been headache, giddiness, numbness and paresthesia of the extremities, vomiting, loss of memory, general weakness, especially in the legs, tenderness and pain along the nerve trunks, and progressive anemia. In acute cases it causes a peculiar intoxication, having the appearance, at the onset, of an attack of hysteria, with laughing, tremors, mydriasis, nystagmus, loss of power in the legs and bladder, failing heart action, delirium, coma and death. In nine fatal cases of chronic poisoning by petroleum benzin, Santesson found a widespread fatty degeneration affecting especially the liver, kidneys and cardiac muscles.

Off. Prep.—Used as a solvent for the fatty substances in various drugs.

BENZOINUM. U.S., Br.

BENZOIN Benzoin.

"Benzoin is a balsamic resin obtained from *Styrax Benzoin* Dryander and other species of *Styrax* (Fam. *Styraceæ*), and known in commerce as Sumatra Benzoin and Siam Benzoin.

"Sumatra Benzoin yields not less than 75 per cent. of alcohol-soluble extractive and not more than 1 per cent. of acid-soluble ash. Siam Benzoin yields not less than 90 per cent. of alcohol-soluble extractive, contains not more than 1 per cent. of foreign organic matter, and yields not more than 0.5 per cent. of acid-soluble ash." *U. S.*

"Benzoin is a resinous solidified balsam obtained from the incised stem of Styrax Benzoin *Dryand.* Known in commerce as Sumatra Benzoin." *Br.*

Resina Benzoe, Asa Dulcis; Gum Benjamin; Benjoin, *Fr.;* Benzoë, *P. G.;* Benzoëharz, *G.;* Benzoino, *It.;* Benjui, *Sp.*

It is generally believed that Siam Benzoin is obtained from *Styrax Benzoin* Dryander. It appears to closely resemble the tree growing in Sumatra, which yields a balsamic resin bearing this name. Tschirch considers that the trees yielding Siam and Sumatra Benzoin are physiological varieties of the same species. (Tschirch, *"Harze,"* II. Aufl., p. 195.) Rordorf (*Schweiz. Apoth. Ztg.,* 1917) concludes that the tree producing Siam Benzoin, while very similar to the *S. Benzoin,* offers distinct differences and proposes a new species, *S. Siamensis* (Rordorf.) Strueff presents a careful morphological paper on the trees of *Styrax Benzoin,* growing in Siam, Sumatra and Java, in *A. Pharm.,* 1911, p. 10.

Styrax Benzoin, or *Benjamin Tree,* is a tall tree of quick growth, sending off many strong round branches, covered with a whitish downy bark. Its leaves are alternate, entire, oblong, pointed, smooth above and downy beneath. The bowers are in compound, axillary clusters, nearly as long as the leaves, and usually hang, all on the same side, upon short slender pedicels. The tree is a native of Sumatra, Java, Borneo, and other islands in the vicinity. By wounding the bark near the origin of the lower branches, a juice exudes, which hardens upon exposure and forms the *Sumatra Benzoin* of commerce. According to the researches of A. Tschirch (*Journ. Roy. Microscop. Soc.,* 1890), the exudation is purely the result of pathological processes, the plant containing no resin receptacles. The trees, which are either wild or cultivated, are deemed of a proper age to be wounded at six years, when the trunks are usually about seven or eight inches in diameter. The operation is performed annually, and the product on each occasion from one tree never exceeds three pounds. The juice which first flows is the purest, and affords the whitest and most fragrant benzoin.

The tree which yields the Siam Benzoin is not certainly determined. According to E. M. Holmes its leaves are thinner and less distinctly venated than those of the Styrax Benzoin. Hartwich believes it to be a new species, *Styrax benzoides* Carib (see *Kew Bulletin,* 1912, p. 391). Holmes (*P. J.,* 1916) attributes it, however, to the *S. tonkinense.* Rordorf (*P. J.,* 1917, xcix, p. 111) received some fruits which were sent him from Bangkok as specimens supposedly derived from the Benzoin tree; these do not agree with any species previously described and he proposed a new species, *S. Siamensis* Rordorf. The territory from which the balsam is derived is a quite limited district in the Province of Laung Probang along the River Mekong.

The *Siam Benzoin* appears in commerce either in the form of separate tears or in masses composed of tears cemented together by a rich amber-colored translucent resin, these masses usually being in cubical blocks which take their form from the wooden boxes in which the soft resin has beeen packed. The tears are small, mostly less than 2 or 3 cm, in length, opaque, brittle and milky white on the interior, but on keeping gradually oxidize into the brownish translucent resin. The finest variety is composed almost entirely of these tears, loosely agglutinated together. *Sumatra Benzoin* is sent into commerce chiefly from Acheen in Sumatra. It differs from the Siam varieties in having a much grayer color; the resin is grayish-brown, the tears are usually fewer than in the finer variety, and the bits of wood, etc., more abundant. The odor differs from, and is less agreeable than, that of Siam Benzoin. *Palenbang Benzoin* resembles Sumatra Benzoin, but is somewhat more transparent, and is stated to yield a larger percentage of benzoic acid. It is also asserted that is can be distinguished by its tincture, when dropped into water, not producing milkiness, but a flocculent deposit. *Penang Benzoin* also resembles Sumatra Benzoin, but has an odor which is more like that of storax, and it is probably yielded by the *Styrax Benzoin;* possibly it is the product of one of the Sumatran species, *S. subdenticulata* Miq. For an account of the cultivation and collection of benzoin in Sumatra, by L. M. Vonck, see *C. D.,* 1891, 486–488; also *D. C.,* 1891, 258. Lüdy made an investigation of the bark and wood of a benzoin tree which was brought from Java by Tschirch. He reached the conclusion that benzoin balsam was produced from the tannin of the bark. (*A. Pharm.,* 1893, 43, 95.) A variety of benzoin known as *Estoraque* or *Benjui,* is produced in Bolivia from the *Styrax Pearcei* Perk. var. *bolivianus.* This has been shown by Wichmann (*S. W. P.,* 1912, p. 237) to be of similar composition to the Asiatic resin. According to this author resins are also collected from a number of other species of *Styrax* in South America.

Properties.—Benzoin has a fragrant odor, with very little taste, but when chewed for some time leaves a sense of irritation in the mouth and fauces. It breaks with a resinous fracture, and presents a mottled surface of white and brown or reddish-brown; the white spots being smooth and shining, while the remainder, though sometimes shining and even translucent, is usually more or less rough and porous, and often exhibits impurities. After long storage it becomes covered with a thin yellow transparent film which Reinitzer finds is due to oxidation of the proper resin (*Schim. Rep.,* April, 1915). In the inferior kinds the white spots are very few, or entirely wanting. Benzoin is easily pulverized, and, in the process of being powdered, is apt to excite sneezing. Its sp. gr. is from 1.063 to 1.092. The U. S. Pharmacopœia recognizes both Sumatra and Siam Benzoins. The official descriptions of these follow:

"*Unground Sumatra Benzoin.*—Blocks or lumps of varying size, made up of tears, compacted together with a reddish-brown, reddish-gray, or grayish-brown resinous mass; tears externally yellowish or rusty-brown, milky-white on fresh fracture; hard and brittle at ordinary temperatures, but softened by heat and becoming gritty on chewing; odor aromatic. When digested with boiling water the odor suggests cinnamic acid or storax; taste aromatic and slightly acrid.

"*Unground Siam Benzoin.*—Pebble-like tears of variable size, compressed, yellowish-brown to rusty-brown externally, milky-white on fracture, separate or very slightly agglutinated, hard and brittle at ordinary temperatures but softened by heat and becoming plastic on chewing; odor agreeable, balsamic, vanilla-like; taste aromatic and slightly acrid.

"The solution of Benzoin in alcohol becomes milky upon the addition of water and is acid to litmus paper. Heat a few fragments of Benzoin in a test tube: Sumatra Benzoin evolves a sublimate consisting of plates and small, rod-like crystals that strongly polarize light. Siam Benzoin evolves a sublimate directly above the melted mass consisting of numerous long, rod-shaped crystals, which do not strongly polarize light. Treat about 0.25 Gm. of Benzoin with 5 cc. of ether, decant about 1 cc. of the ethereal solution into a porcelain dish, and add to it 2 or 3 drops of sulphuric acid: the solution of Sumatra Benzoin produces a deep red-brown coloration of the sulphuric acid and the solution of Siam Benzin produces a deep purplish-red cloration. Heat about 0.5 Gm. of Benzoin in a test tube with 10 cc. of potassium permanganate T.S.: only the Sumarta variety develops in odor of benzaldehyde. Treat about 1 Gm. of powdered Benzoin with 15 cc. of warm carbon disulphide, filter, wash the filter with an additional 5 cc. of carbon disulphide, and allow the filtrate to evaporate spontaneously: the residue does not exceed 12.5 per cent. This residue responds to the tests for identity under *Acidum Benzoicum.* Benzoin does not show the presence of *rosin.*

"**Assay.**—Proceed as directed under alcohol-soluble extractive." *U. S.*

"Hard brittle masses consisting of numerous whitish tears embedded in a greyish-brown translucent matrix. Odor agreeable, similar to that of storax; taste slightly acrid. When cautiously heated in a dry test-tube it melts and evolves whitish fumes with an irritating odor. When 0.5 gramme is slowly heated to about 40° C. with 10 millilitres of *solution of potassium permanganate* an odor of benzaldehyde is evolved (distinction from Siam Benzoin). Not more than 15 per cent. insoluble in *alcohol* (90 per cent.). Ash not more than 5 per cent." *Br.*

When heated it melts, and emits thick, white, pungent fumes, which excite coughing when inhaled, and consist chiefly of benzoic acid. It is wholly soluble, with the exception of impurities, in alcohol, and is precipitated by water from the solution, rendering the liquid milky. It yields to boiling water a notable proportion of benzoic acid. Lime water and the alkaline solutions partially dissolve it, forming benzoates, from which the acid may be precipitated by the addition of other acids.

The percentage of alcohol-soluble matter require to be present by the U. S. P. in benzoin is very high, and if rigidly enforced by the customs would exclude Sumatra Benzoin in all but its very finest varieties. Robt. C. Pursel and Willard Graham obtained from five commercial varieties of Sumatra Benzoin, in the American market, an average of 86 per cent. of soluble matter. (*Proc. Pennsylvania Pharm. Assoc.*, 1902.) John Barclay, in England, found the average of ten samples to be 69.9 per cent. (*P. J.*, Jan., 1903.)

Benzoin retards the oxidation of fatty matters, and thus tends to prevent rancidity.

Constituents.—The chief constituents of benzoin are resin, benzoic and cinnamic acids and their esters. The resinous portion, which constitutes about three-fourths of the drug, is made up of esters of *benzoresinol* (*siaresinol*), constituting from 7 to 8 per cent. of the resin, and of an undetermined alcohol. This latter has been stated to be *sumaresinotannol.* Zinke and Dzrimal (*J. P. C.*, 1921, xxiv, 350) report the presence of a distinctive compound *lubanyl benzoate*, $C_6H_3OH.OCH_3.CH{=}CH.CH_2O.CO{-}C_6H_5$. This occurs in crystalline masses melting at 72° C.

The total amount of free acids is from 15 to 17 per cent. In the Sumatra Benzoin cinnamic acid predominates, and in the Siam Benzoin benzoic acid is more abundant; indeed Beckurts and Brueche state that Siam Benzoin contains no cinnamic acid (see also Tschirch and Lüdy, *A. Pharm.*, 1893, 500). There is present also some 9 or 10 per cent. of esters of these acids, cinnamyl, cinnamate, phenylpropyl cinnamate, and traces of vanillin, benzaldehyde, *styrol* and *styracin.*

Benzoin may be rapidly tested for cinnamic acid by heating a small quantity with a little soda and water and warming the filtrate with potassium permanganate, when the odor of bitter almond will be developed. (*A. Pharm.*, 1892, ccxxx.)

Aschoff recommends the following method of detecting cinnamic acid. Boil the benzoin with milk of lime, filter, decompose with hydrochloric acid, and add either potassium dichromate with sulphuric acid, or potassium permanganate, when, if cinnamic acid be present, the odor of oil of bitter almond will be perceived.

According to T. T. Cocking and J. D. Kettle (*Tr. Br. Ph. Conf.*, 1914, 357), the important analytical data to be considered in valuing benzoin are (1) the percentage soluble in 90 per cent. alcohol, and (2) the quantity of aromatic acids present, both free and combined. Methods of obtaining these factors are given in detail and also tables giving the results of such examinations of a number of commercial samples. Reinitzer (*A. Pharm.*, cclii) has made an exhaustive study of Siam Benzoin, in which he contradicts some of the previously published statements of Tschirch and Lüdy. He claims that the resinotannol of these authors does not exist in the drug, but is an oxidation product created during the analysis.

Rump (1878) treated Siam Benzoin with caustic lime, precipitated the benzoic acid with hydrochloric acid, and agitated the liquid with ether. The latter on evaporating afforded a mixture of benzoic acid and vanillin, $C_8H_8O_3$. Subjected to dry distillation, benzoin affords, as the chief product, benzoic acid, together with empyreumatic products, among which Berthelot has proved the presence (in Siam Benzoin) of *styrol*, C_8H_8. The latter was also obtained in 1874 by Theegarten from Sumatra Benzoin by distilling it with water. (*B. Chem. G.*, 1874.)

Sumatra Benzoin is sometimes heavily adulterated with stony débris, sand and bark. Schneider reports finding as much as 75 per cent. of bark in a commercial article.

Uses.—Benzoin acts as a stimulating expectorant, and was formerly employed in pectoral affections, but, except as an ingredient of the compound tincture of benzoin, it has fallen into disuse. Trousseau and Pidoux recommend strongly its inhalation in *chronic laryngitis.* Either the air of the chamber may be impregnated with its vapor by placing a small portion upon some live coals, or the patient may inhale the vapor of boiling water to which the balsam has been added. It is occasionally employed in pharmacy for the preparation of benzoic acid (see *Acidum Benzoicum*); the milky liquor resulting from the addition of water to its alcoholic solution is sometimes used as a cosmetic, under the impression that it renders the skin soft. A tincture has been strongly recommended in *anal fissure.* In the East Indias, the balsam is burnt by the Hindus as a perfume in their temples of worship.

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Adeps Benzoinatus, *U. S.* (*Br.*); Tinctura Benzoini, *U. S.*; Tinctura Benzoini Composita, *U. S.*, *Br.*; Sevum Benzoatum, *Br.* (*N. F.*); Unguentum Picis Compositum (from Tincture), *N. F.*

BERBERIS. N. F., Br.

BERBERIS Berber [Oregon Grape Root]

"Berberis consists of the dried rhizome and roots of species of the section *Mahonia* (Nuttall) De Candolle of the genus *Berberis* Linné (Fam.

Berberidaceæ). Berberis contains not more than 5 per cent. of the overground parts of the plant or other foreign organic matter. Reject pieces of the rhizome or root over 45 mm. in diameter or with the bark removed." *N. F.*

Oregon grape root; Nepaul Barberry; Barberry; Epine-vinette, Vinettier, Ecorce de Racine de Berbérides, *Fr.;* Fauerach, Gemeiner Sauerdorn, Berberitze, Berberitzen-(Saurach-) Wurzelrinde, *G.;* Berbero, *It., Sp.*

The genus *Berberis* (Fam. *Berberidaceæ*) is a large one, comprising shrubs or trees which are widely distributed throughout temperate regions and in the mountains of the tropics. There are three well-defined medicinal groups: (1) The Rocky Mountain group, including *Berberis Aquifolium,* which yields the Oregon Grape Root. (2) The Asiatic group, which includes *B. aristata* DC., a shrub indigenous to India and Ceylon, and is recognized by the British Pharmacopœia. (3) The European group, which includes the common Barberry (*B. vulgaris* L.), which is naturalized in New England. According to Dragendorff (*Die Heilpflanzen*), about forty different species of berberis have been used in medicine.

Lycium, or *λύκιον* of the ancients, highly valued as a local application in affections of the eye and eyelids, and used for various other purposes, is supposed to be the medicine still used in India for the same affections, under the name of *rusot* or *ruswut,* which is an extract from various species of berberis combined with opium.

Berberis aristata, which furnishes the berberis of the British Pharmacopœia, is a shrub indigenous to the temperate Himalayas, extending from Bhután to Kanawar, the Nilgiri Hills, and Ceylon. It is erect and branching, the leaves being evergreen, obovate or oblong, entire, sometimes possessing spinose teeth. The flowers are yellow and occur in compound, often corymbose racemes. The stigmas are distinguished by being small and subglobose. The berries are few-seeded and taper into a short style. Several varieties of this species are recognized, viz., *floribunda* and *micrantha.* The type *B. aristata* closely resembles *B. asiatica* Roxb., *B. Lycium* Royle and *B. vulgaris* L., and consequently are mistaken throughout India. The same vernacular names are frequently applied to each of these plants and the same medicinal properties attributed to all.

The N. F. IV recognizes, under the title Berberis, "the rhizome and roots of species of the section *Mahonia* Nuttall of the genus Berberis." This section corresponds to the genus *Odostemon* of Rafinesque, and includes *B. Aquifolium* and *B. Nervosa.*

Berberis Aquifolium Pursh., *Berberis,* U. S. VIII, *Oregon Grape Root, Rocky Mountain Grape, California Barberry, Holly-leaf Barberry, Trailing Mahonia.*

The *Oregon grape* is a tall shrub, about six to seven feet high, with evergreen, coriaceous, bright and shining leaves, and having numerous small, yellowish-green flowers in the early Spring, and later clusters of purple berries containing an acid pulp. It is a native in woods from Colorado to the Pacific Ocean, especially abundant in Oregon and northern California.

Rusby believes that a large part of the berberis collected in Oregon is obtained from *B. Nervosa.* (*Ph. Era,* 1909, p. 633.)

Nepaul Barberry (*Berberis vulgaris* L.) is a native of Europe, but grows wild in waste ground in the eastern parts of New England, and is sometimes cultivated in gardens on account of its berries. It is a spreading shrub, from four to six feet or more in height, with thorny branches, a light gray bark and a fine yellow wood.

The *berries* of *B. vulgaris,* which grow in loose bunches, are oblong and of a red color, have a grateful, sour, astringent taste, and contain malic and citric acids. They are refrigerant, astringent and antiscorbutic, and are used in Europe, in the form of drink, in *febrile diseases* and *diarrheas.* An agreeable syrup is prepared from the juice, and the berries are sometimes preserved for the table. The bark of the root of *B. vulgaris* L. was formerly included in the secondary list of the U. S. Pharmacopœia, under the name of *Berberis.* The root and inner bark have been used for dyeing yellow. The bark of the root is grayish on the outside, yellow within, very bitter, and stains the saliva when chewed.

Algerita Root, which has been used by Mexicans and old settlers in Western Texas, is derived from *Berberis trifoliatus* Moric [*Odostemon trifoliatus* (Moric.) Heller]. The shrub grows in Western Texas and New Mexico and extends into Mexico. The root contains, according to Hart (*A. J. P.,* 1916, p. 301), 1.3 per cent. of berberine and 0.1 per cent. of associated alkaloids. Hydrastine is absent. Infusions of algerita root are used for *eye sores,* while chewing the roots is considered reliable as a corrective for *sore mouths.* Injections of an infusion have been used for *gonorrhea.*

The commercial supplies of berberis used in the United States are obtained from Trieste and Oregon.

For a description of the bark of *B. aristata* DC., by Hartwick, see *Ph. Rev.,* 1896, 232.

Description and Physical Properties.—"*Unground Berberis.*—Cylindrical, more or less knotty, strongly branched, usually cut into pieces of varying length and up to 45 mm. in diameter; usually splitting somewhat on drying; externally light yellowish brown, longitudinally wrinkled and short scaly; fracture hard and tough; bark 1 mm. in thickness, easily separable into layers; wood yellow, the color more pronounced upon wetting, distinctly radiate, and showing rings of growth; pith of rhizome small, sometimes excentric. Odor slight; taste distinctive, very bitter; on chewing it tinges the saliva yellow.

"*Powdered Berberis.*—Yellowish-brown; composed chiefly of fragments of medullary rays, and wood fibers associated with a few tracheæ; wood fibers yellowish, with large, simple, transverse pores; tracheæ chiefly with bordered pores, occasionally reticulate; starch grains simple or 2- to 3-compound, the individual grains being irregularly spherical, 0.003 to 0.020 mm. in diameter, or occasionally larger." *N. F.*

The berberis of the British Pharmacopœia occurs "in undulating pieces from two and a half to five centimetres in diameter. Cork orange-brown, removed in places showing the subjacent darker brown cortex; marked with slightly wavy longitudinal striæ and occasional shallow transverse depressions. Transverse section shows a narrow brown cork; a broad, dark brown bast traversed by conspicuous yellow medullary rays; a bright yellow wood composed of numerous narrow vascular rays, containing many vessels, separated by narrow, paler medullary rays. Slight odor; taste bitter." *Br.*

Constituents.—Both the *B. vulgaris* and *B. aquifolium* contain three alkaloids of which the most important is *berberine*, $C_{20}H_{17}O_4N$. This alkaloid is found in numerous other plants of several natural orders, including *Hydrastis, Argemone, Coptis, Xanthoxylum*, etc. It occurs as golden-yellow crystalline needles, differing from most other alkaloidal bases in being soluble in water, yielding yellow solutions. It is also soluble in chloroform or benzol, but almost insoluble in ether or petroleum benzin.

Besides berberine Hesse (*B. Chem. G.*, 1886, xix, 3190) found *berbamine*, $C_{18}H_{19}O_3N$, and *oxyacanthine*, $C_{19}H_{21}O_3N$. For general properties and color reactions of these alkaloids see Rudel (*J. Chem. S.*, 1892, p. 641) and Pommerehne (*A. Pharm.*, 1895, ccxxxiii, p. 127).

Uses.—The various species of berberis appear to have similar medical properties. The alkaloid berberine is physiologically very feeble. (See *Hydrastis.*) Antiperiodic properties have been attributed to it, and T. Lascarato (*La Grèce médicale*, 1899, No. 2) affirms that it has a specific action upon the spleen which renders it very valuable in the treatment of malarial *splenic enlargement*, and that it is so powerful in producing contraction that when the spleen is softened large doses may produce splenic rupture, with *fatal hemorrhage.* The crude drug probably has no real medicinal effect, except that of a bitter tonic and mild laxative. It is by some believed to have an especial tendency towards the liver and hence is used in *jaundice* and *chronic hepatitis.* It is also stated to have alterative powers and has been employed in *syphilis* and *scrofula.*

Dose, from fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Tinctura Berberidis, *Br.;* Fluidextractum Berberidis, *N. F.*

BETANAPHTHOL. U. S. (Br.)

BETANAPHTHOL Betanaph. [Naphtol, U. S. 1890, Naphthol]

"Beta-monohydroxy naphthalene [$C_{10}H_7$-OH]." *U. S.* "Beta-naphthol, or beta-monohydroxy-naphthalene, $C_{10}H_7OH$, may be obtained from naphthalene-sulphonic acid." *Br.*

Naphthol, *Br.;* β-Naphthol, Beta-mono-hydroxy-naphthalene, Iso-naphthol; Naphtol β, *Fr. Cod.;* Naphtylol-β, *Fr.;* Naphtholum, *P. G.;* Beta-Naphtholum, *G.;* Naftol β, *Sp.*

On digesting four parts of naphthalene with three parts of sulphuric acid at 80° C. there is formed α- and *β-naphthalene sulphonic acids,* $C_{10}H_7SO_3H$, which may be separated by means of the barium or lead salts. When heated with sulphuric acid, the α acid passes into the β variety; therefore the latter acid is exclusively produced at higher temperatures, 160° C. Both of the naphthalene sulphonic acids, when fused with alkaline hydroxides, yield the corresponding naphthols, which are designated as α- and β *naphthol,* respectively. The second of these, betanaphthol, is the official naphthol, $C_{10}H_7OH$. It bears to naphthalene the same relation that phenol does to benzene.

Description and Physical Properties.—"Colorless or pale buff-colored, shining crystalline leaflets, or a white or yellowish-white, crystalline powder. It has a faint, phenol-like odor, and is stable in the air. One Gm. of Betanaphthol is soluble in about 1000 cc. of water, 0.8 cc. of alcohol, 17 cc. of chloroform, and in 1.3 cc. of ether, at 25° C. One Gm. is soluble in 80 cc. of boiling water. It is soluble in glycerin and in olive oil and is readily dissolved by solutions of alkali hydroxides. It sublimes readily when heated, and volatilizes with the vapors of alcohol and of water.

"Betanaphthol melts between 120° and 122° C. A cold, saturated, aqueous solution of Betanaphthol, when mixed with ammonia water, develops a faint, bluish fluorescence. Add about 0.1 Gm. of Betanaphthol to 5 cc. of an aqueous solution of potassium hydroxide (1 in 4), then add 1 cc. of chloroform, and gently warm the mixture: the aqueous layer acquires a blue color, changing afterwards, successively, to green and brown. Ferric chloride T.S. produces a greenish color in a cold, saturated, aqueous solution of Betanaphthol, and after some time causes the separation of whitish flakes, which turn brown upon the application of heat.

"Shake 1 Gm. of Betanaphthol with 100 cc. of distilled water at frequent intervals for fifteen minutes, and filter: the filtrate is neutral to litmus paper. Ash: not more than 0.05 per cent. Dissolve 0.5 Gm. of Betanaphthol in 25 cc. of ammonia water: no residue remains (*naphthalene*), and the solution does not have a deeper color than pale yellow (*other organic impurities*). Boil 0.1 Gm. or Betanaphthol with 10 cc. of distilled water until dissolved, allow the solution to cool, and then filter: the addition to the filtrate of 0.3 cc. of normal sodium hydroxide, followed by 0.3 cc. of tenth-normal iodine, produces no violet color (*alphanaphthol*).

"Preserve in well-closed containers, protected from light." *U. S.*

The British Pharmacopœia describes it as "white, or nearly white, crystalline lamellæ, or in powder. Odor resembling that of phenol; taste sharp, pungent. Soluble in about 1000 parts of *water,* and in 75 parts of boiling *water,* the solutions being neutral to *litmus;* soluble in less than 2 parts of *alcohol* (90 per cent.); very soluble in *ether,* in *chloroform,* and in *solution of sodium hydroxide.* Melting point 122° C. A hot saturated aqueous solution develops a blue fluorescence on the addition of 1 drop of *solution of ammonia.* A cold saturated aqueous solution yields a white turbidity with *solution of chlorine,* which, on the addition of excess of *solution of ammonia,* gives place to a green or brown coloration. 0.1 gramme dissolved in 10 millilitres of boiling *water* yields with 10 drops of an aqueous solution (1 in 30) of *ferric chloride* a white precipitate becoming brown, but not violet (absence of alpha-naphthol). No appreciable ash." *Br.*

Gugliamelli finds an arseno-tungstic reagent to give an intense blue color with alphanapthol and no color with bentanaphthol. Deniges employs a sulphotitanic reagent for differentiating between the two naphthols. This gives a green color with the alpha and a red color with the beta variety.

For Yvon's tests to distinguish between alpha- and betanaphthol, see *Proc. A. Ph. A.,* 1892, 955; see also *Chem. News,* 1892, 18. For Liebman's test for the presence of alphanaphthol, see *M. R.,* 1897, 281. See *Alphanaphthol* (Part II).

Uses.—Betanaphthol is locally irritant to mucous membranes, but on account of its insolubility cannot exercise a caustic effect in aqueous solutions. It is powerfully germicidal. Sternberg found that a solution of 1 part in 2000 would destroy the cholera spirillum after 15 minutes' exposure, and Schneider (*Z. Hyg.,* 1906, lii) finds that it is four times as active as lysol. As an antiseptic it is still more efficient, 1 part in 10,000, according to Maximovitch, being sufficient to prevent the development of all bacteria tested.

As a surgical disinfectant it is not commonly used but has been widely employed in *skin diseases* such as *favus, scabies,* etc., for its parasiticide effect. For this purpose it may be applied in the form of an ointment in strengths of from ½ to 5 per cent. Sloboziano (*G. M. P.,* 1920) highly recommends a 5 to 10 per cent. alcoholic solution of betanaphtol in the treatment of itch; he asserts that the betanaphthol has an anesthetic effect which allays the itching and a positive germicidal effect which destroys the parasite.

The most important uses of betanaphthol, however, are based on its relatively low toxicity which makes it one of the most valuable intestinal antiseptics that we possess in the treatment of *enteritis, intestinal fermentation* and similar conditions. More recently it has been considerably used as a vermifuge, especially in the treatment of *uncinariasis.* Schultz (*J. A. M. A.,* 1911, lvii, p. 1103) recommended for this purpose the administration of fifteen to thirty grains (1–2 Gm.) mixed with one-third its weight of milk sugar and enclosed in a capsule, followed by a cathartic. Certain South American physicians have recommended much larger doses, as high as 6 Gm. (90 gr.). From these quantities from 75 to 85 per cent. of cures have been reported, but Smille (*J. A. M. A.,* 1920, lxxiv, p. 1503) in seventy-nine cases had four in which there was severe destruction of the red blood cells and concludes that such doses are too toxic to be justifiable.

It has also been used as a food preservative, both under its proper name and under fanciful trade names, but this use is forbidden by law. The calcium salt known as abrastol, which is used for the same purpose, is described in Part II.

Dose, as an intestinal antiseptic, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Pasta Betanaphtholis, *N. F.;* Petroxolinum Betanaphtholis, *N. F.*

BETEL. Br.

BETEL

"Betel consists of the dried leaves of Piper Betle, *Linn.*" *Br.*

Betel, Betle, Pawn, or *Pinang* are popular Oriental names for *Piper Betle* L. and *P. Siriboa* L., the leaves of which are used by the Malays as a masticatory. The leaves are usually admixed with scrapings of the Areca nut and lime. The betel plants are indigenuous throughout the entire Indian-Malay region and cultivated in Madagascar, Bourbon and West Indies. The plants are climbing shrubs and trained upon trellises and poles in shady but hot places. The leaves are picked while green, pressed together by means of stones and dried.

Betel leaves of the British Pharmacopœia are described as follows: "About fifteen centimetres long, broadly ovate, acuminate, obliquely cordate at base; thin and brittle, upper surface glossy, five or seven conspicuous lateral veins. Mesophyll contains abundant oil-cells filled with brown oleo-resin. Taste warm, aromatic, bitter. As found in commerce the leaves are frequently tied up or stitched together into packets." *Br.*

The warm aromatic taste of the betel leaves is due to an essential oil known as *betel oil.* This is of a color varying from clear yellow to dark brown and of aromatic, somewhat creosote-like odor and burning sharp taste. The specific gravity ranges from 0.958 to 1.044, the lighter oil being that obtained from the fresh leaves. The alcoholic solution of the oil gives a greenish to bluish-green color with ferric chloride.

The betel oil from Siam contains cadinene and a characteristic phenol named *betelphenol,* isomeric with eugenol; the oil from Java contains in addition to the betelphenol, chavicol and a sesquiterpene; while the Manila oil contains betelphenol as the sole phenolic constituent. (Gildemeister and Hoffmann, *Die Ætherische Oele,* 1899.)

Uses.—The essential oil of betel is an active local stimulant and has been used in *doses* of one to two minims (0.06–0.12 cc.) in the treatment of various respiratory *catarrhs,* and as a local application, either by gargle or inhalation, in *diphtheria.* It is said that the juice of four leaves is equivalent in power to one drop of the oil. In India betel leaves are used locally to a considerable extent for the purpose of counter-irritation and applied to the mammary glands for the purpose of suppressing the secretion of milk in *mammary abscesses.* The essential oil has been given internally in doses of from one to two minims (0.06–0.12 cc.).

BISMUTHI SUBCARBONAS. U. S. (Br.)

BISMUTH SUBCARBONATE Bism. Subcarb. [Basic Bismuth Carbonate, Bismuth Oxycarbonate]

" Bismuth Subcarbonate is a basic salt of varying chemical composition, which, when dried to constant weight at 100° C., yields upon ignition not less than 90 per cent. of bismuth oxide [Bi_2O_3]." *U. S.* " Bismuth Oxycarbonate, $(Bi_2O_2CO_3)_2,H_2O$, may be obtained by the interaction of bismuth nitrate and ammonium carbonate." *Br.*

Bismuthi Carbonas, *Br.;* Carbonate of Bismuth, Oxycarbonate of Bismuth, Bismuthyl carbonate; Bismuthum Subcarbonicum, Subcarbonas Bismuthicus; Souscarbonate de Bismuth, *Fr.;* Basisches Kohlensaures Wismutoxyd, Wismutsubcarbonat, *G.*

A process for this salt is no longer official; that of the U. S. P., 1870, will be found in *U. S. D.,* 19th edition, p. 239.

Description and Physical Properties.—" A white or pale yellowish-white powder. It is odorless and tasteless, and is stable in the air. Bismuth Subcarbonate is insoluble in water and in alcohol. It is completely dissolved by nitric and hydrochloric acids with copious effervescence. Bismuth Subcarbonate responds to the reactions for bismuth and for carbonates.

" One Gm. of Bismuth Subcarbonate shows no more *chloride* than corresponds to 1 cc. of fiftieth-normal hydrochloric acid. Dissolve 3 Gm. of the salt in a sufficient quantity (about 4 cc.) of warm nitric acid, and pour the solution into 100 cc. of distilled water: a white precipitate is produced. Filter, evaporate the filtrate on a water bath to 30 cc., again filter the liquid, divide the latter filtrate into portions of 5 cc. each, and subject these several portions to the following tests: Mix one portion with an equal volume of diluted sulphuric acid: the liquid does not become cloudy (*lead*). Precipitate another portion with a slight excess of ammonia T.S.: the supernatant liquid does not exhibit a bluish tint (*copper*). Another portion is not immediately affected by barium nitrate T.S. (*sulphate*). In another portion, hydrochloric acid produces no precipitate which is insoluble in a slight excess of hydrochloric acid, but soluble in ammonia T.S. (*silver*). Boil 1 Gm. of Bismuth Subcarbonate with 20 cc. of a mixture of equal volumes of acetic acid and distilled water, cool the solution, and filter. Add 2 cc. of diluted hydrochloric acid, remove the bismuth by the addition of hydrogen sulphide, boil the mixture, and again filter: the latter filtrate leaves not more than 0.005 Gm. of residue on evaporation and gentle ignition (*alkalies or alkali earths*). Agitate about 0.05 Gm. of Bismuth Subcarbonate with 5 cc. of a solution of equal volumes of distilled water and ferrous sulphate T.S., and cautiously superimpose the mixture upon 5 cc. of concentrated sulphuric acid, no brownish-red zone forms at the line of contact of the two liquids (*nitrate*). The residue resulting from the ignition of 2 Gm. of Bismuth Subcarbonate does not respond to Bettendorf's Test for *arsenic.*

" **Assay.**—Dry about 1 Gm. of Bismuth Subcarbonate to constant weight at 100° C., weigh accurately in a tared porcelain crucible, ignite at a red heat, and weigh the resulting bismuth oxide. The residue of bismuth oxide (Bi_2O_3) corresponds to not less than 90 per cent. of the original weight of Bismuth Subcarbonate taken.

" Preserve protected from light." *U. S.*

" A whitish, inodorous powder. Insoluble in *water;* soluble in *nitric acid* diluted with half its volume of *water.* Yields the *reactions* characteristic of bismuth and of carbonates. Yields when strongly heated from 89 to 91 per cent. of bismuth oxide. Yields no characteristic *reactions* for silver, lead, copper, calcium, selenium, tellurium, or chlorides, and not more than the slightest *reaction* for sulphates. *Arsenic limit* 2 parts per million. On mixing 0.02 gramme with 5 drops of *phenoldisulphonic acid,* adding after five minutes, 10 millilitres of *solution of ammonia,* filtering, washing the precipitate with *water* and adding *water* to the filtrate until it measures 100 millilitres, the color of the filtrate is not deeper than that obtained by similarly treating 0.00013 gramme of *potassium nitrate* (limit of nitrate). The solution obtained by exhausting 5 grammes with boiling *water* requires for neutralisation not more than 1 millilitre of *N/10 solution of sulphuric acid* (limit of alkaline carbonates)." *Br.*

Its sp. gr. is about 4. It effervesces with acids, and, when exposed to heat, loses 9.5 per cent. of its weight in consequence of the escape of carbon dioxide, and is converted into the anhydrous trioxide, of a slight yellow color.

Uses.—Bismuth subcarbonate has the general properties of the insoluble salts of bismuth. (See under *Bismuthi Subnitras.*) In cases of *gastritis* and especially in *gastric ulcer* the fact that it acts as an alkali gives it preference over the subnitrate which is usualy acid in reaction. Loeper (*J. A. M. A.,* 1920, lxxv, 903) has found it valuable for the expulsion of *oxyuris vermicularis.* It is especially preferred over the subnitrate when large quantities are to be taken, as in röntgenography, because of its lower toxicity. For the purpose of rendering opaque to the X-ray the walls of the intestines it is the habit to give one to two ounces of an insoluble salt of bismuth. This quantity of the subcarbonate produces absolutely no disturbances of either the general system or the alimentary canal.

Dose, ten to thirty grains (0.65–2.0 Gm.).

BISMUTHI SUBGALLAS. U. S.

BISMUTH SUBGALLATE Bism. Subgal. [Basic Bismuth Gallate, Bismuth Oxygallate, Dermatol]

"Bismuth Subgallate is a basic salt of varying chemical composition which, when dried to constant weight at 100° C., yields, upon ignition, not less than 52 per cent. nor more than 57 per cent. of bismuth oxide [Bi_2O_3]." *U. S.*

Bismuthyl Gallate; Bismuth Monogallate; Dermatolum; Gallas Bismuthi Basicum; Gallate Basique de Bismuth, *Fr. Cod.;* Sousgallate de Bismuth, *Fr.;* Bismutum subgallicum, *P. G.;* Basisches Wismutgallat, *G.;* Galato basico de bismuto, *Sp.*

Preparation.—Bismuth Subgallate was originally prepared by Bley in 1841; Fischer again prepared and described it in 1891. It was introduced to the medical profession under the proprietary name of *Dermatol.* Its composition has been stated to be $C_6H_2(OH)_3.COOBi(OH)_2$. F. T. Greene proposes the following process: Normal bismuth nitrate, 1 oz. av.; glacial acetic acid, 2 fl. oz. or q. s.; gallic acid, 250 grains. Dissolve the normal bismuth nitrate in the glacial acetic acid; add a pint of water. If bismuth salts should precipitate, add more glacial acetic acid until clear. Filter off impurities. Dissolve the gallic acid in a pint of warm water; mix the solutions; allow the precipitate to subside; decant; wash by decantation with warm water until washings no longer show acid reaction. Dry at 100° C.; rub to powder. See *Ph. Rund.,* 1896, 85; *Ph. Ztg.,* 1901, 1033.

Description and Physical Properties.—"An amorphous, bright yellow powder. It is odorless and tasteless, and is stable in the air. Bismuth Subgallate is practically insoluble in water, alcohol and ether. It is readily dissolved with decomposition by warm, moderately dilute hydrochloric, nitric or sulphuric acid, insoluble in very dilute mineral acids. It is readily dissolved by solutions of alkali hydroxides, forming a clear, yellow liquid, which rapidly changes to a deep red.

"When heated to redness, Bismuth Subgallate at first chars, leaving finally a yellow residue, which is blackened by hydrogen sulphide T.S. A solution of this residue in a slight excess of warm nitric or hydrochloric acid produces a white turbidity when added to twenty-five volumes of distilled water. Agitate thoroughly about 0.1 Gm. of Bismuth Subgallate with an excess of hydrogen sulphide T.S., filter, boil the filtrate to remove the dissolved gas, cool, and add one drop of ferric chloride T.S.: a blue-black color is produced.

"Shake 1 Gm. of Bismuth Subgallate with 20 cc. of alcohol for one minute, filter, and evaporate the filtrate to dryness on a water bath: not more than 0.005 Gm. of residue remains (*free gallic acid*). Boil 1 Gm. of Bismuth Subgallate with 20 cc. of a mixture of equal parts of acetic acid and distilled water, cool the solution, and filter. Free the filtrate from bismuth by the addition of hydrogen sulphide, boil the mixture, and again filter: the latter filtrate leaves not more than 0.005 Gm. of residue on evaporation and gentle ignition (*alkalies or alkali earths*). Mix thoroughly about 0.05 Gm. of Bismuth Subgallate with 5 cc. of diluted sulphuric acid and 5 cc. of ferrous sulphate T.S., filter the mixture, and carefully superimpose the filtrate, without mixing, on 5 cc. of concentrated sulphuric acid, in a test tube: no brownish-red zone forms immediately (*nitrate*). Ignite 3 Gm. of Bismuth Subgallate in a porcelain crucible, cool, and cautiously add, drop by drop, just sufficient nitric acid to dissolve the residue when it is warmed. Evaporate the solution to dryness, again ignite, and cool. Cautiously dissolve this residue in just sufficient nitric acid by the aid of gentle heat, concentrate the solution to about 4 cc., pour it into 100 cc. of distilled water, filter, evaporate the filtrate on a water bath to 20 cc., again filter, and divide this filtrate into portions of 5 cc. each. These portions do not respond to the tests for *lead, copper or silver* under *Bismuthi Subcarbonas.* The residue resulting from the ignition and subsequent treatment of 2 Gm. of Bismuth Subgallate, as described in the following test, meets the requirements of Bettendorf's Test for *arsenic.*" *U. S.*

Uses.—Bismuth subgallate was originally introduced into medicine as a substitute for iodoform in the treatment of *eczema* and other skin diseases and in surgical dressings. It does not, however, act like iodoform, and is only a feeble germicide. It resembles closely in all its medicinal activities the older insoluble preparations of bismuth, than which it is, however, thought by some practitioners to be more astringent, and therefore preferable in *diarrhea;* otherwise its rank in internal medicine is precisely that of the subnitrate.

Dose, seven to thirty grains (0.45–2.0 Gm.).

BISMUTHI SUBNITRAS. U. S., Br.

BISMUTH SUBNITRATE Bism. Subnit. [Basic Bismuth Nitrate, Bismuth Oxynitrate]

"Bismuth Subnitrate is a basic bismuth nitrate of varying chemical composition, which, when dried for twenty-four hours over sulphuric acid, yields upon ignition not less than 79 per cent. of bismuth oxide [Bi_2O_3]." *U. S.* "Bismuth oxynitrate, $BiONO_3,H_2O$, may be obtained by the interaction of bismuth nitrate and water." *Br.*

Subnitrate of Bismuth; Bismuthum Album, *Br.* 1864; Bismuthyl Nitrate; Magistery of Bismuth; White Bismuth; Nitras Bismuthi Basicus, Magisterium Bismuthi, Subazotas (s. Subnitras) Bismuthicus; Azotate (sous) de Bismuth, *Fr. Cod.;* Sous-nitrate de Bismuth, *Fr.;* Bismutum subnitricum, *P. G.;* Basisches Salpetersaures Wismutoxyd, Basisches Wismutnitrat, Wismutsubnitrat, *G.;* Nitrato basico di bismuto, *It.;* Nitrato (sub) bismutico, Magisterio de bismuto, *Sp.*

A process for bismuth subnitrate is no longer official in either the U. S. or Br. Pharmacopœias. In the U. S. formula of 1870 bismuth was dissolved in nitric acid added to a solution of sodium, carbonate, the resulting precipitate dissolved in nitric acid and precipitated with ammonia water, the object of this repeated precipitation being to get rid of arsenic which often contaminates metallic bismuth. The former British process (1867) dissolved purified bismuth in nitric acid, concentrated the solution by evaporation and poured it into a large volume of distilled water collecting the consequent precipitate. For details of these methods see *U. S. D.*, 19th edition, p. 242.

A. de Schulten obtained *crystallized bismuth subnitrate,* $5Bi_2O_3.5N_2O_5.9H_2O$, by dissolving 50 Gm. of bismuth subnitrate in 50 cc. of nitric acid (sp. gr. 1.2) and adding 300 cc. of water while stirring; the crystals which are produced are pressed between folds of filter paper and dried. (*Chem. News,* 1904, 87.) *Bismuth trinitrate,* the salt which is formed by dissolving metallic bismuth in nitric acid, forms colorless crystals of the formula, $Bi_3NO_3.5H_2O$, which are soluble in glycerin and acids but are changed by water to the insoluble subnitrate. This salt was at one time used for medicinal purposes but has been almost completely abandoned. Bismuth nitrate was used by Balmanno Squire dissolved in glycerin, under the name of *Glycerole of Nitrate of Bismuth.* W. W. Moorhead prepares it by taking two troyounces of crystalline bismuth nitrate and dissolving in sufficient glycerin to make eight fluidounces. No heat should be used. This preparation can be diluted with an equal bulk or less of water, or one part can be added to forty-eight of water without precipitation, but one part to twelve, eight, or six of water soon precipitates. (*A. J. P.*, 1877, p. 98.)

Description and Physical Properties.—"A white, slightly hygroscopic powder. Bismuth Subnitrate is practically insoluble in water, insoluble in alcohol, but is readily dissolved by hydrochloric or nitric acid. Bismuth Subnitrate responds to the reactions for bismuth and for nitrates. When heated to redness, it evolves brown vapors of nitrogen oxides, leaving a yellow residue. When brought in contact with moistened blue litmus paper, Bismuth Subnitrate shows a slightly acid reaction.

"Boil 1 Gm. of Bismuth Subnitrate with 20 cc. of a mixture of equal volumes of acetic acid and distilled water, and cool: a clear solution should result. Add 2 cc. of diluted hydrochloric acid, remove the bismuth by the addition of hydrogen sulphide, boil the mixture, and filter: the filtrate leaves not more than 0.005 Gm. of residue on evaporation and gentle ignition (*zinc, iron, alkali earths or alkalies*). Boil about 0.1 Gm. of the salt with 5 cc. of sodium hydroxide T.S.: no odor of ammonia is perceptible nor does the vapor turn moistened red litmus paper blue. One Gm. of the salt shows no more *chloride* than corresponds to 0.5 cc. of fiftieth-normal hydrochloric acid. The residue resulting from the ignition of 2 Gm. of the salt meets the requirements of Bettendorf's Test for *arsenic.* Add 3 Gm. of Bismuth Subnitrate to 3 cc. of warm nitric acid: no effervescence occurs (*carbonate*), and no residue remains (*insoluble foreign salts*). A white precipitate is produced when this solution is poured into 100 cc. of distilled water. Now filter, evaporate the filtrate on a water bath to 30 cc., again filter the liquid, and divide the new filtrate into portions of 5 cc. each. These portions do not respond to the tests for *lead, copper, sulphate or silver* under *Bismuthi Subcarbonas.*

"**Assay.**—Dry about 1 Gm. of Bismuth Subnitrate over sulphuric acid for twenty-four hours, weigh accurately in a tared porcelain crucible, ignite at red heat, and weigh the resulting bismuth oxide. The residue of bismuth oxide (Bi_2O_3) corresponds to not less than 79 per cent. of the original weight of Bismuth Subnitrate taken.

"Preserve protected from light." *U. S.*

"A white, inodorous, microcrystalline powder, with not more than a slight action on *litmus.* Yields the *reactions* characteristic of bismuth and of nitrates. Yields when strongly heated, from 79 to 82 per cent. of bismuth oxide. Yields no characteristic *reactions* for silver, lead, copper, calcium, selenium, or tellurium, and not more than the slightest *reactions* for chlorides or sulphates. *Arsenic* limit 2 parts per million." *Br.*

For examination of commercial bismuth subnitrate by Curtman, see *A. J. P.*, 1896, 422; *Ph. Era,* 1896, 43; also a paper by F. A. Upsher Smith (*P. S.*, 1900, 15).

Bismuth subnitrate is incompatible with potassium iodide (slowly forming a brick-red bismuth iodide) and with alkaline bicarbonates.

Uses.—The almost complete insolubility of the bismuth subnitrate has led to the belief that it is incapable of being absorbed from the gastrointestinal tract, but a number of chemists have found traces of bismuth in the urine and in various internal organs after its oral exhibition. It is evident, therefore, that it may be slowly absorbed from the bowels, but apparently unlimited quantities can be given by the mouth without enough of the metal being absorbed to produce any sign of bismuth intoxication. Although serious symptoms have been reported from the ingestion of doses of two ounces of bismuth subnitrate administered for röntgenographic purposes, it has been shown that the condition was due to the formation of nitrous acid in the intestinal tract and not to the bismuth. When applied to raw surfaces, however, the subnitrate of bismuth undergoes some chemical change and sufficient of the metal may be absorbed to cause fatal poisoning The symptoms of bismuth poisoning which have followed the surgical use of bismuth subnitrate are as follows: There appears first a bluish line on the edges of the gum which spreads and becomes darker in color until the whole tongue and pharynx are almost black. There also develops ulcerative stomatitis with salivation, nephritis, vomiting, and in some cases mental disturbances and methemoglobinemia. The mortality in this poisoning is high. (See David and Kauffmann, *J. A. M. A.*, 1909, lii.)

The insoluble salts of bismuth because of their heaviness, as well as their insolubility, tend to cling to any surface to which they are applied; therefore when they are brought in contact with the mucous membrane they form over it a coating which protects the membrane against the action of a local irritant. Chiefly because of this protective action, but probably also in part because of a feeble antiseptic influence, the insoluble salts of bismuth are of great value in the treatment of all forms of *catarrh,* especially of the acuter types, such as *rhinitis, gastritis,* or *enteritis.* Although in no proper sense an antemetic, in cases of *vomiting* dependent upon irritation of the stomach, bismuth by its sedative influence upon the mucous membrane may relieve the emesis. In the same way in cases of *gastric ulcer* it assuages the pain by protecting the ulcerated surface from the irritant secretion of the stomach. When used in cases of gastric disease it should be given when the stomach is empty, preferably in the form of a suspension or as a dry powder, so that it will spread of itself out over the mucous membrane of this organ before it is carried out into the duodenum, by peristaltic movements. On the other hand, in *enteritis* it should be given after meals. The bismuth salts are also useful as topical applications in the treatment of *coryza, gonorrhea, dysentery,* and similar conditions. For this purpose from 1 to 4 per cent. should be suspended by means of mucilage of acacia. When administered by mouth in fairly large quantities bismuth often causes blackish discoloration of the stools. As a form of suspension of bismuth subnitrate less liable to produce bismuth poisoning, it has been suggested to use 20 Gm. of bismuth subnitrate, 70 Gm. of liquid petrolatum, and 10 Gm. of petrolatum. This preparation is not readily absorbed and may be sweetened and flavored and used for a bismuth meal for radioscopy.

As was first shown by Kocher the insoluble salts of bismuth possess considerable antiseptic virtues when applied to raw surfaces. The subnitrate of bismuth was at one time largely, and it still is to a less extent, used as a dusting powder in various *wounds* and *ulcers.* In 1908 Beck (*J. A. M. A.,* March 14, 1908) described the favorable results following the injection of a mixture containing one part of bismuth subnitrate and two parts of petrolatum into the chronic *fistulas* of *bone tuberculosis.* His method has been followed by a large number of surgeons with mostly favorable results, although in a number of cases the injection of the bismuth paste into abscess cavities has led to bismuth poisoning. This mixture is known as *Beck's bismuth paste,* and it is important that it shall be sterile. Under the title of *Bipp* an ointment of bismuth and iodoform was introduced as a wound dressing during the World War and has been largely used by English surgeons. The formula recommended by Morison is iodoform 440 Gm., bismuth subnitrate 220 Gm., petrolatum 220 Gm.

The bismuth and petrolatum are sterilized by dry heat at temperature of 120° C. for half an hour, the bismuth after cooling is mixed with the iodoform in a mortar that has been sterilized by means of boiling water and solution of formaldehye. The petrolatum is added to the mixture at a temperature of 90° C. and thoroughly mixed. Care must be taken in sterilizing that the temperature does not rise to high, otherwise nitrous fumes will be evolved.

For further information on this paste see *J. A. M. A.*, 1918, lxxi, 300.

The acidity of bismuth subnitrate sometimes leads to the development of explosive mixtures in prescriptions containing sodium bicarbonate.

Dose, five to thirty grains (0.32–2.0 Gm.).

Off. Prep.—Unguentum Resorcinolis Compositum, *N. F.;* Glyceritum Bismuthi, *N. F.;* Magma Bismuthi, *N. F.*

BISMUTHI SUBSALICYLAS. U. S. (Br.)

BISMUTH SUBSALICYLATE Bism. Subsalicyl.

[Basic Bismuth Salicylate, Bismuth Oxysalicylate]

"Bismuth Subsalicylate is a basic salt of varying chemical composition, which, when dried to constant weight at 100° C., yields upon ignition not less than 62 per cent. and not more than 66 per cent of bismuth oxide [Bi_2O_3]." *U. S.* "Bismuth Salicylate, or oxysalicylate, $BiOC_7H_5O_3$, may be obtained by the interaction of bismuth hydroxide and salicylic acid." *Br.*

Bismuthi Salicylas, *Br.;* Bismuth Salicylate; Bismuthyl Salicylate, Bismuth Oxysalicylate; Salicylate Basique de Bismuth, *Fr. Cod.;* Sous-salicylate de Bismuth, *Fr.;* Bismuthum subsalicylicum, *P. G.;* Basisches Wismutsalicylat (salicylsaures Wismutoxyd,) Wismutsubsalicylat, *G.;* Salicilato de bismuto, *Sp.*

Preparation.—This salt is a bismuthyl salicylate of somewhat variable composition, the bismuth oxide resulting from its ignition being about 64 per cent. Samples which show a higher percentage than this either contain bismuth subnitrate or hydroxide. It may be made by Wolff's process, by diluting a glycerin solution of crystallized bismuthous nitrate with one or two parts of water, and decomposing this with a concentrated aqueous solution of sodium salicylate, then washing the precipitate well with hot water and carefully drying. Another method for its preparation will be found in *A. J. P.,* 1891, 401. Fischer and Grützner (*A. Pharm.,* 1894, 680) object to the variable composition of commercial bismuth salicylate, and recommend the following process for making a basic salt of constant composition. Crystallized bismuth nitrate is dissolved in four times its weight of diluted acetic acid, the solution diluted with about forty times its weight of water, and the bismuth precipitated as hydroxide by ammonia water. The precipitate is washed and mixed with the molecular proportion of salicylic acid. After heating on a water bath, a magma of crystals of basic bismuth salicylic is formed; these are drained and dried. B. Fischer recommended the following process: one molecule each of salicylic acid and freshly precipitated bismuth hydroxide are heated together with the necessary amount of water on the water bath; filter, collect and dry the residue at 80° to 100° C. on porous tiling. (*Ph. Centralh.*, 1895, 92, 169.) Duyk perpares bismuth salicylate as follows: 100 Gm. of pure bismuth subnitrate are treated for one or two days with one liter of water, to which 50 Gm. of ammonia water have been added. After shaking sufficiently the subnitrate is completely changed into an oxide, which is collected and carefully washed with water. This oxide, after expression, is heated, under constant stirring, with 25 Gm. powdered salicylic acid on a water bath. After the union has been effected, the salicylate is washed and dried at a gentle heat. (*B. S. Ph. Br.*, 1891.) Thibault prefers the use of crystallized bismuth nitrate and solution of sodium hydroxide to precipitate the bismuth hydroxide. (*Bull. Soc. Chem.*, xxv, No. 16.) The bismuth is combined not only with the hydrogen of the carboxyl group but with the hydrogen of the phenolic group as well. Hence it is not a true salt of bismuth and salicylic acid and the name *salicylated bismuth* would be more correct.

Description and Physical Properties.—"A white, or nearly white, amorphous or crystalline powder. It is odorless, and is stable in the air. Bismuth Subsalicylate is practically insoluble in cold water. Upon prolonged boiling with water, a portion of the salicylic acid passes into solution with the formation of a more basic bismuth salicylate. When treated with a slight excess of warm nitric or hydrochloric acid, it is decomposed, a flocculent white precipitate of salicylic acid separating.

"When heated, Bismuth Subsalicylate at first chars, and above 300° C., leaves a yellow residue, which is blackened by hydrogen sulphide. This residue responds to the reactions for bismuth. Agitate about 0.1 Gm. of Bismuth Subsalicylate with a solution of five drops of ferric chloride T.S. in 10 cc. of distilled water: a deep violet-blue coloration is produced.

"Agitate 1 Gm. of Bismuth Subsalicylate with 20 cc. of chloroform, filter the liquid, and evaporate the filtrate to dryness: not more than 0.005 Gm. of residue remains (*free salicylic acid*). Ignite 3 Gm. of Bismuth Subsalicylate in a porcelain crucible, cool and cautiously add, drop by drop, just sufficient nitric acid to dissolve the residue when it is warmed. Pour the acid solution into 100 cc. of distilled water, filter, evaporate the filtrate on a water bath to 30 cc., again filter, and divide the filtrate into portions of 5 cc. each. These portions do not respond to the tests for *lead, copper, sulphate, or silver* under *Bismuthi Subcarbonas.* Boil 1 Gm. of Bismuth Subsalicylate with 20 cc. of a mixture of equal parts of acetic acid and distilled water, cool the solution, and filter. Free the filtrate from bismuth by the addition of hydrogen sulphide, boil the mixture, and again filter: the latter filtrate on evaporation and ignition leaves not more than 0.005 Gm. of residue (*alkalies or alkali earths*). Triturate about 0.05 Gm. of Bismuth Subsalicylate with 0.1 Gm. of sodium salicylate and 5 cc. of distilled water, and superimpose the mixture upon 5 cc. of concentrated sulphuric acid, no pink or brownish-red zone is observed at the line of contact (*nitrate*). The residue resulting from the ignition and subsequent treatment of 2 Gm. of Bismuth Subsalicylate, as described in the test below, meets the requirements of Bettendorf's Test for *arsenic.*

"**Assay.**—Dry about 1 Gm. of Bismuth Subsalicylate to constant weight at 100° C., and weigh accurately. Ignite in a porcelain crucible, and, after cooling, add 5 cc. of nitric acid, drop by drop, to the residue, warming until solution has been effected. Evaporate this solution to dryness, and carefully ignite it at red heat and weigh the resulting bismuth oxide. The residue of bismuth oxide (Bi_2O_3) corresponds to not less than 62 per cent. and not more than 66 per cent. of the original weight of Bismuth Subsalicylate taken.

"Preserve protected from light." *U. S.*

"A white or nearly white amorphous powder, insoluble in *water.* Yields the *reactions* characteristic of bismuth. When shaken with diluted *T. Sol. of ferric chloride* a violet color is produced. Yields not more than the slightest characteristic *reaction* with the copper test for nitrates. *Arsenic limit* 2 parts per million. When 5 grammes are shaken with 50 millilitres of *ether*, the ethereal solution filtered off and evaporated to dryness leaves not more than 0.005 gramme of residue (limit of free salicylic acid). Yields when strongly heated from 62 to 65 per cent. of bismuth oxide. Free from the impurities indicated under 'Bismuthi Carbonas.'" *Br.*

Uses.—Bismuth subsalicylate differs from the subnitrate in that it exercises a distinctly antiseptic as well as protective effect in the bowels It is used to a considerable extent in the treatment of chronic *intestinal catarrhs* and subacute *diarrheas* with marked tendency to intestinal fermentation; also as a local antiseptic remedy for *wounds* and various inflamations of the mucous membrane.

Dose, from ten to twenty grains (0.65–1.3 Gm.), every four to eight hours.

BISMUTHUM.

BISMUTH

$Bi = 208.0$

Etain de Glace, Bismuth, *Fr.;* Wismuth, Wismut, *G.;* Bismuto, *It., Sp.*

Bismuth occurs usually in the metallic state, occasionally as a sulphide (*bismuthite*) or a telluride, and rarely as an oxide. It is found largely in Saxony, Schneeberg being the chief point of production. It has been found, mainly as telluride of bismuth, in Colorado with gold and silver ores. Small quantities have been found in Utah and Wyoming. It has also been discovered in southern Australia, from whence a quantity of it has been sent into commerce. It is obtained almost entirely from native bismuth ore, which is heated by means of wood or charcoal, whereby the metal is fused, and separated from its gangue. Most of the bismuth of commerce formerly came from Germany and Austria, but it is now largely mined in Bolivia and Australia. The bismuth ore from South America is said to be naturally free from arsenic, and to be therefore preferable for pharmaceutical purposes.

As the production of bismuth in the world far exceeds the demand, there is no regular American production, much of that which accompanies the gold and silver in the ore being allowed to go to waste in the slag.

Bismuth was first recognized as a metal by Agricola in 1520. Before that period it was confounded with lead. It is brittle, pulverizable, brilliant metal, of a crystalline texture, and of a white color with a slight reddish tint. Its crystals are rhombohedral, but with an angle of 87° 40′, which makes it difficult to distinguish them from cubes, in which the angle would be 90°. Indeed, many books still refer to it as cubical in form. It undergoes but a slight tarnish in the air. Its sp. gr. is 9.8 (*B. P.*, 1885, purified 9.38), melting point 264° C. Its most notable property is the ease with which it forms easily fusible alloys used as valves in fire sprinkler systems, for wood cuts, etc. *Wood's metal* consists of cadmium, tin, lead and bismuth and melts at 68° C. *Rose's metal* consists of lead, tin and bismuth and melts at 79° C. *Newton's alloy* also contains lead, tin and bismuth and melts at 95° C. *Lipowitz's alloy* has the same elements present as Woods metal but in slightly different proportions and softens at 60° C. At a high temperature, in close vessels, bismuth volatilizes, and may be distilled over. When heated in the open air to a full red heat, it takes fire, and burns with a faint blue flame, forming an oxide of a yellow color. This is the *trioxide*, or *bismuthous oxide*, and consists of two atoms of bismuth and three of oxygen. There is another compound of bismuth and oxygen consisting of two atoms of the former and five atoms of the latter, which is called *bismuthic oxide*, Bi_2C_5. It is obtained in the form of a hydroxide by boiling bismuth nitrate in solution of potassium hydroxide, washing the precipitate, and mixing it while moist with solution of potassium hydroxide into which chlorine is passed. A mixture of bismuthous and bismuthic oxides is precipitated, from which the former is separated by digestion with nitric acid. The hydroxide remaining, when washed and dried, is in the form of a red powder, which gives up its water at 130° C., and at a higher heat loses oxygen. Bismuth is acted on feebly by hydrochloric acid, but violently by nitric acid, which dissolves it with a copious liberation of red fumes. Sulphuric acid, when cold, has no action on it, but at a boiling heat effects its solution with the liberation of sulphurous acid. As it occurs in commerce, it is generally contaminated with other metals, among which are arsenic in minute quantity, traces of silver, cadmium, nickel, lead and iron, and sometimes a very small proportion of thallium. Claassen has found in so-called "purissimus" bismuth, lead, copper, and iron, and in one sample of bismuth, sold as suitable for scientific purposes, he obtained from 500 grammes 10 grammes of lead chloride. (*Ap. Ztg.*, 1891, p. 121; see also *Chem. News*, 1892, lxv, 28.) It may be purified from all contaminating metals by dissolving the bismuth of commerce in diluted nitric acid, precipitating the clear solution by adding it to water, and reducing the white powder thus obtained with black flux. The same precipitate is obtained by adding ammonia to the nitric solution; if the supernatant liquid in blue, the presence of copper is indicated; if the precipitate is yellowish, iron is present.

Uses.—Bismuth is not used in medicine in an uncombined state, but is employed pharmaceutically to obtain bismuth subcarbonate, subnitrate, subgallate, subsalicylate and other medicinal preparations formed from this metal. In the arts its oxychloride is used to form a cosmetic for the complexion, called *pearl white*, and the metal is an ingredient of the best pewter.

Recently the bismuth salts have been found to be highly toxic to certain protozoa and some of them have been used in syphilis and other protozocal infections (see *Luatol*, Part II).

Although enormous doses of the official salts of bismuth can be given by mouth without injurious effect, when introduced into the circulation the metal is an active poison. Soluble salts of bismuth when injected into the blood stream in sufficient doses stimulate the central nervous system, giving rise to convulsions and depress the circulation. Non-fatal doses cause violent inflammation of the excreting organs, including the kidney, salivary glands and intestine. The type of poisoning seen in human beings from the medicinal use is described under bismuth subnitrate.

BITUMEN SULPHONATUM. N. F.

SULPHONATED BITUMEN Bitum. Sulph.

"Sulphonated Bitumen contains not less than 2.5 per cent. of ammonia, not more than 8 per cent. of ammonium sulphate, and not less than 10 per cent. of total sulphur." *N. F.*

Ichthyol; Ammonii Sulphoichthyolas; Ammonium Sulphoichthyolate; Ammonium Ichthyolsulphonate; Ammonium Ichtholicum; Sulpho-ichthyolas Ammonicus, Ictiol, *Sp.*

There has long been used in medicine a group of tarry preparations obtained by sulphonating bituminous shale. The original preparation of this type was prepared from the distillate of a peculiar deposit found in the Tyrol and was known under the name of *ichthyol.* This distillate when treated with sulphuric acid gave a compound known as *ichthyol-sulphonic* acid which was neutralized before being used, generally with ammonium.

A large number of more or less similar preparations are upon the market. These are described in Part II under the group of *Ichthyol substitutes.* Thompson (*Proc. N. Y. State Pharm. Assoc.,* 1920, p. 198) finds the proportion of sulphur in these substances to vary from 4.5 to 11 per cent.

Description and Physical Properties.—"A viscous fluid obtained by the destructive distillation of certain bituminous schists, sulphonating the distillate and neutralizing the product with ammonia. Sulphonated Bitumen is reddish brown to brownish black in color, with a strong characteristic, empyreumatic odor. It is soluble in water and in glycerin, and is miscible with fixed oils and fats. It is partly soluble in alcohol or ether, and entirely soluble in a mixture of equal volumes of these solvents. An aqueous solution (1 in 10) may be faintly acid or faintly alkaline to litmus paper. The addition of hydrochloric acid to this solution precipitates a dark resinous mass which is soluble in ether.

"Upon boiling an aqueous solution with sodium hydroxide T.S., ammonia is evolved. Upon incineration, the ash of sulphonated bitumen does not exceed 0.5 per cent. Upon drying on a water bath to constant weight, sulphonated bitumen loses not more than 50 per cent.

"**Assay for Ammonia.**—Accurately weigh about 5 Gm. of Sulphonated Bitumen, dissolve in 100 cc. of water, transfer to a distillation flask, add an excess of sodium hydroxide solution and distil slowly; collect the distillate (about 50 cc.) in 15 cc. of normal sulphuric acid. When the distillation is completed, titrate the excess of sulphuric acid with tenth-normal sodium hydroxide, using methyl orange as indicator. Each cc. of tenth-normal sulphuric acid corresponds to 0.001703 Gm. of NH_3.

"**Assay for Ammonium Sulphate.**—Accurately weigh about 1 Gm. of Sulphonated Bitumen, transfer to a 100 cc.-beaker and add 25 cc. of alcohol. Stir thoroughly, filter, and wash the filter with a mixture of equal parts of ether and alcohol until the washings are clear and colorless. Dry the residue on the filter at 100° C., cool, and wash the filter with 200 cc. of warm water slightly acidulated with hydrochloric acid. Determine the sulphate in the solution by precipitation with barium chloride T.S., and after washing, drying, igniting, and weighing, calculate the results to ammonium sulphate.

"**Assay for Total Sulphur.**—Dry about 1 Gm. of Sulphonated Bitumen, on a watch glass, to constant weight at 105° C. Pulverize the dried material and transfer about 0.5 Gm., accurately weighed, to a nickel crucible. Add about 9 Gm. of sulphur-free sodium peroxide, and mix thoroughly. Place the crucible carefully in a beaker containing cold distilled water which should reach about half way to the top. Ignite the dry mixture in the crucible by thrusting a red hot iron wire through a hole in the cover of the crucible. After complete combustion has taken place, tip the crucible and allow the fused mass to dissolve in the distilled water. Add hydrochloric acid in slight excess, heat to boiling and determine the sulphate in the solution by precipitation with barium chloride T.S., and after washing, drying, igniting, and weighing, calculate the results to sulphur. The total sulphur should not be less than 10 per cent." *N. F.*

The *sodium ichthyol* (*sodium sulphoichthyolate*) is a dark, tar-like substance of an alkaline reaction, perfectly soluble in water. Both preparations combine with fat and vaseline in all proportions. According to Baumann, they have a great affinity for oxygen, and are powerful reducing agents. The ichthyol sulphonates of lithium, zinc, mercury, sodium and calcium have also been prepared.

Odorless ichthyol has been made by treating ichthyol with hydrogen dioxide. It is questionable, however, whether the removal of the odorous constituents does not impair the therapeutic activity of the ichthyol.

Uses.—Ichthyol was formerly attributed with almost magic alterative action upon the skin, but is much less highly esteemed today than two decades ago. Such therapeutic value as it possesses appears to be due to a combination of four properties; it is feebly irritant and therefore acts as a local stimulant, tending to improve the peripheral circulation. It possesses reducing properties similar to those of sulphur; it appears to penetrate the skin with comparative readiness; it is feebly antiseptic. Abel (*Cb. B.,* 1893, xiv, p. 413) finds that pure ichthyol kills staphylococci in five minutes but will not destroy the typhoid bacillus even after an hour; that one to two thousand inhibits the growth of streptococci but it requires 5 per cent. to prevent the growth of staphylococci.

Sulphonated bitumen has been used in a very large variety of skin diseases, but is especially prized in the treatment of *acne* and *furunculosis.* It has been used also as a mild counterirritant in *rheumatic* conditions and *sprained joints.* The use of it in *lymphadenitis* is based upon nothing more tangible than a forlorn hope of the desperate. It has also been occasionally prescribed internally as an expectorant.

Dose, from two to five grains (0.12–0.3 Gm.).

Off. Prep.—Collodium Bituminis Sulphonati, *N. F.;* Petroxolinum Bituminis Sulphonati, *N. F.;* Unguentum Bituminis Sulphonati, *N. F.*

BOLDUS. N. F.

BOLDO [Boldo Leaves]

"Boldo is the dried leaf of *Boldu Boldus* (Molina) Lyons (Fam. *Monimiaceæ*). Boldo contains not more than 2 per cent. of its stems or other foreign organic matter and yields not more than 6 per cent. of acid-insoluble ash." *N. F.*

Peumus Boldus Mol. is an evergreen shrub, frequenting the meadows of the Andes in Chili, where its yellowish-green fruit is eaten, its bark used in tanning, and its wood is employed in charcoal making.

Description and Physical Properties.—"*Unground Boldo.*—Broadly ovate or oval, 3 to 7 cm. long and 1 to 4 cm. wide, the base varying from rounded to very slightly indented, the apex rounded or slightly notched, the margin entire and sharply revolute; thick, coriaceous, rigid and brittle; pale green to brownish green, papillose, roughened on both surfaces, the principal veins coarsely reticulate, impressed above, sharply prominent underneath; the petiole stout and rigid, 1 to 5 mm. long, reticulate. Odor peculiar, when crushed very strong, disagreeable, and somewhat like that of oil of chenopodium; taste bitter, warm and pungent, camphoraceous and slightly terebinthinate.

"*Structure.*—Upper epidermis with papilla-like excrescences; a well marked hypodermis; palisade layer with frequent cells containing volatile oil; spongy parenchyma with many large cavities containing cystoliths of calcium carbonate; numerous oil secretion cells; prominent, radial, collateral fibro-vascular bundle in midrib; occasional groups of radiating 1-celled, thick-walled hairs, stomata numerous on the lower surface and hairs somewhat smaller." *N. F.*

The principal constituent of boldo leaves is a volatile oil of which they yield about 2 per cent. This oil has a specific gravity of between 0.915 to 0.945 and a boiling point between 175° and 250° C.; it may be either laevo- or dextro-rotary. It gives a green color with ferric chloride and is composed chiefly of terpenes and containing also some unknown oxygenated bodies. Apparently it is related chemically to the oil of chenopodium. (See *Schim. Rep.*, Oct., 1907.) A peculiar alkaloid, *boldine*, has been found in them by Bourgoin and Verne (*J. P. C.*, 4e sér., xvi, 191), and a glucoside, *boldoglucin*, $C_{30}H_{52}O_8$, a thick syrupy liquid, by P. Chapoteaut. (*C. R. A. S.*, xcviii, 1052.)

Uses.—According to Sigismond Pascaletti (*Terapia Moderna*, 1891), boldine when injected hypodermically paralyzes both the motor and sensory nerves, and also attacks the muscle fibers. When given internally in toxic dose it produces great excitement, with exaggeration of the reflexes and of the respiratory movements, increased diuresis, cramps, disorders of coördination, convulsions, finally death from centric respiratory paralysis, the heart continuing to beat long after the arrest of respiration, finally stopping in diastole. Boldine has been widely used in veterinary medicine as a remedy for *jaundice*. It has also been used in man in the treatment of hepatic affections, in *doses* of one one-hundredth to one-twentieth of a grain (0.0006-0.003 Gm.) in conjunction with calomel. Boldoglucin is said to act on the lower animals as a narcotic, and has been given by Réne Juranviller in *doses* of one to three grains (0.06–0.2 Gm.) in diseases of the liver. Fifteen minims (0.9 cc.) of the oil of boldo cause in man some warmth in the epigastrium; thirty minims (1.8 cc.), much gastric irritation, with pain and vomiting, and passage of urine smelling strongly of the oil. Dujardin-Beaumetz finds the oil useful in *genito-urinary inflammations* in doses of five drops (0.25 cc.) (*B. G. T.*, March, 1875). In France boldo has been employed as a tonic in *chronic hepatic torpor* and in *hepatitis*, and Fedeli (*Il Policlinico*, 1907) reports favorable results in the treatment of *cholelithiasis*.

According to A. T. De Rochebrune (*Toxicol. Africaine*, i, 1897), the tree *Monimia rotundifolia*, of Australia, contains an abundant volatile oil, an alkaloid, and a glucoside, which are very similar to, if they are not identical with, those obtained from the *Boldo*, and may be substituted for the latter in therapeutics.

Dose, five to ten grains (0.3–0.6 Gm.).

Off. Prep.—Fluidextractum Boldo, *N. F.*

BRAYERA. N. F. (Br.)

BRAYERA Brayer. [Kousso, Cusso]

"Brayera is the dried panicle of the pistillate flowers of *Hagenia abyssinica* (Bruce) Gmelin (Fam. *Rosaceæ*). Brayera contains not more than 10 per cent. of staminate flowers or other foreign organic matter and yields not more than 5 per cent. of acid-insoluble ash. Reject stems over 3 mm. in diameter and all binding material before powdering or using the drug." *N. F.*

"Kousso consists of the dried panicles of pistillate flowers of Brayera anthelmintica, *Kunth.*" *Br.*

Cusso, *Br.*; Kooso; Kusso; Koso Flores; Brayeræ Flores; Flos Cousi; Cousso, *Fr. Cod.*; Kousso, *Fr.*; Flores Koso, *P. G.*; Kosoblüthen, Kosso, Kuso, Cusso, *G.*; Kousso, Cosso, *It.*; Flor de Couso, *Sp.*

Hagenia abyssinica Willd. (*Brayera anthelmintica* Kunth) is a handsome monœcious tree, native to northeastern Africa and found growing on the tableland of Abyssinia at an elevation from 3000 to 8000 feet. It is cultivated by the natives of that country as a worm remedy. The plant attains a height of 18 to 38 feet and is characterized by possessing large, imparipinnate leaves with lanceolate, serrate leaflets, paniculate inflorescences and achenial fruits. The panicles which bear pistillate flowers are alone recognized as of medicinal value. Each of these consists of a repeatedly branched axis covered with brown hairs, the branches arising from the axils of bracts and dotted with orange-colored glandular hairs which darken with age. Arising from the smaller branches are numerous, short pedicelled flowers, each of which consists of a greenish epicalyx of 5 segments, a calyx of 5 sepals, a white caducous corolla of 5 slender petals, abortive stamens, and 2 carpels with ovaries enclosed in a receptacular cup.

Corolla and abortive stamens are wanting in the dried flowers. The drug is brought from Abyssinia packed in boxes, reaching Europe chiefly by way of Aden and Bombay. The fruit of the tree is said to be used as an anthelmintic in Abyssinia, but Dragendorff failed to detect any active principle in it. It is stated that in Abyssinia, honey gathered directly after the flowering season from beehives in gardens planted with kousso plants, is used in doses of a teaspoonful as a tænicide.

The drug of commerce consists either of cylindrical rolls or flattened bundles of the dried pistillate inflorescences tied with the stem of a rush or, as it is chiefly seen at present, of dried flowers mixed with fragments of leaves (*loose kousso*). The male flowers are frequently collected, when the general color of the mass is greenish-yellow or light brown; sometimes the female flowers constitute the bulk of the drug, which then has a distinct reddish tint, and is often known in commerce as *red kousso*. The male flowers are often found mixed with the female flowers, when loose (not in bundles), as high as 12 per cent. of this adulteration having been noticed by Meyer and Sandlund. (*Ph. Ztg.*, 1893, No. 99.)

Description and Physical Properties.—"*Unground Brayera.*—In reddish brown rolls or flattened bundles 25 to 50 cm. long, or occurring more or less loose and stripped from the larger portions of the panicles. Panicle branches cylindrical, somewhat flattened, longitudinally furrowed or wrinkled, externally light brown to yellowish, tomentose, glandular; cork brownish, bast- and wood-fibers yellow, fibro-vascular bundles in wedges, pith large and yellowish brown; nodes distinct, each with a scar or branch and subtended by a sheathing bract; internodes mostly 1 to 2 cm. long. Flowers subtended by 2 ovate, reddish, pubescent and glandular bracts; pedicel short; calyx turbinate, pubescent below, subtended by 4 or 5 rigid, spreading, obovate, purple-veined bractlets which are persistent and elongated in fruit, alternating with and larger than the 5 usually shriveled, reflexed calyx lobes; petals 5, caducous, and usually absent in the drug; carpels 2; styles exserted, stigmas broad and hairy with prominent papillæ; fruit an ovoid achene about 2 mm. in diameter, enclosed by the remains of the calyx. The staminate flowers are greenish yellow, with about 20 fertile stamens. Odor slight; taste bitter.

"*Powdered Brayera.*—Light brown or reddish brown; numerous simple, non-glandular, straight or curved hairs, up to about 1 mm. long, with thick, strongly lignified walls, usually enlarged at the base; glandular hairs with 1- to 3-celled stalks, the glandular head unicellular or consisting of 1 or 2 pairs of cells; tracheæ up to 0.050 mm. wide, spiral, annular, scalariform or with bordered pores; fibers long, thick-walled, strongly lignified and with numerous, simple, oblique pores; parenchyma of pith more or less lignified and with large simple pores; fragments of epidermal tissue from the bracts and calyx with elliptical stomata, the latter up to 0.030 mm. long; groups of thin-walled, somewhat branching, parenchyma cells with large intracellular spaces; tissue from the inner surface of the pericarp consisting of numerous elongated, porous, strongly lignified cells; calcium oxalate in rosettes up to 0.040 mm. in diameter; occasionally fragments of tissue containing prisms of calcium oxalate, the latter about 0.015 mm. long; pollen grains few, nearly spherical, from 0.025 to 0.040 mm. in diameter, with three pores. The larger branches of the panicles with simple, non-glandular hairs up to about 5 mm. long; tracheæ up to 0.125 mm. wide and rosettes of calcium oxalate up to about 0.075 mm. in diameter." *N. F.*

"Usually in more or less cylindrical rolls from three to six decimetres long, composed of reddish panicles of pistillate flowers. Panicles much branched, the branches arising from the axils of large sheathing bracts; more or less covered with hairs of glands. Flowers numerous, small, shortly stalked, mostly unisexual, with two roundish, membranous, veined bracts at the base of each. Calyx with reddish veins, hairy externally, and consisting of two alternating whorls each of five segments, the inner whorl being curved inwards over the young fruit and shrivelled. No marked odor; taste bitter and acrid." *Br.*

As the medicine, from its high price, is apt to be adulterated, it should be procured in the unpowdered state, in which the botanical characters of the flower will sufficiently attest its genuineness. It has a fragrant balsamic odor, and the taste, slightly perceptible at first, becomes in a short time somewhat acrid and disagreeable.

Analyzed by Wittstein, it was found to contain, in 100 parts, 6.25 of bitter acrid resin, 24.40 of tannin, 15.71 of ash, besides fatty matter, liguin and chlorophyll. Bedall, of Munich, determined the bitter acrid resin of Wittstein is equivalent to the *tæniin* of Pavesi, and gave it the name of *kosin.* Commercial kosin is a mixture of two inactive yellow, crystalline substances α- and β-kosin. Leichsenring (*A. Pharm.*, 1894, 50) has re-examined kousso, and finds an inactive crystalline principle to which he gives the name *protokosine,* and an amorphous substance, *kosotoxin,* which he considers the active principle of the drug; the latter is a yellowish powder, fusing at 80° C., and not obtainable in a crystalline state. It is easily soluble in alcohol, ether, benzene, carbon disulphide, and insoluble in water. Kosotoxin, which occurs in the unripe fruit as well as the flowers, is hydrolyzed by alkalies into kosin.

Kosotoxin is stated to be a derivative of trimethylphloroglucin, which indicates a relationship between the principles of cusso and of aspidium (see *Aspidium*).

There are also stated to be present an amorphous glucoside *coussin,* $C_{26}H_{41}O_5$, and a crystalline principle *cosine,* $C_{22}H_{32}O_7$, which upon hydrolysis yields isobutyric acid and an unidentified body.

Kosidin and *kosoin* have also been reported present, as well as an iron greening tannin and traces of oxalic, acetic and valeric acids.

Uses.—Kousso is highly valued in Abyssinia as a vermifuge. Bruce speaks of it in his travels, and gives a figure of the plant. Brayer, a French physician practising in Constantinople, published a treatise on it at Paris in 1823. It was in his honor that Kunth adopted the generic title of the plant. Much attention has been attracted to this valuable medicine, and trials made with it have proved its efficacy in the destruction and expulsion of the *tape-worm.* Its effects when taken internally are not very striking. In the ordinary dose it sometimes produces heat of stomach, nausea, and even vomiting, and shows a tendency to act on the bowels, though this effect is not always produced. It appears to act exclusively as a poison to the worms, and has been found equally effectual in both kinds of *tape-worm.* The medicine is taken in the morning upon an empty stomach, a light meal having been made the preceding evening. A previous evacuation of the bowels is also recommended. The flowers are given in the form of powder, mixed with half a pint of warm water, the mixture being allowed to stand for fifteen minutes, then stirred up, and taken in two or three draughts at short intervals. The medicine may be preceded and followed by lemonade. The medium dose for an adult is half an ounce (15.5 Gm.), which may be diminished one-third for a child of twelve years, one-half for one of six years, and two-thirds for one of three years. Should the medicine not act on the bowels in three or four hours, a brisk cathartic should be administered. One dose is said to be usually sufficient to destroy the worm. Should the quantity mentioned not prove effectual, it may be increased to an ounce (31 Gm.).

So far as we know, no cases of human poisoning by kousso or its active principle are on record, but it has been found by Rochebrune to be capable of causing centric convulsions in the lower animals.

Dose, from two to four drachms (8–15 Gm.).

Off. Prep.—Infusum Brayeræ, *N. F.*

BROMUM. N. F.

Bromine

"It contains not less than 99 per cent. of Br. (79.92) and not more than 1 per cent. of Cl." *N. F.*

Bromum; Brominium; Brome, *Fr. Cod.;* Bromum, *P. G.;* Brom, *G.;* Bromo, *It., Sp.*

Bromine is an elementary body, possessing many analogies to chlorine and iodine. It was discovered in 1826 by Balard, of Montpellier, in the bittern of sea salt works, in which it exists as a magnesium bromide. Since then it has been found in the waters of the ocean, in certain marine animals and vegetables, in various aquatic plants, in numerous salt springs, and in the mineral kingdom and in the coal gas liquor of the Paris gas works. In the United States it was first obtained by Silliman, who found it in the bittern of the salt works at Salina, in the State of New York. It is now obtained in largest amount from the brines of Ohio, Pennsylvania, Michigan, and West Virginia. The chief works are located at Parkersburg and Mason City, W. Va.; Pomeroy, Ohio, and Midland County, Mich. The chief source of bromine in Europe is the potash mines at Stassfurt, Germany, where the magnesium bromide remains as a residue after extraction of the potassium salts.

The method of separating the bromine from these various salt liquors is first to concentrate the solution by evaporation which causes the less soluble chlorides and sulphates to crystallize out. The bittern which is left—containing some residue of chlorides with varying percentages of sodium, calcium or magnesium bromides—is treated with an oxidizing agent, either manganese dioxide or potassium chlorate, thereby causing the liberation of chlorine, which in turn decomposes the bromides liberating the bromine which is removed by a current of hot air. In Germany the bittern is decomposed in a continuous process by a current of chlorine and hot steam, the liberated bromine dissolving in the solution from which it may be removed by distillation. In Michigan the bittern is decomposed by an electrolytic process.

The crude bromine obtained in this manner is often contaminated with bromine chloride (BrCl). It is purified by treating it with ferrous bromide thereby liberating the chlorine according to the following reaction:

$$FeBr_2 + 2BrCl = FeCl_2 + 2BrCl_2$$

Recently a vessel has been fitted out for the purpose of recovering bromine from sea-water, and is now (1925) making its first voyage for that purpose. More than two-thirds of the bromine of commerce is used for the manufacture of bromides for medicinal use, and for photography; the remainder is used for aniline colors.

Properties.—The National Formulary gives the following description: "Bromine is a heavy, dark, brownish-red, mobile liquid, evolving, even at ordinary temperatures, reddish fumes, highly irritating to the eyes and lungs, and having a peculiar, suffocating odor, resembling that of chlorine. Specific gravity: about 3.1 at 25° C. Boiling point: about 63° C. One cc. dissolves in about 90 cc. of water; it is freely soluble in alcohol, ether, chloroform, or carbon disulphide.

On exposure to air it volatilizes. It destroys the color of solutions of litmus or indigo, and imparts a yellow color to starch T.S. Add 1 cc. of bromine to 50 cc. of sodium hydroxide T.S.; it combines to form a permanently clear liquid, without the separation of oily drops (*organic bromine compounds*). Shake

10 cc. of a saturated aqueous solution of Bromine with a slight excess of reduced iron until it becomes nearly colorless, filter the liquid and add 1 cc. of ferric chloride T.S. and 1 cc. of starch T.S.; it does not assume a blue color (*iodine*).

Assay.—"Dissolve 10 Gm. of potassium iodide in 25 mils of distilled water, introduce the solution into a 100 cc. measuring flask, stopper and determine accurately the weight of the flask and its contents. Add about 1 Gm. (or 0.3 cc.) of Bromine to the contents of the flask, determine its exact weight and then fill the flask to the mark with distilled water and titrate 25 cc. of this solution with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal sodium thiosulphate used corresponds to 0.007992 Gm. of Br. or 0.003546 Gm. of Cl. Each gramme of Bromine (containing not more than 1 per cent. of chlorine) corresponds to not more than 126.7 cc. of tenth-normal sodium thiosulphate.

"Preserve Bromine in glass-stoppered bottles in a cool place, each bottle being enclosed in a larger vessel with the space between being filled with some substance capable of absorbing and combining with any vapors which might escape." *N. F.*

Bromine congeals at -7° C. and at -20° C. becomes a hard, brittle, crystalline solid, having a dark leaden color, and a luster nearly metallic. It boils at about 63° C., forming a reddish vapor resembling that of nitrous acid, and of the sp. gr. 5.54. It evaporates readily, a single drop being sufficient to fill a large flask with its peculiar vapor.

Bromine is sparingly soluble in water to which it communicates an orange color, more soluble in alcohol, and still more so in ether, chloroform, and carbon disulphide. By the aid, however, of potassium bromide, it may be dissolved to any desirable extent in water. Its alcoholic and ethereal solutions lose their color in a few days and become acid from the generation of hydrobromic acid. It bleaches vegetable substances like chlorine, destroys the color of indigo sulphate, and decomposes organic matters. Its combination with starch has a yellow color. It corrodes the skin and gives it a deep yellow stain. Bromine is intermediate in its affinities between chlorine and iodine, since its combinations with metals are decomposed by chlorine, while, in its turn, it decomposes those of iodine. It forms acids which are analogous in properties and composition to the corresponding acids of chlorine and iodine.

Uses.—In concentrated solution bromine is a powerful caustic and germicide. Its disinfectant properties appear to be somewhat inferior to those of chlorine; according to Koch, a 2 per cent. solution destroys the anthrax spores in twenty-four hours and Miquel gives the antiseptic limit as 1 in 1600. At one time it was employed internally in *scrofulous* and *syphilitic diseases*, but there is no reason to believe that it exercises any different effect upon the system from the salts of hydrobromic acid, and it has been entirely abandoned as an internal remedy. In dilute solution, from 10 to 40 minims to a pint of water, it is occasionally employed as a wash for ulcers but has no advantage over other disinfectants. It was a highly lauded remedy for *hospital gangrene*, which before the days of antiseptic surgery was a frequent condition in military hospitals.

In overdoses bromine is a corrosive poison. About an ounce ingested caused violent inflammation of the lips, mouth, tongue, and esophagus, with incessant burning pain, followed, in two hours and a half, by prostration, ending in death. (Snell, *N. Y. Journ. of Med.*, Sept., 1850.) In a vaporized state, it was one of the poison gases used in the trench warfare in France and Belgium in the European War. The best antidote, according to Alfred Smee, is ammonia, given largely diluted and mixed with sweet oil. Thiosulphates are also antidotes and an effective mask to prevent the inhalation of the fumes is provided by covering the mouth and nose with gauze which has been recently saturated with an aqueous solution of sodium thiosulphate.

BRYONIA. N. F.

BRYONIA [Bryony]

"Bryonia is the dried root of *Bryonia alba* Linné or of *Bryonia diocia* Jacquin (Fam. *Cucurbitaceæ*). Bryonia contains not more than 2 per cent. of foreign organic matter." *N. F.*

The bryonias are climbing or trailing herbs with rough, hairy leaves. The *white bryony* (*B. alba*) is found in central and northern Europe and the red bryony (*B. dioica*) in England. The fruit of the latter is red and that of the white bryony is black. The term "black bryony" has been applied to a very different plant, *Tamus communis* L. which belongs to the *Dioscoreaceæ.* The berries of this plant are irritant poisons and, according to Coutagne, cause in animals paralysis and convulsions (see *Rep. Pharm.*, Nov., 1884; *P. J., Jan.*, 1903). The *B. americana* Lam. of the West Indies and the *B. africana* Thumb. are said to be employed in their respective countries as hydragogue cathartics.

The flowers of the *B. alba* are monoecious and the berries black. The *B. dioica* has dioecious flowers and scarlet berries.

The N. F. recognizes the root which it describes as:

Description and Physical Properties.—"*Unground Bryonia.*—Usually in circular or elliptical slices, from 1.5 to 10 cm. wide and from 3 to 15 mm. thick; the edges light gray or yellowish, rough and striate, the cut surface white or faintly yellow, showing a thin cortex and a wood with numerous projecting, collateral fibrovascular bundles arranged in concentric zones; fracture short and mealy, whitish internally. Odor faint but distinct and characteristic; taste bitter and nauseous.

"*Powdered Bryonia.*—Light yellow; starch grains simple, rounded or 2- or more compound, from 0.004 to 0.024 mm. in diameter, frequently with a central cleft; tracheæ from 0.35 to 0.250 mm. wide, reticulate or with bordered pores; large yellow cork cells.

"Add sulphuric acid to the powdered drug; it becomes reddish-brown and then brownish-purple." *N. F.*

The substance known as *bryonin,* according to Power and Moore (*Tr. Chem. Soc.,* 1911, xcix, 937), is not a pure principle but a mixture of a glucoside and an alkaloid neither of which is physiologically active. Jensen (*P. J.,* 1915, xcv, p. 641) confirms the inertness of bryonin but describes a second glucoside, *bryonidin,* which exercises a paralytic effect upon the central nervous system. Bryonia also contains a dark brown resin known as *bryoresin* to which its purgative properties are probably due.

Uses.—Bryonia is an active irritant hydragogue cathartic. In a number of cases it has produced serious or even fatal poisoning. Vomiting and purging have been commonly present, but in some cases there has been no diarrhea. Giddiness, delirium, and dilated pupils, coupled with fall of the bodily temperature, imperceptible pulse, cold perspiration, and other manifestations of collapse, are the usual symptoms. Eighty minims (5 cc.) of the homeopathic tincture caused very serious but not fatal poisoning. (For cases, see *B. M. J.,* 1883, ii, 1067; *T.G.,* ii, 35.) The fresh root is highly irritant, and is said, when bruised and applied to the skin, to be capable of producing vesication.

Bryonia has real value as a hydragogue cathartic but is little used at present for this purpose. By the medical sect who call themselves eclectics it was highly esteemed in the treatment of various pectoral conditions as *bronchitis, whooping-cough, pleurisy* and *pneumonia* and also in various other inflammatory disorders. It is still used to a certain extent by the regular profession for similar purposes.

Dose, ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Tinctura Bryoniæ, *N. F.*

BUCHU. U. S. (Br.)

BUCHU

"Buchu is the dried leaf of *Barosma betulina* (Thunberg) Bartling et Wendland, or of *Barosma crenulata* (Linné) Hooker, known in commerce as Short Buchu; or of *Barosma serratifolia* (Curtis) Willdenow, known in commerce as Long Buchu (Fam. *Rutaceæ*). Buchu contains not more than 8 per cent. of its stems and not more than 2 per cent. of other foreign organic matter." *U. S.* "Buchu Leaves are the dried leaves of Barosma betulina, *Bart. and Wendl.*" *Br.*

Buchu Folia, *Br.;* Folia Bucco, Folia Diosmæ, s. Barosmæ; Feuilles de Bucco (Booko, Buchu), *Fr.;* Buckublätter, Buccoblätter, *G.*

The leaves of the official and other *Barosmas* (so named from βαρύς, heavy, and ὀσμή, odor), and of some *Agathosmas,* are collected by the Hottentots, who value them on account of their odor ,and under the name of *bookoo* or *buchu,* rub them, in the state of powder, upon their greased bodies.

The medicinal species of Barosma are all erect, slender shrubs with opposite leaves, dotted with conspicuous pellucid oil glands, smooth, angular, purplish branches, often of a purplish color, white flowers, and a fruit of five erect follicles. They are chiefly distinguished by their leaves.

Barosma betulina is a small shrubby plant indigenous to Cape Colony. The leaves are collected while the plant is in flower and fruit, then dried. *B. serratifolia* is a well-developed shrub growing in the mountains of the southwest of Cape Colony. The leaves of both of these plants are collected in the Cape Colony district of South Africa when the plants are in the flowering or fruiting condition. About 90 per cent. of the supply used in the United States comes from Cape Town, South Africa. The other 10 per cent. comes through London. According to Schimmel and Co., the buchu plant thrives best in a very sandy soil, but it is rather difficult to cultivate as the cuttings do not root readily. The buchu of commerce always contains more or less foreign material, such as stems, twigs and old worthless leaves, and the U. S. Pharmacopœia has wisely limited the amount of such admixture to 10 per cent.

Barosma crenulata (L.) Hook, has leaves opposite, ovate or obvate, acute, serrated and glandular at the edge, coriaceous, and full of small pellucid dots on the under surface. The flowers are white or of a reddish tint, and stand solitarily at the end of short, lateral leafy shoots.

The non-official species, which have been seen in European markets occasionally, are said to be used in South Africa as substitutes for the official buchu; they are:

Barosma Eckloniana Bartl., a plant which has been considered to be only a variety of *B. crenulata,* has leaves which are rounded at the base, shorter and proportionately wider than those of *B. crenulata* and also grow upon pubescent shoots.

The leaves of *Barosma venusta* Ecklon and Zeyher, which are said to have appeared in the London markets, are readily distinguished by their being very much smaller than those of *B. betulina,* which they otherwise resemble.

Barosma pulchellum (L.) Bartl. and Wendl.—The leaves closely resemble those of the *B. betulina,* being ovate instead of obovate, that is, they are wider at the base. Their odor is quite different, strongly recalling that of citronella, and Schimmel and Company have demonstrated the presence in them of citronellal.

Under the name of *Karoo buchu,* in 1904 the leaves of the *Diosma succulenta* L., var. *Bergiana* H. and S., appeared in London; they are small and heath-like, thick, obtuse, and slightly recurved, and yielded to C. E. Sage (*C. D.*, lxv, 506, 787) a small semi-solid volatile oil having the odor of peppermint. Another buchu, which has appeared on the market, has leaves resembling very closely those of *Barosma scoparia* E. and Z. (*Pref. & Ess. Oil Rec.*, 1914, p. 375.)

Buchu is subject to many adulterations both by the leaves of other species of the genus as well as more distantly related leaves. The most important of these adulterations are as follows: *Psoralea obliqua* E. Mey, or *P. bracteata* (*P. J.*, 1910, pp. 69 and 464), and *Empleurum serrulatum* Ait. The leaves of the latter have a more acrid taste, are lanceolate or narrowly linear, about 4 cm. in length, yellowish-green and very acute at the summit. They furthermore acrid taste, are lanceolate or narrowly of the teeth. (For description of many other adulterants, see Holmes, *P. J.*, 1910, lxxxv, p. 464.)

Description and Physical Properties.—"*Unground Short Buchu.*—Rhomboidally oval or obovate, from 9 to 30 mm. in length and from 4 to 20 mm. in breadth; apex obtuse or rounded and sometimes recurved, base wedge-shaped or obtuse, margin finely dentate, glandular punctate, with an oil gland at the base of each tooth, papillose, longitudinally striate beneath, coriaceous and with a petiole about 1 mm. in length; color bright green to yellowish-green, occasionally olive-gray; odor aromatic, and mint-like; taste camphoraceous.

"*Unground Long Buchu.*—Linear-lanceolate from 12 mm. to 4 cm. in length and from 4 to 10 mm. in breadth; apex acute, somewhat rounded; margin sharply serrate. Otherwise resembles Short Buchu.

"*Structure.*—Cuticle thick, somewhat uneven and striated; hairs few, simple, 1-celled, non-lignified, up to 0.145 mm. in length (Short Buchu), or 0.180 mm. in length (Long Buchu). Stomata absent on the upper surface, numerous on the lower surface, broadly oval, up to 0.040 mm. in length and surrounded by from 4 to 6 neighboring cells; epidermal cells with inner walls mucilaginous and containing colorless sphero-crystal aggregates of hesperidin which strongly polarize light, the latter form giving a brilliant display of colors; a single row of large hypodermal cells beneath the upper epidermis containing mucilage and frequently brownish, feather-like crystal aggregates; palisade cells in a single row below the mucilage cells, and bordering a loose mesophyll, the cells containing numerous plastids and a few rosette aggregates of calcium oxalate; oil cavities occurring mostly near the margin of the leaf, circular in outline and containing globules of oil. Fibro-vascular bundles of midrib and larger veins collateral, in crescent-shaped groups, composed chiefly of tracheæ, sieve tubes and non-lignified fibers and separated by collenchyma from the lower epidermis.

"*Powdered Buchu.*—Light green; elements of identification are epidermal cells containing sphero-crystals or crystal aggregates of hesperidin, rosette aggregates of calcium oxalate from 0.015 to 0.030 mm. in diameter, a few simple hairs, lower tissue with numerous stomata, oil secretion cavities and oil globules, and fragments of the fibro-vascular bundles." *U. S.*

"From twelve to twenty millimetres long, rhomboid-obovate, dull yellowish-green, rigid, cartilaginous when slightly moist. Surface glabrous, bearing small scattered prominences; margin usually sharply denticulate, apex blunt and recurved. Oil glands visible in the leaf, especially in epidermis cells containing yellow especially near the margin. Transverse section exhibits in epidermis cells containing yellow sphero-crystals; inner walls of these cells thick and rich in mucilage. Odor and taste strong and characteristic." *Br.*

The leaves of *B. betulina* constitute the *short buchu* or *round buchu,* while those of *B. serratifolia* are the *long buchu* of commerce. The leaves of *B. crenulata* are at present comparatively infrequent in commerce, the parcels usually consisting of those of one of the other species almost unmixed. The species can be recognized by the characters already given.

Buchu leaves yield a volatile oil with a peppermint-like odor. The amount of oil present in the short buchu ranges from 1.5 to 2 per cent., but in the long buchu is much less, usually not over 1 per cent. (*Schim. Rep.*, Oct., 1893). This oil on chilling deposits a stearopten which is known as *Barosma camphor* or *diosphenol* (it is, however, said not to occur in the oil from *B. serratifolia*). This substance, which composes about 30 per cent. of the oil, forms crystals which have a melting point of 82° C. and boil at 232° C. with partial decomposition. The residue of the oil after extraction of the diosphenol contains a hydrocarbon, $C_{10}H_{18}$, and a ketone, $C_{10}H_{18}O$, which is probably laevogyrate menthone. Spica (*P. J.*, 1885) found in the leaves of the *B. crenulata,* from which the oil had been extracted, a solid principle *diosmin* which is considered now to be the same as hesperidin found in orange peel. His results were confirmed by Shimoyama (*A. J. P.*, 1888) who also has prepared several derivatives of diosphenol. The yield of ash varies, according to the researches of H. W. Jones (*P. J.*, ix, 673), from 4.69 to 4.40 in *B. betulina,* 4.32 to 5.39 in *B. crenulata,* 5.03 to 5.22 in *B. serratifolia;* the ash itself was remarkable as containing a great deal of manganese.

Uses.—The activity of buchu depends upon the volatile oil, which is eliminated by the kidneys. Under its action there is no marked increase in the amount of the urine, but the oil affects very decidedly the mucous membrane of the genito-urinary tract, perhaps by virtue of some antiseptic power. The remedy is useful in diseases of the urinary organs, such as *gravel,* chronic *cystitis, urethritis* and *diseases of the prostate.* It should not be given when the inflammation is severely acute. An infusion (one ounce in a pint of boiling water) may be given in the dose of one to two fluidounces (30–60 cc.), but the best preparation is the fluidextract.

Dose, one-half to one drachm (2.0–3.9 Gm.).

Off. Prep.—Fluidextractum Buchu, *U. S.;* Infusum Buchu, *Br.;* Tinctura Buchu, *Br.;* Elixir Buchu (from Fluidextract), *N. F.;* Elixir Buchu Compositum (from Compound Fluidextract), *N. F.;* Elixir Buchu et Potassii Acetatis (from Elixir of Buchu), *N. F.;* Fluidextractum Buchu Compositum, *N. F.*

BUTEÆ GUMMI. Br.

BUTEA GUM [Bengal Kino]

"Butea Gum is the inspissated juice obtained from incisions in the stem of Butea frondosa, *Roxb.*" *Br.*

For description and uses, see under butea seeds.

BUTEÆ SEMINA. Br.

BUTEA SEEDS

"Butea Seeds are the seeds of Butea frondosa, *Roxb.*" *Br.*

The *Sacred Tree, Butea frondosa* (Fam. *Leguminosæ*), enters largely into the religious rites of the Hindoos. Its red flowers are offered at the bloody sacrifice of the goddess Kali. Its leaf with three spreading leaflets is supposed to represent the Hindoo deity, and furnishes platters used when the Hindoo boy becomes of age.

Butea gum, which has sometimes been mistaken for African kino, is the concrete juice of the *Butea frondosa* Roxb., or *Dhak-tree* of Hindostan, and also to some extent of *B. superba.* The juice flows from natural fissures, and from wounds made in the bark of the tree, and quickly hardens. It is in small elongated tears, or irregular angular masses, less in size than a grain of barley, apparently black and opaque, but translucent and of a ruby-red color when examined in small fragments by transmitted light; in some specimens the tears are much paler than described, and of a very beautiful ruby tint. Many of the tears have small portions of bark adhering to them. They are very brittle, and readily pulverizable, yielding a reddish powder. They are very astringent to the taste, do not adhere to the teeth when chewed, and tinge the saliva red. The solubilities and reactions of this product to water, alcohol, and other chemical reagents are nearly the same as those of ordinary kino. When freed from impurities, consisting of from 15 to 25 per cent. of wood, bark, and sand, etc., it contains from 20 to 60 per cent. of kinotannic acid besides considerable gum and insoluble substances. It is, however, very seldom imported into England, and never, at present, into this country.

Butea gum occurs in "small irregular shining fragments, very dark ruby color, thinnest flakes transparent when examined by transmitted light. Partially soluble in *water;* about 40 per cent. soluble in hot *alcohol* (90 per cent.), the solution being scarcely colored. No odor; taste astringent. Free from corky or woody particles. On keeping, the fragments may become dull and blackish." *Br.*

"In India and the Eastern Divisions of the Empire, Butea Gum may be employed in making the official preparations for which kino (distinguished in commerce as East Indian, Malabar, Madras, or Cochin kino) is directed to be used." *Br.*

The British Pharmacopœia describes the seeds as "flat, reniform, from twenty-five to thirty-eight millimetres long, sixteen to twenty-five millimetres wide, and one and a half to two millimetres thick. Testa thin, glossy, veined, wrinkled, dark reddish-brown. Cotyledons large, leafy, yellow. Faint odor; taste slightly acrid." *Br.*

For a description of the seeds see also *Ph. Rev.,* 1896, 232.

The seeds contain about 18 per cent. of fat and an equal amount of protein, but no principle has been found to which any therapeutic activity can be attributed. The gum contains from 15 to 60 per cent. of kinotannic acid.

Uses.—Butea gum is used for the same purposes and in the same doses as kino. The seeds have been used by the native practitioners in India as vermifuges against both the *tape worm* and the *round worm.* According to the *Pharmacographica Indica,* the infusion of three seeds exercises a laxative effect. Before being used, the seeds should be soaked in water and the integument carefully removed. The powdered dried kernels may be given in doses of ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Pulvis Buteæ Seminum, *Br.*

BUTYL-CHLORAL HYDRAS. Br.

BUTYL-CHLORAL HYDRATE

"Butyl-Chloral Hydrate, or trichlorbutylidene glycol, $C_4H_7Cl_3O_2$, is a crystalline hydrate obtained by adding water to the liquid butylchloral produced by the action of chlorine gas on aldehyde." *Br.*

Butylchloralum Hydratum, Chloralhydratum Butyli; Trichlorbutylidene Glycol; Hydrous Butyl Chloral; Croton Chloral Hydrate (wrongly so called); Chloralum Butyli Hydratum; Hydrate de Chloral Butylique, *Fr.;* Butylchloralhydrat, Trichlorbutylaldehydhydrat, *G.*

This substance was discovered by Krämer and Pinner, of Berlin, during an examination of the accumulated by-products of the chloral factory of Schering. It was named croton-chloral hydrate because it was believed to bear a relationship to crotonic acid, the peculiar acid of croton oil; this was subsequently disproved by Pinner, who showed that it belonged to the butyl series. (*B. Chem. G.,* vii, 1321, 1561.) It is made by passing dry chlorine through aldehyde cooled to –10° C. in an apparatus similar to that used in making chloral. Fractional distillation is resorted to, and the product boiling between 163° C. and 165° C. is reserved; this is butyl-chloral, a colorless oily fluid. The necessary amount of water is added, and butyl-chloral hydrate is obtained.

Properties.—Butyl-chloride hydrate occurs in the form of crystalline, micaceous scales of a pungent odor, sparingly soluble in water, freely soluble in alcohol, hot water, and glycerin, but insoluble, or nearly so, in chloroform, a property which may be employed to separate it from ordinary hydrated chloral. When treated with caustic alkalies it is converted into formic acid, potassium chloride, and allylene dichloride, $C_3H_4Cl_2$. The British Pharmacopœia describes it as "pearly-white, trimetric laminæ. Odor pungent but not acrid; taste acrid and nauseous. Melts at about 78° C. to a transparent liquid, which, on cooling, begins to solidify at about 71° C. Soluble in about 40 parts of *water,* and in less than 1 part of *glycerin* or of *alcohol* (90 per cent.). The aqueous solution is neutral or but slightly acid to *litmus.* When 0.5 gramme is gently warmed for a short time with 10 millilitres of *solution of sodium hydroxide,* 3 drops of *aniline* added and the mixture well shaken and heated to boiling, no odor of phenyl iso-cyanide is perceptible (absence of chloral hydrate)." *Br.*

Uses.—Butyl-chloral hydrate was proposed by Liebreich, in 1870, as a remedy in the treatment of *trigeminal neuralgia.* He states that a drachm (3.9 Gm.) of it causes deep sleep, accompanied by anesthesia of the head, with complete loss of irritability of the eyeball and of the trigeminal nerve. The circulation is kept up with great tenacity, and, if the dose has been large enough, death results from the arrest of respiration. These statements of Liebreich were contradicted by the research of J. von Mering and of H. W. Schmidt, who found that no anesthesia was produced unless sufficient doses were given to cause complete narcosis, and that the general course of the symptoms caused by the butyl-chloral hydrate was exactly parallel to that of those produced by hydrated chloral. But a number of observers have used butyl-chloral hydrate with asserted good results in *tic douloureux.* The relief obtained is, unfortunately, only temporary and palliative. The drug has been commonly administered in doses of from 5 to 20 grains (0.32–1.3 Gm.) in syrup. The safer plan is to give 5 grains (0.32 Gm.) every half hour until 30 grains (2.0 Gm.) have been taken or relief afforded. The original formula of Liebreich was: butyl-chloral hydrate 5 to 10 parts, glycerin 20 parts, distilled water 130 parts. Dose, half a flouidounce (15 cc.), followed in five minutes by a second dose, ten minutes later by a third dose, unless relief is afforded. That such medication is safe is not certain. For experiments in making and dispensing solutions of butyl-chloral hydrate, see *Proc. A. Ph. A.,* 1894, 578.

Dose, of British Pharmancopœia, from five to twenty grains (0.32–1.3 Gm.).

CACAO PRÆPARATUM. N. F.

COCOA [Prepared Cacao]

"Cocoa is a powder prepared from the roasted, cured kernel of the ripe seed of *Theobroma Cacao* Linné (Fam. *Sterculiaceæ*)." *N. F.*

Chocolat, *Fr.;* Schokolade, Kakao, *G.;* Cioccolata, *It.;* Chocolatl, *Mex.*

Theobroma Cacao L. is a handsome evergreen tree from twelve to twenty feet in height, growing in Mexico, the West Indies, and South America. It is largely cultivated in all tropical countries, particularly in Guayaquil, Venezuela, Mexico, Trinidad, and the Philippines. It possesses alternate, elliptic-oblong, entire leaves and fascicles of small, rose-colored flowers, the latter appearing on the trunk and larger branches. The fruit is an oblong-ovate, ten-ribbed capsular nut, six or eight inches in length, with a thick, coriaceous, somewhat ligneous rind, enclosing a whitish pulp, in which numerous seeds are embedded. These are ovate, somewhat compressed, about as large as an almond, and consist of an exterior thin shell and a brown oily kernel. Separated from the matter in which they are enveloped, they constitute the *cacao,* or *chocolate nuts,* of commerce. The cacao tree is usually cultivated in large estates, where it is grown in the shade of the banana or other large plant, and develops its pods from the stem continually, so that the harvest goes on all the time, although the product is greater in the spring and in the autumn. The pods are cut off, opened, and the beans contained in the glutinous sweet acid pulp are allowed to ferment, during which process the outer integument comes off easily. The beans are finally carefully dried, commonly in the sun, sometimes by means of a steam drying shed. If the sweating process is carried too far, or the beans during drying are wetted by rain, they blacken and are much lowered in value. These blackened beans are sometimes artificially whitened. Cacao beans have a slightly aromatic, bitter, oily taste, and, when bruised or heated, an agreeable odor. (See *Am. Drug.,* 1897, 311; also *Ph. Ztg.,* 1900, 756.)

The average of a number of analyses of raw beans gave H. Weigmann (*König's Nahrungs- und Genussmittel,* 3d ed., vol. i, 1019) water, 7.93 per cent.; nitrogenous matter, 14.19 per cent.; theobromine, 1.49 per cent.; fatty matter (cacao butter), 45.57 per cent.; starch and other carbohydrates, 22.92 per cent.; crude fiber, 4.78 per cent.; pure ash, 3.99 per cent.; sand, 0.62 per cent. The coloring matter is probably the result of chemical change, as the fresh seeds are white. Theobromine has been found also in the shells in the proportion of about 1 per cent. The latter impart to boiling water a taste analogous to that of chocolate, but weaker, and are used for making a table beverage. Chocolate is the solid substance expressed from the cacao bean after roasting. In Great Britain and the United States it is usually made, when pure, exclusively of the kernel of the cacao or chocolate nuts, which are first roasted, then deprived of their shells, and lastly reduced, by grinding between heated stones, to a paste, which is moulded into oblong cakes. Sometimes rice flour or other farinaceous substance, with foreign fats, is added, but these must be considered as adulterations. In the compounded form known as sweet chocolate, sugar is generally incorporated with the paste, and spices, especially cinnamon, are often added; vanilla is a favorite addition in America, France, and Spain. The well-known confection known as *"milk chocolate"* contains either whole or skim milk powder in addition to the foregoing ingredients. The U. S. Department of Agriculture standards for cacao products are as follows:

"1. *Cocoa beans* are the seeds of the cacao tree, *Theobroma cacao,* L. 2. *Cocoa nibs, cracked cocoa,* is the roasted, broken cocoa bean freed from its shell or husk. 3. *Chocolate, plain chocolate, bitter chocolate, chocolate liquor, bitter chocolate coatings,* is the solid or plastic mass obtained by grinding cocoa nibs without the removal of fat or other constituents except the germ, and contains not more than three (3) per cent. of ash insoluble in water, three and fifty hundredths (3.50) per cent. of crude fiber, and nine (9) per cent. of starch, and not less than forty-five (45) per cent. of cocoa fat. 4. *Sweet chocolate, sweet chocolate coatings,* is chocolate mixed with sugar (sucrose), with or without the addition of cocoa butter, spices, or other flavoring materials, and contains in the sugar- and fat-free residue no higher percentage of either ash, fiber, or starch than is found in the sugar- and fat-free residue of chocolate. 5. *Cocoa, powdered cocoa,* is cocoa nibs, with or without the germ, deprived of a portion of its fat and finely pulverized, and contains percentages of ash, crude fiber, and starch corresponding to those in chocolate after correction for fat removed. 6. *Sweet cocoa, sweetened cocoa,* is cocoa mixed with sugar (sucrose), and contains not more than sixty (60) per cent. of sugar (sucrose), and in the sugar- and fat-free residue no higher percentage of either ash, crude fiber, or starch than is found in the sugar- and fat-free residue of chocolate."

Description and Physical Properties.—"*Cocoa:* Brownish-red; oil globules, protein grains and starch grains numerous, the latter, simple or compound and up to 0.012 mm. in diameter. Odor and taste, chocolate-like; free from sweetness.

"Extracted with ether, Cocoa yields not less than 18 per cent., or more than 25 per cent. of fat, and the fatty residue does not have a spicy odor or taste. The residue, insoluble in ether, shows not more than 3 per cent. of cocoa shells. Cocoa yields not more than 6 per cent. of crude fiber and not more than 15 per cent. of starch." *N. F.*

For Emminger's method of determining theobromine in cacao, see *P. J.*, 1896, 289.

Mixed with hot milk or water cocoa is much employed as a drink. It has the advantages over tea and coffee that it is less stimulating to the nervous system and contains some nutriment.

It is officially recognized because of its use as a flavoring agent.

Off. Prep.—Syrupus Cacao, *N. F.*

CACTUS GRANDIFLORUS. N. F.

CACTUS GRANDIFLORUS Cact. Grand.

[Night Blooming Cereus]

"*Cactus grandiflorus* is the fresh succulent stem of the wild growing *Selenicereus grandiflorus* (Linné) Britton et Rose (Fam. *Cactaceæ*)." *N. F.*

Night-blooming Cereus, Vanilla Cactus, Large-flowered Cactus, Sweet-scented Cactus, Queen of a Single Night, Cierge à grandes fleurs, *Fr.;* Königin der Nacht, *G.*

The night-blooming cereus, *Cactus grandiflorus* L. (*Selenicereus grandiflorus* (L.) Brit. and Rose), is a large fleshy shrub bearing terminal and lateral flowers with a diameter of from 8 to 12 inches which open at night, exhaling a vanilla-like odor during their few hours of bloom. It is a native of Jamaica but is frequently grown in hot houses for its showy flowers which, with their outer leaflets of dark brown shading through golden yellow into pure white in the center, are generally deemed among the most beautiful of flowers. The fleshy stems are armed with the spines which are characteristic of the cactus family.

For years most of the cactus supplies have been imported from Mexico. It has been shown that this drug was *Selenicereus spinulosus* Brit. and Rose, and that the genuine *Cactus grandiflorus* (*Selenicereus grandiflorus*), little of which was seen on the market, comes solely from Jamaica. The two can readily be distinguished by the ribs and spines; *S. spinulosus* stems usually possess 5 ribs and the spines are not acicular, in *S. grandiflorus* the stems have 7 to 8 ribs with acicular spines.

Description and Physical Properties.—"*Whole Cactus Grandiflorus.*—In pieces of varying length, from 1.5 to 4 cm. in diameter, and from 5 to 9 angled; the angles at intervals of about 2 cm. with tufts of from 9 to 12 acicular spines about 5 mm. in length, together with about the same number of bristles about 1 cm. in length; at irregular intervals branched roots sometimes present. It has a strong, herby odor; taste acidulous and mucilaginous.

"*Structure.*—The transverse section shows a central cylinder about 8 mm. in diameter and a spongy parenchyma containing large irregular fragments of tetragonal crystals, prisms and raphides of calcium oxalate." *N. F.*

Sultan (*A. J. P.*, 1891, p. 424) claimed to have isolated an alkaloid which he called *cactine* from this plant but subsequent chemists have been unable to confirm his statements. Sharp could find only inert resins.

Uses.—This drug has long been used in tropical America in the treatment of *dropsy.* It was brought into notice as a cardiac remedy by Rubini of Naples in 1896. Boynet and Boy-Teissier (*B. G. T.*, cxxi, p. 343) found that cactus increased the systolic contractions of the frog's heart, but Hatcher and Bailey (*J. A. M. A.*, 1911, lvi, p. 26), from experiments with carefully identified specimens as well as commercial preparations purporting to be of this drug, reached the conclusion that it was physiologically inert. Gordon Sharp (*Pract.* 1894, liii), from review of the literature and his own extensive clinical trials, reached the conclusion that the drug was therapeutically useless. Despite the vigor of the impugnments there still are many competent clinicians who continue to use the drug with apparent benefit in various neurogenic disturbances of *cardiac* rhythm such as seen in *Grave's disease, nicotinism, neuresthenia* and allied affections.

Dose, from five to fifteen grains (0.3–1 Gm.).

Off. Prep.—Tinctura Cacti Grandiflori, *N. F.*

CAFFEINA. U. S., Br.

CAFFEINE Caffein. [Theine]

"Trimethyl-xanthine [$C_5H(CH_3)_3O_2N_4.H_2O$.]" *U. S.* "Caffeine, $C_8S_{10}N_4O_2,H_2O$, is an alkaloid obtained from the dried leaves of Camellia Thea, *Link*, or from certain other plants." *Br.*

Trimethyl-xanthine, Methyl-theobromine; Caffeia; Theina; Caféine, *Fr. Cod.;* Coffeïnum, *P. G.;* Koffein, Kaffein, Thein, *G.;* Caffeïna, *It.;* Cafeina, *Sp.*

Caffeine was first discovered by Runge, and afterwards by Pelletier, Caventou and Robiquet. Strecker first proved it to be methyl-theobromine by making it from theobromine synthetically. (*Ann. Ch. Ph.*, cxviii, 170.) It is now recognized as an immediate derivative of xanthine, $C_5H_4O_2N_4$, being the trimethyl-derivative of the same, and it belongs to the purine group, of which xanthine is the dioxy-derivative. Emil Fischer has accomplished the conversion of uric acid, $C_5H_4O_3N_4$, into xanthine, and this into caffeine. Caffeine may be obtained from a number of plants including coffee, tea, cola, guarana, etc., but because tea leaves contain a much larger percentage of the alkaloid than does the coffee berry, and are frequently thrown into commerce in a damaged condition, unfit for use as a beverage, commercial caffeine is almost always prepared from them. The finely powdered unsalable material known as "tea sweepings" is also used. Dunstan and Shepheard (*J. Chem. S.*, 1893, 195) have thoroughly established the complete chemical identity of the alkaloids of tea and coffee by a study of a number of derivatives.

Caffeine may be isolated as follows: Exhaust powdered coffee or tea by boiling with two successive portions of water, unite the infusions, add lead acetate in order to precipitate various principles accompanying the caffeine, filter, decompose the excess of lead acetate in the filtered liquor by hydrogen sulphide (or sodium phosphate), concentrate by evaporation, and neutralize, with ammonia. The caffeine is deposited in crystals upon cooling, and may be purified by redissolving in water, treating with animal charcoal, and evaporating. H. Leuchsenring obtains caffeine by availing himself of its property of subliming unchanged by heat. He precipitates a concentrated decoction of coffee by a weak solution of lead acetate, filters, evaporates to dryness, mixes the residue with sand, and sublimes as in Mohr's process for procuring benzoic acid. (*A. J.*, xxxii, 25.) Paul and Cownley's process for estimating the caffeine in coffee is to mix finely powdered coffee with moist lime, and exhaust with alcohol by hot repercolation. The alcohol is evaporated off, and the residue mixed with water and a few drops of diluted sulphuric acid; the mixture is filtered, and the filtrate and washings, when cool, treated with chloroform to wash out the alkaloid; the chloroformic solution is evaporated in a tared dish, and the residue weighed as caffeine. (*P. J.*, 1887, p. 565.) Petit and Terrat subsequently found that the presence of lime or magnesia retards the extraction of the caffeine; they recommend direct extraction by chloroform containing a trace of water. (*J. P. C.*, 1896, 529.) A method of determining caffeine in either raw or roasted coffee, suggested by Fendler and Stüber (*Z. Nahr. Genuss.*, 1914, H.1), gives a very white and pure alkaloid. The method is as follows: The coffee is first extracted with chloroform. The residue from the chloroformic filtrate is taken up in hot water and treated with a solution of potassium permanganate in excess and the excess of manganese removed by adding a little solution of hydrogen dioxide, acidulated with acetic acid. After filtration the aqueous liquid is rendered alkaline and extracted with chloroform and the residue dried at 100° C. to constant weight. Power and Chestnut have developed an assay method yielding a very pure product. It is described in *J. Am. C. S.*, 1919, xli, 1298, 1307. For other methods see *A. J. P.*, 1892, 468, and 1893, 338; *Ap. Ztg.*, 1893, 132; *Ph. Era*, 1897, 391.

Caffeine is a feeble base, capable of forming definite compounds with mineral acids but not with organic acids; the latter, however, increase its solubility in water and other liquids. (See *Caffeina Citrata.*) The salts formed with mineral acids decompose when their solutions are evaporated. Caffeine is remarkable for containing a larger proportion of nitrogen than does almost any other proximate vegetable principle, in this respect equalling some of the highly animalized products.

Description and Physical Properties.—"White, flexible, silky, glistening needles, usually matted together in fleecy masses. It is odorless, has a bitter taste, and is efflorescent in dry air. One Gm. of Caffeine is soluble in 46 cc. of water, 66 cc. of alcohol, 50 cc. of acetone, 5.5 cc. of chloroform, 530 cc. of ether, and in 100 cc. of benzene, at 25° C. One Gm. is soluble in

5.5 cc. of water at 80° C., in 22 cc. of alcohol at 60° C., and in 22 cc. of boiling benzene.

"Caffeine rendered anhydrous by drying at about 100° C. melts between 235° and 237° C. A saturated, aqueous solution of Caffeine is neutral to litmus paper. Dissolve about 0.01 Gm. of Caffeine in 1 cc. of hydrochloric acid in a porcelain dish, add 0.1 Gm. of potassium chlorate, and evaporate to dryness on a water bath. On inverting the dish over a vessel containing a few drops of ammonia T.S., the residue acquires a purple color, which disappears upon the addition of solutions of fixed alkalies (*murexide reaction*). A saturated aqueous solution of Caffeine yields with tannic acid T.S., a precipitate which is soluble in an excess of the reagent, but no precipitate is produced by tenth-normal iodine unless the solution is first acidulated with hydrochloric or sulphuric acid.

"Caffeine loses not more than 9 per cent. when dried to constant weight at 80° C. Ash: not more than 0.05 per cent. The solution of 0.5 Gm. of Caffeine in 5 cc. of sulphuric or nitric acid is colorless or only faintly yellow (*readily carbonizable substances*). No precipitate is produced by mercuric potassium iodide T.S. in an aqueous solution of Caffeine (1 in 50) (*alkaloids*)." *U. S.*

The Br. Ph. describes it as "colorless, silky, acicular, inodorous crystals. Soluble in 80 parts of *water*, somewhat more soluble in *alcohol* (90 per cent.), readily soluble in *chloroform*, sparingly in *ether*. Melting point 235° C. Aqueous solution neutral to *litmus* and faintly bitter. Loses part of its water of crystallization on exposure to the air. Loss when dried at 100° C. not more than 8.5 per cent.; the dry alkaloid begins to volatilise at a slightly higher temperature and sublimes readily at about 180° C. A cold saturated aqueous solution is not precipitated by *N/10 solution of iodine*, or by solution *of potassio-mercuric iodide*, but gives a white precipitate with *solution of tannic acid*, soluble in excess of the reagent. 0.1 gramme dissolves without color in 1 millilitre of *sulphuric acid*, and also in 1 millilitre of *nitric acid*. When treated with a crystal of *potassium chlorate* and a few drops of *hydrochloric acid*, the mixture being evaporated to dryness in a porcelain dish, a reddish residue remains which becomes purple when exposed to the vapor of *solution of ammonia*." *Br.*

The apparent difference in solubilities of caffeine between the U. S. and British Pharmacopœias is due to the fact that the standard temperature of the U. S. is 25° C., and of the British 15.5° C. The U. S. solubilities are based upon the studies of Seidell (*J. Am. C. S.*, 1907, xxix, p. 1091).

The solubility of caffeine is increased by the presence of certain neutral salts as sodium benzoate, cinnamate, or salicylate. See *Caffeinæ Sodio-benzoas.*)

Uses.—There have been a few cases of poisoning by caffeine; a drachm of citrated caffeine swallowed by an adult was followed by burning in the throat, giddiness, faintness, nausea, tremor of the extremities, abdominal pain, mental distress, great cardiac oppression and finally collapse. Consciousness was not impaired and there was no headache until the patient began to recover. A decoction of 8 ounces of freshly roasted coffee, taken for the purpose of producing abortion, caused pronounced choreic tremors, great restlessness, quickened respiration, and rapid pulse, with very strong, even violent, heart beats. In doses of 3 to 5 grains caffeine produces in the healthy individual a peculiar wakefulness, with stimulation of the cerebrum, and some increase of the urinary secretion and force of the pulse. There is usually marked increase of the mental activity and of the capability for sustaining mental work. About two hours after the ingestion of 12 grains by Pratt, there were intense physical restlessness and mental anxiety, with obstinate sleeplessness, active and persistent thinking, general muscular tremulousness, and frequent urination.

Given in large dose to the lower animals, caffeine produces hurried respiration, restlessness, slightly lowered, followed by markedly elevated, temperature, tetanic and clonic convulsions, progressive paralysis, and finally death from paralytic arrest of respiration. The cause of the convulsions in mammals is not determined, but in the frog they are of spinal origin, for both Pratt and Le Blond have found that cutting of the cord does not arrest them below the point of section, while destruction of the cord (Pratt and Leven) prevents their development. It would appear, therefore, that caffeine acts upon the frog as a stimulant to the motor side of the spinal cord and a similar effect has been demonstrated in the human being by H. C. Wood, Jr. (*T. G.*, Jan., 1912.) In moderate doses, caffeine exercises a marked stimulating influence upon the muscle, increasing not only the irritability and contractile power of the muscle, but also the resistance to fatigue. Hyde, Root, and Curl (*A. J. Phys.*, 1917, xliii, p. 371) found that caffeine notably increased the muscular work as measured by the ergograph in human beings. When the drug is applied locally, in concentrated solution, it produces death of the muscle, with a condition simulating that of rigor mortis. In certain species of frogs a generalized rigidity of the muscles can be caused by the hypodermic administration of the drug, but it is improbable that sufficiently large quantities could be introduced into the system of any warm blooded animal to exercise this effect.

The effect of caffeine upon the circulation is less powerful than has been believed in the past. After moderate doses, there is generally, although not always, a slight rise in the blood pressure, with usually some slowing of the pulse. The rise in the blood pressure, as has been demonstrated by Sollmann and Pilcher (*J. P. Ex. T.*, 1911, iii, p. 19), is due solely to an increase in the vigor of the contraction of the heart, the blood vessels being usually somewhat dilated. After large doses the pulse becomes extremely rapid, apparently through a direct action upon the muscle of the heart, and the blood pressure shows a tendency to fall. The drop in the blood pressure after these large quantities appears to be due both to a widening of the vessels, and a diminution of the amplitude of the cardiac contractions.

In sufficient quantities, caffeine produces a very marked increase in the quantity of urine. Although the increase is more marked in the watery constituents, and the percentage of solid matter falls, the total quantity of solids eliminated in a given time is somewhat increased. The diuresis is accompanied with a marked widening of the renal vessels. This increase in the flow of urine appears to be due to a direct action on the renal epithelium, for Richards and Plant have shown (*J. P. Ex. T.*, 1915, vii, 485) that diuresis can be caused in the artificially perfused kidney without any acceleration of the blood flow.

The early belief that caffeine exercised some influence upon metabolism and the output of nitrogen has been entirely disproven. The only change in the amount or character of nitrogenous material in the urine is that which is due to the presence of caffeine itself, or its various methylization products in the body; it appears in the urine as a dimethyl- or monomethylxanthine. If the dose is small this reduction is complete, but after large quantities some of the drug may escape unaltered.

The dominant action of caffeine in the human being is upon the cerebrum. The experiments of Hollingworth (*T. G.*, Jan., 1912) have demonstrated that in those forms of psychological tests which involve purely intellectual processes there is a distinct increase in the rapidity and accuracy, an observation which is in entire harmony with the daily experience of millions of men. Not only is the mental activity temporarily stimulated, but the capability for prolonged work is also increased. After large quantities, this cerebral excitation shows itself in nervous restlessness, and a tendency to insomnia.

Although widely employed as a mental stimulant in daily life, caffeine is rarely used medically for this purpose, unless it be that its value in certain types of *headache* is associated with its action upon the cerebrum. Its most important medical uses are as a diuretic, and as a cardiac and respiratory stimulant.

As a diuretic, caffeine is of service, especially in the treatment of *dropsies*. When the dropsy is due to *nephritis* it must be used with some caution because of the possibility of an irritating action upon the diseased kidneys. Its value as a diuretic is lessened by its tendency to produce wakefulness, and because of this objection it has largely been displaced by the closely allied drugs, theobromine and theophylline. It is generally advisable, if using caffeine freely, not to administer the remedy in the latter part of the day. Those who have been habitual users of caffeinic beverages acquire a tolerance to the diuretic effects (see Myers, *J. P. Ex. T.*, 1924, xxxiii, p. 465) so that they require much larger doses or may refuse to respond altogether to the drug.

As a circulatory stimulant, caffeine is of little value as a cardiac tonic in cases of chronic *heart disease*, but finds its chief application in more or less acute *heart failure*, whether occurring during the course of a chronic cardiac condition, or as the result of the ingestion of the depressant *poisons*. Heathcote (*J. P. Ex. T.*, 1920, xvi, p. 327), finding that it actively dilates the coronary vessels, suggests its use in *angina pectoris*. In *surgical shock* the fact that it does not stimulate the vasomotor mechanism—which is generally believed to be the essential factor in these cases—makes it a remedy of only secondary value.

As a stimulant of the respiration it is a remedy of much usefulness, especially when used in connection with other agents of this class. It is more especially employed in cases of *narcotic poisoning*, such as morphine or chloral, in which it is useful, not only because of its direct action upon the respiratory center, but also because it counteracts, to some degree, the tendency to sleep.

Dose, one to five grains (0.065–0.32 Gm.).

Off. Prep.—Caffeina Citrata, *U. S.* (*Br.*); Caffeinæ Citras Effervescens (from Citrated Caffeine), *U. S.*; Pulvis Acetanilidi Compositus, *N. F.*; Caffeinæ Sodio-Benzoas, *U. S.*; Caffeinæ Sodio-Salicylas, *N. F.*; Sal Potassii Bromidi Effervescens Compositus, *N. F.*

CAFFEINA CITRATA. U. S. (Br.)

CITRATED CAFFEINE Caffein. Cit.

"Citrated Caffeine, when dried to constant weight at 80° C., contains not less than 48 per cent. nor more than 52 per cent. of anhydrous caffeine [$C_8H_{10}O_2N_4$]." *U. S.* "Caffeine Citrate, $C_8H_{10}N_4O_2,C_6H_8O_7$, is an unstable compound of Caffeine and Citric Acid." *Br.*

Caffeinæ Citras, *Br.*; Caffeine Citrate; Coffeinum Citricum; Citras Coffeicus; Citrate de Caféine, *Fr.*; Koffeïncitrat, Citronensaures Koffeïn, *G.*; Citrato cafeico, *Sp.*

"Caffeine, 100 grammes; Citric Acid, in powder, 100 grammes; Distilled Water, 16 millilitres. Mix the Caffeine with the Citric Acid, moisten the mixture with the Distilled Water, and dry on a water-bath with constant stirring." *Br.*

No formula is given in the U. S. X.

In this preparation Merson (*P. J.*, 1904, 8) prefers to mix the caffeine with the citric acid without the aid of a liquid; he uses a sieve, water bath, and granulating tray, and asserts that the process yields a superior product. It is not regarded by chemists as a chemical salt, but as a mechanical mixture of the two substances composing it. The British Pharmacopœia gives the following as its chemical formula: $C_8H_{10}N_4O_2,C_6H_8O_7$.

Description and Physical Properties.—"A white, odorless powder, having a slightly bitter, acid taste. One Gm. of Citrated Caffeine is soluble in about 4 cc. of warm water. On diluting the solution with an equal volume of water, a portion of the caffeine gradually separates, but redissolves on the further addition of water.

"The residue obtained in the assay when recrystallized from hot water and dried to constant weight at 80° C. has the melting point given under *Caffeina.* An aqueous solution of Citrated Caffeine (1 in 30) is acid to litmus paper. Dissolve about 0.02 Gm. of Citrated Caffeine in 1 cc. of hydrochloric acid in a porcelain dish, add 0.1 Gm. of potassium chlorate, and evaporate to dryness on a water bath. On inverting the dish over a vessel containing a few drops of ammonia T.S., the residue acquires a purple color, which disappears upon the addition of solutions of fixed alkalies (*murexide reaction*). About 2 cc. of a filtered aqueous solution of Citrated Caffeine (1 in 10) mixed with 50 cc. of lime water remains clear in the cold, but becomes turbid when heated to boiling. Add 1 cc. of mercuric sulphate T.S. to 5 cc. of an aqueous solution of Citrated Caffeine (1 in 100), heat the mixture to boiling, and add 1 cc. of potassium permanganate T.S.: a white precipitate is formed.

"Dried to constant weight at 80° C., Citrated Caffeine loses not more than 5 per cent. (*water*). Ash: not more than 0.1 per cent. Heat a mixture of 0.25 Gm. of Citrated Caffeine and 5 cc. of sulphuric acid in a porcelain dish on a water bath for fifteen minutes, protecting it from dust: it may become yellow but not brown or black (*tartrate*). An aqueous solution of Citrated Caffeine meets the requirements of the test for *heavy metals,* page 439. The addition of a few drops of barium chloride T.S. to 10 cc. of an aqueous solution of Citrated Caffeine (1 in 100), previously treated with a few drops of hydrochloric acid, produces no turbidity (*sulphate*).

"**Assay for Caffeine**—Dissolve about 0.5 Gm. of Citrated Caffeine, previously dried to constant weight at 80° C. and accurately weighed, in 10 cc. of hot distilled water, add 10 cc. of sodium hydroxide T.S., cool the solution, and shake it in a separator with three successive portions of 20 cc., 10 cc., and 5 cc., respectively, of chloroform, or more if necessary to complete the extraction. Evaporate the combined chloroform solutions on a water bath, dry the residue to constant weight at 80° C., and weigh.

"Preserve in well-closed containers." *U. S.*

The British Pharm. describes it as "a white powder with an acid reaction. Inodorous; taste acid and faintly bitter. Soluble in 4 parts of hot *water,* but dissociating on the further addition of *water* with separation of caffeine, which completely redissolves in 32 parts of *water.* Loses not more than 1 per cent. of its weight when dried at 100° C. When 1 gramme is dissolved in hot *water,* the solution made alkaline with *solution of sodium hydroxide* and shaken with three successive portions, each of 10 millilitres, of *chloroform,* the mixed chloroformic solutions, washed with a little *water,* leave on evaporation a residue weighing not less than 0.45 gramme, and responding to the test with *potassium chlorate* and *hydrochloric acid* described under 'Caffeina.' Caffeine Citrate yields the *reactions* characteristic of citrates." *Br.*

Uses.—Citrated caffeine is possessed of the physiological and therapeutic properties of caffeine, but is more liable to disagree with the digestive functions.

Dose, from three to eight grains (0.2 to 0.5 Gm.).

Off. Prep.—Caffeinæ Citras Effervescens, *Br.*

CAFFEINÆ CITRAS EFFERVESCENS. Br.

EFFERVESCENT CAFFEINE CITRATE

"It contains not less than 1.9 per cent. of anhydrous caffeine [$C_8H_{10}O_2N_4 = 194.12$]." *U. S.*

Caffeina Citrata Effervescens, *U. S. IX;* Effervescent Citrated Caffeine; Coffeïnum Citricum Effervescens; Braüsendes Koffeïncitrat, *G.;* Citrato Cafeico Effervescente, *Sp.*

"Sodium Bicarbonate, in powder, 510 grammes; Tartaric Acid, in powder, 270 grammes; Citric Acid, in powder, 180 grammes; Refined Sugar, in powder, 140 grammes; Caffeine Citrate, 40 grammes. Mix the Caffeine Citrate, Tartaric Acid, and Citric Acid; with this mixture thoroughly incorporate the mixed Sodium Bicarbonate and Refined Sugar; place in a dish or pan of suitable form heated to between 90° and 105° C. When the mixture, by aid of careful manipulation, has assumed a granular character, separate it into granules of uniform and convenient size by means of suitable sieves. Dry the granules at a temperature not exceeding 55° C. The product weighs about one thousand grammes." *Br.*

This compound contains about two per cent. of caffeine. Samples of effervescent citrated caffeine have been found in the market very deficient in caffeine; the sweetening is sometimes effected by the use of saccharin instead of sugar. The powder affords an agreeable method of administering citrated caffeine.

Dose, one to two drachms (3.9–7.5 Gm.) in water, to be taken during effervescence.

CAFFEINÆ SODIO-BENZOAS. U. S.

CAFFEINE SODIO-BENZOATE Caff. Sod. Benz.

"A mixture of caffeine and sodium benzoate, which contains, when dried to constant weight at 80° C., not less than 47 per cent. nor more than 50 per cent. of anhydrous caffeine [$C_8H_{10}O_2N_4$ and not less than 50 and not more than 53 per cent. of sodium benzoate [$NaC_7H_5O_2$]." *U. S.*

Coffeinum Natrium Benzoicum; Benzoas Coffeini et Natrii.

Description and Physical Properties.—"A white, odorless powder, having a slightly bitter taste. One Gm. of Caffeine Sodio-Benzoate is soluble in 1.1 cc. of water, a portion of the caffeine usually separating on standing, and in 30 cc. of alcohol, at 25° C. It is partly soluble in chloroform.

"On heating, it is decomposed with the evolution of white vapors of caffeine, leaving a residue which effervesces with acids and colors a non-luminous flame intensely yellow. Ferric chloride T.S. produces a salmon-colored precipitate, and diluted hydrochloric acid produces a white precipitate in an aqueous solution of Caffeine Sodio-Benzoate. The residue obtained in the assay for caffeine when recrystallized from hot water, and dried to constant weight at 80° C., has the melting point of Caffeine, and responds to the other tests for identity under *Caffeina.*

"Its aqueous solution (1 in 20) may be neutral, slightly acid, or slightly alkaline to litmus paper, but is not reddened by phenolphthalein T.S. When dried to constant weight at 80° C., Caffeine Sodio-Benzoate loses not more than 5 per cent. of its weight (*water*). The solution of 0.1 Gm. of Caffeine Sodio-Benzoate in 2 cc. of sulphuric acid is colorless or only faintly yellow (*readily carbonizable substances*). Dissolve about 2 Gm. of Caffeine Sodio-Benzoate in 40 cc. of distilled water in a separator, add 10 cc. of diluted sulphuric acid, extract the liberated benzoic acid with two successive 10 cc. portions of ether, and allow the ether solution to evaporate to dryness at room temperature: one-half Gm. of the benzoic acid so obtained complies with the test for *chlorinated compounds* under *Acidum Benzoicum.* Its aqueous solution (1 in 50) acidulated with hydrochloric acid and filtered, meets the requirements of the test for *heavy metals.*

"**Assay for Caffeine.**—Dissolve about 1 Gm. of Caffeine Sodio-Benzoate, previously dried to constant weight at 80° C. and accurately weighed, in 5 cc. of distilled water in a separator, add 5 cc. of sodium hydroxide T.S., and shake the mixture with four successive portions of 20 cc., 10 cc., 10 cc., and 5 cc., respectively, of chloroform. Pass the chloroform solutions through a filter which has been previously moistened with chloroform, and wash the stem of the funnel and filter with a few cc. of hot chloroform to remove any adhering caffeine. Evaporate the combined chloroform solutions on a water bath, and dry the residue, consisting of anhydrous caffeine, to constant weight at 80° C.

"**Assay for Sodium Benzoate.**—To the aqueous liquid from which the caffeine has been removed in the above assay for caffeine, add 10 cc. of diluted sulphuric acid, and extract the liberated benzoic acid with four successive portions of 20 cc., 10 cc., 10 cc., and 5 cc., respectively, of chloroform. Pass the chloroform solutions through a filter which has been previously moistened with chloroform, and wash the stem of the funnel and the filter with a few cc. of hot chloroform. Evaporate the combined chloroform solutions to about 5 cc. at a temperature not exceeding 40° C., add 25 cc. of diluted alcohol previously neutralized with tenth-normal sodium hydroxide, using 3 drops of phenolphthalein T.S. as indicator, and titrate with tenth-normal barium hydroxide to the restoration of the pink color. Each cc. of tenth-normal barium hydroxide corresponds to 0.01441 Gm. of sodium benzoate ($NaC_7H_5O_2$)." *U. S.*

Uses.—This compound has the physiological effects and therapeutic uses of caffeine. It has the advantage over the alkaloid of being freely soluble in water, and over the citrated caffeine of being less irritant to the stomach; whenever it is desired to exhibit caffeine in solution the preference should be given to caffeine and sodium benezoate. It is especially suitable for hypodermic administration for which purpose it may be dissolved in three parts of water and from ten to twenty minims (0.6–1.3 cc.) of this solution injected at a dose.

Dose, three to ten grains (0.2–0.6 Gm.).

Off. Prep.—Ampullæ Caffeinæ Sodio-benzoatis, *N. F.*

CALAMINA PRÆPARATA. N. F.

PREPARED CALAMINE. Calamin. Praep. [Lapis Calaminaris]

"Prepared Calamine is Zinc Oxide containing a small amount of ferric oxide. It contains, after ignition, not less than 98 per cent. ZnO." *N. F.*

Tutia Grisea; Nihilum Griseum; Galmei, Grauer Galmei, *G.;* Giallamina, *It.*

Calamine is the old name of the native *zinc carbonate,* although in mineralogy the name *calamine* is now applied to *zinc silicate,* while the name *smithsonite* is given to the carbonate. It is found in the United States, as well as in Belgium, Germany, and England. It occurs in compact or earthy masses, or concretions of a dull appearance, readily scratched by the knife, and breaking with an earthy fracture, or it occurs crystallized in rhombic forms. Its color is very variable, being, in different specimens, grayish, grayish-yellow, reddish-yellow, and, when very impure, brown or brownish-yellow. Its sp. gr. varies from 3.4 to 4.4. Before the blow pipe it does not melt, but becomes yellow and sublimes. When of good quality, it is almost entirely soluble in the dilute mineral acids, and unless it has been previously calcined, emits bubbles of carbon dioxide.

Description and Physical Properties.—"Prepared Calamine is a pink powder passing through a No. 100 sieve. It is insoluble in water but dissolves in mineral acids, leaving a small amount of insoluble residue.

"A filtered solution of Prepared Calamine in diluted hydrochloric acid yields the reactions of zinc. Digest 1 Gm. of Prepared Calamine with 20 cc. of warm water, filter and add 2 drops of phenolphthalein T.S. If a red color is produced, not more than 0.2 cc. of tenth-normal sulphuric acid is required to discharge it (*alkaline substances*). 0.2 Gm. of Prepared Calamine dissolved in 5 cc. of diluted sulphuric acid meets the requirements of the Test for arsenic. Dissolve 1 Gm. of Prepared Calamine in 25 cc. of diluted hydrochloric acid, filter, and add to the filtrate ammonia water until the precipitate first formed is redissolved, then add 5 cc. more ammonia water. To 10 cc. of this solution add 2 cc. of ammonium oxalate T.S. Not more than a slight turbidity is produced (*calcium*). To another 10 cc. portion add 2 cc. of sodium phosphate T.S. Not more than a slight turbidity is produced (*calcium* or *magnesium*). To 1 Gm. of Prepared Calamine add 15 cc. of water, stir well, then add 3 cc. of glacial acetic acid, warm on the water bath until dissolved and filter. On adding 5 drops of potassium chromate T.S. to the filtrate no turbidity is produced (*lead*).

" **Assay.**—Ignite about 1.5 Gm. of Prepared Calamine, cool, weigh accurately and dissolve it by warming with 50 cc. of normal sulphuric acid. Filter, wash the residue and filter with hot distilled water until the washings are no longer acid to litmus paper, then titrate the combined cooled filtrate and washings with normal sodium hydroxide, using methyl orange as indicator. Each cc. of normal sulphuric acid corresponds to 0.04069 Gm. of ZnO." *N. F.*

Native zinc silicate, the calamine of the mineralogist, occasionally finds its way into pharmaceutical commerce through error. It may be distinguished by its complete insolubility in diluted hydrochloric acid. A spurious calamine composed of barium sulphate colored with iron oxide or aniline color is still to be found. " Calamina Præparata " made from precipitated carbonate of zinc and iron chloride should be used at the present time, as the natural product is no longer obtainable. (*Proc. New York Pharm. Assoc.*, 1915, p. 89.)

Uses.—Zinc carbonate has similar therapeutic virtues to the zinc oxide as a local application in the treatment of skin diseases. The chief use of native calamine depends, however, on its color; it is used to impart a flesh color to ointments, washes, and powders. As the pure zinc carbonate is white it ought not to be used when calamine is ordered.

Off. Prep.—Linimentum Calaminæ, *N. F.;* Lotio Calaminæ, *N. F.;* Lotio Calaminæ Composita, *N. F.;* Unguentum Calaminæ, *N. F.*

CALCII BROMIDUM. U. S.

CALCIUM BROMIDE Calc. Brom.

" Calcium Bromide is a hydrated salt, containing not less than 84 per cent. of CaBr$_2$." *U. S.*

Calcium Bromatum, Bromure de Calcium, Bromure de Chaux, *Fr.;* Brom Kalk, Calciumbromid, *G.*

Calcium bromide may be made by direct reaction of hydrobromic acid and calcium carbonate. Various other methods have been suggested; that of Macdonald (*A. J. P.*, 1873) is as follows: Dissolve 4 ounces of ammonium bromide in a pint of water. Put into a flask and bring to the boiling point. Keep boiling, and add milk of lime (made from *pure* calcined lime) in small quantities, until ammoniacal vapors cease to be evolved. The operator can easily tell when this point has been reached, by the sense of smell. Filter the solution, evaporate to a syrupy consistency, remove from the fire, and stir until cold. Tasilly prepares *calcium oxybromide* by adding three parts of calcium oxide in small portions to a solution of one hundred parts of calcium bromide in seventy-five parts of hot water; acicular crystals of calcium oxybromide CaBr$_2$3CaO,16H$_2$O, are deposited on cooling the filtered solution.

Description and Physical Properties.—" A white, granular salt, having no odor. It is very deliquescent. One Gm. of Calcium Bromide is soluble in 0.7 cc. of water and in 1.3 cc. of alcohol, at 25° C. One Gm. is soluble in 0.4 cc. of boiling water. It is insoluble in chloroform and in ether. An aqueous solution of the salt (1 in 20) responds to the reactions for calcium, and for bromides.

" An aqueous solution of Calcium Bromide (1 in 20) is neutral or slightly alkaline to litmus paper. Add a few drops of ferric chloride T.S. and 1 cc. of chloroform to 10 cc. of an aqueous solution of the salt (1 in 20), and shake the mixture: the chloroform does not acquire a violet tint (*iodide*). Drop 1 cc. of diluted sulphuric acid upon about 1 Gm. of the powdered salt: no yellow color appears at once (*bromate*). Dissolve 0.1 Gm. of the salt in 5 cc. of distilled water, add an excess of silver nitrate T.S. and a few drops of nitric acid, and filter. Wash the precipitate with distilled water, digest it for ten minutes with 5 cc. of ammonium carbonate T.S., and filter. Dilute the filtrate with enough distilled water to make 40 cc.: a 10 cc. portion of this dilution, acidulated with nitric acid and further diluted with enough water to make 50 cc., shows no more *chloride* than corresponds to 0.5 cc. of fiftieth-normal hydrochloric acid, page 462. A 20 cc. portion of an aqueous solution of Calcium Bromide (1 in 250) does not at once assume a blue color with potassium ferrocyanide T.S. (*iron*). A 5 cc. portion of an aqueous solution of the salt (1 in 20), when acidulated with 1 drop of hydrochloric acid, shows no immediate turbidity with 1 cc. of barium chloride T.S. (*sulphate*). Dissolve 1 Gm. of Calcium Bromide and 1 Gm. of sodium acetate in 5 cc. of distilled water, and render the solution slightly acid by the addition of a sufficient quantity (from 3 to 5 drops) of diluted acetic acid. After boiling and thoroughly cooling the solution, it does not become cloudy within five minutes after the addition, with agitation, of five drops of potassium dichromate T.S. (*barium*). Precipitate the calcium completely from 10 cc. of an aqueous solution of Calcium Bromide (1 in 20) by adding ammonium oxalate T.S., and filter: the filtrate on evaporation and ignition leaves not more than 0.004 Gm. of residue (*magnesium or alkalies*). An aqueous solution of the salt meets the requirements of the test for *heavy metals*.

"**Assay.**—Proceed as directed under the assay for bromides, page 432, using about 0.5 Gm. of Calcium Bromide, accurately weighed in a stoppered weighing-bottle. Each cc. of tenth-normal silver nitrate corresponds to 0.009996 Gm. of $CaBr_2$.

"Preserve in well-closed containers." *U. S.*

Uses.—If the calcium salts have, as there is reason to believe, anticonvulsant properties (see under *Calcium*) then the combination in calcium bromide is a rational one. Its action upon the lower animals has been partially investigated by Guttmann (*P. M. T.,* iv, p. 361) who finds that it is a sedative to the nerve centers and does not depress the heart. It may be used in the place of the other bromides in the treatment of *epilepsy, tetany,* or *hysteria,* but is not largely employed. It is sometimes of service in *asthma.*

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Elixir Bromidorum Quinque, *N. F.;* Syrupus Bromidorum, *N. F.*

CALCII CARBONAS PRÆCIPITATUS.
U. S., Br.

PRECIPITATED CALCIUM CARBONATE Calc. Carb. Præc. [Precipitated Chalk]

"It contains, when dried to constant weight at 200° C. not less than 98 per cent. of $CaCO_3$." *U. S.* "Precipitated Calcium Carbonate, $CaCO_3$, is obtained by the interaction of calcium chloride and sodium carbonate." *Br.*

Carbonas Calcicus Præcipitatus, Creta Præcipitata, Calcaria Carbonica Præcipitata; Precipitated Carbonate of Lime; Carbonate de Chaux Precipité, *Fr.;* Carbonate de Calcium, *Fr. Cod.;* Calcium carbonicum præcipitatum, *P. G.;* Calciumcarbonat; Präcipitirter kohlensaure Kalkerde, *G.;* Carbonato di calcio precipitato, *It.;* Carbonato de cal, *Sp.*

This salt may be made by the process of the U. S. P., 1870. It is as follows: "Take of Solution of Chloride of Calcium *five pints and a half;* Carbonate of Sodium *seventy-two troyounces;* Distilled Water *a sufficient quantity.* Dissolve the Carbonate of Sodium in six pints of Distilled Water. Heat this solution and the Solution of Chloride of Calcium, separately, to the boiling point and mix them. After the precipitate has subsided, separate it from the supernatant liquid by decantation, and wash it with boiling Distilled Water until the washings cease to be affected by a solution of nitrate of silver. Lastly, dry the precipitate on bibulous paper."

Description and Physical Properties.—"A fine, white, microcrystalline powder, without odor or taste. It is stable in the air. Precipitated Calcium Carbonate is practically insoluble in water. The solubility is increased by the presence of ammonium salts and also by carbon dioxide. Alkali hydroxides diminish its solubility. It is insoluble in alcohol, and is dissolved with effervescence by diluted acetic, hydrochloric, or nitric acid, When heated to about 825° C., the salt gradually loses carbon dioxide, and a residue of calcium oxide remains. The addition of acetic acid to Precipitated Calcium Carbonate produces effervescence, and the resulting solution after boiling to expel carbon dioxide and neutralizing with ammonia T.S. responds to the reactions for calcium.

"Mix 2 Gm. of Precipitated Calcium Carbonate with 100 cc. of distilled water and add hydrochloric acid, drop by drop, with agitation until solution takes place. This solution does not impart a green or crimson color to a nonluminous flame, and a 10 cc. portion of the liquid does not respond to the test for *heavy metals,* page 439. Filter any insoluble residue remaining, wash with water until washings show no more chloride, and ignite: the weight of the residue does not exceed 0.004 Gm. Dissolve 0.5 Gm. of Precipitated Calcium Carbonate in 10 cc. of diluted hydrochloric acid, neutralize with ammonia T.S., completely precipitate the calcium by adding ammonium oxalate T.S., and then filter: the filtrate on evaporation and ignition leaves not more than 0.004 Gm. of residue (*magnesium or alkalies*).

"**Assay.**—Dry about 0.3 to 0.4 Gm. of Precipitated Calcium Carbonate to constant weight at 200° C., weigh accurately, dissolve it in 10 cc. of diluted hydrochloric acid and 10 cc. of distilled water, and boil the solution to expel all carbon dioxide. Transfer this solution to a 200 cc. volumetric flask, add 100 cc. of tenth-normal oxalic acid, render it alkaline with ammonia T.S., shake the mixture well, and allow it to stand for three hours at from 60° to 70° C., or over night at room temperature. Cool the liquid if necessary, fill the flask with distilled water to 200 cc., mix well, filter through a dry filter into a dry flask, reject the first 20 cc. of the filtrate, and proceed as follows: Acidulate 100 cc. of the filtrate (corresponding to one-half of the Precipitated Calcium Carbonate taken) with diluted sulphuric acid, then add 25 cc. more of the diluted sulphuric acid, warm the solution to about 65° C., and titrate with tenth-normal potassium permanganate. Each cc. of tenth-normal oxalic acid corresponds to 0.005004 Gm. of $CaCO_3$." *U. S.*

"A white microcrystalline powder insoluble in *water.* Yields the *reactions* characteristic of calcium and of carbonates. Yields no characteristic *reactions* for iron, aluminium, phosphates, or sulphates, and not more than the slightest *reactions* for magnesium or chlorides. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Bertholet has stated that the peculiar properties of precipitated calcium carbonate are largely dependent upon its micro-crystalline form. When precipitation is performed at 0°C. a light hydrated carbonate, almost entirely amorphous, is produced, having a density of only 1.7; if the precipitation is conducted at 30°C., the product consists of minute rhombohedra with a density of 2.7; if boiling solutions are employed, the precipitate consists of prismatic rhombohedra with a density of 2.9.

The denser form being easier to manipulate and wash, constitutes most of the precipitated calcium carbonate of commerce. It is much less readily attacked by acids and may pass through the intestinal tract unchanged.

Uses.—For ordinary purposes, it probably has no such superiority over prepared chalk as to counterbalance its greater expensiveness.

It is not so desirable for tooth powders as chalk because, being in a crystalline state, it is more liable to abrade the tooth enamel.

Dose, from ten to forty grains (0.65–2.6 Gm.).

Off. Prep.—Trochiscus Bismuthi Compositus, *Br.*

CALCII CHLORIDUM. U. S., Br.

CALCIUM CHLORIDE Cal. Chlor.

"Calcium Chloride is a hydrated salt, containing not less than 75 per cent. of $CaCl_2$. Preserve it in well-stoppered bottles." *U. S.* "Calcium Chloride, $CaCl_2$, may be obtained by neutralizing hydrochloric acid with calcium carbonate, and carefully desiccating at a temperature not exceeding 200° C." *Br.*

Calcium Chloratum; Calcaria Muriatica; Chlorurum Calcicum; Chloridum Calcium; Muriate of Lime, Hydrochlorate of Lime; Chlorure de Calcium Cristallisé, *Fr.;* Chlorcalcium, Calciumchlorid, Salzsaures Kalk, *G.;* Cloruro di calcio, *It.;* Cloruro calcico, *Sp.*

The hydrated form of this salt has replaced the fused calcium chloride which was formerly official. Anhydrous calcium chloride may be readily formed by saturating hydrochloric acid with chalk or marble, evaporating to dryness, and heating to redness. The hydrochloric acid, be reacting with the calcium carbonate, forms calcium chloride, carbon dioxide, and water, the latter of which is dissipated at a red heat, $CaCO_3 + 2HCl = CaCl_2 + CO_2 + H_2O$. The crystallized or partly hydrated salt is prepared by allowing a concentrated solution to crystallize in a cool temperature. The Br. Ph. (1885), after neutralizing the acid with calcium carbonate, adds a little solution of chlorinated lime and slaked lime, filters, evaporates until the chloride becomes solid, and, instead of igniting the residue, dries it at about 204.4° C.

Description and Physical Properties.—"White, slightly translucent, hard, odorless fragments or granules. It is very deliquescent. One Gm. of Calcium Chloride is soluble in 1.2 cc. of water, and in about 10 cc. of alcohol, at 25° C. One Gm. is soluble in 0.7 cc. of boiling water and in about 2 cc. of boiling alcohol. An aqueous solution of the salt (1 in 10) responds to the reactions for calcium, and for chlorides.

"An aqueous solution of Calcium Chloride (1 in 20) is neutral or slightly alkaline to litmus paper. Add ammonia water to an aqueous solution of the salt (1 in 20) until alkaline: no turbidity or precipitation occurs either before or after boiling (*iron, aluminum, or phosphates*). Precipitate the calcium completely from 10 cc. of an aqueous solution of the salt (1 in 20) by adding ammonium oxalate T.S., and filter: the filtrate on evaporation and ignition leaves not more than 0.004 Gm. of residue (*magnesium or alkalies*). An aqueous solution of the salt does not respond to the test for *heavy metals.*

"**Assay.**—Proceed as directed under the assay for chlorides, page 432, using about 0.3 Gm. of Calcium Chloride, accurately weighed in a stoppered weighing-bottle. Each cc. of tenth-normal silver nitrate corresponds to 0.00555 Gm. of $CaCl_2$.

"Preserve in well-stoppered bottles." *U. S.*

"Dry, white, very deliquescent masses. Taste warm, slightly bitter. Soluble in 1.5 parts of *water,* and in 3 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of calcium and of chlorides. Yields no characteristic *reactions* for iron, aluminium, or carbonates, and not more than the slightest *reactions* for magnesium. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million. Evolves no chlorine or hypochlorous acid on the addition of *hydrochloric acid* (absence of hypochlorite). Loses not more than 5 per cent. of its weight when dried at 200° C." *Br.*

On account of its avidity for water, the fused salt is used for drying gases and in desiccators. The crystallized salt is also very deliquescent, and has the form of colorless, transparent, striated, six-sided prisms. The crystals, on exposure to heat, first dissolve in their water of crystallization, and, after this has evaporated, undergo igneous fusion. With ice or snow they form a powerful frigorific mixture. Calcium chloride exists in the water of the ocean and of many springs. It is usually associated with common salt and magnesium chloride, from which it is separated with difficulty. When crystallized it normally contains six molecules of water, but other crystalline hydrates have also been obtained.

Uses.—For consideration of the rôle of this element in physiology and the general therapeutic use see under *Calcium.* As an available source of calcium the chloride has been extensively employed in the treatment of internal *hemorrhages* such as *hemoptysis, menorrhagia* and *hemophilia.*

Within recent years calcium chloride has attracted some attention as a diuretic in cases of general *anasarca.* Keith, Barrier and Whelan (*J. A. M. A.*, 1924, lxxxiii, p. 666) attribute its beneficial effect in these cases to the fact that it causes an increased elimination of sodium chloride.

In some way not at present evident the lime salts diminish the susceptibility of guinea-pigs to the condition known as *anaphylaxis* which follows the injection of foreign protein. It has, therefore, been used clinically and with apparent good results not only to prevent the *serum disease* after the injection of antitoxins, but in the treatment of *hay fever, asthma, urticaria, laryngismus stridulus, hemoglobinuria,* etc. Following the example of a Swedish physician named Saxtorph a number of clinicians have used calcium chloride by intravenous injection for the relief of *tubercular diarrhea.* A single injection of 5 cc. of a 5 per cent. solution (equivalent to a dose of 0.25 Gm.—four grains) will often cause permanent relief (Fishberg, *J. A. M. A.,* 1919, lxxii, 1881). The treatment is apparently not entirely free from danger as in one case reported by Fishberg there was serious collapse. Calcium chloride should never be administered hypodermically because of its strong local destructive effect on the subcutaneous tissues (see Seelig, *J. A. M. A.,* 1925, lxxiv).

The *dose* ordinarily recommended is five to fifteen grains (0.32–1.0 Gm.), but it is very doubtful whether such a quantity by the mouth can exercise any effect on the system, and as the salt is relatively innocuous larger doses would seem more rational; a more reasonable dose would be twenty to thirty grains (1.3–2.0 Gm.).

Off. Prep.—Liquor Hydrastinæ Compositus, *N. F.*

CALCII GLYCEROPHOSPHAS. U. S.

CALCIUM GLYCEROPHOSPHATE Calc. Glycerophos. [Calcium Glycerinophosphate]

"The normal calcium salt of glycerophosphoric acid [$C_3H_5(OH)_2PO_4H_2 = 172.11$], containing, when dried to constant weight at 130° C., not less than 98 per cent. of $C_3H_5(OH)_2PO_4Ca$." *U. S.*

Glycerophosphate of Lime, Calcium Phosphoglycerate; Glycerophosphate de chaux, *Fr.;* Glycerophosphate de Calcium, *Fr. Cod.*

There are several theoretically possible *glycerides of phosphoric acid,* but the only one of any practical significance is the *monoglyceride of ortho-phosphoric acid* of the composition $CH_2OH.CHOH.CH_2O.PO(OH)_2$. This compound, called for brevity's sake *glycerophosphoric acid,* was discovered by Pelouze in 1846, while studyng glycerol-sulphuric acid, an analogous compound. Other authors soon discovered the presence of salts of this new acid in yolk of egg, brain tissue and other organic sources. Being called to the attention of the medical profession, a demand soon arose for the glycerophosphates of the various elements, which in some cases, as that of sodium, was supplied by the furnishing of spurious articles, mixtures of inorganic salts and glycerin being substituted for them.

Glycerophosphoric acid is a dibasic acid and therefore is capable of combining with bases to form normal or acid salts, which occur in varying conditions of hydration. The official calcium glycerophosphate is the normal salt and has the formula $Ca.\ C_3H_5(OH)_2.PO_4$. The acid salt has the formula $Ca.[C_3H_5(OH)_2HPO_4]_2$. This latter compound does not exist as a solid salt, but is usually found in the form of a 50 per cent. solution, higher concentrations being unstable. The advantage of the acid salts is their more ready solubility, which, however, is counter-balanced by the acidity, which prevents their use subcutaneously. The solubility of the normal salts can be greatly increased by the addition of a small proportion of lactic acid, citric acid or of sodium citrate. The solubility is diminished by the presence of alcohol, glycerin or solutions of other glycerophosphates.

The normal salt is made by treating glycerophosphoric acid with calcium hydroxide and purifying the product by treatment with alcohol.

Description and Physical Properties.—"A fine, white, odorless powder. It is somewhat hygroscopic. One Gm. of Calcium Glycerophosphate is soluble in about 50 cc. of water at 25° C. It is more soluble in water at a lower temperature; citric acid increases its solubility in water. It is insoluble in alcohol.

"A saturated aqueous solution of Calcium Glycerophosphate is alkaline to litmus paper and to phenolphthalein T.S. A cold, saturated aqueous solution of the salt upon boiling yields white, iridescent scales of anhydrous calcium glycerophosphate. When heated above 170° C., the salt is decomposed, evolving inflammable vapors, and at a red heat is converted into calcium pyrophosphate. A saturated aqueous solution of the salt responds to the reactions for calcium, and for glycerophosphates. With lead acetate T.S. a saturated aqueous solution of the salt yields a white curdy precipitate, which is soluble in nitric acid.

"Dissolve 1 Gm. of Calcium Glycerophosphate in 10 cc. of diluted nitric acid, and add an equal volume of cold ammonium molybdate T.S.: no precipitate is formed within one hour (*phosphates*). An aqueous solution of the salt meets the requirements of the test for *heavy metals.* One Gm. of Calcium Glycerophosphate shows no more *chloride* than 1 cc. of fiftieth-normal hydrochloric acid, page 462. Two-tenths of 1 Gm. of Calcium Glycerophosphate shows no more *sulphate* than 1 cc. of fiftieth-normal sulphuric acid, page 462. Shake 1 Gm. of finely powdered Calcium Glycerophosphate with 25 cc. of dehydrated alcohol, filter the mixture, evaporate the filtrate on a water bath, and dry the residue for an hour at a temperature not exceeding 70° C.: the resulting residue weighs not more than 0.01 Gm. (*alcohol-soluble substances*). The loss on drying a portion of the finely powdered salt to constant weight at 130° C., does not exceed 10 per cent. (*water*). Dry about 3 Gm. of Calcium Glycerophosphate to constant weight at about 130° C., weigh accurately, dissolve it in 250 cc. of distilled water, and then titrate with half-normal hydrochloric acid, using methyl orange T.S. as indicator, to a slight yet distinct pink. Each Gm. of dry Calcium Glycerophosphate requires not less than 9 cc. of half-normal hydrochloric acid (*minimum limit for glycerophosphate*).

"**Assay.**—Dry about 0.4 Gm. of Calcium Glycerophosphate to constant weight at 130° C., weigh accurately, dissolve in 20 cc. of a 5 per cent. solution of acetic acid, and add 30 cc. of distilled water. Heat the mixture to boiling, and add an excess of ammonium oxalate T.S. Collect the resulting precipitate, wash, dry, and ignite to constant weight. This residue of calcium oxide corresponds to not less than 26.1 per cent. of the weight of dried Calcium Glycerophosphate taken. Dry a portion of Calcium Glycerophosphate to constant weight at 130° C., and ignite it to constant weight. The weight of calcium pyrophosphate corresponds to not less than 59.2 per cent. of the weight of Calcium Glycerophosphate taken.

"Preserve in well-closed containers." *U. S.*

Uses.—The phosphorus of the central nervous system exists in the form of an organic combination of glycerophosphoric acid. On the theory that glycerophosphoric acid could be directly absorbed and utilized as a nutriment for the central nervous system, various salts of the glycerophosphates have been introduced into medicine. There is, however, no convincing evidence that the central nervous system can metabolize the glycerophosphates any better than ordinary phosphates; moreover in conditions of nerve weakness in which this group of remedies is supposed to be indicated, the fault is due not to the absence of phosphorus in the food but to errors in the metabolic processes of the nervous system. While theory does not support the use of glycerophosphates as nerve tonics, there is considerable clinical evidence as to their value in conditions of *debility,* as *neurasthenia.* The calcium glycerophosphate represents any virtue that may pertain to the glycerophosphoric acid and adds to it the value of the calcium. It has been used also in various *bone diseases,* such as *rickets* and also in *tubercular* complaints. Blackader (*J. A. M. A.*, 1912, lix) believes that any therapeutic value that calcium glycerophosphate may possess is due to its content of lime. Theoretically it should, for many purposes, be superior to most other calcium salts because it represents both calcium and phosphoric acid in a soluble combination (see *Calcium Phosphate*).

Dose, three to eight grains (0.2–0.5 Gm.).

Off. Prep.—Elixir Calcii et Sodii Glycerophosphatum, *N. F.;* Elixir Glycerophosphatum Compositum, *N. F.;* Elixir Terpini Hydratis et Creosoti Compositum, *N. F.*

CALCII HYDRAS. Br.

CALCIUM HYDROXIDE

"Calcium Hydroxide, $Ca(OH)_2$, is the product, recently prepared, of the interaction of water and Lime." *Br.*

Calcis Hydras; Slaked Lime; Hydrate of Lime; Chaux Eteinte, *Fr. Cod.;* Idrato di calcio, *It.*

The British Parmacopœia no longer gives a detailed process for slaked lime. The process of the Br. Pharm. (1885) is as follows: "Take of Lime *two pounds* [avoirdupois]; Distilled Water *one pint* [Imperial measure]. Place the lime in a metal pot, pour the water upon it, and when vapor ceases to be disengaged cover the pot with its lid and set it aside to cool. When the temperature has fallen to that of the atmosphere, put the slaked lime on an iron-wire sieve, and by the gentle agitation cause the fine powder to pass through the sieve, rejecting what is left. Put the powder into a well-stoppered bottle, and keep it excluded as much as possible from the air. Slaked lime should be recently prepared." *Br.,* 1885. Calcium hydroxide "is a soft, white powder. Yields the *reactions* characteristic of calcium. Strongly heated it loses nearly one-fourth of its weight of water. Yields not more than the slightest characteristic *reactions* for iron, carbonates, chlorides, sulphates, or silica. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million." *Br.*

For an account of the physical and medicinal properties of slaked lime, see *Calx.*

Off. Prep.—Liquor Calcis, *Br.;* Liquor Calcii Saccharatus, *Br.*

CALCII HYPOPHOSPHIS. N. F., Br.

CALCIUM HYPOPHOSPHITE Calc. Hypophos.

"Calcium Hypophosphite contains, when dried to constant weight over sulphuric acid, not less than 98 per cent. of $Ca(PH_2O_2)_2$ (170.18)." *N. F.*

"Calcium Hypophosphite may be obtained by the interaction of phosphorus, calcium hydroxide, and water. It contains not less than 98 per cent. of pure calcium hypophosphite, $Ca(PH_2O_2)_2$." *Br.*

Calcis Hypophosphis; Calcium Hypophosphorosum; Hypophosphite of Lime; Calcaria Hypophosphorosa, Hypophosphis Calcicus; Hypophosphite de Chaux, *Fr. Cod.;* Unterphosphorigsaure Kalkerde, Calcium hypophosphit, *G.;* Hipofosfito calcico, *Sp.*

Calcium hypophosphite may be prepared by the following method, originally devised by Procter: Slake four pounds (avoirdupois) of lime with a gallon of water, add it, in a deep boiler, to four gallons of boiling water, and mix thoroughly. To the mixture add a pound (av.) of phosphorus, and continue the boiling, adding hot water from time to time to keep up the measure, until the combination is complete, and hydrogen phosphide is no longer evolved. It is necessary to provide for the escape of the gas, which takes fire spontaneously in contact with air. There are formed in the liquid calcium phosphate and hypophosphite, the phosphorus oxidizing at the expense of the water, the hydrogen of which has escaped in combination with another portion of phosphorus, which is therefore lost. The liquid is filtered to separate the insoluble phosphate and residuary lime, then concentrated, and refiltered to separate the calcium carbonate formed by the action of the air on a little lime held in solution, and lastly evaporated until a pellicle appears; after which the salt may be allowed to crystallize by setting the liquid aside, or may be obtained in the granular form by continuing the heat and stirring. The salt should be introduced into bottles. The former Br. Pharm. practically adopted this process, but any uncombined lime remaining in the solution was separated by passing carbonic acid gas through it.

Description and Physical Properties.—"Calcium Hypophosphite occurs as colorless, transparent, monoclinic prisms, as small lustrous scales, or as a white, crystalline powder; odorless, having a nauseous and bitter taste. One Gm. of Calcium Hypophosphite is slowly soluble in 6.5 cc. of water at 25° C.; insoluble in alcohol.

"When heated the salt decrepitates and begins to decompose, giving off water and evolving spontaneously inflammable hydrogen phosphide, and on complete ignition leaving a residue of calcium pyrophosphate. When an aqueous solution of the salt (1 in 20), acidulated with hydrochloric acid, is added, drop by drop with agitation, to an excess of mercuric chloride T.S., a white precipitate of mercurous chloride is formed. Upon the further addition of the solution of Calcium Hypophosphite the precipitate becomes gray from reduction to metallic mercury. An aqueous solution of Calcium Hypophosphite (1 in 20) yields with ammonium oxalate T.S. a white precipitate, insoluble in acetic acid, but soluble in hydrochloric acid.

"Dissolve 1 Gm. of the salt in 20 cc. of distilled water; it requires not more than 1 cc. of tenth-normal potassium hydroxide to produce a pink color, phenolphthalein T.S. being used as indicator. When 1 Gm. of the salt is dissolved in 20 cc. of distilled water, not more than 0.005 Gm. of residue remains (*phosphate*). Mix 5 cc. of an aqueous solution of the salt (1 in 10) in a test tube with 0.5 cc. of diluted hydrochloric acid and heat on a water bath; no offensive odor develops within thirty minutes. An aqueous solution of the salt does not respond to the Test for heavy metals. Pour 5 cc. of an aqueous solution of the salt (1 in 25) into a beaker containing 3 cc. of nitric acid, diluted with about 10 cc. of distilled water, and evaporate it to dryness on a water bath. The residue meets the requirements of the Test for arsenic.

"**Assay.**—Dissolve about 0.75 Gm. of Calcium Hypophosphite, previously dried to constant weight over sulphuric acid and accurately weighed, in 10 cc. of distilled water, add 10 cc. of nitric acid and evaporate to dryness on a water bath. Add 5 cc. of nitric acid to the residue, again evaporate to dryness on a water bath and dissolve the residue in sufficient distilled water to measure 100 cc. Transfer 10 cc. of this solution to a 100 cc. graduated flask, add sodium hydroxide T.S. (free from chloride) until a slight, permanent precipitate is produced; then add 50 cc. of tenth-normal silver nitrate and agitate well. Then gradually add zinc oxide (free from chloride) in small portions until the liquid is neutral to litmus. Then add distilled water to make 100 cc., agitate the mixture thoroughly, filter through a dry filter, rejecting the first 20 cc. of filtrate, collect 50 cc. of the subsequent filtrate, add 2 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S. and titrate with tenth-normal potassium thiocyanate to the production of a red color. Each cc. of tenth-normal silver nitrate corresponds to 0.002836 Gm. of $Ca(PH_2O_2)_2$. Each Gm. of Calcium Hypophosphite, dried to constant weight, corresponds to not less than 345.5 cc., of tenth-normal silver nitrate.

"Preserve it in well-closed containers. Caution should be observed in dispensing Calcium Hypophosphite as an explosion is liable to occur if it is triturated or heated with nitrates, chlorates, or other oxidizing agents." *N. F.*

"A white crystalline salt, with a pearly lustre; taste bitter, nauseous. Soluble in 8 parts of *water;* insoluble in *alcohol* (90 per cent.). When strongly heated evolves spontaneously-inflammable hydrogen phosphide and hydrogen, and leaves a reddish residue. Yields the *reactions* characteristic of calcium. Its aqueous solution yields with *T. Sol. of mercuric chloride* a white precipitate turning grey. Yields no characteristic *reactions* for copper or iron, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million. Contains not less than 98 per cent. of pure calcium hypophosphite, $Ca\ (PH_2O_2)_2$, as determined by the following process: Dissolve 2.5 grammes in 40 millilitres of *water;* add 5 millilitres of *solution of lead acetate* and sufficient *water* to produce 50 millilitres; shake the mixture well and allow it to stand for one hour for the precipitate to subside. To 10 millilitres of the clear liquid add 50 millilitres of *N/1 solution of potassium bichromate* and 10 millilitres of *sulphuric acid;* heat on a water-bath for one hour, cool, and add sufficient *water* to produce 250 millilitres. To 25 millilitres of this solution add 2 grammes of *potassium iodide* and titrate the liberated iodine with *N/10 solution of sodium thiosulphate, mucilage of starch* being used as indicator; not more than 27 millilitres are required." *Br.*

The solubility of calcium hypophosphite is increased by the addition of hypophosphorous acid. For a method of purifying alkaline hypophosphites, see *J. P. A.,* 1879, 57; *N. R.,* 1879, 142.

As the soluble salts of mercury, copper, and silver are reduced by the hypophosphites, they are of course incompatible with it in prescriptions. With calcium hypophosphite all the soluble sulphates and carbonates produce precipitates. As the hypophosphites are insoluble in cod liver oil, they should be dissolved in syrup or water before being added to the emulsion of the oil. (See *Syrupus Hypophosphitum* and *Emulsum Olei Morrhuæ cum Hypophosphitibus.*) W. A. H. Naylor considers the presence of sulphites in commercial hypophosphites to be the source of the disagreeable odor of hydrogen sulphide sometimes found in the compound syrup of hypophosphites. (*P. J.,* 1895, 144.)

Uses.—Calcium hypophosphite was at one time largely used in *chronic phthisis,* in various *scrofulous affections,* in *neurasthenia,* and other conditions of impaired nutrition of the nerve centers. Although frequently prescribed for its hypophosphite ion, as pointed out elsewhere, the latter probably is therapeutically inert and it is very doubtful whether it has any therapeutic virtues other than that of the soluble calcium salts generally.

Dose, ten to thirty grains (0.65–2.0 Gm.), three times a day.

Off. Prep.—Syrupus Hypophosphitum, *N. F.;* Emulsum Olei Morrhuæ cum Hypophosphitibus, *N. F.;* Liquor Hypophosphitum Compositus, *N. F.;* Syrups Calcii et Sodii Hypophosphitum, *N. F.;* Syrupus Calcii Hypophosphitibus, *N. F.;* Syrupus Hypophosphitum Compositus, *N. F.*

CALCII IODOBEHENAS. U. S.

CALCIUM IODOBEHENATE Calc. Iodobehen.
[Calioben, Calcium Monoiodobehenate]

"Calcium Iodobehenate consists principally of calcium monoiodobehenate $[(C_{21}H_{42}ICOO)_2Ca]$ and contains, when dried to constant weight at 100° C., not less than 23.5 per cent of iodine [I]." *U. S.*

Erucic acid, one of the higher fatty acids found in the fixed oils of various seeds, notably of the mustards and grapes, is closely related to behenic acid which occurs in smaller quantities in mustard seeds, but is the chief fatty acid of oil of ben (see Part II). When erucic acid is treated with hydriodic acid it yields mono-iodobehenic acid. This latter combines with calcium to form a white odorless salt, analogous to the soaps, containing about 26 per cent. of iodine, which was introduced as a medicine under the trade name of *sajodin.*

Description and Physical Properties.—"A white or yellowish powder, unctuous to the touch. It is odorless or has a slightly fat-like odor. Calcium Iodobehenate is insoluble in water, very slightly soluble in alcohol and in ether, but freely soluble in warm chloroform.

"When strongly heated, Calcium Iodobehenate is decomposed, with the evolution of violet vapors of iodine and of white vapors having an odor of burning fat. Heat about 0.2 Gm. of Calcium Iodobehenate with 2 cc. of sulphuric acid on a water bath during five to ten minutes, cool, add 2 cc. of chloroform, and shake gently: the chloroform, upon separation, is colored violet.

"Add 10 cc. of diluted hydrochloric acid to 1 Gm. of Calcium Iodobehenate: no effervescence occurs (*carbonate*). Add 40 cc. of distilled water, and boil gently: a layer of fatty acid which is soluble in ether and chloroform separates on the surface. Make the aqueous layer slightly alkaline with ammonia T.S., and add an excess of ammonium oxalate T.S. (about 5 cc.): a white precipitate of calcium oxalate is produced. Allow to stand for four hours, filter, evaporate the filtrate to dryness, and ignite: the residue does not exceed 0.003 Gm. (*magnesium or alkali salts*). Dried to constant weight at 100° C., Calcium Iodobehenate loses not more than 2 per cent. (*water*). One Gm. of Calcium Iodobehenate dissolves in 10 cc. of warm chloroform with not more than an opalescence. Triturate 1 Gm. of Calcium Iodobehenate with 10 cc. of distilled water: the mixture is neutral to litmus paper. Add 15 cc. more of distilled water, mix well during five minutes, and filter. Evaporate 10 cc. of the filtrate to dryness on a water bath, and dry to constant weight at 120° C.: the weight of the residue does not exceed 0.001 Gm. (*soluble salts*). Other 5 cc. portions of the filtrate, tested for halogens and sulphate as described under turbidimetric tests, show no greater turbidity than 0.1 cc. of fiftieth-normal hydrochloric acid or sulphuric acid, page 462. Add 40 cc. of tenth-normal hydrochloric acid to about 1 Gm. of Calcium Iodobehenate, previously dried to constant weight at 100° C., and accurately weighed, and boil gently in a flask until thoroughly decomposed. Cool, and titrate the excess of acid with tenth-normal sodium hydroxide, using methyl orange T.S. as indicator: not less than 20 cc. and not more than 20.6 cc. of the tenth-normal acid is consumed.

"**Assay.**—Mix about 0.5 Gm. of Calcium Iodobehenate, previously dried to constant weight at 100° C. and accurately weighed, with about 3 Gm. of anhydrous potassium carbonate. Place the mixture in a platinum crucible, cover with about 1 Gm. more of anhydrous potassium carbonate, and heat moderately, gradually increasing the heat, but not exceeding a dull redness, until completely carbonized. Extract the residue with boiling distilled water, and wash it on the filter with boiling distilled water until the washings produce no opalescence with silver nitrate T.S. Heat the combined filtrate and washings, which measure about 150 cc., on a water bath, and add an aqueous solution of potassium permanganate (1 in 20) in small portions, until the hot liquid remains permanently pink. Add just enough alcohol to remove the pink tint, cool to room temperature, dilute to 200 cc., mix well, and filter through a dry filter, rejecting the first 50 cc. of filtrate. To 100 cc. of the subsequent clear filtrate add about 1 Gm. of potassium iodide (free from iodate) and an excess of diluted sulphuric acid, and titrate the liberated iodine with tenth-normal sodium thiosulphate, adding starch T.S. near the end of the titration. Each cc. of tenth-normal sodium thiosulphate used corresponds to 0.002115 Gm. of iodine.

"Preserve in well-closed containers, protected from light." *U. S.*

Uses.—The action of calioben probably depends entirely on the liberation of iodine and therefore resembles in its general action the alkaline iodides. Its solubility relations, however, give it certain advantages over the older iodides, for some purposes, although for others it is inferior. Being practically insoluble in the gastric juice, it is not irritating to the stomach. Although it has been abundantly demonstrated that it is absorbed from the intestinal canal, its absorption is much slower and apparently somewhat less complete than with the inorganic iodides; Broking (*Z. E. P. T.,* 1905, ii, 416) found that after the oral administration, iodine did not appear in the saliva nor urine for at least one hour and that 84 hours were required for the complete elimination of a single dose. He further showed that from 7 to 10 per cent. of the calioben could be recovered unchanged from the feces. It is not known in exactly what form the iodized fatty acid is absorbed; but evidently the iodine is not liberated from the compound in the intestinal tract. This is shown not only by the fact of its relatively slow excretion, but also by the distribution of the iodine in the body tissues. McLean (*A. In. M.,* November, 1912 and January, 1915) has shown that after the administration of potassium iodide, from 30 to 32 per cent. of the iodine is retained in the lipoid portion of the internal organs and from 67 to 70 per cent. as a water soluble compound, while with an iodized fatty acid, such as calioben, from 50 to 75 per cent. of the iodine is in the tissues in a lipoid soluble form. Because of its slower absorption, iodism is much less likely to occur after calioben than after the iodides, and Boulaire (*C. R. S. B.,* 1906, lvi. 303) has shown that the iodized fats are the least toxic of the iodine compounds. It would appear from the above that calioben is absorbed either from the alimentary tract or from the subcutaneous tissues in a materially unchanged form—perhaps in fatty solution—and deposited in the adipose and lipoid tissues where it is slowly decomposed, liberating ionic iodine. Whether or not the organic molecule—in which form the calioben circulates in the blood—has any effect upon the body functions is, as yet, not determined, but at present the compound is used purely for its iodine action. Where a long-continued mild effect of iodine is desired, calioben is superior to the inorganic iodides, not merely because of the comparative freedom from gastric disturbances and the lesser liability of iodism, but also because the amount of iodine in the blood is much more constant. On the other hand, where a rapid profound effect is required the inorganic salts are superior. Calioben has been especially recommended in the treatment of *chronic bronchitis, asthma, arterio-sclerosis, chronic arthritis* and other chronic conditions where the iodides are indicated.

Dose, from fifteen to forty-five grains (1–3 Gm.).

CALCII LACTAS. U. S., Br.

CALCIUM LACTATE Calc. Lact.

"Calcium Lactate contains not less than 70 per cent. and not more than 75 per cent. of $Ca(C_3H_5O_3)_2$, corresponding to not less than 98 per cent. of the hydrated salt [$Ca(C_3H_5O_3)_2.5H_2O$]." *U. S.* "Calcium Lactate may be obtained by neutralising dilute lactic acid with calcium carbonate and evaporating the resulting solution. It contains not less than 93 per cent. of pure calcium lactate, $Ca(C_3H_5O_3)_2,5H_2O$." *Br.*

Calcium Lacticum; Lactas Calcicus; Milchsaures Kalk, *G.*

This salt was introduced into the U. S. P. IX and the Br. Pharm., 1914. The experiments of C. A. Hill and T. T. Cocking (*Y. B. P.,* 1912, 481) demonstrate that calcium lactate is liable to vary in composition according to the method of preparation, varying particularly in the amount of water of crystallization. It may be neutral or contain either lactic acid, calcium hydroxide, or calcium carbonate. *Pure* calcium lactate is readily prepared by precipitation of ing the precipitate with acetone and then with its cold saturated solution with acetone, wash- ether.

Description and Physical Properties.—"White, granular masses or powder. It is odorless or has a slight odor. It is somewhat efflorescent and at 120° C. becomes anhydrous. One Gm. of Calcium Lactate is soluble in 20 cc. of water at 25° C. It is practically insoluble in alcohol. An aqueous solution of the salt (1 in 20) responds to the reactions for calcium, and for lactates.

"When dried to constant weight at 120° C., Calcium Lactate loses not less than 25 per cent. and not more than 30 per cent. of its weight. A solution of 1 Gm. of Calcium Lactate in 20 cc. of distilled water requires not more than 0.5 cc. of tenth-normal sodium hydroxide for neutralization, using phenolphthalein T.S. as indicator. An aqueous solution of the salt meets the requirements of the test for *heavy metals.* Add ammonium oxalate T.S. to 20 cc. of a hot aqueous solution of Calcium Lactate (1 in 20) until no further precipitate is produced, filter the mixture after three hours, and wash the precipitate with 50 cc. of distilled water: the combined filtrate and washings leave not more than 0.01 Gm. of residue on evaporation and subsequent ignition (*magnesium or alkalies*). Stir about 0.5 Gm. of the salt with 1 cc. of sulphuric acid: the mixture does not emit an odor of volatile fatty acids even on warming.

"**Assay.**—Dry about 2 Gm. of Calcium Lactate to constant weight at 120° C., weigh accurately in a crucible, incinerate, wash the incinerated residue into a flask with about 50 cc. of distilled water, add exactly 50 cc. of half-normal hydrochloric acid, and titrate the excess of acid with half-normal sodium hydroxide, using methyl orange T.S. as indicator. Each cc. of half-normal hydrochloric acid corresponds to 0.05455 Gm. of $Ca(C_3H_5O_3)_2$.

"Preserve in well-closed containers." *U. S.*

"A white powder; almost tasteless. Slowly soluble in 18.5 parts of *water,* forming a clear, colorless solution. Yields the *reactions* characteristic of calcium. The aqueous solution, acidified with *sulphuric acid* and warmed with *potassium permanganate,* develops the odor of aldehyde. A solution of 5 grammes in hot *water* does not become pink on the addition of a few drops of *solution of phenolphthalein,* and requires not more than 0.5 millilitre of *N/1 solution of sodium hydroxide* to produce a pink coloration (limit of acidity). One gramme, treated with *sulphuric* acid and incinerated in a crucible, cooled, again treated with *sulphuric acid* and incinerated, leaves a white residue weighing not less than 0.410 and not more than 0.450 gramme. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Uses.—Calcium lactate affords an excellent means of obtaining the therapeutic effects of lime. It is asserted that it not only is less likely to disturb the stomach than the chloride, but is more readily absorbed. It is used in the treatment of *hemorrhage, rickets,* and other diseases in which the lime salts are indicated. (See *Calcium*). Luckhardt and Goldberg (*J. A. M. A.,* 1923 lxxx, 79) obtained results in *tetany* from the lactate which they could not from other calcium salts.

The *dose* is fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Syrupus Calcii Lactophosphatis, *Br.*

CALCII LACTOPHOSPHAS. N. F.

CALCIUM LACTOPHOSPHATE Calc. Lactophos.

"A mixture in variable proportions of calcium lactate, calcium acid lactate, and calcium acid phosphate, corresponding to not less than 1.5 per cent. and not more than 2 per cent. of phosphate oxide (P_2O_5)."

Calcium Lactophosphoricum; Lactophosphate de Calcium, *Fr. Cod.*

Description and Physical Properties.—"Calcium Lactophosphate occurs in white granules or as a white powder, without odor. It is soluble in water, almost insoluble in alcohol. Its aqueous solution (1 in 20) is acid to litmus.

"The addition of ammonium oxalate T.S. to an aqueous solution of Calcium Lactophosphate produces a white precipitate insoluble in acetic acid but soluble in hydrochloric acid. Add 10 cc. of diluted sulphuric acid and 5 cc. of potassium permanganate T.S. to 5 cc. of an aqueous solution of Calcium Lactophosphate (1 in 20) and gently warm the mixture; the odor of acetaldehyde is evolved. Add silver nitrate T.S. or ammonium molybdate T.S. to separate portions of an aqueous solution of Calcium Lactophosphate (1 in 20); a yellow precipitate is produced.

"Mix 0.5 Gm. of Calcium Lactophosphate with 5 cc. of sulphuric acid; not more than a slight coloration results within one minute (*readily carbonizable impurities*). Ten cc. of an aqueous solution of Calcium Lactophosphate (1 in 100) mixed with 1 cc. of diluted hydrochloric acid, does not at once become turbid on the addition of a few drops of barium chloride T.S. (*sulphate*). Ten cc., of an aqueous solution of Calcium Lactophosphate (1 in 100) when mixed with a few drops of nitric acid, yields not more than an opalescence on the addition of a few drops of silver nitrate T.S. (*chloride*). An aqueous solution of Calcium Lactophosphate does not respond to the Test for heavy metals. Mix 0.2 Gm. of Calcium Lactophosphate with 1 Gm. of potassium nitrate, ignite the mixture cautiously, in small portions at a time, until the carbonaceous matter is all or nearly all burned off, then add to the residue 20 cc. of diluted sulphuric acid and evaporate the mixture until fumes of sulphuric anhydride are evolved. The residue meets the requirements of the Test for arsenic. Dissolve 1 Gm. of Calcium Lactophosphate and 2 Gm. of ammonium chloride in 75 cc. of distilled water, heat the solution to boiling and add an excess of ammonium oxalate T.S. (about 20 cc.). Allow the precipitate to subside completely, then filter and supersaturate the filtrate with ammonia water; not more than a slight turbidity is produced (*magnesium*).

"**Assay.**—Dissolve about 1 Gm. of Calcium Lactophosphate accurately weighed, in a mixture of 15 cc. of distilled water and 10 cc. of nitric acid contained in a 200 cc. beaker, and then add ammonia T.S. to a point just short of neutralization. Dilute the solution to 100 cc., heat to 60° C., add 25 cc. of ammonium molybdate T.S. and agitate well. Allow the mixture to remain at 60° for fifteen minutes, then filter through paper and wash with distilled water until the washings are neutral. Transfer the precipitate and filter back to the beaker, dissolve the precipitate in 30 cc. of half-normal sodium hydroxide, and titrate the excess of alkali with half-normal hydrochloric acid, using phenolphthalein T.S. as indicator. Each cc. of half-normal alkali corresponds to 0.001544 Gm. of P_2O_5." *N. F.*

Uses.—Calcium lactophosphate probably represents the therapeutic virtues of calcium phosphate, its chief advantage residing in its solubility which makes it easier to administer, especially to children. It is largely employed in the treatment of *rickets* and other bone diseases, especially in the form of the syrup.

Dose, five to ten grains (0.3–0.6 Gm.).

Off. Prep.—Elixir Calcii Lactophosphatis, *N. F.;* Syrupus Calcii Lactophosphatis *N. F.;* Syrupus Calcii Lactophosphatis et Ferri, *N. F.*

CALCII PHOSPHAS PRÆCIPITATUS. N. F. (Br.)

PRECIPITATED CALCIUM PHOSPHATE Calc. Phos. Præ.

"Calcium Phosphate ($Ca_3(PO_4)_2 = 310.29$) losing, when dried at 200° C. not more than 4 per cent. of moisture." *N. F.*

"Calcium Phosphate may be obtained by the interaction of calcium chloride with sodium phosphate and excess of ammonia at a boiling temperature." *Br.*

Calcii Phosphas, *Br.;* Calcium Phosphate; Tricalcium Phosphate, Tribasic Calcium Phosphate, Calcaria Phosphorica; Phosphas Calcicus Præcipitatus; Phosphas Tricalcicus; Phosphate Neutre de Calcium, *Fr. Cod.*; Precipitated Phosphate of Lime; Phosphate of Calcium; Phosphate Tricalcique, Phosphate de Chaux hydraté, *Fr.;* Calcium Phosphoricum, *P. G.*; Phosphorsaure Kalkerde, Calciumphosphat, *G.;* Fosfato calcico, *Sp.*

Calcium phosphate is found abundantly in nature; the so-called phosphate rock which is found in the southern parts of the United States contains sometimes as much as 90 per cent. of calcium phosphate. It is found also in other minerals such as *apatite* and *phosphorite.* The U. S. V and the Br. 1885 gave a method for preparing calcium phosphate from bone ash. In this process the carefully calcined bones were treated with hydrochloric acid, which dissolved the calcium phosphate of the bones, and the basic phosphate was precipitated from this solution by the addition of ammonia, in a state of minute division. It was then washed to free it from adhering ammonium chloride. The salt thus obtained is, for the sake of distinction, called *bone calcium phosphate.*

The commercial supply of calcium phosphate today is made by a mutual interaction between calcium chloride, sodium phosphate, and ammonium hydroxide at a boiling temperature.

Description and Physical Properties.—" Precipitated Calcium Phosphate occurs as a white, amorphous or microcrystalline, bulky powder, odorless and tasteless; permanent in the air. At an intense white heat the salt fuses without decomposition. Almost insoluble in cold water; partly decomposed by boiling water; almost insoluble in acetic acid, except when freshly precipitated; easily dissolved by hydrochloric or nitric acid; insoluble in alcohol.

" When moistened with silver nitrate T.S., either before or after ignition, the salt acquires a yellow color (distinction from *acid calcium phosphate,* which, after ignition, when moistened with silver nitrate T.S. remains white). For applying tests of identity and of purity, prepare a solution by shaking 2 Gm. of Precipitated Calcium Phosphate with 20 cc. of distilled water, adding nitric acid, drop by drop, until solution is effected, and then sufficient distilled water to make the liquid measure 40 cc. While making this solution, no effervescence occurs on adding the acid (*carbonate*). To a portion of this solution add a slight excess of ammonia water, then an excess of silver nitrate T.S. and afterwards acetic acid, drop by drop, until the excess of ammonia is neutralized; the color of the precipitate changes from white to yellow. Ammonium molybdate T.S. precipitates from the solution yellow ammonium phosphomolybdate; the reaction is accelerated by a gentle heat, not exceeding 65° C.

" Add to five cc. of the solution, acidulated with nitric acid, 0.5 cc. of silver nitrate T.S.; not more than a slight turbidity is produced (*chloride*). Add to five cc. of the solution, strongly acidulated with nitric acid, 1 cc. of potassium sulphate T.S.; no turbidity appears within fifteen minutes (*barium*). An aqueous solution of Precipitated Calcium Phosphate (1 in 50), obtained by shaking the salt with distilled water, adding hydrochloric acid, drop by drop, and heating until solution is effected, does not respond to the test for heavy metals. Five cc. of a solution of Precipitated Calcium Phosphate in diluted nitric acid (1 in 25), heated with 1 cc. of sulphuric acid until fumes of sulphur trioxide appear, meets the requirements of the Test for arsenic." *N. F.*

"A light, white, amorphous powder, permanent in the air. No odor or taste. Almost insoluble in *water.* Yields the *reactions* characteristic of calcium and of phosphates. Dissolves without residue and without effervescence (absence of carbonate) in *diluted hydrochloric acid* or *diluted nitric acid.* Yields no characteristic *reactions* for barium, ammonium, or silica, and no more than the slightest *reactions* for aluminium or magnesium. *Arsenic limit* 5 parts per million. Its solution in slight excess of *diluted nitric acid* is not rendered more than slightly opalescent by *solution of silver nitrate* (limit of chlorides), or by *solution of barium chloride* (limit of sulphates). Its solution in slight excess of *diluted hydrochloric acid* is not affected by *hydrogen sulphide* (absence of copper and lead), and, on the subsequent addition of excess of *solution of ammonia,* the precipitate produced is quite white (limit of iron)." *Br.*

Joly and Sorel record (*C. R. A. S.,* 1894, 738) the precipitation of tricalcium phosphate by adding crystals of hydrated bicalcium phosphate to boiling water; the acid liquid remaining contains monocalcium phosphate.

Uses.—As the result of an immense amount of investigation it may be regarded as established that the body can synthesize its complex phosphorus-containing tissues from the inorganic phosphates although there is some evidence that the organic forms are used more economically. Evidence is also very strong that for the proper utilization of food phosphorus there is necessary an abundance of calcium in the diet and *vice versa* that phosphoric acid is requisite for normal calcium metabolism. From these facts the conclusion is obvious that calcium phosphate is to be regarded as a useful food-stuff when there is dietetic deficiency in the proportion of these elements. On the basis of these experiments some have jumped to the conclusion that an excess of calcium phosphate in the diet would be beneficial in such diseases as *rickets* where there is a disturbance of bony metabolism. The present evidence indicates, however, that these conditions are due to an inability to properly utilize the requisite compounds in the diet rather than to deficiency of supply. There is at present no convincing evidence that an excess of calcium phosphate is of any great advantage in the treatment of such disorders. If, however, the other factors essential for the utilization of calcium and phosphorus are provided, it seems probable that an excess of these elments in the diet might hasten their deposition in the body. Calcium phosphate should therefore be regarded as a foodstuff, useful in maintaining the health of the tissues or in aiding in the upbuilding of bony and perhaps nervous tissue but, by itself, having little curavite value in disturbances of metabolism. In other words, its rôle is that of a food rather than a medicine. Despite the insolubility of the basic calcium phosphate it is capable of being absorbed from the intestines but, theoretically at least, the more soluble acid phosphate should be more easily absorbed and many authorities prefer, therefore, such preparations as the syrup of calcium lactophosphate in which the lime salt is held in solution by lactic acid.

Dose, ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Liquor Phosphatum Acidus, *N. F.;* Liquor Phosphatum Compositus, *N. F.;* Pulvis Antimonialis, *N. F.;* Syrupus Phosphatum Compositus, *N. F.;* Syrupus Phosphatum cum Quinina et Strychnina, *N. F.*

CALCIUM

CALCIUM

This is the metal characteristic of lime, and, consequently, of all calcareous substances. It was obtained by Matthiessen, in 1855, in masses of the size of a pea, by the electrolysis of calcium chloride with a Bunsen battery. It is, when pure, a yellowish-white crystalline metal, ductile, malleable, with a specific gravity of 1.58 and melting at 760° C. It oxidizes slowly in dry air, more rapidly in moist air, and must therefore be kept under petroleum.

Calcium is a very abundant element in nature, existing in the mineral kingdom chiefly as a carbonate, in the form of limestone, marble, chalk, and calcareous spar; as a sulphate in gypsum and selenite; and as a phosphate and carbonate in the bones and shells of animals.

Therapeutic Action.—Calcium is necessary in the body not only for the stiffening of the bones, but for the correct functioning of nearly all tissues. It has been shown by many investigators that removal of lime salts from muscle tissue, either by washing with sodium chloride solution or by the use of precipitants of calcium, causes spontaneous contractures and eventually paralysis of voluntary muscle fiber, weakens the contractile power of the heart, increases the irritability of the nervous centers both of the brain and spinal cord. See Maxwell (*B. K. Ch.,* 1906, ii, 203). The converse of these reactions are also true; that is, excess of calcium salts lessens irritability of the nerve centers and increases the vigor of the heart beats. The investigations of Roger and Schulmann (*Arch. de Med. Exper. et d'Anat. Path.,* 1916, xxvii, 252) are indicative that the depression of nerve centers in the medulla by large quantities of calcium injected directly into the circulation may cause death through failure of the respiration.

The presence of calcium is essential for the coagulation of the blood; diminution in the proportion of lime salts delays, and the entire absence prevents, clotting. There is also considerable evidence that an increase in the amount of lime salts, at least up to a certain point, will accelerate coagulation.

As a therapeutic agent the lime salts have been used, first, in conditions which are due to deficiency of calcium in the various tissues, and, secondly with the idea that an excess of lime may modify the body functions in a desired direction. Under the first head are various diseases of the bones such as *rickets, osteomalacia,* and *ununited fractures.* There is strong reason to believe that these diseases are due to an inability to utilize calcium rather than to deficiency in the supply. We, therefore, should not expect any great benefit from the use of lime salts in conditions unless the underlying dyscrasia can be corrected; a conclusion that is confirmed by clinical experience. There do occasionally occur cases of bony changes due to deficiencies in the calcium intake; the most common and typical example of this is the softening of the teeth in pregnant women due to the excessive demands for lime salts. This type of case is very greatly benefited by the administration of calcium. It may be remarked in this connection that numerous investigators (see Blaterwick and Lang, *J. Bi. Chem.,* 1922, lii, and Sherman *J. Bi. Chem.,* 1922, liii, 375) have shown that the bodily needs for this element can be derived from an exclusively inorganic source.

In 1909 MacCallum and Voegtlin (*J. Ex. M.,* xi, 118) showed that the convulsive disorder which follows removal of parathyroid bodies is associated with a great reduction of the amount of calcium, both in the blood and in the brain, and that the convulsions could be temporarily controlled by the administration of calcium chloride. This has led to the theory that the disease *tetany* is due primarily to a deficiency of lime in the nerve centers and consequently to a use of salts of this element in the treatment of these convulsions.

As nerve sedatives, the salts of lime have been used in various convulsive diseases as *tetany* and *epilepsy* (Ohlmacher,, *J. A. M. A.,* 1910, liii, 527). Because of the relationship between calcium and phosphorous metabolism (see *Calcium Phosphate*), the lime salts have also been used for their general tonic effects on the nervous system. The administration of large doses of the metal prevents the inflammatory reaction of the conjunctiva to irritants such as abrin or oil of mustard Mayer, (*M. M. W.,* 1910) attributed this fact to the lessened permeability of the walls of the capillary blood vessels, but Nagai and Ito concluded that calcium chloride stimulates phagocytosis. As antiphlogistics the salts of lime have been used in *serum sickness,* inflammation of the serous membranes, as *pleur-*

isy or *peritonitis* (Blum, Press. Med., xxx, 221) in *asthma* and *hay fever.* Whether the value of calcium chloride in *tuberculous enteritis* is to be attributed to its antiphlogistic action or to the effect on the intestinal muscles is as yet uncertain. It may be noted in this connection that although it has been used to a considerable extent in pulmonary *tuberculosis* its value is not established.

Concerning the clinical value of lime salts in *hemorrhage* there has been so much difference of opinion that it is impossible to draw positive conclusions. (For literature see Cohen, *A. I. M.*, 1911, xxiv, 834).

It should be noted in connection with the therapeutic use of calcium that many of the results reported have been from intravenous or hypodermic injections; although the view at one time advanced that inorganic salts of lime would be precipitated in the alimentary canal as insoluble carbonates, and hence not be absorbed, has been shown to be incorrect, the mere fact that the salts are absorbed after oral administration does not establish their therapeutic usefulness. The observations of Dennis and Minot (*J. Bi. Chem.*, 1920, xli, 357), of Howland and Kramer (*Amer. J. Dis. of Children,* 1921, xxii, 105) and others indicate that it is impossible to cause any notable increase in the proportion of lime in the blood by giving the drug by mouth, probably because elimination is more rapid than alimentary absorption. On the other hand, there is considerable evidence that when the blood calcium is subnormal sometimes the administration of lime salts by the mouth will cause an increase.

CALENDULA. N. F.

CALENDULA Calend. [Marigold]

Marigold, Mary-bud, Holligold; Fleurs de Tous les Mois, Souci, *Fr.;* Ringelblume, Todtenblume. Goldblumen, *G.;* Calendula, *Sp.*

"Calendula consists of the dried ligulate florets of *Calendula officinalis* Linné (Fam. *Compositæ*). Calendula contains not more than 2 per cent. of foreign organic matter." *N. F.*

An annual, ornamental herb with spatulate or oblanceolate leaves having toothed margins and terminal flower-heads of yellow to orange-colored ray- and disk-florets. *French* or *African Marigold,* so called, is very frequently substituted for the official drug. It is the *Tagetes patula* L., and *T. erecta* Linn., both of Mexico. The flowers are readily distinguished by the scales of the involucre being united to form a tube, and by the slender, flattish achenes being crowned with a few chaffy or awned scales. The broadly strap-shaped ray-florets are toothed, and of a light or deep orange color sometimes striped with red. Latour and Magnier de la Source isolated from African marigold a yellow crystalline substance, *quercetagetin,* which Perkin examined and gave the composition $C_{15}H_{10}O_8$ (*P. J.*, 1902, 294.) The odor is much stronger in the fresh than in the dry flowers, and on exposure to light, the orange-red or yellow color fades.

Description and Physical Properties.—"*Unground Calendula.*—Florets from 15 to 25 mm. long, yellow- or orange-colored, 1- to 3-toothed, 4- to 5-veined, margin nearly entire, the short hairy tube occasionally enclosing the remnant of a filiform style and bifid stigma. Odor slight, somewhat heavy; taste slightly bitter, faintly saline.

"*Powdered Calendula.*—Light yellow to orange-yellow; a few characteristic, non-glandular hairs, consisting of a double row of thin-walled, more or less collapsed cells with a 1- or 2-celled apex, and up to 0.950 mm. long; elongated epidermal cells with thin, somewhat wavy walls, a striated surface, and containing irregular chromoplasts and oil-like globules, the latter coalescing when mounted in chloral hydrate T.S.; pollen grains, more or less spherical, with numerous spinose projections, three-pored, and up to 0.045 mm. in diameter; tracheæ about 0.009 mm. in width with spiral or annular markings, prisms or rosettes of calcium oxalate from 0.002 to 0.006 mm. in diameter." *N. F.*

It contains traces of a volatile oil, a bitter principle, and an amorphous tasteless substance called *calendulin* (discovered by Geiger most abundantly in the flowers) which swells up in water and is considered by Berzelius as analogous to bassorin, though soluble in alcohol.

Uses.—In the days of therapeutic darkness *calendula* was thought to be medicinally active, but it has no virtues beyond that of a feeble aromatic. Both the leaves and the flowers were used; but the latter were preferred, and were usually administered in the recent state in the form of tea. It has also been used as a local application in various inflamed conditions of the skin or mucous membranes and even as a stimulant to *wounds* and *ulcers.*

Dose, from fifteen to sixty grains (0.9–3.9 Gm.).

Off. Prep.—Fluidextractum Calendulæ, *N. F.;* Tinctura Calendulæ, *N. F.*

CALUMBA. U. S. (Br.)

CALUMBA Calumb. [Columbo]

"Calumba is the dried root of *Jateorhiza palmata* (Lamarck) Miers (Fam. *Menispermaceæ*). Columba yields not more than 2.5 per cent. of acid-insoluble ash." *U. S.* "Calumba Root is the root of Jateorhiza Columba, *Miers,* cut in transverse slices and dried." *Br.*

Calumbæ Radix, *Br.;* Calumba Root; Radix Columbo; Colomba, *U. S.* 1850; Racine de Colombo, *Fr.;* Colombo, *Fr. Cod.;* Radix Colombo, *P. G.;* Kolombowurzel, *G.;* Colombo, *It.;* Colombo, Raiz de colombo, *Sp.;* Kalumbo, *Port.;* Calumb, *Mozambique.*

Calumba is official in nearly all pharmacopœias. The difference in botanical origin as given in the definition in the U. S. and British Pharmacopœias is merely one of synonymy, as *J. palmata* (Lamarck) Miers is merely another name for *J. Columba* Miers. There is considerable confusion in the spelling of both the generic and specific names: *Jateorhiza* is sometimes spelled *Jateorrhiza,* and the specific name is usually given as *Calumba* and not *Columba.*

Jateorhiza palmata is a diœcious climbing plant, with a short fibrous rhizome bearing numerous thick fusiform roots. The stems are twining, cylindrical, hairy and simple in the staminate plant, being branched in the pistillate plant. The leaves, which stand on rounded, glandular, hairy footstalks, are alternate, distant, cordate, with three, five, or seven entire, acuminate, wavy, somewhat hairy lobes, and as many nerves, each running into one of the lobes. The flowers are small and inconspicuous, and arranged in solitary axillary racemes, which in the staminate plant are compound, in the pistillate simple, and in both plants are shorter than the leaves.

The Calumba plant is indigenous to Mozambique, on the southeastern coast of Africa, where it grows wild in great abundance in the thick forests extending from the sea many miles into the interior. It is more particularly abundant in the region between the Zambezi and Rovuma. (*Ap. Ztg.,* 1912, p. 147.) The root is dug up in March, when dry weather prevails. From the base of the rhizome numerous fusiform offsets proceed, less fibrous and woody than the parent stock. These offsets are separated and cut into transverse slices, which are dried in the shade. The old rhizome is rejected.

The plant is said to be cultivated both in Africa and the East Indies for the sake of its root, which under the name of *Calumb* is used in dyeing.

Calumba is sent from the Portuguese dominions in southeastern Africa into India, whence it goes into general commerce. At one time, when thought to be a product of Ceylon, it was supposed to have derived its name from Columbo, a city of that island, but a much more probable derivation is from the African name of the root above given. (See Lloyd's history of columbo root, *West. Drug.,* 1898, 8.)

Description and Physical Properties.—"*Unground Calumba.*—Circular or oval discs, attaining a diameter of 10 cm. and seldom exceeding 2 cm. in thickness, or longitudinal or oblique slices, attaining a length of 30 cm.; the edge brown and roughly wrinkled, the cut surfaces yellowish-brown or grayish-yellow and indistinctly radiate in the region of the dark cambium; often depressed in the central portion; fracture short and mealy; odor slight; taste slightly aromatic and very bitter.

"*Structure.*—A thick corky layer of small cells with yellowish walls; a starch-bearing parenchyma layer with a few characteristic stone cells scattered singly or in small groups; numerous, narrow wood bundles distinct and separated by broad, starch-bearing medullary rays; phloem portion consisting of sieve tissue with cells mostly collapsed; xylem portion of tracheæ and wood-fibers frequently in small groups separated by starch-bearing parenchyma, especially in the inner portion.

"*Powdered Calumba.*—Greenish-brown to grayish-yellow; starch grains numerous, mostly single, occasionally 2- to 3-compound, the individual grains from 0.003 to 0.085 mm. in length, ovoid, ellipsoidal, frequently very irregular, slightly lamellated, with an excentral linear x-shaped or branching cleft; stone cells few, with irregularly thickened, strongly lignified, coarsely porous walls and often containing one or more prisms of calcium oxalate up to 0.030 mm. in length, or numerous sphenoidal microcrystals; fragments with tracheæ few, the latter with reticulate thickenings or bordered pores, and associated with wood-fibers having long, oblique, slit-like pores and few lignified wood parenchyma having large simple pores." *U. S.*

The drug is described in the British Pharmacopœia as follows: "Cork thin, brownish and wrinkled; cortex thick, yellowish and separated by a dark line from the greyish wood, in which the parenchymatous tissue is largely developed and the vessels arranged in narrow elongated groups. In the cortex, in transverse section, numerous isolated sclerenchymatous cells with yellow, irregularly thickened walls enclosing small prismatic crystals of calcium oxalate; in the wood, vessels with yellow reticulated walls. The parenchymatous cells of both wood and cortex filled with starch grains, which are irregularly ovoid in outline, from 20 to 70 microns in length and exhibit a conspicuous, excentric, radiate or cleft hilum." *Br.*

According to the U. S. P. microscopical description, it is inferred that the calcium oxalate crystals occur only in the stone cells. Tunmann (*Ph. Zentralh.,* 1906, p. 1069) asserts that the crystals are distributed throughout the woody portion of the root as well as in the bark, and outlines a method for readily demonstrating their presence.

Along with the disks are sometimes a few cylindrical pieces an inch or two in length. The cortical portion is thick, of a bright yellow, slightly greenish color internally, but covered with a brownish, wrinkled epidermis. The interior or medullary portion, which is readily distinguishable from the cortical, is light, spongy, yellowish, usually more or less shrunk, so that the pieces are thinnest in the center; and is often marked with concentric circles and radiating lines. Those pieces are to be preferred which have the brightest color, are most compact and uniform, and least worm eaten.

The odor of calumba is slightly aromatic. The taste is very bitter, that of the cortical much more so than that of the central portion, which is somewhat mucilaginous. The root is easily pulverized. The powder is greenish, becoming browner with age, and deepening when moistened. As it attracts moisture from the air, and is apt to undergo decomposition, it should be prepared in small quantities.

The crude drug, as well as the powder, is liable to be attacked by insects if kept for any length of time. This can be guarded against by thoroughly drying the drug, keeping it in a dry place, and adding either carbon tetrachloride or chloroform.

Adulterations.—Formerly the high price of calumba led to its frequent adulteration, especially, it is said, with the roots of the *white bryony,* and of *Frasera carolinensis* or *American calumba,* and with the stem of *Coscinium fenestratum,* the *columbo wood* or *false columbo* of Ceylon. According to Stolze of Halle, the American calumba can be readily detected by the fact that while the tincture of true calumba is not affected by ferric sulphate or sesquichloride, and yields with tincture of galls a dirty precipitate, the tincture of Frasera becomes dark green with the former and is not affected by the latter reagent. *Coscinium fenestratum,* a bitter tonic used in Ceylon, is at once to be distinguished by its being a stem, not a root. At present, owing to its great cheapness, calumba root seems to be very rarely adulterated (see *P. J.,* 1901, 502, and Dec., 1904), although a specimen of calumba yielded, on incineration, 16 per cent. of ash. Holmes believes that the fictitious drug is the overground portion of *Jateorhiza palmata,* while Wardleworth believed that the drug is a product of *Tinospora Bakis* (A. Rich.) Miers which is used in Senegal as an antiperiodic.

Constituents.—Calumba differs from most vegetable drugs in not containing tannin and can therefore be combined with iron salts without precipitation. It contains, besides about one-third of its weight of starch, a small proportion of volatile oil, salts of calcium and potassium, ferric oxide, and silica. Wittstock, of Berlin, afterwards isolated a neutral principle, which he called *columbin.* This crystallizes in beautiful transparent quadrilateral prisms of the formula $C_{28}H_{30}O_9$, is without odor, and is extremely bitter. It is but very slightly soluble in water, more soluble in alcohol, ether, or chloroform, and imparts to these fluids a strongly bitter taste. It is more soluble in boiling alcohol, which deposits it upon cooling. The best solvent is diluted acetic acid. It is taken up by alkaline solutions, from which it is precipitated by acids. It melts at 182° C. It is converted by boiling in alkaline solution into *columbic acid.* It is obtained by exhausting calumba by means of alcohol of the sp. gr. 0.835, distilling off three-quarters of the alcohol, allowing the residue to stand for some days until crystals are deposited, and lastly treating these crystals with alcohol and animal charcoal. The mother waters still contain a considerable quantity of columbin, which may be separated by evaporating with coarsely powdered glass to dryness, exhausting the residue with ether, distilling off the ether, treating the residue with boiling acetic acid, and evaporating the solution to crystallization.

Alessandri (*P. J.,* 1882) found in this root an alkaloid which he called columbine, which probably, however, was a mixture of principles. According to the researches of Gunzel (*A. Pharm.,* 1906, ccxliv, p. 257) and of Feist and Sandstede (*A. Pharm.,* 1918, cclvi, p. 1) there are present in calumba three alkaloids: *calumbamine, jateorhizine* (*jatrorrhizine*) and *palmatine.* Although they were unable to isolate these bases in a free state they formed the following iodides: calumbamine $C_{21}H_{22}O_5NI$; jatrorrhizine $C_{20}H_{20}O_5NI$; palmatine $C_{21}H_{22}O_4NI$.

The presence of berberine was asserted by Alessandri and also Bocchiola (*Y. B. P.,* 1891, 162), but has been denied by more recent investigators. The proportion of alkaloid ranges between 2.5 and 3 per cent. Haensel (*P. J.,* 1904, 216) obtained from calumba a volatile oil which exists in very small quantities (0.00568 per cent.). It has a peculiar odor and bitter taste.

There can be little doubt that both columbin and the alkaloids contribute to the remedial effects of calumba. The virtues of the root are extracted by boiling water and by alcohol. Precipitates are produced with the infusion and tincture by infusion of galls, and by solutions of lead acetate and subacetate, but the bitterness is not affected.

Uses.—Biberfeld (*Z. E. P. T.,* 1909, vii) has shown that all the alkaloids of calumba root are depressant to the central nervous system and especially to the respiratory center; palmatine indeed exceeds morphine in its respiratory toxicity; columbamine and jateorhizine increase intestinal tonus. Despite these findings, however, it is improbable that calumba has any medical virtue aside from that of a mild bitter, free from astringency. It is useful in functional atonic conditions of the digestive organs, especially with other tonics, aromatics, or cathartics. A favorite remedy of the late George B. Wood for the cure of a disposition to the accumulation of *flatus* in the bowel was an infusion made with half an ounce of calumba, half an ounce of ginger, a drachm of senna, and a pint of boiling water, and given in doses of a wineglassful three times a day. By the natives of Mozambique it is used in *dysentery* and various other diseases.

Dose, of the powder, from ten to thirty grains (0.65–2.0 Gm.), which may be repeated three or four times a day.

Off. Prep.—Fluidextractum Calumbæ, *N. F.;* Infusum Calumbæ, *Br.;* Tinctura Calumbæ, *U. S., Br.*

CALX. U. S., Br.

LIME [Calcium Oxide, Quicklime]

"Lime contains, when freshly ignited to constant weight with a blast, not less than 95 per cent. of CaO. It loses not more than 10 per cent. of its weight on ignition. Preserve it in air-tight containers in a dry place." *U. S.*

"Lime, CaO, is calcium oxide obtained by calcining marble." *Br.*

Calcii Oxidum, Calcium Oxydatum; Calcaria Usta, Calx Viva, Calx Usta, Oxydum Calcicum; Burned Lime; Oxyde de Calcium, *Fr. Cod.;* Chaux, Chaux vive, *Fr.;* Calcaria Usta, *P. G.;* Aetzkalk, Kalk, Gebrannter kalk, *G.;* Ossido di calcio, Calce, *It.;* Cal viva, *Sp.*

Preparation.—Lime is prepared by calcining, by a strong heat, some form of the native carbonate. The carbon dioxide is thus expelled, and the lime remains. When the lime is intended to be of a high degree of purity, it may be obtained from Iceland spar. For the purpose of the arts it is procured from common limestone, by calcining it in kilns of peculiar construction. When obtained in this way it is generally impure, being of a grayish color, and containing alumina, silica, ferric oxide, and occasionally a little magnesia and manganese oxide.

The official lime of the United States and British Pharmacopœias is usually the lime of commerce. It may be obtained in a purer form by exposing pure white marble, broken into small fragments, in a covered crucible, to a full red heat for three hours, or until the residue, when slaked and suspended in water, no longer effervesces on the addition of hydrochloric acid.

Description and Physical Properties.—"Hard, white or grayish-white masses or granules, or a white powder. It is odorless. One Gm. of Lime is soluble in 840 cc. of water at 25° C., and in 1740 cc. of boiling water. It is soluble in glycerin and in syrup, but is insoluble in alcohol.

"When moistened with water, Lime becomes heated, and is gradually converted into a white powder (calcium hydroxide or slaked lime). When this is mixed with about 3 or 4 times its weight of water, it forms a smooth magma (milk of lime). Water, when agitated with Lime, becomes alkaline to litmus paper. Slake 1 Gm. of Lime with 20 cc. of distilled water and add acetic acid until the lime is dissolved: the resulting solution responds to the reactions for calcium.

"Slake 1 Gm. of Lime, thoroughly mix it with 50 cc. of water, and decant the greater portion of the milky liquid: the addition of an excess of diluted hydrochloric acid to the residue does not cause more than a slight effervescence (*carbonate*). Slake 5 Gm. of Lime, then mix it with 100 cc. of distilled water, followed by hydrochloric acid, drop by drop, with agitation until solution takes place: the resulting solution after boiling and cooling should be acid and should not deposit more than 0.05 Gm. of insoluble matter. Ignite a portion of Lime to constant weight in a tared platinum crucible, with a blast lamp: the loss in weight does not exceed 10 per cent. (*volatile substances*). Dissolve 0.5 Gm. of Lime in 10 cc. of diluted hydrochloric acid, neutralize with ammonia T.S., completely precipitate the calcium by adding ammonium oxalate T.S., and then filter: the filtrate on evaporation and ignition leaves not more than 0.004 Gm. of fixed residue (*magnesium, other alkali earths, or alkalies*).

"**Assay.**—Ignite about 1 Gm. of Lime to constant weight over a blast lamp, weigh accurately, dissolve in 20 cc. of diluted hydrochloric acid, cool the solution, dilute with distilled water to 100 cc., and mix well. Transfer 20 cc. of this solution to a 200 cc. volumetric flask, and proceed with the assay as directed under *Calcii Carbonas Præcipitatus.* Each cc. of tenth-normal oxalic acid corresponds to 0.002804 Gm. of CaO.

"Preserve in air-tight containers, in a dry place." *U. S.*

"Compact whitish masses, which readily absorb water. When rather less than their weight of water is added, the masses swell and fall to powder with the development of much heat. The powder obtained by this process of slaking, when shaken with *water,* gives, after filtration, a clear alkaline solution which yields the *reactions* characteristic of calcium. Yields not more than the slightest characteristic *reactions* for iron, silica, carbonates, chlorides, or sulphates. *Arsenic limit* 5 parts per million." *Br.*

Lime has a sp. gr. of 3.15 to 3.40. Its solubility in water is greatly increased by the addition of sugar or glycerin. (See *Liquor Calcis Saccharatus.*) It is distinguished from the other alkaline earths by forming a very deliquescent salt (*calcium chloride*) by reaction with hydrochloric acid, and a sparingly soluble one with sulphuric acid.

All acids, acidulous, ammoniacal, and metallic salts, borates, alkaline carbonates, and astringent vegetable infusions are incompatible with it.

Uses.—Lime acts externally as an escharotic, and was formerly applied to ill-conditioned *ulcers.* The *lime ointment* of Spender is made by incorporating four parts of washed slaked lime with one part of fresh lard and three parts of olive oil, previously warmed together. Mixed with potassium hydroxide, lime forms *Potassa cum Calce,* official in the U. S. P., 1890. As an internal remedy, it is converted into hydroxide and this is administered in solution. (See *Liquor Calcis.*)

Calcium oxide may cause a form of caustic poisoning like that of the hydroxides (see under *Potassii Hydroxidum*), but it is less common than either sodium or potassium. Local burns from quick-lime are, however, not infrequent. In the treatment of these the first thing is to neutralize the caustic by washing with a weak acid, preferably a dilute solution of acetic acid; after-treatment is on the same lines as other burns.

Off. Prep.—Liquor Calcii Hydroxidi, *U. S.* (*Br.*); Liquor Calcis Saccharatus, *Br.;* Liquor Calcis Sulphuratæ, *N. F.;* Potassa cum Calce, *N. F.;* Soda cum Calce, *N. F.*

CALX CHLORINATA. U. S., Br.

CHLORINATED LIME Calx Chlorin.

"Chlorinated lime is a product resulting from the action of chlorine upon calcium hydroxide, and yields not less than 30 per cent. of available chlorine [Cl]. Preserve it in air-tight containers, in a cool and dry place." *U. S.* "Chlorinated Lime is obtained by exposing slaked lime to the action of chlorine gas until absorption ceases." *Br.*

Chlorinated Calcium Oxide, Calx Chlorata, *U. S.* 1890; Chloride of Lime, Hypochlorite of Lime, Calcium Hypochlorosum; Calcicus Chloruratus; Chloris Calcicus, Chloruretum Calcis, Calcis Chloridum, Calcii Hypochloris, Calcium hypochlorite, Bleaching Powder; Chlorure de Chaux sec, *Fr. Cod.;* Poudre de Tennant ou de Knox, *Fr.;* Calcaria Chlorata, *P. G.;* Chlorkalk, Bleichkalk, *G.;* Cloruro di calcio, *It.;* Hipoclorito calcico clorurado, *Sp.*

This compound, originally prepared as a bleaching agent in 1798 by Tennant, of Glasgow, is now enormously used both in the arts and in medicine. (For a process of manufacture see *U. S. D.,* 19th ed., p. 267.)

It is made on a large scale by passing chlorine vapors into calcium hydroxide. A series of horizontally placed drums or cylinders provided with revolving endless screws receive the dry calcium hydroxide, which, from its entering the top cylinder until discharged from the bottom one, meets a continuous stream of chlorine gas going in the opposite direction. According to Lunge's investigations, the best temperature for the absorption of chlorine by calcium hydroxide is 40° to 45° C.; from pure calcium hydroxide a bleaching powder of 43 per cent. active chlorine can be produced, in which case allowance for 4 per cent. of moisture in the hydroxide is made.

Several electrolytic processes for the decomposition of sodium and potassium chlorides have been introduced in recent years, whereby caustic alkali on the one hand and chlorine on the other hand are produced. The chlorine liberated is almost entirely utilized in the manufacture of bleaching powder. Large quantities are thus produced at present at Niagara Falls.

Description and Physical Properties.—"A white, or grayish-white, granular powder, having the odor of chlorine. It becomes moist and gradually decomposes on exposure to air and when in such condition must not be used. It is partially soluble in water and in alcohol, the insoluble portion settling readily when mixed with water.

"Shake 1 Gm. of Chlorinated Lime with 50 cc. of distilled water, and filter: the filtrate at first turns litmus paper blue and then bleaches it. Dissolve 0.5 Gm. of Chlorinated Lime in 5 cc. of diluted acetic acid: an abundance of chlorine gas is evolved and only a slight residue remains undissolved. Ammonium oxalate T.S. added to this solution yields a white precipitate insoluble in acetic acid, but soluble in hydrochloric acid.

"**Assay.**—Transfer to a mortar, about 4 Gm. of Chlorinated Lime, accurately weighed in a tared weighing bottle, using 50 cc. of distilled water. Triturate thoroughly, and pour the mixture into a graduated liter flask, rinsing the mortar with distilled water to make 1000 cc. Stopper the flask, and allow it to stand for ten minutes. Shake thoroughly, add to 100 cc. of the mixture 1 Gm. of potassium iodide and 5 cc. of acetic acid, and titrate the liberated iodine with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.003546 Gm. of available chlorine (Cl).

"Preserve in air-tight containers, in a cool, dry place." *U. S.*

"A dull white powder with a characteristic chlorinous odor, becoming moist and gradually decomposing on exposure to air. Partially soluble in *water.* The solution yields the *reactions* characteristic of calcium and of chlorides, and evolves chlorine copiously upon the addition of an acid. 0.5 gramme of Chlorinated Lime, mixed with 1.5 grammes of *potassium iodide* dissolved in 200 millilitres of *water,* gives, when acidified with 6 millilitres of *hydrochloric acid,* a reddish solution, which requires for decolorisation not less than 42.3 millilitres of *N/10 solution of sodium thiosulphate,* corresponding to not less than 30 per cent. of available chlorine." *Br.*

When perfectly saturated with chlorine it dissolves almost entirely in water. When exposed to heat, it gives off oxygen and some chlorine, and is converted into calcium chloride. It is incompatible with the mineral acids, carbon dioxide, and the alkaline carbonates. The acids evolve chlorine copiously, and the alkaline carbonates cause a precipitate of calcium carbonate. (See *Liquor Sodæ Chlorinatæ.*) It is said that strong mineral acids, when not used in excess, liberate only hypochlorous acid; dry carbon dioxide at normal temperature does not set free any chlorine, but at moderately elevated temperature drives off almost all the chlorine.

Chlorinated lime is an oxidizing agent, the oxygen being derived from water, the hydrogen of which unites with the chlorine to form hydrochloric acid. It has a powerful action on organic matter, converting sugar, starch, cotton, linen, and similar substances into formic acid, which unites with the calcium. It also acts energetically on the volatile oils, including oil of turpentine, producing chloroform.

Chlorinated lime constantly becomes weaker on exposure to air and light, giving off chlorine or hypochlorous acid, probably through the influence of the atmospheric carbon dioxide, which sets them free by combining with the calcium, after the compound has become damp through the absorption of moisture.

Composition.—The composition of chlorinated lime is represented by the formula $CaOCl_2$, and it was formerly supposed to be a direct compound of lime with chlorine. This view, however, is not consistent with its reactions, for when distilled with diluted nitric acid it readily yields a distilate of aqueous hypochlorous acid, and when treated with water it is resolved into calcium chloride and hypochlorite, the latter of which may be separated in crystals by exposing the filtered solution to a freezing mixture, or by evaporating it in a vacuum over oil of vitriol and leaving the dense frozen mass to thaw upon a filter. A solution of calcium chloride mixed with hypochlorite then passes through, and feathery crystals remain on the filter. These are very unstable, but consist, when recently prepared, of hydrated calcium hypochlorite, $Ca(OCl)_2.4H_2O$. This seems, at first sight, to show that the bleaching powder is a mixture of calcium chloride and hypochlorite, formed according to the equation.

$$2CaO + Cl_4 = CaCl_2 + Ca(ClO)_2$$

but if this were its true constitution the powder when digested with alcohol ought to yield a solution of calcium chloride containing half the chlorine of the original compound, which is not the case. Its constitution is, therefore, better represented by the formula $Ca\left\{\begin{matrix}Cl\\OCl\end{matrix}\right.$ suggested by Odling, this molecule being decomposed by water into chloride and hypochlorite in the manner just explained, and yielding with diluted nitric acid or sulphuric acid a distillate containing hydrochloric and hypochlorous acids,

$$CaCl(OCl) + 2HNO_3 = Ca(NO_3)_2 + HCl + HClO$$

(Lunge and Schaeppi, *A. J. P.*, 1881; Lunge and Naef, *B. Chem. G.*, 1883.) Lunge and Bachofen (*Zeit. angew. Chem.*, 1893, 326) have determined the specific gravities of chlorinated lime solutions at 15° C. (See *Proc. A. Ph. A.*, 1894, 579.)

Impurities and Tests.—Chlorinated lime may contain a great excess of lime, from imperfect impregnation with the gas. This defect will be shown by the large proportion insoluble in water. If it contain much calcium chloride, it will be quite moist, which is always a sign of inferior quality. When long and insecurely kept, it deteriorates from the gradual formation of calcium chloride and calcium carbonate. Much of the chlorinated lime on the market is greatly below the official requirements in available chlorine, probably because of its instability. Several methods have been proposed for determining its bleaching power, which depends solely on the proportion of loosely combined chlorine. The oxidation of an arsenous acid solution is largely used in practice. Lunge (*B. Chem. G.*, 1886, p. 869) has also proposed to use hydrogen dioxide (H_2O_2) solution for the valuation of bleaching powder. The two solutions liberate oxygen in exactly equal amount. This is measured in a nitrometer.

A valuable reagent for the qualitative detection of free or available chlorine, capable of showing a positive reaction in water containing as small proportion as 0.01 part of chlorine to the million, has been described in the *Amer. Journ. of Pub. Health* for 1916, p. 160, by the Committee on Standard Methods of Water Analysis. It consists of a solution of 1 Gm. of orthotolidin in 1000 cc. of 10 per cent. hydrochloric acid. In the presence of chlorine this reagent gives a yellow or greenish-yellow color. It may also be used for quantitative determinations of free or available chlorine by using colorimetric methods of comparison, and permanent comparison standards may be made from copper sulphate solutions according to the directions given in the article.

The following is the test given in the British Pharmacopœia: "0.5 gramme of Chlorinated Lime, mixed with 1.5 grammes of *potassium iodide* dissolved in 200 millilitres of *water,* gives, when acidified with 6 millilitres of *hydrochloric acid,* a reddish solution, which requires for decolorisation not less than 42.3 mllilitres of *N/10 solution of sodium thiosulphate,* corresponding to not less than 30 per cent. of available chlorine." *Br.*

This is similar in principle to the U. S. P. assay method previously described. In this process iodine is separated by the chlorine in equivalent quantity, and imparts color to the liquid, which is removed by the sodium thiosulphate, by forming colorless compounds with the iodine, and the quantity required for this purpose measures the quantity of iodine, and consequently that of the chlorine, present in the chlorinated solution. (See *Sodii Thiosulphas.*)

Chlorinated lime acts exclusively by its chlorine. It should be carefully kept from contact with the air and organic substances, which cause rapid loss of chlorine, and the modern method of putting it up for ordinary use in hermetically sealed zinc boxes is a great convenience. R. C. Bicknell examined commercial chlorinated lime put up in boxes for available chlorine. He found the top layers usually deficient in strength, but in the interior from 30 to 35 per cent. of chlorine. Some of the packages assaying 30 per cent. of chlorine were more than a year old. (*A. J. P.*, 1886, p. 593.) Investigations made more recently show that variations in the percentage of chlorine are found in the chlorinated lime put up in packages. See Puckner, Stephens, and Harding (*Proc. A. Ph. A.*, 1898, 905). All acids, even carbonic, disengage it, and, as this acid is a product of animal and vegetable decomposition, noxious effluvia furnish the means, to a certain extent, of their own disinfection; but the stronger acids disengage the chlorine far more readily, and among these sulphuric acid is the most convenient. Accordingly, the powder may be dissolved in a very dilute solution of this acid, or a small quantity of the acid may be added to an aqueous solution ready formed, if a more copious evolution of chlorine be desired than that which takes place from the mere action of the carbon dioxide of the atmosphere.

Uses.—As the therapeutic virtues of chlorinated lime depend largely upon the chlorine gas which is liberated from it, it may be well to discuss in this place the effects of chlorine. This gas is an extraordinarily powerful germicide, according to Geppert (*B. K. W.*, 1890), 0.03 per cent. being sufficient to kill the highly resistant anthrax spores in two minutes. It should be noted, however, that in the absence of moisture its germicidal power is comparatively slight. Gaseous chlorine has been used for the purpose of disinfecting inclosed spaces, such as ships' holds, but although highly efficient, if properly used, has largely passed out of vogue. Not only is chlorine actively germicidal, but because of its oxidizing effect decomposes hydrogen sulphide and other malodorous substances, thereby acting as a deodorant. For the same reason it is a powerful bleaching agent and destructive to many kinds of organic matters.

Chlorinated lime possesses desiccant, disinfectant, deodorizant, and bleaching powers. As a bleaching agent it is widely used in the arts. As regards its antibacterial properties it probably ranks, except the salts of mercury and silver, as the most active germicide official. Bolton has shown that one part in two thousand of chlorinated lime is sufficient to destroy the viability of the typhoid bacillus within two hours, and that a one per cent. solution would kill the anthrax spores in the same time. Niessen (*Z. Hyg.*, vii, p. 62) finds that a one per cent. solution can be relied on to destroy either typhoid or cholera germs in the feces within ten minutes, while Stokes and Hatchel (*J. A. M. A.*, li, p. 1505) report that chlorinated lime equivalent to from 0.4 to 1.5 parts per million of chlorine killed ninety per cent. of the bacteria in drinking water.

The most important use of chlorinated lime is as a disinfectant. For the purpose of destroying disease germs in urine, feces, sputa, or similar matters it is, taking all things into consideration, the best of all chemical agents. Its advantages are its relative cheapness, the promptness and certainty of its action, and its oxidizing power which enhance its penetration into organic masses. For this purpose sufficient chlorinated lime to equal about two parts for each hundred of excreta should be intimately mixed and the mixture allowed to stand for one or two hours in an agate-ware, china, or glass receptable. A solution of one pound of chlorinated lime to a bucketful of water makes an excellent disinfectant for washing the walls and floors of dissecting rooms, privies, docks, and other places with offensive effluvia, not only for its germicidal, but especially for its deodorizing effect. The same solution is also serviceable for sterilizing dishes and other utensils which have been used by patients with infectious diseases. Because of its decolorizing effect it is not a suitable agent for the sterilization of colored goods or clothing.

Chlorinated lime may be advantageously applied to the purpose of purifying polluted water, a property which makes it invaluable on long voyages. When used for this purpose, from one to two ounces of the chloride may be mixed with about sixty-five gallons of the water. The water must afterwards be exposed for some time to the air, and allowed to settle, before it is fit to drink. For water not grossly polluted it is sufficient to use about one part of available chlorine per million parts of water. This destroys all pathogenic bacteria and communicates scarcely any taste or odor to the water. It is now used on a large scale for this purpose by many municipalities or gaseous chlorine is used directly.

For more directly medicinal purposes chlorinated lime has been used in solution externally as an application to ill-conditioned *ulcers, burns, chilblains,* and the *itch,* also as a gargle in *angina* and as a disinfectant and deodorizant mouth wash in *ulcerated gums* and similar conditions. Binz (*B. K. W.*, 1909) recommends an ointment containing from 10 to 20 per cent. of chlorinated lime for the treatment of *chilblains* and of *erysipelas.* This ointment must be made with petrolatum as the true fats rapidly render the salts inert. For external application the solution may be made of the strength of from one to four drachms (3.9–15.5 Gm.) to a pint (500 cc.) of water. Vincent (*Press. Mèd.*, 1914, Oct. 8) has had success in the treatment of *hospital gangrene* by powdering the wound with a mixture of 1 part of chlorinated lime to 10 parts of boric acid. From one to four drachms of the powder added to a pint of water, and the solution filtered, will form a liquid within the limits of strength ordinarily required. For the cure of *itch,* Derheims has recommended a much stronger solution—three ounces of the chloride to a pint of water, the solution being filtered, and applied several times a day as a lotion, or constantly by wet cloths. When applied to *ulcers,* their surface may be covered with lint dipped in the solution. When used as an ointment to be rubbed upon *scrofulous enlargements* of the lymphatic glands, this may be made of a drachm of the chloride to an ounce of lard. Riehl (*W. M. W.*, 1907) has confirmed the findings of Calmette regarding the value of calcium hypochlorite as an antidote for *snake bite.* For this purpose ten cc. (2½ fluidrachms) of a 1 per cent. solution should be immediately injected in the neighborhood of the wound. (See also *Liquor Sodæ Chlorinatæ Chirurgicalis.*)

It has been used occasionally internally, in *adynamic dysentery, typhus fever,* and various other *low diseases* but the solution of chlorinated soda is usually preferable. The dose internally is from three to six grains (0.2–0.4 Gm.), dissolved in one or two fluidounces (30–60 cc.) of water, filtered and sweetened with syrup. It should never be given in pills. (See also *Chlorine,* Part II.)

Dose, four grains (0.26 Gm.).

Off. Prep.—Liquor Calcis Chlorinatæ, *Br.;* Liquor Sodæ Chlorinatæ, *U. S., Br.;* Liquor Sodæ Chlorinatæ Chirurgicalis, *U. S.*

CALX SULPHURATA. Br.

SULPHURATED LIME

"Sulphurated Lime is a mixture consisting chiefly of calcium sulphide and calcium sulphate. It may be obtained by heating calcium sulphate with carbon. Contains not less than 50 per cent. of calcium sulphide, CaS." *Br.*

Calcii Sulphidum Crudum, *U. S. IX,* Crude Calcium Sulphide; Calcium Sulphuratum, Calcii Sulphidum; Calcaria Sulfurata, Hepar Sulphuris Calcareum, Hepar Calcis; Sulphide of Calcium; Sulfure de Chaux, *Fr.;* Kalkschwefelleber, *G.*

This preparation has been dismissed from the U. S. P. but is recognized by the Br. No process is at present official. The process of the U. S. P. VIII is as follows:

"Exsiccated Calcium Sulphate, in fine powder, *seventy grammes;* Charcoal, in fine powder, *ten grammes;* Starch, *two grammes.* Mix the powder thoroughly, pack the mixture lightly into a crucible, cover this loosely, and heat it to bright redness, until the contents have lost their black color. Allow the crucible to cool, reduce the product to powder, and at once transfer it to small, glass-stoppered vials." *U. S. VIII.*

By subjecting a mixture of seven parts of calcium sulphate and one part of charcoal to a red heat, in a covered crucible, carbonic oxide is formed, and calcium sulphide is produced,

$$CaSO_4 + 2C = CaS + 2CO_2$$

A less convenient method is to pass hydrogen sulphide over red-hot lime, but if the lime be pure a better product is insured. A *phosphorescent calcium sulphide* used in luminous paints is prepared by igniting calcium carbonate and sulphur and activating with one-thousandth of its weight of bismuth.

Properties.—Crude calcium sulphide is "a greyish-white powder with an odor of hydrogen sulphide; taste nauseous. Yields the *reactions* characteristic of calcium. When 0.8 gramme is mixed in a stoppered flask with a cold solution of 1.4 grammes of *copper sulphate* in 50 millilitres of water, and, after the addition of a little *hydrochloric acid,* the mixture is heated to a temperature approaching that of ebullition, well shaken for ten minutes, and then filtered, the filtrate gives a red color with *solution of potassium ferrocyanide* (presence of a due proportion of sulphide)." *Br.* The U. S. IX described it as "a pale gray or yellowish powder, having a faint odor of hydrogen sulphide and a nauseous and alkaline taste. It gradually decomposes on exposure to moist air. Crude Calcium Sulphide is very slightly soluble in cold water; more readily soluble in boiling water with partial decomposition; readily dissolved by solutions of ammonium salts; insoluble in alcohol. When Crude Calcium Sulphide is decomposed by diluted acetic acid, hydrogen sulphide is evolved and a residue of calcium sulphate and carbon frequently remains. The filtered solution yields with ammonium oxalate T.S. a white precipitate insoluble in acetic acid, but soluble in hydrochloric acid." *U. S.*

Calcium sulphydrate, or *calcium hydrosulphide,* $Ca(SH)_2$, the compound produced when calcium sulphide is dissolved in water is also formed when hydrogen sulphide is passed into milk of lime as long as it is absorbed. It may be obtained in the form of a paste of a greenish-gray color, and exhales a strong odor of hydrogen sulphide.

Assay.—The U. S. IX gave the following method for determining the proportion of pure CaS present: "Introduce about 0.2 Gm. of Crude Calcium Sulphide, accurately weighed, into a glass-stoppered bottle or flask; add 50 mils of distilled water, mix, and quickly introduce 30 mils of a 10 per cent. ammonium chloride solution and immediately stopper the flask. Agitate the contents for a few minutes, add quickly 20 mils of a 10 per cent. cadmium chloride solution, immediately insert the stopper and again agitate well for a few minutes. Then add 5 mils of acetic acid, heat the mixture on a water bath for fifteen minutes, decant the supernatant liquid through a filter, agitate the remaining precipitate with 10 mils of diluted acetic acid, transfer the precipitate to the filter and wash with 10 mils of diluted acetic acid. Return the filter and precipitate to the original flask, add 50 mils of tenth-normal iodine V.S. and 20 mils of a mixture of equal valumes of hydrochloric acid and water. Stopper the flask and agitate it vigorously for a few minutes, and then titrate the excess of iodine with tenth-normal sodium thiosulphate V.S. It shows not less than 55 per cent. of CaS. Each mil of tenth-normal iodine V.S. used corresponds to 0.003607 Gm. of CaS. Each gramme of Crude Calcium Sulphide corresponds to not less than 152.5 mils of tenth-normal iodine V.S." *U. S. IX.*

Uses.—Sulphide of lime owes its therapeutic virtues chiefly to the hydrogen sulphide which is evolved during its decomposition. This gas is locally irritant and actively poisonous, not only to bacteria, but to more highly organized forms of life. Because of this latter property calcium sulphide is a useful agent in the treatment of various parasitic *skin diseases,* such as *scabies, ring-worm,* etc. Because of its local stimulating action it is also employed in various other skin diseases, such as *acne.* Its use as a depilatory depends upon its solvent powers towards keratin. It should be stirred up with enough water to form a paste and spread in a thin layer over the area from which it is desired to remove the hair. At the end of fifteen minutes it is removed with a wet sponge, the hair generally coming away at the same time. See Brayton. (*J. A. M. A.,* April 16, 1898.) For the treatment of skin diseases it may generally be employed in strengths of from twenty to thirty grains to the ounce. It is very widely used in the form of *Vleminckx's solution.* (*Liquor calcis sulphurati,* N. F.) Pusey (*J. A. M. A.,* 1920, lxxiv, p. 97) recommends the latter in full strength for removal of *warts.*

The older dermatologists used calcium sulphide largely as an internal remedy in the treatment of *furunculosis* and *acne,* but it is not evident how it can prove beneficial. In recent years it has also been recommended as a chemical antidote for mercuric chloride (see *Hydrargyri Chloridum Corrosivum*).

Dose, one-fourth to one grain (0.015–0.06 Gm.).

CAMBOGIA. U. S.

GAMBOGE Cambog.

"Gamboge is the gum-resin obtained from *Garcinia Hanburyi* Hooker filius (Fam. *Guttiferæ*). Gamboge contains not more than 1 per cent. of foreign organic matter, and yields not more than 1 per cent. of acid-insoluble ash, and not less than 65 per cent. of alcohol-soluble extractive." *U. S.*

Cambogia, *Br.* 1898; Gambogia, *U. S. Pharm.* 1870; Gummi-resina gutti; Gummi Guttæ; Gutta Gamba, Cambodia; Pipe Gamboge; Gommegutte, *Fr. Cod.;* Gutte, *Fr.;* Gutti, *P. G.;* Gummigutt, *G.;* Gumma gotta, *It.;* Gutagamba, Gomo-resina Guta, *Sp.*

Several plants belonging to the family of *Guttiferæ,* growing in the equatorial regions, yield on incision a yellow opaque juice, which hardens on exposure and bears a close resemblance to gamboge; but it is only from a particular tree that the official gum-resin is procured. The name Cambogia (of which Gamboge is a corruption) appears to have been derived from the fact that it originally came from the kingdom of Cambodia, now a part of French Indo-China. Many years ago Hanbury who had received from Singapore specimens of the gamboge plant cultivated in that island, and derived from Siam, found that the plant approached very near to the *Garcinia Morella* of Desrousseaux, from which it could be distinguished only by its pedicellate flowers and classified it as *G. Morella,* var. *pedicellata.* Sir Joseph Hooker, however, determined (*Journ. Linn. Soc.,* xiv, 480) that the var. *pedicellata* is a distinct species, differing from *G. Morella* in having not only its flowers pedicellate, but also its leaves more ovate and much larger, and its fruit larger; he very properly gave it the specific name of *Hanburii.*

G. Hanburii is a tree reaching a height of fifty feet found in a limited district including Cambodia, southern Cochin-China and the islands and sea coast of the Gulf of Siam, where it is known as "*Ton Rong.*"

Gamboge is said to be procured in Siam by breaking off the leaves and shoots of the tree; the juice, which is contained in ducts or latex vessels in the bark, issues in drops, and being received in suitable vessels, gradually thickens, and at length becomes solid. Jamie, of Singapore, states that incising the trunk and larger branches is often practised. The juice is frequently received into the hollow joints of the bamboo, and the water expelled by mild continuous heat. In this way the so-called pipe gamboge is formed, the contraction during drying causing the cylinders to be hollow. According to Beckett, Siam gamboge is obtained only from trees of not less than ten years of age and during the rainy months, from June to October, by cutting long, spiral grooves into the bark and collecting in hollow bamboos the sap which trickles down in a viscous stream. (*Kew Bulletin,* 1895.)

The name *gummi gutta,* by which gamboge is generally known on the continent of Europe, probably originated from the circumstance that the juice escapes from the plant by drops. Although the medicinal properties of this gum were known to the Chinese as far back as the thirteenth century it was first brought to Europe by the Dutch, about the middle of the seventeenth century. We import it mainly from Singapore.

Indian Gamboge, formerly recognized by the Br. Add. under the name of *Cambogia Indica,* is obtained from the *Garcinia Morella* Desrouss. *Ceylon gamboge,* derived from *G. pictoria* Roxb., is procured by incisions, or by cutting away a portion of the bark, and scraping off the juice which exudes. The specimens sent to Christison were in flattish or round masses, eight or nine inches in diameter, apparently composed of aggregated irregular tears, with cavities which are lined with a grayish and brownish powdery incrustation. It resembles coarse gamboge, and was identical in composition. In Ceylon it is used as a pigment and purgative. (Christison.) *New Caledonian gamboge,* derived from *Garcinia collina* Vieil, is described by Heckel and Schlagdenhauffen as very similar in its appearance and reactions to ordinary gamboge; its color is, however, deep orange. A white crystalline compound, which when heated beyond 235° C. produced pyrocatechin, was found in it, and marked the point of difference between it and other varieties of gamboge. (*Rép. de Pharm.,* 1893, 193.)

Varieties.—The best gamboge is in cylindrical rolls, from two to five centimeters in diameter, sometimes hollow in the center, sometimes flattened, often folded double, or agglutinated in masses so that the original form is not always easily distinguishable. The pieces sometimes appear as if rolled, but are in general striated longitudinally from the impression made by the inner surface of the bamboo. They are externally of a dull orange color, which is occasionally displaced by greenish stains, or concealed by the bright yellow powder of the drug, slightly adhering to the surface. In this form the drug is sometimes called *pipe gamboge.* Another variety is imported under the name of *cake* or *lump gamboge.* It is in irregular masses weighing a kilo or more, often mixed with sticks and other impurities, containing many air-cells, less dense, less uniform in texture, and less brittle than the former variety, and breaking with a dull and splintery instead of a shining and conchoidal fracture. The worst specimens of this variety, as well as of the cylindrical, are sometimes called by the druggists *coarse gamboge*. They differ, however, from the preceding only in containing a greater amount of impurities. Indeed, it would appear from the experiments of Christison that all the commercial varieties of this drug have a common origin, and that cake or lump gamboge differs from the cylindrical only in the circumstance that the latter is the pure concrete juice, while to the former, farinaceous matter and other impurities have been added for the purpose of adulteration. The inferior kinds of gamboge may be known by their greater hardness and coarser fracture; by the brownish or grayish color of their broken surface, which is often marked with black spots; by their obvious impurities, and by the green color which their decoction, after cooling, gives with tincture of iodine (starch). When pure, the gum-resin is completely dissolved by the successive action of ether and water, so that the amount of residue left by any specimen treated in the manner just spoken of indicates approximately the measure of the adulteration.

Description and Physical Properties.—"*Unground Gamboge.*—Cylindrical pieces, frequently hollow at the center, from 2 to 5 cm. in diameter, up to 20 cm. in length, longitudinally striate, grayish orange-brown; fracture brittle, conchoidal, presenting a smooth, rather dull, orange-red surface; odorless; taste acrid.

"*Powdered Gamboge.*—Bright yellow; when mounted in chloral hydrate T.S., nearly all the particles slowly dissolve leaving but a few fragments of vegetable tissues and a very few or no starch grains.

"When rubbed with water, Gamboge yields a yellow emulsion which becomes darker and almost transparent upon the addition of ammonia T.S. The emulsion does not turn green upon the addition of iodine T.S. (*starch*).

"**Assay.**—Proceed as directed under alcohol-soluble extractive." *U. S.*

From the brilliancy of its color, gamboge is highly esteemed as a pigment. It has no odor, and little taste, but, after remaining a short time in the mouth, produces an acrid sensation in the fauces. Its sp. gr. is 1.221. If the proportion of starch be unduly large the emulsion will yield a blue, instead of a green, reaction with iodine.

It is a gum-resin, without volatile oil. Christison has shown that the proportion of gum and resin varies in different specimens even of the purest drug. In one experiment, out of 100.8 parts be obtained 74.2 of resin, 21.8 of gum, and 4.8 of water. The gum is quite soluble in water, and of the variety denominated arabin. Flückiger, however, says that the gum is not identical with gum arabic, as its solution does not redden litmus, and is not precipitated by neutral lead acetate, nor by ferric chloride, nor by sodium silicate or biborate. The resin of gamboge, formerly known as *gambogic acid,* is soluble in alkaline solutions—from which it may be precipitated by acids—in alcohol, ether and other organic solvents. From it have been separated α-, β-, and *γ-garcinolic acids.* By fusing purified gamboge resin with potassium hydroxide, Hlasiwetz and Barth (*Ann. Ch. Ph.*, cxxxviii, 61) obtained acetic and other acids of the same series, together with phloroglucin, *pyrotartaric acid,* and *isouvitinic acid,* $COOH.C_6H_4.CH_2COOH$. Sassarini found gamboge to contain the following constituents: 1. Gum anallogous to arabin. 2. Volatile oil, consisting of terpene and a camphor 3. Isouvitinic and acetic acids. 4. A phenol ester. 5. Resin. 6. Methyl alcohol and some higher homoogues. 7. A liquid having a fruity odor resembling aldehyde or acetone. He believes phloroglucin found by others to be a decomposition product. (*Ann. di Chim. Farm.*, 1897.) Gamboge is readily and entirely diffusible in water, forming a yellow opaque emulsion, from which the resin is very slowly deposited. It yields its resinous ingredient to alcohol, forming a golden-yellow tincture, which is rendered opaque and bright yellow by the addition of water. Its solution in ammoniated alcohol is not disturbed by water. Ether dissolves about four-fifths of it, taking up only the resin. It is wholly taken up by alkaline solutions, from which it is partially precipitated by the acids. The strong acids dissolve it; the solution when diluted deposits a yellow sediment. The color, acrimony, and medicinal power of gamboge are thought to reside in the resin. Hirschsohn gives a method for detecting gamboge in mixtures in *Ph. Z. R.*, xxiv. (*A. J. P.*, 1885.)

Uses.—Gamboge is a powerful, drastic, hydragogue cathartic, so very apt to produce nausea and vomiting and much griping when given in the full dose that it is almost never employed except in combination with other cathartics. In large quantities it is capable of causing fatal effects, and death has resulted from a drachm. The full dose is from two to six grains (0.13–0.4 Gm.), which in cases of *tenia* has been raised to ten or fifteen grains (0.65–1.0 Gm.). It may be given in pill or emulsion, or dissolved in an alkaline solution. In the dose of five grains (0.32 Gm.) the resin is said to produce copious watery stools, with little or no uneasiness. If this be the case, it is probable that, as it exists in the gum-resin, its purgative property is somewhat modified, by the other ingredients.

Dose, one to three grains (0.06–0.2 Gm.).

Off. Prep.—Pilulæ Hydrargyri Chloridi Mitis Compositæ, *U. S.*

CAMPHORA. U. S., Br.

CAMPHOR Camph.

"A dextrorotatory ketone [$C_9H_{16}CO$] obtained from *Cinnamomum Camphora* (Linné) Nees et Ebermaier (Fam. *Lauraceæ*)." *U. S.* "Camphor, $C_{10}H_{16}O$, is a white crystalline substance obtained from Cinnamomum Camphora, *T. Nees and Eberm.*, purified by sublimation." *Br.*

Gum Camphor; Camphora Officinarum; Camphre du Japon *Fr. Cod.;* Camphre droit, *Fr.;* Camphora, *P. G.;* Kampher, Kampfer, Campher, *G.;* Canfora, *It.;* Alcanfor, *Sp.*

The name of camphor has been applied to various concrete, white, odorous, volatile products, found in different aromatic plants, and resulting probably from chemical change in their volatile oil. But camphor proper is derived mainly from two plants, the *Cinnamomum Camphora* (L.) of Nees or *Laurus Camphora* of Linnæus (Fam. *Lauraceæ*) and the *Dryobalanops Camphora* Colebrooke (Fam. *Dipterocarpaceæ*); the former of which yields our official camphor, the latter, the Borneo or Baras camphor, a product much valued in the East, but unknown in the commerce of this country and of Europe. Borneo camphor resembles true camphor, but is distinguished by being heavier than water and not being volatile at ordinary temperatures. On treatment with nitric acid it is converted into true camphor. In California, *Ramona stachyoides, Artemisia trifolium* and *Artemisia frigida* are grown for camphor.

The camphor tree (*Cinnamomum Camphora*) is an evergreen which sometimes attains great size, having the aspect of the linden, with a trunk straight below, but divided above into many branches, which are covered with a smooth, greenish bark. Its leaves, which stand alternately upon long foot-stalks, are ovate-lanceolate, entire, smooth and shining, ribbed, of a bright yellowish-green color on their upper surface, paler on the under, and two or three inches in length. The flowers are small, white, pedicelled, and collected in clusters, which are supported by long axillary peduncles. The fruit is a purple, one-seeded drupe, resembling that of the cinnamon. The camphor tree is a native of China, Japan, and adjacent portions of Eastern Asia, but is capable of cultivation in most sub-tropical countries, where the minimum winter temperature is not below –6.6° C., and the summers are warm. It thrives in Formosa, Madagascar, South Africa, Argentina, Egypt, Canary Islands, Southern Europe, and is being cultivated in India, Ceylon, the Federated Malay States, Luzon, Burma, Florida, Southern California, and Texas. The chief obstacle to its cultivation seems to be the extreme slowness of growth of the tree, and the corresponding slowness of returns from the investment. For an account of cultivation in Florida see *D. C.*, Sept., 1902; also True and Hood, *Proc. A. Ph. A.*, 1909, p. 719.

In Japan and Formosa the drug is obtained chiefly from the root, trunk and branches by the process of sublimation, but in the American plantations the leaves and small twigs are utilized, thus avoiding injury to the trees. Only the older trees are employed; indeed, it is said that a tree must be fifty years old before it should be considered available. In the province of Tosa, in Japan, the method of obtaining camphor, as reported by Dewey (Circular 12, *U. S. Dept. of Agric.*, Div. of Botany), is as follows: "The trees are felled and the trunk, larger limbs, and sometimes the roots are cut into chips with a sharp, concave adze. The fresh chips are placed in a wooden tub about 40 inches high and 20 inches in diameter at the base, tapering towards the top like an old fashioned churn. The perforated bottom of the tub fits tightly over an iron pan of water on a furnace of masonry. The tub has a tight fitting cover, which may be removed to put in the chips. It is surrounded by a layer of earth about 6 inches thick to aid in retaining a uniform temperature. A bamboo tube extends from near the top of the tub into the condenser. This consists of 2 wooden tubs of different sizes, the larger one right side up, kept about two-thirds full of water from a continuous stream which runs out of a hole in one side. The smaller one is inverted with its edge below the water, forming an air-tight chamber. This air chamber is kept cool by the water falling on the top and running down over the sides. The upper part of the air chamber is sometimes filled with clean rice straw, on which the camphor crystallizes, while the oil drips down and collects on the surface of the water. In some cases, the camphor and oil are allowed to collect together on the surface of the water, and are afterwards separated by filtration through rice straw or by pressure. About 12 hours are required for distilling a tubful by this method. Then the chips are removed and dried for use in the furnace, and a new charge is put in. At the same time the camphor and oil are removed from the condenser. By this method 20 to 40 pounds of chips are required for 1 pound of crude camphor." In China the comminuted plant is said to be first boiled with water until the camphor adheres to the stick used in stirring, when the strained liquor is allowed to cool, and the camphor which concretes, being alternated with layers of earth, is submitted to sublimation. In the island of Formosa, where the camphor tree abounds, the chips are heated in a rough still. This is usually composed of a furnace surmounted with a trough or similar rude vessel, which is protected by clay. In this reservoir the chips are placed, with water upon them, and a perforated board luted upon the top; on this are set earthenware pots. A fire having been lighted, steam rises through the chips and carries the camphor with it to deposit it in the pots. The crude camphor is taken to the towns in baskets and then put into large vats, with holes in the bottom, through which an oil escapes called *camphor oil,* much used by the Chinese for medicinal purposes. It is said that of recent years hydraulic pressure is largely substituted for drainage.

Crude camphor is of a pinkish color and of a softer consistency than the refined. It is purified by mixing it with about one-fiftieth of its weight of quicklime and heating in an iron vessel, first to a temperature of about 100° C. which drives off the water and volatile oil. Afterwards the vessel is connected with a suitable receiver and heated to a temperature of 175° to 200° C. which causes the camphor to sublime, the vapors condensing in the receiver. It is refined both in Japan and in the United States.

Oil of Camphor.—Two substances occur in commerce under the name of oil of camphor: The one derived from the *Cinnamomum Camphora,* known as the *Formosa* or *Japanese oil of camphor,* and formerly official under the name of *Oleum Camphoræ* in the U. S. P.; the other the product of *Dryobalanops aromatica,* the *East India oil of camphor,* not occurring in American and European commerce.

Oil of camphor, as found in our markets, is a colorless fluid or of a light yellowish-brown color, having a strong odor like that of camphor, a bitterish camphorous taste and a specific gravity, according to Wm. Procter, of 0.940. It acts strongly on polarized light, and is dextrogyrate. Yoshida (*A. J. P.,* 1886, p. 99) found in it besides two terpenes an oxygenated oil, which constituted half of the crude oil, to which he gave the formula $C_{10}H_{16}O,H_2O$, and calls it *camphorogenol.* Schimmel & Co., of Leipsig, have since extracted *safrol* commercially from the Japanese oil of camphor, and give a different account of its composition. They state (*Schim. Rep.,* 1888) that it contains camphor, safrol, eugenol, a sesquiterpene, $C_{15}H_{24}$, and possibly terpinol. They do not consider Yoshida's camphorogenol to be a distinct substance.

Japanese oil of camphor varies in tint from the colorless transparency of water, through pale straw and yellow, to almost black. The specific gravity varies from 0.898 in the colorless oil to 0.990 in the very dark. The oil seems to vary greatly in the amount of camphor it contains, much of it having nearly all the solid principle removed before exportation. The odor is distinctly camphoraceous, with a peculiarity that suggests the odor of sassafras. It is said by Peter MacEwan to differ from the Formosa oil in its behavior towards nitric acid. If half a drachm of the acid be allowed to act upon half a drachm of Japanese oil, and then diluted with half a drachm of water, a crimson color will be produced. The Formosa oil so treated yields a milky color with a scarcely perceptible green shade; hydrochloric acid gives with each oil a salmon color, more marked, however, with the Japanese oil. For further details, see *P. J.,* vols. xv, xvi, and *J. C. S.,* Oct., 1885. The oil is said to be used in Japan for the preparation of Chinese ink and varnishes, and for burning. As a diluent for artists' colors it is useful because its capacity for dissolving resins is greater than that of oil of turpentine and similar liquids.

The oil of camphor has properties similar to those of camphor, but more stimulant, and is especially applicable to affections of the stomach and bowels in which an anodyne and stimulant impression is indicated, as *flatulent colic* and *spasmodic cholera.* It may also be used externally, as a rubefacient and anodyne liniment, diluted with soap, liniment, or olive oil, in *local rheumatism* and *neuralgic pains, bruises, sprains,* etc. The dose is two or three minims (0.12–0.2 cc.).

The *Dryobalanops oil of camphor* is said to be found in trees too young to produce camphor, and is supposed to constitute the first stage in the development of this substance, as it occupies the cavities in the trunk which are afterwards filled with the camphor. The chief constituent of it is a peculiar volatile oil, which is termed *borneene;* it is isomeric with oil of turpentine, $C_{10}H_{16}$, and holds in solution borneol and resin. By fractional distillation this oil may be separated into two portions, the one more volatile than the other, but not differing in composition.

Commercial History.—The commerce of the world is supplied with camphor chiefly from China, Japan, and Formosa, the great bulk of the product coming from the latter island. After the annexation of Formosa by the Japanese, that government, led by the unnecessary destruction of the camphor trees of the island, the inferiority of the camphor obtained, and the waste of the processes employed, and especially by the desire for revenue, made a governmental monopoly of the camphor trade which went into operation in 1900. The camphor is sold by the Japanese government through a single London firm from whose agencies refiners in different parts of the world buy it by contract for a year at a time. Camphor is now cultivated on a commercial scale in Florida. According to an article in the *Oil, Paint, and Drug. Rep.,* Feb. 26, 1917, p. 18, one grove in Florida produces 40 tons of crude camphor annually.

Camphor is imported into the United States in tin-lined or zinc-lined cases. Crude camphor comes to the United States from Hongkong and Foochow, China, and from Formosa; refined camphor from Shanghai, China and from Formosa; synthetic camphor from Germany.

Sumatra Camphor. Borneo Camphor. Dryobalanops Camphor. Bhimsaim Camphor. Baros Camphor, Borneol.—This camphor is produced in the islands of Sumatra and Borneo from *Dryobalanops Camphora* Coleb. This tree is very large, often exceeding one hundred feet in height, with a trunk six or seven feet in diameter and ranks among the tallest and largest trees in India. It is found in Sumatra and Borneo, and is abundant on the northwest coast of the former island. The camphor exists in concrete masses, which occupy longitudinal cavities or fissures in the heart of the tree, from a foot to a foot and a half long, at certain distances apart. The younger trees are generally less productive than the old. The only method of ascertaining whether a tree contains camphor is by incision. When discovered, the tree is felled and cut into logs, which are then split, and the camphor removed by means of sharp-pointed instruments. It is stated that the masses are sometimes as thick as a man's arm, and that the product of a medium-sized tree is nearly eleven pounds; of a large one, double that quantity. The trees which have been wounded and left standing often produce camphor seven or eight years afterwards. Ida Pfeiffer states, in her *Second Journey Round the World,* that the camphor is also found in a concrete state under the bark and is swept down with long brooms. The whole tree is pervaded more or less by the camphor or the oil. The wood retains a fragrant odor, and, being on this account less liable to the attacks of insects, is highly esteemed for carpenter work.

Borneo camphor resembles in appearance ordinary camphor, but has, according to Christison, a specific gravity of 1.009. Its odor is also distinctly different from that of camphor. It usually pulverizes without the addition of alcohol, is less volatile than ordinary camphor and does not sublime on the interior of the bottles in which it is kept. It fuses at 206° C. and boils at 212° C.; is dextrogyrate; has a formula of $C_{10}H_{17}(OH)$; and by the action of boiling nitric acid is converted into common camphor. It does not reach European commerce, being largely consumed in the Batta provinces, especially in funeral rites; and any that is exported is brought up at enormous prices for China, where it is preferred for embalming purposes on account of its being less volatile than the ordinary drug.

Borneo camphor is also produced in Johore, a province of the Malay peninsula, where it is sold in four qualities. The first is composed of transparent crystals, generally a quarter of an inch and upwards in length; the second of brown crystals, inferior in size; the third of powdery, coherent and slightly grayish colored crystals, which resemble Japanese camphor; the fourth quality is brownish, pulverulent, and looks like seashore sand.

Ngai camphor is yielded by the *Blumea balsamifera* DC. (Fam. *Compositæ*), a shrub from 5 to 6 feet high which occurs in India, China, Formosa, Philippines, etc. The crude drug is known to the Chinese as *ngai-fêu,* and when refined in Canton as *ngai-p'ien.* About ten thousand pounds annually are exported from Canton. The refined camphor in appearance, odor, hardness, specific gravity, and volatility agrees almost precisely with Borneo camphor. According to Plowman, it has the chemical composition of Borneo camphor, but differs from it in its alcohol solution, being lævogyrate, and in being converted by boiling nitric acid into a substance thought to be identical with the stearopten of *Chrysanthemum Parthenium* Pers. Another species of Blumea, the *B. grandis,* a weed growing from 6 to 8 feet high, is said to yield a camphor identical with the Japanese product.

The physiological action of *Borneo* and *Ngai camphor* and of artificial *borneol* has been studied by R. Stockman (*J. P.,* 1888, ix) who finds that the action of the three substances is practically identical and closely resembles that of true camphor. The results obtained by A. Lapin (*Med. Age,* 1894, xii) confirm those of Stockman, and show that in its proper dose the drug increases the energy of the heart, and that in frogs it is an especial motor nerve paralyzant.

Artificial Camphor.—Camphor can be made artificially by the oxidation of *camphene,* $C_{10}H_{16}$, with chromium trioxide mixture. Camphene is obtained from either *pinene hydrochloride* (so-called artificial camphor) or from bornyl chloride by treatment with alcoholic potash, and is a solid crystalline mass, fusing at 49° C. In the patented process of Nathan Thurlow, camphor is made by submitting oil of turpentine to the action of anhydrous oxalic acid in steam-jacketed reaction tanks. The liquid mass, containing *pinyl oxalate* and *pinyl formate,* is then distilled in the presence of an alkali with live steam, the resultant products being camphor, Borneol camphor, and certain oily products, which are separated from one another and purified by a somewhat complicated process. It is stated that turpentine yields in this process from 25 to 35 per cent. of its weight, and that oil of lemon and other essential oils, and terpenes are obtained as secondary products. This artificial camphor is either optically inactive or has a very slight dextrorotation, but in general physical properties exactly resembles natural camphor. So far, however, it seems to be difficult to work the process upon a large scale and the artificial product has had little effect upon the general camphor market. Camphor can also be produced from isoborneol, by the action of oxidizing mixtures. The method patented in France, which is said to yield from 95 to 100 per cent. of camphor, consists in suspending ten kilogrammes of isoborneol in ten kilogrammes of benzol, and adding ten kilogrammes of potassium permanganate dissolved in one thousand liters of water, until the color of the permanganate is discharged. The camphor produced is separated by distillation and crystallized from petroleum benzin. Some pine needle oils and also Siberian oil of turpentine contain large proportions of bornyl acetate; the remaining terpenes may be converted into bornyl formate by the action of formic acid and a dehydrating agent. The mixed bornyl esters may then be converted into very pure camphor, free from chlorine compounds. A study of natural and synthetic camphor by Houseman giving complete review of all processes for producing the synthetic article and illustrated with structural formulas is found in *A. J. P.*, 1915, p. 49.

While some writers have used synthetic camphor as a substitute for a natural variety with asserted good results, the facts that Pari and Bruni found the laevo-camphor thirteen times more toxic than the dextro-camphor and that the synthetic product is optically inert emphasizes the necessity of careful research before the artificial camphor can be considered therapeutically equivalent to the natural. (For literature see Borsich, *Ph. Centralh.*, 1920, lxi, p. 403.)

Camphor, $C_{10}H_{16}O$, and borneol, $C_{10}H_{18}O$, are classified together as belonging to the group called in general *camphors*, which are related to the *terpenes*, and are considered to be oxidation products of these.

Borneol is an alcohol, yielding esters when heated to about 200° C. with organic acids. It is a secondary alcohol, and therefore contains the group CH.OH linked to a more complex group. Secondary alcohols by oxidation yield ketones, by the change of the CH.OH group to CO. Common camphor bears this relation to borneol, and is therefore considered as a ketone, and can be formed from borneol by the action of mild oxidizing agents. The action of metallic sodium, on the other hand, upon common camphor, $C_{10}H_{16}O$, yields borneol, $C_{10}H_{18}O$.

Description and Physical Properties.—"White, translucent, tough masses or granules. It has a penetrating, characteristic odor, and a pungent, aromatic taste. It is readily pulverizable in the presence of a little alcohol, ether, or chloroform. It slowly volatilizes at ordinary temperatures. One Gm. of Camphor is soluble in about 800 cc. of water, 1 cc. of alcohol, 0.5 cc. of chloroform, and in 1 cc. of ether, at 25° C. It is freely soluble in carbon disulphide, petroleum benzin, and in fixed or volatile oils.

"Specific gravity: about 0.990 at 25° C. Camphor melts between 174° and 177° C. The specific rotation $[a]_D$ of Camphor, determined at 25° C. in a solution containing 10 Gm. of Camphor in 100 cc. of alcohol and using a 200 mm. tube, is between $+41°$ and $+42°$.

"A solution of Camphor in petroleum benzin (1 in 10) is clear (*water*). Gradually heat about 2 Gm. of Camphor: it sublimes without carbonization and without leaving more than 0.05 per cent. of non-volatile matter. Wind the end of a copper wire into a spiral about 6 mm. in diameter and 6 mm. in length, and hold it in a non-luminous flame until it glows without coloring the flame green. Dip the hot spiral in the Camphor, ignite, allow it to burn outside of the flame, and then bring the spiral into contact with the lower, outer edge of a non-luminous flame: not even a transient green color is imparted to the flame (*chlorinated products*).

"Preserve in well-closed containers, in a cool place." *U. S.*

"Colorless, transparent crystals or crystalline masses of tough consistence; also in rectangular tablets or in pulverulent masses known as 'flowers of camphor.' Penetrating and characteristic odor; taste pungent and somewhat bitter, followed by a sensation of cold. Specific gravity about 0.995. Melting point about 175° C. Soluble in about 700 parts of *water*, in 1 part of *alcohol* (90 per cent.), in 0.25 part of *chloroform*, and in 4 parts of *olive oil;* very soluble in *ether*. Burns readily with a bright smoky flame, volatilises even at ordinary temperatures, and sublimes without residue when heated. Forms a liquid when triturated with chloral hydrate, menthol, phenol, thymol, and certain other substances. A solution of 5 grammes in sufficient *alcohol* (90 per cent.) to produce 20 millilitres exhibits at 15.5° C. an *optical rotation* of about $+10°$ (distinction from synthetic camphor)." *Br.*

Camphor has a peculiar, strong, penetrating, fragrant odor, and a bitter, pungent taste, and a slight sense of coolness. It is beautifully white and pellucid, somewhat unctuous to the touch, brittle, and yet possessed of a tenacity which renders its reduction to a fine powder very difficult unless its cohesion be overcome by the addition of a minute proportion of alcohol, ether, chloroform, glycerin, essential or fatty oils, or other liquid for which it has an affinity. It may be obtained in powder by pulverizing with an equal weight of sugar, by precipitating the tincture with water, or by grating and afterwards sifting it, or by sublimation. A still better plan is to dissolve camphor in one and a half parts of alcohol, and pour this solution with stirring into four parts of water. Collect the precipitate, wash with water, and dry. By noting the quantity of camphor used, the amount left dissolved in the diluted alcohol can be calculated, and this solution used in making tincture. The fracture of camphor is shining, and its texture crystalline. Its sp. gr. varies from 0.9857 to 0.996. When thrown in small fragments upon water, it assumes singular circulatory movements, which cease upon the addition of a drop of oil; and this property has been applied to the detection of grease in liquids, a very small proportion of which is sufficient to prevent the movements. Its volatility is so great that, even at ordinary temperatures, it is wholly dissipated if left exposed to the air. When it is confined in bottles, the vapor condenses on the inner surface, and, in large bottles partially filled, sometimes forms, after long standing, large and beautiful crystals. It melts at 175° C., boils at 204° C., and, in closed vessels, sublimes unchanged. When allowed to concrete slowly from the state of vapor, it assumes the form of hexagonal plates. It is not altered by air and light. It readily takes fire, burning with a brilliant flame, with much smoke, and without residue.

Leo and Rimbach find that the solubility of camphor in pure water is 1 part in 598. The solubility in water falls with rise of temperature. (*J. Soc. Chem. Ind.*, xxxviii, 1919, 738A.) Carbon dioxide increases the solvent power of water, as also does the spirit of nitrous ether. Ordinary alcohol will take up 75 per cent. of its weight of camphor, which is precipitated upon the addition of water. Berzelius states that 100 parts of alcohol, of the sp. gr. 0.806, dissolve 120 parts of 10° C. It is soluble without change in ether, the volatile and fixed oils, strong acetic acid, and diluted mineral acids, and is extremely soluble in chloroform. Nitric acid on prolonged boiling with camphor oxidizes it into *camphoric acid,* $C_{10}H_{16}O_4$ (see Part II), and *camphoronic acid,* $C_9H_{14}O_6$. Schwanert's *camphresinic acid,* $C_{10}H_{14}O_{12}$, is, according to Kachler, a mixture of these two. Sulphuric acid in the proportion of ten parts to one gives, when heated with camphor, an oil isomeric with camphor, boiling at 200° C., and yielding a solid camphor when distilled repeatedly over potassium hydroxide. Sulphuric acid, in the proportion of four to one with camphor, gives, according to Chautard, a volatile product which he calls *camphrene,* and to which Schwanert gives the formula $C_9H_{14}O$. Kachler (*Ann. Ch. Ph.,* clxiv, p. 90) considers, however, that camphrene is only *phorone* (a condensation product of acetone) with slight impurities. Alcoholic potassium hydroxide solution heated with camphor gives a derivative called *campholic acid,* $C_{10}H_{18}O_2$, a white solid, fusing at 95° C., and boiling at 250° C. Resins unite with camphor, forming a soft, tenacious mass, in which the odor of the camphor is sometimes almost extinguished, and frequently diminished; and a similar softening effect results when it is triturated with the solid fats. Exposed to a strong heat, in closed vessels, camphor is resolved into carbonic acid gas and hydrocarbons, among which cymol is especially to be recognized.

Genuine camphor is said to be sometimes adulterated with the synthetic, which may be detected by the action of ammonia upon its alcoholic solution, causing a flocculent precipitate, which does not redissolve, and the quantity of which is proportionate to that of the synthetic product in any mixture of the two. (*A. J. P.,* xxxiv, 189.) As a means of distinguishing camphor from the synthetic camphor, J. W. Bailey recommends that a drop of alcohol, holding in solution a little of the camphor to be tested, be allowed to evaporate on the slide of a microscope. The crystals then formed produce, with polarized light, beautiful colors, if of natural camphor, but not, if of the synthetic. (*Neues Repertorium,* xvi, 763, 1867.)

The best test for distinguishing natural and synthetic camphor is by mixing 0.1 Gm. of the suspected substance, on a watch glass with ten drops of a cooled mixture of equal parts of vanillin-hydrochloric acid and concentrated sulphuric acid. Natural camphor first turns green and after five hours' exposure, dark blue; synthetic camphor remains yellow.

Another point of distinction is said to be the fact that the synthetic camphor does not liquefy when triturated with an equal weight of chloral hydrate, while the natural camphor does.

Uses.—Locally camphor is irritant, with probably a benumbing influence upon the peripheral sensory nerves, and somewhat antiseptic. It is absorbed through mucous membranes not very readily, but easily from subcutaneous tissue. It combines in the body with glycuronic acid and is eliminated in this combination by the kidneys. The systemic action of camphor is not well understood. In frogs it is depressant to the spinal cord and produces no motor disturbance except gradually increasing paralysis. In the mammalia, including man, it causes convulsions which are apparently due to an effect upon the motor tract of the brain. It appears also to have some stimulant action upon the intellectual centers and antagonizes the somnifacient drugs. On the other hand, in conditions of nervous excitement it will frequently produce a sensation of quietude. The effects of camphor upon the circulation have been the subject of an immense amount of scientific investigation but with very contradictory results. The majority of authorities have found that the drug increases the force of the cardiac contractions in cold-blooded animals, but in the studies upon warm-blooded animals the results have been so contradictory that it seems impossible to harmonize them. Most investigators have found that camphor does not produce any consistent change in the blood pressure until large doses are given, when it is likely to cause a fall, but on the other hand, Pilcher and Sollman (*J. P. Ex. T.,* 1915, vi, p. 349) have found that in the great majority of cases it causes a definite rise in the blood pressure. While Gottlieb (*Z. E. P. T.,* 1905, ii) and others have obtained evidence of a stimulant action upon the heart muscle of warm-blooded animals, the majority of experimenters have been unable to determine such an effect. (For review of the literature on this subject, see *J. P. Ex. T.,* 1914, v, p. 571.) On the other hand, several investigators present evidence indicating that it has the power of antagonizing certain poisons such as strophanthin, chloral, phosphorus, etc., and the clinical evidence of the stimulating effect of camphor upon the circulation seems incontestable. Marfori (*Rif. M.,* 1918, xxxiv, p. 567) asserts that it is a remedy of great value in *myocarditis* with irregular rhythm; its action, he believes, is due to a stimulation of the nodal system of the heart. Marvin and Soifer (*J. A. M. A.,* 1925, lxxxiii, p. 94) in careful observations on fourteen patients with chronic heart disease, were unable to note any favorable influence of camphor upon either the circulation or general condition of the patient. For reference to the literature on this subject see the paper of Marvin and Soifer. In cases of heart failure whether due to diseases of the heart itself or secondary to infectious fevers, such as *typhoid* or in *pneumonia,* it is, however, highly esteemed by many clinicians.

In pneumonia camphor has been used not only as a cardiac stimulant but with the idea that it inhibits the growth of the pneumococci. While the evidence for this view is strongly suggestive it cannot be considered in any way conclusive. (For review of the literature on this subject see *J. A. M. A.,* 1920, lxxiv, p. 46.)

Aside from its action as a circulatory stimulant camphor is used internally for its calmative influence in *hysteria,* general *nervousness* and *neuralgia.* Whether the effects in these conditions are due to any action other than a psychic influence from the strong taste of the drug, is open to question. It is also employed in the treatment of *serous diarrheas,* its effects being probably due to a local irritant action upon the mucous membrane of the intestines. Externally it is widely employed as a counter-irritant in *sprains, rheumatic affections, bronchitis,* and other inflammatory conditions. It is also employed as a local application, especially in conjunction with menthol or phenol, in inflammations of the upper respiratory tract.

When a profound influence is desired, as in heart failure, it is necessary to give the drug hypodermically. For this purpose from three to five grains may be dissolved in twenty to thirty minims of sterile olive oil. The effect of a single injection lasts usually about two hours. Attention may be called to the fact that solutions of camphor in liquid petrolatum are entirely unsuited for hypodermic administration. Apparently the camphor is not absorbed under these conditions and not only does it fail to produce the desired physiological action but is often followed by serious local inflammatory changes. In nervous diseases it may be given in substance, in capsule, or as the spirit; the water contains so little camphor that it is scarcely more than a vehicle.

Cases of camphor poisoning, chiefly from the accidental ingestion of camphor liniment, have been reported. Benz (*J. A. M. A.,* 1919, lxxii, p. 1217) reports 20 such cases. The most constant symptom observed has been clonic convulsion, usually accompanied with vertigo, more or less mental confusion often amounting to active delirium and sometimes followed with coma. While sometimes the symptoms are very alarming the mortality is very low. The treatment, aside from evacuation of the stomach, is purely symptomatic.

Dose, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Aqua Camphoræ, *U. S., Br.;* Ampullæ Camphoræ, *N. F.;* Ceratum Camphoræ, *N. F.;* Ceratum Plumbi Subacetatis, *N. F.;* Linimentum Aconiti, *Br.;* Linimentum Belladonnæ, *N. F., Br.;* Linimentum Camphoræ, *U. S., Br.;* Linimentum Camphoræ Ammoniatum, *Br.;* Linimentum Chloroformi (from Soap Liniment), *U. S.* (*Br.*); Linimentum Hydrargyri (from Camphor Liniment), *Br.;* Linimentum Opii, *Br.;* Linimentum Saponis, *U. S., Br.;* Linimentum Sinapis, *Br.;* Linimentum Terebinthinæ, *Br.;* Linimentum Terebinthinæ Aceticum (from Camphor Liniment), *Br.;* Spiritus Camphoræ, *U. S., Br.;* Tinctura Camphoræ Composita, *Br.;* Tinctura Opii Camphorata, *U. S.* (*Br.*); Unguentum Hydrargyri Compositum, *Br.;* Chloral Camphoratum, *N. F.;* Emplastrum Fuscum Camphoratum, *N. F.;* Linimentum Ammonii Iodidi, *N. F.;* Linimentum Opii Compositum, *N. F.;* Linimentum Saponato-Camphoratum, *N. F.;* Linimentum Sinapis Compositum, *N. F.;* Lotio Ammoniacalis Camphorata (from Spirit of Camphor), *N. F.;* Menthol Camphoratum, *N. F.;* Mistura Camphoræ Acida (from Water), *N. F.;* Mistura Camphoræ Aromatica (from Water), *N. F.;* Mistura Opii et Chloroformi Composita (from Spirit), *N. F.;* Mistura Opii et Rhei Composita (from Spirit), *N. F.;* Nebula Aromaticum, *N. F.;* Nebula Mentholis Composita, *N. F.;* Petroxolinum Chloroformi Camphoratum, *N. F.;* Petroxolinum Phenolis Camphoratum, *N. F.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloes, *N. F.;* Pilulæ Opii et Camphoræ, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodicæ sine Aloes, *N. F.;* Tinctura Pectoralis (from Spirit), *N. F.;* Unguentum Camphoræ, *N. F.*

CANELLA. N. F.

CANELLA Canel.

"Canella is the dried rossed bark of *Canella Winterana* (Linné) Gaertner (Fam. *Canellaceæ*). Canella contains not more than 2 per cent. of foreign organic matter." *N. F.*

Cortex Canellæ; Cortex Winteranus Spurius; White Cinnamon; Cassia alba; Jamaica Winter's Bark, Wild Cinnamon Bark; Weisser Zimmt, *G.*

Canella alba Murr. (Fam. *Canellaceæ*).—The Spaniards who noted this bark shortly after the discovery of the West Indies believed, because of its aromatic odor, that it was a species of cinnamon and called it "white cinnamon" (*Canella alba*). The first mention of it was by Clusius in 1605. Subsequently it was confused with Winter's Bark (see Part II).

Canella Winterana is a tree, native of Florida and the Bahama and West India Islands. The bark of the branches, which is the part employed in medicine, is loosened and deprived of its epidermis by beating. After removal from the tree it is dried in the shade. It enters commerce at Nassau, Island of New Providence, West Indies, where it is known as *cinnamon bark,* or as *white wood bark.*

Description and Physical Properties.—"*Unground Canella.*—In quills usually from 1 to 3 cm. long and from 1 to 4 cm. thick, occasionally 2 or 3 times this size, or in irregular fragments of bark, from 1.5 to 5 mm. thick and 2 to 3 cm. wide, the outer periderm mostly removed; outer surface light brownish yellow or pale orange-brown, more or less scaly, with a few very shallow fissures, often more or less reticulate with slight ridges; inner surface pale yellow, somewhat smooth, but showing coarse, longitudinal striæ; fracture short and sharp, pale yellow internally with an irregular, slightly darker band at the center. Odor slight unless the bark is heated, then aromatic, resembling that of cinnamon; taste aromatic, warm, somewhat bitter and mucilaginous.

"*Powdered Canella.*—Light brown to brownish red; numerous, isodiametric, thick-walled stone cells 0.040 to 0.090 mm. in diameter, the walls with simple or branching pores; calcium oxalate in rosettes up to 0.050 mm. in diameter; starch grains simple or 2- to 3-compound up to 0.020 mm. in diameter; oil cells with suberized walls numerous." *N. F.*

Nearly one-fourth the weight of canella is extracted by boiling water but the infusion, though bitter, has comparatively little of the warmth and pungency of the bark. It yields all its virtues to alcohol, forming a bright yellow tincture, which is rendered milky by the addition of water. Canella bark yields by distillation from 0.75 to 1.25 per cent. of a volatile oil, having an odor resembling that of a mixture of cajeput and clove. It contains benzoyl eugenol; l-pinene; cineol and caryophyllene. The bark yielded to Flückiger 0.74 per cent. of oil. According to John P. Frey, it contains volatile oil, 1.28 per cent.; resin, 8.2 per cent.; mannite, 8 per cent.; ash, 8.9 per cent.; also starch, bitter principle, albumen, and cellulose. (*A. J. P.*, 1884, 1.)

Uses.—Canella is a mild, aromatic tonic, very acceptable to the stomach, and especially as an addition to tonic or purgative medicines. It is scarcely ever prescribed except in combination. Its best known compound is the famous *Pulvis Aloe et Canellæ* (see Part III), commonly known as *Hiera Picra*, literally "*Sacred Bitters*," from the esteem in which it was once held. In the West Indies it is employed by the negroes as a condiment and as an antiscorbutic.

Dose, ten to forty grains (0.65–2.6 Gm.).

Off. Prep.—Pulvis Aloes et Canellæ, *N. F.*

CANNABIS. U. S. (Br.)

CANNABIS Cannab.

"Cannabis is the dried flowering tops of the pistillate plants of *Cannabis sativa* Linné (Fam. *Moraceæ*). Cannabis, in the form of the fluidextract, administered by the mouth to dogs in doses not exceeding 0.1 cc. for each kilogram of body weight of dog, produces a degree of incoördination equivalent to that caused by the same dose of the standard fluidextract of cannabis, prepared as directed below. It contains not more than 10 per cent. of its fruits, large foliage leaves, stems over 3 mm. in diameter, and not more than 2 per cent. of other foreign organic matter. It yields not more than 5 per cent. of acid-insoluble ash, and not less than 8 per cent. of alcohol-soluble extractive." *U. S.* "Indian Hemp consists of the dried flowering or fruiting tops of the pistillate plant of Cannabis sativa, *Linn.*, grown in India; from which the resin has not been removed." *Br.*

Cannabis Indicæ, *Br.;* Hemp, Indian Hemp; Guaza, Ganjah, Herba Cannabis Indicæ; Chanvre, Chanvre de l'Inde, *Fr.;* Indischer Hanf, *G.;* Cañamo, *Sp.;* Marihuana, *Mex.*

For many years the official cannabis was restricted to the drug which was used for centuries in India. The reason for this was that the Indian cannabis was more uniformly active. Recently the Indian Government has placed a high tax on every pound of the drug grown. The result has been that other markets have been sought and the hemp plant has been grown in other parts of Asia, Africa and America. While, of course, much of this material is not equal to that grown in India yet the fact that it can be grown, as shown by experiments, in the United States (see Hamilton, *J. A. Ph. A.*, 1913, ii; 1915, iv, 389) of a very high quality has caused the framers of the U. S. Pharmacopœia to permit the use of a cannabis, no matter where it may be grown, provided it comes up to the biological standard as given in the definition. Physiologically active cannabis is obtained at the present time not only from India, but Africa, Turkey, Turkestan, Asia Minor, Italy, Spain and the United States.

The *Cannabis sativa*, or hemp plant, is a tall, rough annual, from four to sixteen feet or more in height, with erect, branching, angular stem. The leaves are alternate or opposite, and palmately-compound, with five to seven linear-lanceolate, coarsely serrated leaflets. The stipules are subulate. The flowers are axillary and greenish; the staminate in long, branched, drooping panicles; the pistillate in erect, simple catkins. The stamens are five, with long pendulous anthers; the pistils two, with long, filiform, glandular stigmas. The fruit is an ovate achene. The whole plant is covered with a fine pubescence, scarcely visible to the naked eye, and somewhat viscid to the touch. The hemp plant of India has been considered by some as a distinct species, and named *Cannabis indica;* but the most observant botanists, upon comparing it with our cultivated plant, have been unable to discover any specific difference. It is now, therefore, regarded merely as a variety. Pereira states that in the female plant the flowers are somewhat more crowded than in the common hemp, but that the male plants in the two varieties are in all respects the same.

C. sativa is a native of the Caucasus, Persia, and the hilly regions in Northern India. It is cultivated in many parts of Europe and Asia, and largely in our Western States.

The most important commercial varieties of cannabis are the India, American and African. Indian cannabis is obtained from plants grown in various districts of India, chiefly north of Calcutta. The flowering tops are collected when they have taken on a brownish color, the fruits shaken out and the herbage allowed to wilt and then subjected to the rolling and treading process in order to work resinous matter from the stems into the inflorescences. There are two commercial grades of Indian cannabis, viz.: round and flat. The round is prepared by kneading each branch into a cylindrical or rounded mass. The flat grade is kneaded into a compressed flattened form. The color is grayish-brown. The commercial supplies of this variety are imported into the United States from Bombay, India.

American cannabis is yielded by *Cannabis sativa* plants cultivated in various sections of the United States. It occurs on the market in the form of broken segments of the inflorescences and more or less crumpled and broken leaves, varying in color from brownish-green to light brown.

African cannabis from *Cannabis sativa* plants growing in various districts of Africa, comes into the market as broken leaves and flowering-tops of a greenish-brown color.

The fruits or "so-called" seeds, though not now official, have been used in medicine. They are from three to five millimeters long and about two millimeters broad, roundish-ovate, somewhat compressed, of a shining ash-gray color, and of a disagreeable, oily, sweetish taste. For a comprehensive monograph on the morphology of cannabis fruits, as well as their history and chemical composition, see Tschirch, *"Handbuch der Pharmakognosie,"* p. 555. They yield by expression about 20 per cent. of a fixed oil, which has the drying property, and is used in the arts. They contain also uncrystallizable sugar and albumen, and when rubbed with water form an emulsion, which may be used advantageously in inflammations of the mucous membrane, though without narcotic properties. The seeds are much used as food for birds, as they are fond of them. They are generally believed to be in no degree poisonous; but Michaud relates the case of a child in whom serious symptoms of narcotic poisoning occurred after taking a quantity of them. It is probable that some of the fruit eaten by the child was unripe, as in this state it would be more likely to partake of the peculiar qualities of the plant.

In Hindostan, Persia, and other parts of the East, hemp has long been habitually employed as an intoxicating agent. The parts are the tops of the plant, and a resinous product obtained from it. *Bhang* is the selected, dried and powdered leaves. *Ganjah* or *gunjah* is the tops of cultivated female plants, cut directly after flowering, and formed into round or flat bundles from two to four feet long by three inches in diameter. It is stated that in the province of Bengal great care is taken to eradicate the male plants from the fields before fertilization of the female, and that thereby the yield and quality of the resin is greatly increased. In Bombay this matter is commonly neglected, so that Bengal ganjah is much superior to Bombay ganjah. It is recognized in India that ganjah rapidly deteriorates on keeping, that which is one year old being not more than one-quarter as potent as the fresh drug, while two-year-old ganjah is practically inert and is required by the Indian government to be burned in the presence of excise officers. It is probable, however, that much old ganjah finds its way into the markets of the world.

The method of collection in Baluchistan is to gently rub the dried plant between carpets. The dust which comes off contains the active principle and is known as "rup." The second shaking produces an inferior variety, known as "tahgalim," and the third shaking is known as "ganja." In Nepal the plant is squeezed between the palms of the hands, and the resin scraped off from the hands. These balls, and also masses formed out of resin mechanically separated from the hemp plant are called *charas* or *churrus*. This is the *hashish* or *hasheesh* of the Arabs.

Hashish is also produced in considerable quantities in Persia by rolling and rubbing the flowers, stalks and leaves of hemp on rough woollen carpets and subsequently scraping off with a knife and making into balls or sticks the adherent resinous substance. The carpets are afterwards washed with water and the extract obtained by evaporation sold at a low price.

Momea or *mimea* is a hemp preparation said to be made in Thibet with human fat.

The pistillate plants are much more active than the staminate and when hemp is grown for its drug it is the custom to eradicate the latter, pruning the remaining female plants so as to make them branch more luxuriantly.

Properties.—Fresh hemp has a characteristic odor, which is much less in the dried tops, which have a feeble bitterish taste.

Description and Physical Properties.—"*Unground Cannabis.*—In separate tops or less agglutinated masses or fragments, consisting of the short stems with their leaf-like bracts and pistillate flowers or more or less developed fruits; color green to dark green or greenish brown; odor agreeable, somewhat heavy and narcotic; taste somewhat acrid and pungent. Leaves digitately compound, usually broken. Leaflets when entire, linear-lanceolate, nearly sessile, margin deeply serrate. Bracts ovate, pubescent, each enclosing 1 or 2 pistillate flowers or more or less developed fruits. Calyx dark green, pubescent and somewhat folded around the ovary. Styles 2, filiform and pubescent. Ovary with a single campylotropous ovule. Stems cylindrical, longitudinally furrowed, light green to light brown, strigose-pubescent.

"*Structure of Stem.*—Cortex composed of collenchyma and, in the larger stems, of numerous strands of more or less lignified bast-fibers; strongly lignified wood with medullary rays 1-cell wide; pith, often hollow; rosette aggregates of calcium oxalate numerous.

"*Powdered Cannabis.*—Dark green; epidermis from lower surface of leaves with sinuate vertical walls and numerous oval stomata, from upper surface with straight walls and no stomata; non-glandular hairs numerous, unicellular, rigid, curved, with a very slender pointed apex and an enlarged base usually containing calcium carbonate masses; glandular hairs of two kinds, one with a short 1-celled stalk, the other with a long multicellular, tongue-shaped stalk, the head being globular and consisting of 8 to 16 cells; fragments of bracts and leaves showing yellowish-brown laticiferous vessels, numerous rosette aggregates of calcium oxalate, 0.005 to 0.030 mm. in diameter, and strands of spiral tracheæ and phloem; fragments of fruits with palisade-like, non-lignified cells with yellowish-brown finely porous walls usually containing air; tissues of embryo and endosperm with numerous oil globules and aleurone grains, the latter from 0.005 to 0.010 mm. in diameter and displaying crystalloids and globoids. Diluted hydrochloric acid added to powdered Cannabis causes effervescence visible under the microscope." *U. S.*

The British Pharmacopœia describes Indian cannabis as follows:

"In compressed, rough, dusky-green masses, consisting of the branched upper part of the stem, bearing leaves and pistillate flowers or fruits, matted together by a resinous secretion. Upper leaves simple, alternate, 1–3 partite; lower leaves opposite and digitate, consisting of five to seven linear-lanceolate leaflets with distantly serrate margins. Fruit one-seeded and supported by an ovate-lanceolate bract. Both leaves and bracts bear external oleo-resin glands and one-celled curved hairs, the bases of which are enlarged and contain crystoliths. Strong, characteristic odor; taste slight. When a mixture of 10 grammes of finely powdered Indian Hemp and 100 millilitres of *alcohol* (90 per cent.) is shaken occasionally during twenty-four hours and then filtered, 20 millilitres of the filtrate, evaporated in a flat-bottomed dish, yield a residue weighing, when dried at 100° C., not less than 0.250 gramme. Ash not more than 15 per cent." *Br.*

For a histological description of the leaf by A. R. L. Dohme, see *Proc. A. Ph. A.*, 1897, 569. The cannabis of the market may consist of fruiting tops and stems and occasionally the staminate tops are admixed with it.

William Beam in Bulletin No. 4 of the chemical Section of the Welcome Tropical Research Laboratories, Khartoum, has discovered a specific color reaction which may be used for the detection of *Cannabis indica* and its preparations. A petroleum ether extract of the suspected material is prepared and evaporated to dryness in a test tube. To this is added a few cc. of a reagent prepared by saturating absolute alcohol with dry hydrogen chloride gas. In the presence of cannabis the liquid assumes a bright cherry red color which is destroyed upon the addition of water or alcohol.

Constituents.—The activity of hemp undoubtedly resides in its resin, but the chemical nature of the active principle is unsettled. By repeated distillation of the same portion of water from relatively large quantities of hemp renewed at each distillation, M. J. Personne obtained a volatile oil, of a stupefying odor, and an action on the system such as to dispose him to think that it was the active principle of the plant. This oil was lighter than water, of a deep amber color, a strong odor of hemp, and composed of two distinct oils, one colorless, with the formula $C_{18}H_{20}$, the other a hydride of the first, $C_{18}H_{22}$, which was solid, and separated from alcohol in plate-like crystals. For the former Personne proposes the name of *cannabene.* It is affirmed that when this is inhaled, or taken into the stomach, a singular excitement is felt throughout the system, followed by a depression, sometimes amounting to syncope, with hallucinations which are generally disagreeable, but an action on the whole slighter and more fugitive than that of the resin. *Cannabindon,* $C_8H_{12}O$, is a dark red syrupy liquid obtained by Kobert (*Chem. Ztg.*, 1894, 741) from *Cannabis indica;* it is soluble in alcohol, ether and oils; it is affirmed to be narcotic in doses of from half a grain to two grains (0.032–0.13 Gm.). As a result of a reinvestigation of charras (churrus) from Indian hemp, Wood, Spivey, and Easterfield (*J. Chem. S.*, vol. lxix, 539) have found the following principles: 1, a terpene, boiling between 150° and 180° C.; 2, a sesquiterpene, boiling at 258° to 259° C.; 3, a crystalline paraffin of probable formula $C_{29}H_{60}$, melting at 63.5° C.; and 4, a red oil, boiling at 265° to 270° C. under a pressure of 20 mm., to which they give the name *cannabinol,* and the formula $C_{18}H_{24}O_2$. This latter constituent they consider the only active ingredient. It is probably the same substance as the dark red syrup of Kobert, mentioned above under the name of cannabindon. The authors found that cannabinol readily underwent superficial oxidation, at the same time losing its toxic activity. It is stated that cannabinol exhibits much more powerful effects when dissolved in a bland oil such as olive oil. Fränkel (*A. E. P. P.*, 1903, p. 266) claims to have isolated the active principle of hashish as a pure and chemically well defined body. It has the formula $C_{21}H_{30}O_2$, and is a phenol-aldehyde. It is of a pale yellow color and of a thick consistency. When heated it becomes quite fluid and distils at 215° C., under a pressure of 0.5 mm. It oxidizes in the air, acquiring a brown tint. It responds to Millon's reaction, and can be acetylized, showing thus its phenol character. Fränkel proposes that the name *cannabinol* be given to it and that the term *pseudo-cannabinol* be given to the substance of Wood, Spivey and Easterfield which Fränkel asserts is inert.

"**Assay.**—Hooper (*P. J.*, 1909, lxxxi, p. 80) describes a method for the chemical standardization of cannabis based upon its iodine value. He finds that the alcoholic extract of old samples has a lower iodine value than that from recent specimens, and there is more or less constancy of relation between the age and the iodine value.

The U. S. Pharmacopœia gives a physiological test for the standardization of *Cannabis indica.* Up to the present no means have been suggested for determining, with even approximate accuracy, the relative potency of different samples of *Cannabis indica,* the physiological test simply demonstrating that the drug possesses a certain indefinite amount of physiological action. The official test is based on the degree of inco-ordination produce in the dog in comparison with that produced by a standard preparation. It is advisable to use the same animal for repeated tests, because the individual susceptibility of the dog varies so greatly, and the experimenter gradually learns the degree of reaction to be expected from a certain dog. It is convenient to employ two dogs (fox terriers usually react well) to one of which will be given the standard and to the other the drug to be tested. Three days later the test should be repeated in reverse order, that is the dog which at the first test received the standard, at the second test should receive the unknown and *vice versa.* A fluidextract of the specimen to be tested is either evaporated into a soft extract and given in the form of a pill or mixed with an inert absorbing powder and enclosed in a capsule; it must not be given hypodermically. The symptoms caused by *Cannabis indica* in the dog recall those of alcoholism in the human being. There is at first a slight loss of control in the hind legs so that the animal staggers as he walks, later the ataxia becomes so marked that the dog is unable to stand up without leaning against some object, and about this time begins to show distinct drowsiness, and may eventually pass into a heavy sleep.

"Use adult dogs which weigh less than 15 kilogrammes and which are susceptible to the action of Cannabis. The dogs must not be fed for twelve hours before being used and observations should be made within one hour after administration The same animal must not be used for testing purposes at shorter intervals than three days. Administer the fluidextract in gelatin capsules by the mouth." *U. S.*

Standard Fluidextract of Cannabis.—In order to obviate the inaccuracies due to variations in susceptibility of the dogs, the present Pharmacopœia directs a comparison to be made with a standard fluidextract of cannabis. This is directed to be prepared as follows:

"Prepare a composite fluidextract, representing at least ten different lots of Cannabis, conforming to the official botanical description, and administer this fluidextract in gelatin capsules to dogs by the mouth. This standard fluidextract must be so adjusted that it will produce incoördination in dogs which have been found to be susceptible to the action of Cannabis when administered in doses of 0.03 cc. for each kilogramme of body weight of dog." *U. S.*

The Bureau of Chemistry, U. S. Department of Agriculture, has indicated its willingness to supply such a standard fluidextract of cannabis for the use of those who desire to make biological assays of this drug.

It has generally been believed that cannabis deteriorates rapidly, but Eckler and Miller (*J. A. Ph. A.,* 1917, vi, p. 872) found that the crude drug showed practically no change after a year's storage but that after two years it had lost about half of its potency; Hamilton (*J. A. Ph. A.,* 1918, vii, p. 117) believes that the loss must be usually much slower because he found a sample fourteen years old to be 70 per cent. of standard, and an extract, which had been constantly used for assay purposes for nine years, has shown no appreciable change.

Uses.—Aside from a slight local irritant effect the action of cannabis seems to be limited almost exclusively to the higher nerve centers. In man this is first manifested by a peculiar delirium which is accompanied with exaltation of the imaginative function and later by a remarkable loss of the sense of time. The delirium is often accompanied with motor weakness and diminished reflexes and generally followed by drowsiness. In the dog the earliest manifestation of the drug's action is a slight degree of restlessness which is soon followed by disturbances of equilibrium and later weakness of the legs and drowsiness.

Cannabis is used in medicine to relieve pain, to encourage sleep, and to soothe restlessness. Its action upon the nerve centers resembles opium, although much less certain, but it does not have the deleterious effect on the secretions. As a somnifacient it is rarely sufficient by itself, but may at times aid the hypnotic effect of other drugs. For its analgesic action it is used especially in pains of neuralgic origin, such as *migraine,* but is occasionally of service in other types. As a general nerve sedative it is useful in *hysteria, mental depression, neurasthenia,* and the like. It has also been used in a number of other conditions, such as *tetanus* and *uterine hemorrhage,* but with less evidence of benefit. One of the great hindrances to the wider use of this drug is its extreme variability. We are inclined to the opinion that one of the important reasons for the lack of confidence in this drug has been insufficiency in dosage. Because of the great variability in the potency of different samples of cannabis it is well nigh impossible to approximate the proper dose of any individual sample except by clinical trial. Because of occasional unpleasant symptoms from unusually potent preparations, physicians have generally been overcautious in the quantities administered. While the inclusion of a physiological assay in the Pharmacopœia has somewhat improved the quality of drug upon the market it must be remembered that the present method of standardization is not quantitatively accurate; all that can be hoped from this assay is the exclusion of inert samples. The only way of determining the dose of an individual preparation is to give it in ascending quantities until some effect is produced. The fluidextract is perhaps as useful a preparation as any; one may start with two or three minims of this three times a day, increasing one minim every dose until some effect is produced. According to C. R. Marshall (*L. L.*, 1897, i, also *J. A. M. A.*, Oct., 1898) the deterioration of cannabis is due to the oxidation of cannabinol, which he has found to act upon dogs and cats as the crude drug.

Dose, of cannabis, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Extractum Cannabis, *U. S.* (*Br.*); Fluidextractum Cannabis, *U. S.*; Tinctura Cannabis (from Extract), *Br.*; Collodium Salicylici Composita (from Fluidextract), *N. F.*; Mistura Chlorali et Potassii Bromidi Composita (from Extract), *N. F.*; Mistura Chloroformi et Morphinæ Composita (from Tincture), *N. F.*

CANTHARIDINUM. Br.

CANTHARIDIN

"Cantharidin, $C_{10}H_{12}O_4$, may be obtained from various species of Cantharis or of Mylabris." *Br.*

Cantharidine, *Fr. Cod.*; Kantharidin, *G.*; Cantaridina, *Sp.*

Cantharidin is the anhydride (lactone) of *cantharidic acid* and is officially recognized by the Br. Pharm. (1914) and the Swiss and French Pharmacopœias. Preparations made from cantharidin are believed to be more uniform in quality than those made from cantharides because they are made from a definite crystallizable product and it is not always easy to extract all of the cantharidin from powdered Spanish flies by the usual methods, as in making the vinegar, tincture, collodion, cerate or plaster. It has also the theoretical advantage that it can be obtained from various other beetles and hence would still be available in case of a shortage of the true cantharides. (See *Cantharis.*)

E. Dieterich prepares cantharidin by macerating 1000 parts of coarsely powdered cantharides in 1500 parts of acetic ether mixed with 20 parts of sulphuric acid; after adding 40 parts of barium carbonate to neutralize the excess of sulphuric acid, the mixture is exhausted with acetic ether in an extraction apparatus, the liquid is distilled, and the residue, consisting of cantharidin, resin, fat, etc., is set aside for eight days to allow the cantharidin to crystallize; 200 parts of petroleum benzin (sp. gr. 0.740) are then added, gently heated in order to dissolve the fatty matter, the liquid filtered, and the cantharidin washed with petroleum benzin and recrystallized from its solution in 90 per cent. alcohol. If perfectly pure cantharidin is needed, the cantharidin may be dissolved in acetic ether or chloroform and the solution passed through animal charcoal, filtered, and allowed to crystallize. (*J. P. C.*, 1893, 375.)

Properties.—"Colorless glistening crystals, inodorous. Very slightly soluble in *water, petroleum spirit,* or *alcohol* (90 per cent.); more soluble in *chloroform,* in *acetic ether,* and in *acetone;* soluble also in fixed oils. A 0.1 per cent. solution in a fixed oil raises blisters when kept in contact with the skin. Melting point 210° to 212° C. Slowly volatilises at 100° C., more rapidly at higher temperatures. Soluble in *solution of sodium hydroxide,* the solution depositing crystals of Cantharidin when acidified. Gently warmed with *sulphuric acid* it yields a colorless solution, from which it is separated unchanged when freely diluted with *water.*" *Br.*

Cantharidin itself has been found to combine like an acid with salifiable and earthy bases, forming soluble compounds with potassium, sodium, and lithium hydroxides, salts of very sparing solubility with baryta, strontia, and lime, and with magnesia a salt which, though feebly soluble in water (100 parts of water dissolving only 0.24 of the salt) (see *P. J.*, March 13, 1880), is much more largely dissolved in cold than hot water, and in cold than in hot alcohol. The potassium salt crystallizes with 3 molecules of water, and is soluble in 25 parts of water. On the addition of strong acids to this solution, cantharidic acid is not precipitated, as might be expected, but the lactone cantharidin. This potassium salt has been recommended by Liebreich for subcutaneous injections. The most satisfactory test of cantharidin is its vesicating property. Notwithstanding the insolubility of this principle in water and cold alcohol, the decoction and tincture of cantharides have the medicinal properties of the insect; and Lewis ascertained that both the aqueous and alcoholic extracts act as effectually in exciting vesication as do the flies themselves, while the residue is in each case inert. Cantharidin probably exists in the insect so combined as to be rendered soluble in water and cold alcohol; if as stated by E. Dieterich (1883), formic acid is present in the Spanish fly, it is possible that the solution of the cantharidin is due to its presence. He also showed that cantharidin was not volatilized with the vapor of benzin, a fact which may prove useful in preparing blistering plasters coated with a benzin solution of cantharidin. (*Ph. Centralh.*, 1901, 464.) H. G. Greenish calls attention to the fact that much loss of cantharidin takes place in making the various pharmaceutical preparations, through insufficient exhaustion by the use of the ordinary solvents. He obtained 0.822 per cent. of cantharidin from exhausted residues. Homolka records (*B. Chem. G.*, 1886, xix, 1082) the results of an investigation of the chemical decompositions of cantharidin.

Uses.—Cantharidin is used for the same purposes as Cantharides (see below). Liebreich strongly recommended hypodermic injections of cantharidin in the treatment of *phthisis,* but general clinical experience has not confirmed the value of the remedy. *Liebreich's cantharidal solution* was made by heating 20 cc. of water with 0.2 Gm. of cantharidin and 0.4 Gm. of potassium hydroxide until solution was obtained, then adding enough water to make 1000 cc. Of this solution he injected from 0.5 to 1.0 cc. at a dose.

Dose, of cantharidin, is from one two-hundred-and-fortieth to one one-hundred-and-twentieth grain (0.00025–0.0005 Gm.).

Off. Prep.—Acetum Cantharidini, *Br.;* Emplastrum Calefaciens, *Br.;* Emplastrum Cantharidini, *Br.;* Liquor Epispasticus, *Br.;* Tinctura Cantharidini, *Br.;* Unguentum Cantharidini, *Br.;* Collodium Vesicans (from Liquor Epispasticus), *Br.*

CANTHARIS. U. S.

CANTHARIDES Canthar. [Spanish Flies, Russian Flies]

"Cantharides consists of dried insects [*Cantharis vesicatoria* (Linné) De Geer (Order *Coleoptera*)]. Cantharides yields not less than 0.6 per cent. of cantharidin and not more than 10 per cent. moisture." *U. S.*

Blistering Flies; Muscæ Hispanicæ; Cantharide, *Fr.;* Cantharides, *P. G.;* Spanische Fliegen, Kantharide, Canthardén, *G.;* Cantaride, Cantarella, Mosca di Spagna, *It.;* Cantarida, *Sp.*

Cantharis is recognized in all of the European Pharmacopœias, but has been dropped by the British authority, being replaced by cantharidin.

The term *Cantharis* was employed by the ancient Greek writers to designate many coleopterous insects or beetles. Linnæus gave the title to a genus not including the official blistering insect, and placed this in the genus *Meloë,* which, however, has been since divided into several genera. Geoffrey made the Spanish fly (beetle) the prototype of a new genus, *Cantharis,* substituting *Cincindela* as the title of the Linnæan genus. Fabricius altered the arrangement of Geoffrey, and substituted *Lytta* for *Cantharis* as the generic name. The former was adopted by the London College, and at one time was in extensive use; but, the latter, having been restored by Latreille, is now recognized in the British and U. S. Pharmacopœias, and is universally employed. By this naturalist the vesicating insects were grouped in a small tribe, corresponding very nearly with the Linnæan genus *Meloë,* and distinguished by the title *Cantharidæ.* This tribe he divided into eleven genera, among which is *Cantharis.*

Cantharis vesicatoria is from 15 to 25 mm. long, and of a shining, golden-green color. The head is large and heart-shaped, bearing a pair of stout mandibles and filiform antennæ; the thorax short and quadrilateral; the wing-sheaths long and flexible, covering brownish membranous wings. (Snyder, *A. J. P.,* 1908, p. 545.) When alive, the Spanish flies have a strong, penetrating, fetid odor, compared to that of mice, by which swarms of them may be detected at a considerable distance. They attach themselves preferably to certain trees and shrubs, such as the white poplar, privet, ash, elder, and lilac, upon the leaves of which they feed. They are most abundant in Spain, Italy, and Southern France, but are found also in all the temperate parts of Europe and in Western Asia. According to the researches of Lichtenstein, the eggs are laid by the female in the latter part of June in small cylindrical holes made in the ground. A week later the larvæ hatch out. They are a millimeter long, with two long caudal threads, and of a brown color. After many efforts, Lichtenstein succeeded in getting them to feed on the honey contained in the stomach of bees. In a few days they changed into milk-white larvæ, and about a month after this buried themselves in the ground, to assume the chrysalis stage and to hatch out the following spring as perfected beetles. In the wild state the larvæ are said to crawl up flowers and attach themselves to bees or other hymenopterous insects; carried by the bee to the hive, the larvæ feed upon the young bees and the honey and bee-bread stored up for use. The beetles usually make their appearance in swarms upon the trees in May and June, when they are collected.

The time preferred for this purpose is in the morning, at sunrise, when they are torpid from the cold of the night, and easily let go their hold. Persons with their faces protected by masks, and their hands with gloves, shake the trees, or beat them with poles; and the insects are received as they fall upon linen cloths spread underneath. They are then plunged into vinegar diluted with water, or exposed in sieves to the fumes of ammonia, vinegar, chloroform, burning sulphur or carbon bisulphide, and, having been thus deprived of life, are dried either in the sun, or in apartments heated by stoves. This mode of killing the flies by the steam of vinegar is as ancient as the times of Dioscorides and Pliny. When perfectly dry, they are introduced into casks or boxes lined with paper and carefully closed, so as to exclude as much as possible the atmospheric moisture.

Cantharides come chiefly from Spain, Southern Russia and Hungary, and other parts of the Mediterranean as Sicily, Poland, and Roumania. The Russian flies are most esteemed. They may be distinguished by their greater size, and their color approaching to that of copper.

In the United States are several species of Cantharis, which have been employed as substitutes for *C. vesicatoria* and found equally efficient; but none of them are now recognized by the U. S. Pharmacopœia, even *C. vittata,* which was at one time official, having been discarded. For description of unofficial blistering beetles, see *U. S. D.,* 19th edition, p. 284. Various other allied insects have been used at one time or another as a substitute for the Spanish beetle.

Cantharis vittata Latreille or "potato fly" was recognized by the U. S. P., 1850. It is rather smaller than *C. vesicatoria,* which it resembles in shape. Its length is about six lines. The head is light red, with dark spots upon the top; the feelers are black; the elytra or wing-cases are black, with a yellow longitudinal stripe in the center, and with a yellow margin; the thorax is also black, with three yellow lines; and the abdomen and legs, which have the same color, are covered with a cinerous down. It inhabits chiefly the potato vine, and appears about the end of July or beginning of August, in some seasons very abundantly. Fahnestock procured 1⅓ per cent. of the cantharidin from this beetle. (*A. J. P.*, xxviii, 195; li, 298.) This insect must not be confounded with the "potato bug," the *Colorado potato beetle* (*Doryphora decemlineata*), which has proved so destructive to potato plants, and which, according to the researches of L. Dembinski (*A. J. P.*, 1877, p. 550) contains no cantharidin.

Mylabris cichorii is thought to be one of the insects described by Pliny and Dioscorides under the name of cantharides, and is to this day employed in Italy, Greece, the Levant, Egypt, and China. W. R. Warner found 500 parts of *M. cichorii* to yield 2.13 parts of cantharidin. (*A. J. P.*, xxviii, 195.) The *M. cichorii* was formerly imported to some extent under the name of *Chinese blistering fly*. It is black, with the powder blackish gray and free from shining particles; it yielded to Fahnestock 1.25 per cent. of cantharidin. (*A. J. P.*, 1879.)

The Br. Add. under the name of *Mylabris* formerly recognized not only the dried beetle, *Mylabris phalerata* Pallas (*M. Sidae* Fabr.) but also allowed the use in the Colonies of other species of the genus, provided that they yield a similar proportion of cantharidin. Mylabris was characterized in the Br. Add. as "usually an inch (twenty-five millimetres) or rather more long, and three-eighths of an inch (nine millimetres) broad; with two long elytra, each three times as long as broad, black with two broad wavy transverse orange-colored bands and a large orange-colored spot at the base of each; one pair of brown membranous wings."

Among other insects that have occasionally found their way into commerce may be mentioned: *Cantharis quadrimaculatus* (*Mexican Cantharides*), *Mylabris lunata, M. bifasciata* (from South Africa), *Epicauta gorhami* (from Japan), *Lytta aspersa* (from Argentina), etc.

Description and Physical Properties.—"*Unground Cantharides.*—From 15 to 25 mm. in length, 5 to 8 mm. in breadth, oblong, somewhat compressed above; of a brilliant green or bluish-green, metallic luster, changing in different parts, especially beneath, to a golden-green; head triangular, separated into two lateral lobes by a faint median line; mandibles stout and partly concealed; antennæ filiform, of eleven conical joints, the upper ones being black; eyes comparatively small; prothorax angulate; legs with five tarsal joints; wings membranous and brownish; elytra or wing sheaths each with two parallel lines and finely wrinkled; odor strong, disagreeable; taste slight, afterwards acrid. Cantharides with an ammoniacal odor must not be used.

"*Powdered Cantharides.*—Grayish-brown, with shining green particles and a number of long, pointed, spicules 0.500 mm. in length and 0.020 mm. in width.

"**Assay.**—Place 15 Gm. of Cantharides, in moderately coarse powder, in a stout bottle of not less than 250 cc. capacity, add 150 cc. of a mixture of benzene, two volumes, and purified petroleum benzin, one volume, and then add 2 cc. of hydrochloric acid. Stopper the bottle tightly, shake it well, and allow it to stand about ten hours. Now gradually warm the bottle and its contents to about 40° C., and maintain it at approximately that temperature with frequent shaking during three hours, avoiding evaporation. If necessary add additional solvent to replace any lost by evaporation. Cool the mixture, decant or filter off 100 cc. of the clear solution, and evaporate this rapidly in a tared beaker or wide-necked flask to a volume of about 5 cc. Add 5 cc. of chloroform to the residue and set it aside in a moderately warm place. When the solvent has all evaporated, add to the crystals 10 cc. of a mixture of equal volumes of dehydrated alcohol and purified petroleum benzin, which has previously been saturated with pure cantharidin, allow the mixture to stand during fifteen minutes, and then decant the liquid through a pledget of purified cotton. Wash the crystals with successive portions of a saturated solution of cantharidin, similar to that directed above, until free from fat and coloring matter, and pass the washings through the same pledget of purified cotton. Then wash the cotton with a very small quantity of warm chloroform to dissolve any adhering crystals, collect the chloroform in the tared flask or beaker containing the washed crystals, evaporate the solvent with the aid of a blast of air, dry the crystals at 60° C. for one half hour, and weigh. The resulting weight will be the amount of cantharidin obtained from 10 Gm. of Cantharides." *U. S.*

For other methods of assay see *U. S. D.*, 20th ed., p. 281; also *P. J.*, 1903, p. 558 and p. 783.

Dried Spanish flies preserve the form and color, and, to a certain extent, the disagreeable odor, of the living insect. They have an acrid, burning, and urinous taste. If kept perfectly dry, in well-stoppered glass bottles, they retain their activity for a great length of time, but exposed to a damp air they quickly undergo putrefaction, and this change takes place more speedily in the powder. Hence the insects should either be kept whole, and powdered as they are wanted for use, or, if kept in powder, should be well dried immediately after pulverization, and preserved in air tight vessels. They should never be purchased in powder, as, independently of the consideration just mentioned, they may in this state be more easily adulterated. Davis (*Proc. Mich. Ph. Ass.*, 1910, p. 62) reports that when cantharis is subjected to a microscopical examination the presence of other kinds of beetles and insects may be detected. But, however carefully managed, cantharides are apt to be attacked by mites, which feed on the interior soft parts of the body, reducing them to powder, while the hard exterior parts are not affected. An idea was at one time prevalent that the vesicating property of the insect was not injured by the worm, which was supposed to devour only the inactive portion. But this has been proved to be a mistake. Farines, an apothecary of Perpignan, has satisfactorily shown that, though the hard parts left by these mites possess some vesicating power, the sound flies are much stronger. Among the best means of preserving them, whether whole or in powder, is the application of the process of Apert, which consists in exposing them for half an hour, confined in glass bottles, to the heat of boiling water, which destroys the eggs of the insect, without impairing the virtues of the flies. (*J. P. C.*, xxii, 246.) Of course, the access of water to the flies should be carefully avoided. The use of chloroform or carbon tetrachloride are among the simplest, safest and best preservatives to prevent the development of insects in drugs. Cantharides will bear a very considerable heat without losing the brilliant color of their elytra; nor is this color extracted by water, alcohol, ether, or the oils, so that the powder might be deprived of all its active principle and yet retain the exterior characters unaltered. The wing-cases resist putrefaction for a long time, and the shining particles have been detected in the human stomach, months after interment.

The activity of cantharides is due to the anhydride cantharidin which was discovered by Robiquet in 1810. (See previous article.) There is present also about 12 per cent. of a fixed oil and, according to Orfila, a volatile principle, upon which the fetid odor of the fly depends. It is separable by distillation with water. The green color is probably not due to chlorophyll as was formerly believed, nor to any pigment at all, but is produced by light interference of their translucent films of tissue. Cantharidin exists in commercial cantharides to the extent of from 0.6 to 0.9 per cent. (See also *Ph. Centralh.*, 1901, 674.)

Adulterations.—These are not common. Occasionally other insects, or even beads, are added, purposely or through carelessness. These may be readily distinguished by their appearance. Flies exhausted of their cantharidin are sometimes substituted for the genuine drug. They are worthless, and are to be distinguished by their lack of substance and their yielding a nearly colorless ethereal tincture.

The percentage of cantharidin found in cantharides furnishes the best test of their virtues.

Uses.—Internally administered, cantharides are a powerful irritant, with a peculiar direction to the urinary and genital organs. Genito-urinary irritation is ordinarily the first symptom produced by small doses of cantharides, and, if the dose has been large enough, it may amount to violent strangury, attended with excruciating pain, and the discharge of bloody urine.

Lipsitz and Cross (*A. I. M.*, 1917, xx, 913) have found that cantharides cause a marked increase in the number of red blood cells, but Morgulis and Muirhead (*A. I. M.*, 1919, xxiii, 190) believe that this is only an apparent increase due to the loss of water from the system.

Cantharides or some similar vesicating insect appears to have been used as far back as the time of Hippocrates in the treatment of dropsy and amenorrhea. While there is no doubt that by its local irritant effect cantharides will increase the quantity of urine, because of the danger of undue irritation of the kidney, it has been almost completely abandoned in favor of less harmful diuretics.

Because of the priapism seen in cantharides poisoning the drug is often used in *sexual impotence* but it is capable of such serious injury that its employment is not often advisable. As an internal remedy, cantharides is of little practical value.

Externally applied, cantharides excite inflammation in the skin, which terminates in a copious secretion of serum under the cuticle. It may be employed either as a rubefacient, or to blister. In the former capacity it has no peculiar value, but as an epispastic it is preferred to all other substances. When blisters are allowed to stay on only long enough to irritate the skin, but not to blister, they are known as *flying blisters*. Used in this way, they are sometimes of service in *neuralgias*, applied directly over the seat of pain. The chief use of cantharides is to produce true blisters for the relief of various internal inflammations as *neuritis, peritonitis, pneumonia, pleurisy*, etc.

It is possible for enough cantharidin to be absorbed by the raw surface of a blister to cause marked irritation of the genito-urinary tract. In order to avoid such genito-urinary irritation, and also as much as possible the pain at the seat of application, the blister should be left on only until it distinctly reddens the skin, when a flaxseed poultice may be applied, and in the course of two or three hours the blister is formed. The time necessary for such reddening of the skin is usually from four to six hours, if the cantharides be active. (See *Ceratum Cantharidis.*)

Toxic doses of Spanish fly produce obstinate and painful priapism, vomiting, bloody stools, severe pains in the whole abdominal region, excessive salivation with a fetid breath, hurried respiration, a hard and frequent pulse, burning thirst, exceeding difficulty of deglutition, sometimes a dread of liquids, frightful convulsions, tetanus, delirium, and death. Orfila has known twenty-four grains of the powder to prove fatal. Dissection reveals severe and acute inflammatory changes in the kidney, the intestines and sometimes the spleen (see *J. A.*

M. A., 1921, lxxvi, p. 50). According to Poumet, if the intestines be inflated, dried, cut into pieces, and examined in the sun between two pieces of glass, they will exhibit small shining yellow or green points, strongly contrasting with the matter around them. (*J. P. C.,* 3e sér., iii, 167.)

The poisonous effects are to be counteracted by the use of emetics, cathartics, and opiates by the stomach and rectum. From the experiments of Schroff it seems that oils somewhat accelerate the poisonous action, probably by dissolving the cantharidin. (See *A. J. P.,* xxviii, 365.) The use of animal charcoal as an antidote was suggested by Thouery, a French apothecary, in 1858, but as far as we know has not been tried in human poisoning.

The dose of cantharides may be stated as one-half to one grain (0.032–0.065 Gm.) but it is rarely prescribed.

Off. Prep.—Ceratum Cantharidis, *U. S.;* Emplastrum Cantharidis (from Cerate), *U. S.;* Tinctura Cantharidis, *U. S.*

CAPSICUM. U. S. (Br.)

CAPISCUM Capsic. [Cayenne Pepper, African Chillies]

"Capsicum is the dried ripe fruit of *Capsicum frutescens* Linné (Fam. *Solanaceæ*), grown in Africa. Capsicum contains not more than 3 per cent. of its stems, calyxes, and not more than 1 per cent. of other foreign organic matter, yields not less than 12 per cent. of non-volatile ether-extractive, and not more than 1.25 per cent. of acid-insoluble ash." *U. S.* "Capsicum is the dried ripe fruit of Capsicum minimum, *Roxb.*" *Br.*

Capsici Fructus, *Br.;* Piper Hispanicum; Capsicum Fruit, African or Pod Pepper, Red Pepper, Chillies, Bird Pepper, Spur Pepper; Fructus Capsici, *P. G.;* Spanischer Pfeffer, Schlotenpfeffer, *G.;* Piment de Cayenne, Piment des Jardins, Poivre d Espagne, Poivre de Guinée, Poivre d'Inde, Poivre de Cayenne, Piment rouge, Capcique, *Fr.;* Peperone, *It.;* Pimiento, Chile, Aji, *Sp.*

Owing probably to its widespread cultivation, the genus *Capsicum* contains a large number of plant forms whose specific relations afford a very difficult problem to the systematic botanist. The probability is that the entire genus was originally confined to the American tropics, although it has been cultivated since the time of Columbus in the temperate and tropical zones of almost the whole world. Its first appearance in literature seems to be in an epistle by Peter Martyn, dated September, 1493, speaking of its having been brought by Columbus. Neither in ancient Sanscrit, Chinese, Greek, Latin, or Hebrew is there a name for it. In 1887 Asa Gray expressed his belief that there are only two species in the genus, although in the last previous revision of the genus, in 1852, Dunal had recorded fifty species. After a very thorough and careful study of the subject, including the cultivation of every procurable variety and species for four years in the Missouri Botanical Garden, H. C. Irish reached the conclusion that the dictum of Gray was correct, and that there are really only two species of the genus, one of which is herbaceous and annual or biennial, the other shrubby and perennial, a conclusion which seems to be accepted.

The first of these species is the one most extensively cultivated in Europe and in this country; it is the *C. annuum* L. The second is in its varieties very largely grown in the tropical and subtropical latitudes, its fruit not ripening at all or only to a slight degree in the temperate zone. It is the species which was described under the name of *C. frutescens,* by Linnæus, in 1737. By Irish it is divided into two varieties—*C. frutescens* proper, which is characterized by its fruit being oblong, acuminate, and usually embraced by the calyx, and *C. frutescens baccatum,* which is characterized by its ovate or subround fruit, usually seated on the calyx. This variety is the *C. baccatum* of Linnæus, 1767. In the first of these varieties are comprised the *C. fastigiatum* of Blume and the *C. minimum* of Miller and of Roxburgh, which yield most of the Cayenne pepper produced in the tropics, although, especially in the West Indies and South America, *C. baccatum* is largely cultivated.

The British Pharmacopœia seems to be in error in ascribing the original description of the *Capsicum minimum* to Roxburgh, since his *Flora Indica* did not appear until 1832, whereas the species was described by Miller, in the *Garden Dictionary,* in 1771.

Capsicum frutescens, the shrubby capsicum, is cultivated in the United States, Mexico, India, Japan and British East Africa. The fruits are collected when fully mature, deprived of their calyces, and carefully dried. Most of the drug used in this country comes from Zanzibar, Mombaza, Nyasal or Sierra Leone.

The following are the characteristics of the plant as given by Irish: "Plants shrubby, perennial, two and a half to six feet high. Branches angular, often channelled, puberulent or pubescent, especially on the younger portions; usually greatly enlarged and slightly purple at the nodes, green or sometimes purplish striate. Leaves broadly ovate, acuminate, 7.5 to 15 cm. long, usually puffed or wrinkled, more or less pubescent, especially around the veins. Petioles medium, usually subciliate; peduncles slender, 2.5 to 5 cm. long, often in pairs, usually longer than the fruit. Calyx usually cup-shaped, embracing base of the fruit; teeth short, corolla white or greenish white, spreading 10 to 20 mm. long, often with ocherous markings in the throat. Fruit red, ovate, obtuse or oblong acuminate, 20 to 30 mm. long and 6 to 18 mm. in diameter."

Capsicum annuum is largely cultivated both in the United States and in Europe, flowering in the early or middle summer, and ripening its fruit in the early autumn. There are numerous varieties of it differing in the shape of their fruit. That which is chiefly cultivated in the United States for market, to be used in the green state in pickling, or cooked for the table, is a large irregularly ovate or conical berry depressed or horned at the extremity, and when ripe varying in color from yellowish to scarlet. A variety with a long, conical, pointed and recurved fruit, which is usually not thicker than the finger, is said to be especially used in the making of red pepper. In another variety the berries are not more than an inch in diameter, spherical and slightly compressed.

When ground into powder the fruit of the *Capsicum annuum* constitutes *paprika,* or as it is sometimes called, *sweet pepper;* it has scarcely more than one-sixth the pungency of real cayenne pepper, so that the addition of it to powdered chillies may be considered an adulteration.

Paprika or *Hungarian pepper* is recognized by the German Pharmacopœia. It is usually imported into the United States in a ground condition, three grades being recognized. 1. *Rosen-paprika* or *Rozsapaprika,* the best grade, possesses a beautiful red color and has a savory taste. It is prepared from the selected pericarp and seeds which are carefully washed before being ground, the stems and placentæ being removed. 2. *Königs-paprika* or *Kiralypaprika* is prepared by grinding the entire pods, including not only the seed but the stems. 3. *Mercantil-paprika* is prepared from the spotted pods, remaining from the selection for the finer grades, and from the pods containing flaws and also contains the stems, seeds and other parts. The last grade has a pale yellow color and is much more pungent. (Tolman and Mitchell, *Bull. No. 163, Bureau of Chemistry, U. S. Dept. of Agriculture.*) The cayenne pepper of the grocery stores is often a mixture of paprika and true pepper. It is possible to distinguish the presence of paprika in powdered capsicum by the microscopic differences of the epidermal cells of the pericarp as seen in a surface view; those of paprika are polygonal and irregularly arranged whereas those of true capsicum are rectangular and arranged in parallel rows.

T. Edward Wallis believes that the different cayenne peppers can be distinguished from one another when powdered by the character of their epidermis and the tissue immediately below it, and gives the following tabulated summary of the differences. (*P. J.*, July, 1902.)

	C. minimum.	*C. annuum.*	*Japanese Chillies.*
Epidermis.	Thick and straight-walled rectangular cells with few pits; often arranged in groups of five to seven in a row and with a uniformly striated cuticle. Size of cells, 25 mkm. to 60 mkm. in either direction.	Irregular polygonal cells with evenly thickened walls, traversed by numerous well-marked, simple pits. The cuticle shows striated ridges. Size of cells, 60 mkm. to 100 mkm. long, and 25 mkm. to 50 mkm. wide.	Cells with strongly thickened walls and a radiated lumen. The pits only rarely penetrate the whole thickness of the wall. No visible striation. Size of cells, 30 mkm. to 80 mkm. long, and 15 mkm. to 45 mkm. wide.
Hypodermis.	Delicate thin-walled cellulose cells.	Several layers of cuticularized collenchymatous cells, having a rounded outline and very few pits.	A single layer of regular polygonal cells with cuticularized, fairly thick walls, traversed with numerous pits, which give them a beaded appearance.

The varieties of cayenne peppers are numerous as they occur in the American market—the pods of the *East African pepper* are about 12 mm. in length, flattened, almost cylindrical, although showing distinctly the conical form; the pods of the *Madagascar pepper* reach the length of 6 to 7 cm. and a breadth of about 20 mm.; those of the *Bombay* or *cherry pepper* are very dark in color, 3.5 to 5 cm. in length, and 12 mm. or more in breadth at the base. They are strictly conical and less likely to be flat than those of the other varieties. *Zanzibar pepper* is smaller than the *East African pepper* but otherwise similar to it. *Japanese capsicum,* whose botanical source is not positively known, occurs in the market in two forms, one in which the pods are large, reaching the length of about 6 cm.; the other in which the small pods are not 2.5 cm. in length. The larger pods are scarcely to be distinguished from *Madras chillies;* the smaller resemble, but are nearly twice the size of, the East African pepper. The color of the pods varies from light yellowish-brown to deep red.

Description and Physical Properties.—"*Unground Capsicum.*—Oblong conical, usually laterally compressed, from 10 to 25 mm. in length, from 4 to 8 mm. in diameter, 2- or 3-locular, the dissepiments united to a short conical placenta at the base of the fruit; pericarp orange to dark brownish-red, glabrous, shriveled, dull, thin, membranous; inner surface longitudinally striate, with 2 or 3 distinct longitudinal ridges; seeds, yellowish or brownish, 6 to 21, circular or irregular, flattened, from 2 to 4 mm. in diameter, with a thickened edge and prominent pointed micropyle; odor characteristic, sternutatory; taste intensely pungent. Calyx light greenish-brown, inconspicuous, inferior, 5-toothed, usually attached to a long, straight peduncle.

"*Structure.*—Outer epidermis of mostly quadrangular cells from 0.020 to 0.080 mm. in length, from 0.020 to 0.045 mm. in width and from 0.015 to 0.020 mm. deep, arranged in irregular rows, with thickened and cutinized outer and radial walls, the surface of the cuticle finely striated, the radial walls somewhat wavy and very slightly beaded; mesocarp of thin-walled parenchyma containing reddish-yellow oil globules; endocarp of elongated cells, some of them very thin-walled, others in large oval areas, with thickened, beaded lignified walls. Epidermal cells of seed irregular in outline up to 0.250 mm. in length, with very wavy, contorted, lignified walls, the cells from the edge of the seed much thicker-walled than those from the flat surface of the seed. Embryo curved and embedded in the endosperm, the latter consisting of small, thin-walled parenchyma, containing small aleurone grains and fixed oil.

"*Powdered Capsicum.*—Yellowish or reddish-brown; consists of thin-walled parenchyma containing oil globules, epidermal cells of pericarp and seed-coat and stone cells of endocarp.

"Fragments of pericarp with outer epidermis consisting of irregular cells up to 0.100 mm. in length, not arranged in regular rows and with strongly beaded radial walls, and with a hypodermis of angular cells with thickened, beaded walls, indicate the presence of Japanese or East Indian Capsicum. Capsicum should meet the requirements of the following test: Mix well 1 Gm. of powdered Capsicum in 50 cc. of alcohol in a stoppered flask and macerate for twenty-four hours. Dilute 0.1 cc. of the clear, supernatant liquid with 140 cc. of distilled water containing 10 per cent. of sucrose: 5 cc. of this dilution swallowed at once will produce a distinct sensation of the pungency of Capsicum in he throat of at least two out of three individuals.

"**Assay.**—For non-volatile ether-soluble extractive, proceed as directed on page 1552." *U. S.*

The Br. Pharm. gives the characteristics of the fruit of *C. minimum* as "Dull orange-red, oblong-conical, obtuse, two-celled fruits, from about twelve to twenty millimetres in length and about six millimetres in diameter; sometimes attached to a five-toothed inferior calyx, and long, straight, slender peduncle. Pericarp somewhat shrivelled, glabrous, translucent and leathery, containing from ten to twenty small flat seeds, either loose or attached to a thin reddish dissepiment. The cells of the outer epidermis of the pericarp have moderately thick walls, are often arranged in rows of five to seven, and exhibit a cuticle uniformly striated (distinction from the fruits of other species of Capsicum). Characteristic odor; taste intensely pungent. Ash not more than 7 per cent." *Br.*

A detailed description of African chillies can be found in Youngken's *Pharmacognosy.*

Gathercoal and Terry (*J. A. Ph. A.*, 1921, x, 423) recommend an organoleptic test; as a standard for pungency they suggest either capsaicin or piperine. The U. S. now includes a test of this type.

The difficulty of distinguishing the source of powdered capsicum is increased by the fact that the red color fades upon exposure to light, and that the powdered African pepper, though very powerful, is a light brownish-yellow. The value of any specimen may be, however, fairly estimated by the intensity of its odor, which is peculiar, somewhat aromatic, and extremely irritant, and by its acrid, burning taste.

Constituents.—The principle described by Braconnot, and named *capsicin,* is a mixed substance, consisting of resinous and fatty matters. In 1876, Thresh isolated a well defined active principle, *capsaicin,* from the extract which he obtained by exhausting Cayenne pepper with petroleum. From the red liquor dilute caustic alkali removes capsaicin, which is to be precipitated in minute crystals by passing carbon dioxide through the alkaline solution. The crystals may be purified by recrystallizing them from either alcohol, ether, petroleum benzin, glacial acetic acid, or hot carbon disulphide; in petroleum, capsaicin is but sparingly soluble, yet it is dissolved abundantly on the addition of fatty oil. The crystals of capsaicin are colorless, and have the formula $C_{18}H_{27}O_3N$, but is not alkaloidal. E. K. Nelson states that capsaicin is a condensation product of vanilylamine (3-hydroxy-4-methoxy-benzylamine) with decylenic acid. They melt at 59° C., and begin to volatilize at 115° C., but decomposition can be avoided only with great care. The vapors of capsaicin are of the most dreadful acridity, and even the ordinary manipulation of that substance requires much precaution. Moerbitz (1898) isolated a pungent principle having a bitter taste, which he states is neither capsicin nor capsicol, and names *capsicutin.* He gives it the formula $C_{35}H_{54}O_4N_3$, and states that it is neither an alkaloid nor glucoside; it does not have acid properties.

Red lead oxide has been added to the powdered capsicin sold in Europe; it may be detected by digestion in diluted nitric acid, and precipitating the lead by sodium sulphate. Capsicum is said to be sometimes adulterated with colored sawdust, which may be recognized by the microscope. It is often adulterated with inert vegetable substances. The British Pharmacopœia requires that capsicum should yield on incineration not more than 6 per cent. of ash; this test would detect the presence of most adulterants. It is frequently attacked by insects.

Uses.—Capsicum is a very powerful local stimulant, producing, when swallowed, a sense of heat in the stomach, and a general glow over the body without any narcotic effect. It is much employed as a condiment, especially in hot climates, and is useful in cases of *atony of the stomach* or *intestines.* It is strongly contraindicated by the existence of gastric catarrh of the ordinary type, but in the chronically inflamed stomachs of persons of intemperate habits it frequently appears to do good. It is also of value in certain cases of serous *diarrhea,* not dependent on true inflammation of the intestines.

Applied externally, Cayenne pepper is a powerful rubefacient, which has the advantage of acting speedily without the danger of producing vesication. It may be applied in the form of cataplasm, or more conveniently and efficiently as a liniment. It may be used in strengths of from 10 to 20 per cent. mixed either with alcohol or cotton-seed oil. The powder or tincture brought into contact with a *relaxed uvula* often acts very beneficially. The tincture has also been used advantageously in *chilblain*. The fluidextract and the oleoresin (*Oleoresina Capsici, U. S.*) are powerfully rubefacient. A gargle may be prepared by infusing half a drachm of the powder in a pint of boiling water, or by adding half a fluidounce of the tinctura to eight fluidounces of rose water.

Dose, of the powder, from one to five grains (0.06–0.3 Gm.), which is most conveniently given in the form of pill.

Off. Prep.—Oleoresina Capsici, *U. S.;* Tinctura Capsici, *U. S., Br.;* Unguentum Capsici, *Br.;* Mistura Chloroformi et Morphinæ Composita (from Tincture), *N. F.;* Mistura Opii et Chloroformi Composita (from Tincture), *N. F.;* Mistura Opii et Rhei Composita (from Tincture), *N. F.;* Pulvis Myricæ Compositus, *N. F.;* Tinctura Capsici et Myrrhæ, *N. F.*

CARAMEL. N. F.

CARAMEL Caram. [Saccharum Ustum, Burnt Sugar Coloring]

"A concentrated aqueous solution of the product obtained by heating sugar or glucose until the sweet taste is destroyed and a uniform dark brown mass results, a small amount of alkali or alkali carbonate being added while heating." *N. F.*

Gebrannte Zucker, *G.*

When sucrose is heated above its melting point but short of a charring temperature it develops a deep brown color, and is finally transformed to a brown, sticky mass which is called caramel. Glucose, when treated similarly, yields a like product. Caramel is undoubtedly a carbohydrate of high molecular weight and condensation or a polymerization product of the monosaccharids or disaccharids. Its formula has been suggested as $C_{125}H_{188}O_{80}$. It is usually found in commerce as a thick liquid which is a concentrated solution of the solid mass which results when anhydrous sugar is used. Solid caramel is an amorphous, reddish-brown, brittle mass, quite porous and highly deliquescent. Caramel made from cane sugar is more soluble in hydroalcoholic liquids than that made from glucose, on account of the dextrins present in glucose, which yield derivatives not readily soluble in alcohol.

Description and Physical Properties.—"Caramel is a thick dark brown liquid having the characteristic odor of burnt sugar and a pleasant, bitter taste. Caramel mixes clear with water in all proportions, 1 part dissolved in 1000 parts of distilled water yielding a clear solution having a distinct sepia tint. The color of this solution is not changed and no precipitate is formed after exposing to sunlight for six hours. It is soluble in diluted alcohol, but is precipitated when the alcoholic content of the solution is increased to 80 per cent. or more by volume. It is insoluble in ether, chloroform, acetone, benzene or petroleum benzin or oil of turpentine. Specific gravity not less than 1.35 at 25° C. Spread a thin layer of Caramel on a glass plate. It appears homogeneous, reddish brown and transparent.

"No precipitate is produced in 20 cc. of an aqueous solution of Caramel (1 in 20) on the addition of 0.5 cc. of phosphoric acid. Caramel swells when incinerated and forms a coke-like charcoal, which burns off only after prolonged heating at a high temperature, and yields not more than 8 per cent. of ash." *N. F.*

Beringer (*A. J. P.*, lxxxiv, p. 160) proposes, for the sake of uniformity (which is difficult to obtain in commercial caramels), a purified caramel made as follows: Caramel, 1000 Gm.; Alcohol, 3500 cc.; Monohydrated Sodium Carbonate, 4 Gm.; Water, *a sufficient quantity.* Weigh the caramel into a capacious bottle or flask, add 250 cc. of boiling water and thoroughly mix. Add gradually 3000 cc. of alcohol, shaking after each addition. Set aside for six hours. Decant the alcoholic solution and wash the precipitate on a filter with two portions of 250 cc. each of alcohol. Allow the precipitate to drain free from alcohol, dissolve it in 1500 cc. of warm water, add the monohydrated sodium carbonate, filter the solution, evaporate it to a thick syrup and spread it upon glass plates to dry. Remove from the plates when dry and place in a desiccator over sulphuric acid until it ceases to lose weight. This process yields about 40 per cent. of purified caramel which has a high coloring power and great uniformity. George A. Menge proposes to make a standard solution of caramel for adjusting the tinctorial power of caramel as follows: Make a sulphuric acid solution by adding 1 cc. of pure concentrated sulphuric acid (sp. gr. 1.84) to 12 cc. of water. Take 0.5 Gm. of sugar in a test-tube, add 5 cc. of the acid solution described and heat the mixture in a bath of boiling water, with the mixture continuously submerged and with constant agitation, for exactly five minutes. Immediately add a little cold water and then 35 cc. of the U. S. P. test solution of potassium hydroxide; finally dilute to 100 cc. The whole procedure takes about fifteen minutes. (*A. J. P.*, 1911, 113.)

A very satisfactory test for the identification of caramel in flavoring extracts and other liquids where it may be used as a color, has been proposed by G. H. P. Lichthardt. (*J. I. and E. C.*, xi, p. 389.) The following solution is required: Tannic acid, 1 Gm.; Sulphuric Acid (sp. gr. 1.84), 0.75 Gm.; Distilled Water, q. s. to make 50 cc. Dissolve the tannic acid in about 30 cc. of water, add the sulphuric acid (the precipitate at first forming will redissolve) and then the remainder of the water. Let it stand twenty-four hours and filter. Add 5 cc. of this solution to 5 cc. of the liquid to be tested, heat gently until the precipitate at first formed is nearly all dissolved, then set aside for twelve hours or over night; a brown precipitate adhering closely to the bottom of the tube will be found when caramel is present. A flocculent, non-adhering precipitate is to be ignored. With highly alcoholic liquids the alcohol should be removed by evaporation and the volume restored by the addition of water before applying the test.

Caramel contains besides some undecomposed sugar, an odorous principle (furfural), a coloring matter, and a white hygroscopic substance called *caramelan.*

Caramelan, $C_{12}H_{18}O_9$, has been exhaustively investigated by Cunningham and Doree (*P. J.,* 1117, xcviii, 408.) It is described as a buff-colored powder melting at 136° C. Various derivatives have been prepared and it is stated to be an intermediate product between cellulose and humus.

F. Ehrlich (*Bull. Chim. Soc.,* 1909, 140) states that the coloring principle in cane sugar caramel is an amorphous, tasteless compound, not precipitated by lead acetate, and having the chemical formula $C_{12}H_{22}O_{11} + 2H_2O$, and to which he gives the name *saccharane.* The yield from sucrose is about 20 per cent. Dextrose, fructose and starch produce no saccharane.

Pure grape sugar and pure cane sugar caramel, for experimental purposes, have been prepared by G. D. Beal and H. F. Greler, according to methods outlined in *J. A. P. A.,* 1914, p. 495. The resulting products are in the form of scales made by evaporating the solutions on glass plates. Sucrose produces a darker caramel than dextrose, when working under exactly the same conditions, in the ratio of about 10 to 1.

Uses.—Caramel is used in medicine only as a coloring agent.

CARBO.

CARBON

$C = 12.$

Carbone, *Fr.;* Kohlenstoff, *G.;* Carbone, *It.;* Carbon, *Sp.*

Carbon is an element of great importance, and very extensively diffused in nature. It exists in large quantity in the mineral kingdom as carbonates and as coal, and is the most abundant constituent of animal and vegetable matter. In the crystallized state it constitutes the diamond; and, more or less pure, it forms the substances called *graphite* (*black lead* or *plumbago*), anthracite and bituminous coal, coke, lampblack, animal charcoal, and vegetable charcoal. Combined with oxygen it forms carbon dioxide, or carbonic acid gas, which is a constituent of the atmosphere, and present in many natural waters, especially those which have an effervescing quality. United with oxygen and a base it forms the carbonates, among others calcium carbonate, which is one of the most abundant minerals. There are three allotropic conditions of carbon, represented respectively by the diamond, graphite, and charcoal.

The *diamond* has been found in quantity in India, in Brazil, and in South Africa, but at the present time is obtained almost exclusively from the last named locality. Several diamonds have been found in the gold regions of Georgia and North Carolina. This gem is perfectly transparent, and the hardest and most brilliant substance in nature. Its sp. gr. is about 3.5 It is fixed and unalterable in the fire, provided air be excluded, but is combustible in air or oxygen, the product being the same as when charcoal is burned, namely, carbon dioxide. It has been made artificially at the temperature of the electric arc (2500° to 3000° C.) by Moissan.

Next to diamond, *graphite* or *plumbago* is the purest natural form of carbon. Graphite is the substance of which "black-lead" crucibles and so called lead-pencils are made. It is found in greatest purity in the mine of Borrowdale, in England, and in Ceylon, from which latter place most of the graphite of commerce is now obtained, but it also occurs very pure in this country, and in deposits at Ticonderoga, N. Y., at Stourbridge, Mass., and in Siberia, Australia, Canada, and Brazil. In physical characters it is utterly different from the diamond; it crystallizes in hexagonal plates, is very soft and unctuous, of 2 to 2.5 sp. gr., and generally contains a little ash. In connection with the production of silicon carbide (carborundum) in the electric furnace, Acheson has produced a very pure artificial graphite by simply increasing the heat until the silicon was volatilized. This artificial graphite has a specific gravity of 2.5, is soft and of high metallic luster. It is extensively used for electrodes in electro-chemical manufacturing processes, and for graphite paint. Graphite is extensively used for lubricating purposes especially in the colloidal form known as deflocculated graphite.

Anthracite, the purest variety of natural coal, occurs in different parts of the world, but particularly in the State of Pennsylvania. The best variety contains from 90 to 95 per cent. of carbon, and several per cent. of ash. Ordinary anthracite for domestic heating purposes contains from 10 to 25 per cent. of ash. *Bituminous coal* is another variety, containing, besides the fixed or free carbon, some 10 to 15 per cent. of volatile hydrocarbons or gas-making material. When this is driven off by the process of charring, as in the manufacture of coal-gas, a kind of mineral charcoal, called *coke,* is obtained, very useful in the arts as a fuel. When peat is charred, it is converted into *peat charcoal,* which forms a cheap deodorizer, which was quite generally used for this purpose at one time but which has almost completely disappeared from commerce.

Carbon may be obtained in a state approaching to purity by several processes. One method is to expose *lamp-black* to a full red heat in a closed vessel. It may also be obtained, in a very pure state, by passing the vapor of volatile oils through an ignited porcelain tube, whereby the hydrogen and oxygen of the oil will be dissipated, and the charcoal left in the tube. The purest lamp-black is now made from natural gas in Western Pennsylvania and in Ohio. This lamp-black is miscible with water, does not color ether, and is free from oily matter.

Colloidal carbon may be easily prepared by gradually adding 2 Gm. of sugar to 20 Gm. of sulphuric acid with continuous agitation and then pouring the mixture into 80 cc. of water and filtering. The sulphuric acid may be removed by dialysis and a clear black solution of colloidal carbon remains.

Carbon, in its uncrystallized state, is an insoluble, infusible solid, generally of a black color, and without taste or odor. It burns when sufficiently heated, uniting with the oxygen of the air, and producing carbon dioxide. Its sp. gr. in the solid state, when in mass, is 3.5. It has great power in resisting and correcting putrefaction in other bodies. When prepared from animal sources, it possesses the property of absorbing the coloring and odorous principles of most liquids. (See *Carbo Animalis.*) Its other physical properties differ according to its source and peculiar state of aggregation. As a chemical element it enjoys a very extensive range of combination. It forms two compounds with oxygen, carbon dioxide (carbonic acid gas) and carbon monoxide (carbonous oxide). With hydrogen it forms a number of compounds, called "hydrocarbons." With nitrogen, carbon constitutes cyanogen, and when united in minute proportion with iron as carbide it is present in cast iron and steel.

CARBO ANIMALIS PURIFICATUS. N. F.

PURIFIED ANIMAL CHARCOAL

"Charcoal prepared from bone, and purified by removing the substances which are dissolved by hot hydrochloric acid and water." *N. F.*

Animal Charcoal; Spodium; Ebur Ustum; Bone Black; Ivory Black; Charbon Animal Ordinaire, Noir Animal Pulvérisé, Noir d'os, *Fr.;* Thierische Kohle, Knochenkohle, Beinschwarz, Thierkohle, *G.;* Nero di ossa, Carbone animale, *It.;* Carbon animal, Carbon de hueso, *Sp.*

The animal charcoal employed in pharmacy and the arts is usually obtained from bones, by subjecting them to a red heat in closed vessels. The residue of the ignition is a black matter, which when reduced to powder forms *bone black,* sometimes incorrectly called *ivory black.*

In manufacturing bone black, the bones, first treated with steam to separate the fat, are subjected to destructive distillation in iron cylinders connected with vessels which receive the ammoniacal liquor, called *bone spirit,* together with a dark tarry liquid (*bone oil*), this being a secondary product of the operation. When the distillate ceases to come over, the residue is charred bone, or bone black. Bone consists of animal matter with calcium phosphate and carbonate. In consequence of the decomposition of the animal matter involved in this destructive distillation, the nitrogen and hydrogen, united as ammonia, and a part of the charcoal, in the form of carbon dioxide, distil over, while the remainder of the charcoal is left in the cylinder, intermingled with the calcareous salts.

Animal charcoal, as it is made by charring bones, necessarily contains bone phosphate and calcium carbonate, the presence of which does no harm in some decolorizing operations; but in delicate chemical processes these salts may be dissolved or decomposed, and thus become a source of impurity. It is on this account that animal charcoal requires to be purified from its calcareous salts; and this is accomplished by diluted hydrochloric acid, which dissolves the phosphate and decomposes the carbonate. For details of process see *U. S. D.,* 19th edition, p. 292. According to Stenhouse, aluminized vegetable charcoal is equally efficacious with purified animal charcoal as a decolorizer.

Description and Physical Properties.—"A dull black powder, odorless, tasteless, and insoluble in water, alcohol or other solvents.

"Boil 1 Gm. of Purified Animal Charcoal during three minutes in a mixture of 3 cc. of potassium hydroxide T.S. and 5 cc. of distilled water, and filter: the filtrate is colorless. The ash from 2 Gm. of Purified Animal Charcoal does not exceed 4 per cent. (*limit of silica and other inorganic matter*)." *N. F.*

It is more dense and less combustible than vegetable charcoal; from which, moreover, it may be distinguished by burning a small portion of it on a red hot iron, when it will leave a residue imperfectly acted on by sulphuric acid, whereas the ashes from vegetable charcoal readily dissolve in this acid, forming a bitterish solution.

The decolorizing power of vegetable charcoal was first noticed by Lowitz, of St. Petersburg; and that of animal charcoal by Figuier, of Montpellier, in 1811. In 1822 the subject was ably investigated by Bussy, Payen, and Desfosses. The decolorizing power of animal charcoal is higher than that of any other commercial product and no substitute for it is available in sugar refining and other industries where large amounts are used. In spite of the smaller percentage of carbon in animal charcoal and the well known gas absorptive power of vegetable charcoal the latter does not possess the decolorizing power of the former. It is probable that the nitrogenous constituent in animal charcoal plays an important part in the decolorozing action which is not yet thoroughly understood.

In the manufacture of potassium ferrocyanide there is obtained a fine black sediment, which has a powerful decolorizing action; this is sometimes attributed to the organic nitrogenous character of the material from which it is made.

In order to determine the commercial value of animal charcoal, Corenwinder has proposed to ascertain its power of absorbing lime from a solution of calcium saccharate of determinate strength. The value is in proportion to the absorbing power of the charcoal. A given weight of the charcoal to be tested is left in contact, for an hour, with a given volume of the solution of the saccharate, taken in excess. The liquid is then filtered, and a small measure of it saturated with diluted sulphuric acid of known strength. The less the acid necessary for this purpose, the greater the amount of lime absorbed, and the better the animal charcoal. (*Scientific American,* April 22, 1876; *A. Pharm.,* 1887; *Proc. A. Ph. A.,* 1887.) See also Laval's investigations, *P. J.,* 1900, 214. Dupuy found that the addition of a few grains of animal charcoal to a few cc. of cold fresh tincture of guaiacum immediately causes the development of a blue color, while wood charcoal does not give this reaction. (*P. J.,* 1897, 190.)

Spent animal charcoal, which has been used by the sugar refiner, may have its decolorizing power restored by calcination, which destroys the organic matters that have become fixed in it, and it is stated that it may be submitted to this process twenty times before becoming unfit for use, although this depends upon the amount of calcium salts it takes up from the raw sugars, beet sugars using up the black faster than sugars from the cane. According to Pelouze, the same object may be accomplished by subjecting it to a weak solution of potassium or sodium carbonate.

Animal charcoal is capable of taking the bitter principles from infusions and tinctures, and iodine from liquids which contain it in solution. Its power, however, of acting on solutions and chemical compounds is stated by Warington and Weppen to be more decided in its purified condition. (See *Ephem.,* 1885, p. 721.) On the other hand, Carswell (*P. J.,* 1893, 615) believes that the purification of animal charcoal is based on erroneous conclusions, as charcoal possesses no inherent powers of decolorization.

Uses.—Animal charcoal is used in pharmacy for decolorizing vegetable principles, such as gallic acid, quinine, morphine, veratrine, etc., and in the arts, principally for clarifying syrups in sugar refining, for depriving spirits distilled from grain of the penetrating impurity, called *fusel oil,* which imparts to them an unpleasant odor and taste, as first distilled, and for the filtration of petroleum residues in the manufacture of petroleum and petroleum jellies. (See *Petrolatum.*) The manner in which it is used as a decolorizer is to mix it with the substance to be decolorized, and to allow the mixture to stand for some time. The charcoal unites with the coloring matter, and the solution by filtration is obtained white and transparent. Its use, however, in decolorizing the alkaloids and other vegetable principles, no doubt causes a loss by absorption, since it has been shown by the experiments of Lebourdais, mentioned under the head of purified animal charcoal, that several of these principles may be obtained by the sole action of charcoal. According to Guthe, a German chemist, bone charcoal, without purification, is to be preferred as a decolorizer in all cases in which the calcareous salts exert no injurious effect. Voilé uses animal charcoal as an absorbent in a pill excipient for making creosote and croton oil pills.

Because of its power in absorbing many toxic principles, animal charcoal has been recommended as an antidote in the treatment of various alkaloidal and mineral *poisonings* (Chinisse, *Press. Med.,* 1920, xxviii, 865) and, according to Secheyron (*Revue Internat. de Méd.,* 1909, p. 120), is especially to be recommended in *mushroom poisoning.* For this purpose a tablespoonful stirred up in water may be given at a dose. Knaffl-Lenz (*M. M. W.,* 1915, 625), having found that animal charcoal will absorb the proteolytic ferment of *Bacillus pyocyaneus,* employed it as a surgical dusting powder in the treatment of infected *wounds* with pleasing results. Because of its absorptive powers it has also been recommended by Adler (*W. K. W.,* 1912) in *enteritis* and by Pribran (*Pr. M. W.,* 1913) in *gastric flatulence.* Starkenstein (*M. M. W.,* 1915, No. 1) finds that the absorptive power of animal charcoal is superior to either vegetable charcoal or kaolin and recommended the drug not only in enteritis but also in *cholera* and in *dysentery.* For these latter conditions it may be administered in teaspoonful doses.

The *dose* given in the N. F. is five grains (0.3 Gm.) but much larger quantities may be safely administered.

Off. Prep.—Tabellæ Carbonis Animalis, *N. F.*

CARBO LIGNI. U. S., Br.

WOOD CHARCOAL Carb. Lig. [Charcoal]

"Wood Charcoal prepared from soft wood, and very finely powdered." *U. S.* "Wood charcoal is wood charred by exposure to a red heat without access of air." *Br.*

Carbo Præparatus, Carbo e Ligno, Carbo Vegetabilis; Wood Charcoal, Vegetable Charcoal; Charbon Végétal, Charbon de bois, *Fr.;* Carbo Ligni Pulveratus, *P. G.;* Gepulverte Holzkohle, Holzkohle, Präparirte Kohle, *G.;* Carbone Vegetale, Carbone di legno, *It.;* Carbon vegetal medicinal, Carbon de lena, *Sp.*

Preparation on the Large Scale.—Billets of wood are piled in a conical form with a central hollow chimney or flue, and covered with earth and sod to prevent the free access of air, several holes being left at the bottom and one at the top of the pile, in order to produce a draught to commence the combustion. The wood is then kindled from the bottom. In a little while the hole at the top is closed, and, after the ignition is found to have pervaded the whole pile, those at the bottom are stopped also. The combustion taking place with a smothered flame, the volatile portions of the wood, consisting of hydrogen and oxygen, are dissipated, while the carbon is left, a portion of it, however, being lost by combustion. Wood, thus carbonized, yields not more than 17 or 18 per cent. of charcoal. A better method is to char the wood in iron cylinders, when it yields from 22 to 23 parts in 100 of excellent charcoal; and, at the same time, the means are afforded for collecting the volatile products, consisting of pyroligneous acid, empyreumatic oil, and tar. This process for obtaining charcoal has been described under another head. (See *Acidum Aceticum.*) A method of preparing charcoal by subjecting wood to superheated steam has been invented by Violette. When the temperature of steam is 300° C., the wood is converted into a peculiar charcoal, called *ed charcoal,* which is intermediate in its qualities between wood and ordinary charcoal. When the temperature is lower, the carbonization is incomplete; when higher, the product is black charcoal. The steam process yields a uniform charcoal for a given temperature, which may be easily regulated, and a product about double that obtained in closed cylinders. Charcoal contains carbon, approximately in proportion to the temperature at which it is formed; varying from 65 per cent. when made at 250° C. to 80 per cent. when made at 400° C. The gaseous matter present, on the other hand, decreases with the temperature of carbonization. Thus, for charcoal made at 300° C. it is one-third of its weight; at 350° C., one-fourth.

E. C. C. Stanford has called attention to a variety of vegetable charcoal, obtained by charring a species of sea weed, *Laminaria digitata,* gathered on the shores of the Hebrides, which, on account of the large proportion of calcium carbonate contained in it (20 per cent.), is unfit for use in refining sugar; it, however, possesses more of the deodorizing and decolorizing power than animal charcoal itself, which, with the exception referred to, it closely resembles in chemical composition. The charcoal from nut shells and the pits of such drupes as the plum, peach, etc., was found to have extraordinary absorptive power for gases during the World War, and was much in demand in connection with the manufacture of gas masks.

Preparation for Medicinal Use.—Belloc recommends that charcoal for this purpose be obtained from poplar shoots, cut at the time the sap rises, and deprived of their bark. The carbonization should be performed in cast iron vessels at red-white heat. The product is a light and brilliant charcoal, which must be purified by being macerated for three or four days in water, frequently renewed. It is then dried, powdered, and placed in bottles, which should be well-stoppered. The charcoal made from willow is generally preferred, although that obtained from maple is also largely employed. A fine charcoal is also made in Europe from the linden and poplar.

Properties.—Charcoal is a black, shining, brittle, porous substance, tasteless and inodorous, and insoluble in water. It is a good conductor of electricity, but a bad one of heat.

It possesses the properties not only of absorbing many times its own bulk of certain gases but also will adsorb many chemicals from their solutions; Kolthoff (*Ph. Wb.,* 1921, lviii, p. 630) found it would adsorb iodine, phenol, mercuric chloride, methylene blue, and various alkaloids, etc. Rosenberg tested the adsorptive powers of various kinds of charcoal with methylene blue; he found that taking the absorptive properties of blood charcoal as 100, that of willow charcoal was 24, and charcoal from a drug store 14 (*Ph. Ztg.,* 1921, lxvi, p. 724).

Description and Physical Properties.—" A black, odorless, and tasteless powder, free from gritty matter. Wood Charcoal burns without a luminous flame, yielding not more than 7 per cent. of ash. Boil 1 Gm. of Wood Charcoal with a mixture of 3 cc. of potassium hydroxide T.S. and 10 cc. of distilled water for one-half minute, and filter: the filtrate has only a slight brown color.

" Preserve in well-closed vessels." *U. S.*

The British Pharmacopœia describes it as " A black powder without odor or taste, free from gritty matter. When 1 gramme of the Charcoal is boiled for a few minutes with 5 millilitres of *solution of sodium hydroxide* diluted with 15 millilitres of *water* and the mixture filtered, the color of the filtrate is not deeper than pale yellow (absence of insufficiently carbonised wood). Ash not more than 7.5 per cent." *Br.*

When exposed to the air after ignition, charcoal increases rapidly in weight, absorbing from 12 to 14 per cent. of moisture. As ordinarily prepared, it contains the incombustible part of the wood, amounting to 1 or 2 per cent., which is left as ashes when the charcoal is burned. This inorganic material may be removed by digesting the charcoal in diluted hydrochloric acid, and afterwards washing it thoroughly with boiling water. Havenhill examined the wood charcoal of the western markets and found the ash to vary from 0.62 to 16.80 per cent. (*D. C.,* 1914, p. 260.) Gane states that imperfectly carbonized samples are of frequent occurrence (*J. A .Ph. A.,* 1912, p. 375). Knecht claims that the more closely the substance approaches in composition to pure carbon the less is its decolorizing power. (*Proc. VIIth Internat. Congress App. Chem.,* Sec. IVb., Coloring, 1909, London, 1910, pp. 17, 18.)

For internal use charcoal is preferred by some in a *granular form* and sweetened. For on account of the method of preparing it in this manner see *U. S. D.,* 20th ed., p. 291.

It has been shown that the presence of certain salts in charcoal increases the absorptive power while others decrease the effect remarkably. Zinc chloride, stannous chloride and magnesium chloride have been found especially valuable as activators.

Eponite and *Norite* are patented forms of vegetable carbon with great decolorizing activity. Microscopic examination of these products revealed the fact that they are probably made from coniferous woods activated by special treatment with calcium or magnesium compounds.

Dorsite is another form of activated charcoal especially useful in gas masks. D. Van Oos (*Pharm. Weekbl.,* 1920, lvii, p. 693) has conducted exhaustive comparative experiments in connection with the selective action of especially activated charcoals.

Stenhouse has devised a process for combining alumina with common vegetable charcoal, forming what he calls *aluminized charcoal,* which is an economical substitute for purified animal charcoal, and equally efficacious as a decolorizer. It is prepared by digesting finely powdered charcoal with sufficient of the solution of aluminum sulphate to give an impregnation of 7.5 per cent. of alumina. The whole is evaporated to dryness, and ignited in a covered Hessian crucible, until the water and acid have been dissipated. Aluminized charcoal is perfectly black, though thoroughly impregnated with anhydrous alumina, and only requires to be carefully pulverized to be ready for use. On similar principles, Stenhouse prepares his *artificial bone black,* by impregnating powdered wood charcoal with 7.5 per cent. of calcium phosphate, by digesting it in a solution of this salt in hydrochloric acid, evaporating to dryness, and igniting in covered vessels. This charcoal decolorizes well, but can be used only for neutral solutions.

Uses.—Charcoal is used in medicine chiefly for its absorbent properties, thus it is used locally in *gangrene* and *foul ulcers* to absorb the putrid gases. Internally it has been used in *meteorism* and *fermentative dyspepsia* with the idea of absorbing the gas. In many cases of *dyspepsia,* however , it appears to have some further action than that of a mere absorbent. Calvert (*J. A. Ph. A.,* 1922, xi, 798) has shown that while moist charcoal has only small power to absorb carbon dioxide it exercises a marked inhibition on yeast fermentation. As is well known, charcoal is capable of adsorbing not only coloring matter but many other organic substances and it has been lauded by Kraus and Barbara (*D. M. W.,* 1915, xli) as an absorbent for toxins. For this action they recommend it internally in the treatment of *diarrhea* and *dysentery* and locally for various infected *wounds;* see also Eisner. (*Ther. Geg.,* lvi.) Oppenheim and Schlifka (abs. *J. A. M. A.,* 1915, lxvii, 1432) have reported excellent results from the injection of a 1 per cent. suspension of charcoal in acute *gonorrhea.*

At one time it was much used as a dressing for ulcers but is at present rarely employed, though the *Cataplasma Carbonis* or charcoal poultice is still occasionally prescribed in Great Britain. Several of its varieties are used as tooth powder. Those generally preferred are the charcoals of the cocoa-nut shell and of bread. It is said that charcoal proves useful in preserving the teeth by absorbing the acid sometimes morbidly present in the mucus of the mouth.

It has long been recommended as an antidote in various forms of poisoning and is one of the ingredients of the mixture sometimes called universal antidote which consists of charcoal, tannic acid and magnesia. There seems to be little doubt that large quantities of charcoal will delay the entrance of many poisons into the system and therefore may be of value, but it is scarcely proper to speak of it as antidotal as it does not destroy the toxicity of the poison but simply delays its absorption. Scoville states that charcoal is a good antidote for phenol poisoning. It acts by absorbing phenol and eliminating it through the intestines rather than through the kidneys. (*Bull. Pharm.,* 1913, p. 393.)

Dose, ordinarily five to twenty grains (0.32 to 1.3 Gm.) but it has been used in teaspoonful doses.

Off. Prep.—Trochisci Carbonis Ligni, *N. F.*

CARBON DISULPHIDUM. Br.

CARBON DISULPHIDE

"Carbon Disulphide, CS_2, may be obtained by combining carbon and sulphur at a high temperature, the product being subsequently condensed and purified." *Br.*

Carbonis Bisulphidum, *Br.,* 1898; Carbon Bisulphide; Carbon Sulphide; Sulphururum Carbonicum; Carbo Sulfuratus, Sulfure de Carbone, *Fr. Cod.;* Bisulphide de Carbone, *Fr.;* Carboneum Sulfuratum, Alcohol Sulfuris, Schwefelkohlenstoff, Kohlensulfid, Schwefelalkohol, *G.;* Solfuro di carbonio, *It.;* Sulfuro de carbono, *Sp.*

This compound is prepared by the direct combination of carbon and sulphur at a moderate red heat. To effect this, charcoal is heated to redness in a vertical cylinder, while sulphur is admitted through a lateral tubulure near the bottom. As the sulphur melts and vaporizes, it combines with the carbon, and the carbon disulphide formed distils over through a series of condensing tubes, which, while they serve to collect the crude carbon disulphide, allow of the escape of the hydrogen sulphide formed at the same time. The crude product is then rectified, first over a solution of chlorinated lime to break up any hydrogen sulphide gas remaining, and then repeatedly either over mercury, mercuric chloride, anhydrous cupric sulphate, or over a pure fatty oil, which withdraws from it all free sulphur and malodorous sulphur compounds.

The most decided improvement in the manufacture of carbon disulphide was made by E. R. Taylor of Penn Yan, New York, who introduced a patented electrothermal process which can be worked continuously. In large furnaces 41 feet high by 16 feet in diameter an alternating current is applied through carbon electrodes. The sulphur passing over the electrodes is vaporized and rises through the glowing carbon, the carbon disulphide being taken off as vapor through a side connection near the top of the furnace. The impure carbon disulphide is purified by forcing lime water in a fine spray through the disulphide liquor until the water runs out of the tank colorless. The carbon disulphide is finally rectified by steam heat. It is used in the arts for the extraction of oils from different oil seeds, for the extraction of sulphur from some varieties of sulphur ores, for the cleansing of wool and recovering the fat, as a solvent for caoutchouc in the manufacture of India rubber goods, for the extraction of perfumes, and on an enormous scale in France as a remedy against the *phylloxera.* It is also used to exterminate rodents and other ground burrowing animals, by pouring a small quantity into each burrow. Its vapor being heavier than air penetrates to the innermost recesses of the burrow and being very toxic the animal dies underground. Von Lengyel describes a carbon sulphide having the composition C_3S_2. (*Proc. A. Ph. A.*, 1893, 1021.)

Properties.—Carbon disulphide is included among the Reagents in the U. S. (see Part III).

"A clear, colorless, highly refractive liquid. Odor charactristic but not fetid. Specific gravity 1.268 to 1.269. Highly inflammable, burning with a blue flame and giving off carbon dioxide and sulphur dioxide. Boiling point 46° to 47° C. Vapor mixed with air is explosive in contact with flame. Evaporated spontaneously in a glass vessel, it leaves no residue (absence of free sulphur)." *Br.*

Uses.—Although carbon disulphide has been recommended by Taar (*B. Thier., W.*, 1907, p. 406) for the destruction of intestinal parasites in the horse, it has not found its way into human medicine as an internal remedy. It is, however, occasionally used externally as a counter-irritant and local anesthetic. Turnbull especially recommended it as an external application in *enlarged lymphatic glands.* He applied it by means of a bottle with a proper sized mouth, containing a fluidrachm of the disulphide, imbibed by a piece of sponge; the skin over the gland is first well moistened with water. He employed the vapor also with benefit in deafness, when dependent on want of nervous energy and a deficiency of wax. For this purpose, the bottle containing the disulphide is made with a neck to fit the meatus, and, being applied to the ear, is held there until considerable warmth is produced. The remedy has been used often with very good results, in a similar manner, in *facial* and other *neuralgias* and various local *pains.* It causes a good deal of smarting, but its disagreeable odor is the chief objection to it. In France the disulphide has been used in *diarrhea* in 3.5 per cent. solution, of which the dose is two tablespoonfuls (30 cc.) four or five times a day.

Its most important use is as a solvent, especially for rubber. Carbon disulphide is an active poison and workmen exposed to the fumes of the disulphide are affected with headache, vertigo, and over-excitement of the nervous system, as evinced by voluble talking, incoherent singing, or immoderate laughter, or sometimes by weeping; and a continuance of the exposure is apt to finally cause a state of cachexia, characterized by general weakness, loss of sexual appetite, dullness of sight and hearing, and impairment of memory. Some writers assert that these phenomena are hysterical, and that what the carbon disulphide does is to produce an hysterical neurosis. (See *Annales de Hygiène*, 1895, xxxiii.) The swallowing by a man of half an ounce of carbon disulphide was followed in half an hour by absolute unconsciousness, very rapid, feeble pulse, slow and stertorous respiration, cold and clammy surface of body, and insensitive conjunctiva, with mobile pupils. Two hours later, death occurred. The blood was found fluid, but there was no marked lesions of irritation in the gastro-intestinal mucous membrane. (*L. L.*, July 17, 1886.) India rubber workers, by whom the disulphide is largely used, are said to suffer frequently from paralytic symptoms. (*L. L.*, Jan., 1886.)

CARBONEI TETRACHLORIDUM. U. S.

CARBON TETRACHLORIDE Carb. Tetrachlor.

"Tetrachlormethane [CCl_4]." *U. S.*

Carbonei Tetrachloridum; Tetrachlormethane; Carboneum Chloratum; Chlorocarbon; Carbon Perchloride; Tétrachlorure de Carbone, Formène Perchloré, *Fr.*; Chlorkohlenstoff, *G.*

Carbon tetrachloride was discovered by Regnault in 1839. It may be prepared by passing the vapor of carbon disulphide with dry chlorine through a red hot porcelain tube. The vapors from this condensed in a well-cooled receiver form a yellowish-red liquid, which is a mixture of carbon tetrachloride and sulphur chloride. The latter substance is removed by slowly adding potassium or calcium hydroxide, the mixture being set aside and agitated from time to time until the sulphur compound is decomposed; the carbon tetrachloride is then recovered by distillation.

Carbon tetrachloride is extensively used as a solvent for fats and for removing grease from garments, replacing petroleum benzine to advantage because of its non-inflammability; proprietary forms used for the latter purpose are known under the trade names respectively of *carbona* and the misnomer *benzinoform.* It is likewise employed as a solvent for alkaloids in assay work and manufacturing processes instead of chloroform. It is also of value as a fire extinguisher and forms the basis of the fluid called *pyrene.* When used, however, to extinguish fires, it generates large volumes of hydrochloric acid gas and in limited spaces may be dangerous, not only from this cause, but also on account of the carbon dioxide formed and the vaporization of undecomposed carbon tetrachloride. It is a good solvent for caoutchouc; and such a solution was at one time suggested for the purpose of coating the hands of the surgeon with a sterile and impermeable covering.

Description and Physical Properties.—"A clear, colorless, mobile liquid. It has a characteristic, ethereal odor, resembling that of chloroform. It is not inflammable. It is slowly decomposed by light if moisture is present.

Carbon Tetrachloride is soluble in 2000 times its volume of water. It is miscible with alcohol, chloroform, ether, benzene, and with petroleum benzin, and dissolves most of the fixed and volatile oils. Specific gravity: from 1.588 to 1.590 at 25° C. Carbon Tetrachloride boils between 76° and 77° C., but volatilizes at lower temperatures.

"Evaporate 50 cc. of Carbon Tetrachloride in a dish on a water bath to about 1 cc., and allow to evaporate spontaneously to dryness: the residue, if any, is odorless. Now dry at 100° C., and weigh: the weight of the residue does not exceed 0.001 Gm. Shake 15 cc. of Carbon Tetrachloride with 25 cc. of distilled water during five minutes, and allow the liquids to separate completely: the aqueous layer is neutral to litmus paper, and 10 cc. portions are not affected by a few drops of silver nitrate T.S. (*chloride*), nor colored blue by the addition of a few drops each of potassium iodide T.S. and starch T.S. (*free chlorine*). Warm 10 cc. of Carbon Tetrachloride with 10 cc. of a 25 per cent. potassium hydroxide solution for five minutes at about 60° C. with frequent agitation: no yellow or brown color develops in either liquid (*aldehyde*). Transfer 20 cc. of Carbon Tetrachloride to a glass-stoppered cylinder previously rinsed with sulphuric acid. Add 5 cc. of sulphuric acid, shake vigorously for five minutes, and allow the liquids to separate completely: the sulphuric acid layer is colorless or nearly so (*readily carbonizable substances*). Mix 10 cc. of Carbon Tetrachloride with an equal volume of a 10 per cent. potassium hydroxide solution in dehydrated alcohol, and allow the mixture to stand for one hour. Add 5 cc. of acetic acid, and follow with 1 cc. of copper sulphate T.S.: no yellow precipitate is formed within two hours (*carbon disulphide*).

"Preserve in well-closed containers, protected from light." *U. S.*

Uses.—Carbon tetrachloride is a powerful narcotic, indeed, the assertion is made by Freymuth (*B. K. W.*, 1921, lviii, p. 1330) that it surpasses chloroform in the vigor of its action. It is, however, depressant to the circulation and therefore not available as a surgical anesthetic. Foster (*U. S. Pub. Health Rep.*, October 25, 1918) has found that carbon tetrachloride is very efficient for the destruction of lice in clothing. Although it was occasionally employed as a local remedy, it attracted little medical attention until 1922 when it was brought forward as a remedy for *hookworms* by Lake (*U. S. Pub. Health Rep.*, May 12, 1922). He found that a dose of 3 cc. (forty-seven minims) was an efficient anthelmintic and that monkeys could take a hundred times the proportional dose without serious intoxication. Lambert (*J. A. M. A.*, 1922, lxxix, 2055) has treated 20,000 cases of hookworm infestation with carbon tetrachloride. In 90 per cent. of the patients a single treatment with a dose of from 3 to 4 cc. (forty-five to sixty minims) caused complete cure. In a few cases the patients complained of a dull headache and nausea, and in a number of instance of drowsiness, but in the whole series there was not a single fatality. In a subsequent communication Lambert (*J. A. M. A.*, 1923, lxxx, 526) reported three deaths from the treatment; these he attributed, however, to impurities in the commercial samples of carbon tetrachloride employed. McVail (*Indian Med. Gaz.*, 1922, lvii, 290) finds that carbon tetrachloride is efficacious against *ankylostoma* and the *oxyuris* but is of little service against the *ascaris*. The drug is of special value in community campaigns against the hookworm because of its relative cheapness and the acceptability to the palate. It should be preferably given on an empty stomach and followed three hours later with a purgative dose of magnesium sulphate. It may be administered by placing the determined quantity in a tablespoon, covering with sugar, and swallowing the whole at once.

Colman (*L. L.*, June 22, 1907) has reported poisoning from the use of carbon tetrachloride in dry shampoos.

Warren (*A. J. P.*, 1923, xcv, 864) gives extensive literature on the use of carbon tetrachloride as an anthelmintic, gives a method for determination of carbon disulphide, also analysis of several commercial samples showing a specific gravity of from 1.5879 up to 1.5897, and a carbon disulphide from 0 up to 0.22 per cent.

Lamson *et al* (*J. P. Ex. T.*, 1923, xxii, 215) find that the oral toxic dose of carbon tetrachloride for dogs is at least seven times as large as that required for rabbits, the difference being due to the absorbability from the intestines. They further find that the simultaneous exhibition of fatty substances or of alcohol increases the absorption and therefore the poisonous effects of the drug.

Dose, thirty to sixty minims (2–4 cc.).

CARBROMALUM. U. S.

CARBROMAL Carbrom. [Bromdiethylacetylurea]

"Brom-diethylacetyl carbamide [$C(C_2H_5)_2Br.CONH.CONH_2$]." *U. S.*

This remedy, which was originally introduced under the proprietary name of *Adalin*, is prepared from diethyl acetic acid by first converting this into a bromine derivative $(C_2H_5)_2CBrCOBr$ (bromo-diethyl-acetyl bromide) and then bringing about a reaction between this compound and urea.

Carbromal contains about 36 per cent. of combined bromine.

Description and Physical Properties.—"A white, crystalline, odorless powder. One Gm. of Carbromal is soluble in about 3000 cc. of water, 18 cc. of alcohol, 3 cc. of chloroform, and in 14 cc. of ether, at 25° C. It is very soluble in boiling alcohol. It dissolves in sulphuric, nitric, and in concentrated hydrochloric acids, from which it is precipitated by dilution with water. It is dissolved by solutions of alkali hydroxides.

" Carbromal melts between 116° and 117° C. On boiling about 0.2 Gm. of Carbromal with 5 cc. of a 10 per cent. aqueous sodium hydroxide solution, ammonia is evolved. Mix 0.1 Gm. of Carbromal with 0.5 Gm. of anhydrous sodium carbonate, and ignite gently until completely decomposed. Dissolve the residue in 5 cc. of hot distilled water, cool, acidulate with acetic acid, and filter: Add to the filtrate 2 cc. of chloroform and then chlorine T.S., drop by drop: the chloroform acquires a red-brown color on shaking.

" The ash from 0.5 Gm. is negligible. A solution of 0.2 Gm. of Carbromal in 2 cc. of sulphuric acid is colorless or at most faintly brown (*readily carbonizable substances*). Shake 1 Gm. of Carbromal with 20 cc. of distilled water during five minutes, and filter: the filtrate is neutral to litmus paper. Five cc. portions of the filtrate obtained in the preceding test show no more *chloride* than corresponds to 0.1 cc. of fiftieth-normal hydrochloric acid, and no more *sulphate* than corresponds to 0.1 cc. of fiftieth-normal sulphuric acid." *U. S.*

Uses.—This compound was introduced into medicine with the idea that it would combine the sedative effects of bromine with the narcotic action of the aliphatic series. Impens (*Ther. Geg.*, 1912, p. 158) has shown that it is partially broken up in the system, eliminated in part as an inorganic bromide but also some of it in the undecomposed state. As the drug represents, however, only approximately 34 per cent. of bromine, in view of the smallness of the dose which is employed it seems highly improbable that this element can play any important part in the action of the drug. This conclusion is borne out by the experiments of Takeda (*A. I. P. T.*, 1911, xxi, p. 203) who concluded from a study of the distribution of the drug in the body that its action must be due to the whole molecule.

Carbromal, in sufficient dose, possesses the somnifacient effects of its aliphatic allies and is frequently used in the milder forms of *sleeplessness.* In severe types of insomnia, however, it is greatly inferior to barbital and some other drugs. Its most important use is as a general nerve sedative in *neurasthenia, hysteria, epilepsy, whooping-cough,* and other similar conditions of hyper-irritability of the central nervous system. It differs from most of the other narcotics of this group in that it possesses marked analgesic properties and is often a remedy of great usefulness in *neuralgia* and other forms of *pain.*

With ordinary caution carbromal seems to be a very safe drug. Nieuwenhuijse (*P. J.*, 1916, xcvi, p. 327) reports a case in which forty-five grains were taken but the patient recovered after sixty hours of narcosis. We know of no other instance of ill-effects from the use of this drug.

The ordinary *dose* as a nerve sedative is from five to ten grains (0.3–0.6 Gm.), as a hypnotic, from ten to fifteen grains (0.6–1 Gm.).

CARDAMOMI SEMEN. U. S. (Br.)

CARDAMOM SEED Cardam. Sem.

" Cardamom seed is the dried ripe seed of *Elettaria Cardamomum* White et Maton (Fam. *Zingiberaceæ*). Cardamom seed yields not more than 5 per cent. of acid-insoluble ash." *U. S.* " Cardamom Seeds are the dried ripe seeds of Elettaria Cardamomum, *Maton.* The seeds should be kept in their pericarps and separated when required for use." *Br.*

Cardamomi Semina, *Br.*; Cardamomum Minus, Cardamomum Malabaricum; Malabar Cardamoms, Cardamoms; Cardamome du Malabar, Petit Cardamome, *Fr.*; Fructus Cardamomi, *P. G.*; Malabar Kardamomen, Kardamomen, Kleine Kardamomen, *G.*; Cardamomo minore, *It.*; Cardamomo, Cardamomo menor, *Sp.*

The fruit of cardamom is official in most of the Pharmacopœias. The U. S. Pharmacopœia in its definition confines cardamom to the seeds. In this it follows the British Pharmacopœia which has always limited the drug to the seeds, but specifically states that the fruit should be kept intact and the seeds separated when required for use. This step was probably a wise one as there has always been some confusion by manufacturers as to whether the article designated as cardamom in a formula was restricted to the seeds or not. On the other hand the pericarp contains some oil and forms an excellent surface for the grinding of the seeds. Furthermore, the decorticated seeds are liable to adulteration with seed of wild cardamom and other foreign seeds which are not detected except upon careful examination.

The term cardamom has been applied to the aromatic capsules of various plants, most of them from India, belonging to the family of *Zingiberaceæ.* Formerly the terms *lesser, middle* and *larger* cardamoms were used to separate these various fruits, but these words have been used so differently by various writers that they no longer possess any precise signification. The *lesser cardamom* of most writers is the variety recognized by the Pharmacopœias and generally kept in the shops. The other varieties, though circulating to some extent in European and Indian commerce, are little known in this country.

The official cardamoms are produced chiefly in Malabar, Mysore, and adjacent regions of India and Ceylon. They have also been cultivated in some extent in tropical America.

The cardamom plant is a perennial herb with a tuberous horizontal rhizome, sending up from eight to twenty erect, simple, smooth, green and shining, perennial stems, which rise from six to twelve feet in height, and bear alternate elliptical-lanceolate sheathing leaves. The flower-stalk proceeds from the base of the stem, and lies upon the ground, with the flowers arranged in a panicle. The fruit is an ovoid, three-celled, loculicidally dehiscent capsule, containing many seeds which are covered by an aril; during drying it is said to lose three-fourths of its weight.

This valuable plant is a native of the mountains of Indo-China, where it springs up spontaneously in the forests after the removal of the undergrowth, and is very extensively cultivated by the natives. For a detailed account of culture, see *P. J.*, 1888; *Bull. des Sc. Pharmacol.*, 1906, pp. 114 and 584 and *Ph. Era*, 1920, liii, 365. The plant begins to yield fruit at the end of the fourth year, and continues to bear for several years afterwards. The capsules just before complete maturity are picked from the fruit-stems, dried over a gentle fire or by sun-heat, and separated, by rubbing with the hands, from the footstalks and adhering calyces. They are then washed and bleached by exposure either to dew and sun or to vapors of burning sulphur. J. W. Mollison describes the method of washing and curing cardamoms employed in the Bombay Presidency, India. The washing and manipulation is performed by women, and water from special wells is employed. The cardamoms are first washed in earthenware vessels containing a mixture of the well water with pounded soap nut and a species of acacia, in the proportion of two pounds of the former to a quarter pound of the latter. About ten pounds of cardamoms are treated at one time. Two women stir them vigorously in the mixture for about one minute and then allow them to rest about an equal length of time, and again stir for another minute. A thick lather results. This completes the first washing, after which the cardamoms are baled out by hand into a basket where they are allowed to drain for a few seconds, and then subjected to a second washing similar to the first except that the mixture contains less of the soap nut preparation and an additional quantity of soap solution. They are then thrown upon a mat and sprinkled with water from the special well at intervals of a half hour, until the next morning, when they are spread upon the roof of a house and allowed to dry for four or five hours. After nipping off the short stalk, an operation performed with a large pair of shears, the cardamoms are sorted, only the most plump fruits being prepared for the foreign market. Besides bleaching by this process, cardamoms are also subjected to starching in India. The starched product has a whiter appearance than the bleached cardamoms. (*B. C. D.*, 1904, see also *Ph. Era*, 1904, 137.)

The fruits, thus prepared, are ovate-oblong, from 10 to 17 mm. long, from 6 to 8 mm. thick, three-sided with rounded angles, obtusely pointed at both ends, longitudinally wrinkled, and of a yellowish-white color. The seeds constitute about 74 parts per cent. by weight. According to Pereira, three varieties are distinguished in commerce: 1, the *shorts*, from 6 to 12 mm. long, from 4 to 6 mm. broad, browner and more coarsely ribbed and more highly esteemed than the others; 2, the *longlongs*, from 14 to 25 mm. in length by 4 to 6 mm. in breadth, elongated, and somewhat acuminate; and 3, the *short-longs*, which are somewhat shorter and less pointed than the second variety. The odor of cardamom is fragrant, the taste warm, slightly pungent, and highly aromatic.

Most of the drug goes through Bombay and Madras to the various parts of the world. That imported into the United States is either shipped direct from Colombo, Ceylon, and Bombay, India, or through London. Malabar cardamom comes from Colombo; Mysore cardamom from Bombay.

UNOFFICIAL VARIETIES.—Besides the official cardamoms the fruit of a large number of related plants has been more or less employed. The more important of these are noted below.

Ceylon Cardamom.—This has been denominated variously *cardamomum majus* and *cardamomum longum*, and is sometimes termed in English commerce *wild cardamom.* It is the *large cardamom* of Guibourt. In the East it is sometimes called *grains of Paradise;* but it is not the product known with us by that name. (See below.) It is derived from a plant cultivated in Candy, in the Island of Ceylon, and also growing wild in the forests of the interior, which was designated by Sir James Edward Smith *Elettaria major,* but is now generally acknowledged to be only a variety of the official plant. (*Elettaria Cardamomum* var. *β-Major* Smith.) The fruit is a lanceolate-oblong, acutely triangular capsule, somewhat curved, about 3.5 cm. long and 6 to 8 mm. broad, with flat and ribbed sides, tough and coriaceous, brownish or yellow ash-colored, having frequently at one end the long, cylindrical, three-lobed calyx, and at the other the fruit-stalk. It is three-locular, and contains angular, rugged, yellowish-red seeds, of a peculiar fragrant odor and spicy taste. Its effects are analogous to those of the official cardamom.

Round or *Siam Cardamom.*—This is probably the Ἄμωμον of Dioscorides and the *Amomi uva* of Pliny, and is believed to be the fruit of *Amomum cardamomum* Willd., growing in Sumatra, Java, and other East India islands. The capsules are usually smaller than a cherry, roundish or somewhat ovate, with three convex sides, more or less striated longitudinally, yellowish or brownish-white, and sometimes reddish, with brown, angular, cuneiform, shrivelled seeds, which have a spicy camphoraceous flavor. They are sometimes, though rarely, met with connected in their native clusters, constituting the *amomum racemosum,* or *amome en grappe,* of the French. They are similar in medicinal properties to the official, but are seldom used except in the southern parts of Europe.

Java Cardamom.—The plant producing this variety is supposed to be the *Amomum maximum* Roxburgh, growing in Java and other Malay islands in the East. The capsules are oval, or oval-oblong, often somewhat ovate, from 1.5 to 3 cm. long, and from 8 to 15 mm. broad, usually flattened on one side and convex on the other, sometimes curved, three-valved, and occasionally imperfectly three-lobed, of a dirty grayish-brown color, and coarse fibrous appearance. When soaked in water, they exhibit as their distinguishing character from nine to thirteen ragged membranous wings along their whole length. The seeds have a feebly aromatic taste and odor. This variety of cardamom affords but a very small proportion of volatile oil, and is altogether of inferior quality.

Madagascar Cardamom.—This is the *Cardamomum majus* of Geiger and some others, and is thought to be the fruit of *Amomum angustifolium,* of Sonnerat, growing in marshy grounds in Madagascar. The capsule is ovate, pointed, flattened on one side, striated, with a broad circular scar at the bottom, surrounded by an elevated, notched, corrugated margin. The seeds have an aromatic flavor similar to that of official cardamom.

Bengal Cardamom.—The fruit of *Amomum aromaticum* Roxb., sometimes known by the name of winged Bengal cardamom. *Morung elachi,* or *Buro elachi,* is about 2.5 cm. in length, obscurely three-sided, ovoid or somewhat obconic, with nine narrow, jagged ridges or wings (best seen after soaking in water) upon its distal end, which terminates in a truncate bristly nipple. The taste is somewhat camphoraceous.

Nepal Cardamom is produced by an *Amomum* of undetermined species probably *A. subulatum* Roxb. and resembles the Bengal cardamom, except in having a long tubular calyx on its summit, and in being usually attached to a stalk.

Grains of Paradise. Grana Paradisi.—Under this name and that of *Guinea grains,* and *Melegueta* or *Mallaguetta pepper,* are found in commerce small seeds of a round or ovate form, often angular, and somewhat cuneiform, minutely rough, brown externally, white within, of a feebly aromatic odor when rubbed between the fingers, and of a strongly hot and peppery taste. Two kinds of them are known in the English market, one larger, plumper, and more warty, with a short conical projecting tuft of pale fibers on the umbilicus; the other smaller and smoother and without the fibrous tuft. The latter are the more common. It is probable that these are produced by *Amomum Melegueta* Roscoe, although they have been ascribed also to the *A. Grana Paradisi* J. E. Smith. Their effects on the system are analogous to those of pepper; but they are seldom used except in veterinary practice, and to give pungency to spirits, wine, beer, and vinegar. J. C. Thresh made a proximate analysis of the seeds, and found volatile oil, resin, tannin, starch, albuminoids, and an active principle in the form of a straw-colored viscid, odorless fluid, pungent, but not so hot as capsaicin. (*P. J.,* 1884, p. 297.) Fred'k Schwartz found in the seeds a reddish-brown acrid resin, and an oil having a burning aromatic taste, upon which the virtues probably depend. (*A. J. P.,* 1886, 118; consult also Hanausek's researches in *Chem. Ztg.,* 1893, 1765.)

Bastard or *Wild Cardamom,* the seeds of *Amomum Xanthioides* Wall., resembles true cardamom in appearance, but is of a dirty green color, and has a very biting, camphor-like taste. They come from Siam.

Description and Physical Properties.—"*Unground Cardamom Seed.*—Mostly agglutinated into groups of 2 to 7 by the adhering membranous aril, the individual seeds oblong-ovoid or irregularly 3- to 4-sided, from 3 to 4 mm. in length; convex on the dorsal surface, strongly longitudinally grooved on the ventral side and coarsely tuberculated; externally reddish-gray brown; odor aromatic; taste aromatic and pungent.

"*Structure.*—Seed coat: an epidermal layer of thick-walled cells, a pigment layer of small cells with brownish contents, a layer of volatile oil cells with suberized walls and a single layer of radially elongated strongly lignified stone cells with inner walls heavily thickened. Perisperm large, white, surrounding a central, greenish endosperm enclosing a small straight embryo.

"*Powdered Cardamom Seed.*—Brown; endosperm and perisperm cells filled with starch grains from 0.001 to 0.004 mm. in diameter or containing one or more prisms of calcium oxalate from 0.010 to 0.025 mm. in diameter; fragments of seed coat with dark brown cells polygonal in surface view and about 0.020 mm. in diameter; fragments of spiral tracheæ with accompanying slightly-lignified bast-fibers relatively few." *U. S.*

"Fruits from one to two centimetres long, ovoid or oblong, bluntly triangular in section, shortly beaked at the apex, pale buff in color, plump and nearly smooth or with slight longitudinal striations. Seeds dark reddish-brown, about three millimetres in length and the same in breadth and thickness, irregularly angular, transversely wrinkled, and enclosed in a thin, colorless, membranous aril. The powdered Seeds exhibit abundant, minute, angular starch grains, often compacted into masses; but no spiral vessels, sclerenchymatous fibres, or strongly elongated sclerenchymatous cells (absence of pericarps). Aromatic odor; taste agreeably warm and aromatic. Ash not more than 6 per cent." *Br.*

The seeds contain 4.6 per cent. of volatile oil, 10.4 of fixed oil, 2.5 of a salt of potassium mixed with a coloring principle, 3.0 of starch, 1.8 of nitrogenous mucilage, 0.4 of yellow coloring matter, and 77.3 of ligneous fiber. (Trommsdorff.) The volatile oil is colorless, of an agreeable and very penetrating odor, and of a strong aromatic, burning, camphorous, and bitterish taste. It is dextrogyrate, and consists essentially of a terpene, $C_{10}H_{16}$, with small quantities of formic and acetic acids. From old specimens of oil Dumas and Peligot claim to have separated crystals of terpene hydrate, $C_{10}H_{20}O_2 + H_2O$, while Flückiger has obtained a crystalline deposit from Ceylon oil which he considers identical with common camphor. Weber (*Ann. Ch. Ph.,* ccxxxviii, 98) found a small amount of a crystalline, non-volatile compound which fuses at 60° to 61° C. Schimmel

& Co. published in their semi-annual reports for April and October, 1897, some results of investigation of several varieties of cardamom oil. The terpenes of Ceylon oil they state to be terpinene and dipentene; both Ceylon and Bengal cardamom contain cineol; Malabar cardamom yields terpineol as well as cineol, while Siam cardamom yields a crystalline sediment composed of borneol and camphor in approximately equal proportions. The sp. gr. of the oil is between 0.92 and 0.94. It cannot be kept long without undergoing change, and finally, even though excluded from the air, loses its peculiar odor and taste. If ether be made to percolate through the powdered seeds, and the liquor obtained be deprived of the ether, a light greenish-brown fluid remains, consisting almost exclusively of the volatile and fixed oils. It has the odor of cardamom, and keeps better than the oil obtained by distillation. (*A. J. P.*, xxi, 116.) The oil of cardamom of commerce is often factitious, being composed of several cheap volatile oils, oils of cajuput, nutmeg, and others being used. Schimmel & Co. announced in 1901 that they no longer distilled the oil from the fruit of *Elettaria cardamomum*, but from the seeds of another species; this oil makes a clear solution with three parts by volume of 70 per cent. alcohol. (*Schim. Rep.*, 1901, 14.) See *Oleum Cardamomi*. The seeds should be powdered only when wanted for use, as they retain their aromatic properties best while in the capsule.

Cardamoms are sometimes adulterated; G. W. Kennedy reported nearly 4 per cent. of orange seeds and unroasted grains of coffee admixed with cardamom. Solstein (1892) found three commercial samples of powdered cardamom containing sodium carbonate.

Uses.—Cardamom is a grateful aromatic, not strongly heating or stimulating, and useful chiefly as an adjuvant. Throughout the East Indies it is largely consumed as a condiment. It was known to the ancients, and derived its name from the Greek language. In this country it is employed chiefly as an ingredient in compound preparations.

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Pulvis Aromaticus, *N. F.* (*Br.*); Pulvis Cretæ Aromaticus, *Br., N. F.;* Tinctura Cardamomi, *U. S.;* Tinctura Cardamomi Composita, *U. S., Br.;* Tinctura Aromatica, *N. F.*

CARMINUM. N. F.

CARMINE Carmina.

Carmine Lake; Chinese, Florentine, Hamburg, Munich, Roman or Venetian Lake; Carmin, *Fr. Cod.;* Karmin Lack, *G.*

"The aluminum lake of the coloring principle obtained from cochineal." *N. F.*

The term *lakes* is applied to a group of coloring substances which are salts of an animal or vegetable coloring matter united with a metal generally aluminum or tin. Carmine is a combination of *carminic acid* (see under *Coccus*), obtained from cochineal, with aluminum. (See also *Lakes,* Part II.)

Description and Physical Properties.—"It occurs in irregular, angular, bright red fragments or as a powder, without odor or taste. When burned, Carmine emits an odor resembling that of burned feathers. Slightly soluble in water to which it imparts a red color; freely soluble in ammonia water and alkaline liquids, forming a dark purplish red solution.

"The yield of ash does not exceed 12 per cent. Fuse the ash from 1 Gm. of Carmine with 1 Gm. of sodium cyanide, dissolve the fused mass in hydrochloric acid with the addition of a few drops of nitric acid, then dilute it with distilled water to 30 cc. and filter the solution. Separate portions of 10 cc. each of this solution yield no precipitate with hydrogen sulphide T.S. or with sulphuric acid (*tin, lead and soluble barium compounds*). Fuse the ash from 1 Gm. of Carmine with a mixture of 1 Gm. of sodium cyanide and 1 Gm. of potassium carbonate, extract the fused mass with boiling distilled water, filter, wash with hot distilled water and dissolve the residue in diluted hydrochloric acid; this solution does not become turbid on the addition of a few drops of sulphuric acid (*barium*).

"Preserve it in well-stoppered, amber-colored bottles." *N. F.*

It is used exclusively as a coloring agent.

Off. Prep.—Liquor Carmini, *N. F.*

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CARUM. U. S. (Br.)

CARAWAY [Carawayseed, Caraway Seed]

"Caraway is the dried ripe fruit of *Carum Carvi* Linné (Fam. *Umbelliferæ*). Caraway contains not more than 3 per cent. of other fruits, seeds or foreign organic matter, and yields not more than 1.5 per cent. of acid-insoluble ash." *U. S.* "Caraway Fruit is the dried ripe fruit of Carum Carvi, *Linn.*" *Br.*

Carui Fructus, *Br.;* Caraway Fruit; Carvies, Cumin des Prés, Carvi, *Fr.;* Fructus Carvi, *P. G.;* Gemeiner Kümmel, Kümmel, Garbe, *G.*

The caraway plant is a biennial herb with a spindle-shaped, fleshy, whitish root from which arises, during the first year, a cluster of bi- to tripinnate leaves. During the second year there arises a slender stem bearing alternate, pinnate to bipinnate leaves, the terminal segments of which are very narrow and pointed. The inflorescence is a long-stalked, compound umbel bearing small white flowers with five minute calyx teeth, five ovate and notched petals, five stamens and a conical stylopod. The fruits are oblong; laterally compressed dark-brown cremocarps.

It is a native of Europe and Asia, growing wild in meadows and pastures, and cultivated in many places. The flowers appear in May and June, and the seeds which are not perfected until the second year, ripen in August. The root, when improved by culture, resembles the parsnip, and is used as food in Northern Europe.

Caraway has been cultivated in Germany, Holland, Morocco, Spain, Norway, Russia, England and to a lesser extent in the northern part of the United States. The plant thrives well in clay soil containing some humus. The plants are mowed down when the oldest fruits are ripe, dried in the field or in the barn loft until they have lost most of their moisture, after which the fruits are thrashed out, cleaned and stored in bags. Most of the commercial supply used by this country comes from Holland in burlap bags.

Description and Physical Properties.—"*Unground Caraway.*—Usually in separated mericarps; curved, tapering towards both ends; up to 7 mm. in length and 2 mm. in diameter; externally dark brown with five yellow filiform ribs; odor and taste aromatic.

"*Structure.*—Mericarps nearly equilaterally pentagonal, with a fibro-vascular bundle in each rib; outer epidermis of tangentially-elongated, rather thick-walled cells, a middle layer of collapsed parenchyma bearing the oil tubes, usually six in number, sometimes one or more additional, and located between the ribs; an inner epidermis of broad parenchyma cells, more or less collapsed and which are coherent with the collapsed cells of the seed coat; endosperm of thick-walled parenchyma containing fixed oil and aleurone grains up to 0.010 mm. in diameter and in which are embedded rosette aggregates of calcium oxalate up to 0.004 mm. in diameter.

"*Powdered Caraway.*—Elements of identification are the outer epidermal cells characterized by a waviness and stripping of the cuticle; the cells of the endosperm containing aleurone grains with the embedded rosette aggregates; tracheæ; lignified fibers and fragments of the oil tubes." *U. S.*

"Mericarps usually separate; each from about four to six millimetres long and about one millimetre broad; brown with paler primary ridges; slightly curved, tapering towards each end, and glabrous. In transverse section, six vittæ in each mericarp. Odor and taste aromatic. Ash not more than 9 per cent." *Br.*

They have an agreeable aromatic odor, and a sweetish, warm, spicy taste. These properties depend on an essential oil, which they afford largely by distillation. (See *Oleum Cari.*) The residue is insipid.

"Drawn caraway seeds," a term applied to such as have been recovered from the still residue after obtaining the volatile oil, are used to adulterate caraway; the exhausted "seeds" are much darker in color than are the genuine and are less odorous. (*P. J.*, 1896, 150.) While this is the principal form of adulteration, they may contain large amounts of stems, gravel, sand, dust, weed seeds and other impurities.

Uses.—Caraway is a pleasant stomachic and carminative, occasionally used in *flatulent colic,* and as an adjuvant or corrective of other medicines. The dose in substance is from fifteen to thirty grains (1–2 Gm.). An infusion may be prepared by adding two drachms of the seeds to a pint of boiling water. The volatile oil, however, is more employed. (See *Oleum Cari.*) Three and a half ounces of the oil of caraway caused violent vomiting and abdominal pain, with loss of consciousness, ending, however, in recovery. The urine contained both acetone and albumin. (*Cb. I. M.*, xxii, 1902.) In culinary operations the seeds are added to cakes, to which they communicate an agreeable flavor, while they stimulate the digestive organs.

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Aqua Carui, *Br.;* Confectio Piperis, *Br.;* Pulvis Opii Compositus, *Br.;* Tinctura Cardamomi Composita, *U. S., Br.;* Tinctura Sennæ Composita, *Br.*

CARYOPHYLLUS. U. S. (Br.)

CLOVE Caryoph. [Cloves]

"Clove is the dried flower-buds of *Caryophyllus aromaticus* Linné (Fam. *Myrtaceæ*). Clove contains not more than 5 per cent. of its stems and not more than 1 per cent of other foreign organic matter, and yields not less than 15 per cent. of volatile ether-soluble extractive, not more than 10 per cent. of crude fiber, and not more than 0.75 per cent. of acid-insoluble ash." *U. S.* "Cloves are the dried flower-buds of Eugenia caryophyllata, *Thunb.*" *Br.*

Caryophyllum, *Br.;* Caryophylli Aromatici; Girofle, *Fr. Cod.;* Gérofle, Clous Aromatiques, Clous de Girofle, *Fr.;* Caryophylli, *P. G.;* Gewürznelken, Nägelein, *G.;* Garofani, *It.;* Clavo de especia, Clavillo, *Sp.;* Cravo da India, *Portug.;* Kruidnagel, *Dutch;* Kerunfel, *Arab.*

The clove-tree is a small tree inhabiting the Molucca Island and Southern Philippines. It has a pyramidal form, is evergreen, and is adorned throughout the year with a succession of beautiful rosy flowers. The stem is of hard wood, and covered with a smooth, grayish bark. The leaves are opposite, petiolate, about four inches in length by two in breadth, obovate-oblong, acuminate at both ends, entire, sinuate, with many parallel veins on each side of the midrib. They have a firm consistence and a shining green color, and when bruised are highly fragrant. The flowers are disposed in terminal corymbose panicles, and exhale a strong, penetrating, and grateful odor.

The natural geographical range of the clove is extremely limited, being confined to the Molucca or, as they were one time called, Clove Islands. According to Flückiger, cloves were known in Western Europe as early as the sixth century, long before the discovery of the Moluccas by the Portuguese. After the conquest of the Molucca Islands by the Dutch, the monopolizing policy of that commercial people led them to extirpate the trees in nearly all the islands except Amboyna and Ternate, which were under their immediate inspection. Notwithstanding their jealous vigilance, a French governor of the Islands of France and Bourbon, named Poivre, succeeded, in the year 1770, in obtaining plants from the Moluccas and introducing them into the colonies under his control. Five years afterwards the clove-tree was introduced into Cayenne and the West Indies, in 1803 into Sumatra, and in 1818 into Zanzibar. At present the spice is cultivated both in the West and East Indies, in tropical Africa, and in Brazil. Approximately seven-eighths of the world's clove supply is grown in Zanzibar.

The unexpanded flower buds are the part of the plant employed under the ordinary name of cloves. They are first gathered when the tree is about six years old. The fruit has similar aromatic properties, but much weaker. The buds are at first white, then become green, and then bright red, when they must be at once collected, which is done by hand picking, or by beating the trees with bamboos and catching the falling buds. In the Moluccas they are said to be sometimes immersed in boiling water and afterwards exposed to smoke and artificial heat before being spread out in the sun. In Zanzibar, Cayenne, and the West Indies they are dried simply by solar heat. The stems of the flowers also enter commerce. They possess the odor and taste of the cloves, but they are worth only about one-fifth the price of the cloves, as they are deficient in volatile oil. They are largely used as an adulterant in ground cloves, and are used in the manufacture of oil of cloves. In France they are generally known by the name of *griffes de girofle*.

Although it is stated that as early as 266 B.C., during the reign of the Han dynasty, the Chinese court officers were accustomed to hold cloves in their mouths before addressing the sovereign, that their breath might have an agreeable odor, the spice seems to have been first introduced into Europe in the fourth century, and became a great source of wealth to the enterprising merchants of mediæval Venice, who obtained it from the Arabians. After the discovery of the southern passage to India, the trade in this spice passed into the hands of the Portuguese, but was subsequently wrested from them by the Dutch, by whom it was long monopolized. (For detailed information as to method of cultivation, see *P. J.*, June, 1890.)

In commerce the varieties of cloves are known by the names of the localities of their growth, and so closely resemble one another as to be distinguished only by experts. The *Penang cloves* have been especially esteemed. The *Bencoolen cloves* from Sumatra are by many druggists deemed equal to them. The Amboyna and Molucca cloves are stated to be thicker, darker, heavier, more oily, and more highly aromatic than those cultivated elsewhere.

Description and Physical Properties.—"*Unground Clove.*—From 10 to 17.5 mm. in length, of a dark brown, or brownish-black color, consisting of a stem-like, solid, inferior ovary, obscurely 4-angled or somewhat compressed, terminated by 4 calyx teeth, and surmounted by a nearly globular head, consisting of 4 petals, which enclose numerous curved stamens and 1 style; odor strongly aromatic; taste pungent and aromatic, followed by slight numbness. Stems sub-cylindrical or 4-angled, attaining a length of 25 mm. and a diameter of 4 mm., either simple, branching, or distinctly jointed, and less aromatic than the flower-buds.

"*Powdered Clove.*—Dark brown; parenchyma fragments showing the large oil reservoirs, spiral tracheæ and a few rather thick-walled, spindle-shaped bast-fibers; calcium oxalate in rosette aggregates, from 0.010 to 0.015 mm. in diameter; pollen grains numerous, tetrahedral, from 0.015 to 0.020 mm. in diameter.

"Stone cells, irregular or polygonal, up to 0.070 mm. in diameter, with thick porous walls and large lumina frequently filled with a yellowish-brown amorphous substance, are few or absent (less than 5 per cent. of *stems*). Starch grains absent (*clove fruit or cereals*).

"**Assay.**—Proceed as directed under volatile ether-soluble extractive." *U. S.*

"About fifteen millimetres long, each consisting of a dark-brown, wrinkled, subcylindrical, somewhat angular calyx tube which tapers below and is surmounted by four thick, rigid, patent teeth, between which are four paler, imbricated petals enclosing numerous stamens and a single style. Odor strong, fragrant and spicy; taste very pungent and aromatic. Cloves emit oil when indented with the finger-nail. Ash not more than 7 per cent." *Br.*

Their color is externally deep brown, internally reddish; their odor strong and fragrant; their taste hot, pungent, aromatic, and very permanent. The best cloves exude a small quantity of oil on being pressed or scraped with the nail. When light, soft, wrinkled, pale, and of feeble taste and odor, they are inferior. Those from which the essential oil has been distilled are sometimes fraudulently mixed with the genuine. For monograph on the microscopical structure of cloves, clove stems and clove fruit see Winton and Moeller, "*The Microscopy of Vegetable Foods.*" Powdered cloves sometime contain an excess of clove stems, and may be adulterated with allspice, wheat middlings and powdered peas or beans. Occasionally clove stems alone are ground and sold as cloves. It is claimed that an enormous quantity of exhausted cloves are dishonestly marketed. The amount of volatile ether extract is the best criterion of the value of cloves.

The most important constituent is a volatile oil (see *Oleum Caryophylli*). Trommsdorff obtained from 1000 parts of cloves 180 of volatile oil, 170 of a peculiar tannin, 130 of gum, 60 of resin, 280 of vegetable fiber, and 180 of water. Wm. L. Peabody (1895) found the percentage of tannin in cloves to range from 10 to 13 per cent., and that it has the same chemical composition as gallotannic acid. Lodibert afterwards discovered a green fixed oil, and a tasteless, white, resinous substance which crystallized in silky needles, soluble in ether and boiling alcohol, and exhibiting neither alkaline nor acid reaction. This substance was called by Bonastre *caryophyllin.* To obtain it, the ethereal extract of cloves is treated with water, and the white substance thrown down is separated by filtration, and treated repeatedly with ammonia to deprive it of impurities. Its formula as determined by Mylius (*B. Chem. G.,* 1873) is $C_{20}H_{32}O_2$. On oxidizing with fuming nitric acid it forms *caryophyllic acid,* $C_{20}H_{32}O_6$. Dumas discovered another crystalline principle, which, like caryophyllin, is soluble in alcohol and ether, but differs from that substance in becoming red when touched with nitric acid. Bonastre proposed for it the name of *eugenin.* (*J. P. C.,* xx, 565.) It has the formula $C_{10}H_{12}O_2$, and is isomeric with eugenol.

Water extracts the odor of cloves with comparatively little of their taste. All their sensible properties are imparted to alcohol; and the tincture when evaporated leaves an excessively fiery extract, which becomes insipid if deprived of the oil by distillation with water, while the oil which comes over is mild. Hence it has been inferred that the pungency of this aromatic depends on a union of the essential oil with the resin. For an account of the oil, see *Oleum Caryophylli.*

The infusion and oil of cloves are reddened by nitric acid, and rendered blue by tincture of ferric chloride, facts of some interest, as morphine gives the same reactions.

Uses.—Cloves are among the most stimulant of the aromatics, but, like others of this class, act less upon the system at large than on the part to which they are immediately applied. They are sometimes administered in substance or infusion to relieve *nausea* and *vomiting* correct *flatulence,* and excite *languid digestion;* but their chief use is to assist or modify the action of other medicines. They enter into several official preparations.

The French Codex directs a *tincture of cloves* to be prepared by digesting for ten days, and afterwards filtering, a mixture of three ounces of powdered cloves and sixteen of 80 per cent. alcohol.

Dose, in substance, from five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Infusum Aurantii Compositum, *Br.;* Infusum Caryophylli, *Br.;* Pulvis Cretæ Aromaticus, *Br., N. F.;* Tinctura Lavandulæ Composita, *U. S.;* Pulvis Aromaticus Rubifaciens, *N. F.;* Pulvis Cretæ et Opii Aromaticus (from Aromatic Chalk Powder), *N. F.;* Pulvis Myricæ Compositus, *N. F.*

CASCARA AMARGA. N. F.

CASCARA AMARGA. Cascar. Amarg.
[Honduras Bark]

"Cascara Amarga is the dried bark of an undetermined species of *Picramnia* (Fam. *Simarubaceæ*). Cascara Amarga contains not more than 2 per cent. of foreign organic matter." *N. F.*

About half a century ago there was brought into this country from Mexico a bark which had been used in that land as a tonic and alterative. This bark was identified by Doctor Vasey, of the Department of Agriculture, as coming from a species of *Picramnia.* No more accurate recognition of its source has since been made.

The genus *Picramnia* includes some 30 species, all of which are found in the American tropics and the West Indies Islands.

Description and Physical Properties.—"*Unground Cascara Amarga.*—In quills up to 500 cm. long and 3 cm. in diameter; bark up to 8 mm. thick, sometimes in broken, irregular, flattened or transversely curved pieces; externally yellowish brown, more or less covered with grayish lichens showing blackish apothecia, longitudinally fissured and roughened with cork layers, or with cork more or less removed and reddish brown; inner surface grayish brown to dark reddish brown, with irregular longitudinal striations and numerous minute transverse markings; internally dark brown with a light yellow zone beneath the cork and numerous yellowish groups of stone cells, the latter especially pronounced in the older bark; fracture short, hard and brittle. Odor faint; taste extremely bitter and persistent.

"*Structure.*—Outer bark of 25 or more rows of thick-walled, more or less lignified cork cells, many of which contain a yellowish to reddish coloring substance; phellogen layer distinct; middle bark with an outer zone of cortical parenchyma, a few isolated stone cells and an inner zone of a nearly continuous ring of stone cells, parenchyma, a few groups of fibers associated with crystal fibers; inner bark with groups of bast fibers associated with crystal fibers; sieve tissue, parenchyma containing starch, and numerous large groups of stone cells more or less transversed by medullary rays, the latter mostly 1 to 4 cells wide and arranged in regular rows.

"*Powdered Cascara Amarga.*—Light brown; numerous groups of bast fibers associated with crystal fibers, the latter with monoclinic prisms of calcium oxalate from 0.020 to 0.040 mm. in length; stone cells isolated or in groups, the individual cells up to 0.100 mm. in diameter; fragments of medullary ray tissue and parenchyma, the latter containing numerous irregular starch grains up to 0.025 mm. in length, rarely larger, occasionally 2- to 4-compound; occasional fragments of brown cork; few slightly lignified or non-lignified fibers." *U. S.*

Thompson (*A. J. P.,* 1884) separated from Honduras bark a yellow amorphous substance, which responded to the ordinary tests of alkaloidal nature such as: solubility in diluted acids, precipitation with Mayer's reagent, tannic acid, etc. He did not obtain either the base nor any salt in a crystalline form. He was satisfied, however, of its alkaloidal nature, and suggested the name *picramnine.* We know of no further chemical study of the drug.

Uses.—Honduras bark appears to have been used as a folk medicine in Mexico in chronic skin diseases, especially those of syphilitic origin. Doctor Atkinson (*T. G.*, 1881) reported a few cases of healing of syphilitic ulcers under the continued use of the remedy; his case histories, however, do not afford any convincing evidence that the healing process was materially hastened by the drug. Honduras bark is used to-day almost solely as an ingredient of the compound fluidextract of trifolium, and the syrup made from it.

Dose, fifteen to forty-five grains (1–3 Gm.).

Off. Prep.—Fluidextractum Trifolii Compositum, *N. F.;* Syrupus Trifolii Compositus, *N. F.*

CASCARA SAGRADA. U. S., Br.

CASCARA SAGRADA. Casc. Sagr. [Rhamnus Purshiana U. S. VIII]

" Cascara Sagrada is the dried bark of *Rhamnus Purshiana* De Candolle (Fam. *Rhamnaceæ*).

" NOTE.—Cascara Sagrada should be collected at least one year before being used for making medicinal preparations." *U. S.* " Cascara Sagrada is the dried bark of Rhamnus Purshianus, *D.C.*, collected at least one year before being used." *Br.*

Cortex Rhamni Purshiani, *P. G.;* Sacred Bark; Chittem Wood Bark, Dogwood bark, Coffee-berry bark, Pigeonberry bark, Bear-berry bark, Bitter bark and Yellow bark; Cascara Sagrada, *Sp.*

A number of species of Rhamnus have been described as growing in California, but according to the best authority there are only four species,—*R. alnifolia,* L'Her., *R. crocea,* Nutt., *R. Purshiana,* D.C., and *R. californica,* Esch. Of these species, *R. alnifolia* is too rare in the Cascara district to be important; while the spinescent twigs, the very thick oval or roundish leaves, and the small roundish red fruit of *R. crocea* make it so distinct that it cannot be confounded with a Cascara, whose bark, moreover, it does not resemble. On the other hand, *R. californica* appears to be very commonly confounded with the official species by collectors, and to have yielded some of the cascara sagrada bark of commerce. *R. californica* is rare in Northern California, but abundant in the countries lying south and southeasterly, while *R. Purshiana* is abundant in Northern California, but scarce in the south, so that any bark collected in Northern California is probably genuine. *R. californica* is chiefly distinguished from the official species by its leaves being thin, and, when not smooth, having a short close pubescence, and the primary veins of the under surface not nearly so numerous, straight, or fine as those of *R. Purshiana.* Rusby thinks that its leaves are especially distinguished by the channel of the midrib of *R. californica* being altogether absent, or shallow, or inconspicuous. Nevertheless the species so run into one another that competent botanists believe them identical.

The *Rhamnus Purshiana* is a small tree, attaining a height of twenty feet. Its leaves are rather thin, elliptic, for the most part briefly acutely pointed, finely serrated, at the base obtuse, somewhat pubescent beneath, from two to seven inches long and from one to three wide. The rather large flowers are in somewhat umbellate cymes; the sepals five; the minute cucullate petals bifid at the apex. The fruit is black, broadly obovoid, four lines long, three-lobed, and three-sided. The seeds are convex on the back, with a lateral raphe. It is found in California, Oregon, Washington and Southwest British Columbia. For details of manner of collecting the bark see an elaborate and illustrated article by Johnson and Hindman, *A. J. P.*, 1914, p. 387. Because of the rapid destruction of natural sources of the bark in the Western United States, experiments have been conducted by the Bureau of Plant Industry, U. S. Department of Agriculture, Washington, D. C., to cultivate it.

The *Rhamnus californica,* or *Californian buckthorn* or *California coffee-tree,* yields a bark which is of a dark brown color externally and bright yellow internally, having an intensely bitter taste, with a persistent nauseous aftertaste, and very little odor. It is said to be much more distinctly purgative than that of *R. crocea.*

It does not seem possible to distinguish with certainty between the barks of the two species by their macroscopic appearance. The bark of *R. Purshiana* is usually more red than is that of *R. californica,* but it may be of a distinctly gray color. The microscopic structure of the two barks is, however, different. The medullary rays in *R. Purshiana* are numerous, thin, for a long distance nearly parallel and straight and converge at their outer ends, run about three-quarters of the distance through the bark, and are one to four cells in width. In *R. californica* the medullary rays are much broader, much shorter, and are one to seven cells in width; further, they are crooked and not parallel throughout their course. Again, the zone of resin spaces is much broader in *R. californica,* and the spaces themselves much larger and more numerous than in the official species. For further details and elaborations, see papers by H. H. Rusby, *Proc. A. Ph. A.*, 1890, and by Gathercoal, *J. A. Ph. A.*, 1915, p. 15. According to L. E. Sayre (*A. J. P.*, March, 1897), the powder of the barks can be distinguished by paying attention to the fact that *R. Frangula* contains no stone cells, while in *R. californica* and *R. Purshiana* such cells are abundant, occurring in large, irregular groups below the cork and usually outside the region of the bast. *R. Purshiana* may also be distinguished from *R. californica* by color tests. After several days' maceration in dilute alcohol the powder of *R. Purshiana* appears of an orange-yellow color, *R. californica* of a purplish color; or if 0.2 Gm. of the powdered bark be placed in a small test tube, and there be added 2 cc. of potassium hydroxide test solution, *R. californica* will give a blood-red and *R. Purshiana* an orange-red color.

The bark of the *Rhamnus crocea,* the so-called *California mountain holly,* occurs in slightly curved pieces, externally of a dark brown color, internally of a characteristic red delicately streaked with numerous white veins. The odor is somewhat aromatic, the taste warming and not unpleasantly bitter. It is affirmed to be a tonic and mild laxative.

Description and Physical Properties.—"*Unground Cascara Sagrada.*—Usually in flattened or transversely curved pieces, occasionally in quills; bark from 1 to 5 mm. in thickness; outer surface dark brown or brownish-red, longitudinally ridged, with grayish or whitish lichen patches, sometimes with numerous lenticels and occasionally with moss; inner surface longitudinally striate, light yellow to dark reddish-brown or dark brown in old matured bark; fracture short with projections of bast-bundles in the inner bark; odor distinct; taste bitter and slightly acrid.

"*Structure.*—Cork yellowish-brown to reddish-brown, of 10 or more rows of small cells; stone cells in yellowish, tangentially elongated groups of 20 to 50 cells; medullary rays 1 to 4 cells wide, 15 to 25 cells deep, frequently diagonal or curved forming converging groups; bast-fibers in small bundles surrounded by crystal fibers and located between the medullary rays; parenchyma with brown walls and containing starch grains or calcium oxalate.

"*Powdered Cascara Sagrada.*—Light brown to olive-brown; consisting of broken bast-bundles with the accompanying crystal fibers containing monoclinic prisms of calcium oxalate; stone cells more or less adhering, with thick, finely lamellated and porous walls; fragments of reddish-brown cork; masses of parenchyma and medullary ray cells, colored red upon the addition of a solution of an alkali; starch grains spheroidal, from 0.003 to 0.008 mm. in diameter; calcium oxalate in monoclinic prisms or rosette aggregates from 0.006 to 0.020 mm. in diameter.

"Add 0.1 Gm. of powdered Cascara Sagrada to 10 cc. of hot water, shake the mixture occasionally until cold, filter, and add sufficient water to make the filtrate measure 10 cc.: this filtrate, on the addition of 10 cc. of ammonia T.S., is colored an orange-yellow. Macerate 0.1 Gm. of powdered Cascara Sagrada with 10 drops of alcohol, boil the mixture with 10 cc. of water, cool, filter, and shake the filtrate with 10 cc. of ether: a yellow ethereal solution separates. Shake 3 cc. of this ethereal solution with 3 cc. of ammonia T.S.: the separated ammoniacal solution on diluting with 20 cc. of water retains a distinct, yellowish-red color." *U. S.*

"In quilled, channeled, or nearly flat pieces from one to two millimetres thick, but varying in length and width. Cork nearly smooth, dark purplish-brown, marked with transversely elongated lenticels, but usually more or less covered with patches of silvery-grey lichen. Inner surface reddish-brown, with faint transverse corrugations and longitudinal striations. Fracture short, but near the inner surface somewhat fibrous. In transverse section, scattered groups of sclerenchymatous cells in both cortex and bast; the parenchymatous cells contain a yellow substance which is colored violet by *solution of sodium hydroxide.* Odor characteristic but not powerful; taste nauseous, bitter and persistent." *Br.*

For articles illustrating the pharmacognosy of Cascara bark see Kraemer, *A. J. P.,* 1912, p. 385; Miller, *J. A. Ph. A.,* 1912, p. 1207; and Farwell, *J. A. Ph. A.,* 1914, p. 649.

Constituents.—A. B. Prescott in the year 1879 found in it a very bitter brown resin (which is colored a vivid purple-red by potassium hydroxide); a red resin; a light yellow resin; a neutral crystallizable substance; a volatile oil and vegetable acids. H. F. Meier and J. LeRoy Webber reported the presence of a ferment, to which they attributed the unpleasant results attending the administration of "fresh bark"; "seasoned bark"—*i.e.,* such as has been kept a year or two—owes its valuable properties as a laxative, *free from griping,* to the fact that the ferment has exhausted itself; the laxative properties, they state, reside in the resins, and the tonic effects are due to the crystalline principle. (*A. J. P.,* 1888, 91.) Schwabe (*A. Pharm.,* ccxxvi, 569) found emodin. Dohme and Engelhardt (*Proc. A. Ph. A.,* 1897, 193) have shown the analogy of cascara sagrada with *Rhamnus Frangula* by obtaining a glucoside to which they give the name of *purshianin.* This decomposes, yielding emodin and a dextro-rotatory non-fermentable sugar, while the frangulin of buckthorn yields emodin and rhamnose as the sugar. Purshianin forms brown-red needles, melting at 237° C. Dohme and Engelhardt failed to obtain in a pure form (*Proc. A. Ph. A.,* 1898, 340) the bitter principle of cascara sagrada. Le Prince (*C. R. A. S.,* 1892, 286) claimed to have obtained the active principle of cascara bark in a crystalline form, which he named *cascarine;* his results are doubted by Jowett who believes that cascarine and purshianin are impure forms of emodin. Jowett (*Proc. A. Ph. A.,* 1904, 288) in an exhaustive paper concludes that the active principle of cascara is contained in that portion of an alcoholic extract which is soluble in water and precipitable by lead subacetate and in that portion of the regenerated lead subacetate precipitate which is soluble in ethyl acetate. Pietsch reported a glucoside, *peristaltin,* having the composition $C_{14}H_{18}O_8$. (*Th. M.,* 1910, No. 1, p. 35.)

Uses.—Cascara sagrada belongs to the group of vegetable cathartics whose activity depends upon the presence of one or more oxides of methylanthraquinone (see *Rheum*). In cascara the active principle appears to be emodin, which is trioxymethylanthraquinone, and which appears also to be the purgative principle of aloes.

The action of this principle is chiefly to excite peristalsis in the colon, although after large doses there is probably also some effect upon the upper bowel. As the action is chiefly upon the lower intestine it is not to be recommended as a laxative where it is desired to clean out the bowel, but in the treatment of *chronic constipation* it acts very favorably. It often appears to restore tone to the relaxed bowel and in this way produce a permanent beneficial effect. McGuigan (*J. A. M. A.*, 1921, lxxvi, 513) says that large doses produce an inflammatory condition of the bowel and that the drug should, therefore, never be used to produce active purgation. The bark itself is rarely used, either the extract or fluidextract being eligible preparations.

The addition of belladonna to overcome any tendency to gripe is an advantage. Ordinarily a single dose is given at bedtime but in some cases better results are obtained by exhibiting smaller doses after meals.

Dose, ten to thirty grains (0.6–2.0 Gm.).

Off. Prep.—Extractum Cascaræ Sagradæ, *U. S.* (*Br.*); Fluidextractum Cascaræ Sagradæ, *U. S.* (*Br.*); Fluidextractum Cascaræ Sagradæ Aromaticum, *U. S.;* Syrupus Cascaræ Aromaticus, *Br.;* Elixir Cascaræ Sagradæ (from Aromatic Fluidextract), *N. F.;* Elixir Cascaræ Sagradæ Compositum (from Aromatic Fluidextract), *N. F.;* Fluidglyceratum Cascaræ Sagradæ, *N. F.;* Fluidglyceratum Cascaræ Sagradæ Aromaticum, *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ (from Extract), *N. F.;* Syrupus Ficorum Compositus (from Aromatic Fluidglycerate), *N. F.*

CASCARILLA. N. F., Br.

CASCARILLA

" Cascarilla is the dried bark of Croton Eluteria, *J. J. Benn.*" *Br.*

Cascarillæ Cortex, *Br.* (1885), Cascarilla Bark, Sweet Bark, Sweetwood Bark; Cascarille officinale, *Fr. Cod.;* Cortex Eluteriæ, Cortex Thuris; Chacrille, Ecorce éleuthérienne Cascarille, *Fr.;* Cortex Cascarillæ, *P. G.;* Cascarillrinde; Cascarilla, Kaskarillrinde, *G.;* Cascarilla, Cascariglia, *It.;* Chacarilla, Quina aromatica, *Sp.*

Croton Eluteria is a shrub or a small tree with a stem from four to eight inches in diameter. The stem is straight, and marked at intervals with white or grayish stains. The leaves are petiolate, often somewhat cordate at the base, obtusely acuminate, pale or grayish-green above, and densely covered beneath with shining silvery scales, appearing white at a distance. They are smaller and narrower in the plants of arborescent growth. The flowers, which have a delicious odor, are monœcious, small, white, petiolate, and closely set in simple terminal or axillary spikes. The shrub is a native of the Bahamas, scarce at present in the island of New Providence, but still abundant in Andros, Long, and Eleutheria islands, from the latter of which is derived its botanical title. Daniell calls the plant *sweetwood.* The name of *sea-side balsam* belongs to another species, *C. balsamiferum* Linnæus, which grows in the Bahamas and other West India islands, and owes its name to the exudation of a balsamic juice from its young branches when wounded.

Under the name of " cascarilla," also " *Quina morada,*" the bark of the *Pogonopus febrifugus* is said to be used in the Argentine Republic as a substitute for cinchona bark. There has been separated from it a blue fluorescent substance, *moradin,* and an alkaloid, *moradeine.* (*P. J.*, xx, 854.)

Copalchi bark has been mistaken not only for cascarilla, but also for a variety of cinchona. Two kinds were noticed: one, in small slender quills, of an ash color, bearing some resemblance to a variety of pale cinchona, but having the flavor of cascarilla, and burning with a similar odor; the other in larger quills, with a thick cork-like epidermis, very bitter, and yielding an aromatic odor when burnt. The former is the product of *Croton Pseudochina,* Schlechtendal (*C. niveus* Jacquin); the latter is of unknown origin, but conjecturally referred to *C. suberosus.* J. E. Howard states that the quilled copalchi bark contains a bitter alkaloid, soluble in ether, and precipitable as a white hydroxide from its acid solution. (*P. J.*, xiv, 319.) Copalchi bark is an aromatic tonic, employed in Mexico in intermittents, and capable of useful application in all cases requiring a mild aromatic bitter.

Croton Cascarilla Bennett, known in the West Indies as *wild rosemary,* was at one time said to furnish the cascarilla of commerce. The bark is also substituted by the barks of *Croton glabellus* L. and *C. lucidus* L. of the Bahamas and which were formerly designated as the " mother plants " of Cascarilla. They are not aromatic but astringent and slightly bitter. They are also distinguished by the presence of stone cells which are wanting in true Cascarilla. (See *U. S. D.*, 19th ed.)

Cascarilla is brought to this market from the West Indies, and chiefly Nassau, on the island of New Providence. It comes in bags or casks. We have observed it in commerce in two forms, so distinct as to merit the titles of varieties. In one, the bark is in rolled pieces of every size, from three or four inches in length and half an inch in diameter to the smallest fragments, covered externally with a dull whitish or grayish-white epidermis, which in many portions is partially, sometimes wholly removed, leaving a dark brown surface, while the inner surface has a chocolate color, and the fracture is a reddish-brown. The small pieces are sometimes curled, but have a distinct abrupt edge as if broken from the branches. The second variety consists entirely of very small pieces, not more than an inch or two in length, very thin, without the white cork, not regularly quilled, but curved more or less in the direction of their length, often having a small portion of woody fiber attached to their inner surface, and appearing precisely as if shaved by a knife from the stem or branches. Whether these two varieties are derived from distinct species, or differ only because of the mode of collection, it is difficult to determine. A. W. Southall describes a bark believed to belong to the genus *Croton,* and obtained from Colombia in *P. J.,* 1894, 574.

According to the Br. it is: "in quills usually from three to ten centimetres in length and from four to twelve millimetres in diameter, or in small curved pieces. Cork greyish-white, easily detached, and often more or less completely removed disclosing a dull brown cortex. Both cork and cortex frequently marked with numerous longitudinal and transverse cracks. Fracture short, the fractured surface exhibiting under a lens a dark reddish-brown bast traversed by numerous, thin, whitish medullary rays. In transverse section cork cells with strongly thickened outer walls, but thin inner walls, in which minute crystals of calcium oxalate are embedded; both cortex and bast free from sclerenchymatous cells. Aromatic odor, especially when burned; taste aromatic and bitter. Ash not more than 11 per cent." *Br.*

Trommsdorff found in the bark 1.6 per cent. of a fixed oil. It is of a greenish-yellow color, has a penetrating odor analogous to that of the bark, and is of the sp. gr. 0.938. G. Feudler (*A. Pharm.,* 1900, p. 671) finds the oil to contain about 2 per cent. of free acid, which consists of a liquid acid, $C_{11}H_{20}O_2$, to which the name of *cascarillic acid* was given, and a solid portion made up of a mixture of palmitic and stearic acids. The oil contains 0.3 per cent. of eugenol, a terpene differing from pinene, cymene, possibly some l-limonene, two sesquiterpenes and an alcohol, $C_{15}H_{23}OH$. Duval in 1845 found in cascarilla a crystalline principle which he called *cascarillin.* This he obtained by treating infusion of the bark with lead acetate; he separated the lead by hydrogen sulphide, filtered, evaporated with the addition of animal charcoal, filtered again, evaporated at a low temperature to a syrupy consistence, and having allowed the semi-liquid substance thus obtained to harden by cooling, purified it by twice successively treating it, first with a little cool alcohol, to separate the coloring and fatty matters, and afterwards with boiling alcohol and animal chacoal. The last alcoholic solution was allowed to evaporate spontaneously. Thus obtained, cascarillin is white, crystalline, inodorous, bitter, very slightly soluble in water, soluble in alcohol and ether. It is not volatile nor a glucoside. Naylor and Littlefield re-investigated Duval's cascarillin and find its melting point to be 203.5° C., and give it the formula $C_{16}H_{24}O_5$. (*Y. B. P.,* 1896, 301.) P. E. Alessandri obtained what he regarded as an alkaloid, by mixing powdered cascarilla with sufficient 3 per cent. aqueous solution of oxalic acid to cover it, shaking the mixture, and heating it to 60° C., then allowing it to cool, expressing the mixture and saturating the filtered liquor with ammonia, then evaporating at a low temperature to two-thirds of its bulk, allowing it to cool, and separating any deposit. The clear liquid is then shaken with ether; this takes up the cascarilline, which may be obtained through evaporation of the ethereal liquid. (*P. J.,* 1882, 993.) R. A. Cripps was unable to obtain the alkaloid by Alessandri's method, and suggests that the bitterness of the so-called cascarilline might be due to adherent resin. (*P. J.,* 1886, 1103.) Either alcohol or water will partially extract the active matters of cascarilla; W. A. H. Naylor has found betaine in cascarilla. (*P. J.,* 1898, 279.)

Uses.—This bark is aromatic and tonic. It was known in Germany as early as the year 1690, and was much used as a substitute for Peruvian bark by those who were prejudiced against that febrifuge in the treatment of *remittent* and *intermittent fevers.* It has, however, lost its reputation, and is now employed only where a pleasant and gently stimulant tonic is desirable, as in *atonic dyspepsia,* and other cases of debility of the stomach or bowels, especially in combination with the more powerful bitters. It may be given in powder or in infusion. In consequence of its pleasant odor when burned, some smokers mix it in a small quantity with their tobacco; but it is said to occasion vertigo and intoxication.

Dose, twenty to thirty grains (1.3–2.0 Gm.).

Off. Prep.—Infusum Cascarillæ, *Br.;* Tinctura Cascarillæ, *Br.*

CASSIA FISTULA. N. F. (Br.)

CASSIA FISTULA Cass. Fist. [Purging Cassia]

"Cassia Fistula is the dried fruit of *Cathartocarpus Fistula* (Linné) Persoon (Fam. *Leguminosæ*). Cassia Fistula contains not more than 2 per cent. of foreign organic matter." *N. F.*

"Cassia Pods are the ripe fruits of Cassia Fistula, *Linn.*" *Br.*

Cassia Fructus, *Br.;* Cassia Pods; Pudding-stick (or pipe); Fructus Cassiæ Fistulæ; Casse Officinale, Casse en bâtons, Pulpe de Casse, Casse, Mondée Casse, *Fr.;* Röhrenkassie, Purgirkassie, Fistelkassie, *G.;* Cassia, *It.;* Cana Fistula, *Sp.*

Cassia Fistula L. (*Cathartocarpus Fistula* (L.) Persoon is a large tree attaining a height of about 15 m. with a trunk of hard, heavy wood, dividing towards the top into numerous spreading branches, and covered with a smooth, ash-colored bark. The leaves are commonly composed of five or six pairs of opposite leaflets, which are petiolate, ovate, pointed, undulated, smooth and of a pale green color. The flowers are large, of a golden yellow color, and arranged in long, pendent, axillary racemes. The fruit consists of long, cylindrical, woody, dark-brown, pendulous loments, which when agitated by the wind strike against each other and produce a sound that may be heard at a distance. This species of Cassia is a native of India, whence it is generally supposed to have been transplanted to other parts of the world. It is at present very extensively diffused through the tropical regions of the old and new continents, being found in insular and continental India, Cochin China, Egypt, Nubia, the West Indies, and the warmer parts of the continent of America. Under the name of *Golden Shower* it is known as an ornamental shade tree in all tropical countries. The fruit is the official part of the plant. Most of the drug used in the United States is imported from the West Indies, and from South America.

Description and Physical Properties.—"*Unground Cassia Fistula.*—Cylindrical, from 25 to 50 cm. long, about 20 mm. in diameter, smooth, chestnut-brown in color, on one side a longitudinal groove and on the other a smooth line or slight ridge, indicating the sutures; indehiscent, the cavity divided transversely into numerous compartments, each containing a reddish brown, glossy, flattish ovoid seed embedded in a blackish brown sweet pulp. Odor resembling that of prunes." *N. F.*

It is described in the Br. as: "Long, narrow, cylindrical, shortly stalked fruits about thirty-five to fifty centimetres in length, and fifteen to twenty-five millimetres in diameter. Pericarp nearly smooth, dark chocolate-brown or nearly black, thin and hard. Internally divided by thin, transverse dissepiments into numerous compartments, each of which contains a smooth, oval, reddish-brown seed surrounded by a nearly black, sweet pulp." *Br.*

The pods of other species of cassia are sometimes substituted for the official. The pods of the *Cassia Braziliana* Lam. (*C. Grandis* L.), sometimes called *horse cassia,* are larger than those of the *Cassia fistula,* being about 4 cm. (1½ inches) in diameter, flattened on the sides, exceedingly rough on the outer surface, and marked by three longitudinal very elevated ridges, corresponding to the bands or furrows of the common cassia. The pulp was rather nauseous, but in other respects seemed to have the properties of the official purging cassia. The fruit of the *C. Moschata* H. B. K. is smaller and narrower than the official variety, from 30 to 50 cm. in length and about 1.5 cm. in diameter; the pulp is of a lighter color and with a musk-like odor.

The heaviest pods, and those which do not make a rattling noise when shaken, are to be preferred, as they contain a larger portion of the pulp, which is the part employed. This should be black and shining and have a sweet taste. It is apt to become sour if long exposed to the air, or mouldy if kept in a damp place The pulp is extracted from the pods by first bruising them, then boiling them in water, and afterwards evaporating the decoction; or, when the pods are fresh, by opening them at the sutures and removing the pulp with a spatula.

Dose, one to four drachms (4–15 Gm.).

Off. Prep.—Confectio Sennæ, *N. F.*

CASSIÆ PULPA. Br.

CASSIA PULP

"Exhaust crushed Cassia Pods by percolation with Distilled Water; strain; evaporate on a water bath to the consistence of a soft extract." *Br.*

Cassia pulp has a slight odor, and a sweet, mucilaginous taste. According to Henry it contains sugar, gum, coloring matter, and a tannin-like substance; while Haensel obtained from it by steam distillation a dark yellow volatile oil, also butyric acid (*Ph. Cb.,* 41). It also apparently contains some anthraquinone derivative, the exact nature of which has not been determined.

Uses.—Cassia pulp is laxative, and may be advantageously given in small doses in cases of *habitual costiveness.* In quantities sufficient to purge, it occasions nausea, flatulence, and griping. In this country it is rarely prescribed, except as an ingredient in the confection of senna, which is a pleasant and useful laxative preparation.

Dose, of the pulp as a laxative, one or two drachms (3.9 or 7.7 Gm.), as a purge one or two ounces (31–62 Gm.).

Off. Prep.—Confectio Sennæ, *Br.*

CASTANEA. N. F.

CASTANEA Castan. [Chestnut Leaves]

"Castanea consists of the dried leaves of *Castanea dentata* (Marshall) Borkhausen (Fam. *Fagaceæ*). Castanea contains not more than 5 per cent. of its stems or other foreign organic matter." *N. F.*

Feuilles de chataignier, *Fr.;* Kastanienblätter, *G.;* Castagna, *It.*

Of the few species included in the genus *Castanea,* two are natives of North America. Of these *C. dentata* has been considered by many botanists as identical with *C. sativa* Mill. (*C. vesca* Gaertn.), of Europe, and was described by Michaux as a variety of that species under the name of *americana.* Botanists at present, however, generally consider the two species as distinct.

Castanea dentata is a large, spreading, deciduous tree with deeply fissured bark, smooth, simple, alternate, oblong-lanceolate leaves with serrate margins. Its staminate flowers are crowded on lower aments while its pistillate flowers appear as spherical structures at the base of the upper aments. Its fruit is a spiny bur containing 1 to 5, usually 2 or 3 nuts. Chestnut leaves are gathered in autumn and carefully dried.

Description and Physical Properties.—"*Unground Castanea.*—Blade entire or slightly broken and usually folded or matted together; about 15 to 25 cm. long and about 5 cm. wide, oblong-lanceolate, apex attenuate, acute at the base, coarsely and sharply serrate with ascending, attenuate teeth, nearly smooth, coriaceous in texture, the upper surface dark green, the lower light green; distinctly pinnately veined, the veins of the first order diverging at an angle of about 60 degrees, each terminating in one of the teeth; petiole stout, about 12 mm. long. Odor slight; taste astringent.

"*Powdered Castanea.*—Few non-glandular hairs from 0.100 to 0.500 mm. long, occasionally up to 1.500 mm. in length, nearly smooth, thick-walled, distinctly yellow, occasionally in groups of 3 to 8 and spreading from the base; numerous calcium oxalate crystals in rosettes or in monoclinic prisms from 0.010 to 0.050 mm. in diameter occasionally in crystal fibers; parenchyma cells containing irregular yellowish brown tannin masses which are colored blue with ammonioferric alum T.S." *N. F.*

Castanea pumila (L.) Mill., *Chinquapin* of the Southern United States, is a bush or small tree usually eight or ten feet in height, but in the Gulf States reaches sometimes thirty feet. The oblong, acute, mucronately serrated leaves are readily distinguished from those of the ordinary chestnut by being whitish and downy underneath. The tree produces a small, edible nut. The bark has been used as an astringent tonic. (For analysis, see *A. J. P.,* 1899.)

Uses.—Chestnut leaves were recommended a half a century ago in the treatment of *whooping-cough* and the superstition still survives to a certain extent. There is, however, no sufficient reason to believe them to possess any therapeutic value except that of a mild astringent which is due to their tannic acid.

Dose, one drachm (4 Gm.).

Off. Prep.—Fluidextractum Castaneæ, *N. F.*

CATARIA. N. F.

CATNEP Catar. [Catmint]

"Catnep consists of the dried leaves and flowering tops of *Nepeta Cataria* Linné (Fam. *Labiatæ*). Catnep contains not more than 5 per cent. of its stems over 4 mm. in diameter or other foreign organic matter." *N. F.*

Catairs, *Fr.*; Katzenmünze, *G.*; Cattara, *It.*; Gatera, *Sp.*

Catnep is a perennial labiate plant which is common near dwellings in the United States, but is indigenous to Europe. Most of the drug is grown in the United States. It is called *catnep* on account of the fondness which cats show for it either in the fresh or the dried condition. The active constituents are volatile oil, and tannin of the kind which produces a greenish color with the salts of iron.

Description and Physical Properties.—"*Unground Catnep.*—Tops, from 10 to 20 cm. long, much branched, or crushed and broken; stems quadrangular, downy, up to 4 mm. in diameter; leaves opposite, the larger, petiolate, from 2 to 7 cm. long, ovate or oblong, rounded or heart-shaped at the base, pointed at the apex, pale gray-green, soft-hairy above, downy beneath, margin deeply crenate; floral leaves small, bract-like; flowers small, in dense, interrupted spikes; calyx hairy, tubular, curved obliquely and sub-equally 5-toothed; corolla whitish, dotted with purple, throat dilated, limb bilabiate, the upper lip erect and two cleft, the lower spreading and three cleft, the middle lobe largest, crenulate; stamens two pairs ascending under the upper lip, lower pair shorter. Odor faintly aromatic and mint-like; taste bitter, pungent and aromatic.

"*Powdered Catnep.*—Light green or grayish green; numerous fragments of parenchyma, the palisade tissue containing green plastids; non-glandular hairs numerous, 1- to 5-celled, tapering, more or less broken, the basal cells up to 0.050 mm. in diameter; glandular hairs with 1-celled stalk and many-celled secreting head, the latter up to 0.070 mm. in diameter; tracheæ with spiral, reticulate, annular or simple pore markings; stomata broadly elliptical up to 0.030 mm. in diameter; collenchyma and lignified wood fiber bundles, few.

"Preserve Catnep in air-tight containers." *N. F.*

Uses.—Catnep has no therapeutic virtues other than that of a mild aromatic. Like other substances of this class it is used, domestically, in the form of a hot decoction as a sudorific in *colds* and *febrile* complaints, and in painful or delayed menses. Chewing the leaves is reputed to relieve *toothache.*

Dose, one to two drachms (4–8 Gm.).

Off. Prep.—Fluidextractum Catariæ, *N. F.;* Elixir Catariæ et Foeniculi, *N. F.*

CATECHU NIGRUM. Br.

BLACK CATECHU

"Black Catechu is an extract prepared from the wood of Acacia Catechu, *Willd.*" *Br.*

Terra japonica, Cutch, Cachou de Pegu, *Fr. Cod.;* Pegu Katechu, *G.;* Caticu, Catto, *It.;* Catecu, *Sp.;* Cutt, *Hindostani.*

Acacia Catechu is a small tree, seldom more than twelve feet in height, with a trunk one foot in diameter, dividing towards the top into many close branches, and covered with a thick, rough, brown bark. Its leaves are bipinnate; the flowers are yellow and arranged on elongated racemes. The fruit is a brown, flattened, legume containing several brown, shiny seeds. This species of Acacia is a native of India and Burma, growing abundantly in various provinces of Hindostan, and in the Burmese Empire. It is also common in Eastern Africa where it is valued for its wood; but no extract appears to be made from it. Pereira says that it is common in Jamaica.

This drug was long known before its source was discovered. It was at first called *Terra japonica,* under the erroneous impression that it was an earthy substance derived from Japan. When ascertained by analysis to be of vegetable origin, it was generally considered by writers on the Materia Medica to be an extract of the *betel nut.* Its true origin was made known by Kerr, assistant surgeon of the civil hospital in Bengal. In the preparation of cutch the exterior white wood is rejected, the brownish heart-wood after being cut into chips is boiled in water, in unglazed earthen vessels, until all the soluble matter is dissolved. The decoction thus obtained is strained and then boiled, until it has assumed a thick consistence, when it is spread out to dry upon a mat or cloth, being, while yet soft, divided by means of a string into square or quadrangular pieces. The account subsequently given by Royle, of the preparation of the extract in Northern India, is essentially the same, but is completed by the pouring of the extract into quadrangular earthen moulds in which it hardens in mases of 40 or 50 pounds. These are afterwards broken up into fragments, in which form it appears in commerce. It is said that the unripe fruit and leaves are also sometimes submitted to decoction. Three colors of catechu are prepared; the light red or red, which is considered best and is especially employed in Burmah and India to chew with the betel nut; the dark red and black, which are made especially for European and American markets, and which are apt to suffer adulteration *en route* in China.

The name "catechu" in the native language signifies the juice of a tree, and appears to have been applied to astringent extracts obtained from various plants. Commerce is chiefly supplied with catechu from Bahar, Northern India, and Nepaul through Calcutta, from Canara through Bombay, and from the Burmese dominions. It is frequently called *cutch* by the English traders, a name derived from the Hindostanee word *cutt.*

Catechu is inodorous, with an astringent and bitter taste, followed by a sense of sweetness. It is brittle, and breaks with a fracture which is rough in some specimens, in others uniform, resinous, and shining. That which is preferred in our market is of a dark color, easily broken into small angular fragments, with a smooth glossy surface, bearing some resemblance to kino. Catechu is often mixed with sand, sticks, and other impurities.

Black catechu is described in the Br. Pharm., 1914, as follows: "In irregular masses of a dark brown color, brittle, having a porous, glossy, somewhat conchoidal fracture. Partially soluble in cold *water,* almost entirely soluble in boiling *water.* Not less than 60 per cent. is soluble in *alcohol* (90 per cent.). No odor; taste sweetish, astringent. Its dilute aqueous solution gives a dark green color with *T. Sol. of ferric chloride,* changing to purple when made slightly alkaline with *solution of sodium hydroxide.* Ash not more than 5 per cent.; ash of the powder not more than 8 per cent. In India, in the Eastern, and in the North American Divisions of the Empire, Black Catechu may be employed in making the official preparations for which Catechu is directed to be used." *Br.*

Its most important constituent is a tannin, called *catechutannic acid,* of which it contains from 25 to 50 per cent. In addition it contains from 20 to 30 per cent. of gum, smaller amounts of a principle allied to the catechin of gambir and known as *acacatechin* and a coloring matter known as *catechu red,* $C_{36}H_{34}O_{15}$, which is evidently the first anhydride of catechin. The catechu tannic acid is of the variety which precipitates iron of a greenish-black color, and differs from most of the other varieties in not yielding grape sugar when digested with diluted sulphuric acid. It is not, therefore, a glucoside. It precipitates gelatin, but not tartar emetic (Kane), and is not, like the tannic acid of galls, converted into gallic acid by the access of the air. Catechu is almost wholly soluble in a large quantity of water, to which it imparts a brown color. The extractive, catechuic acid, is much less soluble than the astringent principle, which may be almost entirely separated from it by the frequent application of small quantities of cold water. Boiling water dissolves it much more readily than cold, and deposits it of a reddish-brown color upon cooling. Both principles are readily dissolved by alcohol or proof spirit, and also by ether.

A. Jossart (*J. P. A.,* 1881, 41) examined a catechu which was adulterated with from 60 to 65 per cent. of ferrous carbonate. For methods of assaying catechu and gambir, see Trimble's *The Tannins;* also *Ph. Rev.,* 1897, 27. (See also *Gambir,* and *U. S. D.,* 19th ed., p. 1436.)

Catechu is used for the same purposes and in the same proportions as *Gambir.*

Dose, five to fifteen grains (0.3–1.0 Gm.).

Off. Prep.—Pulvis Catechu Compositus, *Br.;* Tinctura Catechu, *Br.;* Trochiscus Catechu, *Br.*

CAULOPHYLLUM. N. F.

CAULOPHYLLUM Cauloph. [Pappoose Root, Squaw Root, Blue Cohosh]

"Caulophyllum consists of the dried rhizome and roots of *Caulophyllum thalictroides* (Linné) Michaux (Fam. *Berberidaceæ*). Caulophyllum contains not more than 3 per cent. of foreign organic matter and yields not than 4 per cent. of acid-insoluble ash." *N. F.*

This is an indigenous, perennial, herbaceous plant, with matted, knotty rhizomes, from which rises a single smooth stem, about two feet high which terminates in a panicle of greenish-yellow flowers.

Description and Physical Properties.—"*Unground Caulophyllum.*—Rhizome of horizontal growth, from 7 to 25 cm. long and from 5 to 15 mm. thick, much branched, slightly compressed from above, bearing large, cup-shaped stem scars on the upper surface and underneath roots which frequently conceal the rhizome; roots in a tangled or matted mass, long, curved, tortuous, thin, tough, profusely branched, the branches of about equal size and diverging at angles of about 45 degrees; both rhizome and root of a grayish or yellowish gray color; fracture tough and woody. Odorless but sternutatory; taste bitter-sweet and acrid.

"*Powdered Caulophyllum.*—Light brown; starch grains numerous, spherical in outline, mostly simple, up to 0.016 mm. in diameter; fragments of cork with cells about 0.050 mm. in diameter and having yellowish brown walls; tracheæ up to 0.050 mm. wide and with bordered pores; wood fibers and tracheids with heavily lignified walls: fragments of parenchyma tissue with many of the cells containing starch grains." *N. F.*

Caulophyllum contains a glucosidal saponin to which J. U. Lloyd has applied the name of *leontin.* (See *Drugs and Med. of North Amer.*, vol. 2, p. 152.) It also contains an alkaloid, *caulophylline,* which according to Power and Salway (*Tr. Chem. Soc.*, 1913, ciii) is *methylcytisine.* It has not been investigated physiologically. The fruit has been analyzed by Stockton and Elbridge (*Chem. News,* 1908, p. 190).

Uses.—As suggested by its popular name, caulophyllum was used by the American Indians to facilitate *child-birth.* As it was administered, however, two or three weeks previous to labor this evidence of its value does not seem very conclusive. However, the practice was brought to the attention of the medical profession by Peter Smith in 1813 and many physicians of the past generation attributed to it marked oxytocic properties. It has been used in the treatment of various uterine disorders such as *amenorrhea, dysmenorrhea, menorrhagia,* etc., implying somewhat contradictory properties on the part of the drug. Thus, it has been variously claimed that it is capable of producing abortion and that it will arrest threatened abortion. Pilcher (*J. A. M. A.*, 1916, lxvii, 490) found that it has a marked stimulating effect on the uterine muscle but did not believe this would occur under clinical use. It was also employed by the eclectics in hosts of other diseases such as *chronic rheumatism, bronchitis, intestinal colic* and *hysteria.* Its practical value is certainly open to doubt.

The *dose* of the crude drug, which is sometimes employed in the form of decoction, is ten to thirty grains (0.6–2 Gm.).

Off. Prep.—Fluidextractum Caulophylli, *N. F.;* Elixir Aletridis Compositum, *N. F.;* Elixir Heloniadis Compositum, *N. F.*

CENTAURIUM. N. F.

CENTAURY Centaur.

"Centaury is the dried flowering herb of *Erythræa Centaurium* (Linné) Persoon (Fam. *Gentianaceæ*). Centaury contains not more than 3 per cent. of foreign organic matter." *N. F.*

Common European Centaury; Petite Centaurée, *Fr. Cod.*; Herba Centaurii, *P. G.;* Tausendgüldenkraut, *G.*

The centaury is a small annual herb with an upright branching stem which bears a few small alternate leaves, most of the leaves being arranged in a basal tuft. The flowers which are of a purplish rose color are borne in flat-topped clustered cymes. The plant is a native of Europe but has been naturalized in the United States, especially along the shores of Lakes Ontario and Michigan. For description of "American Centaury" see *Sabbatia,* Part II. *E. acaulis,* which grows in great abundance in the territory of French Algiers bordering on the Sahara, yields a root which, under the name of *rejagnou,* is employed by the natives for dyeing yellow.

Description and Physical Properties.—"*Unground Centaury.*—Glabrous, from 1.5 to 5 cm. in length, much branched from the base, but little branched, if at all, from above; stems slender, sharply angled or narrowly winged, sparsely leafy; leaves opposite, entire, mostly three-nerved, sessile, those at the base obovate and obtuse, from 2 to 5 cm. long, their bases norrowed and petiole-like, those above gradually oval, ovate or even lancelinear, acute; flowers in a terminal and at length compound cyme, rose-colored; calyx from 5 to 7 mm. long, deeply five-parted, the tube short sharply angled, lobes linear-attenuate with a sharp midrib; corolla tube nearly twice the length of the calyx, slender, the limb from 10 to 15 mm. wide, its lobes broadly oblong or oval; stamens five, exserted, bright-yellow, their anthers twisted when old; pistil two-carpelled. Odor faint but characteristic, taste persistently bitter.

"*Powdered Centaury.*—Light brown to darker yellow-orange; with numerous fragments of lignified mechanical tissue composed of wood fibers, wood parenchyma and tracheæ, the latter with bordered pores, annular or spiral markings; leaf tissue containing rosettes or prisms of calcium oxalate up to 0.012 mm. in length; leaf epidermis of cells with irregular vertical walls and surface walls frequently striated; non-glandular hairs from lower margins of leaves; few, simple, elliptical stomata up to 0.035 mm. long; chlorophyll containing parenchyma; epidermal tissue of petals and calyx with papillated cells; abundant pollen grains, 0.025 to 0.030 mm. in diameter, spherical, smooth, with three pores; brownish fragments of reticulated seed-coat composed of small stone cells; abundant pith and cortical parenchyma." *N. F.*

This plant yields a peculiar colorless crystalline non-nitrogenous substance *erythrocentaurin.* This is almost insoluble in cold water, but dissolves in alcohol, melts at 136° C. and is reddened by exposure to sunlight. Various authors assign a different chemical formula to it (see Reis, *Ap. Ztg.*, 1911, p. 148). It is not bitter and therefore cannot be regarded as the active principle. Herissey and Bourdier (*J. P. C.*, 1908) claim to have found a glucoside which they named *erytaurin,* but Reis was unable to confirm their results. The active principle of the drug is unknown.

Uses.—Centaury possesses the bitter properties of the gentians and is useful as a stomachic. There is no reason, however, to suspect that it possesses any virtue beyond that of the more frequently prescribed *Gentiana*. It is more frequently employed as a domestic remedy than by physicians.

Dose, twenty to forty grains (1.3 to 2.6 Gm.).
Off. Prep.—Tinctura Amara, *N. F.*

CERA ALBA. U. S., Br.

WHITE WAX Cer. Alb.

"Yellow Wax, bleached." *U. S.* "White Beeswax is Yellow Beeswax, bleached." *Br.*

White Beeswax; Cire Blanche, *Fr. Cod.;* Cera alba, *P. G.;* Weisses Wachs, *G.;* Cera bianca, *It.;* Cera blanca, *Sp.*

CERA FLAVA. U. S., Br.

YELLOW WAX Cer. Flav. [Beeswax]

"Yellow Wax is obtained by melting and purifying the honey-comb of the bee, *Apis mellifera,* Linné (Fam. *Apidæ*)." *U. S.* "Yellow Beeswax is obtained from the honeycomb of the Hive Bee, Apis mellifica, *Linn.,* and possibly other species of Apis." *Br.*

Yellow Beeswax; Cera Citrina; Beeswax; Cire Jaune, *Fr. Cod.;* Cire d'Abeilles, *Fr.;* Cera Flava, *P. G.;* Gelbes Wachs, *G.;* Cera gialla, Cera vergine, *It.;* Cera amarilla, *Sp.*

The name *Apis mellifera* was given to the honey-bee of Linnæus in 1758, *Systema Naturæ,* 10th edition; subsequently (*Ibid.,* 12th edition, 1767), Linnæus changed the name to *mellifica,* but according to the established rules of scientific nomenclature the first name must hold, and the revisers of the United States Pharmacopœia were therefore correct in adopting it. It was at one time doubtful whether the wax which constitutes the walls of the honey-comb is elaborated or merely gathered by the insect. Huber, however, by feeding bees exclusively on honey and water, determined that under these circumstances wax is produced in the form of scales under the rings of the abdomen. But wax also exists in plants, bearing in this, as in other respects, a close analogy to the fixed oils. Besides the official species other bees are used as honey makers. The extremely vicious, blackish-brown *Apis fasciata* was kept by the ancient Egyptians on floating apiaries, which as the season progressed slowly drifted down the Nile, following the successive opening of the flowers. In Senegal, *Apis adansonii,* and in Southern Africa, *Apis caffra* and *Apis scutellata* produce honey; while the *Apis unicolor* of Madagascar has been domesticated in that island and introduced into other parts of the world. In India honey is made in large quantities by *Apis dorsata* (*Apis indica, Apis florea*) the largest bees known. *India Wax* differs from official wax chiefly in its lower acid value. A wax is also produced in India by the so-called *Kota bees,* belonging to the genus *Melipona;* they are minute stingless insects, which furnish a sticky, dark-colored wax, resembling in physical and chemical characteristics the propolis of the honey bee rather than the true wax.

Propolis or *bee-glue* is a brownish resinous substance sometimes deposited at the base of the hive; apparently it is collected from the resinous exudate of various trees such as the balsam, poplar and conifers. It has been used

1. Cera Flava, or *Yellow Wax.*—This is obtained by slicing the comb taken from the hive, removing the honey by centrifugal action, and melting the residue in boiling water, which is kept hot for some time in order to allow the impurities to separate and either subside or be dissolved by the water. When the liquid cools the wax concretes, and, having been removed and again melted in boiling water, is strained and poured into pans or other suitable vessels. The labor saving device is sometimes adopted of stretching a strainer of cheese cloth upon a hoop and wedging the latter down into the hot mixture below the level of the water; as this cools, the melted wax slowly rises through the cloth, and thus a perfectly clean cake of wax is formed on top on cooling. It is usually brought to market in round flat cakes from three to six inches in thickness.

Description and Physical Properties.—"A solid, varying in color from yellow to grayish-brown. It has an agreeable, honey-like odor, and a faint, characteristic taste. When cold, it is somewhat brittle, and when broken presents a dull, granular, non-crystalline fracture. It becomes plastic from the heat of the hand. Yellow Wax is insoluble in water and sparingly soluble in cold alcohol. Boiling alcohol dissolves the cerotic acid and a portion of the myricin, which are constituents of Yellow Wax. It is completely soluble in chloroform, ether, and in fixed or volatile oils, partly soluble in cold benzene or in carbon disulphide, and completely soluble in these liquids at about 30° C.

"Specific gravity: 0.950 to 0.960 at 25° C. determined as follows: Melt the Wax at a low temperature, and allow it to fall in separated drops from just above the surface into alcohol that has been warmed to from 45° to 50° C. Allow the globules to remain in the alcohol until it has cooled spontaneously to room temperature (20° to 25° C.), then remove the Wax and keep it at room temperature for twenty-four hours. Prepare a mixture of four volumes of alcohol and enough distilled water to make ten volumes, and allow it to stand until free from air bubbles. Moisten the globules of Wax with distilled water by means of a brush, and place them by means of forceps in the alcohol solution just prepared and contained in a beaker. Then add alcohol, or air-free distilled water, as required, to the mixture, kept at 25° C., until the globules of the Wax float and rest indifferently in the liquid. Finally determine the specific gravity of the alcohol-water mixture. The figure thus obtained represents the specific gravity of the Wax examined. Yellow Wax melts between 62° and 65° C.

"Boil 1 Gm. of Yellow Wax for half an hour with 35 cc. of an aqueous solution of sodium hydroxide (1 in 7), the volume being preserved by the occasional addition of distilled water: on cooling, the Wax separates without rendering the liquid opaque, and no precipitate is produced in the liquid after filtration through glass wool or asbestos on the addition of an excess of hydrochloric acid (*fats or fatty acids, Japan wax, rosin or soap*). Warm about 3 Gm. of Yellow Wax, accurately weighed, in a 200 cc. flask with 25 cc. of neutral dehydrated alcohol until melted, add 1 cc. of phenolphthalein T.S., and while warm titrate with half-normal alcoholic potassium hydroxide until a permanent, faint pink color is produced: the acid number so obtained is not less than 18 and not more than 24. Now add 25 cc. of half-normal alcoholic potassium hydroxide and 50 cc. of alcohol, boil the mixture for four hours under a reflux condenser, and titrate the excess of the alkali with half-normal hydrochloric acid: the ester number so obtained is not less than 72 and not more than 77." *U. S.*

"A yellowish-brown solid; somewhat brittle when cold, but becoming plastic by the heat of the hand. Agreeable, honey-like odor. Fracture granular, not crystalline. Soluble in *chloroform,* and in fixed and volatile oils. Specific gravity 0.958 to 0.970. Melting point 61° to 64° C. *Refractive index* at 80° C. 1.4380 to 1.4420. When 5 grammes are boiled for ten minutes with 80 millilitres of an aqueous solution (1 in 10) of *sodium hydroxide,* the water lost by evaporation being made up, the resulting solution, cooled and filtered through asbestos, does not become turbid when acidified with *hydrochloric acid* (absence of fats, fatty acids, Japan wax, resin). 5 grammes heated with 20 millilitres of *absolute alcohol,* and shaken until uniformly distributed, require for neutralisation at boiling temperature not less than 1.5 and not more than 2.0 millilitres of *N/1 alcoholic solution of potassium hydroxide, solution of phenolphthalein* being used as indicator (limits of free acid). Upon the further addition of 20 millilitres of *N/1 alcoholic solution of potassium hydroxide,* and on well boiling for one and a quarter hours in a flask to which a reflux condenser is attached, not less than 13.2 and not more than 13.8 millilitres of *N/1 solution of sulphuric acid* are required for neutralisation. When 5 grammes are boiled with a mixture of 15 millilitres of *N/1 alcoholic solution of potassium hydroxide* and 15 millilitres of *absolute alcohol* until completely saponified, the alcohol evaporated, the residue dissolved in 20 millilitres of *glycerin* on a water-bath and 80 millilitres of boiling *water* added, a clear or translucent solution is obtained (absence of ceresin, paraffin and other waxes). Not more than 1 per cent. is soluble in boiling *water* (limit of honey)." *Br.*

Dieterich examined hundreds of specimens annually, and found the wax to vary in sp. gr. from 0.963 to 0.966. He also determined the specific gravities of the following substances some of which are used to adulterate wax: white wax, 0.973; cera japonica, Japan wax, 0.975; ceresin, half white, 0.920; ozokerite, crude, 0.952; rosin, common, 1.108; cacao butter, 0.980 to 0.981; pure rosin, 1.045; beef suet, 0.952 to 0.953; yellow wax, 0.963 to 0.964; ceresin, white, 0.918; ceresin, yellow, 0.922; spermaceti, 0.960; French rosin, 1.104 to 1.105; paraffin, med. hard, 0.913 to 0.914; stearin, A No. 1, 0.971 to 0.972; mutton suet, 0.961.

2. CERA ALBA, *Bleached Yellow Wax,* or *White Wax.*—The color of yellow wax is discharged by exposing it, with an extended surface, to the combined influence of air, light and moisture. The process of bleaching is carried on to a considerable extent in this country. The wax, previously melted, is made to fall in streams upon a revolving cylinder, kept constantly wet, upon which it concretes, forming thin ribbon-like layers. These, having been removed, are spread upon linen cloths stretched on frames and exposed to the air and light, care being taken to water and occasionally turn them. In a few days they are partially bleached; but, to deprive the wax completely of color, it is necessary to repeat the whole process once, if not oftener. When sufficiently white, it is melted and cast into small circular cakes. Yellow wax may also be decolorized by treatment with animal charcoal or with potassium permanganate, potassium dichromate and sulphuric acid, and hydrogen peroxide. White wax sometimes contains one or more free fatty acids, consequent probably upon the employment of alkalies in bleaching it, which render it an unfit ingredient in the unctuous preparations of certain salts. It may be deprived of these acids by means of alcohol.

WHITE WAX is less unctuous to the touch than the yellow, soft and ductile at 35° C. and fusible at 65° C., retaining its fluidity at a lower temperature.

Description and Physical Properties.—"A yellowish-white solid, somewhat translucent in thin layers. It has a faint, characteristic odor, is free from rancidity, and is nearly tasteless. The acid value is not less than 17 and not more than 23, and the ester value not less than 72 and not more than 79, as determined by the methods under *Cera Flava.* In other respects White Wax has the characteristics of, and responds to, the tests for identity and purity under *Cera Flava.*" *U. S.*

"Hard, nearly white, translucent cakes or masses. 5 grammes heated with a mixture of 10 millilitres of *alcohol* (90 per cent.) and 10 millilitres of *absolute alcohol,* and shaken until evenly distributed, require for neutralisation at boiling temperature not less than 1.5 and not more than 2.2 millilitres of *N/1 alcoholic solution of potassium hydroxide, solution of phenolphthalein* being used as indicator (limits of free acid). In other respects White Beeswax responds to the tests described under '*Cera Flava*'." *Br.*

By a great heat it is partly volatilized, partly decomposed; and, when flame is applied to its vapor, it takes fire and burns with a clear bright light. It is insoluble in water, and in cold alcohol or ether, but is slightly soluble in boiling alcohol and ether, which deposit it in a great measure upon cooling. The volatile and fixed oils dissolve it with facility, rosin readily unites with it by fusion, and soaps are formed by the action of sodium and potassium hydroxides. It is not affected by the acids at ordinary temperatures, but is converted into a black mass when boiled with concentrated sulphuric acid.

Composition.—The chief constituent of beeswax is *myricin* (*myricyl palmitate*); melting point 64° C. It also contains *cerotic acid* (formerly called *cerin*), $C_{26}H_{52}O_2$, and *melissic acid,* $C_{30}H_{60}O_2$. There are also present about 6 per cent. of hydrocarbons of the paraffin series, including *heptacosane,* $C_{27}H_{56}$, and *hentracontane,* $C_{31}H_{64}$. *Myricyl alcohol,* $C_{30}H_{61}OH$, is liberated when myricyl palmitate is saponified, as glycerol is liberated during the saponification of ordinary fats; when fused with potash lime it is converted into *potassium melissate,* $KC_{30}H_{59}O_2$. Hot alcohol extracts the cerotic and melissic acids from beeswax. Saponification, of course, decomposes the myricyl palmitate. Schwalb (*Ann. Chem.*, ccxxiv, 225) found melissic acid and some unsaturated acids of the oleic series; also higher solid hydrocarbons of the saturated series, such as $C_{27}H_{56}$ and $C_{31}H_{64}$. Kebler states that the hydrocarbons in beeswax amount to from 12.72 to 13.78 per cent. (*A. J. P.*, 1893, 587.) T. Marie believes that cerotic acid, as ordinarily obtained, is a mixture of two distinct acids. He gives $C_{30}H_{60}O_2$ as the formula for melissic acid and $C_{25}H_{50}O_2$ for pure cerotic acid.

Adulterations.—Wax has been variously adulterated. Heavy substances sink to the bottom of the vessel when the wax is melted. Starch, meal, and other insoluble substances remain behind when the wax is dissolved in oil of turpentine or petroleum benzin. Water, which is said to be sometimes fraudulently incorporated with it, by agitation when partially melted, is driven off by heat. Fatty substances render lime water turbid when agitated with it and allowed to stand. The best test for fats, fatty acids, or rosin is the pharmacopœial test of boiling with sodium hydroxide solution and testing the filtrate obtained after cooling. For the detection of rosin, cold alcohol is sufficient. It dissolves the rosin, and yields it on evaporation, attended with a very small portion of pure wax, which yields 2.4 per cent. to cold alcohol. F. Jean states that a few drops of sulphuric acid added to the melted wax adulterated with rosin, cause a red color, or, if only 1 per cent. be present, a green tint. (*A. J. P.*, 1881, p. 307.) To detect Japan wax, Dullo boils together for a minute 10 Gm. of wax, 120 Gm. of water, and 1 Gm. of sodium hydroxide; if Japan wax be present, a soap will immediately form, which will slowly solidify on cooling. Beeswax does not saponify under these circumstances. (*J. P. C.*, 4e sér., i, 448.) Ceresin, a principle obtained from ozokerite (see Part II), is also employed as an adulterant, and is manufactured largely for that purpose in Vienna. It is only native paraffin, and of course answers to the tests for that substance. There are other less precise methods of detecting adulterations. Thus, spermaceti and lard render wax softer and less cohesive, of a smoother and less granular fracture, and of a different odor when heated. The melting point and specific gravity are lowered by tallow, suet, lard, and especially by paraffin. *Legrip's cereometer* is based upon the altered specific gravity of wax when adulterated. Anyone may apply this principle by making such a mixture of alcohol and water that pure wax will neither sink nor rise in it, but remain wherever placed. Adulterated wax would either float or sink in this liquid. The most valuable information, however, is obtained by the determination of the chemical constants—viz., acid value, ester value, and saponification value. In yellow wax the iodine value is also of use; in white wax the bleaching process has altered the bodies which absorb the iodine. (See also *Chem. Ztg.*, 1893, 918; *Proc. A. Ph. A.*, 1894, 957; *D. C.*, 1898, 33; *Am. Drug.*, 1898, 97, and 1904, 103, 105.) According to G. Brehner (*Ztsch. Off. Ch.*, 1912, No. 5), who has investigated many samples of beeswax of normal and abnormal character, beeswax may be divided into three groups, according to source, as follows: (1) Ordinary normal beeswax in which the ratio of acid number to ester number is 1 : 3.6 to 1 : 4. (2) Beeswax of African origin in which the ratio is 1 : 3. (3) Beeswax of Indian origin in which the ratio is 1 : 12. A Leijs (*J. P. C.*, 1912, No. 12) describes a method—based on the relative solubility in fuming hydrochloric acid—which, he claims, enables him with certainty to separate paraffin, ceresin, and carnauba wax readily from beeswax.

Under the name of White Wax No. 2 or White Wax for technical use, there has been found in commerce a product put up in exact imitation of white beeswax, and consisting of over 90 per cent. of paraffin.

VEGETABLE WAX.—Many vegetable products contain wax. It exists in the pollen of numerous plants, and forms the bloom or glaucous powder which covers certain fruits, and the coating of varnish with which leaves are sometimes supplied. In some plants it is so abundant as to be profitably extracted for use. Such is the *Ceroxylon andicolum* Humb., a lofty palm growing in the South American Andes. Upon the trunk of this tree, in the rings left by the fall of the leaves, is a coating of wax-like matter, about one-sixth of an inch thick, which is removed by the natives and employed in the manufacture of tapers. It contains, according to Vauquelin, two-thirds of a resinous substance and one-third of pure wax. Two kinds of wax are collected in Brazil, one called *carnauba,* from the leaves of the *Copernicia cerifera,* a palm, which forms large forests in the provinces of Ceara, the other *ocuba,* from the fruit of a shrub of the province of Para. (*J. P. C.,* 3e sér., v, 154.)

Carnauba wax is collected by cutting out the leaf buds of *Copernica cerifera* (Arruda) Mart. (Fam. *Palmaceæ*), commonly called the *Brazilian Wax Palm,* drying and beating them, and melting the powder thus detached, in water. The principal constituent of Carnauba wax is *myricyl alcohol,* $C_{30}H_{61}OH$, which is present to the extent of nearly 50 per cent. *Myricyl cerotate* is also present, as is *cerotic acid,* $C_{26}H_{52}O_2$, and *ceryl alcohol,* $C_{27}H_{55}OH$. There are some unidentified paraffin-like carbohydrates present and a dihydric alcohol of the composition $C_{23}H_{46}(CH_2OH)_2$, and the corresponding acid $C_{23}H_{46}(COOH)_2$. An acid isomeric with *lignoceric acid,* $C_{23}H_{47}COOH$, melting point 72.5° C., is also present. Over 50 per cent. of Carnauba wax is unsaponifiable. The constants, according to Radcliffe (*J. Soc. Chem. Ind.,* 1906, xxv, p. 158) are as follows: Sp. gr. 0.999, melting point 84° C., acid value 2.9, saponification value 88.3, ester value 85.4, iodine value 13.2. It is hard, brittle, and buff-colored, yellow, or greenish, resembling the resins more than wax, and melts at 84° C. which is much higher than the fusing point of other kinds of vegetable wax. It takes a fine polish when rubbed with any soft material, does not receive impressions from the finger at the natural temperature of the hand, and is adapted for polishing furniture, either alone or mixed with other varieties of wax. 2,000,000 pounds of it are said to be annually produced in Brazil, where it is largely used, mixed with tallow, in making candles, etc. (See also *P. J.,* 1904, 26.) (See also *Carnauba Root,* Part II.)

China wax, or *Chinese insect wax,* called *pe-la* by the Chinese, resembles spermaceti in whiteness and crystalline appearance, but is distinguished by greater hardness and friability and a somewhat fibrous fracture. It melts at about 83° C., is very slightly soluble in alcohol or ether, is insoluble in cold oil of turpentine and rectified petroleum, but is dissolved with the aid of heat, and is very soluble in benzene. These solubilities distinguish it from spermaceti. (*P. J.,* xiv, 9.) It was formerly supposed to be of vegetable origin, but has been ascertained to be the product of an insect, *Coccus ceriferus,* deposited on the twigs of the Chinese Ash, *Fraxinus Chinensis* Roxburgh, and investing them closely; the insect becomes embedded in a waxy material, which is scraped off with the insects, and constitutes the crude wax. It is purified by melting and straining. It is one of the chief industries in the province of S'zchuan, second only in importance to the silk culture. It is used over the entire Empire for candles and as medicine. (For details of its collection see *U. S. D.,* 19th ed., p. 307; also *P. J.,* 1885, xv.)

Under the name of *Ocotilla wax,* Helen Abbott Michael described (*A. J. P.,* Feb., 1885) a vegetable wax obtained from the bark of *Fouquiera splendens* (Tor.) Engelm. (Fam. *Tamaricaceæ*) known familiarly in Texas as *coachwhip cactus.*

Pisang Wax from *Ficus cerifera,* according to Greshoff and Sack, occurs in white crystalline cakes, having the sp. gr. 0.963 to 0.970 at 15° C., and melting at 79° to 81° C. It is very sparingly soluble in ethyl alcohol, even when boiling, but readily soluble in boiling oil of turpentine, amyl alcohol, and carbon disulphide. Its acid number is 2 to 3, its saponification number 109. *Pisang-cerylic acid,* obtained by saponification, melts at 71° C., and has the composition $C_{24}H_{48}O_2$; while *pisang-cerylic alcohol,* which was also isolated, melts at 78° C., and has the formula $C_{13}H_{18}O$.

Gondang Wax occurs in brown pieces which are yellowish internally and have a sp. gr. of 1.015. In distinction from pisang wax, gondang wax is soluble in all the usual solvents at a boiling temperature, and it may be almost completely dissolved by prolonged boiling with ethyl alcohol, being, however, again deposited on cooling. Gondang wax purified in this way melted at 61° C., and yielded *fico-cerylic acid* on saponification, which has the formula $C_{13}H_{26}O_2$, and melts at 57° C., while *fico-cerylic alcohol* has the formula $C_{17}H_{28}O$, and melts at about 198° C. In its general character gondang wax is intermediate between wax and caoutchouc. (*Ph. Ztg.,* 1901, 563.)

Japan Wax has been imported into Europe in considerable quantities, either directly from Japan, or through the Chinese ports. It is obtained from the berries of the *Rhus succedanea* of Linnæus, and in small amount from the *R. sylvestris* and *R. vernicifera,* or lacquer plant. The partially dried berries are crushed, winnowed, steamed, placed in hemp cloth bags, steamed again, and pressed in a wooden wedge press. They yield about 15 per cent. of a coarse greenish tallowy mass. It bears a considerable resemblance to purified beeswax, but is not quite so white, having a slightly yellowish tint, is softer, more friable, and has a somewhat rancid odor and taste. Its melting point is below that of wax, varying from 42° C. to 55° C. It is much more soluble in alcohol than is beeswax, and is saponifiable with the alkalies. It is not a true wax, being, in the main, a glyceride of palmitic acid with smaller amounts of the glycerides of stearic and arachidic acids. It has been employed in the preparation of candles, which yield as brilliant light as those made of common wax. It has been found useful in the preparation of cerates, etc.

Myrtle Wax is obtained from several species of *Myrica,* notably the *M. cerifera* L. and the *M. Xalapensis* H. B. K. of Cape Colony. The former known popularly as *wax myrtle,* or *bayberry,* is an aromatic shrub from one to fifteen feet high, growing in the United States, from New Jersey to Louisiana, and flourishing especially along the sea coast. The fruit, which grows in clusters closely attached to the stems and branches, is small, globular, and covered with a whitish coat of wax, which may be separated for use. Other parts of the plant are said to possess medicinal virtues. The bark of the root is acrid and astringent, and in large doses emetic, and has been popularly employed in jaundice. The process for collecting the wax is simple. The berries are boiled in water, and the wax, melting and floating on the surface, is either skimmed off and strained, or allowed to concrete as the liquor cools, and then removed. To render it pure, it is again melted and strained, and cast into large cakes. It is of a pale grayish-green color, somewhat diaphanous, more brittle and unctuous to the touch than beeswax, of a feeble odor, and a slightly bitterish taste. It is about as heavy as water, and melts, according to G. E. Moore, at from 46.6° to 48.8° C. It is insoluble in water, scarcely soluble in cold alcohol, soluble, excepting about 13 per cent., in twenty parts of boiling alcohol, which deposits the greater portion on cooling, soluble also in boiling ether, and slightly so in oil of turpentine. It is readily saponifiable with the alkalies. Myrtle wax consists chiefly of the glycerides of myristic, palmitic and stearic acids with small quantities of olein; it is, therefore, not a true wax but a hard fat. It has been popularly employed in the United States as a remedy for dysentery. It is occasionally substituted by apothecaries for beeswax in the formation of plasters, and is used in the preparaction of tapers and candles. It is somewhat fragrant when burning, but emits a less brilliant light than common lamp oil. It is especially employed for making candles for use at the Christmas season.

A wax which is said to be used, under the name of *Árbol de la Cera,* in Mexico not only for domestic purposes, but also as a remedy in diarrhea and jaundice, is obtained by boiling the fruit of the *Myrica jalapensis* in water. It is greenish or yellow, more brittle and unctuous than beeswax, has a feeble odor, a slightly bitter taste, and a density nearly equal to that of water, and melts at 43° C.; but on exposure the fusing point rises to 47.5° C. It is wholly soluble in boiling ether, insoluble in water, sparingly soluble in cold alcohol, and dissolves in twenty parts of boiling alcohol, depositing the greater part on cooling; alkalies saponify it readily. (*A. J. P.,* xv, 339, 1885.)

Uses.—Wax has little effect upon the system. Under the impression that it sheathed the inflamed mucous membrane of the bowels, it was formerly prescribed in *diarrhea* and *dysentery;* and it is mentioned by Dioscorides as a remedy in the latter complaint; but at the present time, we suppose, no one would think of employing wax for such purposes. Its sole use in modern medicine is in the formation of ointments, cerates, plasters, suppositories, and surgical dressings, etc.; in which it acts mechanically either giving stiffness or serving to protect from water. It is an ingredient in almost all the official cerates, which owe to it their general title.

Off. Prep.—*White wax.*—Ceratum, *U. S.;* Ceratum Camphoræ, *N. F.;* Unguentum Aquæ Rosæ, *U. S., Br.;* Unguentum Cetacei, *Br.;* Unguentum Paraffini, *Br.;* Petroxolinum Spissum, *N. F.*

Yellow wax.—Ceratum Cantharidis, *U. S.* (*Br.*)*;* Ceratum Resinæ, *U. S.* (*Br.*)*;* Ceratum Resinæ Compositum, *N. F.;* Linimentum Terebinthinæ (from Rosin Cerate), *Br.;* Unguentum, *U. S.*

CERATA.

CERATES

Cérats, Céréolés, Elæocéréolés, *Fr.;* Cerate; Wachssalben, *G.*

These are unctuous substances consisting of oil or lard, mixed with wax, spermaceti, or rosin, to which various medicaments are frequently added. Their consistence, which is intermediate between that of ointments and that of plasters, is such that they may be spread at ordinary temperatures upon linen or leather, by means of a spatula, and do not melt or run when applied to the skin. In preparing them, care should always be taken to select the oil or lard perfectly free from rancidity. In reference to the wax, too, there would seem to be a choice, as experience has shown that cerates made with yellow wax keep longer unchanged than those made with white or bleached wax, probably because there is in yellow wax some principle which corrects the tendency of fatty matters to become rancid. The liquefaction should be effected by a very gentle heat, which may be applied by means of a water bath, and during the refrigeration the mixture should be well stirred, and the portions which solidify on the sides of the vessel should be made to mix again with the liquid portion, until the whole assumes the proper consistence. When a large qantity is prepared, the mortar or other vessel into which the mixture may be poured for cooling should be previously heated by means of boiling water. It has been proposed to substitute paraffin for wax in the preparation of the cerates, but the great tendency to produce granulation in the finished cerate has largely prevented its use.

It is, we think, unfortunate that this class of preparations has been abandoned in the British Pharmacopœia, the several cerates having been rejected, or transferred to the class of ointments. Independently of the connection between the name and one of the characteristic constituents of the cerates, there is ground for difference between them and the ointments in their consistence, that of the cerates being such as to render them especially suitable for spreading on linen, while that of ointments is peculiarly adapted to inunction. W. H. Mielcke (*Ph. Cb.,* 1881, Nos. 20, 21) proposes a class of preparations, to which he has given the name "*Steatins.*" These are of about the consistence of cerates, of varied composition, and contain usually a considerable portion of tallow. The *Steatinum Iodoformi* offers a fair specimen of the class. "Take of mutton tallow 18 parts, expressed oil of nutmeg 2 parts, iodoform, in fine powder, 1 part. Melt the tallow and add the other ingredients." For other formulas, see *A. J. P.*, 1881, p. 404.

CERATUM. U. S.

CERATE Cerat. [Simple Cerate]

Ceratum Adipis, *U. S.* 1860; Ceratum Simplex, *U. S.* 1850; Cérat Simple, *Fr. Cod.*; Unguentum cereum, *P. G.*; Einfaches Cerat, Wachssalbe, *G.*; Cerato simple, *Sp.*

"White Wax, 300 Gm.; Benzoinated Lard, 700 Gm.; to make 1000 Gm. Melt the white wax by the heat of a water bath, add the benzoinated lard, continue the heat until the mixture is liquefied, strain if necessary, and stir constantly until it congeals. For use in southern latitudes and during the heated season in other localities, 50 Gm. of benzoinated lard (or more, if necessary) may be replaced by an equal quantity of white wax." *U. S.*

In the U. S. Pharmacopœia VIII 20 per cent. of white petrolatum, and 50 per cent. of benzoinated lard were directed in place of the 70 per cent. of lard used in the U. S. P. (1890) process. In the present official cerate the white petrolatum was omitted. In the preparation of cerate, peculiar care should be taken that the oleaginous ingredient be entirely free from rancidity, and that the heat employed be not sufficient to produce the slightest decomposition, for the value of the preparation depends on its perfect blandness. To avoid change, it should be put up in small jars, and covered closely with tin foil so as to exclude the air. It is used for dressing *blisters, wounds,* etc., in all cases in which the object is to prevent the contact of air and preserve the moisture of the part and at the same time to avoid all irritation. It is sometimes improperly employed as the vehicle of substances to be applied by inunction. For this purpose benzoinated lard should be used in winter, and simple ointment in summer, the cerate having too firm a consistence. George W. Sloan recommended the use of simple cerate as a pill excipient for certain oxidizable substances and special uses. (*Proc. A. Ph. A.*, 1884.)

CERATUM CANTHARIDIS. U. S.

CANTHARIDES CERATE Cerat. Canthar. [Blistering Cerate]

Emplastrum Cantharidini, *Br.*; Cantharides Plaster; Emplastrum Epispasticum, s. Vesicatorium, s. Vesicans, Emplastrum Lyttæ; Blistering Cerate or Plaster; Emplâtre Vesicatoire, *Fr. Cod.*; Pommade Epispastique, Emplâtre de Cantharides, *Fr.*; Emplastrum Cantharidum Ordinarium, *P. G.*; Spanischfliegen Pflaster, Blasenpflaster, *G.*; Pomata di cantaridi, *It.*; Unguento de cantharidas. *Sp.*

"Cantharides, in a very fine powder, 350 Gm.; Glacial Acetic Acid, 25 cc.; Oil of Turpentine, 150 cc.; Yellow Wax, 175 Gm.; Rosin, 175 Gm.; Benzoinated Lard, 200 Gm.; to make 1000 Gm. Moisten the cantharides with the oil of turpentine and the glacial acetic acid, previously mixed, and set the mixture aside in a well-covered container in a warm place for forty-eight hours. Melt together the rosin, yellow wax, and benzoinated lard, strain the mixture through muslin, add the macerated cantharides, and keep the mixture in a liquid condition by heating it on a water bath with occasional stirring until it is reduced in weight to 1000 Gm. Then withdraw the heat, and stir the Cerate until it becomes firm." *U. S.*

This is the commonly called *blistering plaster.* As it can be readily spread without the aid of heat, it is properly a cerate, and is, therefore, correctly named in the U. S. Pharmacopœia. The U. S. P. IX has recognized a plaster in which this cerate is spread upon fabric, while the British Pharmacopœia contains a preparation similar to the U. S. cerate, under the title *Emplastrum Cantharidini.* In the Br., however cantharidin is used instead of cantharides. (See also *Emplastrum cantharidis.*)

"Cantharidin, 2 *grammes;* Chloroform, 100 *millilitres;* Yellow Beeswax, 450 *grammes;* Wool Fat, sufficient to produce 1000 *grammes.* Dissolve the Cantharidin in the Chloroform by the aid of heat, add to the other ingredients previously melted on a water-bath, and stir until cold. This Plaster contains 0.2 per cent. of Cantharidin, which is approximately the proportion contained in the Emplastrum Cantharidis of the British Pharmacopœia, 1898." *Br.*

There can be no question of the advantage of retaining the cantharides in contact with hot liquefied fatty bodies to facilitate the extraction of the cantharidin.

It was at one time recommended that the mixture of cantharides and oil be heated to a temperature of 121° C., the advantage being claimed that the contained moisture of the cerate is boiled off at this temperature and also that the solution of active principle is encouraged, but as it has been shown that cantharidin begins to volatilize at a temperature of 100°, it is evident that the use of this method must be attended with a considerable loss of drug. Dieterich states that the activity is greatly increased by the use of an acid in the manufacture. Thus, for every 250 Gm. of powdered flies used he adds to the melted mass 1 Gm. sulphuric acid and 10 Gm. alcohol (90 per cent.), keeps the mass for two hours at 70° C., and finally adds 2 Gm. barium carbonate rubbed up with 6 Gm. alcohol. (*Ph. Centralh.*, 1892, 425.) It is desirable that the flies should be very finely pulverized. Coarsely powdered cantharides should not be used, because of the imperfect and unequal distribution of the vesicating agent. Powdered euphorbium is said to be sometimes fraudulently added.

Uses.—This cerate is used solely as a vesicant and is one of the most efficient preparations of cantharides for this purpose in ordinary conditions of the system, if the flies are good, and not injured in the preparation. It should be spread on soft leather or linen and applied to skin as a plaster. Heat is not requisite, and should not be employed in spreading the cerate. Some operators sprinkle powdered flies upon the surface of the plaster, press them lightly with a roller, and then shake off the portion which has not adhered; but, if the flies originally employed were good, this addition is superfluous. The practice of applying over the surface with a brush an ethereal tincture of cantharides, which leaves a thin coating of extract, renders the preparation more certain.

For details of the methods of using, see under *Emplastrum Cantharidis.*

Off. Prep.—Emplastrum Cantharidis, *U. S.*

CERATUM RESINÆ. U. S. (Br.)

ROSIN CERATE Cerat. Res.

Unguentum Resinæ, *Br.;* Resin Ointment; Ointment of Resin, Unguentum Basilicum; Basilicon Ointment; Unguentum Tetrapharmacum; Resin Ointment, Resin Cerate; Pommade Basilicum, *Fr. Cod.;* Onguent Basilicum, Cérat de Résine Anglais, *Fr.;* Harzcerat, Harzsalbe, Königsalbe, Zugsalbe, *G.*

"Rosin, 350 Gm.; Yellow Wax, 150 Gm.; Lard, 500 Gm.; to make 1000 Gm. Melt the rosin, add the yellow wax and lard, and continue the heat until liquefied, then strain the liquid through muslin, and allow it to congeal, stirring occasionally.

"NOTE.—In cold weather 530 Gm. of lard and 120 Gm. of yellow wax may be used." *U. S.*

"Resin, 26 *grammes;* Yellow Beeswax, 26 *grammes;* Olive Oil, 26 *grammes;* Prepared Lard, 22 *grammes.* Melt together; strain; stir until cold. In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

The U. S. preparation does not differ greatly from that formerly official except that occasional stirring while congealing is directed; the U. S. P. 1890 process forbade stirring. The British process (1898) discards the simple ointment and almond oil previously used (1885), and substitutes lard and olive oil. *Ceratum Resinæ Composition*—Compound rosin cerate. *Deshler's Salve* was dropped from the U. S. P. IX. It is retained in the N. F. (see Part III). It is made from rosin, yellow wax, prepared suet, turpentine (white) and linseed oil, and is used for the same purposes as Ceratum Resinæ. Rosin cerate, commonly called *basilicon ointment,* is much used as a gently stimulating and protective application to *blistered surfaces, indolent ulcers, burns, scalds,* and *chilblains.* We have found no application more effectual in disposing the *ulcers* which follow *burns* to heal.

Off. Prep.—Linimentum Terebinthinæ, *N. F.*

CEREVISIA FERMENTUM COMPRESSUM. N. F.

COMPRESSED YEAST Cerev. Ferm. Compr.

"Compressed yeast consists of the moist, living cells of *Saccharomyces cerevisiæ* Meyen or of other species of *Saccharomyces* (Fam. *Saccharomytaceæ*), combined with a starchy absorbent base. Compressed yeast must must nor be used unless fresh and free from mildew and musty or foul odors." *N. F.*

Faex Medicinalis; Yeast, Leaven; Hefe, G.; Levure, *Fr.* Fermento, Lievito, *It.*

Baker's Yeast.—As was originally shown by Pasteur, the decomposition of glucose into alcohol and carbonic acid is accomplished by means of a living ferment known as yeast or leaven. The name *Torula cerevisiæ* was first given to the yeast plant, which was subsequently called *Mycoderma vini;* Reess, in his elaborate work (*Alkoholsgährungspilze,* Leipsic, 1870), made a distinct genus of it, *Saccharomyces,* including many species.

The wine-producing yeasts are varieties of the species *Saccharomyces ellipsoideus.* Brewers' yeast and that used for culinary purposes are varieties of *S. cerevisiæ.*

According to Casagrandi, *Saccharomyces ruber,* previously discovered by Demme, produces a *red yeast* which ferments glucose very readily, developing a red pigment. This saccharomyces was found pathogenic to various animals, and when put into milk so modified that liquid as to convert it into a pronounced intestinal irritant. (*P. J.,* Jan., 1898.) A number of yeasts are used in China and Java whose fundamental plants are different from those of the European yeast. See *P. J.,* vol. xlvii.

Two well-marked varieties of the *Saccharomyces cerevisiæ* have been recognized. The one is the most active at the ordinary temperature (16°–20° C.), and carries through its fermentative work in from three to four days; the other works at a lower temperature (6°–8° C.), and the fermentation is much slower. The first placed in a saccharine liquid is carried by the carbon dioxide which it liberates to the surface of the liquid, where it continues its activity; it is, therefore, known as a *surface* or *top yeast.* The second, on the contrary, is not carried up, and rests during its entire activity on the bottom of the fermenting vessel, and is hence called a *bottom yeast.* Two quite distinct methods of beer brewing are practised, depending upon the use of the one or the other of these varieties of yeast. (For fuller information as to the nature of *yeast* and its conditions of culture and activity, see Sadtler's *Industrial Organic Chemistry,* Philadelphia, 4th ed., 1921.)

Brewers' yeast is a flocculent, frothy, somewhat viscid semi-fluid, of a dirty yellowish color, a sour, vinous odor, and a bitter taste. Exposed to a moderate heat the moisture evaporates and it becomes dry, hard, and brittle, and may in this state be preserved for a long time, though with the loss of much of its enzymic power. *Yeast cakes* are made by putting yeast into sacks, washing it with water, then submitting it to pressure, and ultimately drying it.

Description and Physical Properties.—"White or yellowish white, soft and easily broken masses, having a characteristic, slightly sour odor, and not more than a faintly acid reaction to litmus. When examined with the microscope, numerous oidium and mycoderma cells and starch grains are visible." *N. F.*

Compressed yeast usually comes in square blocks weighing about one-half ounce each.

Compressed yeast, according to an analysis by Hawk, Smith and Holder (*A. J. Phys.*, 1919, xlviii) contains on a water free basis 52.4 per cent. of protein, 37.1 per cent. of carbohydrate, 1.7 per cent. of fat and 8.7 per cent. of ash, the latter being chiefly potassium phosphate. Funk, Lyle and McCaskey (*J. Bi. Chem.*, 1916, xxvii, p. 173), from experiments in which yeast was the sole source of protein, reached the conclusion that the yeast nitrogen was so poorly uitilized by the human economy that yeast possessed no food value. Hawk, Smith and Holder, however, found that from 10 to 30 per cent. of the nitrogenous elements of the food can be replaced by yeast nitrogen without detriment to the nutrition. While we believe that it must be conceded that yeast has a definite food value, the quantities that can be employed as a foodstuff are rather limited by two factors: one, the difficulty of preparing large amounts in a palatable form, and the other, the fact that considerable quantities of yeast have a definite laxative action.

Yeast contains a considerable quantity of nucleic acid.

According to Albert Buchner and Rapp, a dried yeast which retains its activity on keeping is obtained as follows: The yeast is freed from water as much as possible by expression, immersed in acetone and rubbed through a sieve. The acetone is decanted, renewed, again decanted, and the residue collected by the aid of a suction filter, then treated with ether for three minutes, and this removed in the same way, after which the yeast is spread out to dry, the drying being completed at a temperature of 45° C. Dried yeast, so obtained, is an almost white powder. (*Ph. Centralh.*, 1903, 36.)

Yeast consists of numerous cells, irregular, roundish, or cylindrical in shape, separate, joined into rows, or budding one from the other. It is most probable that the yeast plant is the mycelium, or early vegetative stage, of more than one species of mucor or mould.

Starch as such is not subject to fermentation by the yeast plant but the latter contains an enzyme which is capable of inverting starch into sugar, the latter of which is utilized by the growing micro-organisms, with the characteristic sugar decomposition. Formerly, it was thought that glucose was the only food necessary for the growth of yeast but more recent evidence indicates that yeast is unable to multiply in the complete absence of protein. In other words, both sugar and nitrogenous principles are requisite for culture media for yeast.

Uses.—Yeast has been employed as a medicine both by the regular profession and as a folk remedy for many years. Its most popular and best supported use has been in skin infections such as *furunculosis* and *acne*. Hawk and his co-workers have found it also of use in *chronic constipation* and Spencer (*T. G.*, May, 1920) in *arthritis deformans*.

Various theories of the mode of action of yeast have been suggested but none of them demonstrated. Some writers have believed that its action is due to the high nuclein content, the latter acting as a stimulant to the formation of leukocytes (see *Nuclein*, Part II). Some investigators have attributed it with a direct bactericidal power. Tsuru (*W. K. R.*, 1909) has shown, however, that this is true only to growing yeast and it could hardly, therefore, explain the benefit which has followed its internal administration. As was first shown by Hopkins (*J. P.*, 1912, xliv, p. 425) and subsequently confirmed by various numbers of investigators, yeast is comparatively rich in the water-soluble vitamine. (See Hawk, Smith and Bergeim, *A. J. Phys.*, 1921, lvi, p. 33.) Osborne and Mendel (*J. Bi. Chem.*, 1919, xxxviii, p. 223) maintained rats in health for over a year on a diet in which yeast was the sole source of both protein and water-soluble vitamine B. Saleeby (*Philippine Journ. Science*, 1919, xiv, p. 11) has found it will cure *beri-beri*. Some have attributed its beneficial effects to the vitamine content but we have no convincing evidence of any beneficial effects of excessive vitamine. It is possible that its ferment action may inhibit the growth of certain putrefactive organisms in the intestinal canal and hence improve the general health or it is at least conceivable that the mild laxative action is the real basis of its curative effects.

In the light of our present knowledge, all that we can say about the medicinal use of yeast is that there is considerable clinical evidence as to its value in staphylococcic infections but that there is no established explanation of its *modus operandi*.

A large number of preparations of yeast have been placed upon the market under the various trade names. Among these the following may be mentioned:

Xerase.—This is stated to be a mixture of yeast and kaolin with glucose and salts. This is a yellowish-gray powder, asserted to possess not only absorbent but also bactericidal powers. It is intended for local application, especially in *gonorrhea* of women.

Cerolin.—A fatty substance derived from yeast, asserted to represent the specifically active constituent of yeast. It is a yellowish to a brownish semi-fluid with an odor resembling that of yeast. It is used in dose of one and a half to three grains (0.1 to 0.2 Gm.). *Bajuvarin* is a preparation of yeast which is used both internally and locally by veterinarians. *Fermentine* is a preparation of yeast containing benzoin, used principally for local application. *Fermocyl:* A mixture of dried yeast, pancreas and sodium phosphate, marketed in the form of tablets, each corresponding to about 30 grains (2 Gm.) of the fresh yeast. Used in diabetes. *Furunculin: Dose,* ten to thirty grains (0.65–2 Gm.). *Levuretin, Levurin,* and *Leuvurinose* are proprietary forms of dried beer yeast; any of them may be given in doses of one drachm (3.9 Gm.). *Mycodermin:* Marketed only in pills. *Dose,* 2 to 4 pills. *Trygase: Dose,* one teaspoonful. *Zymin* is a dried yeast which is marketed either as a powder, intended for external use, or in the form of tablets each of which contains fifteen grains (1 Gm.).

Dose, of compressed yeast, is one to three drachms (4–12 Gm.).

CETACEUM. U. S., Br.

SPERMACETI Cetac.

"A fatty substance, obtained from the head of the sperm whale, *Physeter macrocephalus* Linné (Fam. *Physeteridæ*)." *U. S.* "Spermaceti is a solid wax obtained from the Sperm Whale, Physeter macrocephalus, *Linn.*, and possibly other species." *Br.*

Blanc de Baleine, *Fr. Cod.;* Spermacéti, Cétine Ambre Blanc, *Fr.;* Cetaceum, *P. G.;* Walrat, *G.;* Cetina, *It.;* Esperma de ballena, Sperma ceti, *Sp.*

The spermaceti whale is from sixty to eighty feet long, with an enormous head, not less in its largest part than thirty feet in circumference, and constituting one-third of the whole length of the body. The upper part of the head is occupied by large cavities, separated by cartilaginous partitions, and containing an oily liquid, which, after the death of the animal, concretes into a white spongy mass consisting of spermaceti mixed with oil. This mass is removed, and the oil allowed to separate by draining. The crude spermaceti obtained from a whale of the ordinary size is more than sufficient to fill twelve large barrels. It still contains much oil and other impurities, from which it is freed by expression, washing with hot water, melting, straining, and repeated washing with a weak boiling potash lye. Common whale oil and the oil of other cetaceous animals contain small quantities of spermaceti, which they slowly deposit on standing. According to W. Gilmour, *sperm oil* should contain not less than 4 per cent. of cetin, and if much less be obtained by the following process, adulteration has been practised. Shake one part by weight of sulphuric acid (sp. gr. 1.84) with four parts of the oil; allow to stand 20 minutes, shaking twice; add three parts of distilled water; shake this thoroughly, and allow to stand from 16 to 20 hours; dilute with 3 or 4 times its volume of distilled water; agitate thoroughly. On standing, the cetin floats upon the top, and can readily be skimmed off, washed, dried, and weighed. (See also *Chem. Ztg.*, 1893, 1453, and *Am. Drug.*, 1895, 105.)

Description and Physical Properties.—"White, somewhat translucent, slightly unctuous masses, having a crystalline fracture, and a pearly luster. It has a very faint odor and a bland, mild taste. It is free from rancidity. Spermaceti is insoluble in water, nearly insoluble in cold alcohol, and only slightly soluble in cold petroleum benzin. It is soluble in boiling alcohol, ether, chloroform, carbon disulphide, and in fixed or volatile oils.

"Specific gravity: 0.938 to 0.944 at 25° C., as determined by the method given under *Cera Flava*, using alcohol warmed to from 38° to 40° C. Spermaceti melts between 42° and 50° C. It dissolves completely in fifty parts of boiling alcohol (*paraffin*), and the solution is neutral or not more than slightly acid to moistened litmus paper. Warm a mixture of about 1 Gm. of Spermaceti and 10 cc. of ammonia T.S. in a stoppered vessel until the Spermaceti is melted, shake it thoroughly for a few minutes, cool, and filter: on acidulating this filtrate with hydrochloric acid, it may become turbid, but yields no precipitate (*stearic acid*)." *U. S.*

"Translucent, pearly-white, glistening masses, with a leafy, crystalline structure; slightly unctuous to the touch. Almost inodorous. Specific gravity 0.950 to 0.960; *acid value* not more than 1.0; *saponification value* 125 to 136; *iodine value* 3 to 4.4; *refractive index* at 80° C. about 1.4330. Soluble in 50 parts of hot *alcohol* (90 per cent.), the greater proportion separating again in thin laminæ on cooling. Reducible to powder with the aid of a little *alcohol* (90 per cent.). When 1 gramme is boiled with 10 millilitres of *alcohol* (90 per cent.) for one minute and the mixture cooled to, and filtered at 0° C. the filtrate when poured into *water* may become opalescent, but does not afford a precipitate (absence of stearic acid)." *Br.*

As found in commerce it is not chemically pure, containing a fixed oil, and often a peculiar coloring principle. From these it is separated by boiling in alcohol, which on cooling deposits it in crystalline scales. Thus purified, it does not melt under 49° C., is soluble in 40 parts of boiling alcohol of the sp. gr. 0.821 (Thénard), and is harder, more shining, and less unctuous than ordinary spermaceti.

Spermaceti is a mixture of various fats. The chief constituent is *cetin* (*cetyl palmitate,* $C_{16}H_{33}O.C_{16}H_{31}O$). *Cetyl alcohol,* $C_{16}H_{33}OH$, is also present in appreciable amounts. There are small amounts of lauric, myristic, palmitic, and stearic acids, and also of dodecyl, tetradecyl and octadodecyl alcohols.

L. F. Kebler, after examining about twenty samples of spermaceti, found that commercial specimens have a melting point of from 42° to 47° C., a specific gravity ranging from 0.905 to 0.945 at 15° C., and saponification numbers from 125.8 to 134.6. (*A. J. P.*, 1896, 7, and 1897, 104.)

Uses.—Spermaceti exercises emollient effects like other fatty substances, but it has no other remedial properties. It is used chiefly to add firmness to ointment bases. It may be reduced to powder by the addition of a little alcohol or almond oil, or by melting it at a very low heat, pouring into a warm mortar, and agitating it until perfectly cold; an emulsion may be made by mixing spermaceti first with half its weight of olive oil, then with powdered gum arabic, and lastly with water. Spermaceti Cerate (*Ceratum Cetacei,* U. S. 1890) was made by melting together 10 parts of spermaceti and 35 parts of white wax and then adding 55 parts of warmed olive oil.

Off. Prep.—Unguentum Aquæ Rosæ, *U. S., Br.;* Unguentum Capsici, *Br.;* Unguentum Cetacei, *Br.*

CHIMAPHILA. N. F.

CHIMAPHILA Chimaph. [Pipsissewa]

"Chimaphila consists of the dried leaves of *Chimaphila umbellata* (Linné) Barton (Fam. *Ericaceæ*). Chimaphila contains not more than 5 per cent. of its stems and other foreign organic matter." *N. F.*

Pipsissewa, Prince's Pine, Wintergreen, Bitter Wintergreen, King's Cure, Ground Holly, Love-in-winter, Rheumatism Weed; Herbe de Pyrole ombellée, *Fr.;* Doldenbluthiges Harnkraut, Wintergrün *G.*

The name chimaphila is formed of two Greek words, χεῖμα, winter, and φίλος, to love. There are two American species of the genus *Chimaphila,* only the *C. umbellata,* however, being official. This is a low perennial herb, 4 to 10 inches in height, bearing from 4 to 7 flesh-colored pedunculated flowers. The wedge-lanceolate leaves are sharply serrate and borne in irregular whorls, of which there are usually two on the same stem, thick and shiny, not spotted, remaining green through the winter. This plant is common in dry woods from Nova Scotia to Georgia and westward. It is also found in the northern latitudes of Europe and Asia. The drug is collected for the market chiefly in the southern Applachians and Michigan.

The *C. maculata* (L.) Pursh (*Spotted Wintergreen*) differs in having the leaves obtuse at the base and broader than at the summit, remotely toothed and the upper surface of a deep olive green variegated with white.

Description and Physical Properties.—"*Unground Chimaphila.*—Oblanceolate, from 2.5 to 7 cm. long and from 8 to 20 mm. wide, the upper portion coarsely and sharply serrate, acute or somewhat obtuse, the lower wedge-shaped and nearly entire; coriaceous, smooth and uniformly dark green on the upper surface, paler beneath, the veins prominent. Odor slight; taste astringent and bitter.

"*Powdered Chimaphila.*—Greenish brown; exhibits characteristic epidermal tissue composed of cells with unevenly thickened more or less porous and wavy vertical walls, with outer walls from 0.008 to 0.015 mm. thick; fragments from the lower epidermis with numerous broadly elliptical stomata, the latter up to 0.040 mm. long; fragments of palisade and spongy parenchyma containing chloroplastids; tracheæ with spiral or annular markings; a few characteristic, elongated tracheæ-like cells, about 0.014 mm. wide, thick-walled, slightly lignified and with minute double-spiral bands of delicate reticulations; parenchyma cells containing a reddish brown amorphous substance; calcium oxalate in rosettes mostly about 0.035 mm. in diameter, occasionally up to 0.065 mm. in diameter; starch grains few, rounded, simple, up to 0.016 mm. in diameter and sometimes with a central cleft or fissure, or 2- to 4-compound; hairs absent; a few fragments of epidermis from stems and root-stocks, the cells containing a purplish coloring substance which is intensified when the powder is mounted in chloral hydrate T.S." *N. F.*

Pipsissewa, when fresh and bruised, exhales a peculiar odor. Boiling water extracts the active properties of the plant, which are also imparted to alcohol. Fairbank found in the leaves a peculiar substance which he calls *chimaphilin.*

Chimaphilin was obtained by extracting the tincture with chloroform, or by distilling the stems with water. It occurs in golden-yellow acicular crystals, odorless and tasteless, practically insoluble in water, but dissolving in alcohol, ether, chloroform, and the fixed oils. It is possessed of neither acid nor alkaline properties. Peacock (*A. J. P.,* 1892, p. 295) found that chimaphilin has the chemical composition $C_{24}H_{21}O_4$.

Ridenour (*A. J. P.,* 1895, 236) confirms this formula. He finds the melting point of the purified chimaphilin to be 114° C. He also prepared another crystalline principle melting above 250° C., to which he gives the formula $C_{10}H_{19}O$. *Arbutin* is also found in chimaphila.

Uses.—This plant is stated to have been used internally by the North American Indians in *scrofula* and *rheumatism,* and was a popular remedy among the settlers of this country. It has no medicinal properties, however, beyond a feeble diuretic action and perhaps some antiseptic influence on the urine. It is occasionally prescribed for *cystitis.* The best preparation is the fluidextract, which may readily be made into a syrup.

Dose, thirty to ninety grains (2–6 Gm.).

Off. Prep.—Fluidextractum Chimaphilæ, *N. F.;* Fluidextractum Stillingiæ Compositum, *N. F.;* Syrupus Stillingiæ Compositus, *N. F.*

CHIONANTHUS. N. F.

CHIONANTHUS Chionanth. [Fringe Tree Bark]

"Chionanthus is the dried bark of the root of *Chionanthus virginica* Linné (Fam. *Oleaceæ*). Chionanthus contains not more than 5 per cent. of wood and other foreign organic matter. It yields to 70 per cent. alcohol not less than 25 per cent. of non-volatile alcoholic extractive." *N. F.*

Old Man's Beard, Poison Ash, Flowering Ash, Shavings Tree.

Chionanthus virginica is a low, deciduous tree indigenous to the Southern United States and extending north into Pennsylvania and New Jersey. It bears opposite, petiolate, ovate to obovate-lanceolate leaves and drooping panicles of white flowers. Its fruit is an ovoid, purple drupe. The commercial supplies of the drug come chiefly from Virginia and North Carolina.

Description and Physical Properties.—"*Unground Chionanthus.*—Usually in transversely curved pieces, occasionally in single quills from 1 to 10 cm. long; bark from 2 to 10 mm. thick; heavy, some pieces of the whole drug sinking when thrown into water; outer surface usually reddish brown, occasionally grayish brown, with few transverse wrinkles; scaly, roughened by shallow pits and ridges, whitish cork patches and root-scars; inner surface yellowish brown, more or less striate and undulate; fracture short, hard, and coarsely granular, the broken surface of a light yellowish-white color. Odor characteristic; taste bitter.

"*Structure.*—A thin outer bark of a corky layer and a zone of tangentially elongated cells; middle bark very thick, composed chiefly of thin-walled parenchyma, a few groups of scattered stone cells and occasional bundles of fibers; inner bark of small parenchyma cells, nearly straight tapering medullary rays which penetrate to the middle bark, a few groups of fibers and small sieve groups; parenchyma cells filled with small prismatic crystals of starch grains.

"*Powdered Chionanthus.*—Light brown; exhibits somewhat rounded, simple or 2- to 4-compound starch grains, the individual grains mostly 0.003 to 0.020 mm. in diameter, occasionally up to 0.25 mm. in diameter; numerous stone cells up to 0.115 mm. in length and 0.085 mm. in diameter, in groups and isolated, the walls thick, non-striated, strongly lignified and with simple and branching pores; few short fibers up to 0.200 mm. in length and 0.045 mm. in diameter, with blunt or truncate ends and lignified, lamellated walls with simple pores; numerous resin masses; few fragments consisting of light brown, thin-walled cork cells; parenchyma tissue, many of the cells with small prismatic crystals, a few with starch grains." *N. F.*

In the bark of this plant a saponin was found by R. S. Justice (*A. J. P.*, xlvii, 195), but not by W. von Schulz, who, however (*Ph. Z. R.*, 1893, 579), detected a glucoside.

Uses.—Chionanthus by some is supposed to have special relations towards the liver and has been used in the treatment of *catarrhal jaundice* and *portal congestion* and allied conditions.

Dose, one-half to one drachm (2–4 Gm.).

Off. Prep.—Fluidextractum Chionanthi, *N. F.*

CHIRATA. N. F., Br.

CHIRATA Chirat.

"Chirata is the dried plant of *Swertia Chirayita* (Roxburgh) Lyons (Fam. *Gentianaceæ*). Chirata contains not more than 3 per cent. of foreign organic matter." *N. F.* "Chiretta is the plant, Swertia Chirata, *Buch.-Ham.*, collected when in flower, and dried." *Br.*

East Indian Balmony; Chirayta; Chirette, *Fr.*; Chiretta, Ostindischer Enzian, *G.*

According to Lloyd, this drug has long been held in esteem by the Hindoos. It first attracted attention in England in 1829 and was introduced into the Edinburgh Pharmacopœia in 1839.

Swertia Chirayita (Roxb.) Hamilton (*Ophelia Chirata* Griesbach) is an annual plant, about three feet high, with a branching oblique root, and an erect, smooth, slightly winged branching stem, and furnished with opposite, lanceolate, very acute, entire, smooth, three or five-nerved leaves. The flowers are numerous, peduncled, yellow, with a four-cleft calyx having linear acute divisions, the limb of the corolla spreading and four-parted, four stamens, a single style, and a two-lobed stigma. The capsules are unilocular. The plant is a native of Nepaul and other parts of Northern India. The whole of it is gathered when the flowers are well advanced. Various dried gentianaceous plants occur as adulterants or substitutes of chirata; the most important of these is the *Swertia* (*Ophelia*) *angustifolia* Buch.-Ham. It yields the *Paharee* or *Hill chirata*, which is distinguished by its inferior bitterness, and its rectangular, winged stems, whose section presents a thick woody ring and a center nearly or entirely hollow, with only traces of pith. A false chirata, which resembles the official variety in having a well developed pith, but which is completely lacking in bitterness, is affirmed to be the product of *S. alata* Royle. (*P. J.*, xvii, 903.) Under the name of *Indian chirata*, the dried plant of the *Andrographis paniculata* Nees has appeared in the London market; it resembles much more closely recently dried broom tops than the true chirata. All of the above are readily distinguished from true chirata by their lack of bitterness.

The dried plant is imported into Europe in bundles, consisting mainly of the stems, with portions of the root attached. The stems contain a yellowish pith.

Description and Physical Properties.—"*Unground Chirata.*—Smooth; root simple, about 7 mm. thick near the crown; stem about 1 M. in length, externally yellowish or purplish brown, cylindrical near the base, quadrangular and slightly winged above, with numerous opposite, ascending branches; wood yellowish, thin, enclosing usually a large yellowish easily separable pith; leaves opposite, sessile, ovate-lanceolate, entire, five-nerved, up to 6 cm. long; flowers numerous, panicled, small, with a four-lobed calyx and corolla; capsule ovoid, acute, one-celled, many seeded. Odor slight; taste intensely bitter.

"*Powdered Chirata.*—Dark yellow or brownish; tracheæ numerous, spiral, scalariform or with simple pores, and frequently associated with lignified fibers; abundant pith parenchyma cells with lignified walls and simple pores; fragments of epidermis with stomata, the latter broadly elliptical and up to 0.045 mm. in length; occasionally whole seed about 0.400 mm. long or fragments of seed coat, with small, rather thick and wavy-walled epidermal cells; ellipsoidal pollen grains, smooth and up to 0.030 mm. in length; a few elongated cells with yellowish brown resin and tannin masses." *N. F.*

"Stem about one metre long, smooth, brown, or purplish-brown, slightly winged and much branched above, rounded below and containing a large, continuous, easily separable pith. Root oblique. Branches slender, elongated, decussate. Leaves opposite, ovate, glabrous, entire, usually with three to seven lateral veins. Flowers small, numerous, panicled. Fruits superior, bicarpellary, unilocular. No odor; taste extremely bitter." *Br.*

Flückiger and Höhn found in chiretta: sugar, wax, chlorophyll, soft resin, tannin, an acid which they name *ophelic,* possessing the formula $C_{13}H_{20}O_{10}$, and a peculiar bitter substance denominated *chiratin,* $C_{26}H_{48}O_{15}$. The acid is syrupy, deliquescent, yellowish-brown, at first slightly sour, afterwards intensely bitter. It is soluble in water, with some turbidness, probably owing to resin mixed with it, and completely soluble in alcohol, or a mixture of this with ether. It decomposes certain salts, and forms amorphous compounds with acids. Chiratin—which occurs in smaller amount—is a yellow, hygroscopic powder, difficultly crystallizable, very bitter, sparingly soluble in cold water, more so in hot water, and readily dissolved by alcohol and ether. It is neutral to test paper, and yields a copious precipitate with tannic acid. By the action of acids, chiratin is separated into ophelic acid, and a yellowish-brown, amorphous substance, bitter, scarcely soluble in water, readily soluble in alcohol, and not reducing copper solutions, as the ophelic acid does. Höhn gives it the formula $C_{13}H_{24}O_3$, and names it *chiratogenin.*

Uses.—Chirata has long been used in India. It has been introduced into Europe, and appears to be highly esteemed, but has not been employed to any considerable extent in this country. Its properties are those of the pure bitters, and probably do not differ from those of the other members of the family of *Gentianaceæ.* (See *Gentiana.*) Like these, in over-doses it nauseates and oppresses the stomach. Some have supposed that, in addition to its tonic properties, it exerts a peculiar influence over the liver, promoting the secretion of bile and correcting it when deranged, and restoring healthy evacuations in cases of habitual costiveness. It has been used in *dyspepsia,* and in the *debility* of convalescence, and generally in cases in which corroborant measures are indicated. In India it has been employed in *intermittents* and *remittents,* combined with the seeds of *Guilandina Bonducella* L. It may be given in powder, infusion, tincture, or fluidextract.

Dose, ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Infusum Chiratæ, *Br.;* Tinctura Chiratæ, *Br.;* Fluidextractum Chiratæ, *N. F.*

CHLORAL FORMAMIDUM. Br.

CHLORAL FORMAMIDE

"Chloral Formamide, $C_3H_4Cl_3NO_2$, may be obtained by the direct combination of formamide with anhydrous chloral. Should be preserved in amber-colored bottles." *Br.*

Chloralamide; Chloralum formamidatum, *P. G.;* Chloralformamid, *G.*

Properties.—Chloralformamide is officially described in the Br. Pharm. as in "colorless lustrous crystals. No odor; taste slightly bitter. Soluble in 21 parts of *water;* very soluble in *alcohol* (90 per cent.), the solution being neutral to *litmus;* very soluble in *ether;* slowly soluble in 12 parts of *glycerin.* Melting point 114° to 115° C.; decomposes at a higher temperature. Hydrolyses in aqueous solution at 60° C., yielding chloral hydrate and formamide. Unaffected by dilute acids, but decomposed when warmed with *solution of sodium hydroxide,* chloroform separating and ammonia and sodium formate being produced. Heated with free access of air it volatilises completely without the evolution of inflammable vapors (absence of certain organic impurities). Its solution in *alcohol* (90 per cent.) is not immediately altered in appearance by *solution of silver nitrate* (absence of certain decomposition products)." *Br.*

Chloralimide, $CCl_3.CH{-}NH$, should not be confounded with chloral*a*mide. Chloralimide is in colorless, inodorous, and insipid, long crystalline needles; melting at about 166° C., insoluble in water; readily soluble in alcohol, in ether, in chloroform, and in oils. Concerning its physiological action we have no certain knowledge; it is asserted to be hypnotic in doses of from fifteen to sixty grains (1–3.9 Gm.).

Uses.—Locally, chloralformamide is scarcely at all irritant, and when taken internally is quickly absorbed and is eliminated chiefly as urochloralic acid. When given to the lower animals, it produces lethargy, sleep, muscular relaxation, arrested respiration, followed by coma, failing respiration, and if the dose has been sufficient, death by centric respiratory paralysis. As shown by the experiments of H. C. Wood and Cerna, subsequently confirmed by various observers, its influence upon the circulation and the spinal cord is extremely feeble, and it has no perceptible effect upon the nerve trunks and the muscles. As an hynotic it resembles hydrated chloral, but its action is more slowly developed and is less positive. Confusion, giddiness and headache are the only unpleasant effects following its use, and they rarely occur.

Dose, fifteen to forty-five grains (0.9–3.0 Gm.), half an hour before the desired time of sleep.

CHLORAL HYDRAS. U. S., Br.

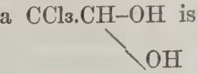
CHLORAL HYDRATE Chloral. Hydrat.

"Chloral Hydrate contains not less than 99.5 per cent. of $CCl_3CHO.H_2O$." *U. S.* "Chloral Hydrate, $C_2Cl_3H_3O_2$, may be obtained by the addition of water to the liquid chloral, C_2Cl_3HO, produced by the action of dry chlorine gas on ethylic alcohol." *Br.*

Chloralum Hydratum, *U. S. IX;* Hydrated Chloral; Trichloraldehyd Hydrate, Trichlorethylidene Glycol; Hydrous Chloral; Chloral Hydraté, *Fr.;* Hydrate de Chloral, *Fr. Cod.;* Chloralum Hydratum, *P. G.;* Chloral Hydrat, *G.;* Cloralio idrato, *It.;* Hidrato de cloral, *Sp.*

Though discovered by Liebig in 1832, it was not until 1869 that its remedial properties were first made known by their discoverer, Otto Liebreich of Berlin; in 1878 the consumption of chloral was estimated at one ton daily in England and America alone; and, although not used now to this extent, it is still largely employed.

Anhydrous Chloral.—In preparing anhydrous chloral, the simple method originally employed by Liebig, of acting directly on alcohol by chlorine, is generally preferred, even, we believe, by the larger manufacturers. This first forms chloral alcoholate which is treated with sulphuric acid to convert it into chloral. It is subsequently rectified by distillation over calcium carbonate and finally hydrated by mixing with molecular proportions of water and allowing it to crystallize. The action of chlorine upon alcohol is said to be aided by the presence of "chlorine carriers," such as iodine, ferric chloride, thallium chloride, etc. The formula of anhydrous chloral is C_2Cl_3HO; in other words, aldehyde, C_2H_4O, in which 3 atoms of hydrogen have been replaced by 3 atoms of chlorine. The name of chloral was derived from the *chlor*ine and *al*cohol from which it is formed. The *anhydrous chloral* thus formed is a colorless liquid, of penetrating disagreeable odor, of little taste, of the sp. gr. 1.502, and boiling at 94° C. It is soluble in ether or chloroform without change. According to A. Trillat, in the formation of chloral from alcohol, the latter is first changed by the action of the chlorine into aldehyde; this unites with alcohol to form acetal, which is changed successively into mono-, di-, and trichloracetal; the action of hydrochloric acid decomposes this latter with the formation of chloral alcoholate and ethyl chloride; sulphuric acid decomposes the alcoholate, liberating chloral, which then is made to combine with water to form the crystalline hydrated chloral. (*Bulletin,* 1897, 17, 230.) As the union of hydrated chloral with water develops heat, it is supposed to be more than the formation of a hydrate, and the formula $\mathrm{CCl_3.CH}\begin{array}{l}-\mathrm{OH}\\ \diagdown\mathrm{OH}\end{array}$ is assigned to the resulting compound. It does not show all the reactions of an aldehyde, as, for example, the red color of a magenta solution that has been decolorized with sulphurous acid, is not restored by it.



Meta-chloral.—By continued contact of anhydrous chloral and concentrated sulphuric acid, a change is effected in the chloral, by which it becomes a solid insoluble in water, which is designated as *insoluble chloral,* or *meta-chloral.* It is tasteless, of a white color resembling porcelain, and insoluble in alcohol and ether. Its formula is $C_6H_3Cl_9O_3$, being formed by the union of three molecules of chloral. It is stated that when perfectly pure, chloral does not become polymerized; the change is also said to be prevented by the addition of a little chloroform. When heated to 180° C., meta-chloral distils with reversion to liquid chloral. (Allen, *Com. Org. Anal.,* 2d ed., i, p. 171.)

Chloral Alcoholate.—A compound obtained by Roussin, which he announced as pure hydrated chloral, was found by Personne to contain no water, but to be in fact a compound of alcohol and chloral, and is now known by the name of *chloral alcoholate,* C_2HCl_3O,C_2H_6O. It results directly from the action of absolute alcohol on anhydrous chloral, and is now known to be formed as a stage in the manufacture of chloral from alcohol. As it is very likely to be confounded with hydrated chloral, the following points of difference should be noted. It forms white crystals melting at 46° C., and boils at 113.5° C., while hydrated chloral crystals melt at 58° C. and boil at 97.5° C.; chloral alcoholate melts without complete solution when warmed with two volumes of water, and, on cooling, congeals below the surface of the water, white hydrated chloral is soluble in one and one-half times its weight of water; chloral alcoholate, gently heated with nitric acid of 1.2 sp. gr., is violently attacked, while hydrated chloral is scarcely acted on; chloral alcoholate, when heated on platinum foil, inflames readily, while hydrated chloral scarcely burns. (Allen, *Com. Org. Anal.,* 2d ed., i, p. 172.)

The three related products, *anhydrous chloral,* polymeric *meta-chloral,* and *alcoholate,* described above, have been more or less introduced into the European markets, and have required some notice to prevent them from being confounded with hydrated chloral, which is alone official. The following observations will be confined to this last compound, and the reader will note that whether the simple term chloral, or the exact designation, hydrated chloral, is used, the same substance is intended.

Chloral hydrate is obtained by simply mixing anhydrous chloral with water. Acicular crystals soon form, which result from the union of a molecule each of the chloral and water, constituting hydrated chloral. It occurs in commerce mainly in two forms; in distinct crystals, which is the official form, or in crystalline plates, about three lines in thickness, broken into small, irregular pieces, so as to be readily introduced into broad-mouthed bottles. These pieces, while retaining their tabular form, are somewhat translucent, but usually covered with a white powder, which somewhat conceals that property. This form is sometimes called "chloral crusts." It is the more common form and the cheaper; but the crystals are to be preferred, as their purity may be relied on. Guerin adds his testimony to the necessity for dispensing only hydrated chloral which has been recrystallized and which is in the form of distinct crystals. He examined many samples, and found acidity in the crust or cake variety, due, as he believes, to the formation of hydrochloric and formic acids, produced by the action of water retained in the cake during the manufacture, and this remaining in contact with the crystals excites decomposition.

Hydrated chloral is white, possessing a peculiar pungent odor, and an acrid pungent taste. Exposed to the air it very slowly volatilizes, and, like camphor, when enclosed in a bottle, covers the interior surface with numerous minute crystals. If the boiling point be under 95° C., it indicates an under-hydrated preparation; if above 98° C., an over-hydrated one. The pure hydrated chloral does not take fire when heated, but evaporates without residue. With the aid of heat, its solution may be effected readily in chloroform; and the solution, on cooling, deposits it in beautiful crystals, which are generally needle-shaped, while those deposited from a solution in carbon disulphide are prisms. The aqueous solution is prone to decomposition, with the development of molds. Hydrated chloral should not, therefore, be kept long in this state.

It is neutral or, according to E. Schering, slightly acid when perfectly pure. When equal parts of hydrated chloral in crystals and of camphor in small fragments are shaken together in a bottle, and allowed to stand, they liquefy, forming a clear solution. When hydrated chloral and sulphuric acid are mixed, the temperature is greatly reduced. A solution of hydrated chloral dissolves morphine, quinine, and most of the vegetable alkaloids. When ammonium sulphide is added to an aqueous solution of hydrated chloral, the mixture rapidly turns yellow, and, after passing through several shades of color, finally becomes dark brown. From this liquid diluted sulphuric acid throws down a bulky brown precipitate. This, purified from precipitated sulphur and dried, is a light-brown powder of the composition $C_{18}H_{24}S_{13}N_4O_6$. Hydrogen sulphide gas forms a sulphydrate by its action on hydrated chloral. These reactions are important, as the detection of metallic poisons in toxicological cases by hydrogen sulphide has been complicated by the presence of hydrated chloral. A still more important chemical reaction of hydrated chloral is that which takes place when the hydrated, or either of its other forms, is acted upon by an alkali. Chloroform is developed, and along with it a formate of the alkali employed. Thus, in a strong solution of potassium hydroxide, put a pinch of powdered hydrated chloral, and almost instantly the odor of chloroform becomes perceptible, and some oil-like globules of chloroform may be seen at the bottom of the vessel. The reaction is as follows:

$$\underset{\text{Hydrated chloral}}{C_2HCl_3O.H_2O} + \underset{\text{potassium hydroxide}}{KOH} = \underset{\text{chloroform}}{CHCl_3} + \underset{\text{potassium formate}}{CHO.OK} + \underset{\text{water}}{H_2O}$$

Description and Physical Properties.—"Colorless, transparent crystals, having an aromatic, penetrating, and slightly acrid odor, and a slightly bitter, caustic taste. It slowly volatilizes when exposed to the air. One Gm. of Chloral Hydrate is soluble in 0.25 cc. of water, 1.3 cc. of alcohol, 2 cc. of chloroform, and in 1.5 cc. of ether, at 25° C. It is very soluble in olive oil and freely soluble in oil of turpentine. Chloral Hydrate is decomposed by caustic alkalies, alkali earths, and ammonia, chloroform and a formate of the base being produced. When warmed with a few drops of aniline and sodium hydroxide T.S., the intensely disagreeable odor of phenylisocyanide is developed.

"Ash: not more than 0.05 per cent. An alcoholic solution of Chloral Hydrate (1 in 20) does not at once redden moistened blue litmus paper, nor does it at once become opalescent on the addition of a few drops of silver nitrate T.S. (*chloride*). Shake about 0.5 Gm. of Chloral Hydrate, at intervals of five minutes during one hour, with 5 cc. of sulphuric acid in a glass-stoppered cylinder, which has previously been rinsed with sulphuric acid: the acid remains colorless or very nearly so when viewed transversely in a tube of about 20 mm. diameter (*readily carbonizable substances*). Gently ignite 2 Gm. of Chloral Hydrate: no inflammable vapors are evolved (*difference from chloral alcoholate*).

"Preserve in tightly stoppered bottles, in a cool place, protected from light." *U. S.*

"In colorless, non-deliquescent, monoclinic plates. Pungent, but not acrid odor; taste pungent and rather bitter. Soluble in less than 1 part of *water, alcohol* (90 per cent.), or *ether,* and in 3 parts of *chloroform.* Aqueous solution neutral or only slightly acid to *litmus.* Melting point 49° to 53° C.; at a slightly higher temperature it volatilises without residue. Decomposed by alkalies with liberation of chloroform. A solution in *chloroform,* shaken with *sulphuric acid,* imparts no color to the acid (absence of certain organic impurities). When 1 gramme of Chloral Hydrate is warmed with 6 millilitres of *water* and 0.5 millilitre of *solution of sodium hydroxide,* the mixture filtered, sufficient *N/10 solution of iodine* added to impart a deep brown color, and the whole set aside for an hour, no yelow crystalline perecipitate is produced (absence of chloral alcoholate). Its aqueous solution yields no precipitate with *solution of silver nitrate* (absence of free chlorides.)" *Br.*

The most delicate test for the presence of chloral alcoholate in hydrated chloral is said to be that with nitric acid. When 1 cc. of nitric acid (1.38 sp. gr.) is poured over 1 Gm.

of hydrated chloral a yellow color should not appear within 10 minutes, even if the mixture be warmed. (*A. J. P.*, 1894, 191.) For other tests for hydrated chloral by Jaworowski, the reader is referred to *Ph. Z. R.*, 1894, 373.

Assay.—"Dissolve about 4 Gm. of Chloral Hydrate, accurately weighed, in 10 cc. of distilled water, add 30 cc. of normal sodium hydroxide, and allow the mixture to stand for two minutes. Add phenolphthalein T.S., and determine the residual alkali at once by titration with normal sulphuric acid. Each cc. of normal sodium hydroxide corresponds to 0.1654 Gm. of $CCl_3CHO.H_2O$." *U. S.*

Chloral hydrate when triturated with phenol, camphor and other organic compounds forms eutectics which liquefy. In aqueous solution it is incompatible with alkalies which decompose it with the production of chloroform. Hydroalcoholic solutions in the presence of bromides or other saline ingredients frequently show a separation into two layers, the upper of which contains part of the alcohol and all of the chloral.

Uses.—The physiological action of hydrated chloral may be summed up as follows:—Its dominant effect is to depress the centers of consciousness, the soundness of the sleep produced being proportional to the quantity ingested. In somewhat larger doses it is depressant to the motor side of the spinal cord and respiratory center but the sensory apparatus is unaffected except after poisonous doses. In full dose it tends to lower blood pressure probably chiefly through an action upon the vasomotor center, although after large quantities there is a direct depressant influence upon the heart muscle. In poisonous doses it produces profound coma with anesthesia. After fatal quantities death is generally due to stoppage of the respiration through paralysis of the nerve centers, although sometimes due to sudden heart failure. Chloral has little effect on the secretions, although it is stated to somewhat increase the flow of urine. It escapes from the body through the kidneys, probably in part unchanged, although partially in the form of urochloralic acid. This latter body has the property of reducing Fehling's solution. The theory of Liebreich which led to the introduction of this drug into medicine, that it was decomposed by the alkalies of the body with the gradual liberation of chloroform, has been abundantly disproven.

Hydrated chloral is used internally in medicine as a somnifacient, as an anticonvulsant, and externally as a local anesthetic, disinfectant and deodorizer. For the relief of *insomnia* not caused by pain it is one of the most certain hypnotics which we possess and is therefore especially employed in the more obstinate forms of sleeplessness such as in *delirium tremens* and certain types of *insanity*. Its action is very prompt, sleep generally beginning within fifteen minutes or half an hour after its oral administration. The effects, however, do not usually last over three or four hours. When the wakefulness is caused by pain it is greatly inferior to the opiates but even here is often of service as an adjuvant. In cases of circulatory weakness it should be used always with great caution if at all, on account of its liability to depress the heart. As a somnifacient it is rarely necessary to give more than 15 grains at a dose.

It is also a remedy of great value in the treatment of various *convulsive disorders*. The determination whether or not to administer chloral in an individual case should be based upon the severity, rather than the type, of the convulsions, thus in *tetanus* and *strychnine poisoning* in which death may be the direct result of the spasm, it is one of the most frequently employed of remedies and justly so. On the other hand, in *epilepsy* ordinarily the convulsions are of little importance and, as the chloral does not lessen the convulsive tendency, it is not often of service; but in the condition known as *status epilepticus* it may prove of great value. It is also occasionally demanded in severe cases of *hysteria* and *chorea*. Certain local spasms, such as *laryngismus stridulus, asthma,* and *hiccough,* are at times greatly benefited by its employment.

Locally it is used to a large extent in combination with camphor or methyl salicylate as an anodyne and counter-irritant. Occasionally it is employed as a stimulating antiseptic to *wounds,* although its antibacterial powers are comparatively feeble. It has, however, been highly recommended by Siegmund (*Th. M.*, 1909) as a deodorizant in *gangrene of the lung* and various other malodorous conditions. It is said also that it is valuable for washing the hands after post-mortem examinations, acting both as a disinfectant and deodorizer. A two per cent. solution has been recommended by Quincke as a spray in *tonsillitis* and other inflamed conditions of the oral or nasal cavities.

Occasionally hydrated chloral in even not excessively large doses may produce very unpleasant symptoms, such as various skin lesions or circulatory failure. The latter may be very alarming and at least one case is recorded in which a single dose of thirty grains caused death. The common symptoms of chloral poisoning are: Deep sleep, passing into coma, the pupil, at first contracted, later dilates; the respirations fall in number; the pulse is weakened and rendered slower, but later may become rapid and irregular; the temperature is reduced; the muscular system is relaxed, and both sensibility and reflex action are diminished or completely abolished. The immediate cause of death is generally a paralytic arrest of respiration but in many cases there appears to have been a simultaneous arrest of the cardiac action, and it is very possible that fatal syncope may at times occur.

In the treatment, if the case be seen early, the stomach should be thoroughly evacuated by a rapidly acting emetic, as zinc sulphate, or the stomach tube, and atropine, strychnine, cocaine, and caffeine, employed as respiratory and circulatory stimulants; at the same time external heat should be applied to maintain the bodily temperature and efforts made to keep the patient awake. For the latter purposes, however, those measures which throw an added strain upon the heart, such as walking, must be sedulously avoided; the electric brush affords the most efficient and least injurious method of preventing sleep.

Hydrated chloral is best administered in solution with syrup of orange flowers, or some simple aromatic. Solutions of chloral hydrate easily undergo decomposition when exposed to light. Dissociation occurs with the formation of hydrochloric acid, trichloracetic acid and formic acid. Solutions of chloral hydrate, therefore, should be preserved in the dark. The French sometimes employ *chloral cream,* made of hydrated chloral 5 parts, water 15 parts, white sugar finely powdered 100 parts, flavored with mint, orange, or vanilla. One teaspoonful is equivalent to about 3 grains of hydrated chloral. This preparation keeps well, and the dose may be dissolved in a little water. *Chloral liniment* may be made by dissolving 6 parts of hydrated chloral in 30 parts of oil of sweet almonds. *Chloral ointment,* 6 parts hydrated chloral, 3 parts white wax, 27 parts lard; the lard and wax are melted at a gentle heat, the hydrated chloral added in powder and dissolved. *Chloral plaster,* to produce counter-irritant effects, is prepared by spreading powdered hydrated chloral on Burgundy pitch plaster; care should be taken to distribute it uniformly.

Dose, ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Syrupus Chloral, *Br.;* Chloral Camphoratum, *N. F.;* Mistura Chloralis et Potassii Bromidi Composita, *N. F.*

CHLORAMINA. U. S.

CHLORAMINE Chloram. [Sodium Paratoluenesulphonchloramide, Chloramine - T]

"Chloramine [$C_6H_4(CH_3)(SO_2NNaCl).3H_2O$] contains not less than 11.5 per cent. and not more than 13 per cent. of active chlorine." *U. S.*

Chlorazene, Tolamine, Tochlorine.

This compound was first made by Chattaway in 1905 (*Tr. Chem. Soc.,* 1905, lxxxvii, p. 153) but its introduction as a medicine was due to the studies of Dr. Dakin in 1915, who suggested for it the name of chloramine. This name is somewhat unfortunate as it has been also applied to the substance NH_2Cl, which is used for very different purposes.

According to Eicher (*J. A. Ph. A.,* 1917, iii, p. 387), in aqueous solution it liberates NCl to which its disinfectant properties are attributable.

Chloramine is prepared from toluene as the starting point. This is first converted into toluene-para-sulphonic acid, the sodium salt of which, when treated with phosphorus pentachloride, yields toluene-para-sulphonic chloride. This compound, which is an abundant by-product in the manufacture of saccharin is sometimes used as the starting point. It is then converted into toluene-para-sulphonamide by treatment with ammonia under pressure. This is finally treated with sodium hypochlorite in the presence of an alkali, the chloramine being obtained from this solution by crystallization. It is twice recrystallized from hot water and finally dried at 35° to 40° C.

Description and Physical Properties.—"White or faintly yellow crystals or a crystalline powder, having a slight odor of chlorine. It slowly decomposes on exposure to air, losing chlorine. One Gm. of Chloramine is soluble in about 7 cc. of water at 25° C. and in about 2 cc. of boiling water. It is decomposed by alcohol, and is insoluble in benzene, chloroform, and ether. At about 95° to 100° C. Chloramine loses its water of crystallization without decomposition.

"An aqueous solution of Chloramine (1 in 20) is alkaline to litmus paper or phenolphthalein T.S. The addition of potassium iodide T.S. to an aqueous solution of Chloramine (1 in 20) causes the liberation of iodine, but bromine is not liberated from alkali bromides unless the mixture is acidulated with an acid (*difference from dichloramine*). Acids produce in an aqueous solution of Chloramine (1 in 20) a white turbidity or precipitate which redissolves in an excess of alkali hydroxide solutions. When strong mineral acids are used, chlorine is also liberated. On adding 2 cc. of sulphuric acid to 0.1 Gm. of Chloramine, chlorine is evolved but no appreciable darkening occurs (*readily carbonizable substances*).

"**Assay.**—Dissolve about 0.5 Gm. of Chloramine, accurately weighed, in 50 cc. of water, add 5 cc. of potassium iodide T.S. and 5 cc. of acetic acid, and allow the mixture to stand in a glass-stoppered bottle for ten minutes. Titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.001773 Gm. of active chlorine.

"Preserve in well-closed containers, protected from light." *U. S.*

Bebie (*J. A. Ph. A.,* 1920, ix, 974) found that solutions of chloramine—provided the latter be pure—showed no perceptible deterioration after six months' storage.

Uses.—Chloramine was brought to the notice of the medical profession by Dakin in 1915 as a surgical disinfectant possessing the advantages over sodium hypochlorite of being more stable in solution and less irritant to the tissues (*B. M. J.,* Aug. 25, 1915 and Jan. 29, 1916). It is a powerful germicide; according to Hamilton, tested by the Hygienic Laboratory method it showed a phenol coefficient of about 50, one part in 2000 being sufficient to destroy the bacillus typhosus in two and one-half minutes. But Tilley (*Journ. Agricul. Res.,* 1920, xx, 85) found that in the presence of organic matter (blood serum) its strength was greatly reduced, a 1 to 500 solution requiring 2 hours to kill typhoid bacilli. Tilley also tested chloramine against other bacteria and while in most cases he found it to approach mercuric chloride in power it was comparatively inefficient against anthrax spores and against the tubercle bacillus; a 1 per cent. chloramine solution failed to kill the tuberculosis germ in 10 minutes and required 24 hours to destroy anthrax spores. In contrast to these results Vincent (*J. Ex. M.*, 1917, xxvi, 83) found that 0.2 per cent. of chloramine was not only not germicidal to the staphylococcus but was not even a complete antiseptic; it required 0.22 per cent. to certainly inhibit the growth of these bacteria.

Taylor and Austin (*J. Ex. M.*, 1918, xxvii, p. 635) and Fantus and Smith (*J. P. Ex. T.*, xiv, p. 259) have both found that when introduced into the blood stream, chloramine is a violent systemic poison. According to the former investigators it ranks in toxicity close to mercuric chloride, being fatal to mice in the proportions of 0.01 Gm. per kilo body weight; Fantus and Smith found the fatal dose for the rabbit to be 0.025 Gm. per kilo. It is a depressant to the whole central nervous system.

The value of chloramine in infected *wounds*, which was so abundantly proven in military surgery during the recent great war, has since been confirmed by civilian surgeons. Although its action appears to depend, like that of the hypochlorites, on the liberation of chlorine its range of usefulness is slightly different from that of the inorganic chlorinated compounds. In ordinary wounds, because of its lower irritating qualities, it is usually preferable to the alkaline hypochlorites, but where there is much necrotic tissue, chloramine, as has been shown by Taylor and Austin, has a distinctly lesser power of dissolving this undesirable detritus. It is mostly employed in dilute solutions for irrigating deep wounds, but Carrel and Hartmann (*J. Ex. M.*, 1917, xxvi, p. 95) assert that by packing wounds with a paste, devised by Daufresne, it is possible to render them completely sterile. The basis of this paste contains 8.6 per cent. of neutral sodium stearate in distilled water, and is usually made to contain from ½ to 1 per cent. of chloramine; it should be freshly prepared as it loses its active ingredient at the rate of about 10 per cent. a month.

Chloramine may also be employed as an antiseptic mouth wash and for irrigation of the bladder, uterus, and other internal cavities. It is not suitable for a gastric antiseptic because it is decomposed by the secretions of the stomach, but Carnot and Bondouy (*A. J. P.*, 1919, xvi, 474) state that if protected from the action of gastric juices it may be used advantageously as an intestinal antiseptic. As a surgical disinfectant it may be used in strengths of from 0.5 to 4 per cent. It should not be confused with dichloramine.

CHLOROFORMUM. U. S., Br.

CHLOROFORM Chlorof.

"Chloroform contains not less than 99 per cent. and not more than 99.5 per cent. of $CHCl_3$, the remainder consisting of alcohol. *Caution—Care should be taken not to vaporize Chloroform in the presence of a naked flame, because of the production of noxious gases.*" *U. S.*

"Chloroform is trichlormethane, $CHCl_3$ to which 2 per cent. of Absolute Alcohol has been added. It may be obtained from ethylic alcohol, industrial methylated spirit, or acetone, by heating with chlorinated lime, slaked lime, and distilled water, and subsequent purification. Should be kept cool and in a dark place." *Br.*

Trichlormethane, Methenyl Trichloride; Chloroformum Purificatum, *U. S.* 1880; Formylum Trichloratum; Chloroforme Anesthésique, *Fr. Cod.*; Chloroformium pro Narcosi, *P. G.*; Reines Chloroform, Chloroform, *G.*; Cloroformio, *It.*; Clorido Formico, Cloroformo, *Sp.*

Chloroform is tri-chlor-methane and may be produced by the interaction of chlorine and methane although the process is not economically practicable.

It was at first made from alcohol by the action of chlorinated lime, but is now made on the large scale, by the distillation of acetone with chlorinated lime; indeed, this process has entirely replaced the manufacture from alcohol. Liebig, as long ago as 1832, described the reaction, but it was thought to be not adapted for commercial use until 1882. To get a satisfactory yield, a very pure acetone is necessary. When such acetone is taken, a yield of nearly or quite 200 per cent. of chloroform can be obtained. (For an account of the methods of purifying the acetone and distilling with chlorinated lime, see *A. J. P.*, 1889, p. 321.) In July, 1885, a patent was taken out by G. Michaelis of Albany, for the manufacture of chloroform from the liquid products resulting from the decomposition of crude acetates at high temperatures. These liquid products are acetone and other higher ketones. Pure methyl alcohol does not yield chloroform. The erroneous statements on this point are probably due to the fact that commercial wood spirit contains a large percentage of acetone.

E. R. Squibb preferred acetic acid to the acetates in the intermediate step of making acetone, thus avoiding impurities likely to be present in acetates; he believed that the grant of a patent for "acetone chloroform" was deficient in equity. (*Ephem.*, 1896, 1743 to 1757.)

Chloroform has been prepared electrolytically but the method has been criticized as yielding a product of unsatisfactory quality.

Chloroform is also made by the Besson process which consists in passing chlorine into ethyl alcohol until the liquid has a specific gravity of 1.32, a mixture of bleaching powder and milk of lime is added and distillation conducted. The yield is said to be over 95 grammes of chloroform for each 100 grammes of alcohol employed. (*Revue Scientifique*, Feb., 1893.)

Carbon tetrachloride (CCl_4) has also been proposed (1896) as a source of chloroform, and as this is now made cheaply on a large scale, the process may come into use. By the action of hydrochloric acid and zinc, hydrogen is liberated and attacks the carbon tetrachloride, forming chloroform and hydrochloric acid,

$$CCl_4 + H_2 = CHCl_3 + HCl$$

As hydrochloric acid is a product of the reaction, fresh quantities of zinc are attacked, and a new liberation of chloroform follows.

Pure chloroform will not keep, but after some time becomes so loaded with decomposition products as to be altogether unfit for respiration. Squibb showed, in 1857, that it is rendered more stable by the addition of a small proportion of alcohol. He recommended adding alcohol in the proportion of ten drops to each fluidounce of good chloroform of maximum density. This recommendation has been adopted by both the U. S. and Br., and explains the addition of alcohol before distillation. Even preserved in this manner, by the addition of alcohol, chloroform will undergo deterioration if kept for long periods. Gregory also attributes the tendency to decomposition to its purity, and to the action of sunlight; having found that those portions which he had purified with the greatest care were soonest decomposed under the influence of light. For methods of preserving chloroform by the use of sulphur, hypophosphorus acid, etc., see *P. J.*, 1895, 261; also 1896, 249.

The intermediate formation of hydrated chloral as a result of the reaction between alcohol and chlorinated lime suggested the preparation of chloroform from hydrated chloral. The advantages which were anticipated from decomposing pure hydrated chloral with alkalies have not altogether been realized, for the product is much more expensive, and the claim of greater stability has not been sustained, as it requires just as much alcohol to preserve it as that made in the usual way.

History.—Chloroform was discovered by Samuel Guthrie of Sackett's Harbor, N. Y., in 1831, and about the same time by Soubeiran in France, and Liebig in Germany. Guthrie obtained it by distilling a gallon from a mixture of three pounds of chlorinated lime and two gallons of alcohol of the sp. gr. 0.844, and rectifying the product by redistillation, first from a great excess of chlorinated lime, and afterwards from potassium carbonate. (*Silliman's Journal,* 1832, xxi, p. 64 and xxii, p. 105.) Guthrie states that the substance which he had obtained, "distilled of sulphuric acid, has the specific gravity of 1.486, or a little greater, and may then be regarded as free from alcohol; and if a little sulphuric acid which sometimes contaminates it be removed by washing it with a strong solution of potassium carbonate, it may then be regarded as *absolutely pure.*" It is thus evident that Guthrie obtained, in a pure state, the substance now called chloroform; but he erroneously supposed his product to be the well known oily liquid of the Dutch chemists, which it greatly resembles, and for the preparation of which he believed he had fallen on a cheap and easy process. Under this impression he called the substance, in his communications, *chloric ether,* one of the names by which *Dutch Liquid,* or *ethene dichloride,* is designated. Chloroform was used internally in *asthma* and other conditions as early as 1832 by Ives of New Haven, and subsequently in various conditions by several European physicians, but it was not until November, 1847, that Sir James Y. Simpson of Edinburgh brought it forward as a general anesthetic.

Description and Physical Properties.—"A clear, colorless, mobile liquid, having a characteristic, ethereal odor, and a burning, sweet taste. It is not inflammable, but its heated vapor burns with a green flame. Chloroform is soluble in 210 volumes of water. It is miscible with alcohol, ether, benzene, petroleum benzin, and with fixed or volatile oils. Specific gravity: 1.474 to 1.478 at 25° C. Chloroform boils at about 61° C., but is volatile even at lower temperatures.

"Evaporate 50 cc. of Chloroform in a platinum or porcelain dish on a water bath, and dry to constant weight at 100° C.: the weight of the residue does not exceed 0.001 Gm. Pour 20 cc. of Chloroform, in small portions, upon a piece of clean, odorless, filter paper, laid flat upon a warmed glass plate, and rock the plate from side to side, until the liquid is completely evaporated: no foreign odor becomes perceptible as the last portions disappear from the paper, and the paper remains odorless. Agitate 10 cc. of Chloroform with 25 cc. of distilled water, and allow the liquids to separate completely. The aqueous layer is neutral to litmus paper and separate portions of 10 cc. each are not affected by a few drops of silver nitrate T.S. (*chloride*), or colored blue by the addition of a few drops each of potassium iodide T.S. and starch T.S. (*free chlorine*). Transfer 40 cc. of Chloroform to a 50 cc. glass-stoppered cylinder of colorless glass, having an internal diameter of about 20 mm. and previously rinsed with sulphuric acid, add 4 cc. of colorless sulphuric acid, and shake the mixture vigorously for five minutes. Allow the liquids to separate completely, so that both are transparent: the Chloroform remains colorless, and the acid is colorless or nearly so, when viewed transversely in the cylinder (*substances decomposable by sulphuric acid*). Dilute 2 cc. of the sulphuric acid separated from the Chloroform in the preceding test with 5 cc. of distilled water: the liquid is colorless and clear, and while hot from the mixing emits but a faint, vinous or ethereal odor (*odorous decomposition products*). When further diluted with 10 cc. of distilled water, it remains clear, and is not affected within one minute by the addition of three drops of silver nitrate T.S. (*chlorinated decomposition products*).

"Preserve in well-stoppered bottles, in a cool place, protected from light. Protect Chloroform from contact with cork stoppers by covering them with tin foil or other suitable material." *U. S.*

"A colorless, volatile liquid. Characteristic odor; taste pungent, sweet. Specific gravity 1.483 to 1.487. Does not begin to boil below 60° C. On allowing 10 millilitres to evaporate from a large piece of filter paper placed on a warm plate, no extraneous odor is perceptible at any stage of the evaporation. *Water* which has been shaken for five minutes with half its volume of Chloroform, and separated from the undissolved Chloroform, is neutral to *litmus* (absence of acid), does not give any color with 1 millilitre of *solution of cadmium iodide* and 2 drops of *mucilage of starch* (absence of free chlorine), and yields not more than a very slight opalescence with 4 drops of *solution of silver nitrate* (absence of chlorides). After shaking *sulphuric acid* with twice its volume of Chloroform for five minutes, and setting aside for fifteen minutes, both the acid and the Chloroform are nearly colorless. 2 millilitres taken from the layer of *sulphuric acid,* and diluted with 5 millilitres of *water,* remain very nearly colorless, and have a pleasant odor. When this acid liquid is further diluted with 10 millilitres of *water,* and stirred with a glass rod, it is transparent and colorless, and the addition of 4 drops of *solution of silver nitrate* causes not more than a slightly diminished transparency. *Water* which has been shaken with half its volume of Chloroform, previously treated with *sulphuric acid* as described above, yields not more than a slightly diminished transparency with *solution of silver nitrate.* Evaporates without residue." *Br.*

Besnou gives the densities of various mixtures of alcohol and the purest commercial chloroform at 4.5° C. as follows:

Specific Gravity.	Chloroform, per cent.	Alcohol, per cent.	Specific Gravity.	Chloroform, per cent.	Alcohol, per cent.
1.4945	100.0	0.0	1.4772	97.5	2.5
1.4908	99.5	0.5	1.4602	95.0	5.0
1.4874	99.0	1.0	1.4262	90.0	10.0
1.4840	98.5	1.5	1.4090	87.5	12.5

The alcoholic solution, when moderately diluted with water, forms a sweetish, aromatic liquid of a very grateful taste. A strong alcoholic solution is decomposed by an abundance of water, the chloroform separating and subsiding, and the alcohol uniting with the water.

It is liable to decomposition by sunlight, or even diffused daylight; and hence the propriety of keeping it in bottles covered with dark paper, in a rather dark place. Chloroform has extensive solvent powers, being capable of dissolving camphor, caoutchouc, gutta-percha, mastic, elemi, tolu, benzoin, and copal. Amber, sandarac, lac, and wax are only partially soluble. It also dissolves iodine, bromine, many alkaloids, the fixed and volatile oils, most resins, and fats. It dissolves sulphur and phosphorus sparingly. As a general solvent, it has the advantage over ether of not being inflammable, the inflammability of the latter being the cause of frequent accidents.

When chloroform vapor, however, comes in contact with a naked flame the chloroform is dissociated with the liberation of irritating chlorine derivatives, hence the warning usually given against administering under such conditions.

Traces of hydrochloric acid in chloroform may be detected by adding a minute quantity of para-dimethylaminoazobenzene. A violet color is produced in the presence of free hydrochloric acid.

The addition of benzidine serves for the detection of phosgene which produces a turbidity or a precipitate, and of chlorine which first produces a red and finally a blue color. Fuming nitric acid, heated with chloroform to 100° C. in a closed tube for 120 hours, forms a new substance, *chloropicrine* (see *chlorpicrin,* Part II).

Uses.—Locally chloroform is actively irritant and somewhat anesthetic. When applied to the skin in ordinary manner it produces pain and redness and if evaporation be prevented will frequently blister. The pain is followed by a sensation of numbness.

Chloroform is actively antiseptic and even germicidal. A one per cent. solution is sufficient to kill most non-sporulating bacteria if the contact be sufficiently prolonged; but against spore-forming organisms it is of little avail. J. B. Barnes has found that in the proportions of 20 minims to the pint it prevents fermentation of such fluids as malt, milk or mucilage.

Taken into the stomach in doses of about five minims (0.3 cc.), it induces only gastric symptoms, chiefly due to its irritant properties; but when there is excessive flatulence, colic, or gastralgia, it not only causes an increased peristalsis and expulsion of any flatus present, but evinces a distinct local narcotic influence by quieting pain and spasm. Taken in doses of 1 to 2 fluidrachms (3.75–7.5 cc.), it produces a narcotism similar to that seen when it is administered in inhalation, the narcotism, however, developing and passing off much more slowly than in the latter case.

The action of chloroform upon the system like that of ether, is predominantly upon the central nervous system. The first portion to feel the effect of the drug is the higher cerebral centers. After larger quantities there is depression of the spinal cord, first of the sensory side and later of the motor tract, and finally paralysis of the medullary centres, especially the respiratory and vasomotor. It differs from ether not only in the power of its action but especially in the fact that it is directly depressant to the heart. A discussion of the relative advantages and disadvantages of these two great anesthetics would occupy too much space to be permissible here and the reader is referred for details to H. C. Wood, Jr.'s *Text-book of Pharmacology.* It may, however, be remarked that under ordinary circumstances chloroform, although more pleasant to take than ether, is much more dangerous.

Aside from its use in surgery chloroform is sometimes used to relieve severe *pain,* as in *neuralgia, gallstone colic,* and the like. It is also capable of relieving the asthmatic paroxysm. For these properties it is generally administered by inhalation but should only be employed with the greatest caution. Internally it is used as a carminative in *flatulent colic* and as a stimulant in combination with other drugs in the treatment of *serous diarrheas.* It has also been recommended as an anthelmintic, especially in the treatment of *hookworm,* but appears to be more dangerous than other equally efficient drugs. Externally it is very widely employed as a counter-irritant, especially in the form of the liniment. Langenbeck, of Berlin, prefers chloroform to tincture of iodine as an injection for the radical cure of *hydrocele.*

Chloroform ointment is made by adding twenty parts of chloroform to a mixture of ten parts of white wax and ninety parts of lard, previously melted together, and allowing the whole to cool. Chloroform may be gelatinized by agitating it with an equal weight of white of egg in the cold. In three hours it takes the gelatinous form. A stronger preparation may be made by shaking together, in a bottle, four parts of chloroform and one of white of egg, and placing the mixture in water at 60° C. In four minutes the gelatinization is completed. *Gelatinized chloroform* may be applied to the skin, spread on linen, or by friction. *Syrup of chloroform* may be made by adding one fluidounce of spirit of chloroform to fifteen fluidounces of syrup.

When an overdose of chloroform is taken by the mouth, it is essential to empty the stomach by the pump or siphon tube, and then treat the case much as in serious narcosis from inhalation. In a case of suicide by swallowing chloroform in which death took place in about thirty-four hours, the lining membrane of the larynx and trachea was found inflamed, the bronchi were loaded with a dirty-gray purulent fluid, the lungs were inflamed as in the first stage of pneumonia, and the brain and its membranes congested; but these morbid appearances are not constant.

Dose, of chloroform, five to fifteen minims (0.3–0.9 cc.).

Off. Prep.—Aqua Chloroformi, *U. S., Br.;* Linimentum Chloroformi, *U. S., Br.;* Spiritus Chloroformi, *U. S., Br.;* Tinctura Chloroformi et Morphinæ Composita, *Br.;* Linimentum Aconiti et Chloroformi, *N. F.;* Mistura Chloroformi et Morphinæ Composita, *N. F.;* Mistura Chloroformi et Morphinæ Composita, *N. F.;* Mistura Opii et Chloroformi Composita, *N. F.;* Petroxylinum Chloroformi Camphoratum, *N. F.;* Syrupus Pini Albæ Compositus, *N. F.;* Deutilinimentum Aconiti Compositum, *N. F.;* Deutilinimentum Aconiti et Iodi Compositum, *N. F.;* Solutio Mastiches Chloroformica Compositum, *N. F.;* Solutio Resinæ Chloroformica, *N. F.*

CHONDRUS. N. F.

CHONDRUS Chondr. [Irish Moss, Carrageen]

"Chondrus is the dried bleached plant of *Chondrus Crispus* (Linné) Stackhouse or of *Gigartina Maruillosa* (Goodenough et Woodard) J. Agardh (Fam. *Gigartinaceae*). Chondrus contains not more than 2 per cent of foreign organic matter." *N. F.*

Caragahen, Fucus Crispus, Pigwrack, Killeen, Pearl Moss; Hen's Dulse; Carragheen; Carragaheen; *Fr. Cod.;* Mousse Marine perlée, *Fr.;* Carrageen, *P. G.;* Irländisches Moos, Perlmoos, Knorpeltang, *G.;* Fuco carageo, Musco d'Irlanda, Fuco crispo, *It.;* Caragaen, Musgo marino perlado, *Sp.*

Chondrus crispus grows upon rocks and stones on the coast of Europe, and is especially abundant on the southern and western coasts of Ireland, where it is collected. It is also a native of the United States, and is gathered largely on the coast of Massachusetts, below Boston, where it is partly torn from the rocks and partly collected from the beach, on which it is thrown up during storms. It is prepared for market by spreading it out to dry and bleach in the sun. For elaborate accounts of the plant, of its distribution on the sea coast of Massachusetts, and of the mode of gathering and curing, see *A. J. P.,* 1895, 596; 1899, 483. Henry Kraemer witnessed the methods pursued on the Massachusetts coast in the collection of Irish moss at Scituate, which appears to be a particularly favorable situation. The season for collection begins late in May and continues to September, June and July being the best months. The moss at present is only found on rocks that are from 15 to 20 feet below the tide, hence women no longer engage in its collection. The men go out in their sail boats or dories at half tide, come in at half flood. With their long rakes they scrape the moss off the rocks, collecting thus about 50 pounds to the boat, the total for the season at Scituate being about 10,000 pounds. The moss is spread out on the high beach for a week or so, the action of the sun and dew bleaching it. It is then enclosed in hogsheads, in which it is again saturated with sea water by rolling them in the marshes; after which it is again spread out and subjected to the bleaching process, this alternate treatment being repeated four or five times, until the product is of a yellowish or white color. The final drying is done in barns, where the moss is stored until it is packed in 100 lb.

barrels at the end of the season. In the course of this journey he had opportunity to observe the *Chondrus* growing and gathered in different localities along the coast, and found it to consist chiefly, if not entirely, of *Chondrus crispus.* While it is stated in Dr. Farlow's "The Marine Algæ of New England" that the closely resembling *Gigartina mamillosa* is common from Boston northward, Kraemer is inclined to believe that *Chrondus crispus* (L.) Lyngbye, is practically the only source of the American drug. (See *Proc. Penn. Pharm. Assoc.*, 1899, 113–116.) Tunmann (*Apoth. Zeit.*, 1909, pp. 91 and 151) has given an elaborate account of the morphology and composition of *Chondrus.*

Girgartina mamillosa Ag. resembles the true Irish moss, and, growing with it upon the rocks, may be gathered with it. It can, however, be at once distinguished by the numerous papillæ which cover the surface and margins of the fronds and bear the fruit (cystocarps). In chemical and medicinal properties it is probably identical with *C. crispus.*

The commercial supplies of Chondrus are chiefly obtained from Boston (Massachusetts), Nimes (France) and Dublin (Ireland).

Irish moss when collected is washed and dried. It is probably sometimes bleached by the use of potassium permanganate and sodium thiosulphate by the same process as that used for bleaching sponge. Schack was led to suspect this through discovering the presence of sulphurous acid in a German specimen. (*Ph. Ztg.*, 1886, p. 87.) The presence of arsenic has been determined in some commercial lots, being caused, no doubt, by the impurities in the sulphur used for bleaching Chondrus. Some "faked" samples have yielded as much as 35 per cent. of ash which contained a large quantity of calcium sulphate. The gelatinizing value of specimens of this kind is about 60 per cent. below normal. In the fresh state it is of a purplish color, but as found in the shops, is yelowish or yellowish-white, with occasionally purplish portions.

Description and Physical Properties.—"*Whole Chondrus.*—Entire plants matted together, consisting of a slender stalk from which arises a series of dichotomously branching, more or less flattened segments, emarginate or deeply cleft at the tips; from 5 to 15 cm. in length, and 1 to 10 mm. in width; yellowish-white; translucent, frequently coated with a calcareous deposit which effervesces with hydrochloric acid; sometimes with fruit bodies or sporangia embedded near the apex of the segments (in *C. crispus*) or with sporangia borne on short tuberculated projections or stalks, more or less scattered over the upper portion of the segments (in *G. mamillosa*); somewhat cartilaginous. Odor slight, seaweed-like; taste mucilaginous, saline.

"Boil one part of Chondrus for about ten minutes with 30 parts of water, replacing the water lost by evaporation; the strained liquid forms a thick jelly upon cooling. When softened in cold water, Chondrus becomes gelatinous and transparent, the thallus remaining nearly smooth and uniform and not swollen except slightly at the tips; a solution made by boiling 0.3 Gm. of the drug in 100 cc. of water and filtering gives no precipitate on the addition of tannic acid T.S. (absence of *gelatin*), and when cold does not give a blue color on the addition of iodine T.S. (absence of *starch*)." *N. F.*

It swells in cold water, but does not dissolve. Boiling water dissolves a large proportion of it, and the solution, if sufficiently concentrated, gelatinizes on cooling. Herberger found 79 per cent. of a mucilaginous substance resembling pectin, and 9.5 of mucus, with fatty matter, free acids, chlorides, etc.

This gum-like substance, which is known as *carrageenin,* is distinguished from acacia by affording, when dissolved in water, no precipitate with alcohol; from starch, by not becoming blue with tincture of iodine; from pectin, by yielding no precipitate with lead acetate and from mucic acid by the action of nitric acid. It is probably not a pure principle but a mixture of carbohydrate derivatives. According to Sebor (1900) it yields, when hydrolized, galactose, dextrose, levulose and salts of sulphuric acid. Muther and Tollens (1904) found also hydroxy-methylfurfuraldehyde. Blondeau in 1865 prepared a substance which he called *goemine* by boiling chondrus for several hours and precipitating the resulting mucilage with alcohol. *Fucusol* is an oily liquid, isomeric with furfural, which is obtained by boiling the seaweed with dilute sulphuric acid. Carrageenin has been used as a substitute for acacia under the name of "imitation gum Arabic"; it occurs in three forms, white, pale yellow and yellow. These differ from the true acacia not only in chemical properties, but in being much less adhesive (Federer, *Ph. Era*, 1887).

The ash of chondrus amounts to from 8 to 15 per cent. and contains traces of iodine. On oxidation with nitric acid the dry moss yields from 21.6 to 22.2 per cent. of mucic acid. There is present also about 7 per cent. of protein material. The mucilage of Irish moss has come into considerable use as an emulsifying agent. (*Proc. A. Ph. A.*, 1887; *A. J. P.*, 1888, 170.)

Uses.—Chondrus is nutritive, and, being easy of digestion and not unpleasant to the taste, forms a useful article of diet in cases in which the farinaceous preparations, such as tapioca, sago, barley, etc., are usually employed. It was formerly employed as a demulcent in *chronic pectoral affections, diarrhea,* and *disorders of the kidneys and bladder,* but is rarely so employed to-day. It may be used in the form of decoction, made by boiling a pint and a half of water with half an ounce of the moss down to a pint. Sugar and lemon juice may usually be added to improve the flavor. It is recommended to macerate the moss for about ten minutes in cold water before submitting it to decoction;

any unpleasant flavor that it may have acquired from the contact with foreign substances is thus removed.

Dose, four drachms (15.5 Gm.).

Off. Prep.—Mucilago Chondri, *N. F.*

CHROMII TRIOXIDUM. U. S. (Br.)

CHROMIUM TRIOXIDE Chrom. Triox. [Chromic Anhydride]

"Chromium Trioxide contains not less than 95 per cent. of CrO_3. *Caution—Chromium Trioxide should not be brought into intimate contact with organic substances, as serious explosions are liable to result.*" *U. S.* "Chromic Anhydride, CrO_3, may be obtained by the interaction of sulphuric acid and potassium bichromate. It should be preserved in well-stoppered bottles." *Br.*

Acidum Chromicum, *Br.,* Chromic Acid; Anhydrum Chromicum, Anhydride Chromique, *Fr. Cod.;* Chromic Acid, Acide Chromique Cristallisé, *Fr.;* Acidum Chromicum; *P. G.;* Chromsäure, *G.;* Anidride cromica, Acido cromico, *It.;* Acido cromico, *Sp.*

No method for this anhydride is official; it is usually prepared by decomposing potassium dichromate with sulphuric acid and crystallizing out the resultant chromic oxide. For details see *U. S. D.,* 20th ed., p. 329. According to Kebler there may also be found in commerce an impure "chromic acid" made by mixing a solution of sodium dichromate with sulphuric acid and drying the product; it sometimes contains 60 per cent. of acid sodium sulphate (*Am. Drug.,* 1901, 344). The requirements of the U. S. Pharmacopœia are that even traces of sulphuric acid shall be absent, and that the color of the crystals be not scarlet.

Description and Physical Properties.—"Small, needle-shaped crystals or rhombic prisms, of a dark purplish-red color and metallic luster. It is odorless, and is deliquescent in moist air. Chromium Trioxide is destructive to animal and vegetable tissues. One Gm. of Chromium Trioxide is soluble in 0.6 cc. of water at 25° C. One Gm. is soluble in 0.5 cc. of boiling water. When Chromium Trioxide is brought into contact with organic solvents (*e.g.,* alcohol), decomposition takes place, sometimes with dangerous violence. When Chromium Trioxide is heated, it darkens and finally becomes black, but the color is restored on cooling. At about 190° C. it fuses to a reddish-brown liquid, which on cooling forms a dark red, brittle mass (often enclosing cavities filled with crystals), yielding a scarlet powder. Above 250° C. it begins to decompose into green chromic oxide and free oxygen, and after protracted heating leaves a residue of green chromic oxide.

"When Chromium Trioxide is warmed with hydrochloric acid, chlorine is evolved. Chromium Trioxide responds to the reaction's for chromates, page 441. A solution of 1 Gm. of Chromium Trioxide in 100 cc. of distilled water, previously acidulated with 3 cc. of hydrochloric acid, is not rendered turbid within one mnute on the addition of 1 cc. of barium chloride T.S. (*sulphuric acid*).

"Preserve in glass-stoppered bottles." *U. S.*

"Crimson acicular crystals, very deliquescent, inodorous, acting corrosively on the skin. Very soluble in *water* and in *ether.* Strongly heated it first melts and then evolves oxygen, leaving, after heating to redness, a green residue, which yields little or nothing to *water.* Warmed with *hydrochloric acid,* chlorine is evolved. In contact with relatively small proportions of *alcohol* (90 per cent.), *ether, glycerin,* or certain other organic substances, sudden combustion or explosion may ensue. When 4 grammes are dissolved in a mixture of 20 millilitres of *water* with 10 millilitres of *hydrochloric acid,* 5 millilitres of *solution of barium chloride* added and the mixture filtered, the filtrate yields no further precipitate on the addition of more of the reagent (limit of sulphates)." *Br.*

Chromium trioxide, at a heat above the melting point, gives off half its oxygen, and is converted into the green sesquioxide, Cr_2O_3. It is a powerful oxidizing and bleaching agent, and gives up its oxygen with great facility to organic matter. The oxidation of weaker alcohol is attended with the production of aldehyde, recognized by the odor, that of stronger alcohol, by inflaming.

"**Assay.**—Dissolve about 1 Gm. of Chromium Trioxide, accurately weighed in a stoppered weighing bottle, in sufficient distilled water to make 100 cc. Mix 15 cc. of this solution with 3 cc. of hydrochloric acid and 2 Gm. of potassium iodide in a glass-stoppered container, agitate the mixture, allow it to stand for five minutes, then dilute it with 100 cc. of distilled water, and titrate the liberated iodine with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.003333 Gm. of CrO_3." *U. S.*

Uses.—In dilute solution chromium trioxide is a powerful coagulant of albumin and is therefore astringent. In more concentrated solution because of its oxidizing power it destroys all forms of tissue and is a rapid and powerful caustic. It is also an active germicide; according to Koch a 1 per cent. solution is sufficient to destroy anthrax spores after two days' exposure. By virtue of its oxidizing effect it destroys decaying organic matter, combining with and neutralizing the ammonia and decomposing hydrogen sulphide, thereby acting as a deodorizant.

As a caustic the liquid formed by the spontaneous deliquescence of the crystals may be used; it is most frequently applied by means of a glass rod.

Much care should be exercised in the use of this agent as it is a powerful poison both because of its local irritant effect and its systemic action. A single drop of the saturated solution taken internally has caused violent symptoms and fatal results have followed the too free external use of the drug. (See Shaw, *Virginia Med. Semi-monthly,* 1901, v.)

In dilute solution (5 per cent.) it is used as an antiseptic and astringent wash in *leucorrhea, ozena,* and *hyperidrosis.* In the Prussian army it has been found useful as a foot wash for preventing *sweating of the feet* and to harden the skin. In more concentrated solution it is used as a caustic for the removal of *warts, syphilitic condylomata, nasal polypi,* and other foreign growths. It has been highly lauded by Ganley (*B. M. and S. J.,* Oct. 14, 1920) in the treatment of *Vincent's angina.*

Although chromium oxide has not been used internally in medicine Kolipinski (*Monthly Cyclopedia of Pract. Med.,* Sept., 1908) asserts that *chromium sulphate* is a valuable remedy in the treatment of various chronic nervous diseases as *alcoholism, neurasthenia, locomotor ataxia, exophthalmic goiter,* etc. He administers it in doses of from one to eight grains (0.065–0.5 Gm.).

Those whose work brings them in contact with chromic acid or its salts, according to Hermann (*M. M. W.,* April 2, 1901), often suffer with lesions, the result of the local irritant action of these compounds either upon the mucous membrane of the respiratory tract or upon the skin. In a large number of cases there was ulceration of the nasal mucosa eventually with perforation of the septum while other patients developed *bronchitis, eczema, gastritis,* or other inflammatory disorders.

Dose, of chromium trioxide, should not exceed one-fourth of a grain (0.016 Gm.). It is very rarely, if ever, used internally.

Off. Prep.—Liquor Acidi Chromici, *Br.*

CHRYSAROBINUM. U. S., Br.

CHRYSAROBIN Chrysarob.

"A mixture of neutral principles obtained from Goa powder, a substance deposited in the wood of *Vouacapoua Araroba* (Aguiar) Druce (Fam. *Leguminosæ*)." *U. S.* "Chrysarobin is a mixture of substances extracted from Araroba by hot benzene. It consists of a definite chemical compound, $C_{15}H_{12}O_3$, also known as pure chrysarobin, or chrysophanolanthranol, associated with certain other substances of similar composition." *Br.*

Acidum Chrysophanicum Crudum; Araroba Purifié, *Fr. Cod.;* Chrysarobinum, *P. G.;* Crisarobina, *It.*

The British Pharmacopœia recognizes under distinct headings Crude Chrysarobin (Goa Powder or Araroba) and the Purified Chrysarobin. (See *Araroba.*)

The question of the chemical composition of chrysarobin is not yet completely solved.

Hesse (*Ann. Ch. Ph.,* 1912, p. 388) found that chrysarobin is a complex body containing at least five different substances, namely: *chrysophanol-anthranol,* its methyl-ether *emodinol* and its methyl ether, and *chrysarobol.* Of these chrysophanol-anthranol is the one to which the drug owes its characteristic properties. (See also Tutin and Clewer, *Tr. Chem. Soc.,* 1912.)

According to Eder (*A. Pharm.,* 1915, 1) chrysarobin yields on oxidation 0.2 per cent. of emodin, 32 per cent. of a methoxyl containing chrysophanic acid, 18 per cent. dihydro-emodin-anthranol-monomethyl ether and about 26 per cent. unidentified colored decomposition produtcs. Eder also found in chrysarobin free chrysophanic acid, emodin and methyl ethers of the latter; all partly in reduced form and partly as easily oxidizable *anthranols.*

Description and Physical Properties.—"A brownish to orange-yellow, microcrystalline powder. It is tasteless, odorless, and irritating to the mucous membrane. Chrysarobin is very slightly soluble in water. One Gm. dissolves in 385 cc. of alcohol, 30 cc. of benzene, 180 cc. of carbon disulphide, 13 cc. of chloroform, and in 160 cc. of ether, at 25° C.

"Chrysarobin dissolves in solutions of alkali hydroxides and in sulphuric acid, producing deep red solutions. On pouring the sulphuric acid solution into water, Chrysarobin is deposited unchanged. Mix about 0.002 Gm. of Chrysarobin with 2 drops of fuming nitric acid: a red-brown mixture is produced which becomes violet-red on the addition of a few drops of ammonia T.S. (*difference from chrysophanic acid,* which produces a yellow liquid). Boil 0.1 Gm. of Chrysarobin with 20 cc. of distilled water, and filter: the filtrate is neutral to litmus paper. Ash: not more than 0.25 per cent.

"Preserve in well-closed containers, protected from light." *U. S.*

"A light, microcrystalline, yellowish powder; inodorous; tasteless. Entirely soluble in hot *chloroform* and in hot *benzene,* almost entirely soluble in hot *alcohol* (90 per cent.), partially and sparingly soluble in *petroleum spirit,* almost insoluble in *water.* Almost entirely soluble in hot *solution of sodium hydroxide,* with production of a deep brownish-red color. Shaken with *solution of ammonia* the liquid slowly becomes violet. About 1 milligram mixed on a white tile with a drop of *fuming nitric acid* produces a brownish-red liquid, becoming violet on the addition of excess of *solution of ammonia.* Melts when heated, giving off yellow fumes. Ash not more than 1 per cent." *Br.*

Chrysarobin in alkaline solution takes up oxygen readily, even from the air, and changes into chrysophanic acid according to the reaction:

$$C_{30}H_{26}O_7 + 4O = 3H_2O + 2C_{15}H_{10}O_4$$

The difference in physical properties between chrysarobin and chrysophanic acid is well described by Andouard. (See *Proc. A. Ph. A.,* 1895, 864.)

Uses.—When taken internally in sufficient amount, chrysarobin acts as a decided gastro-intestinal irritant, producing large, very watery, brownish stools, and repeated vomiting without much nausea; it has, however, failed to secure a place as an internal remedy. Chrysarobin has long been used in South America and India as a remedy in skin diseases, but the attention of the general profession was first called to it in 1874 by Sir Joseph Fayrer. It is a remedy of the greatest value in the treatment of *psoriasis* and is also of service in chronic *eczema.* Schamberg, Kolmer and Raiziss (*Jour. of Cutaneous Dis.,* 1915, xxxiii) in an elaborate research on its mode of action reach the conclusions that chrysarobin is without germicidal properties and that its beneficent effects are probably due to its chemical affinity for the keratin elements of the skin, the drug abstracting the oxygen for its oxidation, which takes place simultaneously with this union, from the epithelium.

It may be applied in the form of an ointment with good success, although this method of application has the objection of staining the clothing. For this reason a number of dermatologists prefer the solution in collodion, which may be prepared by dissolving a drachm of chrysarobin in a fluidounce of the official flexible collodion. This is painted over the lesions with a camel's hair brush and after it is thoroughly dried the film may be coated with plain collodium as a further protection against staining the clothing. Another method of applying the drug is to dissolve it in chloroform in the proportion of one to two drachms to the ounce. This solution is painted on the skin, the chloroform evaporating and leaving a thin film of chrysarobin behind. Kossobudskji highly recommends in the treatment of *hemorrhoids* an ointment containing twenty-five grains of chrysarobin, nine grains of iodoform, and eighteen grains of extract of belladonna to the ounce of petrolatum. Benzin is said to be useful for removing the stains caused by chrysarobin.

Off. Prep.—Unguentum Chrysarobini, *U. S., Br.*

CIMICIFUGA. U. S.

CIMICIFUGA Cimicif. [Black Cohosh, Black Snakeroot, Macrotys]

"Cimicifuga is the dried rhizome and roots of *Cimicifuga racemosa* (Linné) Nuttall (Fam. *Ranunculaceæ*). Cimicifuga contains not more than 2 per cent. of its stems or other foreign organic matter, and yields not more than 4 per cent. of acid-insoluble ash." *U. S.*

Cimicifugæ Rhizoma, *Br.*, 1898, Actææ Racemosæ Radix; Cohosh; Macrotys; Rattleroot; Squaw Root; Rattle Snake Root; Bugbane; Rattle Weed; Richweed; Bugwort, Rattletop; Racine d'Actée à Grappes, *Fr.;* Schwarze Schlangenwurzel, *G.*

Cimicifuga was dismissed from the Br. Pharm., 1914.

Cimicifuga racemosa is a tall, stately plant, having a subterranean knotty rhizome, and a simple herbaceous stem, which rises from below to eight feet in height. The leaves are large, and ternately decompound, having oblong-ovate leaflets, incised and toothed at their edges. The flowers are small, white, and disposed in a long, terminal, ward-like raceme, with occasionally one or two shorter racemes near its base. The calyx is white, four-leaved, and deciduous; the petals are minute, and shorter than the stamens; the pistil consists of an oval ovary and sessile stigma. The fruit is an ovoid capsule containing numerous flat seeds. The plant grows in shady or rocky woods from southern New England to Wisconsin and southward, flowering in June and July. The drug is gathered for the market in Michigan, Indiana, Illinois, and the southern Applachians.

Description and Physical Properties.—"*Unground Cimicifuga.*—Rhizome more or less branching, from 2 to 15 cm. in length and from 1 to 2.5 cm. in thickness; externally dark brown, slightly annulate, the upper surface with numerous hard, erect, somewhat curved branches having deep, cup-shaped, radiating scars; lower and lateral surfaces marked by numerous root scars and occasional short roots; fracture horny; internally dark brown and waxy or whitish and mealy; bark thin, wood distinctly radiate and about the same thickness as the pith; odor slight; taste bitter and acrid. Roots nearly cylindrical or obtusely quadrangular from 3 to 12 cm. in length and from 1 to 3 mm. in thickness, externally dark brown and longitudinally wrinkled; fracture short; internally, cortex thin and dark brown, wood yellowish or light-brown, 4- to 6-rayed.

"*Structure.*—Rhizome with a yellowish-brown epidermal layer; cortex of starch-bearing parenchyma cells; tracheæ with bordered pores; wood-fibers numerous, thin-walled and strongly lignified; the vascular bundles separated by starch-bearing parenchyma; pith cells resembling those of the cortex. Roots with thin epidermis; endodermis distinct; fibro-vascular bundles 4 to 6, developed in older roots as separate collateral bundles.

"*Powdered Cimicifuga.*—Light to dark brown; starch grains numerous, single or compound, the individual grains spherical or more or less polygonal, each with a somewhat central cleft, from 0.003 to 0.015 mm. in diameter; fragments of tracheæ and of wood-fibers; irregular, yellowish-brown fragments of suberized epidermis made up of more or less tabular cells, which are sometimes elongated and considerably thickened." *U. S.*

For a detailed description of the microscopic character of the root, see *A. J. P.,* 1884, 460; also 1895, 121; Holm, *M. R.,* 1911, p. 6.

The roots "exhibit in transverse section from three to five wedge-shaped wood-bundles, separated by as many broad medullary rays. Both rhizome and roots are blackened by *test-solution of ferric chloride* (presence of tannic acid)." *Br.,* 1898.

The odor, though not strong, is peculiar and rather disagreeable, and is gradually lost with age. The drug of commerce is likely to be unintentionally admixed with other species of *Cimicifuga* and *Actæa.*

Cimicifuga yields some 15 to 20 per cent. of resin. The substance known as *cimicifugin,* or *macrotin,* is made by pouring a concentrated tincture of the drug into a large volume of water whereby a mixture of resinous and other bodies is precipitated. Finnemore has made a systematic examination (*P. J.,* 1910, lxxxv, p. 142, 178) of this rhizome. He found besides palmitic, oleic, also isoferulic acid, 3 crystalline bodies apparently alcohols, phytosterol, and indications of alkaloid. There appears to be present also a crystallizable bitter principle to which the name *racemosin* has been applied. There is no evidence that any of these substances are physiologically important. The principle reported many years ago by Conarb (*A. J. P.,* 1871) was probably an artefact as subsequent investigators have been unable to confirm his results.

Uses.—In 1831 cimicifuga was introduced to the notice of the profession by Young. In overdoses it is said to cause general relaxation, vertigo, tremors, decided reduction of the pulse; occasionally it causes vomiting, but its emetic action is never violent, and is probably simply the result of a mild gastric irritation. In large doses it produces giddiness, with intense headache and prostration. It has been found by R. Hutchinson to cause in frogs complete anesthesia by a direct action upon the sensory side of the spinal cord. The same observer noted that toxic doses produce in mammals slowing of the pulse and fall of the arterial pressure, results which appear to be due in part to a direct depressant action upon the heart muscle or its ganglia, in part to a paralysis of the vasomotor center. Clinical experience has shown this drug to be a useful remedy in the treatment of *chorea.* It has also been employed, though with less certainty of benefit, in *chronic rheumatism, urticaria, neuralgia,* and *dysmenorrhea.* It is also asserted to act as a specific in *tinnitus aurium.*

In *chorea* it is necessary to give large doses. The proper method of administration is to start with about fifteen minims of the fluidextract three times a day, increasing one minim daily until the occurrence of frontal headache or improvement in the condition. The practitioners calling themselves eclectics use, under the name of *cimicifugin,* or *macrotin,* an impure resin obtained by precipitating a saturated tincture of the root with water; dose, a grain or two (0.065–0.13 Gm.). (See *N. J. Med Rep.,* viii, 247.)

Dose, of powdered cimicifuga, five to thirty grains (0.3–2.0 Gm.).

Off. Prep.—Fluidextractum Cimicifugæ, *U. S.;* Elixir Tongæ et Salicylatis Compositum (from Fluidextract), *N. F.;* Syrupus Cimicifugæ Compositus (from Fluidextract), *N. F.;* Tinctura Cimicifugæ, *N. F.*

CINCHONA. U. S. (Br.)

CINCHONA Cinch. [Peruvian Bark]

"Cinchona is the dried bark of *Cinchona succirubra* Pavon or of its hybrids, known in commerce as Red Cinchona or of *Cinchona Ledgeriana* Moens, *Cinchona Calisaya* Weddell and of hybrids of these with other species of *Cinchona,* known in commerce as Calisaya Bark or Yellow Cinchona (Fam. *Rubiaceæ*). Cinchona yields not less than 5 per cent. of the alkaloids of Cinchona." *U. S.*

"Red Cinchona Bark is the dried bark of the Cinchona succirubra, *Pav.*" *Br.*

Cinchonæ Rubræ Cortex, *Br.;* Red Cinchona Bark; Cortex Chinæ Ruber, Quinquina, *Fr.;* Cortex Chinæ, *P. G.;* Chinarinde, Rothe Chinarinde, *G.;* China, *It.;* Quina, *Sp.*

The U. S. recognizes under the name of cinchona any one of three species of bark, but the Br. recognizes only the *C. succiruba.* Formerly the U. S. recognized this under a distinct title of *Cinchona rubra.*

History.

There is no certain evidence that the medicinal properties of cinchona bark were known to the natives. The first authentic record of its use was in 1630 when Francisco Lopez de Canizares, Corregidor of the province of Loxa in southern Peru, was cured of a malarial fever. One tradition ascribes his treatment to an old Indian medicine-man, while according to others the original prescriber of the bark was a Jesuit priest. A few years later the wife of the Viceroy of Peru—Ana de Osorio, Countess of Chinchon—being seized with the same malady, Canizares sent to her physician, Dr. Juan del Vega, a package of the bark which was used upon her with the same gratifying results. In 1639 the Countess of Chinchon returning to Spain carried some of this wonderful remedy to Europe, where she distributed it among the afflicted in her extensive domain. Dr. del Vega also took some of the bark back to Europe with him, but the first general introduction of the drug into Europe was by the Order of Jesuits who for many years had a monopoly of the distribution, hence the popular mediæval name of *Pulvis Jesuiticus.* The remedy rapidly attracted tremendous attention and was sold in the 17th century at fabulous prices. In 1679 the English physician Sir Robert Talbot (or Talbor) cured the Dauphin of France of a malarial fever and sold his secret to Louis XIV for 2000 Louis d'or and a title of nobility.

For nearly a hundred years the source of the bark was entirely unknown to Europeans, but in 1735 Charles Marie de la Condamine, the commander of a scientific expedition sent out by the French government, collected a number of young plants which he transported down the Amazon River for 2000 miles, but all of them were lost in a storm which overtook his fleet in the mouth of the river. He, however, succeeded in bringing back specimens of the tree, the description of which he published in 1738.

Linné, from La Condamine's specimens, established a new genus which he named, in honor of the Countess of Chinchon, cinchona. The botanist of this expedition, Joseph de Jussieu, remained for 15 years in South America studying the sources of the drug, but on the eve of sailing for France, was robbed of his fine collection of young cinchona plants. The loss of the rewards of his long labor drove him insane. In 1846 Dr. Weddell succeeded in bringing back to Paris some seeds from which a few cinchona trees were grown in the Jardin des Plantes in Paris. The first considerable exportation of cinchona trees were brought back by the Dutch botanist Hasskarl in 1854 and afforded the beginning of the cinchona plantation in the Island of Java. This plantation, however, did not flourish at first. In 1859 the English government sent out an expedition under Clements R. Markham who succeeded in establishing a plantation in the Neilgherry hills of India. Among other botanists who contributed to the early knowledge of this species may be mentioned especially Ruiz and Pavon, Ledger, Karsten, etc. At the present time there are recognized more than 30 species of the genus, many of which, however, are medicinally unimportant.

The word quinine is derived from the Indian word "quina" or "kina," which means a bark.

Geographical Distribution.

The Cinchona trees are natives exclusively of South America. In that continent, however, they are widely diffused, extending from the 19th degree of south latitude, to about the 10th degree of north latitude. They follow, in this distance, the circuitous course of the great mountain ranges, and for the most part occupy the eastern slope of the second range of the Cordilleras. They require a moderate and equable temperature and an abundant and fairly constant supply of water. Irrigation cannot supply the place of a humid climate, for the atmosphere as well as the soil must be well charged with moisture. A certain amount of dry weather is, however, required for the ripening of the capsules. Free drainage is an important condition. In their natural habitat the temperature rarely goes below 2° C. or above 21° C.

The limits of altitude and climatic conditions are closely drawn. In the most southern districts, the trees descend to about 2500 feet, while in the warmest regions they scarcely ascend to the 10,000-foot level. The individual species are for the most part rigidly restricted as to altitude and latitude, and, indeed, it has not always been found easy to detect the climatic conditions which would cause one species or variety to thrive while another very near it would languish. This is especially true of the more valuable forms.

The ever increasing demand for cinchona and the wanton carelessness in methods of collecting the bark, made such terrible inroads on the natural supplies that as early as the beginning of the 19th century the necessity of cinchona culture was universally recognized. It was this solicitude for a future source of a substance that had become almost essential for human civilization, that led to the repeated efforts of various governments to establish plantations in other parts of the tropics.

The earliest cinchona plantation was in Java, there being in that island in the year 1860, 947,000 young cinchona plants, most of them, however, being of species worthless as medicine. The second plantation was that started in India by Markham in 1861. In 1865 Chas. Ledger obtained some seeds of the superior species of cinchona known today by his name, which he sold to the Dutch government from which they grow what is generally regarded as the finest variety of bark. There are at present large plantations in Java, Southern India, in Sikkim, Darjeeling, Bengal, Lingmulla, in Bombay, in the Valley of Kangra and in the Punjab. The plantations which were established in Ceylon have been in recent years largely abandoned in favor of tea culture. The Portuguese have established plantations on the West Coast of Africa which are now yielding commercial quantities. A small amount of wild cinchona still appears in the market and the tree is being cultivated artificially in South America. The most important plantations are in the head-water districts of the Beni affluents of the Amazon in Bolivia; a large plantation in the United States of Colombia is also commercially productive and a smaller one in Ecuador. In 1918 the Igorot Exchange, a missionary institution at Sagada on the Island of Luzon, obtained seeds of the *C. Ledgeriana* from the plantation at Ootacamund, Madras, and this species is now growing in the mountains around Sagada in the Philippines. Successful plantings have also been made in East Africa of *C. ledgeriana, C. succiruba, C. robusta* and hybrids. In 1918, an examination of these barks indicated as high as 8.41 per cent. of quinine.

The history of cinchona cultivation affords a striking illustration of the importance of government aid in the establishment of a new industry of this kind. The early and repeated disappointments and failures, owing to the natural obstacles in the way of securing stocks, and to an almost total ignorance of the conditions determining the successful propagation and growth of the plant, and the composition of its bark, were such as to have discouraged the most hopeful of private enterprises. Repeated and expensive expeditions were necessary before the first transplantings were accomplished, and these stocks were preserved and propagated only through the instrumentality of well appointed public gardens and plantations. In Java, after these early difficulties had been surmounted and success apparently attained, it was found that owing to cross fertilization much of the progeny was entirely worthless, and the work of propagation had to be begun anew. The same difficulty was encountered elsewhere, and the slow and expensive method of propagation by cuttings was largely resorted to. In Ceylon the public was slow to become interested, and the officials were obliged not only to give away the young plants, but to solicit experiments with them as a personal favor. In Jamaica a hurricane visited the young and flourishing plantations and almost completely destroyed them. But at length, in spite of all, not only were thriving and permanent government plantations established, but private capital and enterprise upon a vast scale were enlisted. The question of commercial success is dominated not simply by climatological surroundings, but also by the price of labor.

The total world production of cinchona bark is today probably over 25 million pounds of which nearly 90 per cent. is produced in the Island of Java.

For detailed accounts of the Javanese cinchona industry see Howard (*J. Soc. Chem. Ind.*, 1906, p. 97) and Blokzeyl (*Ph. Era*, 1920, p. 69).

Description of Plants.

As the result of much experimentation, practical growers of cinchona have limited their efforts to the cultivation of the four species described below.

C. Calisaya Weddell yields the *Calisaya bark* or *Yellow Cinchona.* It is a tall tree, usually surpassing those about it, the trunk often more than two feet in diameter. Leaves petiolate, the blade ovate-oblong to slightly obovate, 7 to 17.5 cm. long by 2.5 to 7 cm. broad, obtuse, the base acute or slightly attenuated, very thin, smooth, and, especially below, with a satiny luster, above dark green, below emerald-green or deep purple-green, scrobiculate, the glands scarcely visible above. Stipules oblong, about equalling the petioles, very smooth, very obtuse. Panicles ovate to subcorymbose. Calyx pubescent, with a cup-shaped limb and short triangular teeth. Corolla rose-colored (in cultivation often white or nearly so), the tube cylindrical and about 8 mm. long, the laciniæ more deeply colored, the edges white-hairy. Stamens included. Capsule ovate, scarcely as long as the flowers. Seeds elliptical lanceolate, the margin irregularly fimbriate-toothed. The species presents many forms, and two varieties are recognized.

C. Ledgeriana Moens., formerly recognized as a variety of *C. Calisaya,* differs from the type chiefly in its thicker, narrower, oblong leaves, with attenuate base, often bluish-green below. It yields a thick and remarkably rich bark, and is probably the most valued of all the cinchonas. This species was named in honor of Ledger, who first brought seed of this species from Bolivia.

C. succirubra Pavon, from which comes the *Red cinchona,* has an extreme size even greater than that of the last. Branches silvery. Petiole pubescent, leaf ovate to oval, acute with a very short point, the base more or less narrowing, often 6 to 9 inches, dark green and smooth above, below paler and pubescent to a variable degree, especially on the veins, not scrobiculate, the margin slightly revolute. Stipules entire, oblong, obtuse subamplexicaul. Flowers much as in the last, but rather smaller. Fruit lanceolate.

C. officinalis Hooker fil.—Petioles smooth, cylindrical, and, like the veins, reddish; blade 10 to 12.5 cm. long, varying from broadly oval to lanceolate, acute at both ends, the margins usually recurved, smooth and deep green above, paler, but bright green below, scrobiculate, the principal veins pubescent. Stipules equalling the petioles, ovate, acute, entire, pubescent. Flowers and fruit much as in *C. Calisaya.* Widely distributed in the equatorial Andes, at an elevation of from 5000 to 7500 feet. The source of the barks known as Pale, Crown, Loxa, Cuenca, and Huanuco. This is the original species, upon which the genus *Cinchona* was founded.

The specific variations produced by hybridization in the above characters may not be here considered, though it may be stated that they are entirely characteristic. The parentage of a hybrid is ordinarily fully and strongly indicated in its appearance. As a rule, also, the alkaloidal yield takes a mean between that of the parents, but sometimes this is conspicuously not the case. Goris and Reimers (*Trav. Lab. Nat. méd. Ecol. supe. Pharm.*, in *Bot. Centralbl.*, 1906, p. 462) pointed out the use of *Cinchona robusta* Trimen as a collective name for all hybrids of *C. succirubra* and *C. officinalis.* Rosenthaler gives an account of the structural characteristics and alkaloidal content of *C. robusta* and other cinchona hybrids produced by grafting. (*B. P. G.*, 1908, p. 126.)

Methods of Cultivation and Collection of Bark.

The history of Cinchona cultivation teems with evidence as to the difficulty of obtaining pure seeds, owing to the tendency of the plants towards cross-pollination. In every locality where the industry has been established has the disgust of the gardener been excited by the discovery that the plants which he had reared with great care, and upon which he had based great expectations, were contaminated by the admixture of foreign pollen. This was especially true in case of the earlier attempts, before this tendency had become known. Experience at length established the fact that absolute isolation of the seed-trees was essential. One of the curious developments of these experiments was the fact, already referred to, that the value of the progeny was not always assured by the value of its parentage. Some of the hybrids, even when least expected, would develop a surprisingly rich yield; and this tendency has been utilized to develop the most valuable stocks in existence. Propagation by cuttings, extensively practised in some localities, has been found too slow and expensive to become general. A thorough preparation of the soil is as beneficial in the case of cinchona as in that of other crops. Thorough tillage after transplantation is also essential, a free growth of weeds meaning destruction to a large number of the young trees. The cultivation of a secondary crop between the rows of trees is, however, practicable. A large percentage of profit depends upon the selection of a suitable age for collecting the bark. There comes a time when the use of the ground for starting a new crop is more valuable than the gain by permitting the present crop to remain, and after some years an actual deterioration of the bark sets in. This age is not the same for all the trees in the plantation. Several years' difference may occur in the maturing of trees germinated at the same time. In the case of calisaya it occurs at from six to nine years from seed, and its indication is the "chicken-leg" scaliness of the bark. The "officinalis" matures somewhat less early.

Four methods of collecting the bark are in vogue, these being variously modified in different sections. The first is *uprooting,* the most primitive, by which the trees are simply uprooted at the proper age, and the ground replanted. The barks of root, stem, and branches are preserved and marketed separately. The second method is *coppicing,* by which, after peeling a quill from the lower portion of the trunk, the latter is cut a few inches from the ground and the remainder of the stem bark and the branch bark is removed. The "coppice" is formed by a second growth of two shoots from each of the stumps. A second coppice is commonly grown, and this is harvested by uprooting. By the third method, *scraping,* the outer bark is scraped off, leaving the liber untouched. This has been found especially applicable to young trees, in which the second growth of bark is rapidly formed and contains 20 to 30 per cent. more alkaloid than that which has been taken off. It seems to be a general opinion among the planters that scraping checks the growth of the tree after it is five years old, so that from three to five years is the age at which it is best practised. The fourth method is known as *mossing.* It having been noticed that the cinchona alkaloids, especially in any other form than that of sulphate, were apt, on exposure to the direct light of the sun, to become reddened by the generation of coloring matter, at the expense of the alkaloid, it was a very natural inference that a similar change might take place in the living plant, as a consequence of which the proportion of alkaloids they were capable of producing might be greatly diminished. It was also observed that the bark upon that side of the tree where the sun struck it was less rich than that upon the shady side. To obviate this presumed effect, MacIvor was induced to make the experiment of covering the stems of the growing trees with a layer of moss, so as to completely protect the bark against the influence of sunlight. The result was favorable beyond all expectation, and the yield of alkaloids in the bark thus protected is said to be doubled, tripled, or increased even in larger proportion. A tree can thus be made continuously productive; for if a slip is removed longitudinally from the trunk, from top to bottom, by covering the decorticated portion with moss, the bark is renewed at least as rich as previously in the alkaloids, while from time to time other strips may be taken, until the whole of the old bark is removed, and the new ready for removal by a repetition of the same process; and the tree is thus preserved indefinitely, probably for the whole normal length of its life. Hooper says that renewed bark is always of greater value than the mossed, and mossed than the natural, so long as the trees are under twenty years old, for it has been found that after that time the bark ceases to thicken, and the alkaloids remain stationary or even decrease. Perhaps twenty years is even too old. The practical difficulty with the process is that it requires skilled workmen, not always attainable, and hence the "coppicing system" still largely prevails in India.

The bark which is stripped from the trunk of the tree is known as "quina tabla" and that which is stripped from the branches is called "quina canuto" or "quill." The quills, after thoroughly drying, are carefuly packed in bales, or preferably in boxes, to avoid breakage, and are marketed in packages of from 100 to 250 pounds. Large quantities of cultivated bark are still marketed in this way, but, increasing competition having lowered prices so that the economy in freight has become a very important item, most of the bark is now broken up, and its bulk even reduced by high pressure.

By scientific methods of arboriculture the quality of bark produced has been greatly improved. This is well shown by the facts that in 1889 the average percentage of quinine (calculated as sulphate) in Java bark was 4; in 1893 it has risin to 4.6; while in the five years, from 1900 to 1904 inclusive, the average quinine percentage of all the Java barks sold in the Amsterdam market was 5.37; in 1924 it was 6 per cent.

For some years, in India, the attempt was made largely to increase the general average in total alkaloids rather than in quinine, so as to increase the production of the impure alkaloids which are so largely used as febrifuges in the British East Indies. Of recent years, however, even in India, efforts have been directed to the obtaining of quinine rather than of inferior alkaloids.

One of the most important developments of the modern bark trade is the fixing of the price in accordance with the quality as determined by assay. The most accurate method of selecting a characteristic sample for assay is a subject which has received much study, without the discovery of any method which does not depend for its value upon the discrimination and care exercised in its employment. The plan which is regarded as the safest, is to take a given weight, say eight ounces, from the inner portion of each package constituting the lot, mix and powder the whole of it, and furnish to applicants the required amount of the resulting powder. If any portion of any bale or bales is damaged, care is taken to add a proportionately large fragment of such portion. The bark is then recorded as containing so many units, a "unit" being each per cent. of quinine contained in a pound of bark. In rich bark the units are of course worth more than in poor, owing to the increased yield of alkaloid for the same cost of manufacture.

The finer appearing packages of unbroken bark, having been marketed at greater cost, are necessarily held at higher prices. Possessing no special value for manufacturing purposes, these fall to the share of the druggist, but at higher prices than broken bark of the same richness. This fact has led to the recognition of two distinct classes, known as *manufacturers' bark* and *druggists' bark*. Druggists' bark, though in quills or unbroken pieces, and of a much finer appearance than manufacturers' bark, is, on the average, inferior in quinine percentage. The druggists' bark finds its entrance into commerce through various channels but the bulk of the cinchona trade, including practically all that is known as manufacturers' bark, centers in Amsterdam and London; of these marts that at Amsterdam is much the more important. The bark which is sold in Amsterdam comes almost exclusively from Java; that in London from India and South America. Manufacturers' bark is sold, without respect to its physical characters or place of origin, entirely by its chemical analysis, the buyer in London being furnished with samples of the different lots of the bark sufficient time before the sale to enable him to make his own analysis, while in Amsterdam the percentage of quinine sulphate in any lot is given in the catalogue and often tagged upon the bale.

At present the commercial cinchona barks entering the United States come from plants cultivated in Java and India and from trees growing wild in South America. Java cinchona either comes direct or through London or Amsterdam. Indian cinchona comes through London or direct from India. South American cinchona comes direct from Cartagena, Colombia, from La Paz, Bolivia and from Guayaquil, Ecuador.

Cinchona barks have been divided according to their external form as follows: (1) the small chips or broken bark, referring in large part to the root bark, and to other bark broken for close packing; (2) the shaved bark, referring to some root bark and to stem bark taken from dry stems, but chiefly to branch bark; (3) the quill bark, referring to natural bark taken from the stem and root in quill form, this including the uncultivated pale bark and all the varieties of cultivated bark; and (4) the renewed and mossed bark, which may be of any cultivated variety.

In structure the root barks correspond very closely to the stem barks of the same variety. They can be readily distinguished from the latter by being thinner, having lighter external and darker inner color, greater softness, and twisted or contorted shape. They occur in short, irregular quills or chips, or sometimes as shavings, and contain very much more dust than any other form. Except partly as regards structure, the description of stem barks will not apply to branch barks of the same variety, for the characteristic markings do not appear in the young condition. The branch bark appears in shavings, to the inner surfaces of many of which more or less wood adheres. If the branches were shaved while yet fresh, these shavings will be more or less rolled up and curled; but if dry before being removed, this rolling and curling will not occur. Shaved bark taken from living trees is thin, soft, and brittle, consisting of the outer bark only. The large quills are of uniform length from the same plantation, but not necessarily so from different plantation or different sections. They are commonly from two to three feet in length, but some have been marketed having a length of five feet. Usually they represent the entire circumference of the stem, but occasionally only half of it. In drying they roll up very tightly from one or both edges, and rarely one will be wholly or partly involved in another. The periderm, with all its markings, remains intact, and no other form so well displays the natural appearance as this. Mossed bark differs from natural stem bark in its great thickness and weight, less breadth of the quills, freedom from lichens, very dark color, and rough, corrugated or warty surface. The outer bark or cellular portion bears a greater ratio to the inner or fibrous portion than in natural bark. Renewed bark is lighter, both in color and weight, thinner, soft and brittle, and marked by a very peculiar external smoothness, sometimes very marked indeed. In its general appearance it is strikingly like a root bark, except for the relative straightness of its fibers. Like the mossed bark, it is in narrow, only partly rolled quills or bands, and is entirely free from lichens.

As they differ so greatly among themselves in coloration, lichen-growth, degree and form of exfoliation, structure and consequent fracture, there are but few characters which can be combined in a general description of the Cinchona barks which we consider. The external color varies from light ashy gray to nearly black, the inner varies less in its shades of yellow-brown and red-brown. All are more or less bitter, and most are astringent, but only Loxa bark has a distinctive odor. The fracture is never very long-splintery and never tough. As to structure, the bast fibers are loosely arranged, the radial rows being neither continuous nor very long. The fibers themselves are always unbranched, which distinguishes the true from the false barks, are rather short and obtuse, brittle, and usually easily detached from the bark. Laticiferous ducts and stone-cells may or may not be present. The former become less conspicuous as the bark grows older, so that their relative absence becomes indicative of a stage in which the due proportion of alkaloid should have been acquired.

It may be noted here that by far the greater portion of the alkaloid, particularly quinine, is stored in the outer bark, though that in the inner bark is in a purer state. The latter is not stored in the fibers, but in the cellular tissue between them.

The classification of barks by color refers chiefly to the powder. These colors, never regarded as absolutely characteristic as the three barks, yellow, red and pale, exhibit gradations by which they mingled at their extremes, have become even more indistinct, because of hybridization. The U. S. Pharmacopœia classifies as *Yellow Cinchona* either the *C. Ledgeriana* or *C. Calisaya* and as *Red Cinchona* the *C. Succirubra,* and their respective hybrids.

Description and Physical Properties.—"*Unground Cinchona.*—In quills or curved pieces or in broken fragments; bark from 2 to 8 mm. in thickness; externally brown or reddish-brown, usually with white or gray lichens, more or less roughened with corky ridges or protuberances, and with transverse fissures, rarely numerous or much intersected and having their sides sloping (Red Cinchona), or with numerous intersecting transverse and longitudinal fissures having nearly vertical sides (Yellow Cinchona); inner surface brown or reddish-brown and striate; fracture short and granular in the outer bark, rather splintery in the inner bark; odor faintly aromatic; taste astringent and very bitter.

"*Structure.*—Cork, frequently bearing dense masses of lichen tissues on its outer surface, conissts of rectangular, thin-walled cells with brown contents; parenchyma brown-walled, containing starch grains, or in some widely scattered cells microcrystals; laticiferous ducts widely separated in a single row near the inner edge of the primary cortex, circular or oval in transverse section, up to 0.120 mm. in diameter; medullary rays usually 1 to 3 cells wide with rectangular thin-walled cells, frequently tangentially elongated in the outer part of the ray; bast-fibers numerous, isolated or in small groups between the medullary rays.

"*Powdered Cinchona.*—Brown; bast-fibers, frequently whole, spindle-shaped, from 0.30 to 1.35 mm. in length, and from 0.050 to 0.135 mm. in width, with thick, strongly lignified, lamellated walls having numerous simple or branched pores; parenchyma and cork fragments brown; starch grains inconspicuous, single or 2- to 5-compound, up to 0.020 mm. in diameter; sphenoidal microcrystals very minute." *U. S.*

In the British Pharmacopœia it is described as: "In quilled or curved pieces, length varying from 5 to 30 cm. or more; usually from about 2.5 to 6 mm. thick; cork brownish or reddish-brown, with longitudinal ridges which are most apparent in the branch bark, and sometimes with reddish warts; inner surface brick-red or deep reddish-brown, irregularly and coarsely striated; fracture shortly fibrous in the smaller, and finely fibrous in the larger, pieces. In transverse section in the cortex, cells filled with minute crystals of calcium oxalate, and also large secretion tubes; in the bast numerous, large strongly-thickened fibers usually 0.050 to 0.070 mm. wide and about 1 mm. long, isolated or in small groups. The powdered Bark is brownish or reddish-brown, exhibits abundant parenchymatous tissue with brownish cell-walls, and often with brownish contents, small starch grains, and large isolated bast fibers about 0.060 mm. in diameter, with distinctly striated walls. No marked odor; taste bitter and somewhat astringent." *Br.*

Yellow bark, or *calisaya,* has lichens thin and closely adherent, not rendering it shaggy. External markings very characteristic, consisting of a very light longitudinal ridging or none at all, but of numerous transverse and longitudinal fissures or cracks, the presence and arrangement of which constitute the chief characteristics of Calisaya. Upon the young stems and branches they do not appear. The first to appear are the usually large primary fissures, which encircle the stem at the nodes, or points where pairs of leaves once stood. Subsequently, numerous smaller secondary transverse fissures appear upon the internodes, and these quickly become connected and crossed by longitudinal cracks, thus dividing the periderm up into more or less quadrangular checks, which may remain attached or fall away. This gives to mature Calisaya bark an appearance of scaliness like that upon the tarsus of a fowl, and this is known to the South American collectors by a term which signifies the "chicken-leg appearance." It has also been spoken of as a "carving-like" marking. Like the roughness upon a musk-melon, its great development is regarded as an indication of high quality, and especially is this true of a close proximity of the primary fissures. This roughness is also regarded as a sure indication of maturity. There are excellent distinctions between these and the somewhat similar fissures upon the bark of *C. officinalis.* In the latter they are coarser and more gaping. Even more important is the absence from Pale Bark of most of the longitudinal cracks, so that it does not become "chicken-legged," or at most only very slightly so. The external color of Yellow Bark is lighter than that of the Pale Bark. Longitudinal ridges are few if any, short, irregular, and inconspicuous. In fine South American bark some very small bright-red spots can be detected upon the periderm. East Indian Calisaya can commonly be recognized by its somewhat dingy or brownish shade of gray, the gray of the South American bark being bright and somewhat bluish-steel-colored.

In structure, the zone of large, rather numerous laticiterous ducts just outside the bast is conspicuous in young, and therefore inferior, samples. The rather small bast fibers are loosely scattered, almost uniformly single or a radial arrangement being apparent. The fracture is rough-splintery, though not coarse. Stone cells few or none. Odorless, more bitter, and less astringent than the Pale Bark. Ledger Bark is the same as Calisaya in all its essential characters, but does not reach so great a size. In hybrids of Calisaya with succirubra the characters and quality of the latter appear to predominate.

Yellow Cinchona is scarcely collected in a wild state, but is cultivated in all plantations. It is the largest quinine yielder, its amount being 70 to 80 per cent. of the total alkaloids contained in the bark. The var. *Ledgeriana* yields a very valuable hybrid bark with *C. succirubra*. *C. Calisaya* also hybridizes with the latter species. Hartwich describes the microscopical characteristics of Cinchona and related barks in *S. W. P.*, 1909, p. 249. Grutterink discusses the microchemistry of Cinchona alkaloids, with illustrations in *Zeit. anal. Chem.*, 1912, p. 215. Rosenthaler reviews the pyro-analytical results that have been obtained with Cinchona Bark and describes the crystals found in the tar. (*B. P. G.*, 1911, p. 203.)

The quills of *Red Bark* are similar to those of Calisaya, though running somewhat broader and thicker. Externally of a dingy brown gray, less lichen-bearing than either of the others. Inner surface of a more reddish cinnamon-brown than in calisaya. Powder reddish-brown. The important characteristic of red bark is the prominent longitudinal ridges, many of them short and confluent, with intervening furrows or elongated meshes. The ridges are suberous, bear numerous small warty protuberances, and may be traversed by faint fissures. Transverse fissures may or may not be present in Red Bark. If so, they are few, short, and irregularly disposed, and not connected by longitudinal cracks to give the checkered appearance of Calisaya. Hybrids with "officinalis" display numerous transverse fissures, and the external color is lighter and more dingy. Fracture short-splintery, not coarse. Odor none. Taste bitter and astringent.

It is scarcely collected in a wild state, but cultivated in all plantations except those of South America. Demand and production are rapidly decreasing. A large alkaloid yielder, but of this only about 20 per cent. is quinine. Largely hybridized with *C. officinalis*. Also hybridized with *C. Calisaya* and its var. *Ledgeriana*.

Under the titles of *Pale Bark, Crown Bark, Loxa* or *Loja Bark, Cuenca Bark, Huanuco Bark,* the bark of *C. officinalis,* while not official, is important as a source of quinine. It occurs above Loxa and other parts of Ecuador, and is cultivated in all plantations except the South American, especially in India. Quinine constitutes 60 to 70 per cent. of the total alkaloids. Largely hybridized with *C. succirubra.*

The quills of Pale Bark are single or double, irregularly broken or entire, attaining a length of nearly 2 dm., a width of nearly 2.5 cm., and having a very wide range in thickness, the natural mostly 2 to 4 mm. thick. Shaggy, with more abundant lichens than in any other species, the abundance of these having been considered, not entirely without reason, as an indication of the relative quality. Color of periderm darker than in the other species, but varying much from a brown gray to nearly black. Inner surface of a paler brown than in the other species, finely striate. Color of powder pale brown. The external markings consist of transverse fissures and longitudinal ridges, some of them wart-bearing. It is only in the thinner samples, in which the warts and fissures scarcely appear, that the ridges are continuous and conspicuous. In the prominence and breadth of its fissures and the inconspicuousness of its ridges, this bark is most distinct from the Red Bark. These characters are yet sufficiently distinct from the somewhat similar ones of Calisaya, as noted in describing that bark. Fracture short, the inner fibrous zone sharp and narrow. Taste not so bitter as in the others. Odor of the genuine Loxa variety peculiar and characteristic. Its structure shows the rather short and not numerous bast fibers in short interrupted single or double radial rows, and much disposed to occur in bundles of three to six or more. Stone cells rarely seen, and laticiferous ducts conspicuous only when young.

Description of various other species as the *C. Pelletierana* (*Cusco Bark*), the *C. cordifolia* (*Maracaibo Bark*), the *C. lancifolia* Mutis (*Cartagena Bark*) which were at one time of some commercial importance but have entirely disappeared from our markets can be found in the *U. S. D.*, 16th edition.

Constituents.—Deschamps, an apothecary of Lyons, obtained from the bark a crystallizable salt of lime, the acid of which Vauquelin afterwards separated, and called *kinic acid* (*quinic acid*). The latter chemist also arrived at the conclusion that those barks were most efficient which gave precipitates with tannin or the infusion of galls. Ruess, of Moscow, succeeded in isolating a peculiar coloring matter from red bark, which he designated by the name of *cinchonic red,* and obtained a bitter substance which probably consisted in part of the peculiar alkaline principles subsequently discovered. The first step, however, towards the discovery of the true active principle appears to have been taken by Duncan of Edinburgh, so early as 1803. He believed the precipitate afforded by the infusion of cinchona with that of galls to be a peculiar vegetable principle, and accordingly denominated it *cinchonin.* Gomez (1816), a Portuguese physician, obtained, by the action of potassium hydroxide upon an aqueous infusion of the alcoholic extract of the bark, what he believed to be a pure form of the same principle found by Duncan and which was probably the principle now known by the name of *cinchonine.* But Gomez was ignorant of its precise nature, considering it to be analogous to resin. To Pelletier and Caventou was reserved the honor of crowning all these experiments, and applying the results which they obtained to important practical purposes. In 1820 they demonstrated the alkaline character of the principle discovered by Gomez, and gave it definitively the name of *cinchonine.* They discovered in the yellow or Calisaya bark another alkaline principle, which they denominated *quinine.* Both these bases they proved to exist in the bark, combined with *quinic* or *kinic acid.* It was, moreover, established by their labors that the febrifuge property of bark depends upon the presence of these two principles.

Subsequent investigators have isolated some twenty or more alkaloids from various species of cinchona. Of these, four—quinine, quinidine, cinchonine and cinchonidine—afford salts which are officially recognized and are discussed under their respective titles. The others are briefly described immediately below. Wherry and Yanobsky (*J. Am. C. S.,* 1918, xl, 1063) have studied the refractive indices, optical activities and crystal measurements of quinine, cinchonine, quinidine and cinchonidine and demonstrate the possibility of detecting any of these alkoloids in a mixture.

In a very careful series of experiments made at the Java governmental cinchona plantations, Lotsy (*Bull. Inst. Botanique Buitenzorg,* 3, 1900) found that the seeds of *C. succirubra* and *C. Ledgeriana* contain no alkaloids, but that these alkaloids appear in the cotyledons shortly after they become green. They exist chiefly in the bark in combination with a tannic acid. Lotsy found that the percentage of alkaloids is ten times greater in young than in old leaves; also that the petioles are richer in alkaloids than is the blade, and that the branch bark contains more than the trunk bark, and that the root bark is practically free from alkaloids. During the active life of the parenchymatous cells of the leaves, wood, and cortex, the alkaloids can always be found in the active protoplasmic contents, but when these cells pass into the inactive condition, are deposited in the cell-walls. The alkaloids found in the leaves are, however, never crystalline, hence it would appear that these organs produce by direct synthesis, probably as the result of the action of cinchonic acid with ammonia, a fundamental alkaloidal base, which, probably in the cambium layer of the tree during its deposition in the growing bark, is elaborated into the true cinchona alkaloids.

The total amount of alkaloids, as well as the relative proportions of different ones, varies greatly in individual samples of bark. In a general way it may be said that the Red Bark contains from 5 to 7 per cent. (occasionally more) of which about one-fifth two two-fifths is quinine; Calisaya runs about 6 to 8 per cent. of which approximately one-half is quinine; Ledger Bark averages from 6 to 10 per cent. with usually three-fourths of this quinine. The richest specimen of which we know was a sample of Ledger containing 14.5 per cent. of alkaloids. Generally speaking, the root barks contain more than the stem barks.

Under the name of *quinetum* or *febrifuge* a compound is produced in India and other Eastern countries, which consists of the mixed alkaloids of Red Bark, the object being to produce a cheap febrifuge which will answer all practical purposes and save the cost of refining. It is largely produced at Sikkim, India, by a modification of Dubreuil's process, which consists in extracting the powdered mixed barks with hydrochloric acid, precipitating the alkaloids by the addition of solution of sodium hydroxide, and shaking out with petroleum, adding to the petroleum solution a calculated quantity of diluted sulphuric acid, evaporating and crystallizing.

Besides the natural bases we have a number of alkaloids formed by the alteration or treatment of these natural bases, or in some cases molecular compounds of two of the natural bases.

Chinoidine or *Quinoidine* is a term now applied to the resinous substance consisting not only of the *amorphous* natural alkaloids, but of those which are produced artificially through the action of the heat and acids upon the crystalline alkaloids. (See Part II.)

The following list of bases from Cinchona or allied sources is arranged alphabetically.

ARICINE or *quinovatine,* $C_{23}H_{26}O_4N_2$, found in the *C. cordifolia* var. *Pelletieriana,* melting point 188° C., optical rotation —58° 18′ (see Hesse, *Ann. Chem.,* 1873, clxvi, 1877, clxxxv; Moissan and Landrin, *Bull. Soc. Chim.,* 1890, iv).

CINCHOTINE, $C_{19}H_{24}ON_2$, also known as *hydrocinchonine* and *cinchonifine,* found in many species of cinchona, usually a constituent of commercial cinchonine and also prepared by the catalytic hydrogenation of cinchonine. (Heidelberger and Jacobs, *J. Am. C. S.,* 1919, xli.) Crystallizes in prisms, melting point of 268° to 269° C. Optical rotation + 204.5, in alcohol, is diacidic.

CUSCONINE and *concusconine,* isomeric with aricine, like it occur in the cusco bark. This bark also contains, according to Hesse (*Ann. Chem.,* 1880, cc), *cuscamine, cuscamidine* and *cusconidine,* the composition of which are unknown.

DICINCHONINE, $C_{38}H_{44}O_2N_4$ found in the *C. rosulenta* and *C. succirubra,* also known as *dicinchonicine* and as *apodicinchonine.* It is amorphous and dextrorotary (Hesse, *Ann. Chem.,* 1885, ccxxvii).

DICONQUININE, $C_{40}H_{46}O_4N_4$, also known as *diquinicine* or *apodiquinidine,* forms the chief ingredient of the mixture known commercially as *quinoidine.* It is amorphous and dextrorotary. (Hesse, *B. Chem. G.,* 1877, x.)

HOMOCINCHONIDINE, $C_{19}H_{22}ON_2$, isomeric with cinchonidine, occurs in several barks but especially in the *C. rosulenta.* It is also produced by the action of hydrochloric acid on cinchonidine. It does not give the thalleioquin reaction. Its physical constants are so close to those of cinchonidine that its separate identity has been denied.

HYDROCINCHONIDINE, $C_{19}H_{24}ON_2$, also known as *cinchamidine,* first isolated by Forst and Börhinger (*B. Chem. G.,* 1881, xiv) from *C. Ledgeriana,* but also occurs in other species. Is best prepared by hydrogenation of cinchonidine. Its crystals have a melting point of 229° C. and an optical rotation of -98.4 in alcohol, the salts exhibit no fluorescence nor thalleioquin reaction (Heidelberger and Jacobs, *J. Am. Chem. S.,* 1919, xli).

HYDROQUINIDINE (*hydroconquinine*), $C_{20}H_{26}O_2N_2 + 2\frac{1}{2}H_2O$, is found in commercial quinidine and may be separated by potassium permanganate treatment. It is crystalline, dissolving freely in hot alcohol and in chloroform, but less freely in ether. It gives the thalleioquin reaction like quinine. (Forst and Böhringer, *B. Chem. G.,* 1882, xv; Heidelberger and Jacobs, *J. Am. C. S.,* 1919, xli.)

HYDROQUININE (*methyl-hydrocupreine*), $C_{20}H_{26}O_2N_2$, was discovered by Hesse in the mother liquors from *C. Ledgeriana* after quinine sulphate has been crystallized (*B. Chem. G.,* 1882, xv). It is a frequent constituent of the commercial quinine sulphate. Its crystals melt at 172.3° C. and show an optical rotation of -142.2 in alcohol. It shows the thalleioquin reaction and is a diacidic base. Quinine cannot be perfectly freed from hydroquinine even by repeated crystallization of the neutral sulphates, but the hydroquinine can be completely separated by converting the alkaloid into the acid sulphate and recrystallizing this from water or alcohol, when the hydroquinine remains in the mother liquor. (Allen.) The hydrochloride, $C_{20}H_{26}O_2N_2HCl.2H_2O$, forms crystals which are readily soluble in water and alcohol. Morganroth and Hallberstadter (*B. K. W.,* 1911) assert that this agent will cause a disappearance of trypanosomes from infected animals, which quinine will not do. Giemsa and Werner (*Cb. G. T.,* 1912, p. 492) assert that *hydroquinine* is more efficacious in *malaria* than quinine. It has also been commended by Lenzmann (*M. M. W.,* 1912, p. 2193) as a local application in *whooping cough.* The *dose* used by Giemsa and Werner was three grains (0.2 Gm.) three or four times a day. It is of commercial importance as a material for the manufacture of *hydrocupreine* (see *Optochine,* Part II).

JAVANINE.—Found in the *C. Calisaya* var. *Javanica,* composition unknown. (Hesse, *B. Chem. G.,* 1877, x.)

PARICINE, $C_{16}H_{18}ON_2$, optically inactive, melting point 130°, forms amorphous salts, found in the *C. succirubra.* (Hesse, *Ann. Chem.,* 1873, clxvi.)

QUINAMIDINE (*Conquinamine* of Hesse), $C_{19}H_{24}O_2N_2$, is found in *C. rosulenta* and *C succirubra,* and probably exists in other species of Red Bark. It crystallizes in long, brilliant prisms, which melt at 123° C. It may be formed in acid solutions of quinamine through decomposition. (Hesse, *Ann. Chem.,* 1881, ccix.)

QUINAMINE, *Quinamia,* $C_{19}H_{24}O_2N_2$.—Hesse discovered this cinchona alkaloid in the bark of *C. succirubra.* He has since found it in several other species, and particularly *C. Ledgeriana.* Melting point 172° C.; optical activity, $+104.5$ in alcohol. Quinamine is almost tasteless, but its solutions in acids are very bitter. Its sulphuric acid solution is not fluorescent.

QUINICINE, $C_{20}H_{24}O_2N_2$, was first formed by Pasteur, 1853, by heating quinine bisulphate and subsequently by Hesse in a similar manner from quinidine; the latter named it *quinotoxine.* It also occurs naturally in cinchona bark. (Howard and Chick, *J. P.,* 1917, xcix, p. 143.)

Besides the genus *Cinchona* certain of the allied genus *Remijia* contain quinine or related alkaloids and have been used in medicine. Of these the *R. pedunculata* Triana (*Cinchona pedunculata* Karsten) formerly appeared in commerce under the name of *cuprea bark* and the *R. Purdieana* Weddell as *false cuprea.* In these barks are found the following alkaloids in addition to some of those which occur in the cinchona barks.

CINCHONAMINE, isomeric with cinchotine, occurs in the *R. Purdieana.* It is said to be a more potent antipyretic than quinine and also poisonous. Melting point 194° C., optical rotation, $+121.1$ in alcohol. It does not respond to the thalleioquin test. See Howard (*J. Soc. Chem. Ind.,* 1905, xxiv, 1909, xxviii.) Physiologically, cinchonamine, according to the experiments of Sée and Bochefontaine, has six times the toxic power of quinine, and has decided sialagogue properties. (*P. J.,* 1885, p. 761.)

CHAIRAMINE and *Chairamidine, Conchairamine* and *Conchairamidine;* these isomers have the formula $C_{22}H_{26}O_4N_2$ and are found in the *R. Purdieana.* For method of separating them see Hesse (*Ann. Chem.,* 1884, ccxxv, p. 211).

CUPREINE.—This is the chief alkaloid of the *R. pedunculata.* The anhydrous crystals melt at 198° C. and have an optical activity of -175.5 in dehydrated alcohol. It gives the thalleioquin reaction. The substance known as *homoquinine* is probably a molecular combination of quinine and cupreine. The anhydrous crystals melt at 177° C. Cupreine is a diacidic base which on methylation is converted into quinine. (Howard, *Tr. Chem. Soc.,* 1882, xli; *J. Soc. Chem. Ind.,* 1909, xxviii; Paul and Cownley, *P. J.,* 1881, xii, 1884, xv.)

In addition to the numerous alkaloids, several other more or less interesting substances have been found in cinchona barks. The most important of these are as follows:

TSCHIRCHIN is a green coloring matter, not identical with chlorophyll, which has been extracted from *Cinchona Succirubra* by Glücksmann.

Cinchocerotin, $C_{27}H_{48}O_2$.—This substance was discovered by Kerner in flat Calisaya bark from South America. He obtained it in white, very light, crystalline scales. It is not soluble in boiling water, nor in hydrochloric, diluted sulphuric, or glacial acetic acid, but dissolves readily in ether, chloroform, and alcohol. (See Helms, *A. J. P.*, 1883, p. 357.)

Cinchofulvic Acid.—The *cinchonic red* of Reuss, identical with the *insoluble red coloring matter* of Pelletier and Caventou, $C_{12}H_{14}O_7$, is reddish brown, insipid, inodorous, largely soluble in alcohol, especially when hot, and almost insoluble in ether or water, though the latter dissolves a little at the boiling temperature. The acids promote its solubility in water. It precipitates tartar emetic, but not gelatin; but if treated with a cold solution of potassium or sodium hydroxide, or with ammonia, lime, or baryta with heat, and then precipitated by an acid, it acquires the property of forming an insoluble compound with gelatin. It yields protocatechuic acid, $C_7H_6O_4$, when fused with potassium hydroxide. It is most abundant in the red bark (over 10 per cent.), and least so in the pale.

Cinchotannic Acid. *Cinchotannin*, $C_{14}H_{16}O_9$.—Is present as a glucoside in cinchona barks in the proportion of 3 to 4 per cent. It has a brownish-red color and an austere taste, is soluble in water and alcohol, and produces precipitates with the salts of iron, which vary in color according to the variety of bark, being deep green with the pale bark, blackish-brown with the yellow, and reddish-brown with the red. Rembold has shown that when cinchotannic acid is boiled with diluted sulphuric acid, cinchonic red is produced, sugar being formed at the same time.

Quinic Acid (*Hexahydrotetraoxybenzoic Acid*), $C_7H_{12}O_6$.—This acid was isolated as early as 1790 by Hofmann, an apothecary of Leer, who obtained it from the calcium salt from cinchona. It exists in a number of important plants—ivy, oak, elm, ash, coffee, etc. It is usually prepared from calcium quinate, the residue obtained in the manufacture of quinine sulphate (see *Quininæ Sulphas*) by decomposing an aqueous solution of calcium quinate with oxalic acid, filtering out the precipitated calcium oxalate, and evaporating the filtrate to the crystallizing point. The crystals are transparent and colorless, sour to the taste, soluble in 2 parts of water, but less soluble in alcohol, and almost insoluble in ether. By heating quinic acid or a quinate with manganese dioxide and sulphuric acid, we get yellow crystals of *kinone*, better known as *quinone*, $C_6H_4O_2$, a reaction which may be used for ascertaining the presence of quinic acid. It is non-toxic and seems, like other vegetable acids, to be decomposed in the system, forming, when taken in the state of an alkaline salt, a carbonate of the alkali in the blood, and rendering that fluid alkaline. Several esters of quinic acid and compounds with synthetic bases have been introduced into medicine, viz.—*chinotropin, sidonal, new sidonal, urosin,* and *ural.* (See Part II.)

Quinovin, *Kinovin,* or *Chinovin,* $C_{38}H_{62}O_{11}$.—This bitter glucoside probably exists, in greater or less proportion, in all the Cinchona barks. It is white, uncrystallizable, almost insoluble in water, but readily dissolved by alcohol and ether. Winckler gives, as a certain test of its presence in any bark, copper sulphate, which indifferent to infusion of bark containing none of this principle, produces a dirty-green color, soon followed by the deposition of a fine similarly colored powder. This salt of copper, has a bitter and metallic taste. (See *A. J. P.*, xxv, 343.) Quinovin in alcoholic solution under the influence of hydrochloric acid hydrolyzes into *quinovic acid,* $C_{24}H_{38}O_4$, and an uncrystallizable sugar, *mannitan,* $C_6H_{12}O_5$, by assimilation of H_2O.

Liebermann and Giesel (*B. Chem. G.*, xvi, 987) believe that two modifications exist, *α-quinovin* and *β-quinovin,* the former in Cinchona, the latter in Cuprea bark: α-quinovin is a white crystalline powder, nearly insoluble in cold and hot water, but soluble in caustic alkalies, lime water, ammonia water, and glacial acetic acid, soluble with difficulty in chloroform, ether, and petroleum benzin; it dissolves in 57 parts of nearly absolute alcohol. β-quinovin closely resembles α-quinovin, but is not soluble in ether, and crystallizes readily from diluted alcohol.

Quinovic Acid (*Kinovic Acid*), $C_{32}H_{48}O_6$, occurs as white, rhomboidal crystals, insoluble in water, slightly soluble in ether or alcohol, but very soluble in ammonia and the fixed alkalies, the solutions frothing like soap water. On adding an acid to an alkaline solution of quinovic acid, a hydrate of quinovic acid is thrown down as a very voluminous jelly, the whole contents of the vessel gelatinizing.

The odor of bark appears to depend on a *volatile oil,* which Fabroni and Trommsdorff obtained by distillation with water. The oil floated on the surface of the water, was of a thick consistence, and had a bitterish, acrid taste, with the odor of bark.

Scoville (*J. A. Ph. A.*, 1921, x, 844) has reported on experiments in the extraction of cinchona, from which he concludes that hydrochloric acid is of material aid both in extraction of the alkaloids and in reducing precipitaton from the fluidextract. He recommends as the most favorable proportion a menstruum containing 1.6 per cent. of the acid. The complete extraction is slow and tedious and necessitates the use of a large quantity of menstruum.

Assay.—The U. S. assay for cinchona is as follows: "Heat 5 Gm. of Cinchona, in fine powder, for one hour, in a 500 cc. flask on a water bath, with 5 cc. of diluted hydrochloric acid and 10 cc. of distilled water. Cool, add 200 cc. of ether-chloroform mixture, and 10 cc.

of strong ammonia T.S. Proceed by Type Process A, decanting an aliquot portion of 160 cc., representing 4 Gm. of Cinchona, and determine the alkaloids gravimetrically. Use chloroform for the final extraction (Proximate Assays)." *U. S.*

The British directions are as follows:

Test.—"Red Cinchona Bark when used for official purposes other than the preparation of alkaloids or their salts, is required to yield from 5 to 6 per cent. of total alkaloids, of which not less than one-half consists of quinine and cinchonidine, as determined by the following process: Mix 10 grammes of Red Cinchona Bark, in No. 60 powder, with 6 grammes of *calcium hydroxide;* add 22 millilitres of *water,* mix intimately in a small porcelain dish or mortar, and set aside for an hour or two. Transfer this mixture to a suitable flask fitted with a reflux condenser, add 130 millilitres of *benzolated amylic alcohol,* boil for about half an hour, and then decant the liquid on to a filter, leaving the sediment in the flask; add more of the *benzolated amylic alcohol* to the sediment, and boil and decant as before; repeat this operation a third time; then transfer the contents of the flask to the filter, and wash by percolation with more of the *benzolated amylic alcohol* until the Bark is exhausted. Introduce the collected filtrate, while still warm, into a stoppered glass separator; add to it 2 millilitres of *diluted hydrochloric acid,* mixed with 12 millilitres of *water;* shake well together, and allow the liquids to separate; draw off the acid liquid, and repeat the process with *water* slightly acidified with *hydrochloric acid,* until the alkaloids have been completely removed. Carefully and exactly neutralise the acid liquid, while warm, with *solution of ammonia,* and concentrate by evaporation to the bulk of 16 millilitres. To the concentrated solution add about 1.5 grammes of *sodium potassium tartrate,* dissolved in twice its weight of *water,* stirring with a glass rod; after about one hour collect the precipitate, wash dry at 100° C. and weigh; the weight in grammes multiplied by 8 gives the percentage of quinine and cinchonidine in the Bark. To the mother-liquor and washings from the preceding process add *solution of ammonia* in slight excess and shake with three successive portions of 10 millilitres of *chloroform;* evaporate the mixed chloroformic solutions to dryness, dry the residue at 110° C and weigh. The weight in grammes multiplied by 10 and added to the percentage of the quinine and cinchonidine, gives the percentage of total alkaloids." *Br.*

The German Pharmacopœia gives the following method: "The powdered bark is assayed as follows: Shake 20 Gm. of it strongly and repeatedly with a mixture of 10 Gm. of water of ammonia, 20 Gm. of alcohol, and 170 Gm. of ether, and, after a day, decant 120 Gm. of the clear liquid. To this liquid add 3 cc. of volumetric hydrochloric acid, remove the ether by distillation or evaporation, and again add, if necessary, enough hydrochloric acid to render the solution acid. Then filter, and mix the cold filtrate with 3.5 cc. of volumetric solution of potassa. When the alkaloids have subsided, drop more of the solution of potassa into the clear supernatant liquid, until nothing more is thrown down. Finally, collect the whole of the precipitate on a filter, and wash it repeatedly with small portions of water, until drops of the wash water allowed to come in contact with the surface of a cold, aqueous, neutral, saturated solution of sulphate of quinine no longer produce a turbidity. When the alkaloids have drained, press them gently between bibulous paper, and, having dried them sufficiently in the air to permit their being removed to a watch-glass, dry them completely, first over sulphuric acid, and, finally, by means of a water-bath. The weight of alkaloids procured by this method should not be less than 0.42 Gm. When a small portion of the same is boiled with 300 parts of water, the filtrate, after cooling, should yield flakes of quinine. When to 5 parts of this solution, after being cooled and decanted, 1 part of chlorine water is added, and water of ammonia immediately dropped in, the liquid should acquire a beautiful green color." For E. R. Squibb's method of assay, see *U. S. D.,* 18th ed., p. 412.

It is sometimes desirable to ascertain not only the quantity of total alkaloids but also the proportion of quinine. For the latter purpose the total alkaloids extracted by the U. S P. method may be exactly neutralized N/10 sulphuric acid, the resulting liquid then diluted with sufficient water that it contains one part of total alkaloid in 70 parts of solution by weight. This is then heated to 90° for 5 minutes and cooled to 15° and set aside at this temperature for 30 minutes when crystals of quinine sulphate will separate out. These crystals are collected on a tared filter and washed with water at 15° until the filtrate weighs 90 Gm. for each Gm. of total alkaloid taken, then dried and weighed. A correction representing the solubility of quinine sulphate in water at 15° is required and for this purpose 0.00817 Gm. should be added for each gramme of filtrate and washings. The sum divided by 0.855 gives the yield of crystallized quinine sulphate (Henry, *Plant Alkaloids,* 1924). For another method of separating the cinchona bases see Leger (*J. P. C.,* 1904, xix, 427).

Uses.—When taken into the stomach, the bark usually excites in a short time a sense of warmth in the epigastrium, which often diffuses itself over the abdomen and even the breast, and is sometimes attended with considerable gastric and intestinal irritation. Nausea and vomiting are sometimes produced, especially if the stomach was previously in an inflamed or irritated state; and its action is not unfrequently accompanied by purging. If the dose of the cinchona bark has been large enough, the symptoms of cinchonism may result. (See *Quinina.*) At one time cinchona bark and its preparations were used as antiperiodics, but at present for such purpose one or another of its alkaloids is always selected. MacGilchrist (*Indian Journ. Med. Res.,* 1915, iii, p. 1) arranges the chief alkaloids in the following order of efficacy in malarial fevers: hydroquinine, cinchonine, quinine, quinidine, optochin, cinchonidine, and quinoidine. The best preparation for use as a tonic is the compound tincture.

Dose, ten grains to one drachm (0.65–3.9 Gm.).

Off. Prep.—Fluidextractum Cinchonæ, *U. S.;* Tinctura Cinchonæ, *U. S.;* Extractum Cinchonæ Liquidum, *Br.;* Infusum Cinchonæ Acidum, *Br.;* Tinctura Cinchonæ, *Br.;* Tinctura Cinchonæ Composita, *U. S.* (*Br.* from Tincture).

CINCHONIDINÆ SULPHAS. U. S.

CINCHONIDINE SULPHATE Cinchonid. Sulph.

"The sulphate [$(C_{19}H_{22}ON_2)_2H_2SO_4.3H_2O$] of an alkaloid obtained from cinchona bark." *U. S.*

Cinchonidinum Subsulfuricum; Sulphate of Cinchonidine; Schwefelsaures Cinchonidin, Cinchonidinsulfat, *G.;* Sulfate de Cinchonidine basique, *Fr.;* Solfato di cinconidina, *It.*

This salt is prepared from the mother liquors obtained in the manufacture of quinine sulphate, and is separated from the sulphates of the other alkaloids by fractional crystallization.

Owing to some confusion in naming cinchonidine and quinidine, this alkaloid is sometimes incorrectly called in Germany *chinidine.* Skraup's researches on the composition of cinchonine and cinchonidine (1879) established the correctness of the formula $C_{19}H_{22}ON_2$, instead of the long-accepted formula of Pasteur (1853), $C_{20}H_{24}ON_2$. Skraup's formula has been confirmed by Hesse, and is generally accepted by chemists.

Basic *cinchonidine* is not official. It crystallizes in large trimetric prisms with a melting point of 207.2° C. (Lenz), or 202.4° C. (Hesse), and an optical activity of -111 in alcohol. It is practically insoluble in cold water, soluble in about 20 parts of alcohol, requires about a thousand parts of dry ether to dissolve it but is somewhat more soluble in the official ether.

Cinchonidine is found in most varieties of cinchona bark, but is especially abundant in the *C. succirubra.* It is a diacidic base and may be readily distinguished from quinine and quinidine by the absence of fluorescence in the solutions of its salt and by not giving the thalleioquin reaction.

Description and Physical Properties.—"White, glistening, silky needles or prisms. It is odorless, and has a very bitter taste. One Gm. of Cinchonidine Sulphate is soluble in 65 cc. of water, 90 cc. of alcohol, and in 620 cc. of chloroform, at 25° C. One Gm. is soluble in 22 cc. of water at 80° C. and in 41 cc. of alcohol at 60° C. It is nearly insoluble in ether.

"An aqueous solution of Cinchonidine Sulphate is lævorotatory. The addition of ammonia T.S. to an aqueous solution of Cinchonidine Sulphate (1 in 100) produces a white precipitate of cinchonidine, which is but slightly soluble in ammonia T.S. or in ether. Sodium tartrate T.S. produces in an aqueous solution (1 in 100) a white precipitate of cinchonidine tartrate (*difference from cinchonine*). An aqueous solution of Cinchonidine Sulphate yields with barium chloride T.S. a white precipitate, insoluble in hydrochloric acid.

"A saturated aqueous solution of Cinchonidine Sulphate is neutral or faintly alkaline to litmus paper. Dried to constant weight at 100° C., Cinchonidine Sulphate loses not more than 12 per cent. (*water*). Ash: not more than 0.1 per cent. A solution of 0.1 Gm. of Cinchonidine Sulphate in 2 cc. of sulphuric acid is not darker than faint yellow (*readily carbonizable substances*). A 10 cc. portion of a solution of the salt (1 in 1000) in diluted sulphuric acid exhibits only a faint, blue fluorescence (*quinine or quinidine*). Macerate 0.5 Gm. of Cinchonidine Sulphate, with frequent agitation, at room temperature, with 20 cc. of distilled water, then add 0.5 Gm. of potassium and sodium tartrate, and continue the maceration with repeated agitation for one hour at 15° C., and filter the mixture. The addition of 1 drop of ammonia T.S. to the filtrate produces not more than a slight turbidity (*cinchonine or quinidine sulphate*).

"Preserve in well-closed containers, protected from light." *U. S.*

The *acid sulphate* (sometimes called *bisulphate*) is much more soluble in water than the official sulphate. *Cinchonidine salicylate* is neutral and crystalline, insoluble in cold water, sparingly in hot water, easily soluble in alcohol and diluted alcohol. It may be prepared by the direct combination of salicylic acid with the alkaloid. The *hydrobromide* has been employed by Gubler hypodermically. Königs and Husmann having claimed to have converted cinchonine into cinchonidine by the long-continued action of boiling amyl alcohol and solution of potassium hydroxide, Paul and Cownley have investigated this treatment. They failed to get such conversion, and consider that the cinchonine used by Königs and Husmann must have been impure. (*P. J.,* Feb. 20, 1897.)

Uses.—So far as our knowledge goes, this alkaloid influences the system similarly to quinine, the only difference being that it is less powerful. It may be given in doses one-third greater than those of quinine, but should not be relied on in severe cases.

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Elixir Cinchonæ Alkaloidorum and in other Elixirs containing Cinchona Alkaloids in combination with Iron, Bismuth, etc., *N. F.*

CINCHONINÆ SULPHAS. N. F.

CINCHONINE SULPHATE Cinchonin. Sulph.

"The sulphate [$(C_{19}H_{22}ON_2)_2.H_2SO_4.2H_2O =$ 722.68] of an alkaloid obtained from the bark of several species of cinchona." *N. F.*

Cinchoniæ Sulphas, *U. S.* 1870; Sulfate de Cinchonine basique, *Fr.* Schwefelsaures Cinchonin, Cinchoninum Sulfuricum, Cinchoninsulfat, *G.;* Solfato Cinchonico, *It.;* Sulfato de cinconina, *Sp.*

Cinchonine is present in nearly all species of cinchona bark; it is especially evident in the *C. micrantha.* Commercially it is obtained from the mother liquors after separation of quinine. The addition of sodium hydroxide to this liquor causes the precipitation of the remaining alkaloids, chiefly quinidine, cinchonidine and cinchonine. Because of the sparing solubility of cinchonine in ether, this precipitate is first shaken out with ether to remove the two other alkaloids, and the insoluble residue extracted with successive portions of boiling alcohol from which the cinchonine crystallizes out on cooling.

Its formula is now generally accepted as $C_{19}H_{22}ON_2$, the molecular weight of which is 292.03. It is, therefore, isomeric with cinchonidine. The base occurs in "white, lustrous prisms or needles, without odor, at first almost tasteless, but soon developing a bitter aftertaste; permanent in the air. Soluble, at 15° C., in 3760 parts of water, and in 116 parts of alcohol; in 3500 parts of boiling water, and in 26.5 parts of boiling alcohol. Also soluble in 526 parts of ether, and in 163 parts of chloroform. At 240° C. the crystals fuse together, and at 258° C. they melt, forming a brown liquid. When ignited, they are consumed without leaving a residue." *U. S.,* 1890. The optical rotation is $+229°$ C. in dry alcohol. It is a strongly alkaline, diacidic base, forming two series of salts, neutral and acid.

It differs from quinine by its rotating the plane of polarization to the right, by the want of fluorescence in its solutions, and by its failing to respond to the thalleioquin test. Chlorine water dissolves it or any of its salts without change; but if ammonia be now added, a white precipitate is produced. It is thus distinguishable from quinine. (See *Quinina.*) J. W. Bill, proposed potassium ferrocyanide as a very delicate test of cinchonine. If added to the solution of a salt of this alkaloid, it produces a yellowish-white curdy precipitate, which is dissolved upon the application of a gentle heat, but is again deposited, when the liquid cools, as an abundant crop of golden-yellow crystals. No other alkaloid exhibits the same reaction. A cloudy precipitate is produced by the same reagent with a salt of quinine; but this does not happen when the ferro-cyanide is in excess; and, if the precipitate be dissolved by heat, no subsidence takes place on cooling. Hence, in the application of this test to cinchonine, a slight excess of the ferrocyanide should be added.

The substance known as *homocinchonine* is an impure form of cinchonine.

There are two cinchonine sulphates, the neutral and the acid sulphate. The official salt is the neutral sulphate.

Description and Physical Properties.—"Cinchonine Sulphate occurs as white, lustrous prismatic crystals; odorless and having a very bitter taste; permanent in the air. One Gm. of Cinchonine Sulphate dissolves in 60 cc. of water, 12.5 cc. of alcohol, 47 cc. of chloroform, and in 3230 cc., of ether at 25° C.; also in 33 cc. of water at 80° C. and in 7 cc. of alcohol at 60° C.

"A saturated aqueous solution of the salt is neutral or slightly alkaline to litmus and is dextrorotatory. An aqueous solution of Cinchonine Sulphate (1 in 100) yields with barium chloride T.S. a white precipitate insoluble in hydrochloric acid. Dried to constant weight at 100° C. Cinchonine Sulphate loses not more than 5 per cent. of its weight.

"Incinerate about 1 Gm. of Cinchonine Sulphate; not more than 0.1 per cent. of ash remains. Ten cc. of a solution of the salt (1 in 1000) in diluted sulphuric acid exhibits only a slight, blue fluorescene. One-tenth Gm. of the powdered salt dissolves completely or nearly so, when shaken with 10 cc. of chloroform at ordinary temperatures (*quinine* or *cinchonidine sulphate*). Add 0.1 Gm. of the salt to 2 cc. of sulphuric acid; it imparts not more than a faint yellow tinge to the acid (*readily carbonizable, organic impurities*)." *N. F.*

The *acid sulphate,* or *bisulphate,* $C_{19}H_{22}ON_2.H_2SO_4.3H_2O$, is prepared by adding sulphuric acid to the neutral sulphate. According to Baup, 100 parts are soluble in 45 parts of absolute alcohol; it is insoluble in ether. It crystallizes in rhombic octahedrons.

Uses.—Cinchonine undoubtedly possesses in marked degree the anti-malarial properties of quinine; indeed, MacGilchrist reaches the conclusion that the two alkaloids are of approximately equal powers but is inclined to the view that cinchonine is slightly superior. Rogers (*B. M. J.,* 1918, ii, 459) used a bi-hydrochloride of cinchonine by intramuscular injection with very satisfactory results in all forms of *malaria,* especially in the malignant tertian variety, he found experimentally that this salt was absorbed much more rapidly than the corresponding salt of quinine. As to whether it possesses the other therapeutic properties of quinine, we have no definite information.

Dose, tonic, a grain or two (0.065–0.13 Gm.) three or four times a day; antiperiodic dose, fifteen to forty grains (1.0–2.6 Gm.) between the paroxysms.

Off. Prep.—Elixir Cinchonæ Alkaloidorum and in other Elixirs containing Cinchona Alkaloids in combination with iron, bismuth, etc., *N. F.*

CINCHOPHENUM.

CINCHOPHEN Cinchophen. [Acidum Phenylcinchoninicum, U. S. P. IX, Phenyl-quinoline carboxylic Acid]

"Cinchophen, when dried to constant weight over sulphuric acid, contains not less than 99 per cent. of $C_6H_5.C_9H_5N.COOH$." *U. S.*

Cinchophen, Atophan, Phenylcinchoninic Acid.

Phenylcinchoninic acid is produced by a complicated process of manufacture in which pyruvic acid (prepared by the distillation of tartaric acid) is first heated with benzaldehyde, in molecular proportions, and a solution of one molecular equivalent of aniline in absolute alcohol then added. The reaction is completed by boiling under a reflux condenser for three hours. Upon cooling, crystals of the crude product separate. These may be purified by reprecipitation and recrystallization.

In another process, isatin, acetophenone, alcohol and an alkali are used in the initial stages.

For description of related compounds, see *Cinchophen Derivatives,* Part II.

Description and Physical Properties.—"Small, colorless, needle-like crystals, or a white to yellowish-white powder. It is odorless, has a slightly bitter taste, and is stable in the air. Cinchophen is almost insoluble in cold water. One Gm. is soluble in about 400 cc. of chloroform, 100 cc. of ether, and in 120 cc. of alcohol, at 25° C. It is more readily soluble in hot than in cold alcohol.

"Cinchophen melts at about 210° C. with partial decomposition. A saturated solution of Cinchophen in hot diluted hydrochloric acid yields with platinic chloride T.S. a precipitate of yellowish-brown crystals. Dissolve about 1 Gm. of Cinchophen in an excess of ammonia T.S., evaporate the solution to dryness on a water bath, or until free from the odor of ammonia, dilute to 20 cc. with distilled water, and filter: portions of the filtrate yield a white, flocculent precipitate with silver nitrate T.S., a yellowish, flocculent precipitate with lead acetate T.S., and a green, flocculent precipitate with copper sulphate T.S. The ash from 0.2 Gm. is negligible. A solution of 0.1 Gm. of Cinchophen in 5 cc. of sulphuric acid is not darker than yellow (*readily carbonizable substances*). On adding three drops of nitric acid to this solution, no reddish or brown color is produced.

"**Assay.**—Weigh accurately about 0.5 Gm. of Cinchophen, previously dried to constant weight over sulphuric acid, and dissolve it in 60 cc. of alcohol which has been neutralized with tenth-normal sodium hydroxide, using three drops of phenolphthalein T.S. as indicator, and warming gently to facilitate solution. Cool, and titrate the solution with tenth-normal sodium hydroxide until the pink color is restored. Each cc. of tenth-normal sodium hydroxide corresponds to 0.02492 Gm. of $C_6H_5.C_9H_5N.COOH$.

"Preserve in well-closed containers, protected from light." *U. S.*

Uses.—In 1908 Nicolaier and Dohrn (*D. K. M.,* 1908, xciii) showed that phenylcinchoninic acid caused an extraordinary increase in the excretion of uric acid; as this excretion was increased in persons upon a purin-free diet, they believed that it was due to increased output of the endogenous uric acid. That it produces a marked increase in the quantity of uric acid eliminated through the kidneys—in some cases amounting to as much as 100 or 200 per cent.—without a corresponding increase in the quantity of urea, seems to be established beyond question. Starkenstein (*A. E. P. P.,* 1911, lxv, p. 177) believes, however, that the increase in the uric acid is due to a diminished ability to oxidize the purin foods, but Folin and Lyman (*J. P. Ex. T.,* 1913, iv, p. 539) have shown that the increased elimination is accompanied by the diminution in the quantity of uric acid in the blood. It is generally accepted, therefore, that the increased elimination of uric acid is due to a greater capacity of the kidneys to excrete this substance, in other words, to a type of stimulation of kidney function. Myers and Killian (*J. P. Ex. T.,* 1921, xvi, 213) have shown that this stimulation of the kidney leads to a reduction not only of the amount of uric acid in the blood but also of the urea and that in cases of diseased kidneys its too free use may have an injurious effect upon the renal structure.

Phenylcinchoninic acid is a valuable remedy in the treatment of both acute and chronic *gout* and in those allied disorders generally spoken of as the *lithemic diathesis.* The improvement in these conditions is due probably in chief part to the increased output of the purin substances through the kidney, but in part, perhaps, also to its anodyne properties. Weintraud recommends that when using cinchophen in gouty disorders alkalies should be administered simultaneously in order to prevent the precipitation of uric acid in the kidney or bladder. Hanzlik and Scott (*J. A. M. A.,* 1921, lxxvi, 1728) have shown that large doses of cinchophen produce the same type of relief in *rheumatic* fever as is seen from the salicylates, that these quantities of cinchophen caused the characteristic ringing in the ears, nausea, etc., which are seen after full doses of the salicylates and also albuminuria and other evidences of renal irritation. From their observations they conclude that cinchophen is about equally efficient with the salicylates in acute rheumatism and that it is slightly less injurious to the kidney. Barron (*J. A. M. A.,* 1924, lxxxii, 2010) has reported severe circulatory collapse, which he believes an allergy, from a single dose of 15 grains. Mendel (*D. M. W.,* 1922, xlviii, 829) believes that cinchophen exerts an antiphlogistic action in all sorts of inflammatory conditions. This he attributes to an effect on the leucocytes.

In ordinary gouty or rheumatic conditions, phenylcinchoninic acid may be given in doses of from five to fifteen grains (0.3–1 Gm.) three times a day. In rheumatic fever Hanzlik and

Scott administered 1 Gm. (15 grains) every hour until there was evidence of its action, in improvement of the patient's condition or the occurrence of toxic symptoms. They found that partial relief occurred usually after about 4 or 5 such doses and that continued administration produced still more therapeutic effect so that most of their patients received eventually from 10 to 12 Gm. (2½ to 3 drachms). When given in small doses it may be administered in the form of tablet or enclosed in a capsule but when used freely the powder should be stirred up in the water as otherwise it is liable to cause considerable irritation of the stomach.

Dose, from eight to fifteen grains (0.5–1.0 Gm.) three times a day.

CINNAMOMUM. U. S. (Br.)

CINNAMON Cinnam. [Cinnamomum Saigonicum, U. S. P. IX]

" Cinnamon is the dried bark of *Cinnamomum Loureirii* Nees (Fam. *Lauraceæ*). Cinnamon yields not less than 2 per cent. of volatile ether-soluble extractive." *U. S.*

" Cinnamon Bark is the dried inner bark of shoots from the truncated stocks of Cinnamomum zeylanicum, *Breyn.* Obtained from cultivated trees. Imported from Ceylon, and distinguished in commerce as Ceylon cinnamon." *Br.*

Cinnamomi Cortex, *Br.;* Cinnamon Bark; Cortex Cinnamomi; Cannelle, *Fr.;* Zimmt, *G.;* Cannella, *It.;* Canela, *Sp.;* Kurundu, *Cingalese;* Karua Puttay, *Tamil.*

Both *cinnamonum* and *cassia* were terms employed by the ancients, but whether exactly as now understood it is impossible to determine.

From what source the ancients derived their cinnamon and cassia is not certainly known. Neither the plants nor their localities, as described by Dioscorides, Pliny, and Theophrastus, correspond precisely with our present knowledge; but in this respect much allowance must be made for the inaccurate geography of the ancients. It is probable that the Arabian navigators at a very early period conveyed this spice within the limits of the Phœnician and Grecian and subsequently of the Roman commerce.

The three principal varieties of cinnamon are known as Saigon Cinnamon, Ceylon Cinnamon and Cassia Cinnamon. Of these the U. S. P. has favored various ones in its previous editions. At present the U. S. P. recognizes only the Saigon variety and the Br. Ph. only the Ceylon. The genus Cinnamomum is a group of evergreen trees with mostly three-nerved leaves. The flowers which are either perfect or polygamous are of a pale yellow color and borne in panicles.

Cinnamomum Loureirii (Nees), the botanical source of Saigon Cinnamon, is of medium height, native to China and Japan. Its branches are glabrous and bear opposite and alternate, rigid, entire, elliptic to oblong, attenuate-acuminate leaves having a coriaceous texture. The petioles of these are one-half inch or less in length, the blades three to five inches long. The flowers are very small; they were, in the dried state, formerly an article of commerce under the name of *Flores Cassiæ.* The fruit is a berry which adheres to the receptacle.

The *Saigon cinnamon* is collected chiefly from wild trees especially in the mountainous districts of Annam, in French Indo-China. The greater portion of it is from branches and small stems and of good quality, although sometimes chips of the thick trunk bark are mixed with the quills. This variety is called Saigon because it is exported from the city of that name in the southern part of Cochin-China.

Cinnamomum zeylanicum (Nees) is a native of Ceylon and the neighboring Malabar coast. In the wild state it is a tree about 20 or 30 feet high, covered with a thick, scabrous bark. The branches are numerous, strong, horizontal, and declining, and the young shoots are beautifully speckled with dark green and light orange colors. The leaves are 4 to 7 inches long, petiolate, opposite for the most part, coriaceous, entire, ovate or ovate-oblong, obtusely pointed, and three-nerved, with the lateral nerves vanishing as they approach the point. There are also two less obvious nerves, one on each side arising from the base, proceeding towards the border of the leaf, and then quickly vanishing. In one variety the leaves are very broad and somewhat cordate. When mature, they are of a shining green upon their upper surface, and lighter-colored beneath. The tree emits no odor perceptible at any distance. The bark of the root has the odor of cinnamon with the pungency of camphor, and yields this principle upon distillation. The leaves have a spicy odor when rubbed, and a hot taste. A volatile oil has been distilled from them. The petiole has the flavor of cinnamon. The flowers have a disagreeable, fetid odor. The fruit has a terebinthinate odor when opened, and a taste in some degree like that of juniper berries. A fatty substance, called *cinnamon-suet,* is obtained from it when ripe, by bruising it and then boiling it in water, and removing the oleaginous matter which rises to the surface and concretes upon cooling.

The *Ceylon cinnamon* is produced chiefly from cultivated plants, the principal gardens being in the vicinity of Colombo. Here the plant is never allowed to become a tree but by vigorous cutting back is forced to produce a bushy growth of slender stems. The seeds are planted four or five in a hill and the first five or six years the stems are pruned to be straight, then cut down and by coppicing produce a new crop of shoots. The cinnamon harvest commences in May and continues until late in October.

Before decortication the shoots are trimmed up, and the small pieces, when dried, constitute *cinnamon chips.* The bark is divided by longitudinal incisions, of which two are made in the smaller shoots, several in the larger, and is then removed in strips by means of a suitable instrument. The pieces are next collected in bundles, and allowed to remain in this state for a short time, so as to undergo a degree of fermentation, which facilitates the separation of the epidermis. This, with the green matter beneath it, is removed by placing the strip of bark upon a convex piece of wood and scraping its external surface with a curved knife. The bark now dries and contracts, assuming the appearance of a quill. The peeler introduces the smaller tubes into the larger, and connects them also endwise, thus forming a congeries of quills which is about forty inches long. When sufficiently dry, these cylinders are collected into bundles weighing about thirty pounds and bound together by pieces of split bamboo.

The *C. zeylanicum* is also cultivated to a limited extent in some of the West India islands—especially Martinique and Cayenne—and in Brazil. The bark from this source is generally regarded as inferior to that from Ceylon; it is known commercially as *Cayenne cinnamon.* The commercial supplies are imported from Colombo (Ceylon) and Calcutta (India).

Cinnamomum cassia (Nees) Blume is cultivated for the bark, buds and oil of cassia in the southeastern provinces of China. The bark after collection is scraped and dried. It is then made into bundles weighing from ½ to 1 kilo. which are tied with split bamboo, packed into bamboo cases which are then covered with bamboo mats. Very frequently these bundles contain chips and dirt in the center which are obscured from view by long quills on the outside. The commercial supplies of Cassia Cinnamon bark come from China and Calcutta, India. The poorer grades are known as "*Cassia lignea.*" From this tree is derived the spice known as *Cassia buds.* This consists of the calyx surrounding the young ovary. Cassia buds have some resemblance to cloves, and are compared to small nails with round heads. The enclosed ovary is sometimes removed, and they are then cup-shaped at top. They have a brown color, and the flavor of cinnamon.

C. iners Reinw. is distinguished from *C. zeylanicum* by the nervation of its leaves, which are also paler and thinner. It is probably only a variety, not a distinct species. It yields the so-called *wild cinnamon* of Japan. *C. obtusifolium* Nees, growing in Ceylon, Java, and on the mainland of India, is said to have been the chief source of the drug known formerly by the name of *Folia Malabathri* and consisting of the leaves of different species of Cinnamomum mixed together. *C. Culilawan* Blume of the Moluccas yields the aromatic bark called culilawan, noticed in Part II of this work; and similar barks are obtained from *C. Sintoc* of Java. *Massoy bark,* from which an aromatic volatile oil is obtained called *oil of massoy,* is the product of *Sassafras Goesianum* Leijom. In the mountains of Eastern Bengal, at a height of 1000 to 4000 feet, flourish *C. obtusifolium* Nees, *C. pauciflorum* Nees, and *C. Tamala* Nees et Ebern., and these, with other unknown species, afford quantities of bark which are shipped from Calcutta, Java, Timor, etc., to Europe under the name of *wild cassia.* The bark of the *C. pedatinervium* Meissn., a tree indigenous to Fiji, yields nearly one per cent. of a white aromatic volatile oil, with a pungent spicy taste. For constitution, etc., see *Proc. Chem. Soc.,* xix. These barks are mostly highly aromatic, resembling cinnamon more or less closely in flavor, and are distinguished by yielding to cold water an abundant mucilage. Holmes described the bark of *C. pedativum* Meis., and concludes that it might be of value as a source of safrol and linalool in *P. J.,* 1904, p. 892.

Description and Physical Properties.—"*Unground Cinnamon.*—In quills up to 30 cm. long and 4 cm. in diameter, the bark from 0.5 to 3.0 mm. in thickness, or in broken irregular pieces or in flattened slabs up to 8 mm. in thickness; the outer surface light brown to dark purplish-brown, with grayish patches of crustose lichens and numerous bud-scars, finely wrinkled when from young twigs, otherwise, more or less rough from corky patches surrounding the lenticels; inner surface reddish-brown to dark brown, granular and slightly striate; fracture short; odor characteristic and aromatic; taste sweetish, aromatic and pungent.

"*Structure.*—A narrow outer layer of more or less lignified cork cells followed by a layer of starch-bearing parenchyma with scattered stone cells and a nearly continuous zone of stone cells among which are small groups of bast-fibers with thickened and slightly lignified walls; inner bark with medullary rays 1 to 3 cells wide, inconspicuous sieve tissue, bast-fibers in groups of 2 to 20, mucilage and oil cells numerous and about the size of the parenchyma cells; parenchyma cells usually filled with starch or containing very small raphides of calcium oxalate; the lumina of parenchyma cells, stone cells and bast-fibers frequently filled with an amorphous reddish-brown substance, which is for the most part insoluble in the ordinary reagents. In the bark of the young twigs there is an epidermal layer with a thick, yellowish cuticle, fewer stone cells in the zone associated with bast-fibers, the inner bark narrower and with fewer secretion cells than in the older bark.

"*Powdered Cinnamon.*—Yellowish- or reddish-brown; starch grains numerous; single and 2- to 4-compound, the single grains from 0.005 to 0.025 mm. in diameter; stone cells irregular in shape, occasionally with one wall much thinner than the other walls, sometimes containing starch; bast-fibers from 0.3 to 1.5 mm. in length, with very thick and slightly lignified walls; parenchyma cells with reddish-brown walls; oil cells and mucilage cells not readily distinguishable.

"**Assay.**—Proceed as directed under volatile ether-soluble extractive.

"Preserve in tightly-closed containers." *U. S.*

According to Siebold, the bark of the large branches is of inferior quality and is rejected;

that from the smallest branches resembles the Ceylon cinnamon in thickness, but has a very pungent taste and odor, and is little esteemed, while the intermediate branches yield an excellent bark, about 2 mm. in thickness, which is even more highly valued than the cinnamon of Ceylon, and yields a sweeter and less pungent oil.

Ceylon cinnamon occurs "in closely rolled quills, each about nine millimetres in diameter, and containing numerous smaller quills or channelled pieces. Dull, pale yellowish-brown, darker on the inner surface; thin, brittle and splintery; entirely free from cork; marked with small scars or holes and with faint, shining, wavy longitudinal lines. The powdered Bark exhibits abundant parenchymatous tissue with brown cell-walls, isolated bast-fibers not more than 30 microns in diameter, small simple or compound starch grains and thick-walled sclerenchymatous cells, but no cork or fragments of wood. Fragrant odor; taste warm, sweet and aromatic. Ash not more than 5 per cent." *Br.*

"Under the microscope, sections of Ceylon Cinnamon usually show no cork but an almost continuous outer layer of stone cells, among which are small groups of bast-fibers resembling those found in *Saigon Cinnamon;* in the inner bark occur numerous bast-fibers singly or in small groups, medullary rays 1 to 2 cells in width, usually with raphides of calcium oxalate; parenchyma with either reddish-brown contents or more or less filled with starch grains; scattered throughout the parenchyma occur oil secretion cells and mucilage cells. The powder is light brown or yellowish-brown; starch grains numerous, varying from spherical to polygonal, from 0.003 to 0.02 mm. in diameter, frequently in small aggregates; bast-fibers from 0.3 to 0.8 mm. in length, usually single, spindle-shaped, with attenuated ends, the walls being very thick and but slightly lignified; colorless stone cells resembling those of *Saigon Cinnamon;* numerous cellular fragments with yellowish-brown walls or contents; cork cells few or none; calcium oxalate in raphides, from 0.005 to 0.008 mm. in length. Ceylon Cinnamon yields not less than 0.5 per cent. of volatile extractive soluble in ether." *U. S. IX.*

When distilled Ceylon Cinnamon affords but a small quantity of essential oil, which, however, has an exceedingly grateful flavor. It is brought to this country from England, but it is costly. The inferior sorts are browner, thicker, less splintery, and of a less agreeable flavor, and are little if at all superior to the best Chinese. The finer variety of *Cayenne cinnamon* approaches in character that above described, but is paler and in thicker pieces, being usually collected from older branches. That which is gathered very young is scarcely distinguishable from the cinnamon of Ceylon.

Chinese cinnamon, or *Cassia* (*Cinnamomum Cassia,* U. S., 1890), occurs in quills, usually single, sometimes double, very rarely more than double, from 30 to 60 cm. long, 2 to 5 cm. wide, and 0.2 to 3 mm. thick. In some instances the bark is rolled very much upon itself, in others is not even completely quilled, forming segments more or less extensive of a hollow cylinder. It is of a redder or darker color than the finest Ceylon cinnamon, thicker, rougher, denser, and breaks with a shorter fracture. It has a stronger, more pungent and astringent but less sweet and grateful taste, and though of a similar odor, is less agreeably fragrant. It is the kind almost universally kept in our shops. Under the name of cassia have also been brought to us very inferior kinds of cinnamon, collected from the trunks or large branches of the trees, or injured by want of care in keeping, or perhaps derived from inferior species. It is said that cinnamon from which the oil has been distilled is sometimes fraudulently mixed with the genuine. These inferior kinds are detected, independently of their greater thickness and coarseness of fracture, by their deficiency in the peculiar sensible properties of the spice. Chinese cinnamon is "in quills of varying length and about 1 mm. or more in thickness; nearly deprived of the corky layer, yellowish-brown; outer surface somewhat rough; fracture nearly smooth; odor fragrant; taste sweet, and warmly aromatic." *U. S.* 1890. Cassia is no longer official in the U. S. P., it having been dropped at the 8th Revision.

Powdered cinnamon is often grossly adulterated with sugar, ground walnut shells, galanga rhizome and various other substances. Galanga, according to Schmitz-Dumont, may be detected by the presence of small club-shaped, rod-shaped, partly bent, microscopic pieces of resinotannol. (*Zeit. oeff. Chem.*, 1903, No. 2.) Powdered cassia buds are frequently added to the inferior cinnamon powders, but can hardly be looked upon as an adulterant, as they contain a larger proportion of volatile oil than the lower grades of cinnamon.

The *Pharmacographia* gives the following tests for distinguishing powdered cassia from powdered cinnamon, and for recognizing the inferior varieties of cassia. Make a decoction of powdered cinnamon of known genuineness, and one of similar strength of the suspected powder; when cool and strained, test a fluidounce of each with one or two drops of tincture of iodine. A decoction of cinnamon is but little affected, but in that of cassia a deep blue-black tint is immediately produced. The cheap kinds of cassia known as *cassia vera* may be distinguished from the more valuable Chinese cassia as well as from cinnamon by their richness in mucilage; this can be extracted by cold water; it is a thick glairy liquid, giving dense ropy precipitates with corrosive sublimate or neutral lead acetate, but not with alcohol.

The coarser cassia bark, or *cassia lignea,* usually has some of the external or corky layer adherent to it, and always the parenchymatous mesophlœum or middle bark, but the inner bark constitutes the chief mass. Isolated bast fibers and thick-walled stone cells are scattered even through the outer layers of a transverse section. In the middle zone they are numerous, but do not form a coherent sclerenchymatous ring as in Ceylon cinnamon. The innermost part of the bast shares the structural character of cinnamon, with differences due to age, as, for instance, the greater development of the medullary rays. Oil cells and mucilage cells are likewise distributed among the parenchyma of the former. The finest cassia or Chinese cinnamon has the three layers described in Ceylon cinnamon, but is distinguished by the adherent outer parenchymatous and suberous layer. For an excellent description of the microscopical structure of the commercial cinnamon see Winton and Moeller, "*The Microscopy of Vegetable Foods.*" Spaeth gives the microscopical characteristics of the several kinds of cinnamon, discusses the adulterants of powdered cinnamon and the means of detection in *Ph. Centralh.*, 1908, pp. 724, 729. Rosenthaler and Reis give an excellent pharmacognostical study of Seychelles Cinnamon in *B. P. G.*, 1909, p. 490.

The chief substitute and adulterant for both Saigon and Cassia barks within recent years has been the *Fagot* or *Batavia cassia.* This bark is obtained from *Cinnamomum Burmanni* Blume, a tree native to Java and probably other East India islands. It occurs mostly in double quills that are scraped, up to 3 mm. thick, light-brown to reddish externally, extremely mucilaginous and less aromatic than the other 3 main varieties. The powdered bark, unlike the other cinnamon barks described, forms a shiny mass in water and may also be distinguished from these by the presence therein of tabular and prismatic crystals of calcium oxalate.

R. Windisch reports that in the case of nine samples of cinnamon bark, which he examined four yielded an ash, dark-brown in color, which was shown to contain considerable iron. The ash in these samples varied from 6 to 10 per cent. as compared with 2.11 per cent. in normal samples. The addition was found to consist of iron ochre, from 6 to 10 per cent. of this material having been added. (*Ztsch. Unters. Nahr.-u. Gennssm.*, 41, 1921, p. 78.)

Constituents.—Cinnamon bark contains from 0.5 to 1.0 per cent. of a peculiar essential oil (see *Oleum Cinnamomi*), some gum, a coloring matter and a tannin of the variety which gives blue-black precipitate with ferric salts. Thornton (*A. J. P.*, 1895, 400) has examined the tannin of *C. Cassia.* He found it to amount to about 3.90 per cent., as an average of three different determinations on different samples. He found it impossible to extract the tannin by any one of several methods tried, and concludes that it either has the phlobophene (anhydride) character as it exists in the drug or acquires such character when brought into contact with water. Bucholz found in 100 parts of *cassia lignea* 0.8 of volatile oil, 4.0 of resin, 14.6 of gummy extractive (probably including tannin), 64.3 of lignin and bassorin, and 16.3 of water, including loss.

Assay.—As the therapeutic value of cinnamon depends upon the volatile oil, of which the most important ingredient is cinnamic aldehyde, Fellenberg (*D. C.*, 1916, lx, 755) has suggested the *assay* of cinnamon for this aldehyde by the following process: 1 Gm. of the powdered bark is heated with 40 cc. of alcohol for ten minutes in a flask provided with a reflux condenser. The alcohol is then distilled until about 30 cc. is obtained, when 100 cc. of water is added to the flask and distillation continued until the distillate measures 100 cc.; 5 cc. of this distillate are mixed with 2 cc. of a 5 per cent. alcoholic solution of isobutyl alcohol and 3 cc. of 38 per cent. alcohol. To this is added 20 cc. of concentrated sulphuric acid and allowed to stand for forty-five minutes. The color produced is compared with that of a 2 per cent. solution of cinnamic aldehyde in 38 per cent. alcohol produced by the same method. He found the proportion of cinnamic aldehyde in Ceylon cinnamon to be from 1.3 to 1.8 per cent. and in Chinese cinnamon from 1.25 to 2.77 per cent. (For another method of assaying cinnamon see Lanten Schläger, *A. Pharm.*, 1918, cclvi, 87.)

Uses.—Cinnamon is among the most grateful and efficient of the aromatics. It is warm and cordial to the stomach, carminative, distinctly astringent, and, like most other substances of this class, more powerful as a local than as a general stimulant. It is seldom prescribed alone, though, when given in powder or infusion, it will sometimes allay *nausea,* check *vomiting,* and relieve *flatulence.* It is chiefly used as an adjuvant, and enters into a great number of official preparations. It is often employed in *diarrhea,* in connection with chalk and astringents.

Dose, of powder, ten to twenty grains (0.65 to 1.3 Gm.).

Off. Prep.—Aqua Cinnamomi, *Br.;* Pulvis Cinnamomi Compositus, *Br.;* Pulvis Cretæ Aromaticus, *N. F.*, *Br.;* Tinctura Cardamomi Composita, *Br.;* Tinctura Cinnamomi, *N. F.*, *Br.;* Tinctura Lavandulæ Composita, *U. S.*, *Br.;* Pulvis Aromaticus, *U. S.;* Tinctura Cardamomi Composita, *U. S.;* Tinctura Lavandulæ Composita, *U. S.;* Elixir Taraxaci Composita (from Tincture), *N. F.;* Syrupus Cinnamomi, *N. F.;* Tinctura Aromatica, *N. F.*

COCAINA. U. S., Br.

COCAINE Cocain.

"An alkaloid [$C_{17}H_{21}O_4N$] obtained from the leaves of *Erythroxylon Coca* Lamarck and other species of *Erythroxylon* (Fam. *Erythroxylaceæ*)." *U. S.* "Cocaine, $C_{17}H_{21}NO_4$, is an alkaloid obtained from the leaves of Erythroxylum Coca, *Lam.*, and its varieties." *Br.*

Benzoyl-ecgonine-methyl-ester; Benzol-methyl-ecgonine; Cocainum; Cocaine, *Fr. Cod.;* Cocain, Kokain, *G.*

For description of Coca, from which this alkaloid is obtained, see Part II.

Squibb's process for cocaine and its hydrochloride is as follows: Coarsely ground coca leaves are repercolated with an aqueous five per cent. solution of sulphuric acid, and a very dense, slightly acid percolate is obtained; this is thoroughly agitated with pure coal oil and an excess of sodium carbonate; the liberated alkaloid is retained by the coal oil, and is nearly free from coloring matter; the oily solution is then agitated with acidulated water, and again precipitated by sodium carbonate in the presence of ether. The ethereal solution of cocaine is treated with diluted hydrochloric acid fractionally, and the nearly colorless solutions of cocaine hydrochloride are cautiously evaporated in shallow porcelain pans almost to dryness. The product is in the form of a white, crystalline, granular powder, and is a nearly pure anhydrous salt. (*Ephem.*, 1887, 906.) For Henrique's process see *Proc. A. Ph. A.*, 1895, 999.

Owing to the small yield, it is found more profitable to manufacture cocaine in South America and export it, thus saving the expense of transporting the bulky coca leaves.

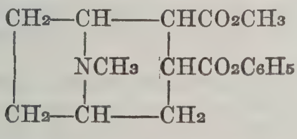
The cocas contain a number of alkaloids which Henry (*Plant Alkaloids*, 1924, p. 95) divides into four groups; (1) the cocaines, (2) pseudotropeines, (3) acylecgonines, (4) hygrines. In the first group is cocaine (methyl benzoyl ecgonine), *cinnamyl-cocaine* (methyl-cinnamoylecgonine), and alpha- and beta-*truxilline*, $C_{38}H_{46}O_8N_2$. Alphatruxilline is also known as *cocamine* and *isatropyl-cocaine.*

The second group comprises one alkaloid, tropacocaine, which is a benzoyl-pseudotropein. This alkaloid is important not merely because of its use in medicine but also because the base *pseudotropine* is isomeric with the base tropine found in atropine. Tropacocaine is described in Part II.

In the fourth group are *hygrine,* $C_8H_{15}ON$, *cuscohygrine,* $C_{13}H_{24}ON_2$ and *betahygrine,* $C_{14}H_{24}ON_2$. These are comparatively simple compounds and are liquid at ordinary temperatures.

With the exception of ecgonine and anhydroecgonine, all of the bodies in the foregoing list are easily decomposable, splitting up when heated to from 80° to 100° C. with hydrochloric acid, or when boiled with alcoholic potassium hydroxide.

Cocaine has the following structural formula:



The characteristic group conferring the anesthetic properties is the benzoyl group.

It may be identified by treatment with strong acids and heating, the decomposition into methyl alcohol and benzoic acid being followed by the production of methyl benzoate with its very characteristic odor. It is easily decomposed by heat in the presence of moisture on solutions of its salts may not be sterilized by heat.

Much of the cocaine used in this country is prepared from the crude alkaloid which is manufactured in the countries where the plant grows. The alkaloids are extracted from the leaves by kerosene or some other cheap immiscible solvent in the presence of an alkali, the alkaloids being separated from the solvent with dilute sulphuric acid from which cocaine is precipitated by sodium carbonate. This crude substance represents about 90 per cent. of cocaine. A good deal of cocaine is manufactured in Germany from the Java coca leaves which contain chiefly cinnamyl cocaine. This alkaloid is hydrolized by boiling with diluted hydrochloric acid and the ecgonine so obtained treated with benzoic anhydride and methyl iodide. The other coca bases may also be converted into cocaine by a similar process as suggested by Liebermann (*B. Chem. G.*, 1888, xxi, 3196).

Description and Physical Properties.—"Colorless crystals, or a white, crystalline powder. It is odorless, and is stable in the air. One Gm. of Cocaine is soluble in about 600 cc. of water, 6.5 cc. of alcohol, 0.7 cc. of chloroform, 3.5 cc. of ether, 12 cc. of olive oil, and in 30 to 50 cc. of liquid petrolatum, at 25° C. One Gm. is soluble in 270 cc. of water at 80° C. It is very soluble in warm alcohol.

"Cocaine melts between 96° an 98° C. Its saturated aqueous solution is alkaline to litmus paper. Its solution in diluted acids is lævorotatory. Heat about 0.1 Gm. of powdered Cocaine with 1 cc. of sulphuric acid for five minutes at 100° C., then cautiously mix with 2 cc. of distilled water: the aromatic odor of methyl benzoate is noticeable and on cooling crystals of benzoic acid separate.

"The ash from 0.5 Gm. is negligible. Dissolve 0.1 Gm. of finely powdered Cocaine in 1 cc. of sulphuric acid: not more than a slightly yellow tint is produced (*readily carbonizable substances*). Dissolve 0.3 Gm. of finely powdered Cocaine in 1 cc. of normal hydrochloric acid, gently warming, if necessary, to aid solution, and dilute with distilled water to 15 cc.: 5 cc. portions of this solution do not respond to the tests for *cinnamyl-cocaine* and for *isoatropyl-cocaine* under *Cocainæ Hydrochloridum.*" *U. S.*

The British Pharmacopœia gives the following description: "In colorless monoclinic prisms. No odor; taste bitter, followed by a sensation of tingling and numbness. Soluble in 10 parts of *alcohol* (90 per cent.), in 4 parts of *ether,* in 0.5 part of *chloroform,* and in 24 parts of *olive oil;* almost insoluble in *water.* Melting point 98° C. The dry salt obtained by dissolving Cocaine in *water* acidified, with *hydrochloric acid,* and evaporating the solution, responds to the tests described under 'Cocainæ Hydrochloridum.'" *Br.*

Uses.—For most purposes cocaine hydrochloride is preferred to the base, but the latter is used in ointments and oily solution because of its greater solubility in fatty substances. Other salts of cocaine have been used in medicine. *Cocaine borate* has been recommended for ophthalmological uses. *Cocaine hydriodide* which occurs in colorless crystals moderately soluble in water, has been recommended by R. Marcus as being especially suitable for use by cataphoresis for the production of anesthesia. For medicinal uses, see *Cocaine Hydrochloride.*

Dose, one-eighth to one-fourth grain (0.008–0.016 Gm.).

Off. Prep.—Oleatum Cocainæ, *N. F.;* Unguentum Cocainæ, *Br.*

COCAINÆ HYDROCHLORIDUM. U. S., Br.

COCAINE HYDROCHLORIDE Cocain. Hydrochl. [Cocainum Hydrochloricum P. I.]

"[$C_{17}H_{21}O_4N.HCl$]." *U. S.* "Cocaine Hydrochloride, $C_{17}H_{21}NO_4,HCl$, is the hydrochloride of the alkaloid cocaine." *Br.*

Cocainæ Hydrochloras, *U. S.* 1890; Cocaine Chloride; Hydrochlorate of Cocaine; Cocainæ Chlorhydricum; Chlorhydrate de Cocaine, *Fr. Cod.;* Cocainum hydrochloricum, *P. G.;* Cocainhydrochlorid, *G.;* Cloridrato di Cocaina, *It.;* Cloruro de Cocaina, *Sp.*

For account of sources and chemical structure see under *Cocainæ.*

Description and Physical Properties.—"Colorless, transparent crystals, lustrous leaflets, or a white, crystalline powder. It is odorless and is stable in the air. One Gm. of Cocaine Hydrochloride is soluble in 0.4 cc. of water, 3.2 cc. of alcohol, and in 12.5 cc. of chloroform, at 25° C. One Gm. is soluble in 2 cc. of alcohol at 60° C. It is soluble in glycerin and insoluble in ether.

"Melting point not below 183° C. Add five drops of a solution of chromium trioxide (1 in 20) to 5 cc. of a solution of Cocaine Hydrochloride (1 in 50): a yellow precipitate is produced which redissolves on shaking the mixture. On the addition of 1 cc. of hydrochloric acid, a permanent, orange-colored, crystalline precipitate is formed. A solution of about 0.01 Gm. of Cocaine Hydrochloride in 1 cc. of distilled water yields on the addition of 2 cc. of tenth-normal potassium permanganate a violet, crystalline precipitate which appears brownish-violet when collected on a filter, and shows characteristic, crystalline aggregates under the low power of a microscope. Heat about 0.1 Gm. of powdered Cocaine Hydrochloride with 1 cc. of sulphuric acid for five minutes, then cautiously mix with 2 cc. of distilled water: the aromatic odor of methyl benzoate is noticeable and on cooling crystals of benzoic acid separate. Silver nitrate T.S. produces in an aqueous solution of the salt (1 in 20) a white precipitate insoluble in nitric acid.

"The ash from 0.5 Gm. is negligible. Dissolve 0.5 Gm. of Cocaine Hydrochloride in 1 cc. of sulphuric acid: not more than a slightly yellow tint is produced (*readily carbonizable substances*). A solution of 0.5 Gm. of Cocaine Hydrochloride in 10 cc. of distilled water requires for neutralization not more than 0.5 cc. of fiftieth-normal sodium hydroxide, using one drop of methyl red T.S. as indicator. Mix 5 cc. of an aqueous solution of the salt (1 in 50) with 0.3 cc. of normal sulphuric acid and 0.1 cc. of tenth-normal potassium permanganate: the violet color does not disappear entirely within a half hour (*cinnamyl-cocaine*). Dilute 5 cc. of an aqueous solution of the salt (1 in 50) in a beaker with 80 cc. of distilled water, add 0.2 cc. of ammonia T.S., and stir the solution vigorously during five minutes, occasionally rubbing the sides of the beaker with a stirring rod: a crystalline precipitate of cocaine is formed and the supernatant liquid is clear (*isoatropyl-cocaine*). The presence of 0.5 per cent. of isoatropyl-cocaine will prevent the formation of nearly all of the precipitate, and will cause the supernatant liquid to be milky." *U. S.*

"In colorless prismatic crystals, or a crystalline powder. No odor; taste bitter, followed by a sensation of tingling and numbness. Soluble in 0.5 part of *water,* and in 3 parts of *alcohol* (90 per cent.); insoluble in *olive oil.* Melting point 182° to 186° C. Yields the *reactions* characteristic of chlorides. An aqueous solution is neutral to *litmus,* and when applied to the eye dilates the pupil. When moistened with *nitric acid,* the mixture evaporated to dryness, and 1 millilitre of *alcoholic solution of potassium hydroxide* added, a characteristic odor is evolved, recalling peppermint. The addition of 3 drops of *N/10 solution of potassium permanganate* to a solution of 0.1 gramme of the salt in 5 millilitres of *water* to which 3 drops of *diluted sulphuric acid* have been added, gives a violet color, which, if dust is excluded, does not fade in half an hour (absence of cinnamyl-cocaine and certain other coca alkaloids). If 0.1 gramme is dissolved in 100 millilitres of water in a glass beaker, 0.25 millilitre of *solution of ammonia* stirred in, and the mixture set aside for fifteen minutes, the sides of the beaker being occasionally and not too vigorously rubbed with a glass rod, a crystalline deposit separates, leaving the supernatant liquid clear (limit of amorphous alkaloid). 0.05 gramme dissolves in 1 millilitre of cold *sulphuric acid* or cold *nitric acid* without coloration, but with hot *sulphuric acid* the salt chars, evolving an agreeable odor and yielding a sublimate of benzoic acid. Loses not more than 1 per cent. of its weight when dried at 100° C. No appreciable ash." *Br.*

D. Scherbatschew recommends for differentiating cocaine and several of its commoner substitutes placing three drops of the aqueous solution of the suspected substance on a glass slide and adding one drop, respectively, of each of the following reagents: (1) Ten per cent. solution of NH_3. (2) Ten per cent. solution of KOH. (3) A saturated solution of $NaHCO_3$. Stovaine and holocaine give precipitates with all three reagents; betaeucaine gives only a slight precipitate with KOH and none with the other two; nirvanine gives a precipitate with NH_3 and a slight one with KOH but none with $NaHCO_3$; alypine precipitates decidedly with NH_3 and KOH, but not with $NaHCO_3$; novocaine precipitates with KOH but not with the other two. Cocaine and tropacocaine are identified by Hankin's $KMnO_4$ test.

Alphaeucaine hydrochloride gives a yellow precipitate when 5 cc. of a 1 per cent. solution are treated with three drops of a 5 per cent. solution of chromic acid. Cocaine hydrochloride does not. Betaeucaine hydrochloride when rubbed with dry mercurous chloride and then moistened with alcohol yields no color, cocaine hydrochloride when similarly treated turns grayish black. Holocaine hydrochloride gives in aqueous solution a violet precipitate with calcium hypochlorite, cocaine hydrochloride does not. Cocaine and procaine are distinguished by the potassium permanganate test (see *Procainæ Hydrochloridum*).

Batta and Jenot describe in detail (*Chem. News.*, 1921, cxxiii, 65) a number of tests for distinguishing between cocaine, stovaine and procaine.

Uses.—It is necessary to distinguish clearly between the local and systemic effects of cocaine. When locally applied cocaine is a paralyzant to the peripheral ends of the sensory nerves, and to a lesser degree to the motor nerves, and stimulating to the muscular coats of the blood vessels. As a result of these actions when painted over mucous membranes it causes a blanching of the part and diminished sensation. It produces not only lessened sensibility to pain and touch but also of the acuity of the special senses, thus it diminishes in the mouth the power of taste and in the nose that of smell.

Systemically it is a stimulant to all parts of the central nervous system including the brain, the spinal cord, and the medulla. Its effects upon the brain are shown by an exaltation of the intellectual faculties similar to that which is produced by caffeine. In overdose it produces a delirium somewhat suggesting that of atropine, to which it is chemically related. Its action upon the spinal cord is shown by increased activity of the reflexes but the convulsions which are seen in cocaine poisoning both in the lower animals and in man seem to be due to an action upon the motor area of the brain, rather than to its effect on the cord. The effects on the medullary centers are shown by an increase of the rapidity of the respiration and sometimes also of its depth. After toxic doses the primary stimulation is followed by a depression of the respiratory center. The blood pressure is elevated chiefly through an action upon the vasomotor center, although there is some evidence that it also stimulates the heart. Concerning the changes in the pulse rate there is difference of opinion. According to Reichert (*P. M. J.*, 1902) small doses slow the pulse rate by stimulating the cardio-inhibitory center, moderate quantities increase the rate by depressing the inhibitory mechanism, while after large toxic doses there may be a second slowing of the heart through depression of its motor ganglia. Cocaine in moderate quantities also stimulates both the voluntary and involuntary muscle fibers. It appears also to have some effect upon the nutritive processes since it causes a marked rise in the bodily temperature. Whether this increase in temperature is due to a direct action upon the thermogenic centers or is simply the result of muscular activity, is as yet not definitely settled. When instilled into the eye it causes dilatation of the pupil, usually without paralysis of accommodation. The widening of the pupil seems to be the result of an action upon the peripheral ends of the sympathetic nerve and can be further increased by the instillation of atropine.

Cocaine is used in medicine both as a local and a systemic remedy. Internally it is of value as a circulatory and respiratory stimulant and is occasionally of use as a cerebral stimulant or as a tonic. Its employment, however, in any condition which requires prolonged administration of the drug is fraught with so great danger of formation of a habit that it is rarely justifiable. In *narcotic poisonings* the simultaneous stimulation of the respiration, circulation, and cerebrum makes it a remedy of particular value.

The most important use of cocaine is as a local application to mucous membranes either for the purpose of contracting the blood vessels or of lessening sensation. For the former action it is useful to relieve congestions such as *hay fever, coryza,* or *laryngitis,* and to control or prevent *hemorrhage* from the nose and throat. There are two great drawbacks to cocaine in this use, the first that the primary contraction of the blood vessels is liable to be followed by a reactive relaxation, and the second is the ever present peril of habit-formation. As a local anesthetic it is useful in operations on the eye, nose, throat, etc., in painful *hemorrhoids, fissure in ano, vomiting, gastralgia,* and other painful diseases of the mucous membranes. While cocaine passes through all mucous membranes with greater or less ease, the unbroken skin offers a practically impassable barrier. Nevertheless, the drug is often used as a local anesthetic, especially for operative purposes, in all parts of the body. To obtain its action it is necessary that the drug be introduced beneath the skin in some manner; it may be either simply injected hypodermically or introduced into the vicinity of the large nerve trunks, or even injected into the spinal canal. The methods of using cocaine as a local anesthetic are too numerous and complex for consideration in this work and the reader is referred to treatises on Surgery. There is a widespread belief among both pharmacists and physicians that solutions of cocaine cannot be sterilized by heat without danger of decomposition, but a number of chemists have shown that if the solution is not allowed to become alkaline the degree of hydrolysis is insignificant.

Cocaine is also useful for the purpose of dilating the pupil, where paralysis of accommodation is not desired, as for example in ophthalmoscopy.

For local application to mucous membranes an aqueous solution of one of the salts of cocaine, ordinarily the hydrochloride, is usually preferred; Gross, however (*A. E. P. P.*, 1910, lxiii, p. 80) presents evidence that the basic cocaine is a much more powerful anesthetic than its salt and some authorities give preference to oily solutions of basic cocaine.

TOXICOLOGY.—As has been pointed out by Kamenzove (*A. I. P. T.*, 1911, xxi, p. 5) there are two distinct types of cocaine poisoning, one characterized by circulatory failure and the other by neurotoxic symptoms. The first type is usually seen after relatively small doses of the drug in persons who possess an idiosyncrasy against it. The prominent symptoms are pallor of the face, vertigo, nausea, failure of the pulse, and usually more or less complete loss of consciousness. The treatment of this type of poisoning is to place the patient in a horizontal position, give rapidly acting stimulants such as hypodermic injections of ammonia or camphor. Kamenzove believes that these symptoms are due to arterial spasm causing anemia of the brain.

The other group of cocaine poisonings is characterized by delirium, increased reflexes, more or less violent convulsions, the pulse usually being rapid and fairly strong but later may become weak, and syncope and cyanosis may intervene. The delirium is frequently associated with hallucinations and at times the patient may develop a violent mania of even homicidal character, as in a case reported by Mattison. In fatal cases death is usually due to respiratory failure although the circulation is also depressed.

In the treatment of cocaine poisoning, as the alkaloid rarely enters the system through the alimentary canal, emptying the stomach and the use of chemical antidotes is generally not indicated. Eggleston and Hatcher (*J. P. Ex. T.*, 1919, xiii, p. 433) from an experimental study highly recommend, in the treatment of cocaine poisoning, the intravenous injection of epinephrin combined with artificial respiration. Nielsen and Higgins (*J. Lab. Clin. M.*, 1923, viii, 440) finds that pituitary solution exercises both a preventive and curative effect. In the convulsive type of poisoning, Tatum (*J. A. M. A.*, 1925, lxxxiv, 1177) finds that the intravenous injection of barbital sodium is of much value provided it is administered promptly. The assertion that calcium chloride is antidotal to cocaine has been shown erroneous by Weiss (*J. A. M. A.*, 1923, lxxxi, 1282).

The habitual use of cocaine as a narcotic stimulant has reached an extent of sociological importance. In the United States the conditions under which it may be prescribed or dispensed are strictly limited both by Federal and, in many states, by state laws. (See *U. S. Pub. Health Rep.*, 1916, xxxi, and 1924, xxxix.) The cocaine habit is not only one of the most seductive but also one of the most rapidly injurious and difficult of eradication of all drug habits. The characteristic symptoms are changes in the mental and moral qualities, especially characterized by alternate periods of exaltation and depression, loss of appetite and of weight, peculiar pallor of the skin, insomnia, and general failure of health. A symptom which is seen in many cases and is said to be characteristic of chronic cocaine poisoning, is a sensory hallucination, as of some foreign body under the skin or of insects crawling over the person.

Dose, of the salts of cocaine, from one-fourth to one-half grain (0.016–0.03 Gm.).

Off. Prep.—Injectio Cocainæ Hypodermica, *Br.;* Lamellæ Cocainæ, *Br.;* Trochiscus Krameriæ et Cocainæ, *Br.*

COCCULUS. N. F.

COCCULUS [Fish Berry, Cocculus Indicus, Indian Bevy]

"Cocculus is the dried ripe fruit of *Anamirta Cocculus* (Linné) Wight et Arnott (Fam. *Menispermaceæ*). Cocculus contains not more than 2 per cent. of foreign organic matter." *N. F.*

Fish Berry, Indian Berry, Levant Berries; Coque du Levant, *Fr.*; Kokkelskörner, Fischkörner, Tollkörner, *G.*; Oriental Berries.

Anamirta Cocculus (L.) Wight et Arnott is a perennial woody climber with alternate pinnate-reticulate, cordate leaves, axillary panicles of small flowers and red kidney-shaped drupaceous fruits, each containing an urn-shaped seed. It is indigenous to mountainous districts of Southern Asia and the East Indies and particularly abundant along the Malabar coast.

The natives collect the fruits (drupes) from wild plants and dry them in the sun. Most of the drug is sent to Calcutta and Bombay whence it is shipped to London and the United States.

The fruit bears some resemblance to the bay laurel berry, but is not quite so large, and may be distinguished by the fact that in the *Cocculus Indicus* the kernel never wholly fills the shell. When the fruit is kept long, the shell is sometimes almost empty. The Edinburgh College directed that "the kernels should fill at least two-thirds of the fruit."

Description and Physical Properties.—"*Unground Cocculus.*—Reniform, 8 to 13.5 mm. long, 7 to 11 mm. wide and 7 to 10 mm. thick, blackish brown or reddish brown, wrinkled; hilum and micropyle close together; separated by a shallow sinus and connected by an obscure ridge running around the convex side; distinct circular stalk-scar. Pericarp tough, about 1 mm. thick, outer layer brownish, inner layer light yellow enclosing a single seed. Seed whitish yellow, urn-shaped, its longitudinal and transverse sections crescent-shaped, taste bitter, the seed intensely bitter.

"*Powdered Cocculus.*—Brown; numerous fragments of epicarp which become reddish brown on the addition of alkalies; endosperm parenchyma containing many fixed oil globules, aleurone grains up to 0.050 mm. in length, and acicular crystals, the latter soluble in dilute hydrochloric acid and insoluble in water, alcohol, and potassium hydroxide T.S.; numerous thick-walled, mostly non-lignified fibers; tracheæ, spiral." *N. F.*

According to Merck its main constituents are *menispermine, paramenispermine, picrotoxin,* $C_{30}H_{34}O_{13}$, *picrotoxic acid* and *cocculin.*

Picrotoxin, a neutral principle, is found in the seed portion, while the alkaloids menispermine and paramenispermine are found in the fruit wall. According to Tunmann, picrotoxin sublimes mostly at 215° to 225° C. without forming crystals. Heating the sublimate with 5 per cent. ferric chloride solution under the cover glass until bubbles appear, yields, upon cooling, typical pentagonal crystals. For further description of these principles see *Picrotoxin,* Part II.

Uses.—*Cocculus Indicus* is used in India to stupefy fishes. Both its poisonous properties and any therapeutic virtues it may contain depend upon picrotoxin (see Part II). It has been used in medicine for the purpose of destroying vermin in the hair, but it is an extremely dangerous drug. For cases of poisoning see Sozinsky (*M. News,* 1883, xliii, p. 485), Swift (*N. Y. M. J.,* 1897, lxvi, p. 664), and Haines (*P. M. T.,* 1884, xiv, p. 748).

Off. Prep.—Tinctura Cocculi, *N. F.*

COCCUS. U. S., Br.

COCHINEAL

"Cochineal consists of the dried female of the insect *Coccus cacti* Linné (Fam. *Coccidæ*), enclosing the young larvæ." *U. S.* "Cochineal is the dried fecundated insect, Coccus cacti, *Linn.*" *Br.*

Coccionella; Cochenille, *Fr. Cod.;* Scharlachwurm, *G.;* Cochinilla, *Sp.*

The cochineal insect is indigenous to Mexico, Peru and Central America and in general appearance resembles a wood louse. It is usually found upon certain flat-stemmed forms of the Cactus family, chiefly species of *Nopalea.* The red dye found in the remains of the female insect has been long esteemed by the old races in these subtropical countries. Indeed, not only did they appreciate its value, but in order to increase the supplies, the cacti with the insects were successfully cultivated many years before even Cortez landed in Mexico in the early part of the sixteenth century.

The cochineal insect belongs to the order *Hemiptera,* suborder *Homoptera,* family *Coccidæ.* The latter includes the scale-like insects which are characterized by the fact that the wingless female dies shortly after producing her eggs, the latter being covered up by her dead scale-like body. In the case of the cochineal insect the larvæ are found, as will be shown later on, within her inflated body. In the group of the *Coccidæ* we find a number of interesting scale insects. Here we find the lac insect from which stick-lac of commerce is produced, the latter being a resinous substance excreted by the *Coccus* (*Carteria*) *lacca* which inhabit the branches of several tropical trees. From the bodies of these insects also certain coloring agents known as "lac dyes" are produced. China wax, the excretion of an insect known as "Pela" (*Ericerus pela*) is also the product of a scale insect belonging to this family. Comstock states that there are many species of the *Coccidæ* which excrete wax in considerable quantity.

The cochineal insect was first described by Hernandez in 1651. It is ordinarily in scientific works referred to as *Coccus Cacti* Linné. In the eighth edition of the U. S. Pharmacopœia the name was changed to *Pseudococcus Cacti* (Linné) Burmeister. In a "Catalogue of The Coccidæ of the World," Maria E. Fernaldo gives preference to the name *Dactylopius Coccus* Costa. In Pharmacopœial work we are justified, however, in using the Latin title that has been given precedent by usage, namely *Coccus Cacti,* as otherwise we might change the name with each revision as our knowledge of these insects is extended.

The cochineal insect feeds upon various species of the *Cactaceæ,* more especially the Nopal plant, *Nopalea* (*Opuntia*) *coccinellifera* (Mill.) S.-Dyck, a native of Mexico and Peru. It has spread into other parts of South and Central America and has been introduced into the West Indies, East Indies, Canary Islands, Southern Spain, Algeria, and is said to be found in Florida and California.

The cultivation of cochineal is rather simple in a tropical climate, all that is necessary is to have the cochineal insects and the proper cacti. During the rainy season the insects are protected by spreading shelters over the plants on which they are propagated. When the weather conditions have become favorable the insects are "sown" on the cacti in the open fields, where fecundation takes place. After this the females attach themselves to the plant and when their bodies have become swollen from the development of the enormous number of eggs, they are scraped off and killed either by boiling water or by the fumes of burning sulphur. Some of the insects are left behind and deposit their eggs, the female dying after the eggs are laid; these furnish a seed for a new crop.

Kraemer has written an extended monograph on the nature and structure of cochineal (*A. J. P.,* 1913, p. 444), and gives the following facts concerning the life history of the cochineal insect. The female insect is without wings, about 2 mm. in length and consists of from 9 to 12 segments. It is somewhat globular, becoming later distinctly ovoid. In general appearance, as it creeps over the cactus stems, it is convex on the upper, that is the dorsal surface, and somewhat flattened or concave below, that is, on the ventral surface. It is covered with glaucous dust formed of wax. This wax is a protective secretion and is formed as a glandular secretion by the "wax pores" and wax hairs, the anatomy of which has been worked out by Mayer. The antennæ are rather short, consisting of 8 parts. The threadlike beak or proboscis, forming a sucking apparatus, is a very fully developed. There are 3 pairs of legs which in the commercial article do not show more than 3 joints. Projecting from the posterior portion of the abdomen there are 2 short hairs or bristles, which are wanting in the commercial article.

The male is more elongated and ellipsoidal in outline and is provided with 2 transparent wings which reach beyond the extremity of the abdomen and cross each other longitudinally on the back. The head is distinguished from that of the female in being furnished with a rudimentary beak and with 2 long feathery antennæ. It is said that the male insect is reproduced in large numbers; the larvæ in the commercial cochineal does not show this to be the case. As a matter of fact, actually only one male is necessary for about 300 females. Upon performing their functions the male insects die and are blown away. They are therefore never seen in the commercial article.

The female insect after fecundation grows larger as the young larvæ develop, becoming eventually about twice her original size. She meanwhile attaches herself to the surface of the stems of the cacti, her body penetrating into the upper layer of cells. The upper dorsal surface becomes more or less cartilaginous in structure and more or less convex in shape. The lower surface is drawn toward the upper surface and in this membranous cradle the larvæ are developed. It requires about eight days for the larvæ to become full grown, when they are said to resemble the parents with the exception that they are covered with a short hairy coating. In another week they attain maturity and the females of the new generation are ready to form broods in their turn. The life history of the cochineal insect is completed in about six weeks, two weeks being required for the development of the mature insect from the egg; during the next two weeks the female crawls over the fleshy stems of the cacti, the male in the meanwhile being able to fly about; then the female attaches herself to the tissues of the Nopal plants, her body becoming a membranous cradle for the larvæ of the next generation, and after which she dies. From three to five generations of the cochineal insect may be produced in a single year. The first generation usually is richer in coloring matter and is considered the most valuable. It is estimated that from an area of about an acre of Nopal plants approximately 100 kilos of cochineal may be gathered; this would represent about 14,000,000 of the membranous cradles with larvæ, or the dried insects of commerce.

Description and Physical Properties.—"*Unground Cochineal.*—Somewhat ovate in outline, convex above, concave beneath, from 3.5 to 5 mm. in length, consisting of from 9 to 12 segments; externally grayish-purple or grayish; in the shell-like, somewhat horny abdomen lie numerous larvæ less than 1 mm. in diameter; the mature larvæ with 8-jointed antennæ, 3 pairs of legs, the lower having from 6 to 8 segments, and a characteristic beak or rostrum composed of 4 thread-like parts which pair off into 2 coils; easily pulverizable; odor characteristic; taste slightly bitter.

"*Powdered Cochineal.*—Dark red; odor, taste, and structure resembling the unground drug.

"The red color of dilute aqueous solutions of Cochineal is changed to purple with alkalies and to light orange with acids. When whole Cochineal is macerated in water, no insoluble powder separates." *U. S.*

"About five millimetres long; somewhat oval in outline, flat or concave beneath, convex above, transversely wrinkled, purplish-black or purplish-grey; easily reduced to powder, which is dark-red or puce-colored. Macerated in *water*, no insoluble powder is separated. Ash not more than 6 per cent." *Br.*

As found in commerce, the finer cochineal, *grana fina* of Spanish commerce, is in irregularly circular or oval, somewhat angular grains, about one-eighth of an inch in diameter, convex on one side, concave or flat on the other, and marked with several transverse wrinkles. Two varieties of this kind of cochineal are known to the druggist, distinguished by their external appearance. One is of a reddish-gray color, formed by an intermixture of the dark color of the insect with the whiteness of a powder by which it is almost covered, and with patches of a rosy tinge irregularly interspersed. From its diversified appearance, it is called by the Spaniards *cochinilla jaspeada.* It is the variety commonly found in commerce. The other, *cochinilla renegrida,* or *grana nigra,* is dark-colored, almost black, with only a minute quantity of the whitish powder between the wrinkles. The two are distinguished in our markets by the names of *silver grains* and *black grains.* Some suppose the difference to arise from the mode of preparation, the gray cochineal consisting of the insects destroyed by a dry heat; the black, of those destroyed by hot water, which removes the external whitish powder; it is also said that cochineal is blackened by placing the insects with black sand in a bag and swinging backward and forward until some of the juice exudes. According to Faber, who derived his information from a merchant residing in the neighborhood where the cochineal is collected, the silver grains consist of the impregnated female just before she has laid her eggs; the black, of the female after the eggs have been laid and hatched. (*A. J. P.*, xviii, 47.) There is little or no difference in their quality. *Cake cochineal* and *grana sylvestra* are forms which have entirely disappeared from commerce, see *U. S. D.*, 20th ed., p. 365.

Composition.—Cochineal has a faint, heavy odor and a bitter, slightly acidulous taste. Its powder is of a purplish-carmine color, tingeing the saliva intensely red. According to Pelletier and Caventou, it consists of a peculiar coloring principle, a peculiar animal matter constituting the skeleton of the insect, stearin, olein, an odorous fatty acid, and various salts. Tyrosin has also been found by De la Rue, and its presence in cochineal confirmed later on by von Miller and Rohde. (*B. Chem. G.*, xxvi, 2660.) It was also analyzed by John, who called the coloring principle *cochinilin.* It is, however, universally known now as *carminic acid.* Hlasiwetz and Grabowski (*Ann. Ch. Ph.*, cxli, 329) gave it the formula $C_{17}H_{18}O_{10}$, and considered it to be a glucoside, which was decomposed by boiling with diluted sulphuric acid into a non-fermentable sugar and *carmine red,* $C_{11}H_{12}O_7$. The incorrectness of this view has, however, been demonstrated by von Miller and Rohde, who have shown that the purified carminic acid is a dioxymethyl-α-naphthoquinone of the formula $C_{12}H_{11}O_7$, or the double formula $C_{24}H_{22}O_{14}$, and that the carmine red is identical with it. Schunk and Marchlewski (*B. Chem. G.*, xxvii, 2979) have shown that the reason that the carminic acid as freshly extracted from the cochineal gave the apparent glucoside reaction was that it is impure. They prepared the pure crystallized carminic acid, its anilide, and identified its character as a naphthoquinone derivative. Their analysis indicated a composition of $C_{11}H_{12}O_6$. Still more recent work by Liebermann, Höring and Wiedermann (*B. Chem. G.*, 1900, xxxiii, 149) and indicates a formula of $C_{22}H_{22}O_{13}$. Dimroth and Karumerer believe carminic acid to be a derivative of oxyanthra-purpurin and assign the formula $C_{18}H_{20}O_{13}$. It shows no sharp melting point, beginning to decompose at 130° C. Carminic acid is of a brilliant purple-red color, unalterable in dry air, is very soluble in water, soluble in cold and more so in boiling alcohol, insoluble in ether. It may be obtained by macerating cochineal in ether, and treating the residue with successive portions of boiling alcohol, which on cooling deposits a part of the carminic acid, and yields the remainder by spontaneous evaporation. It may be freed from a small proportion of adhering fatty matter by dissolving it in official alcohol and then adding an equal quantity of ether. The pure carminic acid is deposited in the course of a few days. Chlorine readily destroys the carminic acid, and nascent hydrogen reduces it to a leuco body, which again becomes red on exposure to the air.

The aqueous infusion of cochineal is of a violet-crimson color, which is brightened by the acids and deepened by the alkalies. The coloring matter is readily precipitated. The salts of zinc, bismuth, and nickel produce a lilac precipitate, and those of iron a dark purple approaching to black. The salts of tin, especially the nitrate and the chloride, precipitate the coloring matter of a brilliant scarlet, and form the basis of those splendid scarlet and crimson dyes which have rendered cochineal so valuable in the arts. With alumina the coloring matter forms the pigment called *lake* (see *Carmina*).

Cochineal-carmine requires for its production a decoction of cochineal itself, and not of carminic acid, the nitrogenized matters being essential to its formation. Liebermann (*B. Chem. G.*, xviii, p. 1971) considers cochineal-carmine to be no ordinary compound of a coloring matter with alumina, but to be an alumina albuminate of the carmine coloring matter comparable in some respects to the product from alizarin and alumina with "Turkey-red oil." (See also *C. D.*, 1893, 199.)

Liebermann found that the coating of the silver cochineal consisted of a peculiar wax, which he named *coccerin,* $C_{30}H_{60}(C_{31}H_{61}O_3)_2$; this is soluble in benzene, but nearly insoluble in ether. (*P. J.*, 1885, 186.) J. J. Hess proved that if fatty matters found in cochineal were removed by treatment with alcohol, a much more brilliant carmine could be produced. (Dingler, *P. J.*, lxxxviii, 235.) The degree of coloring power in cochineal may be approximately measured by the decolorizing effect produced by solution of potassium permanganate. For a method of applying this process, the reader is referred to a paper by J. M. Merrick, of Boston, in *A. J. P.*, 1871, 263. The Pharmacopœias require that when cochineal is macerated in water no insoluble powder shall be separated, and that when incinerated with free access of air it shall yield not more than 6 per cent. of ash.

Cochineal may be detected when used as a coloring reagent by acidulating the suspected solution with hydrochloric acid, agitating with amyl alcohol, separating the latter solvent and shaking it with an aqueous solution of uranium acetate. Cochineal shows a violet color in the aqueous layer and carmine a green color.

Cochineal has been adulterated by causing certain heavy substances, such as powdered talc, lead carbonate, and barium sulphate, by shaking in a bag or otherwise, to adhere, by means of some glutinous material, to the surface of the insects, and thus increase their weight. This fraud is detectable either by a high percentage of ash or by microscopic examination which shows the absence of a woolly appearance which characterizes the white powder upon the surface of the unadulterated insect. (For other adulterants formerly encountered see *U. S. D.*, 20th ed., p. 366.)

The importations of cochineal have diminished, owing to the gradual replacement of this dye by the newer coal-tar colors.

The commercial supplies used in the United States come chiefly from Teneriffe, an island of the Canaries, and from Mexico.

Uses.—Cochineal was at one time supposed by some to possess anodyne properties, and used in *whooping-cough* and *neuralgia*. At present it is employed only as a coloring agent.

Off. Prep.—Tinctura Cardamomi Composita, *U. S., Br.;* Tinctura Cocci, *Br.;* Liquor Cocci, *N. F.*

COCILLANA. N. F.

COCILLANA Cocillan. [Guapi Bark]

"Cocillana is the dried bark of *Guarea Rusbyi* (Britton) Rusby (Fam. *Meliaceæ*). Cocillana contains not more than 5 per cent. of wood or other foreign organic matter." *N. F.*

Cocillana Bark, Huapi Bark, Trompillo.

The plant yielding Cocillana is a tree indigenous to the upper slopes of the eastern Andes in Bolivia. It possesses leaves which are paripinnate with a bud at the top of the rachis between the last pair of leaflets. Its fruits are pear-shaped when young, becoming nearly spherical when ripe. The bark of this tree was long used by the aborigines of the Andes as an emetico-cathartic. Its use in this country is largely due to its introduction by Dr. H. H. Rusby who, in 1886, first collected it at Guanai, a town on the Mapiri River and for a number of years thereafter was the sole importer in the United States. Since 1908 a substitute Cocillana bark has frequently appeared on the market. The tree yielding this bark is *Guarea Bangii* Rusby as determined by H. H. Rusby who collected specimens in October, 1921, from trees growing at Rurrenabaque, Bolivia. (For description of trees yielding this substitute bark and possible future substitutes see *Bull. Torrey Bot. Club,* 1922, xlix, p. 262.) This substitute may be distinguished from the genuine article by the more reddish cast of its cork, its tougher and more fibrous fracture, the fibers projecting throughout the middle and inner bark, by its smaller stone cells and less numerous crystals. The powdered bark is light chocolate brown whereas that of the genuine article is grayish-brown. (Ballard, *A. Ph. A.,* 1922, xi, p. 781–787.)

Description and Physical Properties.—"*Unground Cocillana.*—In flat or curved pieces of variable length and width up to about 2 cm. thick; outer surface shallowly or deeply fissured, according to age and thickness; gray-brown, often ashy-gray from lichen growths, or of an orange-brown where the cork has been removed; inner surface of medium brown color, strongly and coarsely longitudinally striate, the striæ straight or wavy; inner bark usually much thicker than the outer, its fracture coarsely splintery-fibrous and soft. Odor characteristic; taste slightly astringent, peculiar and slightly nauseous.

"*Structure.*—Outer bark composed of one or more zones of cork alternating with layers composed of parenchyma and isolated stone cells; middle bark composed of starch-containing parenchyma, groups of thick-walled stone cells, and a few bundles of fibers; inner bark with large groups of yellow fibers, surrounded by crystal fibers and separated tangentially by parenchyma and sieve tissue, and radially by wavy medullary rays 1 to 3 cells in width, the latter with porous walls and frequently lignified; many of the medullary ray cells contain reddish amorphous masses, and occasionally starch grains; secretory cells in the middle and inner bark containing a yellowish white granular substance.

"*Powdered Cocillana.*—Light brown; numerous groups of lignified fibers, the individual fibers up to 0.800 mm. in length with nearly straight walls and attenuated ends; crystal fibers, showing prisms of calcium oxalate mostly from 0.010 to 0.025 mm. in length; parenchyma and medullary ray cells with reddish brown contents or starch grains, the latter single and spheroidal, or 2-4 compound, the individual grains measuring from 0.005 to 0.020 mm. in length; stone cells abundant, yellowish, with thick porous walls, angular to irregular in shape, up to 0.150 mm. in length. Many fragments of dark brownish cork tissue." *N. F.*

Cocillana contains a small quantity of an alkaloid, about 2.5 per cent. of resin, 2.5 per cent. of fixed oil and a white crystalline hydrocarbon, melting at 80° C., sublimable with a peculiar aromatic odor.

Uses.—In *doses* of from twenty to fifty grains (1.3–3.2 Gm.) the bark causes vomiting, with prostration and some purging; also, it is said, much sneezing, dull frontal headache, and discharge from the nasal mucous membrane. The therapeutic action of the drug resembles that of ipecac, although as an expectorant it is somewhat more stimulant. (See *N. Y. M. J.,* Dec., 1889, and April, 1890). It has been used in various forms of *bronchitis* with asserted success.

Dose, eight to fifteen grains (0.5–1.0 Gm.).

Off. Prep.—Fluidextractum Cocillanæ, *N. F.*

CODEINA. U. S., Br.

CODEINE Codein. [Methylmorphine]

"An alkaloid [$C_{17}H_{18}(CH_3)O_3N.H_2O$ = 317.19] obtained from opium, or prepared from morphine by methylation." *U. S.* "Codeine, $C_{18}H_{21}NO_3,H_2O$, is an alkaloid obtained from opium or prepared from morphine." *Br.*

Codeia, Methylmorphine; Codeinum, Codéine, *Fr. Cod.;* Codein, Kodein, *G.;* Codeina, *It., Sp.*

Preparation.—*Codeine* was discovered in 1832 by Robiquet in morphine hydrochloride prepared according to the process of Gregory. It exists in opium combined like morphine with meconic acid, and is extracted along with that alkaloid in the preparation of the hydrochloride. (See *Morphina.*) When the solution of the mixed morphine and codeine hydrochlorides is treated with ammonia, the former alkaloid is precipitated, and the codeine, remaining in solution, may be obtained by evaporation and crystallization. It may be purified by treating the crystals with hot ether, which dissolves them and yields the codeine in colorless crystals on spontaneous evaporation. Codeine is the methyl derivative of morphine, as shown in the formula $C_{17}H_{18}(CH_3)O_3N$. It may be formed artificially from morphine by treating this latter successively with methyl iodide and fixed alkali. (Grimaux, 1881, *J. Chem. S.*, xliv, 358.) Codeine may be made also by the following process: Morphine, 285 Gm., and nitrosomethylurethane, 132 Gm., are dissolved in 1 kilo. of methyl alcohol. With the solution is mixed, constantly stirring, a solution made by mixing 50 Gm. of potassium hydroxide in 800 Gm. of methyl alcohol. When the reaction is complete, the methyl alcohol is distilled off, and codeine is extracted from the residue with benzene, from which it afterwards separates in characteristic crystals. (*C. D.*, 1898, 237.)

Description and Physical Properties.—"Colorless, translucent crystals, or a white, crystalline powder. It is odorless, and is slightly efflorescent in warm air. One Gm. of Codeine is soluble in 120 cc. of water, 2 cc. of alcohol, 0.5 cc. of chloroform, 18 cc. of ether, and in 13 cc. of benzene, at 25° C. One Gm. is soluble in 1.2 cc. of alcohol at 60° C.

"When heated in an amount of water insufficient for complete solution, Codeine melts to oily drops, which crystallize on cooling. Codeine rendered anhydrous by drying at 80° C. melts between 154° and 156° C. A saturated, aqueous solution of Codeine is alkaline to litmus paper, and is lævorotatory. Sulphuric acid, containiny 0.005 Gm. of selenous acid in each cc. produces with Codeine a green color, which changes rapidly to blue, then slowly back to green. Dissolve about 0.01 Gm. of Codeine in 5 cc. of sulphuric acid, add a drop of ferric chloride T.S., and warm: the solution becomes blue, changing to red on the addition of a drop of nitric acid.

"When dried to constant weight at 80° C., Codeine loses not more than 6 per cent. of its weight (*water*). The ash from 0.5 Gm. is negligible. About 0.01 Gm. of Codeine dissolves in 5 cc. of sulphuric acid (free from nitrous compounds without producing other than a transient, pinkish tint (*readily carbonizable substances*). Dissolve about 0.05 Gm. of potassium ferricyanide in 10 cc. of distilled water, add 1 drop of ferric chloride T.S. and 1 cc. of a neutral or slightly acid, aqueous solution of Codeine (1 in 100) made with the aid of sulphuric acid: no blue color is produced at once (*morphine*).

"Preserve in well-closed containers, protected from light." *U. S.*

"Colorless or nearly colorless crystals. Soluble in 80 parts of *water,* and in 80 parts of *solution of ammonia,* readily soluble in *alcohol* (90 per cent.), and in *chloroform.* The aqueous solution has a bitter taste and an alkaline reaction. Melting point 155° to 156° C. 0.1 gramme dissolves in 1 millilitre of cold *sulphuric acid* without coloration or with the production at most of a faint pink tinge; but when the solution is gently warmed with a trace of *ammonium molybdate* or of *ferric chloride* a deep bluish-violet color is developed which, on the addition of a drop of *diluted nitric acid,* changes to scarlet and finally orange. When a little of the powdered alkaloid is sprinkled on *nitric acid* the liquid becomes yellow but not red (distinction from morphine). A saturated aqueous solution, acidified with *hydrochloric acid,* gives no blue color, but only gradually a dull green, on the addition of diluted *T. Sol. of ferric chloride* and very dilute *solution of potassium ferricyanide* (absence of morphine). A solution (1 in 50) in *water* acidified with *hydrochloric acid* yields a white precipitate with *solution of sodium hydroxide* but not with *solution of ammonia.*" *Br.*

When added in excess to boiling water, the undissolved portion melts and sinks to the bottom, having the appearance of an oil. It may be separated from morphine by a solution of potassium or sodium hydroxide, which dissolves the morphine and leaves the codeine. It has an alkaline reaction on test paper, and combines with acids to form salts, some of which are crystallizable. Its capacity of saturation is almost identical with that of morphine. According to Robiquet, 1 part of hydrochloric acid is saturated by 7.837 of codeine, and by 7.88 of morphine. It is distinguishable, however, from the latter principle by the different form of the crystals, which are octahedral, by its solubility in boiling ether, greater solubility in water, and insolubility in alkaline solutions, and by not assuming a red color with nitric acid, or a blue one with ferric salts. Tincture of galls precipitates from its solutions a codeine tannate. Crystallized from an aqueous solution, it contains about 6 per cent. of water, which is driven off at 100° C. The crystals obtained from a solution in ether contain no water.

Uses.—Codeine resembles morphine in its general physiological action. Von Schroeder (*A. E. P. P.*, 1883, xvii) has shown that it heightens the reflex activity of the spinal cord. It also exerts a depressant effect on the higher cerebral centers; Macht (*J. P. Ex. T.*, 1916, viii, p. 1) has shown that it lowers the threshold of pain perception, the efficient dose being approximately 3 or 4 times as large as that of morphine. Its sedative action upon the respiratory center is similar in type to that of morphine, although it requires, according to the observations of Macht (*J. P. Ex. T.*, 1915, viii, 339), almost ten times as much codeine as it does morphine to produce a corresponding effect.

Like morphine it also tends to increase the tone of unstriped muscle tissue (Macht, *J. P. Ex. T.*, 1918, xi, 389). Its narcotic action differs in type from that of morphine, especially in the fact that it is much less likely to give rise to habit.

It has been highly lauded in the treatment of *diabetes mellitus,* and cases of recovery under its use reported. In the grave form of this disorder we have seen it fail to exert any perceptible influence, but the evidence is sufficient to demand a fair trial of the remedy in any individual case. Medical practitioners often use it to quiet *cough,* to allay *intestinal pain,* and to fulfil various other of the minor narcotic indications for which opium is commonly administered. Although less efficient than morphine it has the advantage of being less constipating and less liable to habit formation. On account of its frequent contamination with morphine, care should be exercised as to the commencing dose, but no marked effect is to be expected, if the alkaloid be pure, from less than one grain (0.065 Gm.), and this dose may be rapidly increased until some symptoms are produced. It may be given in pill or in syrupy solution.

The symptoms of codeine *poisoning* in man differ considerably from those of morphine. There is usually narcosis, sometimes preceded by a feeling of exhilaration and followed by convulsions. In most of the reported cases nausea and vomiting have been prominent symptoms and there has also been evidence of circulatory depression. The pupils are contracted, the pulse rate usually increased. We are not familiar with any case of fatal codeine poisoning, but alarming symptoms have followed the ingestion of 4 grains (Myrtle, *B. M. J.*, 1874), and Boissonnas (*R. M. S. R.*, 1919, xxxix, 581) reports a case of violent poisoning in a child of 3 years from 0.04 Gm. ($\frac{3}{5}$ of a grain). The treatment of codeine poisoning should be along the same lines as that of morphine poisoning.

Dose, one-fourth to two grains (0.015–0.13 Gm.).

Off. Prep.—Elixir Terpini Hydratis et Codeinæ, *N. F.*

CODEINÆ PHOSPHAS. U. S., Br.

CODEINE PHOSPHATE Codein. Phos.

"Codeine Phosphate [$C_{17}H_{18}(CH_3)O_3N.H_3PO_4.2H_2O$] contains not less than 67 per cent of anhydrous codeine ($C_{17}H_{18}(CH)_3O_3N$)." *U. S.* "Codeine Phosphate, $C_{16}H_{21}NO_3,H_3PO_4,2H_2O$, is the phosphate of the alkaloid codeine." *Br.*

Phosphate de Codéine, *Fr.;* Codeïnum phosphoricum, *P. G.;* Kodeinphosphat, Phosphorsaures Kodein, *G.*

This salt has been introduced because of its easy solubility and stability; it may be made by dissolving 1 part of codeine in 1.25 parts of 25 per cent. phosphoric acid (the solution should be slightly acid in reaction); sufficient alcohol is added to precipitate the codeine phosphate. On account of its large percentage of codeine (about 70 per cent.) it is well fitted for hypodermic injections.

Description and Physical Properties.—"Fine, white, needle-shaped crystals, or a white, crystalline powder. It is odorless. Codeine Phosphate readily loses water on exposure to air. One Gm. of Codeine Phosphate is soluble in 2.3 cc. of water, 325 cc. of alcohol, 4500 cc. of chloroform, and in 1875 cc. of ether, at 25° C. One Gm. is soluble in 0.5 cc. of water at 80° C., and in 125 cc. of boiling alcohol.

"An aqueous solution of Codeine Phosphate (1 in 20) is acid to litmus paper. It responds to the identity tests with selenous acid, ferric chloride and nitric acid under *Codeina.* In an aqueous solution of Codeine Phosphate neutralized with ammonia water, silver nitrate T.S. produces a yellow precipitate, which is soluble in diluted nitric acid and in ammonia water.

"Separate portions of 10 cc. each of an aqueous solution of Codeine Phosphate (1 in 100) show no turbidity at once on the addition of a few drops of barium chloride T.S. (*sulphate*), and no opalescence with a few drops of silver nitrate T.S. (*chloride*). Codeine Phosphate complies with the test for *morphine* under *Codeina.*

"**Assay.**—Dissolve about 0.5 Gm. of Codeine Phosphate, accurately weighed, in 10 cc. of distilled water, in a separator, add 10 cc. of sodium hydroxide T.S., and extract the codeine by shaking with four successive portions of 15 cc., 10 cc., 10 cc., and 5 cc. of chloroform, or a sufficient quantity to complete the extraction. Shake the combined chloroform solutions with 5 cc. of distilled water, and completely separate the chloroform from the aqueous layer. Evaporate the chloroform almost to dryness on a water bath, dissolve the residue by warming with 15 cc. of tenth-normal sulphuric acid, heat the solution on the water bath until the odor of chloroform is no longer evolved, cool, dilute with about 10 cc. of distilled water, and titrate the excess of acid with tenth-normal sodium hydroxide, using 2 drops of methyl red T.S. as indicator. Each cc. of tenth-normal sulphuric acid corresponds to 0.02993 Gm. of anhydrous codeine ($C_{18}H_{21}O_3N$).

"Preserve in well-closed containers, protected from light." *U. S.*

"White efflorescent crystals. Taste slightly bitter. Soluble in 3.5 parts of *water.* An aqueous solution (1 to 20) has a slightly acid reaction and yields a white precipitate with *solution of sodium hydroxide,* but not with *solution of ammonia.* Loses its water of crystallisation at 100° C. Yields the *reactions* characteristic of phosphates, and responds to the color-tests described under 'Codeina.'" *Br.*

Uses.—The medicinal properties of codeine phosphate are the same as those of codeine.

Dose, one-fourth to two grains (0.015–0.13 Gm.).

Off. Prep.—Syrupus Codeinæ Phosphatis, *Br.*

CODEINÆ SULPHAS. U. S.

CODEINE SULPHATE Codein. Sulph.

"$[C_{17}H_{18}(CH_3)O_3N]_2H_2SO_4.5H_2O$." *U. S.*

Codeinum sulfuricum; Sulfate de Codéine, *Fr.;* Kodein ulfat, Schwefelsaures Kodein, *G.*

Preparation.—Codeine sulphate may be made by dissolving codeine in warm water, adding sufficient sulphuric acid to neutralize, evaporating and crystallizing; 16.71 Gm. of sulphuric acid of official strength will be required to neutralize 100 Gm. of codeine.

Description and Physical Properties.—"Long, glistening, white, needle-shaped crystals or rhombic prisms, or a crystalline powder. It is odorless, and is efflorescent in the air. One Gm. of Codeine Sulphate is soluble in 30 cc. of water and in 1280 cc. of alcohol, at 25° C. One Gm. is soluble in 6.5 cc. of water at 80° C. and in 440 cc. of alcohol at 60° C. It is insoluble in chloroform and in ether. It responds to the identity tests with selenous acid, ferric chloride and nitric acid under *Codeina.* Barium chloride T.S. produces in an aqueous solution of the salt a white precipitate which is insoluble in hydrochloric acid.

"When dried to constant weight at 100° C., Codeine Sulphate loses not more than 12 per cent. of its weight (*water*). The ash from 0.5 Gm. is negligible. A solution of 0.5 Gm. of Codeine Sulphate in 15 cc. of distilled water requires not more than 0.3 cc. of fiftieth-normal sodium hydroxide for neutralization, using one drop of methyl red T.S. as indicator. Codeine Sulphate complies with the tests for *morphine* and *readily carbonizable substances* under *Codeina.*

"Preserve in well-closed containers, protected from light." *U. S.*

Uses.—The medicinal properties of this salt are those of the alkaloid codeine.

Dose, one-fourth to two grains (0.015–0.13 Gm.).

COFFEA TOSTA. N. F.

COFFEE Coff. Tost. [Roasted Coffee]

"Coffee is the dried ripe seed of *Coffea arabica* Linné or *Coffea liberica* Bulliard (Fam. *Rubiaceæ*), deprived of most of the seed coat and roasted until a dark brown color and characteristic aroma are developed. Coffee yields not less than 1 per cent. of caffeine, not less than 3 per cent. and not more than 5 per cent. of total ash, and not less than 10 per cent. of fat." *N. F.*

Coffee, Semen Caffeæ; Kaffee, *G.;* Café, *Fr.;* Caffe, *It.;* Café, *Sp.;* Bun, *Ar.;* Copi Cotta, *Cingalese;* Kaeva, *Malay.*

Coffea arabica L. and *C. liberica* Bull. are small evergreen trees with opposite, oblong-ovate, acuminate leaves of leathery texture, axillary clusters of white, tubular flowers and globular, red to purplish, berry fruits. The coffee berries are about the size of a cherry. Each of these consists of a 2-celled pericarp surrounding 2 plano-convex seeds. The seeds are longitudinally grooved on their plane surfaces and enveloped by a thin membranous endocarp called "parchment." Between each seed and the parchment is a thin covering called "silver-skin." When divested of their coverings they constitute coffee. *Coffea arabica* is indigenous to Abyssinia, while *C. liberica* is native to Liberia. *C. robusta* has recently been cultivated in Java. For description see Vichoever and Lepper (*J. Assoc. Off. Agr. Chem.,* 1921, v, 274).

About the year 1690 coffee was introduced by the Dutch from Arabia into Java, and in 1718 into their colony of Surinam. Soon after this latter period the French succeeded in introducing it into their West India islands, Cayenne, and the Isles of France and Bourbon. Within a comparatively short time coffee cultivation was taken up by many other tropical countries of the western hemisphere.

To-day the coffee plants are extensively cultivated in Arabia, Java, South America, Central America, Mexico, West Indies, India and Hawaii. Brazil and Java are the largest producers, Brazil giving to the world about 80 per cent. of all the coffee produced.

The coffee trees are grown from seeds which, when sown in properly prepared soil, germinate in less than a month. Within a year the young plants are transplanted and set out at suitable distances. They yield mature fruits in two or three years but generally require five years before bearing a good crop and continue to be productive for thirty to thirty-five years. Two crops are generally harvested each year. The fruits are gathered when fully mature and prepared for the market by either the dry or wet methods.

The dry method is the more primitive and at present almost restricted to Arabia which yields much of the Mocha coffee. It consists of spreading the fruits out in a thin layer on a drying floor and exposing them to the drying action of the sun. Later the pulp and parchment are removed, liberating the two seeds contained in each fruit. In the wet or West Indian method which is the one now most generally employed, the fruits are placed in a tank of water. The mature fruits sink and are drawn through pipes to a pulping machine where the fleshy portion is reduced to a pulp, and the pulp and free seeds, enclosed in their membranes, conveyed to a second tank of water. Here they are stirred, the pulp being separated by washing and the seeds sinking to the bottom. The parchment membranes are removed by allowing them to slightly ferment and by washing, accompanied by trampling with bare feet and stirring. The seeds are then dried in trays, or barbecues, by natural or artificial heat. In this condition they constitute "raw coffee." They are subsequently graded by passing them through sieves having large, medium and small apertures. They are then garbled to remove split or otherwise defective seeds and foreign matter. They are usually packed in bags and imported in the unroasted condition.

The finest coffee grown is that commercially known as "Java coffee" from the East Indies, mostly from Sumatra. *Mocha* coffee is a sharp, aromatic type which is grown in Arabia; little of it comes to this country. The chief varieties or types of coffee grown in Brazil are those designated commercially as "Santos Rio," "Mocha Seed Santos" and "Victoria."

Raw coffee has a faint, peculiar odor and a slightly sweetish, somewhat harsh taste.

During the roasting process coffee swells to almost double its original volume, losing from 15 to 23 per cent. of its weight, and acquires a new, peculiar odor and a bitter taste. An active empyreumatic oil (*caffeol,* $C_8H_{10}O_2$) is developed during the process, probably at the expense of a portion of the caffeine. Much of the alkaloid, however, escapes change, and a portion of it is volatilized. The excellence of the flavor of roasted coffee depends much upon the manner in which the process is conducted, and the extent to which it is carried. It should be performed in a covered vessel, over a moderate fire, and the grains should be kept in constant motion. When they have acquired a chestnut-brown color, the process should cease. If too long continued, it renders the coffee bitter and acrid, or, by reducing it to charcoal, deprives it entirely of flavor. During a severe roasting the coffee loses a portion of caffeine, which sublimes, while in a slight roasting it loses none; yet ordinary coffee for drinking, prepared by percolation, contains rather more caffeine when prepared from strongly roasted than from slightly roasted coffee, because the caffeine is more easily extracted from the former. Paul and Cownley found in preparing "low and medium roasted" coffee no perceptible loss of alkaloid, while in "over-roasted" coffee the loss amounted to one-third. The average of caffeine in roasted coffee they give as at 1.3 per cent. (*P. J.*, 1887, 822.)

Parry (*Food and Drugs,* vol. i, 1911, p. 31) gives the following comparative figures for coffee before and after roasting:

	Raw (per cent.)	Roasted (per cent.)
Moisture	11.90 to 12.45	3.7 to 4.1
Ash	3.66 to 3.72	3.82 to 3.95
Cellulose	26.82 to 28.5	25.00 to 26.8
Caffeine	1.2 to 1.36	1.36 to 1.40
Sugar	3.2 to 4.0	1.1 to 1.5

Seissir has devised a method for removing the caffeine from coffee. About 5 kilos of unroasted coffee berries are placed in a closed centrifugal drum which is surrounded by a hot-water jacket. After the addition of about 15 kilos of ethyl acetate, the drum is set in motion, so that the solvent and berries are thoroughly mixed, the temperature being maintained at 68° C. At the end of three hours the solvent is drawn off, and replaced by a further quantity of about 10 kilos, and the mixing and extraction are continued for a further two hours. The ethyl acetate is then run off, the berries are heated to 100° C. to remove the last traces of solvent, and finally dried at 40° to 46° C., the drum being rotated meanwhile. The ethyl acetate may be recovered by distillation, and the caffeine separated from the residue. The method is the subject of a French patent. (*J. Soc. Chem. Ind.*, 1909, 622.)

Description and Physical Properties.—"*Unground Coffee.*—Oval, of variable size, having one side strongly convex, the other flat with a longitudinal groove, and showing traces of the papery seed coat in the cleft. It has a characteristic aroma and a pleasantly bitter taste.

"*Powdered Coffee.*—Numerous fragments of the seed coat made up of parenchyma and irregular stone cells, the latter up to 1.000 mm. long and up to 0.135 mm. wide, with walls having simple pores; numerous brownish endosperm cells having porous walls about 0.010 mm. thick and containing oil and aleurone grains; starch grains few or absent; reticulate tracheæ wanting.

"Percolate 1 Gm. of powdered Coffee with ether until exhausted and evaporate the percolate to dryness; the residue weighs not less than 0.1 Gm. (presence of at least 10 per cent. of fat). Boil 1 Gm. of powdered Coffee with 10 cc. of distilled water, filter and acidify the filtrate with 1 cc. of diluted sulphuric acid, and then decolorize it by the cautious addition of potassium permanganate T.S. This decolorized solution shows no blue or purple coloration upon the addition of iodine T.S. (*starch*) Shake 1 Gm. of Coffee with 20 cc. of water; the strained liquid shows no colored or heavy deposit. Shake 1 Gm. of Coffee with 20 cc. of alcohol; the strained liquid shows no colored or heavy deposit nor is any color imparted to the alcohol (*artificial colors or facings*).

"**Assay.**—Place 6 Gm. of Coffee, in fine powder, in a suitable flask or bottle, add 120 cc. of chloroform and shake. Allow to stand five minutes, then add 6 cc. of ammonia water and shake the mixture continuously during one hour, or intermittently (see *Proximate Assays,* Type Process A) during two hours. Allow the mixture to stand over night, again shake intermittently during one-half hour, then allow the drug to settle. Decant or filter off through a pledget of purified cotton, 100 cc. of the chloroformic liquid, representing 5 Gm. of Coffee, and evaporate to dryness. Treat the residue with 10 cc. of weak (about 1 per cent.) sulphuric acid with the aid of a gentle heat, allow to cool, filter through a small filter into a separator, and wash the dish and filter with successive small portions of distilled water until no test for alkaloid is obtained by acidulating a few drops of the filtrate strongly with sulphuric acid and adding iodine T.S. Now add ammonia water until the liquid is distinctly alkaline to litmus, and completely extract the caffeine with successive portions of chloroform, as shown by testing with iodine T.S. Evaporate the combined chloroform solutions, and dry the residue at 80° C. to constant weight. The weight is the amount of caffeine from 5 Gm. of Coffee." *N. F.*

Adulterations.—Both whole and ground roasted coffee have been and still are adulterated by irresponsible dealers. The whole article has been adulterated with artificial coffee seeds made by moulding and roasting dough as well as masses of pea hulls, ground cereals and molasses. The ground article has been adulterated with the following ground roasted materials: chicory root, identified by its short, pitted and reticulate tracheæ from 25 to 50 μ in breadth and numerous laticiferous vessels; dandelion root, identified by its pitted and reticulate tracheæ up to 80 μ in width and numerous laticiferous vessels; cereals and cereal products, identified by their hairs, cross cells and starch grains; coffee hulls, characterized by a layer of curved palisade cells with yellowish contents; leguminous seeds, characterized by fragments of palisade cells and typical starch grains; figs, identified by fragments of the mesocarp of receptacle containing abundant branching latex tubes up to 50 μ in breadth, and numerous rosette crystals of calcium oxalate and by numerous small achenes usually imbedded in the roasted pulp; ivory nuts, identified by the large, endosperm cells with porous walls of reserve cellulose that are up to 35 μ or more in thickness; acorn kernels, identified by their distorted, ellipsoidal or elongated starch grains, each with prominent elongated hilum.

Chicory, dandelion and other similar roots used as adulterants may be detected microscopically, but a chemical method of detection has been proposed by LaWall and Forman (*J. A. Ph. A.*, 1914, iii, p. 1669), which depends upon the determination of the ratio of reducing sugars to extractive matter in the aqueous decoction.

Mussaenda coffee, so called, is not a true coffee, but the seeds of *Gaertnera vaginata* Lam. (Fam. *Loganiaceæ*). (*P. J.*, Nov., 1889.)

C. Griebel (*Nahr. Genussm,* 1918, xxxv, 272) finds among the numerous coffee substitutes chicory and beets play the main rôle. In addition, however, waste products have been used, like potato pulp, husks of grapes or other fruits, tree bark, the stony part of fruit shells and kernels or stone fruits of plants such as hawthorne, rose, etc. Spurry as well as locust seeds (see *Robinia,* Part II) have been used as coffee substitutes, and Griebel discusses them in detail. Spurry (*Spergula arvensis,* Fam. *Caryophyllaceæ*), growing quite generally as a weed on sandy soil, is under cultivation for feed in western Germany.

Constituents.—The most important substances present in raw coffee are: the alkaloid caffeine, a peculiar tannin, and a sugar, probably glucose, which is almost completely caramelized in the roasting process. *Caffetannic acid* has been ascertained by Hlasiwetz to be a glucoside with the formula $C_{14}H_8O_7$ and resolvable into glucoside and a peculiar crystallizable acid, $C_8H_8O_4$, named by him *caffeic acid* (*J. P. C.*, 1867), and which may be obtained from coffee by boiling a solution of the extract with potassium hydroxide, treating the resulting liquid with sulphuric acid in excess, and extracting the caffeic acid with ether, which yields it somewhat impure by evaporation. (*J. P. C.*, 1868, 75.) Caffeic acid has the constitution of a dihydroxy-cinnamic acid, and on fusion with potassium hydroxide yields protocatechuic and acetic acids. The *coffee fat,* which ranges in different varieties from 14 to 21 per cent., is, when purified, white, without odor, of a buttery consistence, melting at 37.5° C., and becomes rancid on exposure. According to Rochleder (*Wien. Akad Ber.*, xxif, 40), it contains glycerides of palmitic acid and of an acid of the composition $C_{12}H_{24}O_2$.

The caffeine, according to Payen, is present partly free and partly as a *potassium and caffeine chlorogenate,* but H. Gorter (*Ann. Ch.*, ccclix, 217, ccclxii, 237), in investigations made upon Liberian coffee, stated that caffeine does not exist free in coffee, but is all combined. The compound is given the following formula: $C_{32}H_{36}C_{19}K_2(C_8H_{10}O_{12}N_4)_2 + 2H_2O$. It decomposes at 225° C., without melting. The salt is scarcely decomposed by dry chloroform, but is easily decomposed by the presence of water and then gives up its caffeine. This explains the fact observed by the manufacturers of decaffeinated coffees, that dry coffee yields only a small amount of its caffeine to chloroform, but that the extraction takes place readily and almost completely if the coffee is simultaneously treated with water or steam.

Chlorogenic acid is given the formula, $C_{32}H_{38}O_{19}$, and is a colorless, crystalline compound, melting at 206° C., and with a marked lævorotatory power. It is hydrolyzed by alkalies into caffeic and quinic acids. When strongly heated it emits an odor of roasted coffee and by some is believed to be the principle to which the flavor of the beverage is to be attributed. It is stated that when acted on by sulphuric acid and manganese dioxide it is converted into quinone, being in this respect analogous to quinic acid. Another acid was found which the author named *coffalic acid.* The coffee also contained citric acid, trigonelline, a pectin and an oxydase.

Julian E. Walter (*Ph. Rec.*, May 5, 1890, 176) found the percentage of caffeine in various samples of unroasted coffee to range from 0.54 to 1.24 per cent. Bertrand (*Bull. Sc. Pharm.*, iv) gives the following results of studies of the percentage of caffeine in various coffee berries: In *Coffea arabica* the percentage varied from 0.69 to 1.60; *C. canephora* was found to be rich in alkaloid, the berries yielding 1.97 per cent., while those of the *C. humboldtiana,* Baill., were remarkable by reason of their containing a bitter principle, *cafamarin,* but no caffeine at all; the berries of *C. mauritiana* contained only 0.07 per cent.

The *leaves* of the coffee plant possess properties analogous to those of the fruit, and are extensively used by the Malays. Stenhouse found them to contain caffeine in larger proportion than the coffee bean, and also caffeic acid. The leaves are prepared for use by drying over a clear fire and then powdering by rubbing in the hands. The powder is made into an infusion like common tea. The taste is like that of tea and coffee combined. (*P. J.*, xii, 443; xiii, 207 and 382, and xvi, 1067.)

The effects of coffee are due chiefly, if not solely, to the caffeine which it contains. Some writers, however, believe that the volatile oil, *caffeol* (*caffeone*) possesses stimulating properties. The evidence of this point, however, is so contradictory as to render conclusions impossible. (See Reichert, *M. News*, 1890, lvi; Erdmann, *A. E. P. P.*, 1902, xlviii; Geiser, *A. E. P. P.*, liii, p. 112.)

Uses.—As a medicine coffee has been almost entirely replaced by the alkaloid caffeine. The infusion is, however, sometimes administered by rectal injection in cases of narcotic poisoning. The chief reason for the recognition as a drug is its agreeable flavor. The disturbances of digestion which follow excessive coffee drinking are not considered by J. Burmann to be due to caffeine, but to a volatile toxic substance formed during roasting and only partly volatilized, named *cafeotoxin,* which can be eliminated by subjecting roasted coffee to successive treatments with steam under pressure of several atmospheres (*J. P. C.*, 1913, 8, 281.)

Dose, thirty to sixty grains (2–4 Gm.).

Off. Prep.—Fluidextractum Coffeæ, *N. F.*

COLCHICI CORMUS. U. S., Br.

COLCHICUM CORM Colch. Corm. [Colchici Radix, U. S. 1890, Colchicum Root]

"Colchicum Corm is the dried corm of *Colchicum autumnale* Linné (Fam. *Liliaceæ*). Colchicum Corm yields not less than 0.35 per cent. of colchicine." *U. S.* "Colchicum Corm is the fresh corm of Colchicum autumnale, *Linn.*, collected in early summer; or the same deprived of its coats, sliced transversely, and dried at a temperature not exceeding 65° C." *Br.*

Bulbus s. Tuber Colchici; Meadow Saffron Root; Bulbe de Colchique, de Safran bâtard, *Fr.;* Zeitlosenknollen, *G.;* Bulbo di colchico, *It.;* Bulbo de colquico, *Sp.*

COLCHICI SEMEN. U. S. (Br.)

COLCHICUM SEED Colch. Sem. [Colchici Semen P. I.]

"Colchicum Seed is the dried ripe seed of *Colchicum autumnale* Linné (Fam. *Liliaceæ*). Colchicum Seed yields not less than 0.45 per cent. of colchicine." *U. S.* "Colchicum Seeds are the dried ripe seeds of Colchicum autumnale, *Linn.*" *Br.*

Colchici Semina, *Br.;* Colchicum Seeds; Semence de Colchique, *Fr.;* Semen Colchici, *P. G.;* Zeitlosensamen, *G.;* Semi di Colchico, *It.;* Semilla de colquico, *Sp.*

Colchicum autumnale, often called *meadow saffron,* is a perennial plant, the leaves of which appear in spring, and the flowers in autumn. Its underground portion consists of an ovoid corm. Its manner of growth is peculiar, and deserves notice as connected in some measure with its medicinal efficacy. In the latter part of summer, a new *corm* begins to form at the lateral inferior portion of the old one, which receives the young offshoot in its bosom and embraces it half round. The new plant sends out roots from its base, and is furnished with a radical spathe, which is cylindrical, tubular, cloven at top on one side, and half under ground. In September, from two to six flowers, of a lilac or pale-purple color, emerge from the spathe, unaccompanied by leaves. The corolla consists of a tube from 10 to 12 cm. long, concealed for two-thirds of its length in the ground, and of a limb divided into six segments. The flowers perish by the end of October, and the rudiments of the fruit remain under ground until the following spring, when they rise upon a stem above the surface, in the form of a three-lobed, three-celled capsule. The leaves of the new plant appear at the same time, so that in fact they follow the flower instead of preceding it, as might be inferred from the order of the seasons in which they respectively show themselves. The leaves are radical, spear-shaped, erect, numerous, about 12 cm. long, and 2.5 cm. broad at the base. In the meantime, the new corm has been increasing at the expense of the old one, which, having performed its appointed office, perishes; while the former, after attaining its full growth, sends forth shoots, and in its turn decays. The old corm in its second spring, and a little before it perishes, sometimes puts forth one or more small corms, which are the sources of new plants. The usual method of propagating colchicum is by planting the bulbs about August or September in deep rich soil, about 2 or 3 inches below the surface and about 3 inches apart in the row. (*D. C.*, 1912, p. 134.) Most of the commercial supplies of the drug are imported from Leghorn, Italy and Amsterdam, Holland.

C. autumnale is a native of the temperate parts of Europe and of Northern Africa, growing in moist pastures and meadows. Attempts have been made to introduce its culture into this country, but with no great success, though small quantities of the corm, of apparently good quality, have entered commerce. The flowers possess virtues similar to those of the corm and are recognized by the French Codex.

Colchici Cormus.—The medicinal virtue of the corm depends much upon the season at which it is collected. Early in the spring it is too young to have fully developed its peculiar properties, and late in the fall it has become exhausted by the nourishment afforded to the new plant. The proper period for its collection is from the early part of June, when it has usually attained perfection, to the middle of

August, when the offset appears. It may be owing, in part, to this inequality at different seasons that entirely opposite reports have been given of its powers. Krapf ate whole corms without inconvenience; Haller found them entirely void of taste and acrimony, and we are told that in Carniola the peasants use them as food with impunity in the autumn. On the other hand, there can be no doubt of its highly irritating and poisonous nature, when fully developed, under ordinary circumstances. Perhaps soil and climate may have some influence in modifying its character.

Christison found the roots collected in April to be more bitter than those gathered in July, and conjectures that the common opinion of their superior efficacy at the latter season may not be well founded. Schroff states, as the result of his observation, that the autumnal root is much stronger than that dug in the summer. (See *A. J. P.*, xxix, 324.)

The corm is often used in the fresh state in the countries where it grows, it is apt to be injured in drying, unless the process is carefully conducted. The usual plan is to cut the corm, as soon as possible after it has been dug up, into thin transverse slices, which are spread out separately upon paper or perforated trays and dried with a moderate heat. The reason for drying it quickly after removal from the ground is that it otherwise begins to vegetate, and a change in its chemical nature takes place; and such is its retentiveness of life that, if not cut in slices, it is liable to undergo a partial vegetation even during the drying process. Houlton recommends that the corm be stripped of its dry coating, carefully deprived of the bud or young bulb, and then dried whole. It is owing to the high vitality of the bud that the corm is so apt to vegetate. During desiccation there is great loss of weight, 70 per cent. being the average for a number of years in the laboratory of Allen & Hanbury, in London.

The recent corm of *C. autumnale* resembles that of the tulip in shape and size, and is covered with a brown membranous coat. Internally it is solid, white and fleshy, and, when cut transversely, yields, if mature, an acrid milky juice. There is often a small lateral projection from its base, which is the bud for the development of a new plant; this bud is frequently broken off in drying. When dried, and deprived of its external membranous covering, the corm is of an ash-brown color, convex on one side, and somewhat flattened on the other, where it is marked by a deep groove extending from the base to the summit. As found in commerce, it is always in the dried state, sometimes in segments made by vertical sections of the corm, but generally in transverse, reniform or longitudinal ovate slices.

Description and Physical Properties.—"*Unground Colchicum Corm.*—Usually in reniform transverse slices or in ovate longitudinal slices from 2 to 5 mm. in thickness; flat surfaces whitish, slightly roughened, and of a crystalline appearance under a hand lens; epidermal surface light brown and finely wrinkled; fracture short and mealy; odor slight; taste bitter and acrid.

"*Powdered Colchicum Corm.*—Light brown or grayish-brown; starch grains numerous, single or 2- to 6-compound, the individual grains varying from spherical or ovoid to polygonal, from 0.003 to 0.030 mm. in diameter and marked with a triangular or star-shaped central cleft; tracheæ few and with spiral or scalariform thickenings; occasional fragments of epidermal cells with thin, reddish-brown walls.

"**Assay.**—Proceed as directed under *Colchici Semen.*" *U. S.*

"Fresh corm about thirty-five millimetres long and twenty-five millimetres broad, somewhat conical, hollowed on one side where a new corm is in process of development, and rounded on the other; covered with a thin brown membranous outer coat, and an inner reddish-yellow one; internally white and solid, and when cut yielding a whitish, turbid juice of a disagreeable odor and bitter taste. Dried slices two or three millimetres thick, yellowish at their circumference, somewhat reniform in outline; firm, whitish, amylaceous; breaking readily with a short fracture. No odor; taste bitter." *Br.*

The cut surface is white, and of an amylaceous aspect. Examined with the microscope, the corm is seen to be composed of large irregular cells, full of ovoid, angular, sometimes compound, starch grains, and interspersed with spiral vessels in vascular bundles. The odor of the recent corm is said to be hircine. It is diminished, but not lost, by drying. The taste is bitter, hot, and acrid.

A. T. Thompson stated that the milky juice of fresh colchicum produces a fine blue color if rubbed with the tincture of guaiac, and that the same effect is obtained from an acetic solution of the dried corm. He considered the appearance of this color, when the slices were rubbed with a little distilled vinegar and tincture of guaiac, a proof that the drug was good and had been well dried. J. M. Maclagan has shown that the value of the test consists simply in proving that the drying has not been effected at a heat above 82.3° C; the color being due to the action of an oxydase. A very deep or large notch in the circumference of the slices is an unfavorable sign, as it indicates that the corm has been somewhat exhausted in the nourishment of the offset. The decoction yields a deep blue precipitate with solution of iodine, white precipitates with lead acetate and subacetate, mercurous nitrate, and silver nitrate, and a slight precipitate with tannic acid.

Colchici Semen.—The seeds of the meadow-saffron ripen in summer, and should be collected about the end of July or beginning of August. They never arrive at maturity in plants cultivated in a dry soil or in confined gardens. (Williams.)

Description and Physical Properties.—"*Unground Colchicum Seed.*—Ovoid or irregularly globular, minutely pointed at the hilum, and with a distinct beak or caruncle approximately opposite to the hilum; from 2 to 3 mm. in diameter and, when fresh, with a tendency to cohere in small clumps; externally dark brown, finely pitted; tough and of bony hardness; internally whitish or light brown; nearly inodorous; taste bitter and acrid.

"*Structure.*—Seed coat of a few layers of more or less collapsed cells with thin, reddish-brown walls; the endosperm parenchyma, with thick porous walls, containing fixed oil and aleurone grains, the latter from 0.003 to 0.015 mm. in diameter; the embryo small; the beaked portion or caruncle containing thin-walled parenchyma with ovoid, ellipsoidal or polygonal starch grains from 0.005 to 0.020 mm. in diameter." *U. S.*

"About two and a half millimetres in diameter, subglobular, slightly pointed at the hilum, rough and of a dull reddish-brown color, minutely pitted, very hard and tough. Endosperm oily; its cells with thickened walls and large pits. No odor; taste bitter and acrid." *Br.*

They are chiefly composed of a gray horny endosperm constituted of very thick-walled cells, and surrounded by a closely adherent testa. The leafless embryo is very small, and is situated close to the surface opposite the strophiole. It has been found that the percentage of alkaloids in colchicum seeds is in inverse proportion to the specific weight of the seeds. There is present nearly 20 per cent. of a semi-drying oil of pungent taste and from 2 to 5 per cent. of reducing sugars. The seeds and powder are very seldom adulterated. Judd, however, reports examining a powder which contained fully 50 per cent. of powdered fœnugreek seed. (*Bull. A. Ph. A.*, 1909, p. 193.)

The therapeutic value of both colchicum seed and corm probably depend on their alkaloid (see *Colchicina*).

The U. S. Pharmacopœia directs that colchicum seed should contain not less than 0.45 per cent. of colchicine, and the corm not less than 0.35 per cent., to be determined by the following process:

Assay.—"Place 15 Gm. of Colchicum Seed, in fine powder, in a 500 cc. flask and add 290 cc. of distilled water and 10 cc. of solution of lead subacetate. Weigh the flask and contents, and digest the mixture at from 60° to 70° C. for three hours with occasional agitation. Cool, add distilled water to restore the original weight, and filter off 200 cc. Add 2 Gm. of sodium phosphate to the clear filtrate, or sufficient to completely precipitate the lead, shake the mixture frequently during half an hour, and filter off 100 cc., representing 5 Gm. of Colchicum Seed. Shake out the alkaloid from the filtrate with chloroform until completely extracted, as shown by testing with iodine T.S., and evaporate the chloroform solution. Add about 1 cc. of alcohol, and again evaporate. Repeat this operation once more, and dry the residue to constant weight at 100° C. To this weighed residue contained in a flask add 5 cc. of tenth-normal sulphuric acid and 5 cc. of distilled water, adding a few drops of chloroform, and heat the mixture for ten minutes at 70° C. Filter the liquid through a pledget of purified cotton, wash the flask and cotton with distilled water, reject the filtrate and washings, and remove as much of the water from the cotton as possible. Dissolve any insoluble residue that may remain on the cotton by washing it first with a little alcohol and then with ether; collect the alcohol-ether washings in the flask, evaporate, and dry the residue to constant weight at 100° C. Deduct this weight from the weight of residue previously obtained. The difference will be the weight of colchicine obtained from 5 Gm. of Colchicum Seed (Proximate Assays)." *U. S.*

For other methods of assay see Schwickerath (*Ph. Rund.*, 1893, 282) and Bredemann (*Ap. Ztg.*, 1903, xviii).

Uses.—The investigations into the physiological action of colchicum have not as yet yielded a very clear explanation of its therapeutic effects. Dixon and Malden (*J. P.*, 1908, xxxviii, p. 50) have found that it is an active stimulant to the unstriped muscle, increasing intestinal and uterine contractions and bronchial tonus. After large doses it depresses the vasomotor system, causing a marked fall in the blood pressure. When injected subcutaneously in somewhat smaller doses it producse a transient decrease in the number of leukocytes followed after twenty-four hours by an enormous increase, the alterations being especially notable in the number of polymorphonuclear corpuscles. These effects appear to be the result of an action upon the bone marrow. Jackson and Blackfan (*J. A. M. A.*, 1906, xlvii) find an increased output of uric acid under its influence, but they believe this is due rather to an increased formation than a more active elimination, but Denis (*J. P. Ex. T.*, 1915, vii, 609) was unable to detect any change in the amount of uric acid either in the urine or blood.

The poisonous properties of colchicum were known to the ancients, but, while it is generally supposed that the hermodactyls were derived from some species of the genus, the use of meadow-saffron cannot be certainly traced back further than the sixteenth century. Although it has from time to time been recommended for various complaints, it is used to-day only in the treatment of *gout*. There is considerable clinical evidence that full doses of colchicum administered during the acute attack of a *podagra* will often abort it. The treatment, however, is not without serious danger and most clinicians urge caution in the use of colchicum during the attack. It appears also to be of service in those more chronic conditions of disturbed metabolism known variously as uric acid diathesis or *lithemia*.

In preparing colchicum pharmaceutically, if it be desired to retain the colchicine unchanged, both acids and alkalies should be avoided and as far as possible also heat. As pointed out below, under various conditions colchicine may be decomposed into colchiceine, colchicinic acid, and various allied products. Whether these derivatives of colchicine possess the therapeutic virtues of the natural alkaloid is uncertain, but Fuehner (*A. E. P. P.*, 1913, lxxii, p. 228) has shown that colchiceine is very much less toxic than colchicine.

When taken internally in therapeutic dose, colchicum usually produces no other symptoms than intestinal pains and looseness of the bowels. In some rare cases it is said to give rise to copious diuresis or diaphoresis instead of purging. When larger amounts are exhibited, the purging is more pronounced, and there may be also vomiting. With these symptoms there may be some depression, which seems to be due to the gastro-intestinal irritation rather than to the direct action of the poison. In an overdose, it may produce dangerous and even fatal effects. Excessive nausea and vomiting, abdominal pains, purging and tenesmus, great thirst, sinking of the pulse, coldness of the extremities, and general prostration, with occasional symptoms of nervous derangement, such as headache, delirium, and stupor, are among the results of its poisonous action. A peculiarity of its influence is that when its dose is increased beyond a certain point there is not a corresponding increase in the rapidity of the fatal issue. This is probably because it kills not by a direct influence upon the heart or the nervous system, but by causing gastro-enteritis. On post-mortem examination the alimentary mucous membrane is found much inflamed.

Dose, of the dried corm and seed, from two to eight grains (0.13–0.52 Gm.), which may be repeated every four or six hours until its effects are obtained.

Off. Prep.—*Colchicum corm.*—Extractum Colchici, *U. S.* (*Br.*); Vinum Colchici, *Br.;* Fluidextractum Colchici Cormi, *N. F.;* Tinctura Colchici Cormi Fortior, *N. F.* *Colchicum seed.*—Fluidextractum Colchici, *U. S.;* Tinctura Colchici, *U. S.* (*Br.*).

COLCHICINA. U. S.

COLCHICINE

"An alkaloid [$C_{22}H_{25}O_6N$] obtained from colchicum." *U. S.*

Colchicine, *Fr.;* Colchicin, *G.*

Colchicine is found in various species of *Colchicum* and in *Gloriosa superba* (see Part II) and in species of *Merendera* (Clewer, Green and Tutin, *Tr. Chem. Soc.*, 1915, cvii, p. 835).

When hydrolized, as by boiling with diluted acids, colchicine is first split into methanol and *colchiceine* (acetyltrimethyl-colchicinic acid). By the further action of hydrochloric acid the latter is decomposed eventually into *colchicinic acid* (Windaus, *Sitzungsber. Heidelb. Akad. Wiss.*, 1910, 1911, and 1914; also *Chem. Soc. Abstr.*, 1924, i, 72). Colchiceine, according to Oberlin (*M. Chem.*, 1888, ix, 870), occurs naturally, along with colchicine, in the autumn corms and seeds, but according to Zeisel was probably formed by decomposition during extraction.

Colchicine has also been built up synthetically from colchiceine, sodium methylate, and methyl iodide, which are heated together to 100° C. (Johanny, *M. Chem.*, ix, 868.) It forms precipitates with the usual alkaloidal reagents. Its solutions are strongly lævo-rotary.

Description and Physical Properties.—"Pale yellow, amorphous scales, or powder, turning darker on exposure to light. It is odorless, or nearly so. *Caution—Colchicine is extremely poisonous.* One Gm. of Colchicine is soluble in 22 cc. of water, 220 cc. of ether, and in 100 cc. of benzene, at 25° C. It is freely soluble in alcohol and in chloroform, and is insoluble in petroleum benzin.

"Colchicine melts between 142° and 146° C. Its aqueous solution (1 in 30) is neutral to litmus paper, and is lævorotatory. An aqueous solution of Colchicine (1 in 30) is yellow, its color becoming intensified by the addition of inorganic acids. Mix about 0.001 Gm. of Colchicine with a few drops of sulphuric acid: a lemon-yellow color is produced, which, on the addition of a drop of nitric acid, changes to greenish-blue, rapidly becoming reddish and finally yellow, or almost colorless. On adding an excess of sodium hydroxide T.S., the color is changed to red.

"The addition of 2 drops of ferric chloride T.S. to 5 cc. of an aqueous solution of Colchicine (1 in 100) produces no color (*colchiceine*), but on heating, a brownish-red color is developed, which changes to brownish-black. One drop of ferric chloride T.S. added to 1 cc. of an alcoholic solution of Colchicine (1 in 20) at once produces a garnet-red color. The ash from 0.1 Gm. is negligible. Heat a mixture of about 0.01 Gm. of Colchicine, 2 cc. of sodium hydroxide T.S., and one drop of aniline: no odor of phenylisocyanide is developed (*chloroform*).

"Preserve in well-closed containers, protected from light." *U. S.*

Vanderkleed and E'we (*Proc. P. Ph. A.*, 1916, p. 279) point out that some commercial samples of colchicine contain chloroform in comparatively stable form, which might be called chloroform of crystallization. This not only interferes with the melting point determination, but inasmuch as the amount of chloroform present is sometimes over 20 per cent. it becomes a fraud as well.

Uses.—The alkaloid colchicine acts like colchicum, according to Maret and Combemale, in doses of one-twelfth of a grain (0.005 Gm.) producing violent diarrhea, with diminished urinary secretion; in doses of one thirty-second of a grain (0.002 Gm.) causing some abdominal disturbance, with increased diuresis. According to J. Sprega, three grains (0.2 Gm.), repeated in three hours, caused violent gastro-enteritis, ending in death in thirty-one hours. (*Gazz. d. Ospitali,* Oct., 1890.) *Colchicine salicylate* is a yellow amorphous powder, soluble in water, alcohol, and ether, the dose being one-hundredth of a grain (0.0006 Gm.) every four hours.

Dose, one one-hundred-and-fiftieth to one one-hundredth of a grain (0.0004–0.0006 Gm.).

Off. Prep.—Elixir Tongæ et Salicylatum, *N. F.*

COLLODIUM. U. S. Br.

COLLODION Collod.

Collodion, *Fr. Cod.;* Collodium, *P. G.;* **Kollodium**, *G.;* Collodio, *It.;* Colodion, *Sp.*

"Pyroxylin, 40 Gm.; Ether, 750 cc.; Alcohol, 250 cc.; to make about 1000 cc. Add the alcohol to the pyroxylin contained in a suitable bottle, shake the mixture thoroughly, add the ether, and again shake the mixture until the pyroxylin is dissolved. Cork the bottle well, and set it aside until the liquid becomes clear. Finally decant the clear portion from any sediment which may have deposited, and transfer it to containers which must be well closed." *U. S.*

"Pyroxylin, 21 grammes; Ether, 750 millilitres; Alcohol (90 per cent.), 250 millilitres. Immerse the Pyroxylin in the Alcohol; add the Ether, shake occasionally until dissolved; set aside for a few days; decant if necessary." *Br.*

Collodion is a solution of pyroxylin in alcohol and ether. Formerly the U. S. Pharmacopœia directed that the gun cotton be prepared at the time of making the collodion, giving directions for the purpose, but at the revision of 1870 the process of the British Pharmacopœia was substantially adopted, a formula for the preparation of pyroxylin being given separately in the Pharmacopœia. A process for the preparation of pyroxylin is not official in the U. S. Pharmacopœia, but the British Pharmacopœia still retains a process. (See *Pyroxylinum.*)

Acetone has been used as a solvent for pyroxylin, and collodion so prepared is on the market.

Description and Physical Properties.—"A clear, or slightly opalescent, syrupy liquid. It is colorless, or slightly yellowish and has the odor of ether. *It is highly inflammable.* Specific gravity: 0.765 to 0.775 at 25° C. When exposed to the air in a thin layer, it leaves a transparent, tenacious film. When mixed with an equal volume of distilled water, a viscid, stringy mass of pyroxylin separates. The aqueous liquid is not acid to litmus paper.

"**Assay.**—Pour quickly about 10 cc. of Collodion into a tared flask, stopper, and weigh accurately, then warm it on a water bath, and add 10 cc. of distilled water, drop by drop, with constant stirring. Evaporate the mixture on a water bath, and dry the residue to constant weight at 110° C. The pyroxylin so obtained corresponds to not less than 5.1 per cent. of the Collodion taken, corresponding to about 4 Gm. of pyroxylin in 100 cc. of Collodion at 25° C. The pyroxylin obtained burns rapidly, with a yellow flame.

"Preserve in well-closed containers, in a cool place, remote from fire." *U. S.*

"A colorless, highly inflammable liquid of syrupy consistence and ethereal odor. Dries quickly upon exposure to the air, and leaves a thin transparent film, which contracts rapidly on drying and is insoluble in *water* or *alcohol* (90 per cent.)." *Br.*

When applied to a dry surface, the ether quickly evaporates, and a transparent film is left, having remarkable adhesiveness and contractility. On account of the great volatility of ether, collodion must be kept in bottles well stoppered. When insecurely kept, the liquid thickens and becomes less fit for the use of the surgeon. The thickened liquid sometimes contains acicular crystals. The addition of a mixture of 3 volumes of ether and 1 volume of alcohol will generally restore the collodion to its original condition.

Uses.—Collodion was first applied to the purposes of surgery by J. Parker Maynard, of Boston, when a student of medicine, in January, 1847, although, as pointed out by Kahlbaum, Schoenbein, the discoverer of gun-cotton, suggested the surgical use of an ethereal solution in 1846. (*Nat. Drug.,* 1902, 8.) It is employed for holding together the edges of incised *wounds,* for covering *ulcers,* abraded or diseased surfaces, *chilblains, chapped nipples,* etc., with an impervious film not acted upon by water, and for encasing parts which require to be kept without relative motion. It should be remembered that while it protects the underlying tissues from external contamination, it also prevents the escape of any toxic materials already present; to hermetically close an infected wound, as with collodion, is an invitation to blood-poisoning. It is applied brushed over the part, or by means of strips of muslin. In whatever way applied, the solvent quickly evaporates, and leaves the solid adhesive material, which is soluble neither in water nor in alcohol. The rigid film thus formed contracts with a good deal of force. This property adapts collodion for certain purposes, such as drawing together the edges of wounds, exciting pressure on buboes, etc. When, however, the surgeon desires simply to protect a surface, a flexible, non-contracting film is preferable, and the official flexible collodion should be used. Collodion has been variously medicated, and thus made the vehicle of several important medicines for external application. *Iodized collodion* has been proposed by C. Fleming, for the purpose of obtaining the specific effects of iodine in a rapid manner, especially on *tumors.* See *Collodion Iodi,* N. F., Part III. Aran has proposed a *ferruginous collodion,* made of equal parts of collodion and tincture of ferric chloride, as a remedy in *erysipelas.* A *caustic collodion* may be prepared by dissolving 4 parts of corrosive sublimate in 30 of collodion. Macke, of Sorau, has used this preparation for destroying *nævi materni.* The eschar formed is one or two lines in thickness, and separates in from three to six days, leaving but a trifling cicatrix. (For formulas in which collodion is made the vehicle of croton oil, iodoform, salicylic acid, tannin, etc., see National Formulary, Part III.) All these medicated collodions are best applied by means of a camel's-hair brush.

Off. Prep.—Collodium Flexile, *U. S., Br.;* Collodium Stypticum, *N. F.*

COLLODIUM FLEXILE. U. S., Br.

FLEXIBLE COLLODION Collod. Flex.

Collodion élastique, *Fr.;* Collodium elasticum, *P. G.;* Elastiches Collodium, Kollodium, *G.;* Collodio elastico, *It.;* Colodion elastico, *Sp.*

"Camphor, 20 Gm.; Castor Oil, 30 Gm.; Collodion, a sufficient quantity to make 1000 Gm. Weigh the ingredients, successively, into a dry, tared bottle, stopper, and shake the mixture until the camphor is dissolved. Keep the product in well-closed containers, in a cool place, remote from fire." *U. S.*

"Collodion, 940 *millilitres;* Canada Turpentine, 40 *grammes;* Castor Oil, 20 *grammes.* Mix." *Br.*

The contractility of the collodion film has long been felt as a drawback to its use simply for the purposes of protection. C. S. Rand proposed to obviate this by dissolving one part of gun cotton and three of Venice turpentine in twenty parts of ether. To give more flexibility to the film, Sourisseau, of Kaiserberg, suggested the addition of one part of elemi to twelve of collodion. According to Startin, of London, opacity and elasticity may be imparted at the same time by adding from half a drachm to a drachm of lard, or some similar fatty matter, previously dissolved in ether, to an ounce of collodion. The qualities of softness and elasticity may also be given by combining collodion with castor oil, in the proportion of thirty parts to two, agreeably to the plan of Guersant, who found it useful, thus modified, in *erysipelas;* and the proportion of castor oil may be increased if thought desirable. This is the method preferred by the French Codex. According to Cap and Garot, the most successful way for obtaining an elastic collodion is to mix two parts of glycerin with one hundred of collodion. *Glycerized collodion* is exceedingly supple, does not crack and scale off from the skin, and accommodates itself to the motions of the part. In order to imitate the color of the skin, an ethereal tincture of turmeric or saffron may be added, so as to produce the desired tint. Meller has proposed a solution of shellac in highly rectified alcohol, so as to have a gelatinous consistence, as a substitute for collodion. Of all these plans, probably that followed in the official direction is the best.

Off. Prep.—Collodium Bitumini Sulphonati, *N. F.;* Collodium Salicylici Compositum, *N. F.;* Collodium Stypticum, *N. F.;* Collodium Tiglii, *N. F.*

COLLODIUM VESICANS. Br.

BLISTERING COLLODION Collod. Canth.

Collodium Cantharidatum, *U. S. IX;* Cantharidal Collodion; Vesicating Collodion; Collodium Cantharidale, Collodion vésicant (cantharidé), *Fr.;* Collodium Cantharidatum, *P. G.;* Spanischfliegen-Kollodium, Blasenziehendes Collodium, *G.*

"Pyroxylin, 25 *grammes;* Cochineal, in powder, 10 *grammes;* Blistering Liquid sufficient to produce 1000 *millilitres.* Shake together until the Pyroxylin is dissolved, set aside till clear, and decant the clear liquid." *Br.*

The U. S. IX recognized an analogous preparation, but made directly from cantharides. The formula for this was:

"Cantharides, in fine powder, *sixty grammes;* Glacial Acetic Acid, *five mils;* Flexible Collodion, *eighty-five grammes;* Acetone, *a sufficient quantity,* to make *one hundred grammes.* Mix the cantharides with *fifty-five mils* of acetone, to which the glacial acetic acid has been added, and set the mixture aside in a closely covered container for twenty-four hours. Then transfer it to a percolator and continue the percolation with acetone until the drug is practically exhausted. Reduce the percolate by distillation on a water bath, in a tared flask, to *fifteen grammes* and, when cold, dissolve this concentrated extract in *eighty-five grammes* of flexible collodion. Finally allow the solution to stand for several hours, and decant the clear liquid from any sediment which may have deposited, and transfer the product to containers, which must be well-closed. Keep Cantharidal Collodion in a cool place, remote from fire." *U. S. IX.*

Cantharidal collodion is a convenient but uncertain epispastic. It may be applied to the surface by means of a camel's-hair brush, and after the evaporation of the ether, which takes place in less than a minute, may be reapplied if the surface should not be well covered. It produces a blister in about the same time as the ordinary cerate, and has the advantages that it is applied with greater facility, is better adapted to cover uneven surfaces, and retains its place more certainly. According to Rand, if the evaporation of the ether be restrained by a piece of oiled silk immediately after its application, it will act much more speedily.

COLOCYNTHIS. U. S. (Br.)

COLOCYNTH Colocyn.
[Colocynth Pulp, Bitter Apple]

"Colocynth is the dried pulp of the unripe but fully-grown fruit of *Citrullus Colocynthis* (Linné) Schrader (Fam. *Cucurbitaceæ*). Colocynth contains not more than 5 per cent. of seed and not more than 2 per cent. of epicarp, and yields not more than 2 per cent. of extractive with purified petroleum benzin, and not more than 6 per cent. of acid-insoluble ash." *U. S.*

"Colocynth Pulp is the dried pulp of the fruit of Citrullus Colocynthis, *Schrad.*, freed from seeds." *Br.*

Colocynthidis Pulpa, *Br.;* Colocynth Pulp, Bitter Gourd, Apple, or Cucumber; Fructus Colocynthidis; Poma Colocynthidis; Coloquinte, *Fr. Cod.;* Pulpe de Coloquinte, *Fr.;* Fructus Colocynthidis, *P. G.;* Coloquintenapfel, Koloquintenmark, Koloquinten, *G.;* Coloquintide, *It.;* Coloquintida, *Sp.*

Although the U. S. Pharmacopœia has followed the British authority and defined Colocynth as the dried pulp, since it is not commercially possible to exclude the seeds entirely, a few being imbedded in the pulp itself, the U. S. P. wisely allows a maximum of 5 per cent. of seeds. It is estimated that every 100 pounds of colocynth fruit will yield 30 pounds of pulp and about 70 pounds of seeds. Tunmann (*Suedd. Apoth. Zeit.*, 1907, p. 503) states that the seeds do not contain medicinally active constituents. Francis (*Proc. A. Ph. A.*, 1906, p. 336), on the other hand, says that if the seeds are first deprived of their fixed oil with benzin, dried and then extracted with 75 per cent. alcohol, the extract is almost as active as the U. S. P. product.

Citrullus Colocynthis, or *bitter cucumber,* is an annual plant, bearing considerable resemblance to the common watermelon. The stems, which are herbaceous and beset with rough hairs, trail upon the ground, or rise upon neighboring bodies, to which they attach themselves by their numerous tendrils. The leaves, which stand alternately on long petioles, are triangular, many-cleft or parted variously sinuated; obtuse, hairy, of a fine green color on the upper surface, rough and pale on the under. The flowers are yellow, and appear singly at the axils of the leaves. The fruit is a globular berry, of the size of a small orange, yellow and smooth when ripe, and contains, within a hard, coriaceous rind, a white, spongy pulp, enclosing numerous ovate, compressed, white or brownish seeds.

The plant is a native of Asia and Africa. Burckhardt, in his travels across Nubia, found the country covered with it; Thunberg met with it at the Cape of Good Hope, and Ainslie says that it grows in many parts of Lower India, particularly in sandy places near the sea. It is said to be cultivated in Spain, the island of Cypress, Morocco and in the neighboring countries, and even to have been collected in Japan. Colocynth is imported in wooden cases; the bulk of the present supplies to the United States is collected in the Soudan and shipped from Cairo. That from the maritime plain between the mountains of Palestine and the Mediterranean is chiefly shipped from Jaffa, and is known as *Turkish colocynth.* It is said to be of superior quality. The fruit is gathered in autumn, when it begins to become yellow, and, having been peeled, is dried quickly in a stove or in the sunshine. Thus prepared, it is imported from the Levant. Small quantities are said to be imported into England from Mogador in the form of brown, unpeeled globular gourds. The so-called *Persian colocynth* is very small, and has apparently been compressed in a fresh state, so that the position of the seeds is perceptible through the dry pulp. The microscopic structure and the proportion of the pulp to the seed appear to be the same as in other colocynths. Colocynth has been grown in New Mexico, but, according to Sayre, the American colocynth is less active.

As found in commerce, colocynth is in whitish, globular berries, from 6 to 7 cm. in diameter, very light and spongy, and abounding in seeds which constitute three-fourths of the fruit.

Description and Physical Properties.—"*Unground Colocynth.*—In light, spongy, easily-broken pieces; yellowish-white or light brown with occasional small patches of darker epicarp; odor slight; taste intensely bitter. Fruits, before removal of seed, nearly globular, from 4 to 10 cm. in diameter, with three large lenticular cavities between the three carpels, hence easily separable longitudinally into three parts. Seeds ovoid compressed, light yellow to brown.

"*Structure.*—Large, thin-walled pitted parenchyma tissue traversed by bicollateral vascular bundles having spiral tracheæ and accompanied by occasional irregular tubular laticiferous vessels.

"*Powdered Colocynth.*—Yellowish-white or buff and characteristically flaky; consisting chiefly of fragments of the parenchyma and vascular bundles. Presence of epicarp and seed indicated by characteristic stone cells, and of the seed, by aleurone grains, and globules of fixed oil.

"**Assay.**—Proceed as directed under non-volatile ether-soluble extractive, using purified petroleum benzin as the solvent." *U. S.*

"White, spongy, light fragments. The powdered Pulp exhibits abundant débris of large, thin-walled parenchymatous cells but no starch, and not more than an occasional sclerenchymatous cell or group of such cells. No odor; taste intensely bitter. Yields not more than 2 per cent. of fixed oil to *petroleum spirit.* Ash not less than 9 per cent." *Br.*

Barclay considers the estimation of ash in powdered colocynth useful in proving its freedom from seeds. The pulp yields from 8.6 to 14 per cent. of ash, the seeds from 2 to 4 per cent., the whole apple 4.6 per cent. (*Am. Drug.*, 1896, 152.) Water and alcohol extract the virtues of colocynth. It is a matter of importance to be able to determine whether the drug miller who usually powders colocynth is careful to reject the seeds. If the seeds have been ground with the dried pulp, the microscope will show the presence of numerous albuminous granules derived from the cotyledons. These are best found by putting a small amount of the powder on the glass slide, adding a drop of water, and gently rubbing the cover glass over it; fragments of the double-walled embryo sac show on the outer side elongated, more or less hexagonal, thin-walled cells, and on the inner side irregular, tabular, thick-walled cells. If powdered colocynth contains a large number of starch granules it has probably been adulterated.

Constituents.—Power and Moore (*Tr. Chem. Soc.,* 1910, xcvii, p. 99) found in colocynth an alkaloidal principle which has a violent purgative effect, but this is not the only active principle of the crude drug, because both ether and chloroform extracts of the resin, when free from the alkaloidal principle, were still purgative. They find also alpha-elaterin, but none of the active beta-elaterin. (See *Elaterinum.*) The bitter principle of colocynth obtained by Vauquelin and by him called *colocynthin* (also known as *citrullin* by Ahrends), according to Power and Moore, is a mixture of the alkaloid and a crystallizable alcohol, *citrullol.* Waltz supposed that he had found another peculiar principle, *colocynthitin.* It was obtained by treating with ether the alcoholic extract previously exhausted by water, decolorizing the ethereal solution with animal charcoal, evaporating to dryness, and dissolving the residue in anhydrous alcohol, which deposited it in crystals on spontaneous evaporation. It is white and tasteless, and is probably a resin. (*N. Jahrbuch der Pharm.,* xvi, 10.)

An infusion of colocynth, made with boiling water, gelatinizes upon cooling. Neumann obtained from 768 parts of the pulp, treated first with alcohol and then with water, 168 parts of alcoholic and 216 of aqueous extract. (See also paper by George Wagner, *Proc. A. Ph. A.,* 1893, 179.)

Uses.—The pulp of colocynth is a powerful drastic, hydragogue cathartic, producing, when given in large doses, violent griping, and sometimes bloody discharges, with dangerous inflammation of the bowels. Death has resulted from a teaspoonful and a half of the powder. (Christison.) Even in moderate doses it sometimes acts with much harshness, and it is therefore seldom prescribed alone. By some writers it is said to be diuretic. It was frequently employed by the ancient Greeks and the Arabians, though its drastic nature was not unknown to them. Among the moderns it is occasionally used in obstinate *dropsy,* and in various affections depending on disordered action of the brain. In combination with other cathartics it loses much of its violence, but retains its purgative energy, and in this form is extensively employed. It is best administered in minute division, effected by trituration with gum or farinaceous matter.

Thunberg states that the fruit of *C. Colocynthis,* at the Cape of Good Hope, is rendered so mild by being properly pickled that it is eaten both by the natives and by the colonists; but, as it is thus employed before attaining perfect maturity, it is possible that the drastic principle may not have been developed.

Dose, one to five grains (0.065–0.32 Gm.).

Off. Prep.—Extractum Colocynthidis, *U. S.;* Extractum Colocynthidis Compositum (from Extract), *U. S., Br.;* Pilula Colocynthidis Composita, *Br.;* Pilula Colocynthidis et Hyoscyami (from Compound Pill), *Br.,* (from Extract), *N. F.;* Pilulæ Catharticæ Vegetabiles (from Compound Extract), *N. F.;* Pilulæ Hydrargyri Chloridi Mitis Compositæ (from Compound Extract), *U. S.*

CONDURANGO. N. F.

CONDURANGO

"Condurango is the dried bark of *Marsdenia Cundurango* (Triana) Nichols (Fam. *Asclepiadaceæ*). Condurango contains not more than 2 per cent. of wood or other foreign organic matter." *N. F.*

Condurango Cortex; Cortex Condurango, *P. G.*

According to an official investigation made in 1873 by Passed Assistant Surgeon Joseph G. Ayers, U. S. N., there are at least ten different plants known in the republic of Colombia as *condurango.* The variety which has been used in *cancer,* and which may be considered as genuine condurango, is the *condurango blanco,* the product of a climbing asclepiadaceous vine from ten to thirty feet in length and from one to two inches in diameter. The plant is the *Marsdenia Condurango* of G. H. Reichenbach. (*Gonolobus Condurango,* Triana.) It is indigenous to Ecuador but also grows in other parts of South America. The bark is prepared by pounding the stem with a mallet to separate it, and then drying it in the sun.

Under the name of *Guayaquil condurango* a drug has appeared in the European markets composed of pieces of bark and fragments of woody branches, believed to be derived from an asclepiadaceous plant closely related to the genus *Gonolobus. Mexican condurango* is composed of split stems or thin adherent bark, and is thought to be yielded by an Aristolochia. For full description, see *Ph. Rund.,* May, 1888.

Description and Physical Properties.—"*Unground Condurango.*—In quills or transversely curved pieces, usually from 4 to 13.5 cm. long; bark 1 to 6 mm. thick; outer surface light grayish brown to dark brown, nearly smooth and with numerous lenticels, or more or less scaly and considerably roughened, occasionally with whitish lichens bearing brownish black apothecia; inner surface grayish white or light brown, longitudinally striate; fracture short-fibrous in the outer portion and granular in the inner portion. Odor slightly aromatic, especially marked in the fresh drug; taste bitter and aromatic.

"*Structure.*—Corky layer consisting of several rows of thin-walled cells, walls occasionally lignified and frequently with yellowish brown contents; a layer of phelloderm of eight to ten rows of cells, containing starch grains and crystals of calcium oxalate; a layer of collenchyma more or less interrupted by parenchyma, and containing chloroplastids, starch grains, and rosettes of calcium oxalate; a layer of parenchyma, with groups of bast fibers and laticiferous vessels in an interrupted circle; inner bark with large groups of stone cells, medullary rays one or two cells in width, numerous laticiferous cells accompanied by small groups of sieve cells, parenchyma containing either starch grains or rosettes of calcium oxalate, and an occasional isolated bast fiber or small group of stone cells.

"*Powdered Condurango.*—Light yellowish brown, consisting chiefly of groups of stone cells and parenchyma the latter containing calcium oxalate crystals and starch grains; calcium oxalate chiefly in rosettes from 0.015 to 0.040 mm. in diameter, occasionally in single prisms, 0.010 to 0.035 mm. in length; starch grains simple or 2- to 4-compound, the individual grains being from 0.003 to 0.020 mm. in diameter; stone cells up to 0.190 mm. in length, chiefly in large groups, the individual cells being more or less irregular in shape and with very thick porous yellow walls, the lumina being usually filled with air; bast fibers non-lignified very long and from 0.010 to 0.035 mm. wide; fragments of thin-walled latex tubes from 0.015 to 0.030 mm. in diameter and filled with a granular substance; fragments of cork grayish or light yellowish brown.

"Macerate 1 Gm. of powdered Condurango in 5 cc. of cold water; filter and heat the filtrate in a test tube; it becomes cloudy, but on cooling assumes its original transparency." *N. F.*

Vulpius (*P. J.*, 1885, 1066) found in it *condurangin*, a glucoside, very closely allied to *vincetoxin* of Tanret, but it was probably a mixture of various glucosides. Carrara (*A. J. P.*, 1892) obtained from the so-called condurangin of commerce two principles: One insoluble in water, soluble in benzene, a light, almost white, powder, melting at from 60°–61° C., and of the composition $C_{20}H_{32}O_6$. Both compounds are decomposed by acids, yielding a brown pitchy substance, insoluble in water. Merck gives the following constituents of condurango: *Alpha-condurangin*, $C_{20}H_{32}O_6$; *Beta-condurangin*, $C_{18}H_{28}O_7$; *Conduransterin*, $C_{30}H_{50}O_2$, and also a trace of an alkaloid resembling strychnine in action. Boehm (*M. M. W.*, lv, p. 1775) regards condurangin as a derivative of cinnamic acid. According to Firbas, condurangin, in solution, can be recognized by freeing from alcohol with gentle warmth, precipitating with a saturated solution of sodium chloride, dissolving the precipitate in chloroform, and adding a liquid composed of equal parts of sulphuric and hydrochloric acids and alcohol. On warming, the mixture assumes a green color, which turns a beautiful greenish-blue on the addition of a trace of ferric chloride. This *Lafon reaction* is given also by adonidin, oleandrin, sapotoxin and digitoxin.

Uses.—Brunton reached the conclusion that *Condurango blanco* was inert, but Kobert found condurangin to be a violent poison, causing convulsions followed by paralysis; he believes it to be a mixture of several principles. (*S. Jb.*, 1889, No. 9.) H. Chiriboga states that three drachms of the bark taken by himself in the form of decoction produced considerable activity of the circulation, copious diaphoresis, increased secretion of urine, and even some vertigo and disturbance of vision. Condurango was at one time reputed to possess value in the treatment of *cancers* and was also used in South America in *syphilis* but there is no satisfactory evidence of its usefulness in either condition.

Prof. P. E. Hommell recommends *Mistura condurango et ulmi* and *Fluidglycerate of condurango* for the internal administration of the drug. (See *Proc. N. Jersey Pharm. Assoc.*, 1913, 80; also *M. R.*, 1913, 231.)

Dose, sixty grains (4 Gm.).

Off. Prep.—Fluidextractum Condurango, *N. F.*

CONFECTIO PIPERIS. Br.

Electuarium Piperis; Electuaire de Poivre, *Fr.*; Pfefferlatwerge, *G.*

"Black pepper of commerce, in powder, 100 *grammes;* Caraway Fruit, in powder, 150 *grammes;* Purified Honey, 750 *grammes.* Mix." *Br.*

This preparation was intended as a substitute for *Ward's Paste*, which acquired some reputation in Great Britain as a remedy in *piles* and ulcers of the rectum. To be of service, it must be continued, according to Brodie, for two, three, or four months. Its stimulating properties render it inapplicable to cases attended with much inflammation.

Dose, from one to two drachms (3.9–7.7 Gm.), repeated two or three times a day.

CONFECTIO ROSÆ GALLICÆ. Br.

CONFECTION OF ROSES

Conserva Rosarum; Conserve de Rose rouge, *Fr.*; Rosen-Conserve, *G.*; Conserva de Rosso, *Sp.*

Confection of Rose is not recognized by the U. S. but is official in the N. F. (See Part III.)

"Fresh Red-Rose Petals, 250 *grammes;* Refined Sugar, 750 *grammes.* Beat together in a stone mortar." *Br.*

The formula given in the N. F. for confection of rose differs in several particulars, from the Br. Dried roses have been substituted for the fresh as the latter are not brought to our market. A part of the sugar has been replaced by honey and added odor given by the use of stronger rose water.

Confection of Rose is slightly astringent; it is used almost exclusively as a vehicle, and is admirably adapted as an excipient and to impart consistence to the pilular mass.

Off. Prep.—Pilula Hydrargyri, *Br.*

CONFECTIO SENNÆ. Br.

CONFECTION OF SENNA

Electuarium Sennæ Compositum, Electuarium Lenitivum; Electuaire de Séné composé, Electuaire lenitif, *Fr.;* Electuarium e Senna, *P. G.;* Sennalatwerge, *G.;* Elettuario lenitivo, *It.*

Confection of Senna is not official in the U. S., but the National Formulary recognizes a similar preparation. (See Part III.)

"Senna Leaves, in powder, 100 *grammes;* Coriander Fruit, in powder, 40 *grammes;* Figs of commerce, 160 *grammes;* Tamarinds, 120 *grammes;* Cassia Pulp, 120 *grammes;* Prunes of commerce, 80 *grammes;* Extract of Liquorice, 15 *grammes;* Refined Sugar, 400 *grammes;* Distilled Water sufficient to produce 1000 *grammes.* Boil the figs and prunes gently with three hundred and fifty grammes of Distilled Water in a covered vessel for four hours; add more Distilled Water to make up the quantity to its original weight, and then incorporate the Tamarinds and Cassia Pulp; digest for two hours; rub the softened pulp of the fruits through a hair sieve, rejecting the seeds and other hard parts; to the pulp thus obtained add the Refined Sugar and Extract of Liquorice, dissolving them by the aid of gentle heat; while the mixture is still warm, add to it gradually the mixed Senna and Coriander powders; mix the whole thoroughly; make the weight of the resulting Confection one thousand grammes, either by evaporation or by the addition of more Distilled Water." *Br.*

The preparation of the N. F. differs from the Br. in that it omits the extract of licorice, using a larger amount of sugar and substituting the oil of coriander for the seed. The latter is an improvement because it is almost impossible to powder coriander fine enough to avoid hard particles except by drying it to such an extent as to deprive it of its volatile oil. The oil of coriander should be dropped upon a portion of the powdered senna contained in a mortar or suitable vessel and this lightly triturated with the rest of the powdered senna so as to distribute it uniformly and the mixture should then be added to the pulpy mass.

A very good, pleasant laxative, admirably adapted to cases of habitual costiveness, especially in pregnant women, and in persons affected with *piles.*

Dose, one to two drachms (3.9–7.7 Gm.), at bedtime.

CONFECTIO SULPHURIS. Br.

CONFECTION OF SULPHUR

Electuarium Sulphuris; Electuaire de Soufre, *Fr.;* Schwefelatwerge, *G.*

"Precipitated Sulphur, 450 *grammes;* Acid Potassium Tartrate, in powder, 110 *grammes;* Tragacanth, in powder, 5 *grammes;* Syrup, 210 *millilitres;* Tincture of Orange, 55 *millilitres;* Glycerin, 170 *millilitres.* Mix." *Br.*

This is merely a mode of administering the two laxatives, sulphur and potassium bitartrate, and the relative proportion of the latter is so small that it can have little effect. The addition of tragacanth is due to a suggestion of Peter Boa, who found that without it a syrupy layer of liquid formed on top of the confection. (*P. J.,* 1882, 682.) The syrup of orange peel, formerly directed, has been replaced in the last two editions by syrup and tincture of orange, evidently because the syrup of orange peel did not keep well, while the glycerin serves to retain the proper consistence of the confection.

Dose, one to two drachms (3.9–7.7 Gm.) or more.

CONFECTIONES

CONFECTIONS

Electuaries; Conserves, Electuaries, Saccharolés mous, *Fr.;* Konserven, Latwergen, *G.;* Elettuario, *It.;* Electuario, *Sp.*

Under the general title of Confections, the Pharmacopœias include all those preparations having the form of a soft solid, in which one or more medicinal substances are incorporated with saccharine matter, with a view either to their preservation or more convenient administration. But two confections, Rose and Senna, were retained in the Eighth Revision of the U. S. Pharmacopœia and in the Ninth Revision both were dropped but admitted to the National Formulary. The old division into Conserves and Electuaries has been abandoned; but, as there is some ground for the distinction, we shall make a few general remarks upon each division before proceeding to the consideration of the individual preparations.

Conserves consist of undried vegetable substances and refined sugar beaten into a uniform mass. By means of the sugar, the vegetable matter is enabled to resist for some time the decomposition to which it would otherwise be exposed in the undried state, and the properties of the recent plant are thus retained to a certain extent unaltered. But, as active medicines even thus treated undergo some change, and those which lose their virtues by desiccation cannot be long preserved, the few conserves now used are intended rather as convenient vehicles of other substances than for separate exhibition. The sugar used in their preparation should be in fine powder.

Electuaries are mixtures consisting of medicinal substances, especially dry powders, combined with syrup or honey, in order to render them less unpleasant to the taste, and more convenient for internal use. They are usually prepared extemporaneously; and it is only when their complex nature renders it convenient to keep them ready made, or some peculiarity in the mode of mixing the ingredients requires attention, that they become proper objects for official direction. Their consistence should not be so soft, on the one hand, as to allow the ingredients to separate, nor so firm, on the other, as to prevent them from being swallowed without mastication. Other information on conserves, electuaries and confections with formulas for those which were formerly official, will be found in previous editions of the *U. S. D.*

CONIUM. N. F.

CONIUM [Poison Hemlock]

"Conium consists of the dried full grown, but unripe fruit of *Conium maculatum* Linné (Fam. *Umbelliferæ*). Conium contains not more than 2 per cent. of foreign fruits, seeds, or other foreign organic matter and yields not less than 0.5 per cent. of coniine. After being kept for more than two years, it is unfit for use. Conium should be carefully dried and preserved." *N. F.*

Conii Fructus, *Br.*, 1898.; Hemlock, Spotted Hemlock or Parsley, Fool's Parsley, St. Bennett's Herb; Spotted Cowbane; Herba Cicutæ (Majoris); Fructus Conii; Ciguë officinale, Grande Ciguë, *Fr. Cod.*; Schierling, Gefleckter Schierling, *G.*; Cicuta maggiore, *It.*; Cicuta (Fruto), *Sp.*

Conium maculatum is an umbelliferous plant, native of Europe, but naturalized in the United States. It is sometimes referred to as *cicuta* but this name properly belongs to another genus of *Umbelliferæ* (see *Cicuta*). The conium usually grows in clusters along road-sides or on waste grounds and is found most abundantly near old settlements. It reaches a height of from 2 to 5 feet and is characterized by large, pinnately decompound leaves—the lower being sometimes more than a foot in length, the upper leaves being sessile and the lower petioled—a spotted stem and umbels bearing white flowers in June and July. The whole plant, during midsummer, exhales a fetid odor, compared by some to that of mice, by others to that of the urine of cats, and narcotic effects result from breathing for a long time air loaded with the effluvia. The plant varies in narcotic power according to the weather and climate, being most active in hot and dry seasons and in warm countries.

All parts of the plant contain the toxic principle and the leaves were at one time recognized by the British Pharmacopœia. Because of the rapidity of their deterioration, however, they were never satisfactory. The fruits (sometimes, incorrectly, called the seed) retain their activity much longer than the leaves. Conium fruits should be collected from plants fully grown but before their color changes from green to yellow, and thoroughly dried.

The commercial supplies of conium are from Europe. Commercial conium occasionally contains other umbelliferous plants, or it may be almost wholly composed of such plants, and even anise has been used as an adulterant of the fruit. (See *Anise.*)

Description and Physical Properties.—"*Unground Conium.*—Broadly ovoid, greenish gray, the two mericarps often separated, each about 3 mm. long and about 1.5 mm. in diameter, ovoid, somewhat curved; the inner flattened side marked by a deep longitudinal groove; the outer convex side with five, pale yellow, somewhat crenate ribs; the intervening surfaces wrinkled; pericarp without oil-tubes. Odor slight, but when triturated with a solution of potassium hydroxide T.S., strong, disagreeable, and mouselike; taste characteristic, disagreeable, afterwards somewhat acrid.

"*Structure.*—Transverse sections of the mericarp pentangular in outline, the angles projecting and forming the ribs, four of the sides being almost equal in length, the fifth or commissural side being about twice as long as one of the dorsal sides and usually concave near the middle; a distinct fibro-vascular bundle at each angle composed of thick-walled fibers about 0.013 mm. in diameter and a few tracheæ; epidermis consisting of one layer of cells, without hairs; pericarp thin, without oil-tubes, enclosing a single seed and extending inwardly on the commissural side for about one-third the diameter of the section; endocarp composed of two layers of cells with yellowish brown walls, the outer layer with cells from 0.060 mm. to 0.140 mm. in tangential length and with thickened radial and inner walls, the inner layer with thin-walled cells from 0.030 to 0.080 mm. in tangential length and about 0.030 mm. in radial diameter; the seed coat composed of small thick-walled cells about 0.015 mm. in radial diameter, often obliterated; a large endosperm somewhat pentangular-rounded in outline, with a deep channel on the commissural side and composed of polygonal parenchyma cells, the latter containing globules of fixed oil and aleurone grains with rosettes of calcium oxalate.

"*Powdered Conium.*—Greenish gray; numerous angular or rounded, light colored fragments of endosperm tissue, composed of parenchyma cells containing fixed oil, aleurone grains and rosettes of calcium oxalate, the latter from 0.002 to 0.008 mm. in diameter; a few more or less curved groups of lignified fibers; fragments of the seed-coat with yellowish brown walls; a few rounded starch grains about 0.005 mm. in diameter; spiral or annular tracheæ few; numerous oil globules separate on mounting the powder in chloral hydrate T.S.

"**Assay.**—Place 15 Gm. of Conium, in a moderately fine powder, in a 250 cc. flask or bottle, add 150 cc. of purified petroleum benzin, allow to stand five minutes, then add 15 cc. of solution of sodium hydroxide U.S.P., stopper securely and shake the flask vigorously at intervals during two hours. Allow it to stand over night and again agitate vigorously at intervals during one hour. Allow the mixture to settle, decant 100 cc. of clear fluid (representing 10 Gm. of Conium) and extract the alkaloids from this by shaking out with successive portions of weak hydrochloric acid, until a few drops of the acid washings give no test for alkaloid with iodine T.S. Evaporate the combined acid washings on a water-bath to a volume of about 10 cc., cool and transfer to a separator and render it alkaline by the cautious addition of sodium carbonate. Extract the alkaline liquid with successive small portions of purified petroleum benzin until a portion gives no test for alkaloid with iodine T.S., and to the combined benzin washings add 10 cc. of tenth-normal sulphuric acid. Stir thoroughly during two minutes, to bring the acid in contact with the benzin solution, then evaporate the benzin layer in a current of warm air. Titrate the acid solution, using cochineal T.S. or methyl red T.S. as indicator. Each cc. of tenth-normal sulphuric acid corresponds to 0.0126 Gm. of coniine." *N. F.*

The active principle seems to be most abundant in the seeds. Even these, however, deteriorate rapidly when kept. Farr and Wright (*P. J.*, Feb., 1904) found the average alkaloidal content of fresh seed to be 2.13 per cent. and of the commercial dried seed, 0.674 per cent. The N. F. requires not less than 0.5 per cent.

Constituents.—In the root Harley found three proximate principles, a bitter resin, which he names *conamarine,* and two crystallizable bodies, named respectively *rhizoconin,* and *rhizoconolein.* They are all neutral, and, so far as known, medicinally inert. (See *P. J.*, Aug., 1867.)

The activity of conium is due to the presence of five alkaloids which are as follows:

Coniine, the most important of these, was discovered in 1827, by Giesecke. The formula, $C_8H_{17}N$, is universally accepted; it is a propylpyridine. When pure it is a colorless, strongly alkaline liquid with a peculiar odor, similar to that of the plant. It boils at 166°–167° C. and solidifies at –2° C. It is naturally dextrorotatory but l-coniine has been prepared. It forms crystalline salts with a number of acids. Coniine has been prepared synthetically by several authors in various manners (see Ladenburg, *B. Chem. G.*, 1907, xl; Lautenschlager and Onsager, *B. Chem. G.*, 1918, li). Hess and Eichel (*B. Chem. G.*, 1917) have shown that pelletierine of pomegranate, is an aldehyde of coniine. Coniine is freely soluble in alcohol, ether, and the fixed and volatile oils, and slightly so in water. It unites with about one-fourth of its weight of water to form a hydroxide. Like ammonia, it occasions a white cloud when approached by a rod moistened with hydrochloric acid; and the resulting hydrochloride is crystallizable, and not in the least deliquescent. When exposed to the air, coniine speedily assumes a deep brown color, and is ultimately converted into a resinous matter, and into ammonia, which escapes. Under the influence of heat this change takes place with much greater rapidity. The presence of coniine may be detected in an extract or other preparation of hemlock by rubbing it with potassium hydroxide, which instantly develops its peculiar odor. It is a most energetic poison.

Methyl-coniine (N-methyl-*d*-coniine), $C_8H_{16}N.CH_3$, occurs in very small amounts. It is a colorless oily liquid, boiling point 173°–174° C., more strongly dextro-rotatory than coniine (see Braun, *B. Chem. G.*, 1905 and 1917, l).

Conhydrine, discovered by Wertheim in 1857, is an oxygenated base with the formula $C_8H_{17}ON$. It is crystalline, melting at 121° C. Isomeric with it is *pseudo-conhydrine* (see Loffler, *B. Chem. G.*, 1909) which has a melting point of 105°–106° C.

Conieine, $C_8H_{15}N$.—A series of isomers have been prepared by chemists, in various ways, from coniine. Of these bases at least one—gamma-coniceine—appears to occur in the natural drug. (Wolffenstein, *B. Chem. G.*, 1895; see also Loffler, *B. Chem. G.*, 1909, xlii) but has been formed by the action of fuming hydrochloric acid on conhydrine. It is a coniine-like oily liquid almost insoluble in water, strongly alkaline and optically inactive. All of these alkaloids seem to be similar in their physiological effects (Albahare and Loffler, *C. R. A. S.*, 1908, cxlvii, p. 996). Gamma-coniceine is the most toxic, coniine the next and conhydrine the least.

Uses.—Hemlock or conium is supposed to be the narcotic used by the Athenians to destroy the life of condemned individuals, and by which Socrates and Phocion died. It was also used by the ancients as a medicine, but fell into entire neglect until Störck employed and extravagantly praised it. Though fatal to some animals, hemlock is eaten with impunity by others, as horses, goats, and sheep.

The alkaloids of conium all have the same physiological properties, although there is a difference in the degree of their power. Their most important effect is a paralysis of the peripheral endings of the motor nerves. In the account of the death of Socrates reference is made to loss of sensation as one of the prominent symptoms of his poisoning and there is evidence that the drug has an effect upon the sensory as well as upon the motor nerves, but the dominant action is certainly upon the motor system. Hayashi and Muto (*A. E. P. P.*, 1901, xlviii) have shown that the phrenic nerve is more susceptible to the drug than the other motor nerves of the body. It is evident, therefore, that if given in sufficient dose to control spasms, conium would stop the movements of the diaphragm and therefore cause death through asphyxia.

The drug has, however, been used in spasmodic disorders, such as *whooping cough, paralysis agitans,* and *acute mania* and by some with asserted good results. It was in the days of superstitious medicine believed to exercise an alterative effect in *scrofulas* and similar diatheses, but was long ago abandoned for this purpose.

Coniine acts precisely as does hemlock, and may be used for the same purposes. The *dose* is from one-fortieth to one-twelfth of a grain (0.0015–0.005 Gm.). Its solution has been used locally in the spasmodic contraction of the *orbicularis oculi* and *ophthalmia* with *photophobia* in scrofulous children. For these purposes from one-half to one per cent. may be employed. Various salts have been prepared, but the *hydrobromide* is the one most frequently used.

This occurs in colorless prismatic needles, soluble in water and alcohol, less so in ether and chloroform, inodorous and almost tasteless, and are not deliquescent. It should be kept in the dark, otherwise it assumes a red tint.

Dose, of conium, three to five grains (0.2 to 0.32 Gm.).

Off. Prep.—Extractum Conii, *N. F.*

CONVALLARIÆ RADIX. N. F.

CONVALLARIA ROOT Convall. Rad.

[Lily-of-the-Valley Root]

"Convallaria Root consists of the dried rhizome and roots of *Convallaria majalis* Linné (Fam. *Liliaceæ*). Convallaria Root contains not more than 5 per cent. of leaves or other foreign organic matter and yields not more than 6 per cent. acid-insoluble ash." *N. F.*

Lilium Convallium; Muguet, *Fr.*; Maiblumen, *G.*; Mughetto, *It.*; Convalaria, Lirio de los valles, *Sp.*

Convallaria majalis L. is a low, acaulescent, perennial herb native to mountainous regions of Europe, Asia and Southeastern United States. It is widely cultivated for the beauty and fragrance of its flowers. Its above ground portion first exhibits two to three oblong, parallel-veined leaves and later a slender one-sided raceme of small, white, nodding bell-shaped flowers. The fruits are red berries.

Both the root and flowers were formerly official but the N. F. V recognizes only the rhizome and roots.

Description and Physical Properties.—"*Unground Convallaria Root.*—Rhizome horizontal, elongated, usually branched cylindrical, variable in length, from 1 to 3 mm. in diameter; externally yellowish white or pale brown, with a few circular stem scars, and from 3 to 5 thin, tortuous, dark brown, branching roots arising from the lower portions of the nodes; fracture short or fibrous; internally whitish. Odor faint; taste sweetish, becoming bitter and acrid.

"*Structure.*—Rhizome; an epidermis with a thick outer layer of cutin; a hypodermal layer of a single row of collenchyma; a cortex made up of about twenty rows of parenchyma cells, some of which contain starch and others raphides of calcium oxalate; a prominent endodermis, the radial and inner walls, strongly thickened and lignified; inside the endodermis an interrupted circle of collateral fibro-vascular bundles, the woody portion V shaped in cross section; inside the first circle of bundles, another interrupted circle of fibro-vascular bundles of the concentric type, the sieve tissue being surrounded by the xylem; parenchyma cells of the pith separated by large inter-cellular spaces. The root shows a hairy epidermal layer; a hypodermis of a single row of cells; a cortex of about six rows of cells, some of which contain starch or raphides of calcium oxalate, and oil; the cells of the endodermal layer resemble those of the rhizome; fibro-vascular bundles mostly five.

"*Powdered Convallaria Root.*—Brown; tending to cake on standing; a few simple or compound starch grains the latter, the simple grains nearly spherical and from 0.003 to 0.012 mm. in diameter; raphides of calcium oxalate few, from 0.020 to 0.060 mm. in length, rarely up to 0.150 mm.; cells of endodermis with slightly oblique ends and considerably thickened, lignified porous walls; fragments of tracheæ with spiral and scalariform thickenings, or with porous walls." *N. F.*

G. F. Walz found in lily of the valley two glucosides, *convallarin* and *convallamarin.* (*A. J. P.*, 1859, p. 577.) Convallarin is in colorless, rectangular prisms, scarcely soluble in water, but sufficiently so as to render the solution acrid. It is decomposed by long boiling with diluted acids into sugar and *convallaretin.* J. Lindner (*J. P. C.*, 1916, xiii, 290) examined convallarin of commerce. He finds it has the formula $C_{22}H_{40}O_{10}$ and not the formula ($C_{34}H_{62}O_{11}$) ascribed to it by its discoverer. According to Kobert convallarin is related to the saponins. Convallamarin is a white powder, very bitter and afterwards sweetish, soluble in water and alcohol, but not in ether. Its composition is $C_{23}H_{44}O_{12}$, and it is decomposed by heating with diluted sulphuric acid into sugar and *convallamaretin.* For preparing convallamarin, Tanret modifies Walz's method, as follows. An alcoholic tincture made from the whole plant is precipitated with lead subacetate and filtered; the excess of lead is removed with diluted sulphuric acid, avoiding the use of more than is necessary, and, after neutralizing, the tincture is distilled, the last portion of alcohol being driven off in the open air, then the cooled and filtered liquor is treated with tannin, care being taken to keep the liquid neutral by cautiously adding a diluted solution of sodium carbonate. A compound of tannin and convallamarin is precipitated, which, after washing, is dissolved in 60° alcohol, the solution decolorized with charcoal, decomposed with zinc oxide, filtered, and evaporated to dryness. In this way convallamarin is obtained nearly white. To free it from the salts that are sometimes carried down by the tannin precipitate, it is a good plan to redissolve it in 90° alcohol, filter, and then evaporate. One kilogramme of the fresh plant collected in the first days of August yielded two grammes of convallamarin. (*P. J.*, 1882, p. 423.)

Uses.—Taken internally the flowers are said to be emetic and cathartic, and their extract purges actively in the *dose* of half a drachm. They were formerly used in *epilepsy* and against *worms.* The root, which is also bitter, has similar purgative properties, and in powder is said to be sternutatory. Convallaria, like digitalis, in moderate doses slows the pulse rate and in toxic doses stops the heart in systole and has been used in the treatment of *heart disease.* Marvin and White (*J. A. M. A.*, 1921, lxxvii, p. 1868), however, found that in *auricular fibrillation,* although it produced the ventricular slowing characteristic of the digitalis group, in the majority of cases it failed to lead to any clinical improvement.

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Fluidextractum Convallariæ Radicis, *N. F.*

COPAIBA. U. S., Br.

COPAIBA Copaib. [Balsam Copaiba]

"An oleoresin derived from South American species of *Copaiba* (Fam. *Leguminosæ*)." *U. S.* "Copaiba is the oleo-resin obtained by incision from the trunk of various species of Copaifera, *Linn.*" *Br.*

Balsamum Copaiferarum; Balsam of Copaiba, Balsam Capivi; Copahu, *Fr. Cod.;* Baume de Copahu, *Fr.;* Balsamum Copaïvæ, *P. G.;* Copaiva; Copaivabalsam, *G.;* Balsamo d Copaive, *It.;* Oleoresina de Copaiba, Bálsamo de Copaiva, *Sp*

Copaiba was first noticed in a work published by Purchas, in England, in 1625. It is derived from several South American trees of the genus *Copaiba* Mill. (*Copaifera,* L.). The most important of these are: *C. officinalis* (L.) Jacquin, *C. guyanensis* (Desf.) O. Kuntze, *C. Langsdorffii* (Desf.) O. Kuntze, and *C. coriacea* (Mart.) O. Kuntze.

The plants yielding the drug are large, much branched trees having in their full grown condition huge trunks. The branches have smooth bark and bear alternate, paripinnate leaves, each with 6 to 10 entire, ovate, coriaceous pellucid-punctate leaflets. The flowers are small and white, each with a receptacle bearing 5 sepals, 10 stamens and a monocarpellary pistil. The fruit is a one-seeded legume.

Copaiba is considered a morbid product of the cell walls of the wood parenchyma. It accumulates in cavities, within the trunk of the tree, that enlarge and join to form great reservoirs, the latter often holding several gallons of oleoresin.

The juice is obtained by making a square chamber in the trunks of the trees, reaching to the very center; and the operation is said to be repeated several times during the same season. It is asserted that single trees have yielded as much as forty liters. As it flows from the wound, it is clear, colorless, and very thin, but it soon acquires a thicker consistence, and a yellowish tinge. It is most largely collected in the provinces of Para and Maranham, in Brazil, and is brought to this country from the port of Para, in small casks or barrels. Smaller quantities of it come from Maracaibo, in Venezuela, and from other ports on the Caribbean Sea, whence it is brought in casks, demijohns, cans, jugs, etc.

C. officinalis is a native of Venezuela, and grows in the province of Carthagena, mingled with the trees which afford the balsam of Tolu. It grows also in some of the West India islands, particularly Trinidad and Martinique. This is the source of the Maracaibo or Venezuela copaiba, which is also obtained in part from *C. guianensis.* This variety of copaiba is distinguished by being lævogyrāte, more viscid and darker in color.

Numerous varieties of true South American copaiba exist in commerce, known under the name of the various ports of shipment. The most important of these varieties besides Maracaibo is the Para or Maranham copaiba, which is derived from *C. Langsdorffii* and *C. coriacea,* which is characterized by being optically lævogyrate. The other varieties are Bahia, Carthagena, Maranham, and Cayenne. Each one of these varieties has been referred (see *P. J.,* 1901, lxvi, 325) to a special species of the genus Copaiba, but there is little reason for supposing that this reference is accurate, and there is much reason for believing that various trees contribute to a single variety of copaiba.

Most of our copaiba is either of the Maracaibo or Para varieties. Although the individual specimens from each of these regions differ so much among themselves that it is impossible to draw a sharp distinction in the physical properties between the two varieties, the Para variety is generally comparatively low in proportion of resin, consisting of from 55 to 90 per cent. of volatile oil. Because of the large proportion of oil the Para copaiba is more liquid and of a lower specific gravity than that which comes from Maracaibo. Much of the Para copaiba fails to meet the pharmacopœial requirements in the percentage of resin and specific gravity. The U. S. requires a specific gravity of 0.94 or over and not less than 36 per cent. of resin; The Br. requires a specific gravity of 0.975 to 0.995 and about 55 per cent. of resin.

According to E. Keto, copaiba of Maracaibo has a density of 0.999; a coefficient of acidity of 85.4; of etherification of 6.7; while that of Para has a density of 0.92; a coefficient of acidity of 19.4; of etherification of 7.4.

The German Pharmacopœia requires that the specific gravity shall be 0.98 to 0.99, and that the acid number shall fall between 75.6 and 84, and the ester number be not more than 8.4.

Surinam copaiba is a yellowish or brownish-yellow liquid, of varying consistence; it may be distinguished from Maracaibo copaiba by the fact that one drop of it dissolved in 1 cc. of acetic anhydride gives a fine blue color on the addition of a drop of sulphuric acid. (*P. J.,* Nov., 1904.)

African copaiba, or *Balsam of Illurine,* which reached the London market first in 1891, from West Africa, is a brownish substance, having a consistency similar to the Maracaibo copaiba, and a greenish fluorescence. Its aromatic odor is entirely different from that of copaiba; its taste is biting, with an after-taste of bitterness. According to Keto (*J. P. C.,* 1902, 381), its density is 0.9905; its coefficient of acidity 55.5; of etherification 8.3. It is soluble in chloroform and petroleum benzin, also in ether, with which it makes an opalescent liquid. Its solution in absolute alcohol, or alcohol of 95 per cent. is not limpid. From it Keto separated *illurinic acid.* Its volatile oil is of a pale yellow color, with a strong odor entirely different from that of copaiba. The residue which remains after the distillation consists of two resins, one soluble, the other insoluble, in alcohol. This oleoresin probably is the product of *Hardwickia Mannii* Oliver, a tree closely allied to the true copaibas. (See *Ap. Ztg.*, 1894, p. 9.) J. C. Umney (*A. J. P.*, 1893, 544) found in African copaiba 39 per cent. of an oil of 0.918 specific gravity and with a rotation of + 20° 42′, the last character distinguishing it from the other varieties which yield lævorotatory oils.

Solid Copaiba or *Mass of Copaiba* is official in the National Formulary, Part III. See also U. S. Dispensatory, 19th edition, p. 398.

Description and Physical Properties.—"A pale yellow to brownish-yellow, more or less viscid liquid, either without fluorescence or with only a slightly greenish fluorescence. It has a peculiar, aromatic odor, and a persistent, bitter, acrid taste. Copaiba is insoluble in water, partly soluble in alcohol, more completely soluble in dehydrated alcohol. It is soluble in carbon disulphide and in fixed or volatile oils, completely soluble in chloroform and in ether; also soluble in an equal volume of petroleum benzin, the further addition of the solvent producing a flocculent precipitate.

"Specific gravity: 0.940 to 0.995 at 25° C. Heat about 2 Gm. of Copaiba, accurately weighed, in a shallow dish on a water bath: no odor of oil of turpentine is evolved. Continue the heating until all of the volatile oil has been driven off: a resin remains, corresponding to not less than 36 per cent. of the original weight of the Copaiba taken. This resin when cooled is hard and brittle (*paraffin or fatty oils*). Its acid number is not less than 28 and not more than 95, page 427. Shake 5 cc. of Copaiba with 15 cc. of alcohol, boil the mixture for one minute, and cool: no oil separates after standing for one hour (*paraffin oils*). Mix one drop of nitric acid and 3 cc. of glacial acetic acid in a test tube, and carefully add four drops of the oil separated from the Copaiba by distillation with steam: no reddish zone appears, nor does the liquid become red or purple after being shaken (*gurjun balsam*). Dissolve 2 Gm. of Copaiba in 40 cc. of dehydrated alcohol, filter on counterbalanced filters or with the aid of a Gooch crucible, and wash with small portions of dehydrated alcohol until the washings are colorless or nearly so: the residue dried at 80° C. does not exceed 5 per cent. The volatile oil separated from Copaiba by distillation with steam does not boil below 250° C., and shows an angle of rotation in a 100 mm. tube of not less than –7° at 25° C. (*African copaiba*)." *U. S.*

"A more or less viscous liquid, generally transparent and occasionally fluorescent, yellow to golden brown. Specific gravity 0.975 to 0.995. Entirely soluble in *absolute alcohol;* soluble in four times its volume of *petroleum spirit*, the solution yielding only a slight filmy deposit on standing. Aromatic, characteristic odor; taste acrid, somewhat bitter, persistent. Loses about 45 per cent. of its weight when heated for forty-eight hours to 100° C. Forms a transparent solution with one-third of its volume of *solution of ammonia.* Four drops carefully added to a mixture of 5 millilitres of *glacial acetic acid* with four drops of *nitric acid* do not yield a purplish or violet color (absence of gurjun balsam). One gramme dissolved in 25 millilitres of *absolute alcohol,* requires for neutralisation not less than 2.7 millilitres of *N/2 alcoholic solution of potassium hydroxide, solution of phenolphthalein* being used as indicator (presence of a due proportion of acid resins). The volatile oil distilled from it responds to the tests described under 'Oleum Copiabæ.'" *Br.*

Copaiba, upon exposure to the air, acquires a deep color, a thicker consistence, and greater density, and; if spread out upon an extended surface, ultimately becomes dry and brittle. This change is owing partly to the volatilization and partly to the oxidation of the essential oil. As it is the soft resin that results from the oxidation of the oil, it follows that the proportion of this resin increases with age. Considerable diversity must, therefore, exist in the drug, and in its physical properties and in the proportions of its ingredients, according to its age and degree of exposure. Similar difference also exist in the copaiba procured from different sources. It is not impossible that differences may exist in the drug according to the circumstances of its collection. The species of *Copaiba* from which the oleo-resin is collected, as well as the age of the tree, its position, and the season of collection, must also have influence over the product. It is highly probable that the resinous matter results from the oxidation of the oil in the cells of the plant, and that the less elaborated the oleoresin may be, the larger proportion it will contain of the oil. It is said that a volatile oil flows abundantly from a tree near Bogotá, which is employed to adulterate the copaiba collected in that vicinity and shipped from Maracaibo and other neighboring ports.

Copaiba is often adulterated. The substances most frequently used for this purpose are: (1) Some fixed oil, especially castor oil, as this cannot be distinguished by its insolubility in alcohol. (2) Gurjun balsam (see *Oil of Wood,* Part II). (3) Volatile oils, especially oil of turpentine or of sassafras. (4) Colophony. (5) Liquid petroleum. Most of these adulterants are excluded by the requirements of the U. S. P.

For additional tests and criticisms by Beckurts and Brueche, see *A. Pharm.*, 1891, p. 90; also *Proc. A. Ph. A.*, 1892, 635. For Hager's test, see *C. D.*, 1894, 740. Dodge and Olcott (*Am. Drug.*, 1895, 5) describe a test to detect gurjun balsam in copaiba, which Kebler regards as the most reliable yet proposed; it is as follows. Four drops of the suspected sample, dissolved in half a fluidounce of glacial acetic acid, will, if pure, remain colorless and clear, or but slightly cloudy, if from four to six drops of pure nitric acid be dropped into the solution.

If the sample be pure gurjun balsam, the mixture will have a deep purple color; if a mixture of the two balsams, the depth of color will vary according to the amount of the adulterant, as small a proportion as 2 per cent. being discoverable; a modification of this test is now official. (See also *A. J. P.*, 1896, 143, and 1897, 394.) For a valuable paper on Copaiba by A. R. L. Dohme, see *Proc. A. Ph. A.*, 1904, 322.

Constituents.—The essential ingredients are volatile oil and resin, with at times small quantities of acid. As it contains no benzoic acid, it cannot properly be called *balsam of copaiba*. The substances which it most closely resembles, both in composition and in properties, are the turpentines. (See *Oleum Copaibæ*.) For a description of an apparatus for distilling the volatile oil, see a paper by R. A. Cripps in *C. D.*, 1892, 282. The proportion of oil varies greatly, ranging from 30 to 75 per cent.

The *resinous* mass which remains after the distillation of the oil is hard, brittle, translucent, greenish-brown, and nearly destitute of odor and taste. It is of an acid character, and yields a series of amorphous salts; it may be obtained pure by exposing a mixture of 9 parts of copaiba and 2 parts of aqueous ammonia (sp. gr. 0.95) to a temperature of 10° C. Tschirch (*Harze and Harzbehälter*, 1900, p. 297) obtained from Maracaibo balsam a crystalline resin acid corresponding in many respects with Strauss's metacopaivic acid, to which, however, he gave the formula $C_{11}H_{16}O_2$, finding a melting point 89° to 90° C. as against 205° to 206° C. for Strauss's acid. Para balsam was found by Tschirch to contain two crystallizable resin acids together with several uncrystallizable ones. Illurinic acid has also been reported in Maracaibo balsam. Keto (*J. P. C.*, 1902, p. 381) finds in Para balsam the two crystallizable acids referred to above, one of which he names *paracopaivic acid* with the formula $C_{20}H_{32}O_3$ and fusing point 142° to 145° C., and the other *homoparacopaivic acid*, $C_{18}H_{28}O_3$, fusing at 111° to 112° C. To *illurinic acid* mentioned by Tschirch he gives the formula $C_{20}H_{28}O_3$ and the melting point 128° C.

For description of the volatile oil see *Oleum Copaibæ*.

Uses.—Copaiba is gently stimulant, diuretic, laxative, and in very large doses often actively purgative. It produces, when swallowed, a sense of heat in the throat and stomach, and extends an irritant action not only throughout the alimentary canal, but also to the urinary passages, and in fact, in a greater or less degree, to the whole mucous membrane, for which it appears to have a strong affinity. The urine acquires a peculiar odor during its use, and its odor may be detected in the breath. It sometimes occasions an eruption upon the skin resembling that of measles, and attended with disagreeable itching and tingling; in rare instances vomiting, painful purgation, stranguary and bloody urine, and a general state of fever are caused by excessive doses.

As a remedy it has been found useful in *catarrhs*, particularly those of a chronic character. Thus, it is given with occasional advantage in *leucorrhea, chronic cystitis, chronic diarrhea, hemorrhoids,* and *chronic bronchitis.* The complaint, however, in which it is most employed is *gonorrhea.* It should not be administered in the first stages, when the inflammation is severe and acute, nor is it applicable to very chronic forms of the disorder, such as gleet. It was formerly much esteemed as a vulnerary and as an application to *ulcers,* but it is now seldom used externally. Ruschenberger recommends it locally in *chilblains.*

Both the volatile oil and the resin are eliminated by the kidneys in an altered condition; if to the urine of a person taking the drug, nitric acid be added, a precipitate is thrown down, which may be mistaken for albumin. The volatile oil is more active than is the resin, which is not, however, inert.

It may be given dropped on sugar, but in this form is often so exceedingly offensive as to render some concealment of its nauseous qualities necessary. A less disagreeable form is that of emulsion, sweetened with sugar and flavored with some aromatic water, as that of mint or cinnamon.

Dose, of copaiba, from fifteen minims to a fluidrachm (1.0–3.75 cc.) three times a day, or a smaller quantity repeated more frequently.

Off. Prep.—Massa Copaibæ, *N. F.;* Mistura Copaibæ, *N. F.;* Mistura Copaibæ et Opii, *N. F.;* Oleum Copaibæ, *Br.*

COPTIS. N. F.

COPTIS [Goldthread]

"Coptis is the dried plant of *Coptis trifolia* (Linné) Salisbury (Fam. *Ranunculaceæ*). Coptis contains not more than 3 per cent. of foreign organic matter." *N. F.*

Coptide, *Fr.;* Gelbe (Kleinste) Niesswurz, *G.*

Coptis trifolia (L.) Salisbury is a low perennial herb characterized by having a slender (filiform) orange-colored rhizome from which spring several radical, evergreen, long-petioled, trifoliate leaves and a slender scape terminating in a single white flower which opens from May to July. The fruit consists of seven follicles containing small black seeds. This plant inhabits the northern region of this continent and of Asia, and is found in Greenland and Iceland. It delights in the dark shady swamps and cold morasses of northern latitudes and alpine regions, and abounds in Canada and in the hilly districts of the Northern United States.

Description and Physical Properties.—"*Unground Coptis.*—In loose, matted masses consisting of long, much branched rhizome and small roots, together with the leaves; rhizomes orange or golden-yellow; leaves evergreen, long and slenderly petioled, trifoliate, the segments broadly obovate-cuneate, crenately lobed and toothed with sharp-pointed teeth, prominently veined, smooth, coriaceous, dark green and shining but often drying to a dull brownish hue; flowers, if present, small, solitary, terminating slender scapes; sepals 5 to 7, oblong, obtuse, deciduous; petals 5 to 6, pale yellow, small, club-shaped; stamens numerous. Odor faint; taste purely bitter without astringency.

"*Powdered Coptis.*—Yellowish green; exhibits numerous, mostly simple, starch grains, somewhat rounded, up to 0.007 mm. in diameter; fragments of leaf epidermis, composed of cells with wavy vertical walls and broadly elliptical stomata, the latter up to 0.024 mm. long; fragments of the nerved scales from the nodes, composed of cells with yellow walls; leaf parenchyma cells containing chloroplastids; few simple, thick-walled hairs from the midrib of the leaf, from 0.035 to 0.075 mm. long; elongated, epidermal cells from the roots having yellow walls and filled with reddish contents; fragments of epidermal and sub-epidermal cells from the rhizome, similar to those from the root, but without reddish contents, though often with yellowish content; groups of elongated parenchyma cells about 0.060 mm. long and about 0.010 mm. wide, many of the cells being filled with starch grains; tracheæ about 0.020 mm. wide; with bordered pores or spiral markings; narrow thin-walled, porous fibers." *N. F.*

It imparts a bitterness and yellow color to water and alcohol, but most perfectly to the latter, with which it forms a bright yellow tincture. The infusion is precipitated by silver nitrate and lead acetate. It affords no evidence of either resin, gum, or tannin. The plant contains berberine, which appears to be associated with another alkaloid. Gross states that the second alkaloid, which he calls *coptine,* differs from berberine in its colorless crystals, and by forming with mercuric potassium iodide (Mayer's reagent) a crystalline instead of flocculent precipitate. (See also John J. Schulz, *A. J. P.,* 1884, 261.)

Uses.—Goldthread is a simple bitter tonic. In New England it is employed as a local application in *aphthous ulcerations* of the mouth, but it probably has no other virtues in this complaint than such as are common to the simple bitters. It may be given in substance, infusion, or tincture.

The *Coptis Teeta* of Wallich, which grows in the mountainous regions bordering on Assam, the *C. trifolia* Salisb. of India, and the *C. anemonefolia* Sieb. et Zucc. of Japan, also contain berberine and have been used as gastrointestinal tonics.

The *dose* of the powder is from ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Fluidextractum Coptis, *N. F.*

CORIANDRUM. N. F. (Br.)

CORIANDER Coriand. [Coriander Seed]

"Coriander is the dried ripe fruit of *Coriandrum sativum* Linné (Fam. *Umbelliferæ*). Coriander contains not more than 5 per cent. of other fruits, seeds, or other foreign organic matter and yields not more than 1.5 per cent. of acid-insoluble ash, nor less than 0.5 per cent. of volatile ether-soluble extractive." *N. F.* "Coriander Fruit is the dried ripe fruit of Coriandrum sativum, *Linn.*" *Br.*

Coriandri Fructus, *Br.;* **Coriander Fruit; Coriandre, Coliander,** *Fr. Cod.;* **Koriander,** *G.;* **Coriandro,** *It.;* **Cilantro** *Sp.*

Coriandrum sativum is an annual plant, with an erect branching stem rising about two feet, and furnished with compound leaves, of which the upper are thrice ternate, with linear pointed leaflets, the lower pinnate, with the pinnæ cut into irregular serrated lobes like those of parsley. The flowers are white or rose-colored, and in compound terminal umbels; the fruit globular, and composed of two concavo-convex mericarps. *C. sativum* is a native of Italy, but at present grows wild in most parts of Europe, having become naturalized in consequence of its extended cultivation. The flowers appear in June, and the fruit ripens in August. It is a singular fact that all parts of the fresh plant are extremely fetid when bruised, while the fruit becomes fragrant by drying. This is the official portion.

Coriander is cultivated in India, Asia Minor, northern Africa and the United States. The plants are propagated from seeds sown in the spring. In August and early September, when the fruits are ripe, the plants are mowed down, partially cured in the field and dried under cover. The fruits are then thrashed out and cleaned. The chief supplies come from Tangier, Morocco and from Marseilles, France. Attempts have been made to cultivate the plant in Vermont.

Description and Physical Properties.—"*Unground Coriander.*—Mericarps usually coherent; cremocarp nearly globular, from 2 to 5 mm. in diameter; externally light brown or rose colored; apex with 5 calyx teeth and a short stylopodium, each mericarp with 5 prominent, straight, longitudinal primary ribs and 4 indistinct, undulate secondary ribs; mericarps easily separated, deeply concave on the inner or commissural surface.

"*Structure.*—An epidermis of small cells with thick walls; a layer of several rows of thin-walled, more or less collapsed parenchyma separated from a broad zone of strongly lignified fibers which extend as a continuous layer in the mesocarp of each of the mericarps; 2 or 3 layers of large, tangentially elongated, thin-walled parenchyma cells, frequently with numerous large, intercellular spaces and bearing on each commissural side 2 large, elliptical oil-tubes; endocarp of large tabular cells, the inner yellowish walls being considerably thickened and closely coherent to the brownish cells of the seed-coat, except on the commissural side where the endocarp is separated from the seed-coat forming a large elliptical cavity; endosperm distinctly reniform in outline and consisting of tabular or polygonal thick-walled cells containing fixed oil, and numerous large aleurone grains each with a rosette or prism of calcium oxalate.

"*Powdered Coriander.*—Light brown, consisting chiefly of endosperm and lignified tissues of the pericarp; calcium oxalate crystals numerous, from 0.003 to 0.010 mm. in diameter, mostly in rosettes, either isolated or in aleurone grains; fibers irregularly curved, having thick, yellowish, lignified walls and numerous simple pores; numerous globules of fixed oil; few fragments of light yellow oil-tubes, associated with elongated polygonal epidermal cells." *N. F.*

"Nearly globular, about five millimetres in diameter, uniform brownish-yellow in color, and glabrous. Mericarps usually closely united, and crowned by the calyx teeth and stylopod. Primary ridges wavy and inconspicuous; secondary ridges straight and more prominent. In transverse section, two vittæ on the commissural surface of each mericarp. Aromatic odor, especially when bruised; taste agreeable." *Br.*

The aromatic taste and odor of coriander depend on a *volatile oil* (see *Oleum Coriandri*), which may be obtained separate by distillation. One pound of the seeds yields forty-two grains of the oil. (Zeller.)

The drug not infrequently contains a large admixture of earthy and stony substances as well as stems and similar inert matter. Blome reports finding a sample of coriander that contained 20 per cent. of flaxseed. LaWall has found leguminous starch in a specimen of powdered coriander, probably from vetch seed which is sometimes accidentally present.

Uses.—Coriander is a rather feeble aromatic. It is almost exclusively employed in combination with other medicines, either to cover their taste, to render them acceptable to the stomach, or to correct their griping qualities. It was well known to the ancients.

Dose, twenty to sixty grains (1.3–3.9 Gm.).

Off. Prep.—Confectio Sennæ, *Br.;* Syrupus Rhei, *Br.;* Tinctura Rhei Composita, *Br.;* Tinctura Sennæ Composita, *Br.;* Fluidextractum Stillingiæ Compositum, *N. F.;* Syrupus Stillingiæ Compositus, *N. F.*

CORNUS. N. F.

CORNUS [Dogwood Bark]

"Cornus is the dried root bark of *Cornus florida* Linné (Fam. *Cornaceæ*). Cornus contains not more than 5 per cent. of adhering wood or not more than 2 per cent. of other foreign organic matter." *N. F.*

Flowering Dogwood; Flowering Cornel; Cornouiller à grandes fleurs, *Fr.;* Grossblüthige Cornelrinde, *G.*

Cornus florida L. or Flowering Dogwood is a small tree usually 15 to 25 feet high, a native of the woods of the eastern and central United States. It is readily distinguished by its opposite branches, alligator bark, bright red or occasionally greenish twigs, small lateral buds that are covered by the persistent bases of leaf stalks, large spherical flower-buds and terminal leaf-buds with a single pair of bud-scales. Its leaves are opposite, simple, ovate, acute at apex, cuneate at base, entire to wavy along margin and with very prominent midrib and lateral veins. Its flowers appear during April. Each so-called "flower" is in reality a glomerule consisting of a dense cluster of small, greenish florets imbedded on a compound receptacle that is surrounded by a white involucre of four obcordate bracts. The fruit appears in autumn as a scarlet, ovoid drupe.

The barks of two other indigenous dogwoods were formerly substituted for that of *C. florida* L. Each of these is a shrub with opposite leaves, the flowers in flat spreading cymes, and the fruit globular and bright red. *C. circinata* L'Her. is further distinguished by its long branches being greenish and warty; its leaves round-oval, abruptly pointed, and woolly underneath. *C. Amomum* Mill. (*C. sericea* L.), *Silky Cornel* or *Swamp Dogwood,* is to be recognized by its purplish branches, and by the fact that the branchlets, stalks, and lower surface of the elliptical pointed leaves are silky and downy. (See also *Chem. News,* 1908, 191.)

These dogwoods are found in all portions of the United States east of the Mississippi.

Description and Physical Properties.—"*Unground Cornus.*—In irregular, chip-like pieces, or portions of quills, usually less than 5 cm. in length; bark from 1 to 4 mm. in thickness; externally scaly and of a dingy-brown color, with few minute root scars or finely roughened; and of a reddish color where the corky layers have been removed; heavy cork patches wanting (absence of trunk bark); inner surface varying from pinkish brown to reddish brown, roughened from numerous short striæ; fracture short, the broken surface purplish or pinkish white and roughened from light-colored projecting groups of stone cells. Odor slight; taste bitter and astringent.

"*Structure.*—Outer bark of several layers of more or less exfoliating cork cells; middle bark of tangentially elongated parenchyma cells, many of which contain rosettes or prismatic crystals of calcium oxalate, a few with starch grains; inner bark with nearly straight medullary rays up to 10 cells wide, some of which extend nearly to the cork and separated by sieve tissue, parenchyma cells and non-lignified fiber-like cells, many of the latter having large simple pores and exhibiting distinctly beaded radial walls when examined in tangential section; many of the parenchyma cells, particularly of the medullary rays contain rosettes or prismatic crystals of calcium oxalate, others contain a brownish amorphous substance; stone cells either isolated or in groups, the individual cells often with branching pores and a reddish brown amorphous content, some with thinner walls, usually non-porous containing one or more prisms of calcium oxalate; lignified bast-fibers are absent.

"*Powdered Cornus.*—Numerous fragments of small thin-walled, non-lignified fibers and parenchyma cells, the latter often containing a brownish or purplish brown amorphous substance, many of the fragments becoming distinctly purplish pink upon mounting in chloral hydrate T.S.; stone cells isolated and in groups, the individual cells up to 0.125 mm. in length; numerous prism and rosette crystals of calcium oxalate up to 0.060 mm. in diameter, the prisms frequently occurring in stone cells; starch grains few, simple or 1- to 3-compound, rounded to oval or narrowly elliptical in outline, usually 0.003 to 0.025 mm. in length, occasionally larger; few fragments of cork, the cells containing a brownish pigment; lignified fibers and tracheæ very few or wanting (absence of trunk bark and wood)." *N. F.*

Geiger in 1836 obtained from dogwood a bitter principle, *cornin* (or *cornic acid*), concerning which, however, there does not appear to be any recent information. C. F. Kramer (*A. J. P.*, 1882) found in the bark about 3 per cent. of tannic acid.

Dogwood bark was used many years ago as an antiperiodic in *intermittent fever,* but it is only a feeble, astringent tonic. Formerly from one to two ounces of the powder were given in the interval between the paroxysms of intermittent fever.

Dose, of the fluidextract, from one-half to one drachm (1.8–3.75 cc.).

Off. Prep.—Fluidextractum Corni, *N. F.*

CORYDALIS. N. F.

CORYDALIS Corydal. [Turkey Corn, Squirrel Corn]

"The dried tubers of *Dicentra canadensis* (Goldie) Walp or of *Dicentra Cucullaria* (Linné) Bernh. (Fam. *Fumariaceæ*). Corydalis contains not more than 3 per cent. of foreign organic matter." *N. F.*

Dicentra canadensis and *D. Cucullaria* are delicate, low, perennial herbs indigenous to rich woodlands from Nova Scotia to Minnesota south to North Carolina, Kentucky and Missouri. The former is commonly known as *Turkey Corn* or *Squirrel Corn* while the latter is called *Dutchman's Breeches.* The aerial portions of both of these plants agree in possessing narrow-stalked, ternately-compound, dissected leaves and few-flowered racemes. The plants differ mainly in respect to their tubers and flowers. *Turkey corn* has scattered, pea-like tubers arranged on subterranean shoots, whereas the tubers of *Dutchman's Breeches* are somewhat scale-like and attached to the subterranean shoots in clusters of three. The flowers of *Turkey corn* are heart-shaped, greenish-white, tipped with rose, each showing 2 short, rounded spurs, whereas those of *Dutchman's Breeches* are irregularly heart-shaped, white, tipped with cream color, each possessing two more elongated and divergent spurs.

Description and Physical Properties.—"*Unground Corydalis.*—Tubers of *D. canadensis* spheroidal, frequently vertically depressed, one surface more or less concave, up to 15 mm. in diameter; usually single, rarely two or more in a cluster; externally, minutely pitted or nearly smooth, grayish brown, grayish black, or amber-colored and more or less translucent; one of the flattened surfaces with a triangular scar from detached roots, the other usually with remains of the slender rhizome; fracture, hard and horny, exhibiting a yellowish, waxy interior, or somewhat tough and granular, exhibiting a yellowish white interior. Tubers of *D. cucullaria* ovoid or triangular-ovoid, up to 12 mm. long; the larger distinctly concave on one surface, with a scar at the apex from the detached petiole, and usually attached to the short rootstock in clusters of three; the smaller grains usually separated from the rootstock, with an acute apex and a scar at the base; externally, yellowish, or grayish brown, usually translucent; fracture hard and horny, exhibiting a grayish, waxy interior, or granular and tough, exhibiting a whitish interior. Nearly odorless; taste slightly bitter.

"*Powdered Corydalis.*—Light yellow or yellowish gray; numerous oval, ovoid or oblong, simple starch grains, the broad end of the grain sometimes truncate, up to 0.060 mm. long and frequently with a cleft or horse-shoe-shaped fissure in the small end of the grain; occasionally in 2-compound grains, altered starch grains up to 0.090 long; numerous angular or rounded parenchyma cells isolated or in groups and containing more or less altered starch grains the outlines of which are indistinct; tracheæ few, with reticulate, simple pores, annular or spiral markings; fragments of epidermal cells with thin brownish walls; fibers very few or absent; few characteristic stone cells, often irregular in outline, mostly elongated, up to about 0.750 mm. long and 0.150 mm. wide, walls heavily lignified and about 0.020 mm. thick and porous, occurring isolated or in groups of from 2 to 4; very few rosette crystals of calcium oxalate, up to 0.020 mm. in diameter.

"An infusion prepared by placing 5 Gm. of powdered Corydalis in 100 cc. of hot distilled water, stirring occasionally during ten minutes and then filtering, is of a light amber color, and gives a precipitate with mercuric-potassium iodide T.S. and a dark blue color with iodine T.S." *N. F.*

As far as we know the constituents of this drug have never been determined. Several species of the closely allied genus *Corydalis* have, however, been carefully studied, especially the *C. cava* Schweig. and the *C. tuberosa.* The bulbs of these plants yield quite a variety of alkaloids which Gadamer (*A. Pharm.*, 1910, 1911, 1916) classifies into three groups as follows: 1. *Corydaline, dehydrocorydaline, corybulbine, iso-corybulbine,* and *corypalmine;* 2. *Corycavine, corycavamine, corycavidine;* 3. *Bulbocapnine, corytubine* and *corydine.* The alkaloid protopine is also found in several species. All of these alkaloids have narcotic actions but the first group are primary depressants of the spinal cord while the second and third excite before paralyzing the motor centers. (For further information concerning these substances see Henry, *Plant Alkaloids,* 1924.)

The tubers of bicuculla are asserted to be tonic, diuretic, and alterative, and are given in *syphilitic, scrofulous,* and *cutaneous affections,* They are used in the form of tincture or decoction. *Corydalin* or *corydalia,* of the eclectics, is an impure resinous mixture.

Dose, ten to thirty grains (0.6–2.0 Gm.).

Off. Prep.—Fluidextractum Corydalis, *N. F.;* Elixir Corydalis Compositum, *N. F.;* Fluidextractum Stillingiæ Compositum, *N. F.;* Syrupus Stillingiæ Compositus, *N. F.*

COTARNINÆ CHLORIDUM. U. S.

COTARNINE CHLORIDE Cotarn. Chlor. [Cotarninæ Hydrochloridum, U. S. P. IX]

"The chloride [$C_{12}H_{14}O_3NCl$] of an alkaloid prepared from narcotine." *U. S.*

Description and Physical Properties.—"A yellow, odorless, crystalline powder. It is deliquescent in moist air. Cotarnine Chloride is very soluble in water and in alcohol, the solutions being yellow.

"Dissolve about 0.5 Gm. of Cotarnine Chloride in 10 cc. of distilled water, and add 2 cc. of a 15 per cent. aqueous solution of sodium hydroxide: a milk-white precipitate is produced which dissolves on agitation, but is reprecipitated from the solution after standing for some time, leaving the supernatant liquor clear but faintly yellow. Silver nitrate T.S. added to an aqueous solution of Cotarnine Chloride produces a white precipitate insoluble in nitric acid. About 0.2 Gm. of Cotarnine Chloride dissolved in 10 cc. of distilled water yields a brown precipitate of cotarnine periodide on the addition of 10 cc. of tenth-normal iodine. When this precipitate is collected on a filter, and dried to constant weight over sulphuric acid, it melts between 142° and 144° C.

"An aqueous solution of Cotarnine Chloride (1 in 20) is neutral to litmus paper. Heat gradually 0.1 Gm. of Cotarnine Chloride over a Bunsen burner: it is decomposed, evolving characteristic, disagreeable vapors and yielding a reddish-brown liquid, which gradually changes to a hard, charred mass. The ash remaining on the incineration of this mass is negligible." *U. S.*

Cotarnine is an artificial alkaloid prepared by the oxidation of narcotine with nitric acid, *opianic acid* being obtained as a by-product. It has been synthesized by Salway (*Tr. Chem. Soc.,* 1910, xcvii) from myristicin.

Uses.—The fact that the only chemical difference between hydrastinine and cotarnine is that in the latter OCH_3 is substituted for one atom of hydrogen led Freund to suggest the substitution of cotarnine for hydrastinine. It has been physiologically studied by Falk (*Th. M.,* 1896, x), Kehrer (*Monat. für Geburts. und Gynakol.,* 1907, xxvi, p. 709), Laidlaw (*Bio-Chem. J.,* 1910, v, p. 243), and others. It differs in its action from hydrastinine, in that it has practically no influence upon the circulation, but resembles it in its depressant action upon the spinal cord, and in its stimulant effect upon the uterine muscle. Because of its stimulating action upon the uterine muscle, it has been found of service in various forms of uterine hemorrhage, such as *menorrhagia* and *metrorrhagia.* On false analogy some have jumped to the conclusion that it should be useful in other forms of *hemorrhage,* and it was at one time extensively employed in the treatment of various forms of internal bleeding, under the trade names of *Stypticin* and *Styptol,* the latter being *cotarnine phthalate.* Hanzlik, however, has shown (*J. P. Ex. T.,* 1918, x, and 1919, xii, 71) that whether applied locally or administered internally cotarnine tends to increase rather than diminish the rapidity of the bleeding.

A double salt of cotarnine hydrochloride and ferric chloride appears on the market under the trade name of *cotargit* and is alleged to contain still better styptic properties than cotarnine. It occurs as a ruby-red crystalline powder freely soluble in water.

The *dose* is ordinarily from three-fourths to one and one-half grains (0.05 to 0.10 Gm.) but in emergency as high as three or four grains (0.2–0.25 Gm.) may be given as a single dose.

COUMARINUM. N. F.

COUMARIN Coumar.

"The anhydride of ortho-oxycinnamic acid [$C_6H_4(CH)_2OCO$ (146.09)] occurring naturally in Tonka, Melilot and other plants, or prepared synthetically." *N. F.*

Coumarin is found widely distributed through the vegetable kingdom, notably in the tonka bean (see Part II), in several species of clover (see *Melilotus*), in several sweet-scented grasses, in the *Trilisa odoratissima,* commonly known as *vanilla leaf* and also in *Asperula odorata* and some species of orchids.

It may be extracted from the above plants by boiling with 80 per cent. alcohol; the resultant tincture is evaporated until faint turbidity, when four volumes of water are added, which precipitates both coumarin and fats. The solution is then heated and filtered hot, which causes the fat to remain on the filter and the coumarin passes through and crystallizes out of the solution on cooling. It is also prepared synthetically by boiling a mixture of salicylic aldehyde, acetic anhydride and anhydrous sodium acetate under a reflux condenser, distilling the oily liquid which separates and crystallizing the distillate. It is also produced by the action of ethyl acetoacetate or of malic acid upon phenol in the presence of sulphuric acid.

Description and Physical Properties.—"Coumarin occurs in colorless, prismatic crystals, having a characteristic, fragrant odor and a bitter, aromatic and burning taste. It is sparingly soluble in cold water, more readily soluble in hot water, freely soluble in alcohol, ether or chloroform; also soluble in fixed or volatile oils.

"When heated to between 67° and 68° C. it melts, and at about 100° C. it commences to sublime; at from 290° to 291° C. it boils without decomposition. Coumarin dissolves in solution of sodium or potassium hydroxide, producing a yellow color and forming sodium or potassium coumarate, from which carbon dioxide precipitates the Coumarin. Coumarin is precipitated in colorless needles on the addition of hydrochloric acid to its hot concentrated sodium or potassium hydroxide solution. A saturated aqueous solution of Coumarin forms a precipitate upon the addition of iodine T.S. The precipitate is at first brown and flocculent and afterwards clots on shaking, forming a dark green curdy mass and leaving the liquid clear (distinction from *vanillin*). Coumarin is not extracted from its solution in ether by ammonia water (distinction from *vanillin*). Warm 0.1 Gm. of Coumarin with 1 cc. of an alcoholic solution of sodium hydroxide (1 in 4), add a few drops of chloroform and again warm; the mixture does not possess the disagreeable odor of phenylisocyanide (*acetanilid*)." *N. F.*

Coumarin is free from medicinal properties, and is used only for its odorous qualities. It is especially valuable for covering the odor of iodoform and is also an ingredient in aromatized castor oil. It finds a prominent place in *imitation vanilla extracts* of commerce. Its adulteration with terpin hydrate has been reported by J. C. Umney who finds the melting point of the ether-soluble portion the best method of its detection.

Off. Prep.—Oleum Ricini Aromaticum, *N. F.*

CREOSOTI CARBONAS. U. S.

CREOSOTE CARBONATE Creosot. Carb.

"Creosote Carbonate is a mixture of the carbonates of various constituents of creosote, chiefly guaiacol and creosol." *U. S.*

Creosote carbonate is known also by the trade names of *creosotal* and *creosotal-Heyden;* it is made by treating a solution of creosote and sodium hydroxide with carbonyl chloride.

Description and Physical Properties.—"A clear, colorless or yellowish, viscid liquid. It is odorless and tasteless, or has a slight odor and taste of creosote. On prolonged exposure to a low temperature, crystals of guaiacol carbonate may separate, which redissolve on warming. Creosote Carbonate is insoluble in water, but is freely soluble in alcohol. It is soluble in petroleum benzin and in fixed oils, and is miscible with chloroform and with benzene. Heat about 0.5 cc. of Creosote Carbonate for a few minutes with 10 cc. of alcoholic potassium hydroxide T.S., and cool the mixture: a crystalline precipitate forms, which effervesces with acids.

"Specific gravity: not below 1.145 at 25° C. Ash: not more than 0.1 per cent. An alcoholic solution of Creosote Carbonate (1 in 5) is neutral to moistened litmus paper, and acquires only a yellow color on the addition of a drop of ferric chloride T.S. (*free creosote*). Heat 25 cc. of Creosote Carbonate on a water bath for half an hour with a solution of 15 Gm. of potassium hydroxide in 100 cc. of alcohol, add about 50 cc. of water, and evaporate the alcohol. Treat the residue with an excess of hydrochloric acid, and allow the liquid to separate into two layers. Separate the creosote layer, wash it by shaking at first with 15 cc. of a 20 per cent. aqueous solution of sodium chloride, then with 10 cc. of water, and distil: eighty-five per cent. of the creosote thus obtained, allowance being made for adhering moisture, distils between 200° and 220° C., when determined by method II, page 433. The distillate, after the separation of adhering water, does not respond to the test for *hydrocarbons and "coal-tar creosote"* under *Creosotum." U. S.*

Uses.—Creosote carbonate has been used in medicine with the idea that it would be decomposed by the acid secretions of the stomach and exercise the characteristic beneficial effect of creosote, especially in *chronic bronchitis* and *tuberculosis.* The advantage of this preparation is that it is comparatively free from odor or taste and that it is much less irritant to the stomach. On the other hand, the *a priori* reasoning that it would be decomposed by the hydrochloric acid in the stomach is based upon false assumption. There is no chemical reason to suppose that this compound would be decomposed by the fluids of the digestive tract and we know of no convincing evidence that it is decomposed anywhere in the alimentary canal or that it liberates its creosote in the body. Although it is enormously prescribed, the question of its therapeutic value seems open to serious doubt.

Dose, from five to thirty minims (0.3–1.8 cc.) preferably in emulsion or capsules.

CREOSOTUM. U. S., Br.

CREOSOTE Creosot. [Creasote]

"A mixture of phenols, principally guaiacol [$C_6H_4(OH.OCH_3)1:2$] and creosol [$C_6H_3(CH_3)OH.OCH_3\ 1:2:3$] obtained from wood tar." *U. S.* "Creosote is a mixture of phenols which may be obtained by the distillation of beech tar, and consists chiefly of guaiacol and creosol." *Br.*

Creasotum, *Br.* (1885); Créosote Officinale, *Fr. Cod.;* Kreosotum, *P. G.;* Kreosot, Buchenholztheerkreosot, *G.;* Creosoto, *It.;* Creosota, *Sp.*

The destructive distillation of wood yields products analogous to one fraction of the coal tar, obtained by the destructive distillation of bituminous coal. This fraction is the heavy oil of coal tar, which comes over between 165° C. and 200° C.; it is often called *"coal tar creosote,"* and contains a group of phenols, including carbolic acid. Wood tar is a complex mixture of phenoloid bodies with acetic acid, varying considerably in its composition according to the species of wood from which it is made (see *Pix Pini*). The tars from the hard woods yields larger proportions of creosote. This is a mixture of methyl ethers of pyrocatechin and its homologues. It contains from 60 to 90 per cent. of guaiacol with *creosol* and small amounts of *phlorol* and methyl-creosol.

Preparation.—Creosote is obtained either from wood tar or from crude pyroligneous acid. When wood tar is used, it is distilled until it has attained the consistence of pitch. The distilled liquid divides itself into three layers, an aqueous between two oily layers. The inferior oily layer, which alone contains the creosote, is separated, and saturated with sodium carbonate to remove acetic acid. The liquid is allowed to rest, and the new oil which separates is decanted from it. This oil is distilled and yields products lighter than water, and a liquid heavier. The latter alone is preserved, and, after having been agitated repeatedly with weak phosphoric acid to neutralize ammonia, is allowed to remain at rest for some time. It is next washed until it is free from acidity, and then distilled with a fresh portion of weak phosphoric acid, care being taken to cohobate from time to time. The oily liquid thus rectified is colorless, and contains much creosote, but also a portion of light oil distillate. To separate the latter the liquid is mixed with a solution of sodium hydroxide of the density 1.12, which dissolves the creosote, but not the light oil. The oil, which floats from its levity, is then separated, and the alkaline solution of the creosote is exposed to the air, until it becomes brown in consequence of the decomposition of a foreign matter, and is then saturated with sulphuric acid. This sets free the creosote, which is decanted and again distilled. The treatment by solution of soda, sulphuric acid, etc., is to be repeated until the creosote no longer becomes brown by exposure to the air, but only slightly reddish. It is then dissolved in a stronger solution of soda, and distilled again, and finally redistilled for the last time, rejecting the first portion which comes over, on account of its containing much water, and collecting the next portion; care being taken not to push the distillation too far. The product collected is creosote.

When creosote is extracted from pyroligneous acid, the first step is to dissolve sodium sulphate in the acid to saturation. The oil which separates and floats above is decanted, and, having been allowed to remain at rest for a few days, is saturated with potassium carbonate with the assistance of heat, and distilled with water. The oily liquid obtained is of a pale yellow color, and is to be treated as above detailed, in relation to the treatment of the corresponding oil obtained from wood tar.

Creosote, when pure, is a colorless oleaginous liquid, but as met with in commerce, it has frequently a brownish tinge. Mixed with water, it forms two layers, one consisting of one part of creosote and about eighty of water, the other, of one part of water and ten of creosote. It dissolves a large proportion of iodine and phosphorus, and a considerable amount of sulphur, especially when assisted by heat. Allen states that in Rhenish creosote guaiacol predominates, while a sample of Morson's creosote from "Stockholm tar," examined by him, boiled at about 217° C., and consisted chiefly of creosol.

Description and Physical Properties.—"An almost colorless or yellowish, highly refractive, oily liquid, having a penetrating, smoky odor, and a burning, caustic taste. It does not readily become brown on exposure to light. Creosote is inflammable, burning with a luminous, smoky flame. Creosote is slightly soluble in water, but is miscible with alcohol, ether, and with fixed or volatile oils.

"Add 1 drop of ferric chloride T.S. to 10 cc. of a saturated aqueous solution of Creosote: a violet-blue color, which is very transient, develops. The liquid becomes cloudy almost instantly, the color changing rapidly from grayish-green to muddy brown, with the formation, finally, of a brown precipitate.

"Specific gravity: not below 1.076 at 25° C. It begins to distil at about 200° C., and not less than 90 per cent., by volume, distils between 200° and 220° C., when determined by method II, page 1536. Creosote is neutral or faintly acid to moistened litmus paper. Mix equal volumes of Creosote and collodion in a dry test tube: no permanent coagulum is produced (*phenol* and so-called *"coal-tar creosote"*). Mix 4 cc. of Creosate and 4 cc. of glycerin, add 1 cc. of water, shake the mixture gently, and allow it to stand: a creosote layer separates equal to or greater in volume than the Creosote taken (so-called *"coal-tar creosote"*). A 2 cc. portion of Creosote requires not less than 10 cc. and not more than 18 cc. of normal sodium hydroxide to produce a clear liquid. This liquid remains unclouded on diluting with 50 cc. of distilled water (*hydrocarbons and bases*). Shake gently 1 cc. of Creosote with 2 cc. of petroleum benzin and 2 cc. of freshly prepared barium hydroxide T.S. until a uniform mixture results: upon complete separation three distinct layers are visible, the upper layer being neither blue nor muddy (*cærulignol*).

"Preserve in tightly-stoppered, dark amber-colored bottles." *U. S.*

The British Pharm. describes creosote as "a colorless or pale yellow, highly refractive liquid, neutral or faintly acid to *litmus*. Freely soluble in *alcohol* (90 per cent.), in *ether*, in *chloroform*, and in *glacial acetic acid*. Specific gravity not below 1.080. Commences to boil below 200° C. Not less than 75 per cent. distils between 200°

and 220° C. A solution (1 in 100) in *alcohol* (90 per cent.) produces with a drop of *T. Sol. of ferric chloride* a green coloration rapidly changing to reddish brown. Dropped on white filter paper and exposed to a temperature of 100° C., it leaves no translucent stain (absence of less volatile liquids)." *Br.*

Creosote dissolves a number of metallic salts and reduces some of them to the metallic state, as, for example, silver nitrate and acetate. *Froehde's reagent* (a solution of 0.1 Gm. of sodium molybdate in 100 cc. of concentrated sulphuric acid) is recommended by E. W. Davy as a distinguishing test for phenol. A drop or two of the doubtful liquid is to be agitated with two fluidrachms of distilled water, the whole filtered, and a drop or two of the test solution added. Pure creosote gives a brown or reddish-brown reaction on standing or slight warming, passing to a light yellowish-brown; with phenol, the brown passing to a maroon soon develops a more or less intense purple. The name creosote refers to its antiseptic properties, being derived from χρέας, *flesh,* and σώζω, *I preserve.*

Impurities and Adulterations.—Creosote is sometimes adulterated with rectified oil of tar and the fixed and volatile oils. All these substances are detected by strong acetic acid, which dissolves the creosote, and leaves them behind, floating above the creosote solution. Creosote from beechwood tar, however, is only partially dissolved by hot acetic acid of ordinary strength. Fixed oils are also discovered by a stain on paper not discharged by heat. Any trace of the matter which produces the brownish tinge is detected by the liquid becoming discolored by exposure to sunshine. Commercial creosote sometimes contains phenol and cresol, from coal tar; and, indeed, much of what has been sold for creosote was nothing more than impure phenol. (See *Phenol.*) It has been already stated that phenol strongly resembles creosote; but the effects of the two on the system are very different. The presence of phenol is excluded by the official tests. The large doses in which creosote is now sometimes given makes the sale of the so-called "coal tar creosote" dangerous, for there would be a strong probability that a patient might be given a large dose of phenol with disastrous effects; all pharmaceutical manufacturers have ceased to label or market "coal tar creosote."

Uses.—Although the constitution of even genuine beechwood creosote varies very greatly in the proportion of guaiacol and creosol, the physiological and therapeutic action of its various constituents is so closely allied as to make variability in the proportion of these constituents of little importance.

The physiological effects produced by creosote have not been closely studied, but it would appear in many of its properties to resemble phenol. It is, however, much less poisonous and doses as high as thirty to sixty minims have been administered three times a day without harmful results. Freudenthal (*N. Y. M. R.,* April, 1892) reports a case of a woman who took six hundred drops of creosote in a very short time, the ingestion being followed almost immediately by unconsciousness with intense trismus, contracted immobile pupil, and general cyanosis, but recovery was made practically without administration of remedies; subsequently this same patient by graduating the dose was able to take five hundred drops daily without ill effect. Thorling (*Upsala Lakaref. Förh.,* Sept. 1, 1921) has reported a case of fatal poisoning in an infant of two months from what was estimated to be 0.6 cc. of creosote. Icterus and evidence of destruction of the blood cells were prominent symptoms.

Creosote is absorbed readily from the intestinal tract and its elimination is fairly rapid. It escapes chiefly through the kidneys in combination with sulphuric and glycuronic acids, but appears also to be in part eliminated by the lungs. Like phenol, it is, when locally applied, a paralyzant to the sensory nerves. Creosote is distinctly superior to phenol in its antibacterial properties, especially in dilute solutions. According to Guttmann (*Z. K. M.,* 1887, xiii) one part of creosote to three thousand completely inhibits the growth of bacteria.

Creosote was originally introduced in the treatment of *phthisis* with the idea that it would exercise an antiseptic action in the lungs. It is, however, extremely questionable whether the drug can reach the pulmonic tissue in sufficient concentration to have any direct antibacterial properties. Its beneficial influence in this disease can be ascribed to its stimulating effect upon the bronchial mucous membrane. For this action it is also a very valuable drug in the treatment of all types of *chronic bronchitis,* especially when there is over-secretion. In tubercular conditions it is generally necessary to give the drug in large doses. The secret of doing this successfully is to see that it is well diluted before ingestion. When being used freely it should never be given in the form of capsules but dissolved in either water or milk. A good rule is that the patient should take at least one-half an ounce of fluid for every drop of creosote; thus if ten minims were to be administered it would require five ounces of water. Perom has recommended the hypodermic administration in *phthisis.* For this purpose he uses a ten per cent. solution in oil of sweet almonds, two injections of eighty minims being given daily. Dor employed intratracheal injections of five per cent. solution in sterile olive oil.

Creosote is also a valuable gastro-intestinal antiseptic in the treatment of *fermentative gastritis* and *enteritis.* It is of service in *nausea* and *vomiting* for its local anesthetic action upon the gastric mucosa. Externally it has been used as a surgical disinfectant, but because of its stronger odor and greater cost is inferior to phenol, but when there is foul discharge, as in fetid *leukorrhea, otorrhea, empyema* or *gan-*

grene, is by many preferred. It is also useful in various *skin diseases,* both for its local anesthetic and antibacterial properties and has been recommended in *chilblains.* In capillary *hemorrhages* it has some power as a hemostatic but is not capable of arresting bleeding from large vessels. For this effect it has been used locally in the milder types of *uterine hemorrhage* and to stop the bleeding from *leech bites.* As a local application it may be employed in strengths of from one to ten per cent., according to the purpose for which it is used. On account of its local anesthetic and antiseptic influence, it is much employed by dentists for the obtunding of sensitive dentine and as an ingredient of pastes for the destruction of nerves. One or two drops of the pure substance must be carefully introduced into the hollow of the tooth on a little cotton, avoiding contact with the tongue or cheek. To render it effectual, the hollow of the tooth must be well cleansed before it is applied.

In an overdose creosote acts as a poison, producing giddiness, obscurity of vision, depressed action of the heart, convulsions, and coma. Medicinal treatment consists in evacuation of the poisons and administration of ammonia and other stimulants.

Under the name of *Vapor Creasoti* (*Inhalation of Creasote*), the British Pharmacopœia (1885) directed a preparation consisting of 12 minims of creosote and 8 fluidounces of boiling water, which were directed to be mixed in an inhaling apparatus, so arranged that the air should be made to pass through the solution, and then inhaled. It may be used in chronic inflammation of the air passages.

Mistura Creosoti, Br. Pharm., 1898, is no longer official, it was made by shaking 16 minims each of creosote and spirit of juniper with 1 fluidounce of syrup and enough distilled water to make 16 fluidounces of the mixture.

Dose, of creosote, five to ten minims (0.3–0.6 cc.), which may be gradually increased.

Off. Prep.—Unguentum Creosoti, *Br.;* Mulla Creosoti Salicylata, *N. F.;* Elixir Terpini Hydratis et Creosoti Compositum, *N. F.*

CRESOL. U. S., Br.

CRESOL

"A mixture of isomeric cresols [$C_6H_4.CH_3.OH$] obtained from coal tar." *U. S.* "Cresol is a mixture of isomers of the formula C_7H_7OH, obtained from coal tar. Should be preserved in stoppered amber-colored bottles." *Br.*

Cresolum, Cresolum Crudum; Cresylic Acid, Tricresol, Methylphenol, Oxytoluene; Crésylol Officinale, *Fr. Cod.;* Enterol, Trikresol, Kresol, *G.*

Preparation.—Cresol is prepared from coal tar by collecting the distillates coming over between 140° C. and 220° C., and purifying these by treatment with solution of sodium hydroxide and hydrochloric acid.

There are three isomeric cresols: *orthocresol,* melting at 31° C. and boiling at 188° C.; *metacresol,* a liquid boiling at 201° C., but not solidifying even at –80° C.; and *paracresol,* forming colorless prisms, melting at 36° C. and boiling at 198° C. These cresols are all obtainable by fractional distillation from that portion of coal tar boiling between 190° and 210° C. The official drug is a mixture of all three.

Description and Physical Properties.—"A colorless, or yellowish to brown-yellow, or a pinkish, highly refractive liquid, becoming darker with age and on exposure to light. It has a phenol-like, sometimes empyreumatic odor. One cc. of Cresol is soluble in about 50 cc. of water, usually forming a cloudy solution. It is miscible with alcohol, ether, benzene, petroleum benzin, and with glycerin, and is dissolved by solutions of the fixed alkali hydroxides.

"Specific gravity: 1.030 to 1.038 at 25° C. Not less than 90 per cent. by volume of Cresol distils between 195° and 205° C., when determined by method II, page 433. A saturated aqueous solution of Cresol is neutral or slightly acid to litmus paper, and becomes bluish-violet on the addition of ferric chloride T.S. A solution of 1 cc. of Cresol in 60 cc. of distilled water shows no greater turbidity than that produced in 58 cc. of distilled water by the addition of 1.5 cc. of fiftieth-normal sulphuric acid and 1 cc. of barium chloride T.S., comparison being made after the control mixture has been well shaken and allowed to stand for five minutes (*hydrocarbons*).

"Preserve in well-closed containers, protected from light." *U. S.*

It is stated that much of the commercial cresol does not comply with the U. S. P. requirements for specific gravity and boiling point (Ewe, *Proc. Penna. Pharm. Assoc.,* 1915, p. 1.6.)

"A straw-colored liquid, becoming brown on keeping or on exposure to light. Soluble in 50 parts of *water,* the solution being neutral to *litmus;* freely soluble in alcohol (90 per cent.), in *ether,* in *chloroform,* in *glycerin,* and in the fixed and volatile oils. Specific gravity 1.040 to 1.050. When 0.5 millilitre is shaken with 300 millilitres of *water* and filtered, the filtrate gives a transient bluish color on the addition of *T. Sol. of ferric chloride.* Not less than 90 per cent. distils between 195° and 205° C. 10 millilitres shaken with 10 millilitres of an aqueous solution (1 in 10) of *sodium hydroxide* form an almost clear liquid, from which no appreciable oily layer separates on standing for twenty-four hours (limit of hydrocarbon oils). 5 millilitres mixed with 5 millilitres of *glycerin* form a clear solution from which, on the addition of 5 millilitres of *water,* the cresol completely separates (absence of phenol)." *Br.*

Uses.—Cresol is used in medicine solely for its disinfectant properties. It far surpasses phenol in power, both as a germicide and antiseptic. Reed (*Trans. of the Association of Military Surgeons,* U. S., 1894, iv) finds that a one-half per cent. solution of cresol is sufficient to destroy the staphylococcus in less than twenty minutes; a one per cent. solution killed in thirty seconds and is equivalent to a four or five per cent. solution of phenol. Ditthorn (*J. Soc. Chem. Ind.*, 1920, xxxix, 799A) finds that of the isomers meta-cresol is the most actively germicidal and that the orthocresol is slightly weaker than the para. Because of the sparing solubility of cresol in water it is generally employed in the form of a soapy solution or emulsion (see *Liquor Cresolis Compositus*). This solution retains the germicidal properties of the cresol, thus Fox (*Report of the Commissioner of Health of the State of Pennsylvania,* 1907, p. 123) finds that one per cent. of the official compound solution of cresol kills non-sporulating bacteria after two minutes' exposure and is superior to a one per cent. solution of phenol. McClintock (*U. S. Hygienic Laboratory Bulletin,* No. 82, April, 1912) gives the phenol coefficient of compound solution of cresol: Without organic matter 3.0, with organic matter 1.87. (For a list of some of the proprietary preparations of cresol, see Part II.) There is probably some difference in the germicidal powers of the various cresols so that the mixture which is known officially as cresol varies more or less in activity. According to Sage (*P. J.*, 1908, lxxx, p. 730) the compound solution of cresol of the British Pharmacopœia has a phenol coefficient varying from 1.25 to 3.75 according to the value of the cresylic acid from which it is made. Other authorities, however, do not find so great a variation.

The statement has been made that cresol is practically non-poisonous, but such is certainly incorrect. It is perhaps somewhat less toxic than phenol, but the difference is not very great, and there have been a number of fatal cases of cresol poisoning reported, as well from its use as a douche as from swallowing. The symptoms have been nausea and vomiting, general depression with a tendency towards stupor, gradually developing into coma, smoky albuminous urine, fall of bodily temperature, and collapse. Friedlander (*Th. M.*, 1907) recommends as antidotes large quantities of oil or the white of egg, which he believes act by preventing absorption; milk and watery fluids are to be avoided.

Cresol is used chiefly as a surgical disinfectant, both for the purpose of sterilizing instruments and as a wound dressing. For the former three to five per cent. of the compound solution should be employed, while for application to wounds one per cent. of the compound solution (representing one-half per cent. of cresol) is generally recommended. Cresol is also employed to a limited extent as a gastro-intestinal antiseptic in various types of *enteritis* and *gastritis.* For this purpose one or two minims (0.06–0.12 cc.) of the cresol, well diluted, may be given.

Vanderkleed and Ewe report that cresol acts as an alkaloidal precipitant under certain conditions and advise against the use of cresol as a preservative in ampules of alkaloidal solution.

Dose, from one to three minims (0.06–0.2 cc.).

Off. Prep.—Liquor Cresolis Compositus, *U. S.* (*Br.*).

CRETA PRÆPARATA. U. S., Br.

PREPARED CHALK Cret. Præp. [Drop Chalk]

"Prepared chalk is a native form of calcium carbonate freed from most of its impurities by elutriation and containing, when dried to constant weight at 200° C., not less than 97 per cent. of $CaCO_3$." *U. S.* "Prepared Chalk is native calcium carbonate, freed from most of its impurities by elutriation." *Br.*

Creta Lævigata; Craie Lavée, Craie préparée, *Fr.;* Präparirte Kreide, Schlämmkreide, *G.;* Creta preparada, *Sp.*

Preparation.—Calcium carbonate, in the extended meaning of the term, is the most abundant of simple minerals, constituting, according to its state of aggregation and other peculiarities, the different varieties of calcareous spar, common and shell limestone marble, marl, and chalk. It occurs also in the animal kingdom, forming the principal part of shells, and a small proportion of the bones of the higher orders of animals. It is present in small quantity in most natural waters, being held in solution as the bicarbonate, $Ca(HCO_3)_2$, by the carbon dioxide which they contain. In the waters of limestone districts it is a very common impregnation, and causes purging in those not accustomed to its use. In all such cases, boiling the water, by expelling the carbon dioxide, causes the carbonate to be deposited. It has been shown, however, that calcium carbonate is itself in a slight degree soluble in water; so that a small proportion remains in limestone water which has been long exposed to boiling.

Chalk occurs abundantly in the south of England and the north of France. It exists in massive beds, and very frequently contains nodules of flint, and fossil remains of land and marine animals. According to F. V. Hayden, chalk beds identical with those of Europe extend for 400 miles along the Missouri River in Dakota. Chalk is an insipid, inodorous, insoluble, opaque, soft solid, generally white, but grayish-white when impure. It is rough to the touch, easily pulverized, and breaks with an earthy fracture. It soils the fingers, yields a white trace when drawn across an unyielding surface, and when applied to the tongue adheres slightly. Its sp. gr. varies from 2.3 to 2.6. It is never a perfectly pure calcium carbonate, but contains besides gritty siliceous particles, small portions of alumina and ferric oxide. If pure, it is entirely soluble in hydrochloric acid, but usually a little silica is left. If this solution be not precipitated by ammonia, it is free from alumina and iron. Chalk, on account of the gritty particles which it contains, is unfit for medicinal use until it has been prepared by the following process: It is first reduced to a very fine powder. This powder is agitated with water, which upon standing a short time deposits the coarser particles, and, being then poured off, slowly lets fall the remainder in an impalpable state. This process of purification is called elutriation or water sifting. The soft mass which remains after the decanting of the clear liquor is made to fall upon an absorbent surface in small portions, which when dried have a conical shape. This part of the operation is known as trochiscation.

The by-product of the manufacture of prepared chalk, which contains earthy impurities, is commonly sold as *whiting*.

Description and Physical Properties.—"A white to grayish-white, very fine, amorphous powder, often formed into 'conical drops.' It is odorless and tasteless, and is stable in the air. When heated to about 825° C., Prepared Chalk gradually loses carbon dioxide and is converted into calcium oxide. Dissolve about 0.1 Gm. of Prepared Chalk in 5 cc. of diluted acetic acid, and filter the solution: this solution responds to the reactions for calcium.

"Prepared Chalk is practically insoluble in water and is insoluble in alcohol. It is decomposed and dissolved by diluted acetic, hydrochloric, or nitric acid, with copious effervescence. When a weighed amount of Prepared Chalk is dissolved in diluted hydrochloric acid and the insoluble residue collected and ignited, it yields not more than 2 per cent. of the amount of Prepared Chalk taken.

"**Assay.**—Proceed as directed under *Calcii Carbonas Præcipitatus.*" *U. S.*

"White friable masses or a white powder. Yields the *reactions* characteristic of calcium and of carbonates. Yields not more than the slightest characteristic *reactions* for iron, aluminium, magnesium, phosphates, sulphates, or silica. *Arsenic limit* 5 parts per million. A solution of Prepared Chalk in *diluted acetic acid* yields no precipitate with *solution of potassium chromate* (absence of barium carbonate)." *Br.*

Uses.—Prepared chalk is an excellent antacid; and, as the salts which it forms in the stomach and bowels, if not astringent, are at least not purgative, it is admirably adapted to *diarrhea* accompanied with acidity. It is also used in *acidity of stomach,* when a laxative effect is to be avoided, and it is one of the best antidotes for oxalic acid. It has been employed as an application to *burns* and *ulcers,* which it moderately stimulates, while it absorbs the ichorous discharge and thus prevents it from irritating the diseased surface or the sound skin. It is given internally in the form of powder, or suspended in water by the intervention of gum arabic and sugar. (See *Mistura Cretæ.*) Prepared chalk is better fitted for chalk mixture than the precipitated calcium carbonate, in consequence of its more impalpable character and greater powers of adhesion.

Dose, from ten to forty grains (0.65–2.6 Gm.).

Off. Prep.—Mistura Cretæ, *U. S.* (from Compound Chalk Powder), *Br.;* Pulvis Cretæ Compositus, *U. S.;* Pulvis Cretæ Aromaticus, *Br., N. F.;* Pulvis Cretæ Aromaticus cum Opio (from Aromatic Chalk Powder), *Br.;* Dentifricium, *N. F.;* Hydrargyri cum Creta, *U. S.*

CROCUS. N. F.

SAFFRON Croc.

"Saffron is the stigma of *Crocus sativus* Linné (Fam. *Iridaceæ*). Saffron contains not more than 10 per cent. of yellow styles, or other foreign organic matter and yields not more than 7.5 per cent. of total ash." *N. F.*

Autumnal Crocus; Stigmata Croci; Spanish Saffron; Safran, *Fr. Cod.;* Crocus, *P. G.;* Safran, *G.;* Zafferano, *It.;* Azafran, *Sp.*

Crocus sativus is a perennial plant, with a rounded and depressed bulb or corm, from which the flower rises a little above the ground, upon a long, slender, white, and succulent stem. The flower is large, of a beautiful lilac or bluish-purple color, and appears in September or October. The leaves are radical, linear, slightly revolute, dark green upon their upper surface, with a white longitudinal furrow in the center, paler underneath, with a prominent flattened midrib; they are enclosed at their base—together with the tube of the corolla—in a membranous sheath, from which they emerge soon after the appearance of the flower. The style hangs out on one side between the two segments of the corolla, and terminates in three long convoluted stigmas, which are of a rich orange color, highly odorous, rolled in at the edges, and notched at the summit. The stigmas of the *Crocus orientalis* are used in the East.

C. sativus is believed to be a native of Greece and Asia Minor, where it has been cultivated from the earliest ages. There are three main varieties of it, the French, the Grecian, and the Chinese. The first of these is superior in color and flavor, the second in the amount of yield, while the third is said to unite these qualities. Saffron is also cultivated for medicinal use in Sicily, Spain, France, England, and other temperate countries of Europe. Large quantities of saffron are raised in Egypt and Persia. We cultivate the plant in this country chiefly as a garden flower, although some of the drug of very fine quality has been produced in Pennsylvania; the high cost of labor in America will probably prevent the possibility of its coming into commerce. Wild saffron is found growing in uncultivated fields in Southern Russia; Tichomirow believes that these are varieties of *C. sativus* and *C. speciosus* Marsh. Biebr., var. *β-Pallassii* (*C. Palassii* Marsh. Biebr.). He further states that wild saffron from these sources is in no way inferior to the cultivated. (*A. Pharm.,* 1903, 656.)

For an account of the cultivation in England, see *P. J.*, June, 1887. The Spanish saffron is generally considered the best in the United States.

Saffron has a peculiar, sweetish, aromatic odor, a warm, pungent, bitter taste, and a rich deep orange color, which it imparts to the saliva when chewed.

Description and Physical Properties.—"*Unground Saffron.*—Stigmas 3, united or separate, attached to the apex of the style; usually about 25 mm. long, cornucopia-shaped, of a dark, rich red color, the margin dentate or fimbriate; styles about 10 mm. long, more or less cylindrical, solid, yellowish. Odor strong, peculiarly aromatic; taste bitterish, aromatic. When chewed it colors the saliva orange-yellow.

"*Structure.*—Upper end of the stigma with numerous cylindrical papillæ about 0.150 mm. long, among which occur a few spherical pollen grains, the latter being nearly smooth, and from 0.040 to 0.120 mm. in diameter; occasionally some of the pollen grains germinated, and with pollen tubes.

"When placed in sulphuric acid, the stigmas are immediately colored blue, gradually changing to violet, and finally become a deep wine-red color. Add 0.01 Gm. of finely powdered Saffron to 100 cc. of cold water, allow it to macerate for several hours and filter; on adding 10 cc. of this filtrate to 100 cc. of water, it gives a distinctly yellow-colored solution. Macerate 0.01 Gm. of Saffron in 5 cc. of methyl alcohol; a deep orange color is imparted to the liquid. Macerate 0.01 Gm. of Saffron in 5 cc. of acetone, alcohol, or dehydrated alcohol; a distinct, lemon-yellow color is produced. With corresponding quantities of Saffron and ether a very light lemon-yellow color is produced. With corresponding quantities of Saffron and chloroform a very slight yellow tinge is imparted; and with corresponding portions of Saffron and xylene, benzene, carbon disulphide, or carbon tetrachloride, the solvents remain colorless. When Saffron is pressed between filter paper, the paper does not display transparent spots due to the absorption of oil. Saffron loses not more than 12 per cent. of its weight when dried at 100° C.

"Preserve it in tightly closed containers, protected from light." *N. F.*

Constituents.—Analyzed by Vogel and Bouillon-Lagrange, saffron afforded 65 per cent. of a peculiar extractive matter, which they named *polychroïte,* but later researches have shown that it is a mixture of the glucoside *crocin,* sugar, and essential oil. (Planchon, *Drogues Simples,* vol. i, 210.) Kayser obtained (*B. Chem. G.*, 1884, 2228) pure *crocin,* having the formula $C_{44}H_{70}O_{28}$, as a yellow powder, easily soluble in water and diluted alcohol, only slightly soluble in absolute alcohol, and giving with concentrated sulphuric acid a deep blue color, which turns violet, then cherry-red, and finally brown. It is easily hydrolyzed into *crocetin* and a dextro-rotatory sugar which Kayser calls *crocose.* The crocetin is a red powder, not soluble in water, but easily soluble in alcohol and ether. Its solution in alkalies shows an orange-yellow color, from which solution acids separate it again in orange-colored flecks. Its formula is $C_{34}H_{46}O_9$, or, according to Schmuck and Marchlewski, $C_{15}H_{20}O_4$. Kayser also found a colorless bitter principle, to which he gave the name *picro-crocin* or *saffron bitter,* and the formula $C_{38}H_{66}O_{17}$, which is also of glucoside character. Winterstein and Teleczky (*Helv. Chim. Acta.*, 1922, v, 376) isolated a colorless crystalline ketonic compound having the composition $C_{10}H_{14}O$, which they also call picro-crocin. They believe this principle to have accompanied and contaminated the crocin of previous investigators. It belongs to the terpene series and is related to carvone. According to T. Munesada (*J. Pharm. Soc. Jap.*, 1922, 486, p. 661) *Gardenia grandiflora* also contains crocetin which he gives the formula $C_{10}H_{13}O.OH$ and states that it is a derivative of saffron. Saffron contains, according to Henry, about 10 per cent. of essential oil. This has the formula $C_{10}H_{14}O$, boils at 208° to 210° C., is yellow, of a hot, acrid, bitterish taste, and heavier than water.

Adulterations.—The high price of this medicine gives rise to frequent adulterations. Water is said to be very often added in order to increase its weight. Oil or glycerin is also added for the same purpose, or to improve the appearance. In some specimens the dyed corolla of the crocus with the attached stamens is abundant. Sometimes the flowers of other plants, particularly *Carthamus tinctorius,* or *safflower, Calendula officinalis,* or marigold, and *arnica* are fraudulently mixed with the genuine stigmas. They may be known by their shape, which is rendered obvious by throwing a portion of the suspected mass into warm water, to expand them. A ready method of detecting Carthamus in powdered saffron suggested by Vicari is based on the fact that saffron gives a blue coloration with a reagent made by mixing 60 cc. of concentrated sulphuric acid with 40 cc. of a 10 per cent. solution of sodium phosphomolybdate. The powder is spread over a glass slide and a drop of the reagent added and well mixed. When examined by the microscope the particles of carthamus stand out because of their reddish color, in contrast with the blue of the true crocus. According to Heim, *Crocosma aurea* Pl., which is cultivated in Southern Africa as a dye-stuff, affords an excellent substitute for saffron, the dried petals giving, when treated with water, a brilliant yellow solution. The partly dry aqueous extract gives with sulphuric acid a blue coloration, passing to violet, similar to that obtained from saffron. Other adulterations are the fibers of dried beef, the stamens of the crocus, distinguishable by their yellow color, the stigmas previously exhausted in the preparation of the infusion or tincture, and various mineral substances, easily detected upon close examination. The ligulate florets of *Calendula officinalis* have been factitiously colored and employed to adulterate Crocus. This article, known as *Feminell,* has a carmine-red color and when mounted in chloral solution and examined microscopically shows elongated epidermal cells bearing near the tube of the corolla large multicellular hairs, yellowish oil globules in the parenchyma and spiny pollen grains.

An adulteration which has been largely practised appears to consist of yellow-colored chalk or barium sulphate, made into a thin paste, probably with honey, and attached to the stigmas, sometimes isolated, sometimes in groups of five or six, enveloping them almost completely. If this saffron be kept in a dry place, and often handled, the paste becomes partly broken up, and the colored powder spreads itself in the mass and the envelope. The chalk can at once be detected by shaking the suspected saffron with water, and treating the precipitated powder with hydrochloric acid, when effervescence will occur. A less than the ordinary brightness of color in the saffron should lead to suspicion of this adulteration. Much can be told as to the purity of saffron by agitating the suspected flowers in distilled water; if the drug be pure the liquid will remain clear, slowly assuming a fine pure yellow tint; the saffron also will retain its red color for hours. Another excellent plan is to scatter a pinch of the flowers upon the surface of warm water, when the stigmas should spread out and display their proper form. Minute fragments of red saunders, which are occasionally added to saffron, may be separated by agitating with water. Adulterations of crocus may sometimes be detected by remembering that the pollen grains of *Crocus sativus* are spheroidal, nearly smooth, and from 0.040 to 0.075 mm. in diameter. In various European markets there has been offered a saffron largely adulterated with borates, chlorides, and other salts of sodium and potassium, and yet retaining the physical properties of saffron of high character. These and other adulterations with inorganic salts can be detected by the amount of ash left on burning, genuine saffron leaving from five to seven per cent. The borated saffron also yielded immediately to water an orange-yellow color. Further, some of it at least was hygroscopic, so that when rubbed up between the fingers into a ball it retained that form instead of being elastic as is true saffron.

A more recent adulterant for Crocus consisted of the florets of a species of *Onopordon* artificially dyed with Tartrazine and commercial Ponceau 2 R, and weighted with borax, glycerine and saltpeter. This adulterant may be detected by the presence of tubular florets, the corollas of which bear club-shaped multicellular, glandular hairs, by the pollen grains with a peculiarly thickened triangular coat and by the narrow extension of the stamens above the anthers. The artificial dyes may be determined by the pink to red color produced when the material is placed in an organic solvent.

A product called *Cape Saffron* formerly attracted some attention but is now rarely met with. It consists of the flowers of a scrophulariaceous shrub, *Lyperia atropurpurea* Benth., which grows in South Africa.

Uses.—Saffron was extensively used by the ancients and by medieval physicians, as a nerve sedative and emmenagogue, and is still employed to some extent in Europe; but in Great Britain and the United States it has fallen into well deserved and almost complete desuetude. In domestic practice saffron tea is occasionally used in *exanthematous diseases,* to promote the eruption. At present it is chiefly used to impart color and flavor. Saffron should be preserved in tightly-closed containers protected from light.

Dose, from ten to thirty grains (0.65 to 2.0 Gm.).

Off. Prep.—Tinctura Croci, *N. F.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodica sine Aloe, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.;* Tinctura Opii Crocata, *N. F.*

CUBEBA. U. S. (Br.)

CUBEB Cubeb. [Cubebs]

"Cubeb is the dried, nearly full-grown, unripe fruit of *Piper Cubeba* Linné filius (Fam. *Piperaceæ*). Cubeb contains not more than 5 per cent. of its shriveled immature fruits or stems, or not more than 2 per cent. of other foreign organic matter, and yields not less than 10 per cent. of volatile ether-soluble extractive." *U. S.* "Cubebs are the dried full-grown unripe fruits of Piper Cubeba, *Linn. fil.*" *Br.*

Cubebæ Fructus, *Br.;* Fructus (s. Baccæ) Cubebæ, Piper Caudatum; Tailed Pepper; Cubèbe, *Fr.Cod.;* Poivre à Queue, *Fr.;* Cubebæ, *P. G.;* Kubeben, *G.;* Pepe Cubebe, *It.;* Semilla de Cubeba, *Sp.;* Kebabeh, *Ar.*

Piper Cubeba is a climbing perennial plant, with a smooth, flexuous, jointed stem, and entire, petiolate, oblong or ovate-oblong, acuminate leaves, rounded or obliquely cordate at the base, strongly nerved, coriaceous, and very smooth. The flowers are diœcious and in spikes, with peduncles about as long as the petioles. The fruit is a globose, pedicelled drupe. This species of Piper is a native of Java, Borneo and Sumatra. It is extensively grown in the coffee plantations, supported by the trees which are used for shade, and has been introduced into Ceylon and the West Indies. The fruits are found in numbers of 50 or more on each spike. They are collected while still green, though full grown, and dried in the sun. They are then sent to Batavia or Singapore for export. The commercial supplies coming into the United States are shipped either direct from Singapore or through London and Amsterdam. Our knowledge of the false cubeb of commerce up to 1894 was epitomized in the 17th edition of the *U. S. D.*, p. 457. To this account the reader is referred for historical details. (See also *U. S. D*,. 19th ed., p. 410.)

Description and Physical Properties.—"*Unground Cubeb.*—The upper portion of fruit nearly globular, from 3 to 6 mm. in diameter, abruptly contracted into a slender stem-like portion seldom exceeding 7 mm. in length; pericarp brown to very dark brown externally, rarely gray, coarsely reticulate, about 0.3 mm. in thickness; 1-locular, 1-seeded, the seed attached at the base of the pericarp and usually not completely filling the loculus; odor aromatic, characteristic; taste strongly aromatic and pungent.

"*Structure.*—Pericarp with an outer epidermis of tabular cells with thickened, undulate outer walls, a nearly continuous hypodermis of stone cells; of wide parenchyma, scattered in which are numerous large, oval secretion cells containing volatile oil and occasionally crystals in the form of short rods, the contents of the secretion cells being colored a deep crimson upon the addition of sulphuric acid; a layer of several rows of collapsed cells in which occurs occasionally a small wood bundle with a few lignified bast-fibers; and an endocarp of one or two rows of isodiametric stone cells; seed-coat of several rows of reddish-brown, tangentially elongated, more or less collapsed cells; perisperm of thin-walled parenchyma cells, more or less polygonal in shape and containing either small starch grains, or globules of fixed oil or occasionally a crystal of calcium oxalate; endosperm small in amount, near the apex of the seed and embedding a very small embryo.

"*Powdered Cubeb.*—Brown to very dark brown. Starch grains numerous, single and compound, the individual grains from 0.002 to 0.012 mm. in diameter; stone cells numerous in palisade-like groups, with rather prominent dark lumina and yellowish, much-thickened, lamellated, porous walls; fragments of wood bundles few, with spiral tracheæ and fibers, the latter from 0.05 to 1.00 mm. in length with blunt, rounded or very much attenuated ends, the walls strongly lignified and with numerous oblique pores.

"Cubeb, powdered or crushed, mixed with a drop of sulphuric acid on glass, and viewed against a white background produces a crimson-red coloration of the acid.

"**Assay.**—Proceed as directed under volatile ether-soluble extractive." *U. S.*

"Nearly globular, about four millimetres in diameter, greyish-brown or nearly black. Pericarp reticulately wrinkled, thin, brittle, and abruptly prolonged at the base into a slender, rounded stalk about one and a half times as long as the globular portion. Seed almost spherical, sometimes much shrivelled, attached by the base. In the transverse section of the pericarp two layers of sclerenchymatous cells, one near the outer, the other near the inner surface, those of the latter being radially elongated and usually arranged in a single row. Strong, aromatic, and characteristic odor; taste warm, aromatic, and somewhat bitter. When 2 grammes of powdered Cubebs are macerated with 20 millilitres of *ether* for twenty-four hours, and shaken occasionally, 10 millilitres of the clear ethereal solution, allowed to evaporate in a flat-bottomed dish, yield a residue which, dried for one hour in a desiccator over *sulphuric acid*, weighs not less than 0.200 gramme. Crushed Cubebs impart a crimson color to *sulphuric acid*. Ash not more than 8 per cent." *Br.*

Commercial cubebs are not infrequently admixed with and entirely substituted by other fruits, some of which contain volatile oils which possess very different properties from the genuine oil of cubeb, being in some instances highly toxic. Hartwich (*A. Pharm.*, 1898) gives the following classification for the identification of spurious fruits:

I. *Fruits of the Piperaceæ having slender stalks.*

- A. STONE CELLS IN EPICARP, ENDOCARP AND DISTRIBUTED IN THE MESOCARP: *Piper ribesioides* Wallich (identical with *Padang Cubeb*). Fruits not colored red with sulphuric acid.
- B. STONE CELLS ONLY PRESENT IN THE EPICARP AND ENDOCARP: *Piper Cubeba* L.f. *Rinoe Katoentjor,* the official variety, which is colored red with sulphuric acid; *Rinoe badak,* distinguished by not being colored red with sulphuric acid; *Piper crassipes* Korthals. Sections not colored red with sulphuric acid.
- C. STONE CELLS PRESENT ONLY IN THE EPICARP: *Piper mollissimum* Blume (*Keboe Cubeb. Karbauw berries*) sections not colored red with sulphuric acid; *Piper venosum* DC. colored red with sulphuric acid.
- D. STONE CELLS ABSENT IN THE PERICARP:
  - (*a*) African varieties: *Piper clussi* DC. sections colored red with sulphuric acid; *Piper guineense* Schum. sections not colored red with sulphuric acid; *Piper borbonense* DC. (*Cubèbe du pays*) sections not colored red with sulphuric acid.
  - (*b*) Indian varieties: None of which are colored red with sulphuric acid; *Piper Lowong* Blume secretion cells colored bluish-green with sulphuric acid; *Ceylon pepper,* secretion cells colored yellow with sulphuric acid; *Piper canium* Blume and *P. phyllostitum* DC.

II. *Fruits of the Piperaceæ without stalks.*
- A. STONE CELLS PRESENT IN EPICARP AND ENDOCARP: *Piper nigrum* L. sections colored red with sulphuric acid.
- B. STONE CELLS ONLY IN THE EPICARP: *Dangdang boeroeng,* a fruit obtained from Java, the origin of which is unknown.
- C. STONE CELLS ABSENT IN PERICARP: *Cubeb from Bangil,* origin unknown. Sections at first colored red with sulphuric acid, then becoming brown.

III. *Fruits obtained from plants belonging to other families than the Piperaceæ.*
1. *Xanthoxylum Budrunga* Wall. (*Fagara Budrunga* Roxb.) (*Rutaceæ*); *Bridelia tomentosa* Bl. (*Euphorbiaceæ*); *Tetranthera citrata* N. v. Esenbeck (*Litsea citrata* Bl.) (*Lauraceæ*); *Daphnidium Cubeba* Nees. (*Lauraceæ*); *Pericampylus incanus* Miers. (*Menispermaceæ*); *Xylopia frutescens* Gaertner. (*Anonaceæ*); *Helicteres hirsuta* Bl. (*Sterculiaceæ*); *Grewia tomentosa* Juss. (*Tiliaceæ*).

Constituents.—The most obvious constituent of cubeb is the volatile oil, the proportion of which yielded by the drug varies from 5 to 20 per cent. It is, as shown by Oglialoro, a mixture of a terpene, boiling at 158° to 163° C., which is present in very small amount, and is probably pinene or camphene, some dipentene, and two oils of the formula $C_{15}H_{24}$, boiling at 262° to 265° C. One of these, known as *cadinene,* is strongly lævogyrate, and yields a crystallized compound having the formula, $C_{15}H_{24}2HCl$, and melting at 118° C., while the other is less lævogyrate, and does not combine with HCl.

The oil distilled from old cubeb on cooling at length deposits large transparent inodorous octahedra of *camphor of cubeb,* $C_{15}H_{26}O$. E. Schmidt found that this camphor melts at 66.5° C.; simply by standing over sulphuric acid, more rapidly on heating, it gave up water and passed into that fraction of cubeb oil which boils at 260° C., of which it is, therefore, simply the hydroxide.

Another constituent of cubeb is *cubebin.* This is an inodorous substance, crystallizing in small needles or scales, melting at 132° C., having a bitter taste in alcoholic solution, it dissolves freely in boiling alcohol, but deposits on cooling, and is abundantly soluble in chloroform. Its composition is $C_{20}H_{20}O_6$. It contains no hydroxyl nor carbinol groups and is not acted upon by oxidizing agents. It is without important physiological properties. Upon decomposition with hydriodic acid in glacial acetic acid solution it yields *cubebinic ether* which, upon redection with sodium in the presence of alcohol, produces *cubebinol.* E. Schaer calls attention to the similarity in reaction between cubebin and veratrine, aconitine, morphine, and digitalin. (*A. Pharm.,* 1887, p. 531.) *Cubebic acid,* a white amorphous substance, is present in the proportion of about 1 per cent.; the therapeutic value of the drug has been attributed as largely due to this constituent. There is also about 3 per cent. of amorphous resin. Cubeb gradually deteriorates by age, and in powder becomes rapidly weaker, in consequence of the escape of its volatile oil. It should be kept whole, and pulverized when dispensed. The powder is said to be sometimes adulterated with that of pimenta.

Uses.—Cubeb in considerable quantities excites the circulation, increases the heat of the body, and sometimes occasions headache and giddiness. At the same time it frequently produces an augmented flow of the urine, to which it imparts a peculiar odor. Among its effects are also occasionally nausea and moderate purging, and it is said to cause a sense of coolness in the rectum during the passage of the feces. We have no evidence that it was known to the ancients.

Cubeb, because of its local irritant action, acts as a stimulant to the mucous membranes. Its active principles appear to be capable of absorption and elimination through the kidneys exerting their characteristic effects upon the mucous membrane of the genito-urinary tract. It is probable also that it possesses some antiseptic virtues. Formerly it was widely used in the treatment of a large variety of inflammatory complaints but at present is used as an internal remedy only in the latter stages of *gonorrheal urethritis* after the subsidence of the first inflammatory symptoms, and occasionally in *chronic bronchitis.* Even for these purposes its use is passing out of vogue. It is a widely employed local remedy in the form of lozenges for the relief of various relaxed conditions of the throat.

Dose, of powdered cubeb, ten grains to one drachm (0.65–3.9 Gm.).

Off. Prep.—Fluidextractum Cubebæ, *N. F.;* Oleoresina Cubebæ, *U. S.;* Tinctura Cubebæ, *Br.;* Trochisci Cubebæ (from Oleoresin), *U. S.;* Elixir Buchu Compositum (from Compound Fluidextract of Buchu), *N. F.;* Fluidextractum Buchu Compositum, *N. F.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloes, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloes, *N. F.;* Tinctura Cubebæ, *N. F.*

CUPRI SULPHAS. U. S., Br.

CUPRIC SULPHATE Cupr. Sulph. [Copper Sulphate]

"Cupric Sulphate contains not less than 63 per cent. and not more than 66.8 per cent. of $CuSO_4$, corresponding to not less than 98.5 per cent. of the crystallized salt [$CuSO_4.5H_2O$]." *U. S.* "Copper Sulphate, $CuSO_4,5H_2O$, may be obtained by the interaction of sulphuric acid, copper or copper oxide, and water." *Br.*

Cuprum Vitriolatum; Blue Vitriol, Roman Vitriol, Blue Stone; Sulfate de Cuivre, *Fr. Cod.;* Vitriol bleu, Couperose bleu, *Fr.;* Cuprum Sulfuricum, *P. G.;* Schwefelsaures Kupfer, Kupfersulfat, Kupfervitriol, Blauervitriol, Blauer Galitzenstein, *G.;* Solfato di rame, Vitriolo di rame, *It.;* Sulfato cuprico, Vitrolo azul, *Sp.*

Preparation.—Copper sulphate occasionally exists in nature, in solution in the water which flows through copper mines. In this case the salt is procured by merely evaporating the waters which naturally contain it. Another method of obtaining it is to roast the native sulphide in a reverberatory furnace, whereby it is made to pass, by absorbing oxygen, into the state of sulphate. Too high a temperature must be avoided during the roasting process to avoid the production of hard masses from which the copper is extracted with great difficulty, subsequent chlorination of the product sometimes being necessary. The roasted mass is lixiviated, and the solution obtained evaporated that crystals may form. The salt procured by either of these methods contains a little ferric sulphate, from which it may be freed by adding either an excess of cuprous oxide, which precipitates ferric oxide, or recently precipitated copper subcarbonate, which causes the deposition of the iron as a carbonate. (*A. J. P.*, xxxiv, 507.) A third method is to dissolve copper scales to saturation in sulphuric acid contained in a wooden vessel lined with sheet lead. The scales consist of metallic copper mixed with oxide, and are produced in the process for annealing sheet copper.

Most of the copper sulphate produced at present is obtained as a by-product by the gold, silver, and copper refiners. The production of copper sulphate in the United States is very large, and there is a considerable exportation.

In the U. S. Pharmacopœia copper sulphate is presumed to be obtained pure from the manufacturer; the British Pharmacopœia suggests the method in which it may be prepared, without entering into the details of the process. The German Pharmacopœia has two kinds official, *Cuprum sulfuricum,* which corresponds with the former *Cuprum sulfuricum purum,* and *Cuprum sulfuricum crudum,* or commercial sulphate.

Description and Physical Properties.—"Deep blue, triclinic crystals or a blue, granular powder. It is odorless, and has a nauseous, metallic taste. It is slowly efflorescent in dry air. One Gm. of Cupric Sulphate is soluble in 2.5 cc. of water, 500 cc. of alcohol, and in 2.8 cc. of glycerin, at 25° C. One Gm. is soluble in 0.5 cc. of boiling water.

"When heated to 30° C., Cupric Sulphate loses part of its water of crystallization and is converted into a pale, blue, amorphous powder. More water is lost at 100° C., and finally at 200° C. a white, anhydrous powder remains. At a still higher temperature, sulphur dioxide and oxygen are given off, and a residue of black cupric oxide remains. An aqueous solution of the salt (1 in 20) has a blue color, and is acid to litmus paper. An aqueous solution of the salt (1 in 10) responds to the reactions for copper, and for sulphates.

"Dissolve 1 Gm. of Cupric Sulphate in 50 cc. of distilled water, add 1 cc. of diluted hydrochloric acid, and pass hydrogen sulphide through the solution until all of the copper is precipitated: upon evaporating the filtrate and igniting, the weight of the residue does not exceed 0.003 Gm. (*other metals*).

"**Assay.**—Dissolve about 1 Gm. of Cupric Sulphate, accurately weighed, in 50 cc. of distilled water, add 4 cc. of acetic acid and 3 Gm. of potassium iodide, and titrate the liberated iodine with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.01596 Gm. of $CuSO_4$. Cupric Sulphate may also be assayed by the electrolytic method.

"Preserve in well-closed containers." *U. S.*

"Blue triclinic prisms. Soluble in 3.5 parts of *water,* very soluble in *glycerin,* almost insoluble in *alcohol* (90 per cent.). The aqueous solution is acid to *litmus.* Yields the *reactions* characteristic of copper and of sulphates. Yields no characteristic *reactions* for lead, zinc or aluminium. *Arsenic limit* 10 parts per million. Contains not more than 0.1 per cent. of iron, calculated as iron, Fe, when tested by the following process:—Dissolve 5 grammes in 25 millilitres of *water,* add 2 millilitres of *nitric acid,* heat to boiling, cool, and add *strong solution of ammonia* until the precipitate which first forms is redissolved and the liquid has a distinct odor of ammonia. Filter. Wash the filter paper thoroughly with *water* made alkaline with *solution of ammonia,* redissolve in *hydrochloric acid* any precipitate that has been collected, reprecipitate with *solution of ammonia,* collect, wash, dry, ignite, and weigh the residue. It weighs not more than 0.007 gramme." *Br.*

When heated, copper sulphate first liquefies in its water of crystallization, and then dries and becomes white. If the heat is increased, it next undergoes the igneous fusion, and finally, at a high temperature, loses its acid, cupric oxide being left. Four of the molecules of water of crystallization can be driven off at 100° C., but the fifth goes off only at a temperature of from 220° to 240° C., when the anhydrous salt remains. Potassium hydroxide, sodium hydroxide, and ammonia throw down from it a bluish-white precipitate of hydrated cupric oxide, which is immediately dissolved by an excess of the last mentioned alkali, forming a rich deep blue solution, called *aqua sappharina.* It is decomposed by the alkaline carbonates, and by borax, lead acetate and subacetate, ferric acetate, silver nitrate, mercuric chloride, potassium tartrate, and calcium chloride, and it is precipitated by all astringent vegetable infusions. If it becomes very green on the surface by the action of the air, it contains ferric oxide. This oxide may also be detected by ammonia, which will throw it down along with the copper oxide, without taking it up when added in excess. When copper sulphate is obtained from the *dipping liquid* of manufacturers of brass or German silver ware, it is always contaminated with zinc sulphate, as pointed out by S. Piesse. This liquid is at first a mixture of sulphuric and nitric acids, but becomes, at last, nearly saturated with copper. When zinc is present in copper sulphate, it will be taken up by solution of potassium hydroxide added in excess, from which it may be thrown down, after filtration, in white flocks, by a solution of bicarbonated alkali.

The industrial uses of copper sulphate are many and important. It is used in copper plating, in dyeing, in calico printing, in the manufacture of numerous pigments and in water purification and in the combating of plant diseases caused by certain low forms of plant or animal life.

Copper sulphate is incompatible with alkalies and liberates iodine from iodides.

Uses.—Copper sulphate is irritant or mildly escharotic, and when in diluted solution, stimulant and astringent. At one time it was given in *epilepsy* and other nervous diseases, but at present it is never used internally, except for its influence upon the gastro-intestinal mucous membrane. In *chronic diarrhea* with ulceration it is sometimes a useful remedy. In doses of 5 grains it acts as a powerful, prompt emetic, without causing general depression or much nausea, but is too irritant to be used freely; it is useful as an emetic in *phosphorus poisoning* because it not only empties the stomach but acts also as a chemical antidote to the phosphorus. Externally it is employed in solution as a stimulant to ill-conditioned *ulcers,* as an escharotic for destroying *warts,* fungous *granulations,* and callous edges, and as a styptic to bleeding surfaces. It is found, in not a few instances, to promote the cicatrization of ulcers, and is not infrequently employed, with that view, as a wash for *chancres.* Bevan (*S. M.,* 1905, p. 558) has used copper sulphate successfully in *actinomycosis.* He gave from one to three grains (0.065–0.2 Gm.) daily and applied a 1 per cent. solution to the ulcerated area.

Copper sulphate is highly poisonous to certain of the lower forms of vegetable life, thus it has been found serviceable for destroying the algæ in ponds. While in general its antibacterial properties are not very powerful it seems to be especially poisonous towards the *Bacillus typhosus,* Gildersleeve (*A. J. M. S.,* 1905, cxxxix, p. 757) having shown that as little as one part to a million is sufficient to destroy this bacterium in a period of three hours. It was at one time suggested as a means for purifying drinking water but is not practically available because the presence of various impurities destroys its action.

The preparation called *Cuprum Aluminatum* (*lapis divinus—pierre divine*) is made, according to the French Codex, by mixing, in powder, three ounces, each, of copper sulphate, potassium nitrate, and alum, heating the mixture in a crucible, so as to produce aqueous fusion, then mixing in a drachm of powdered camphor, and, finally, pouring out the whole on an oiled stone to congeal. The mass, when cold, is broken into pieces, and kept in a well-stoppered bottle. It is often desirable to employ copper sulphate, as a caustic, in the form of pencil. Its tendency to effloresce interfers with its use in this way in the pure state. Llovet recommends for the purpose a mixture of one part of potassa-alum and two of copper sulphate, which are to be first powdered, and then gradually melted together in a porcelain vessel, and poured into moulds made of bronze. Another mode of preparing *pencils of copper sulphate* is to rub briskly together four parts of that salt and one of borax, and to mould the plastic mass which results, into the desired form. An elongated cone is the best form, made by selecting suitable crystals and turning them in a lathe to the desired form; or they may be made by filing the crystals, and finishing with sand paper.

Dose, of copper sulphate, as an astringent, one-fourth of a grain (0.016 Gm.); as an emetic, five grains (0.32 Gm.), repeated in fifteen minutes if necessary, but not oftener than once. As a stimulant wash, the solution may be made of the strength of two, four, or eight grains to the fluidounce of water. For its effects as a poison, see *Cuprum.*

Off. Prep.—Liquor Zinci et Ferri Compositus, *N. F.;* Mistura Adstringens, *N. F.*

CUPRUM.

COPPER

Cu = 63.57.

"Fine Copper wire, about No. 25 wire gauge or about 0.02 inch." *Br.,* 1885.

Cupreum Filum: Fil de Cuivre, Cuivre, *Fr.;* Kupfer, Kupferdraht, *G.;* Rame, *It.;* Cobre, *Sp.*

This metal is very generally diffused in nature, and exists principally in four states; as native copper, as an oxide, as a sulphide, and as a salt. Its principal native salts are the sulphide (*chalcopyrite* $CuS.FeS$, and *chalcocine* Cu_2S), silicate, carbonate (*malachite* $CuCO_3.3Cu(OH)_2$, and *azurite* $2CuCO_3.Cu(OH)_2$), arsenate, oxide (*cuprite* Cu_2O), and phosphate. In the United States it occurs in various localities, but especially in the neighborhood of Lake Superior, in Montana, Arizona, Alaska and East Tennessee. The principal producing copper mines of Europe are those of Sweden, Spain and Portugal and Germany and the Ural Mountains. Chili, China and Japan are also relatively large producers at present. It is one of the metals used by man from remote periods of antiquity.

The total production of copper in the United States has increased very rapidly in recent years, and now is more than two-thirds of the world's annual production. The three most productive states are Arizona, Montana, and Michigan, in the order named.

Properties.—Copper is a brilliant, sonorous metal, of a reddish color, and very ductile, malleable, and tenacious. It has a slightly nauseous taste, and emits a disagreeable odor when rubbed. Its texture is granular, and its fracture hackly. Its sp. gr. is 8.92 to 8.95, and its fusing point 1080° C. Exposed to the air it undergoes a slight tarnish. Its combinations are numerous and important. With oxygen it forms two well characterized oxides, a red suboxide, better known as *cuprous* oxide, Cu_2O, and a black oxide, known as *cupric* oxide, CuO. While a cuprous chloride, iodide, and sulphide are known, it is the cupric oxide chiefly that unites with the several acids to form the copper salts. With metals copper forms numerous alloys, of which that with zinc, called *brass,* and that with tin, called *bronze,* are the most useful. *Bell metal, gun metal, delta metal, phosphor bronze, statuary bronze, silico bronze, manganese bronze,* and *German silver* are other alloys in frequent use in which copper is the predominating constituent.

Characteristics.—Copper is recognized by its color, and the effects of tests on its solution in nitric acid. This solution, with potassium hydroxide, sodium hydroxide, and ammonia, yields a blue precipitate, soluble in excess of the latter alkali, with which it forms a deep azure-blue liquid. Potassium ferrocyanide occasions a brown precipitate of copper ferrocyanide, and a bright plate of iron immersed in the solution of copper nitrate immediately becomes covered with a film of metallic copper. Thoms (*Zeit. An. Chem.,* 94, 464) asserts that if to a solution, too dilute to give a sensible reaction with potassium ferrocyanide, be added a solution of potassium iodide, a yellow coloration is produced which becomes violet with starch paste. This test, in absence of deoxidizing agents, will show as little as 1 to 500,000. Potassium ferrocyanide is a very delicate test for minute portions of copper in solution. Another test, proposed by Verguin, is to precipitate the copper in the metallic state on platinum by electro-chemical action. For this purpose a drop of the (acid) liquid to be examined is placed on a slip of platinum foil, and a slip of bright iron is brought in contact with the platinum and the liquid. If copper be present it will be instantly precipitated on the surface of the platinum. Copper compounds when present in food or drug products in appreciable amounts may be detected by the simple test of immersing a bright piece of steel or iron (as a knitting needle or spatula) into the material which has been brought to a pasty condition and acidulated with hydrochloric acid. The copper will be deposited upon the iron or steel in the form of a very thin easily perceptible film.

Action on the Animal Economy.—Copper in its pure state is nearly inert, but in combination it is highly deleterious. Nevertheless, a minute portion of the metal has been found in the human body. Wackenroder found copper in the blood of man, but does not consider it a constant and normal constituent. He also detected this metal in the blood of domestic animals living on a mixed diet, but not in their blood when nourished on vegetable food only. It has been found in the feathers of certain birds, as of a grass-green paroquet from Australia, which is said to frequent districts of the country where copper is found.

The soluble combinations of copper, when taken in poisonous doses, produce a coppery taste in the mouth; nausea and vomiting; violent pain in the stomach and bowels; frequent black and bloody stools; small, irregular, sharp, and frequent pulse; faintings; burning thirst; difficulty of breathing; cold sweats; paucity of urine, and burning pain in voiding it; violent headache; cramps, convulsions, and finally death. The best antidote is potassium ferrocyanide, given freely, which forms with the poison the insoluble copper ferrocyanide. Soap and alkalies are also antidotal. Before the antidote can be procured, large quantities of albuminous substance of milk or white of eggs should be given mixed with water, which act favorably by forming copper caseinate and copper albuminate, respectively, but these compounds should be evacuated as soon as possible by vomiting and purging. Should vomiting not take place, the stomach tube may be employed.

There is some difference of opinion as to whether the prolonged injection of copper can give rise to a chronic type of poison. Although some of the older writers attributed various cachectic symptoms to copper poisoning, the experiments of Huber (*J. P. Ex. T.,* 1918, xi, p. 303) who tested the effects of prolonged administration of a large number of salts of copper from the lower animals, without noting any ill effects, is in harmony with the clinical evidence that if copper has any deleterious influence upon the general health, it is very slight.

In medico-legal examinations, where cuprous poisoning is suspected, Orfila recommends that the viscera be boiled in distilled water for an hour, and that the matter obtained by evaporating the filtered decoction to dryness be carbonized by nitric acid. The carbonized product will contain the copper. By proceeding in this way there is no risk of obtaining the copper which may happen to pre-exist in the animal tissues. This method of search is preferable to that of examining the contents of the stomach and intestines, from which copper may be absent, while it may have penetrated the different organs by absorption, especially the abdominal viscera.

Vessels of copper which are not coated with tin should not be used in pharmaceutical or culinary operations, for although the metal uncombined is inert, yet the risk is great that the vessels may be acted on and a poisonous salt formed.

CYPRIPEDIUM. N. F.

CYPRIPEDIUM Cypriped. [Lady Slipper Root]

"Cypripedium consists of the dried rhizome and roots of *Cypripedium bulbosum* Miller, *Cypripedium pubescens* Willdenow, or of *Cypri-*

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pedium parviflorum Salisbury (Fam. *Orchidaceæ*). Cypripedium contains not more than 3 per cent. of other parts of the same plant or other foreign organic matter and yields not more than 6 per cent. of acid insoluble ash." *N. F.*

Lady's Slipper; Rhizoma Cypripedii; Yellow Lady's Slipper Root; Yellow Indian Shoe; Yellow Moccasin Flower; Yellow Noah's Ark; Venus' Shoe; Male Nervine; American Valerian; Racine de Cypripède jaune, Valériane américaine, *Fr.;* Gelbfrauenschuhwurzel, *G.*

Under the common name of *lady's slipper,* or *moccasin plant,* about 30 species of *Cypripedium* inhabit the woods in different parts of the north temperate zone. They are small plants, with large, many-nerved, plaited leaves, sheathing at the base, and large, often beautiful terminal flowers, of a shape not unlike the Indian moccasin, whence they derive one of their common names. Their generic name of *cypripedium* (Κύπρις, *Venus,* and πόδιον, *sock*) had a similar origin. Several of them have been used by American physicians, the root being the part employed. R. P. Stevens of Ceres, Pennsylvania, says of them that he has found the *C. reginæ* Walt. (*C. spectabile* Salisb.), and *C. acaule* Ait., especially when growing in dark swamps, to be possessed of narcotic properties, and to be less safe than the *C. parviflorum* Salisb. The rhizomes and roots of the two species, *C. hirsutum* and *C. parviflorum* are indiscriminately found in commerce and sold under the same name.

Cypripedium hirsutum Mill. (*C. pubescens* Willd.), or *Large Yellow Lady's Slipper,* has a simple, often flexuous, pubescent, leafy stem, from one to two feet high. The leaves are pubescent, ovate-lanceolate, acuminate, narrowing at the base, about four or five inches long by two in breadth, alternate, sessile, and sheathing. The flower is usually solitary and terminal, with four divisions of the perianth, the two outer cohering nearly to the apex, the inner longer, narrower, undulatory or twisted, and the lip an inch or two in length, swelling sac-like, and of a yellow color. The fruit is an oblong capsule, tapering at each end, recurved, pubescent, and peduncled. The plant is indigenous, growing abundantly in rich, moist woods from Newfoundland to Georgia, west to Minnesota and Eastern Kansas.

Cypripedium parviflorum Salisb., or *Small-flowered Yellow Lady's Slipper,* is a perennial plant with a leafy stem, a foot or two in height, and comparatively small, bright yellow flowers, appearing in May. The specific character of the flower is that the lobe of the style is triangular and acute; the outer petals are oblong-ovate and acuminate; the inner linear and contorted; the lips shorter than the petals, and compressed. This species has the same range as *C. hirsutum.*

The rhizomes and roots are gathered after the flowering of the plant in the spring, washed and dried. The commercial supplies are obtained from Michigan, Wisconsin, North Carolina, Kentucky, Virginia, Indiana and Missouri.

Description and Physical Properties.—"*Unground Cypripedium.*—Rhizome of horizontal growth, curved, 3 to 10 cm. long, 2 to 6 mm. thick, orange-brown to dark brown, the upper side showing numerous circular, cup-shaped scars, closely covered below with simple, wiry roots, the latter varying from 3 to 15 cm. in length; fracture of rhizome short, white; that of roots somewhat fibrous. Odor distinct, heavy; taste sweetish, bitter, and somewhat pungent.

"*Structure.*—Rhizome: epidermis composed of small cells with reddish brown walls; cortex of about twelve layers of thick-walled parenchyma cells, the latter being filled with starch or resin, a few containing raphides of calcium oxalate; stele without endodermis and consisting of irregularly distributed concentric fibro-vascular bundles surrounded by thick-walled porous parenchyma cells, the latter containing starch, resin, or calcium oxalate in raphides, no distinct pith present. Root; epidermis of small cells with reddish brown walls usually without root hairs, hypodermis of a single layer of small cells with yellowish walls; about seven layers of parenchyma cells containing starch, resin, or calcium oxalate in raphides; stele composed of from five to eight radial fibro-vascular bundles with the sieve in small groups adjoining a pericambium composed of a single layer of thin-walled cells; endodermis continuous, and composed of thin-walled cells, except opposite the sieve where two or three cells are thickened, more or less lignified and fiber-like.

"*Powdered Cypripedium.*—Yellowish brown; numerous rounded or somewhat angular, simple and compound starch grains up to 0.014 mm. in diameter; calcium oxalate in raphides up to 0.070 mm. in length and occurring isolated or in bundles, occasionally imbedded in a mucilage-like plasma; tracheæ spiral, scalariform, or with simple or bordered pores; a few tracheids, fibers, long, thin-walled and lignified; a few non-lignified, thick-walled fibers; fragments of epidermal tissue composed of elongated cells with reddish brown walls; groups of thick-walled parenchyma cells with numerous simple pores, and containing starch, resin, or calcium oxalate." *N. F.*

Locally poisonous properties have been attributed to *C. reginæ* Salisb. and *C. parviflorum* var. *pubescens* (see *Geol. Nat. Hist. Survey, Minnesota Bull.,* 9, part i), but it has been shown that the secretion from the glandular hairs simply exerts an irritant action.

Cypripedium has a somewhat aromatic odor, which diminishes by time, and a bitter, sweetish, peculiar, and in the end somewhat pungent taste.

Cypripedium contains a volatile oil, tannin and a bitter principle, perhaps glucosidal (Beshore, *A. J. P.,* 1887). The eclectic preparation *cypripedin* is said to be a resinoid, obtained by precipitating with water a concentrated tincture of the rhizome.

Uses.—Cypripedium appears to be a gentle nervous stimulant or antispasmodic, and has been used for the same purposes as valerian, though less powerful. E. Ives of New Haven, Conn., commends the remedy in *hypochondriasis* and *neuralgia.* It may be used in powder, infusion, or tincture.

Dose, of the powder, fifteen grains (1.0 Gm.), three times a day. The resinoid, obtained by precipitating the tincture, has been given in doses varying from half a grain to three grains (0.032 to 0.20 Gm.).

Off. Prep.—Fluidextractum Cypripedii, *N. F.*

DAMIANA. N. F.

DAMIANA [Turnera]

"Damiana is the dried leaf of *Turnera diffusa* Willdenow et Schultes, or of *Turnera aphrodisiaca* Ward (Fam. *Turneraceæ*). Damiana contains not more than 15 per cent. of its stems, not more than 3 per cent. of other foreign organic matter and yields not more than 4 per cent. of acid-insoluble ash." *N. F.*

The genus *Turnera* is represented by about 85 species of tropical and subtropical American, African, and Madagascar plants that vary in habit from herbs, subshrubs or shrubs. Only one species, *Turnera diffusa* and its variety *aphrodisiaca* yield the drug, *damiana.* Both of these are shrubs indigenous to southern California, Mexico, South America and the West Indies. The commercial supplies of Damiana are imported chiefly from Bolivia and Mexico.

Description and Physical Properties.—"*Unground Damiana.*—Obovate to lanceolate, 10 to 25 mm. long and from 4 to 10 mm. wide, short-petioled, obtuse or acute at the apex, and with a short, cuneate base; sharply 2- to 10-toothed on each side; the veins ascending, generally strong, straight and simple and running to the sinuses of the teeth, but sometimes branched and sending the branches into teeth; the upper surface smooth and light green or yellowish green, the lower glabrous or with a few hairs on the ribs (*Turnera aphrodisiaca*) or densely tomentose over the entire surface (*Turnera diffusa*). Intermixed with the leaves are frequently found some reddish twigs, the young tips and buds of which are grayish with appressed pubescence (*Turnera aphrodisiaca*) or white floccose (*Turnera diffusa*), also flower buds, yellowish flowers, and globose pods. Odor aromatic; taste characteristic, aromatic and resinous.

"*Powdered Damiana.*—Light yellowish green; fragments of epidermal cells and mesophyll of leaf, the cells of the former with somewhat wavy, vertical walls and associated with stomata up to 0.030 mm. long, numerous rough simple hairs, up to 0.900 mm. in length and 0.030 mm. in width at the base, with a narrow lumen usually distinct at the base only and with heavy, mostly non-lignified walls, often curved near the base so that the major portion of the hair lies nearly parallel to the surface of the stem or leaf; fragments of the periderm from the stems composed of somewhat rectangular cells up to about 0.070 mm. in length and about one-third as broad, with square or somewhat pointed ends, with few broadly elliptical stomata about 0.030 mm. long; subepidermal cells from the stem resembling those of the epidermis in shape but with lignified walls; tracheæ, spiral, up to 0.020 mm. wide, or with bordered pores and up to about 0.035 mm. wide; tracheids from stem few; strongly lignified, thick-walled sclerenchyma cells or fibers few; lignified pith-parenchyma with large simple pores; numerous crystals of calcium oxalate in rosettes up to 0.030 mm. in diameter and occasionally in prisms; starch grains few, simple, up to 0.012 mm. in diameter." *N. F.*

Parsons (*A. Pharm.*, 1881, p. 133) obtained 0.2 per cent. of a volatile oil; 8.06 of a soft resin, fixed oil and chlorophyll; 3.46 per cent. of tannin; 7.08 per cent. of a bitter principle; 6.39 per cent. of a hard brown resin; 10 per cent. of extractive; 13.5 per cent. of a gum; 6.15 per cent. of starch, etc.

The leaves of the composite plant *Aplopappus discoideus* DC. (*Bigelovia Veneta* Gray) were, formerly, also sold under the name of damiana and are found occasionally as adulterants in the drug of commerce.

Uses.—Although damiana has achieved some repute in the treatment of sexual *impotence,* it is worthy of note that it is always given in conjunction with strychnine, phosphorus or some other stimulant; it is probably nothing more than a feeble tonic.

Dose, one-half to one drachm (2–4 Gm.) of the leaves, either in the form of infusion or fluidextract.

Off. Prep.—Fluidextractum Damianæ, *N. F.*

DATURÆ FOLIA. Br.

DATURA LEAVES

"Datura Leaves are the dried leaves of Datura fastuosa, *Linn.*, var. alba, *Nees* and also of Datura Metel, *Linn.*" *Br.*

DATURÆ SEMINA. Br.

DATURA SEEDS

"Datura Seeds are the dried seeds of Datura fastuosa, *Linn.*, var. alba, *Nees.*" *Br.*

The genus *Datura* consists of fifteen species, which are distributed throughout the warmer portions of the whole world, the greatest number being found in tropical America. Nearly all of them are used locally in medicine. The plants vary from herbs to shrubs and even trees. The leaves of *Datura Stramonium* L. are official in the U. S. Pharmacopœia. (See *Stramonium.*)

Datura fastuosa L. is an annual herb attaining a height of 4 to 5 feet which is indigenous to India but naturalized in the tropics of both hemispheres. It is characterized by possessing ovate-lanceolate, acuminate, toothed or wavy-margined leaves, trumpet-shaped flowers, up to

7 in. in length and erect; spiny, subglobular, capsular fruits. The var. *alba* Nees has white or nearly white flowers.

Datura Metel L. is another Indian annual herb somewhat resembling *D. fastuosa.* It differs from the latter in possessing entire or only slightly toothed, pubescent leaves and nodding capsules. The flowers are white.

Datura meteloides DC. is a perennial herb in the wild state but an annual as cultivated in temperate regions. It is native to northern Mexico and the southwestern United States and is especially characterized by its slender, forked, glaucous branches, unequally ovate, nearly entire leaves, acute at base and apex, its fragrant white flowers which are suffused with violet, and its succulent, erect and prickly capsules.

Of the varieties of *D. fastuosa,* the British Pharmacopœia recognizes that known as *alba.* From it the Thugs prepared the poison *Dhât* (whence is derived the generic name), which they used to stupefy their victims.

The *leaves* are described as "Brownish or yellowish-green, attaining twenty centimetres in length and thirteen centimetres in breadth; ovate, acuminate, with sinuate-dentate margins and long petioles; often unequal at the base; bearing scattered glandular or simple hairs. Characteristic odor; taste bitter." *Br.*

The trumpet-shaped corolla, together with the stamens, is sometimes found mixed with the leaves. The drug has a slight unpleasant odor, and a bitter taste.

The *seeds* are "yellowish-brown, somewhat wedge-shaped, flattened, with rounded, thickened, furrowed, wavy margins; from four to five millimetres broad and about one millimetre thick. Hilum large, extending from about the middle to the acute end of the seed. Surface finely pitted and reticulated. Endosperm narrow and translucent, enclosing a curved embryo. No odor; taste slightly bitter." *Br.*

Constituents.—The *D. fastuosa* differs chemically from the *D. Stramonium,* which is official in the U. S., in that its dominant alkaloid is scopolamine (Andrews, *Tr. Chem. Soc.,* 1911, xcix, p. 1876), but it also contains traces of hyoscyamine. The proportion of alkaloid in the leaves is usually about 0.12 per cent., and in the seeds approximately double this quantity (Schmidt, *A. Pharm.,* 1906, ccxliv, p. 66). The alkaloids of the *D. Metel* and of the *D. meteloides* are very similar to those of the official species, but Pyman and Reynolds (*Tr. Chem. Soc.,* 1908, xciii, p. 2077 and 1912, ci, 946) have found small amounts of two new alkaloids—*meteloidine* and *nor-hyoscyamine.*

Uses.—While this drug produces effects more or less similar to those of belladonna its precise action has not been clearly determined. It is used in India to a considerable extent as a criminal poison; cases have been reported by Banerja (*Indian Med. Gaz.,* 1885, xx, p. 209) and by Gimlette (*B. M. J.,* 1903, i, p. 1137). In India the *Datura fastuosa* leaves have been used for the same purposes as the stramonium leaves.

Off. Prep.—Tinctura Daturæ Seminum, *Br.*

DECOCTA. U. S.

DECOCTIONS

Tisanes par décoction, Décoctions, *Fr.;* Abkochungen, *G.;* Decotti, *It.;* Cocimiento, *Sp.*

Decoctions are solutions of vegetable principles, obtained by *boiling* the substances containing these principles in water. Vegetable tissues generally yield their water-soluble constituents more readily, and in larger proportion, to water maintained at the point of ebullition, than to the same liquid at a lower temperature. Hence decoction is occasionally preferred to infusion as a mode of extracting the virtues of plants, when the call for the remedy is urgent, and the principles which are to be extracted are not injured by heat. The process should be conducted in a covered vessel. The boiling, moreover, should not, as a rule, be long continued for the same reason. The substance submitted to decoction should if dry be either powdered or well bruised, if fresh should be sliced, so that it may present an extensive surface to the action of the solvent; and previous maceration for some time in water is occasionally useful. Should the physician not happen to prescribe this preliminary preparation, the pharmacist should not omit it.

All vegetable substances are not proper objects for decoction. In many the active principle is volatile at a boiling heat, in others it undergoes some change unfavorable to its activity, and in still others inert matter is too freely extracted, and in the large class of drugs containing resinous principles, water is of very little use in extracting the virtues of the drug. In some of these instances, infusion is preferable to decoction. Besides, by the latter process more matter is often dissolved than the water can retain, so that upon cooling a precipitation takes place and the liquid is rendered turbid, and this constitutes the greatest objection to this class of preparations. When the active principle is thus dissolved is excess, the decoction should always be strained while hot, so that the matter which separates on cooling may be mixed again with the fluid by agitation at the time of administering the remedy. In compound decoctions several of which were vary popular at one time, the ingredients were advantageously added at different periods of the process, according to the length of boiling requisite for extracting their virtues; and, if one of them owed its activity to a volatile principle, the plan followed, at the close of the process, was to pour upon it the boiling decoction of the other ingredients, and allow the liquor to cool in a covered vessel.

As a rule, glass or earthenware vessels should be preferred, as those made of metal are sometimes corroded by the ingredients of the decoction, which thus become contaminated. Vessels of block tin are preferable to those made of copper, brass, or zinc; but iron pots should not be used where astringent vegetable substances are concerned.

Decoctions, on account of the presence of fermentable constituents and the absence of any preservative solvent such as alcohol or glycerin are apt to spoil in a short time. Hence they should be prepared only when wanted for use, and should not be kept, when the weather is warm, for a longer period than forty-eight hours.

The tendency of modern medicine and pharmacy has been decidedly against the employment of decoctions; their nauseous taste, bulky dose, repulsive appearance, and non-permanent character have been powerful reasons for causing their retirement, while the use of tinctures and fluidextracts has largely increased.

There is, at present, no decoction specifically recognized by the U. S. Pharmacopœia, but the following general formula is given:

"Decoctions must be freshly made, and when their strength is not otherwise directed, they are to be prepared by the following general formula: The Drug, coarsely comminuted, 50 Gm.; Water, a sufficient quantity to make 1000 cc. Place the drug in a suitable vessel provided with a cover, pour upon it 1000 cc. of cold water, cover it well, and boil for fifteen minutes. Then allow it to cool to about 40° C., express, strain the expressed liquid, and pass enough cold water through the strainer to make the product measure 1000 cc.

"Caution.—The strength of decoctions of energetic or powerful drugs should be specially directed by the physician." *U. S.*

DECOCTUM ACACIÆ CORTICIS. Br.

DECOCTION OF ACACIA BARK

"Acacia Bark, bruised, 60 *grammes;* Distilled Water sufficient to produce 1000 *millilitres.* Boil the Acacia Bark with twelve hundred *millilitres* of Distilled Water, in a suitable vessel, for ten minutes; strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

This decoction was transferred from the British Addendum (1900) to the British Pharm. (1914). It is used in India as an astringent gargle, lotion, or injection. The *dose* is from four fluidrachms to two fluidounces (15–60 cc.).

DECOCTUM AGROPYRI. Br.

DECOCTION OF COUCH GRASS [Decoction of Triticum]

"Couch Grass, cut small, 50 *grammes;* Distilled Water sufficient to produce 1000 *millilitres.* Boil the Couch Grass with twelve hundred *millilitres* of Distilled Water, in a suitable vessel, for ten minutes; strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

This decoction was transferred from the British Addendum (1900) to the British Pharm. (1914). It is used in *cystitis* and *urinary diseases. Dose,* four fluidrachms to two fluidounces (15–60 cc.).

DECOCTUM GOSSYPII RADICIS CORTICIS. Br.

DECOCTION OF COTTON ROOT BARK

"Cotton Root Bark, bruised, 200 *grammes;* Distilled Water sufficient to produce 1000 *millilitres.* Boil the Cotton Root Bark with two thousand *millilitres* of the Distilled Water, in a suitable vessel, until the volume is reduced to one thousand *millilitres;* strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

This decoction was transferred from the British Addendum (1900) to the British Pharm. (1914). It is used as an emmenagogue and in *uterine hemorrhage. Dose,* from four fluidrachms to two fluidounces (15–60 cc.).

DECOCTUM ALOES COMPOSITUM. Br.

COMPOUND DECOCTION OF ALOES

Tisane (Décocté) d'Aloès composée, *Fr.;* Zusammengesetztes Aloëdecoct, *G.*

"Extract of Aloes, 10 *grammes;* Myrrh, Potassium Carbonate, of each, 5 *grammes;* Extract of Liquorice, 40 *grammes;* Compound Tincture of Cardamoms, 300 *millilitres;* Distilled Water sufficient to produce 1000 *millilitres.* Reduce the Extract of Aloes and the Myrrh to coarse powder, and boil them and the Potassium Carbonate and the Extract of Liquorice with four hundred *millilitres* of Distilled Water in a covered vessel for five minutes; cool; add the Tincture of Cardamoms; set aside for two hours; strain through flannel; pass sufficient Distilled Water through the strainer to produce the required volume." *Br.*

This is essentially the former process of the British Colleges. The effect of the alkaline carbonate is, by combining with the resin of the myrrh and the insoluble portion of the aloes, to render them more soluble in water, while the licorice assists in the suspension of the portion not actually dissolved. The tincture of cardamom is useful not only by its cordial property, but also by adding preservative qualities. This decoction is said not to filter clear when first made, but, if kept for some time, to deposit insoluble matter, and then to become bright and clear on filtering. (*P. J.*, xiv, 491.) J. F. Brown proposes to prepare a concentrated decoction which keeps for a long time unchanged. (*C. D.*, 1896, 425.)

Long boiling impairs the purgative property of aloes, and the same effect is thought to be produced, to a certain extent, by the alkalies, which certainly qualify its operation and render it less apt to irritate the rectum. This decoction, therefore, is milder as a cathartic than aloes itself; it is also more tonic and cordial, from the presence of the myrrh, saffron, and cardamom, and derives antacid properties from the potassium carbonate. It is given as a gentle cathartic, tonic, and emmenagogue, and is especially useful in *dyspepsia, habitual constipation,* and atonic *amenorrhea.* The decoction should not be combined in prescription with acids, acidulous salts, or other bodies incompatible with the alkaline carbonate.

Dose, from one-half to two fluidounces (15–60 cc.).

DECOCTUM HÆMATOXYLI. Br.

DECOCTION OF LOGWOOD

Tisane (Décocté) de Bois de Campêche, *Fr.;* Blauholz Abkochung, *G.*

"Logwood, in chips, 50 *grammes;* Cinnamon Bark, bruised, 10 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Boil the Logwood with twelve hundred *millilitres* of Distilled Water in a suitable vessel for ten minutes, adding the Cinnamon Bark towards the end of the time; strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

We prefer the old U. S. formula, which ordered an ounce of the logwood to be boiled with two pints down to a pint, and doubt whether the wood is exhausted by a boiling of ten or fifteen minutes. The cinnamon of the Br. formula is in general a very suitable addition, but there might be circumstances under which it would be better omitted, and in this case, as in others, any addition to the simple decoction might be left to the judgment of the prescriber.

This is an excellent astringent in *diarrheas* of relaxation.

Dose, from one-half to two fluidounces (15–60 cc.).

DECOCTUM ISPAGHULÆ. Br.

DECOCTION OF ISPAGHULA

"Ispaghula, bruised, 15 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Boil the Ispaghula with twelve hundred *millilitres* of Distilled Water, in a suitable vessel, for ten minutes; strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

This decoction was transferred from the British Addendum (1900) to the British Pharm. (1914). It is used as a demulcent drink in India for *diarrhea.*

Dose, from four fluidrachms to two fluidounces (15–60 cc.).

DECOCTUM SAPPAN. Br.

DECOCTION OF SAPPAN

"Sappan, in chips, 50 *grammes;* Cinnamon Bark, bruised, 10 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Boil the Sappan with twelve hundred *millilitres* of Distilled Water, in a suitable vessel, for ten minutes, adding the Cinnamon Bark towards the end of the time; strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

This decoction was transferred from the British Addendum (1900) to the British Pharm. (1914). It is used like logwood decoction in India as an astringent in *diarrhea* in *doses* of four fluidrachms to two fluidounces (15–60 cc.).

DELPHINIUM. N. F.

LARKSPUR SEED Delphin.

"Larkspur Seed is the dried, ripe seed of *Delphinium Ajacis* Linné (Fam. *Ranunculaceæ*). Larkspur Seed contains not more than 2 per cent. of foreign seeds or other foreign organic matter." *N. F.*

Knight's Spur; Lark's Heel; Lark's Claw; Staggerweed; Flores Calcatrippæ; Rittersporn, *G.;* Dauphinelle, Pied d'Allouette, *Fr.*

Both of the official species of Larkspur are natives of Europe but have become sparingly naturalized in the Middle Atlantic States. They differ from our native species in being annuals instead of perennials having only two petals instead of four and a single pistil. The leaves are divided into narrowly linear segments. The delphiniums are very closely related to the staphisagria, indeed their seeds are often substituted for this. The *D. Consolida* seeds do not appear to be commercially common.

Description and Physical Properties.—"*Unground Larkspur Seed.*—Irregularly tetrahedral, or somewhat triangulate, acute at one end, obtuse or rounded at the other, about 2 mm. in length and equally broad or slightly narrower; surface black or blackish brown, occasionally grayish with from 8 to 12 rows of centrifugally elongated epidermal cells transversely encircling the seed and forming wavy continuous vertical walls or ruffles occasionally intersecting and with narrow channels between; seed-coat crustaceous; endosperm whitish, fleshy and oily; embryo small, in fleshy endosperm. Odor very faint; taste bitter, afterward biting and acrid.

"*Structure.*—Epidermis of non-lignified cells with thick light-yellowish walls some of which extend outwardly forming more or less continuous, ruffle-like projections; several layers of cells containing a dark brown pigment; inner seed-coat composed of non-lignified cells with thick, porous walls; occasionally cells near the micropyle containing a few starch grains; a large endosperm of thick-walled parenchyma, the cells being filled with fixed oil and aleurone grains.

"*Powdered Larkspur Seed.*—Gray-brown. Numerous fragments of endosperm parenchyma filled with fixed oil and aleurone grains, the latter up to 0.012 mm. in length; fragments composed of elongated epidermal cells, the latter up to about 0.045 mm. in diameter and 0.300 mm. in length; groups of elongated cells from the inner layer of seed-coat up to 0.010 mm. in width, with characteristic beaded walls." *N. F.*

Despite the close botanical relation, the toxic principles of delphinium are not the same as those of staphisagria. Indeed the two species recognized by the N. F. differ from each other in their composition. Keller and Volker (*A. Pharm.,* 1913, ccli, 207) have found in the *D. Ajacis* two alkaloids—*ajacine,* $C_{15}H_{24}O_4N$ and *ajaconine,* $C_{17}H_{29}O_2N$. From the *D. Consolida,* Hopkins (*A. J. P.,* 1839) obtained the alkaloid which he called *calcatripine.* Keller (*A. Pharm.,* 1910, ccxlviii, 468) found in this species three alkaloids neither of which was identical with delphinine from staphisagria. For literature on the alkaloids of other species of Delphinium see Miller (*J. A. Ph. A.,* 1923, xii, 492).

Uses.—All of the larkspurs appear toxic and the indigenous *D. exaltum* and *D. azureum* are frequently fatal to sheep and cattle. As far as we know the official species have not been subjected to physiological investigation. One of the bases separated by Keller from *D. Consolida* was found to paralyze the motor nerves like delphinine (see *Staphisagria*). The *D. Consolida* was formerly used for the relief of various spasmodic disorders such as asthma, dysmenorrhea, etc., and was also attributed with diuretic powers. It is, however, at present, almost never employed as an internal remedy, being used only as a local application for the destruction of lice in the hair.

Off. Prep.—Tinctura Delphinii, *N. F.*

DEXTRINUM ALBUM. N. F.

WHITE DEXTRIN Dext. Alb.

"A mixture of soluble carbohydrates, amylodextrin, achroodextrin, erythrodextrin and maltodextrin, together with a variable amount of unconverted starch, obtained by the incomplete hydrolysis of starch by the action of an acid." *N. F.*

Dextrin; Artificial Gum; British Gum; Stärkezucker, *G.;* Dextrine, *Fr.*

The dextrins are a group of carbohydrates which may be regarded as partially hydrolized starch. In their chemical structure as well as their phyisical properties they are closely allied to the gums and mucilages, but do not yield mucic acid by the action of nitric acid. The following stages in the hydrolysis of starch by boiling with dilute acids have been recognized: (1) The starch is converted into soluble starch (some times called *amylodextrin*); this gives a blue reaction with iodine. (2) Maltose is split off leaving behind *erythrodextrin;* this gives a red color with iodine. (3) Maltose is in turn split off from the erythrodextrin forming *achroödextrin;* this gives no reaction with iodine, (4) The last named yields *maltodextrin.* (5) The final stage gives maltose as the result of complete hydrolysis. The chemical formula for the dextrines is homologous to that for starches, namely—$(C_6H_{10}O_5)n$.

Dextrin may be prepared from starch either by a torrefaction process applied to starch which has been moistened with acid and then dried, or in aqueous suspension by the action of acids or of diastase. Commercially it is usually manufactured by the Heuse Process, a torrefaction process which is as follows: One thousand kilos of starch are moistened with 2 kilos of nitric acid diluted with 300 liters of water, the mass is then made into loaves which are dried in the air, ground finely, and heated for about two hours at 100° to 120° C. The powder is then heated in a suitable oven or placed in a circular Uhland apparatus, it is heated with superheated steam, and continually stirred to secure intimate mixture. If the temperature is raised to 130° to 140° C. the duration of heating is shortened, but yellow and not white dextrin is obtained. For further detail, consult *General and Industrial Chemistry,* Molinari.

Description and Physical Properties.—"White Dextrin occurs as a white, glistening, non-hygroscopic, amorphous powder, producing a peculiar and characteristically harsh sensation when rubbed in the hand; odorless and having a sweetish taste. Only partly soluble in cold water, but completely soluble in three parts of water on boiling.

"An aqueous solution prepared in the cold and filtered is colored wine-red by iodine T.S.; an aqueous solution prepared with boiling water is colored blue by iodine T.S. Alkaline cupric tartrate solution is not changed by a solution of White Dextrin in the cold, but is reduced on boiling.

"Separate portions of a freshly prepared, filtered solution in cold water do not become turbid on the addition of calcium chloride T.S., or of calcium hydroxide T.S. (*oxalic acid*). Not more than 5 per cent. of White Dextrin is soluble in boiling alcohol (*dextrose*). Dry White Dextrin at 110° C.: it loses not more than 10 per cent. in weight (*moisture*). Separate portions of a filtered aqueous solution of White Dextrin (1 in 20) are not immediately precipitated by lead acetate T.S., or by basic lead acetate T.S., but upon the addition of a few drops of ammonia water to the mixtures, precipitation occurs (difference from *natural gums*). A solution of White Dextrin does not darken on the addition of hydrogen sulphide T.S. even when supersaturated with ammonia water (*metals*). White Dextrin yields not more than 0.5 per cent. of ash." *N. F.*

Dextrin is used in medicine solely for its pharmaceutical properties, occasionally as an emulsifying agent, more frequently to give consistency to medicinal pastes.

Off. Prep.—Pasta Dextrinata, *N. F.*

DEXTROSUM. U. S.

DEXTROSE Dextros. [d-glucose]

"A sugar [$C_6H_{12}O_6.H_2O$] usually obtained by the hydrolysis of starch." *U. S.*

Anhydrous Glucose; Pure Glucose; Saccharum Amylaceum.

Anhydrous dextrose is prepared from granular hydrated glucose (dextrose), which is produced in a manner similar to that employed for the preparation of syrupy glucose (see *Glucosum*), the conversion being carried to completion and the dextrose crystallized by reducing the temperature, adding previously formed dextrose crystals, and centrifuging the granular crystalline mass which results, to remove dextrin and other impurities. The details are as follows: *Cerealose,* the crude crystalline product obtained by the complete hydrolysis of starch, is mixed in a kneading machine with enough water to enable it to be centrifuged. Washing with cold water in this manner raises the purity to 99 per cent. The partly purified product is then heated with water to make a solution of sp. gr. 63° to 68° Brix, and is filtered through bone black filters at a high temperature (about 80° C.). The syrup is then crystallized for 72 hours without seeding. The crystalline residue is then centrifuged, and washed with cold water and subsequently dried in a hot air drier at 40° to 50° C. to constant weight. In this manner a purity of 99.9 per cent. has been reached and the article contains no bleaching agents or chemicals. (*J. I. E. C.,* 1922, xiv, 217.)

Description and Physical Properties.—"A white, crystalline powder, or white granules. It is odorless, and has a sweet taste. One Gm. of Dextrose is soluble in 1 cc. of water, and in 59 cc. of alcohol, at 25° C. It is more soluble in boiling water and in boiling alcohol.

"An aqueous solution of Dextrose (1 in 20) is neutral to litmus paper and is dextrorotatory. The specific rotation $[a]_D$ of Dextrose determined at 25° C. in an aqueous solution containing in each 100 cc. 10 Gm. of Dextrose, previously dried to constant weight at 100° C., and using a 200 mm. tube, is not less than $+52.5°$ and not more than $+53.0°$. The solution must be allowed to stand twenty-four hours before observing the rotation. Add a few drops of its aqueous solution (1 in 20) to 5 cc. of hot alkaline cupric tartrate T.S.: a copious red precipitate of cuprous oxide is formed (*difference from sucrose*).

"Dextrose loses not more than 10 per cent. when dried to constant weight at 105° C. Ash: not more than 0.1 per cent. One Gm. of finely powdered Dextrose dissolves completely on boiling with 15 cc. of alcohol under a reflux condenser (*dextrin, lactose*). Add 1 drop of iodine T.S. to a solution of 1 Gm. of Dextrose in 10 cc. of distilled water: the liquid is colored yellow (*soluble starch, sulphite*). Its aqueous solution (1 in 20) meets the requirements of the test for *heavy metals.* Dissolve 1.5 Gm. of Dextrose in 5 cc. of distilled water, add 5 cc. of diluted sulphuric acid and 1 cc. of bromine T.S., and heat for five minutes on a water bath. Add 0.5 Gm. of potassium iodide, follow with 5 drops of stannous chloride T.S., cool, and test for *arsenic.* The stain produced, if any, is not greater than that produced in a test made with the same quantitites of reagents and 2 cc. of the standard arsenic solution. Two Gm. portions of Dextrose show no more *chloride* than 0.5 cc. of fiftieth-normal hydrochloric acid, and no more *sulphate* than 0.5 cc. of fiftieth-normal sulphuric acid.

"Preserve in well-closed containers." *U. S.*

It melts at 146° C., and at higher temperatures decomposes with the production of caramel. Nitric acid oxidizes it and forms a number of decomposition products of which *saccharic acid.* $H_2C_6H_8O_8$, is the most important. Saccharic acid is an amorphous, deliquescent solid easily soluble in water and forming salts with metallic bases. Dextrose has strong reducing properties and is estimated quantitatively by means of Fehling's solution.

Uses.—It is generally held by physiologists of to-day that all carbohydrates are converted into dextrose before they are utilized by the body cells. There is reason to believe that increasing the amount of this sugar in the blood, thereby offering to the working muscle readily-oxidizable, energy-yielding form of carbon, not only increases its immediate efficiency but lessens the call upon the fuel stored up with it. It is to this mechanism and the rapidity of its absorption that sugar owes its power of banishing the sense of fatigue from muscular exertion. Thus Dixon (*J. P.,* 1907, xxxv, p. 346) has found that the injection of glucose into the blood stream may cause an immediate increase in the force of the cardiac contractions presumably by furnishing an easily oxidizable food.

Kleiner (*J. Ex. M.,* April, 1916) has found that after the intravenous injection of large amounts of dextrose in dogs, the blood sugar returns to its normal quantity within 1½ hours. Of the excess dextrose introduced, the major part is eliminated through the kidneys but about 40 per cent. escapes from the blood vessels, by the process of dialysis, into the surrounding tissues and a small amount is destroyed by increased oxidation. It has long been known that in conditions where there is an inability to oxidize blood sugar, as in diabetes mellitus, there is a tendency towards the diminution of the alkalinity of the blood; a condition known commonly although inaccurately as acidosis. There is strong evidence that a similar disturbance occurs when there is a deficiency in the food supply, especially of the carbohydrate foods. Conversely flooding the system with excess of sugar in cases of acidosis, even when the result of diabetes, will usually—at least temporarily—ameliorate this condition.

Chemically pure dextrose has been introduced into medicine in order to provide a form of sugar suitable for intravenous administration.

Buedingen (*D. A. K. M.*, 1914, cxiv, 534), Pfalz (*D. M. W.*, 1919, xlv, 1181) and others have injected intravenously a dextrose solution, isotonic with the blood, in the treatment of *heart disease* with asserted benefit. Litchfield (*J. A. M. A.*, 1918, lxxi, 503) introduced the use of dextrose intravenously in the treatment of *pneumonia.* In his earlier cases he employed an isotonic solution, but later much more concentrated solution, as high as 25 per cent. Of this solution 250 cc. (8½ fluidounces) is injected very slowly into the vein so that upwards of an hour is required for the complete dose. This method has been followed, more or less modified in details, by John (*A. J. M. S.*, 1920, clx, 542) and others with apparently satisfactory results. Fisher and Snell (*J. A. M. A.*, 1924, lxxxiii, p. 1906) report prompt relief of the symptoms of surgical *shock* by the conjoint administration intravenously of dextrose and insulin. They used 1000 cc. of a 10 per cent. solution of glucose, with a simultaneous administration of 30 units of U-20 insulin. Titus and Givens (*J. A. M. A.*, 1922, lxxviii, 92) employed glucose intravenously in pernicious *vomiting of pregnancy* and also in *eclampsia,* on the theory that these toxemias were due to a carbohydrate deficiency; they report an immediate clinical improvement in individual patients and a general lowering of the mortality rate.

For intravenous use it is essential that the dextrose shall be of the highest purity. Titus and Givens find that even with the best quality of dextrose it is advisable to filter the solutions because of the presence of dust particles. It is, of course, also essential that the solutions should be completely sterilized, which may be accomplished by heating in the autoclave, under 15 pounds' pressure, for 30 minutes. In a number of cases unpleasant symptoms have been caused apparently from the acidity of the solution. Williams and Swett (*J. A. M. A.*, 1922, lxxviii, 1024) find that heating solutions of glucose increases the hydrogen ion concentration —that is the acidity—and recommend, for the purpose of counteracting this, the addition of a " buffer " salt composed of a mixture of monopotassium and dipotassium phosphate. The solutions of dextrose employed have ranged in concentration from 5.1 per cent., which is isotonic with the blood, up to 25 per cent. The solutions may be made directly in distilled water, the addition of sodium chloride being unnecessary with these concentrations.

DIAMORPHINÆ HYDROCHLORIDUM. Br.

DIAMORPHINE HYDROCHLORIDE

" Diamorphine Hydrochloride, $C_{21}H_{23}NO_5$,-HCl,H_2O, is the hydrochloride of an alkaloid obtainable by the action of acetic anhydride on morphine." *Br.*

Diacetylmorphinæ Hydrochloridum, *U. S. IX; Hydrochloridum, Br.;* Diacetylmorphine Hydrochloride; Heroin Hydrochloride; Diacetylmorphinum Hydrochloridum, *P.G.*

Because of a Federal law forbidding its importation or manufacture in this country, this alkaloid has been dropped from the U. S. Pharmacopœia. It was introduced under the trade-name of *Heroin.* It is made by treating morphine with acetyl chloride, washing the product with a dilute alkaline solution and crystallizing from alcoholic solution. The base, diamorphine, is " a white, crystalline powder without odor. One Gm. of Diacetylmorphine dissolves in about 1700 cc. of water, 31 cc. of alcohol, 1.4 cc. of chloroform, and in 100 cc. of ether at 25° C. Its saturated alcoholic solution is alkaline to moistened litmus paper. It melts between 171.5° and 173.5° C. Dissolve about 0.01 Gm. of Diacetylmorphine in a few drops of nitric acid; a yellow color is produced, which gradually changes to greenish-blue. Heat about 0.1 Gm. of Diacetyl-morphine with 1 cc. of alcohol and 1 cc. of sulphuric acid; ethyl acetate is produced, recognizable by its odor." *U. S. VIII.*

For further details of the properties of this base see *U. S. D.*, 20th ed., p. 401.

The hydrochloride is a " white, crystalline powder; taste bitter. Melting point from 231° to 232° C. Soluble in 3 parts of *water* and in 11 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of chlorides. 0.1 gramme dissolved in 2 millilitres of *alcohol* (90 per cent.), mixed with 1 millilitre of *sulphuric acid* and warmed, develops an odor of acetic ether. A solution of 0.1 gramme in 1 millilitre of *sulphuric acid* heated on a water bath, cooled and diluted with 6 millilitres of *water,* gives a deep blue color on the addition of an aqueous solution (0.5 in 100) of *potassium ferricyanide* to which 1 drop of *T. Sol. of ferric chloride* has been added. Treated with a few drops of *nitric acid* a yellow color is produced, which changes to greenish-blue on warming, and finally becomes yellow again. 0.02 gramme added to 5 millilitres of an aqueous solution (0.5 in 100) of *potassium ferricyanide,* to which 1 drop of *T. Sol. of ferric chloride* has been added, produces a greenish color and not a deep blue (absence of morphine)." *Br.*

A method for the rapid determination of small quantities of heroin or its salts, especially adapted for revenue officers who are required to give testimony concerning seizures under the Harrison Narcotic Act, was devised by Reginald Miller and is described in *A. J. P.*, 1915, p. 248. It is a colorimetric method, using the formaldehyde sulphuric acid reagent. Duran (*J. A. Ph. A.*, 1916, p. 163) makes use of the insolubility of morphine in carbon tetrachloride to separate the two bases.

Uses.—In its general physiological action diamorphine acts much like morphine except that, according to Ott, it is depressant to the spinal cord. It is, however, about twice as powerful in its depressant action upon the respiratory center. For this reason it is greatly inferior to morphine as an analgesic. Its most important use in medicine is as a sedative to the respiratory center; thus it is employed to allay *cough* whether due to *bronchitis* or of nervous origin, to relax the *asthmatic* paroxysm, in *whooping cough, cardiac dyspnea,* and similar conditions. According to Impens (*A. G. P.*, 1899, lxviii, p. 527), although actually more poisonous to the respiratory center, it is relatively safer than morphine as disproportionally smaller quantities are needed to exercise therapeutic sedation.

Diamorphine has been employed by physicians in cases in which formation of the drug habit is feared but it is fully as dangerous a drug in this regard as morphine itself, indeed, the heroin habit is apparently the more rebellious addition of the two. Cases of acute poisoning are not very numerous but Trawick (*Kentucky Med. Journ.*, 1911) reports a case, following a dose of one-half a grain, with serious symptoms of the opium type—marked slowing of the respiration, and contracted pupils. In some cases there is also a semi-delirious condition somewhat resembling that seen in scopolamine poisoning.

Dose, one-sixteenth to one-sixth of a grain (0.004–0.01 Gm.).

DICHLORAMINA. U. S.

DICHLORAMINE Dichloram. [Paratoluenesulphondichloramide, Dichloramine-T]

" Dichloramine [$C_6H_4(CH_3)(SO_2NCl_2)$] contains not less than 28 per cent. and not more than 30 per cent. of active chlorine." *U. S.*

This is the acid of which chloramine is the sodium salt. It differs from its sodium salt in that it is soluble in certain organic bases, notably, eucalyptol and liquid petrolatum, although insoluble in water.

When perfectly pure, dichloramine keeps unchanged but commercial varieties decompose with a rapidity in proportion to the amounts of impurities present, solutions in chlorcosane show a noticeable diminution in strength within a month. Sollmann (*J. A. M. A.*, 1919, lxxii, 992) determined the rate of destruction of dichloramine by various forms of petrolatum. With liquid petrolatum from 25 to 50 per cent. of the dichloramine was decomposed in one day and 71 per cent. decomposed in two months. With various ointment petrolatums from 80 to 95 per cent. was decomposed in one day. With chlorcosane the loss in strength was about 10 per cent. in one day and about 25 per cent. in one week. The destruction by these ointments was practically the same for the white as for the yellow. Kerosene and olive oil decomposed dichloramine with extraordinary rapidity. Solutions in carbon tetrachloride were practically stable for a week and at the end of two months showed loss of only 21 per cent.

It is prepared by the following method: Chlorinated lime (from 350 to 400 Gm.) of good quality is shaken with 2 liters of water on a shaker for half an hour, and then the mixture allowed to settle. The supernatant fluid is siphoned off and the remainder filtered. Powdered toluene-parasulphonamid, 75 Gm. (the crude product may be used), is then added to the hypochlorite solution and shaken till dissolved. The mixture is filtered, if necessary, placed in a large separating funnel, and acidified by the gradual addition of acetic acid. The mixture is then extracted with chloroform; the chloroform solution, after drying over calcium chloride and filtration, is allowed to evaporate in the air. The residue is usually sufficiently pure without recrystallization.

Description and Physical Properties.—" Pale yellow crystals or a yellowish crystalline powder, having an odor of chlorine. It gradually decomposes on exposure to air, losing chlorine. Dichloramine is almost insoluble in water. It is soluble in eucalyptol and in chlorinated paraffin hydrocarbons, also in glacial acetic acid. One Gm. is soluble in about 1 cc. of benzene or chloroform and in about 2.5 cc. of carbon tetrachloride. It is decomposed by alcohol.

" Dichloramine melts at about 80° C. Add about 0.1 Gm. of Dichloramine to 5 cc. of an aqueous solution of sodium bromide (1 in 10): bromine is liberated (*difference from chloramine*). Strong mineral acids added to Dichloramine liberate chlorine. One Gm. of Dichloramine dissolves completely in 5 cc. of chloroform. Add 1 cc. of sulphuric acid to 0.1 Gm. of Dichloramine: chlorine is evolved but no appreciable darkening occurs (*readily carbonizable substances*).

"**Assay.**—Dissolve about 0.1 Gm. of Dichloramine, accurately weighed, in 20 cc. of glacial acetic acid, in a dry, glass-stoppered bottle. Add 10 cc. of potassium iodide T.S. and 50 cc. of distilled water, allow the mixture to stand for ten minutes, and titrate the liberated iodine with tenth-normal sodium thiosulphate. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.001773 Gm. of active chlorine.

" Preserve in well-closed containers, protected from light." *U. S.*

Uses.—Dichloramine, like its near relation chloramine, is a powerful germicide. McMaster (*J. Inf. D.*, 1919, xxiv, 378) finds that the oily solution will destroy *Bacillus typhosus* in strength of five parts in 10,000, which makes it about eight times as strong as phenol when tested by the same method.

As dichloramine is practically insoluble in water, it is usually employed in the form of a solution in eucalyptol diluted with liquid petrolatum. Ordinary petrolatum has such an affinity for chlorine as to decompose the dichloramine, so that it is necessary that the solvent be saturated with this element and the Pharmacopœia therefore recognizes a chlorinated paraffine as a solvent (see *Paraffinum Chlorinatum*).

Dichloramine is used as a disinfectant. Sweet (*J. A. M. A.*, 1917, lxix, 1076) reported from a large hospital experience during the World War, that in infected *wounds* it not only gave as good surgical results as any method of treatment, but was of great practical value because of its ease of application and economy of dressing material and that it is much less irritating to the surrounding healthy skin than other disinfectants. It has also been used as an antiseptic application to the mucous membranes of the nose and throat and even of the eye. As a surgical disinfectant it may be employed in strengths of from 2 to 10 per cent. As an application to the mucous membranes from 0.5 to 2 per cent.

Horan (*Illinois M. J.*, 1921, xl, 123) finds dichloramine dressings of great value in *burns* because the oily solvent makes the changing of dressings painless while they are actively antiseptic. Dakin and Dunham (*B. M. J.*, May 20, 1917) have introduced also, under the name of *Halazone,* the para-sulphone dichloramide-benzoic acid, which is intended for the sterilization of drinking water.

DIGITALIS. U. S. (Br.)

DIGITALIS Digit. [Foxglove, Digitalis Folium P. I.]

"Digitalis is the dried leaf of *Digitalis purpurea* Linné (Fam. *Scrophulariaceæ*). Digitalis, in the form of the tincture, properly diluted and injected into the ventral lymph sac of a frog, has a mimimum systolic dose (the minimum dose producing in one hour a stoppage of the ventricle of the heart in systole) not exceeding 0.006 cc. of tincture, equivalent to 0.00,000,05 Gm. of ouabain, for each gram of body weight of frog. It contains not more than 2 per cent. of browned leaves, stems, flowers, or foreign organic matter, and yields not more than 5 per cent. of acid-insoluble ash." *U. S.*

"Digitalis Leaves are the dried leaves of Digitalis purpurea, *Linn.*, collected from plants commencing to flower, thoroughly dried at a low temperature, and kept dry in well-filled air-tight containers. When powdered no portion should be rejected." *Br.*

Digitalis Folia, *Br.*, Digitalis Leaf; Digitalis Leaves, Foxglove Leaves; Fairy Cap, Fingers, Thimbles, or Bells, Lady's Glove, Purple Foxglove, Flop-dock, Throatwort, Cottagers; Digitale, *Fr. Cod.;* Feuilles de Digitale Pourprée (de grande Digitale), Digitale Pourprée, Doigtier, *Fr.;* Folia Digitalis, *P. G.;* Purpurrother Fingerhut, Fingerhutkraut, Fingerhutblätter, *G.;* Digitale, *It.;* Digital (Hoja de), Dedalera, *Sp.*

The common foxglove, *Digitalis purpurea,* is a biennial or occasionally perennial plant, native to Europe, but now widely cultivated both for medicinal and ornamental purposes in the United States and other parts of the world. It has become naturalized in several sections of the United States, particularly in Washington, Oregon and New York.

The underground portion of the plant consists of a fibrous root system which, during the first year, sends forth a rosette of long stalked, ovate to ovate-lanceolate, radical leaves. During the second summer, a single, erect downy and leafy stem arises from the center of a leaf rosette to the height of 1 to 1.5 meters and terminates in an elongated raceme of large, purple, tubular-campanulate flowers. The lower leaves are ovate to ovate-lanceolate, pointed, about eight inches in length and three in breadth, and stand upon short, winged petioles; the upper are alternate, sparse, and lanceolate; both are irregularly crenate to dentate, and have wrinkled pubescent surfaces, of which the upper is a fine deep green, the under paler and more downy. The flowers are numerous, and attached to the upper part of the stem by short pedicels, in such a manner as generally to hang down upon one side. At the base of each pedicel is a floral leaf, which is sessile, ovate, and pointed. The calyx is divided into five segments, of which the uppermost is narrower than the others. The corolla is gamopetalous, tubular-bell-form, swelling on the lower side, irregularly divided at the margin into short obtuse lobes, and in shape and size not unlike the end of the finger of a glove, a circumstance which has suggested most of the names by which the plant is designated in different languages. Its mouth is guarded by long soft hairs. Externally, it is in general of a bright purple; internally, it is sprinkled with dark spots upon a white ground. There are four didynamous stamens whose filaments are white, curved, and surmounted by large yellow anthers. The style is simple, and supports a bifid stigma. The seeds are numerous, very small, grayish-brown, and contained in a pyramidal two-celled capsule.

Several varieties of *Digitalis purpurea* have occurred in cultivation, the leaves of which have been commonly collected with those of the pure species as a source of the drug of commerce. The var. *gloxinæflora* Hart. has longer racemes with larger and more spotted flowers; the var. *alba* Hart. possesses white flowers; the var. *campanulata* Hart. is a large form whose upper flowers are united into a large bell-shaped bloom; the var. *monstrosa* is a double peloric form. All of the species of the genus *Digitalis* seem to have similar effects upon the system. Miller and Baker (*J. A. Ph. A.*, March, 1914) examined 23 different species or varieties of *Digitalis* and found one or two, indeed, surpassed the *D. purpurea* in power.

The leaves of the *D. Thapsi* L. have appeared commercially under the name of *Spanish Digitalis.* Guerin states that these have practically no simple hairs and that the glandular hairs are averagely longer stalked than those of *D. purpurea.* For further details see *C. D.,* 1919, p. 1151.

Foxglove grows wild in the temperate parts of Europe, where it flowers in the middle of summer. In this country it is cultivated both for ornamental and for medicinal use. (For methods of cultivation in the United States, see Newcomb, *A. J. P.,* 1911, p. 529; Borneman, *A. J. P.,* 1912, p. 547; Miller, *A. J. P.,* 1913, p. 297.) The leaves are the part generally employed. The U. S. Pharmacopœia IX departed from the ancient requirement, and in our opinion properly so, that digitalis should be collected only in the second year. Modern investigators, such as Sharp (*P. J.*, lxxxix, 131), Miller and Baker (*J. A. Ph. A.*, 1913, ii, 198), and Carr (*A. J. P.*, 1913, lxxxv, 297) are unanimous that the first year's leaves are fully as powerful as those collected just before flowering. Hale (*Proc. A. Ph. A.*, 1910, 294), as well as Miller and Baker, finds that there is no difference between the wild and cultivated plants; indeed, the latter say, even if grown in hot houses. Likewise the formerly accepted view that digitalis leaves deteriorate rapidly has been shown to be erroneous. If properly dried, the loss of strength is practically negligible during a year's storage (Haskell and Miller, *J. A. Ph. A.*, 1914, iii, 306) and probably for several years (Pick and Wasicky, *C. D.*, 1917, lxxxix, 320); the last named authors have shown that when improperly stored the loss of potency may be quite considerable. Various methods of drying the leaves have been recommended. Joachimglu (*Ph. Wb.*, 1920, lvii, 799) recommends drying at a temperature of 60° C., while Haskell and Miller state that any temperature below 120° C. is not injurious. Pick and Wasicky recommend that the air of the container be kept dry by the use of burnt lime. Straub (*D. M. W.*, 1921, xlviii, 791) finds that, of the three chief principles of digitalis, digitalein is the most readily decomposed, digitoxin the least, and gitalin stands midway between.

The seeds contain more of the active principle than the leaves, are less likely to suffer in drying, and keep better, but are nevertheless little used. So far as the relative strength of these two parts can be determined from that of their alcoholic extracts, it would appear, from the experiments of Hirtz, that the seeds are ten times stronger than the leaves. (See *A. J. P.*, xxxiii.)

The commercial supplies of digitalis used in the United States are obtained chiefly from plants grown in Germany and the U. S. A.

Fresh digitalis leaves are without odor but acquire a characteristic odor when dried and rubbed in the hollow of the hand. The color of the dried leaf is a dull pale green, modified by the whitish down upon the under surface; that of the powder is a fine deep green.

Description and Physical Properties.—"*Unground Digitalis.*—More or less crumpled or broken; blades ovate to ovate-lanceolate, about 25 cm. in length and contracted into a winged petiole; margin crenate or irregular; thin, lower surface densely pubescent, upper surface wrinkled, finely hairy; venation conspicuously reticulate, the midrib and principal veins broad and flat and the lower veins continued into the wings of the petiole; color of upper surface dark green, of lower surface grayish from the dense tomentose pubescence, the larger veins often purplish; odor slight when dry, peculiar and characteristic when moistened; taste very bitter.

"*Structure.*—Upper epidermis with slightly wavy vertical walls, no stomata, and numerous hairs; lower epidermis with wavy, vertical walls, numerous oval stomata and many hairs and not attached over irregular areas to the cell layer within, especially near the veins; chlorenchyma of a single layer of short palisade cells and several layers of spongy parenchyma, vascular bundles of larger veins and petiole, numerous, separated by medullary rays 1-cell wide.

"*Powdered Digitalis.*—Dark green; numerous irregular fragments of epidermis; non-glandular hairs frequently curved or crooked, up to 0.5 mm. in length, uniseriate, 2 to 8 cells, some of the cells collapsed so that the planes of adjoining cells may be at right angles, the terminal cell pointed; glandular hairs few, small, usually with a 1- or 2-celled stalk and a 1- or 2-celled head; fragments of veins and petioles with tracheæ annular, reticulate or spiral or with simple pores; calcium oxalate absent.

"**Assay.**—Prepare a tincture according to the official process and proceed as directed under *Tinctura Digitalis.*

"Preserve Digitalis, thoroughly dried, in airtight containers." *U. S.*

The British Pharmacopœia description is as follows: "Hairs of two kinds, either simple, mostly 3–5 celled and bluntly pointed, or glandular and consisting of a short pedicel bearing a unicellular or bicellular gland. In transverse section, no sclerenchymatous cells or fibers, and no crystals of calcium oxalate. In the powdered Laves, groups of epidermal cells with more or less sinuous walls, numerous fragments of multicellular hairs with thin, granular walls; but no sclerenchymatous cells or fibers, of crystals of calcium oxalate. No marked odor; taste very bitter." *Br.*

For a comprehensive description of the morphology and anatomy of the leaves of *Digitalis purpurea* and the adulterants of this drug, see Bohny's article in *Bot. Centralbl.*, 1906, p. 267. Collin reviews the pharmacognosy of Digitalis (*J. P. C.*, 1905, p. 56), showing the characteristics of the powder and the detection of the principal leaf adulterants, such as *Inula Conyza, Verbascum phlomoides, Artanthe elongata,* and *Salvia Sclarea.* Kraemer (*A. J. P.*, 1912, p. 35) discusses the morphology of digitalis leaves and shows the variation and the forms of hairs in different commercial specimens. Youngken (*J. A. Ph. A.*, 1919, p. 923) investigated the structure and pharmacodynamics of *D. Sibirica.* He found that a 10 per cent. tincture of the leaves of this Siberian herb was about 75 per cent. stronger in the physiologic effects than the U. S. P. tincture of digitalis. The chief adulterants for digitalis in recent years have been the leaves of Mullein species which may be readily detected as an admixture even in small quantities, by their candelabra-shaped trichomes and velvety texture.

Constituents.—Despite an enormous amount of labor, the chemical problems in connection with digitalis are not completely solved. While the statement made below concerning the active constituents of this drug may be revised by future investigations, we believe that it fairly represents the conclusions of the most recent and competent investigations.

It should be remarked in the first place that the term digitalin has been applied to at least four distinct substances and therefore, unless qualified, is meaningless. *Homolle's digitalin* (*French digitalin*) is an amorphous powder, probably an impure form of Kiliani's digitalin. *Nativelle's digitalin* (*digitaline cristallisée*) is apparently an impure form of the substance now known as digitoxin. *Merck's digitalin* (*German digitalin*) is a concentrated extract from the seeds; it is a yellowish-white amorphous powder soluble in either water or alcohol and contains over 50 per cent. of digitonin with 5 to 6 per cent. of Kiliani's digitalin as well as other glucosides.

The most important researches upon the chemistry of digitalis are those of Schmiedeberg (*A. E. P. P.*, 1874, iii, 19; 1882, xvi, 149), Kiliani (*A. Pharm.*, 1895, 1899; 1914, cclii), Keller (*P. J.*, July 24, 1897), Kraft (*S. W. P.*, 1911, xlix), Berry (*P. J.*, 1915, xcv, 783) and McGill (*J. Am. C. S.*, 1920, xlii, 1893).

Digitalis contains a number of glucosides; these may be divided into two groups, those that possess the characteristic physiological properties of the drug, and those whose action places them among the saponins. Of the first group there are three whose identity appears to be satisfactorily established: *digitoxin, digitalin Kiliani,* and *gitalin.* The status of *digitophyllin* is not yet settled. The saponin glucosides which do not act upon the heart include *digitonin, digitoflavone* (*luteolin*) and perhaps *gitonin.*

For account of clinical applications of various principles see under *Uses.*

DIGITONIN forms fully one-half of the mixed glucosides from the digitalis seed and the principal portion of "German digitalin," from which it may be prepared by extraction with and crystallization from 85 per cent. alcohol. Digitonin softens at 225° C., and melts completely at 235° C. The crystals dissolve sparingly in cold water, more readily in hot, to an opalescent solution which froths on agitation. It cannot be crystallized from water. The aqueous solution is lævorotatory ($[a]_D = -49$ at 25° C., and is precipitated by tannin, ammoniacal lead acetate, and baryta water. Digitonin is only slightly soluble in absolute alcohol, and still less so in ether, chloroform, or petroleum benzin. It forms a crystalline compound with amyl alcohol. According to Kiliani, digitonin has the formula $C_{27}H_{46}O_{14} + 5H_2O$, and when boiled with strong alcohol and hydrochloric acid splits up into dextrose, galactose, and *digitogenin,* the last body separating in warty masses on cooling. Digitonin does not possess the characteristic physiological properties of digitalis; its action is similar to that of the saponins.

Kraft believes that there are two substances which have been described under the name of digitonin and suggests that one of these be called *digitsaponin.* The substance described by Schmiedeberg under the name of *digitin* is probably an impure form of digitonin.

DIGITOXIN is characterized by its free solubility in alcohol and chloroform, slight solubility in ether, and insolubility in petroleum benzin. It crystallizes from alcohol in pearly scales or needles which melt at 240° C. It is quite insoluble in water, to which it does not impart even a bitter taste. Warmed with strong hydrochloric acid, it gives a yellow or greenish coloration. Schmiedeberg states that it is not a glucoside, but Kiliani asserts that upon heating its alcoholic solution with hydrochloric acid it splits up into *digitoxigenin* and a sugar, *digitoxose.* The reaction for this is now considered to be:

$$C_{34}H_{54}O_{11} + H_2O = C_{22}H_{32}O_4 + C_6H_{12}O_4$$

Digitoxin is found mainly in the leaves (Kiliani stating that it is not found in the seeds at all), but Keller (*P. J.*, July 24, 1897) finds it also in the seeds in smaller amount. It is the most poisonous of the constituents of digitalis so far isolated.

DIGITALIN (*Digitalinum verum* of Kiliani) forms a white amorphous powder or soft white grains which remain unchanged when heated to 200° C., at 210° C. begin to aggregate, and towards 217° C. melt, becoming yellow. When treated with water the particles of digitalin swell up and dissolve slightly, giving a solution which foams strongly on agitation. It is dissolved sparingly (1 to 100) by cold proof spirit, but in considerable amount by hot rectified spirit or absolute alcohol. When a minimum of alcohol is used, the solution on cooling becomes almost solid from the separation of a thick magma of granules, which are, however, destitute of crystalline structure. This peculiar behavior affords a valuable means of testing its purity, as only a small percentage of the other glucosides with the digitalin prevents the formation of the granules. The minutest admixture of amorphous glucosides also rapidly causes an intense yellow coloration. Digitalin is very sparingly soluble in ether or chloroform. When digitalin is heated with diluted hydrochloric acid, an insoluble resinous substance almost immediately separates out; Schmiedeberg termed this *digitaliresin.* By operating in alcoholic solution, Kiliani avoids the separation of resin, and finds that digitalin splits up as a glucoside into *digitaligenin, glucose,* and *digitalose,* thus:

$$C_{29}H_{46}O_{12} + H_2O = C_{16}H_{22}O_2 + C_6H_{12}O_6 + C_7H_{14}O_5$$

Kiliani found that commercial *digitalinum purum* contained but 5.5 per cent. of true digitalin.

GITALIN has been described by Kraft (*S. W. P.*, 1911, xlix) as an amorphous white powder soluble in 600 parts of water. It can be obtained also as a crystalline hydrate. *Digitalein* of Schmeideberg is regarded by Kraft as an impure gitalin. Kiliani doubts the chemical individuality of gitalin. There is on the market a substance called *verodigen* which is asserted to be gitalin.

Digitalis contains, besides active principles, a volatile oil, a fatty matter, a red coloring substance analogous to extractive, chlorophyll, albumen, starch, sugar, gum, lignin, and salts of potassium and lime, among which, according to Rein and Haase, is acid potassium oxalate. Morin, of Geneva, discovered in the leaves two acids: one fixed, called *digitalic acid,* the other volatile and resembling valerianic acid, which he proposed to name *antirrhinic acid* (*P. J.,* vii, 294). England (*A. J. P.,* 1892, 361) found about 5 per cent. of fixed oil in digitalis leaves. Morries obtained a narcotic empyreumatic oil by the destructive distillation of the leaves. The yield of ash from digitalis leaves is usually put down at from 7 to 10 per cent., and this is in accord with the result reached by F. H. Alcot with British leaves. (*P. J.,* Jan., 1903.) On the other hand, M. Greshoff (*P. J.,* Dec., 1902) has obtained in various samples of German digitalis, after the leaves have been freed from sand and the leaf-stalks removed, a yield of from 16.4 to 25 per cent. of ash.

Assay.—The three animals most commonly used as reagents for the biological standardization of digitalis are the frog, the guinea-pig, and the cat. Although a number of writers had employed physiological tests to determine the relative potency of different digitalis bodies, the first to use the biological assay in a systematic manner was Houghton, who used what is now known as the "twelve hour frog method."

The U. S. P. IX gave an optional biological standard for digitalis based upon the so-called one hour frog method. The same test has been made compulsory in the U. S. X (for official description see under *Tinctura Digitalis*). In the second part of the U. S. P. IX this method was described somewhat more in detail than it is in the present Pharmacopœia. As this description contains much that is of practical interest, it is here repeated: "For the members of the digitalis series the so-called 'one hour frog' method is recommended. This method consists essentially in ascertaining the dose of a drug or preparation which will bring the heart of a standard sized frog to systolic standstill in one hour's time. The method is carried out as described below; all measurements being performed with the same degree of accuracy used in ordinary quantitative chemical estimations.

"*Frogs.*—The frogs to be employed in an assay should be in a healthy condition and of the same species. Those most commonly obtainable in this country are the common grass frogs (*Rana viridis* or *Rana pipiens*). While the dose for a frog is estimated according to its weight, it is best to use frogs of a fairly uniform size, the most convenient weight for such work being between 15 and 25 Gm.

"*Storage.*—Before use the frogs should be stored in tanks kept in a cool room, preferably where the temperature does not rise above 15° C. The bottom of the tanks should be covered with running water or, if running water is not convenient, standing water may be used if it is changed from two to four times daily. An hour before the frogs are to be used for an assay a sufficient number should be taken to the operating room, each one carefully weighed to within 0.1 Gm. [0.5 Gm. *U. S. X*] and placed in an individual wire cage or container, these are then placed in a tank containing water to the depth of about 1 cm. (½ inch), which is kept during the process of assay at a uniform temperature of 20° C. The maintaining of a uniform temperature at which all assays of the members of this group should be carried out is important, as the susceptibility of frogs differs very considerably at different temperatures.

"*Dosage.*—After the frogs have been weighed as described, the doses to be given are calculated according to their weights and are measured into small conical glasses by means of a finely graduated pipette. The doses of the preparation which are to be injected should be as uniform in quantity as possible and should not exceed 0.015 mil for each gramme of body weight of frog. The members of the digitalis series may be assayed in either fluidextract or tincture strength, being diluted with water as may be necessary to get the volume dose. In case the alcohol content in any preparation after dilution is higher than 20 per cent., the preparation may be subject to careful evaporation and subsequent dilution with an aqueous solution containing 0.7 per cent. of sodium chloride until the original volume is restored and the alcohol content is not above the per cent. named. It is always best to have the alcohol content of different preparations uniform. In case there is a precipitate the preparation to be assayed should be shaken each time a dose is measured out. When the doses are ready, they may be injected into the anterior lymph sac of the animal. This is done by means of a glass pipette which is drawn out to a fine point [the so-called 'tuberculin' hypodermic syringe, which is graduated in 0.01 cc., is more convenient]. The frog is held on its back in one hand and the pipette with the contained drug in the other, the mouth of the frog is opened with the point of the pipette and, carefully avoiding the tongue, the floor of the mouth is punctured and the point of the pipette is then seen to enter the anterior lymph sac of the frog. The contents of the pipette are now forced into the sac either by gravity or by gently blowing, if necessary. In the latter case, care should be taken not to introduce air into the sac. Care should also be taken not to puncture the skin. The animal is then replaced in its cage in the tank, the temperature of which is maintained as stated at 20° C. At the end of one hour from the time of injection each frog is pithed, both brain and cord, the heart is exposed and its condition examined. For the correct end reaction the ventricle should be in systolic standstill while the auricles should be widely dilated. Following mechanical stimulation feeble contractions may be allowed in the auricles and localized contractions in the ventricle, but no general contraction is allowable. If when the heart of an animal is being exposed for examination, remains of the injected drug are found in the lymph sac unabsorbed, such an animal should be discarded and not considered in the results obtained. It happens sometimes that one frog out of a large series may prove a decided exception to the others in the way of increased or decreased susceptibility to the drug. Such an animal should also be discarded. After the primary or trial assay has been carried out and the approximate strength of the preparation ascertained, a second series of frogs is injected in like manner, using doses the limits of which are considerably narrower than the first series. A third or even fourth series of injections may be necessary to confirm the earlier results. The dose thus found is then compared with the dose of a standard which is similarly ascertained upon another series of frogs of the same lot. From such a comparison the strength of the unknown preparation can be suitably adjusted. The use of a standard is made necessary by the fact that frogs differ in their susceptibility to the members of the digitalis series at different seasons of the year. The condition of susceptibility is ascertained and allowed for by the use of a solution of ouabain (see Part III) as a standard which in appropriate doses is injected into a series of frogs and their resistance thus determined." *U. S. IX.* The necessary strength of an unknown preparation may be calculated from the dose actually found by the ratio of the standard dose of ouabain to the dose of ouabain found necessary to kill. Thus:

"Standard dose of ouabain : Found dose of ouabain :: Standard dose of drug being assayed : Necessary dose of unknown.

"The standard dose of ouabain is 0.0000005 Gm. per gramme of body weight of frog. The standard dose of Tincture of Digitalis to correspond is 0.006 mil per gramme of body weight of frog. If, therefore, in a certain series of frogs the resistance to ouabain is found to be increased so that a dose of 0.00000075 Gm. is necessary to stop the heart in systole in one hour, the dose of Tincture of Digitalis would also have to be increased to 0.009 mil, and the actual dose found calculated against this, instead of against the standard dose of 0.006 mil. For example, in frogs showing the increased resistance as indicated above, if the Tincture being examined assays 0.018 mil per gramme of body weight it is one-half strength." *U. S. IX.*

In carrying out this method it is well to make a preliminary series of observations on 5 or 6 frogs, using doses rising in equal gradations from 0.2 to 1.0 milligrammes of the digitalis per gramme of frog. At the same time a similar series of frogs should be tested with ouabain solution, using doses ranging between 0.0003 to 0.0007 milligramme per Gm. The ouabain may conveniently be made up into a solution containing 5 parts per 100,000; of such a solution 0.01 cc. would represent the standard dose per gramme of frog-weight for ordinarily susceptible frogs. In standardizing frogs the doses for a 25-gramme frog of such a solution would be from 0.2 to 0.5 cc. for the preliminary series. A second set of experiments is then performed using as the limit of doses the largest amount which failed to arrest the heart and the smallest amount which caused cardiac spasm and using two frogs for each of the doses in the middle. Houghton prefers that the observation be made at the end of 14 or 15 hours, instead of one hour. Focke (*A. Pharm.*, 1907) modifies the frog's heart method by using a constant dose, the time of arrest being the variant which furnishes the index to relative potency.

The "guinea-pig method" consists in simply finding the minimum lethal dose for a guinea-pig. To a series of previously weighed guinea-pigs is administered hypodermically ascending doses of a tincture of the sample to be tested. The end-point of the test is the smallest dose which will kill the guinea-pig within twenty-four hours. The method is essentially similar to that employed for aconite. (See *Aconitum.*)

A much more elaborate method has been suggested by Hatcher (*J. A. M. A.*, 1910, lv, p. 746). He has found that the lethal dose of crystalline strophanthin (ouabain) for the cat is very constant, being almost exactly 0.1 milligramme per kilogramme of body weight when administered intravenously. The method of assay is to give a quantity of the sample to be tested, of about two-thirds of the expected fatal dose for the cat, and then run slowly into a vein a solution of strophanthin until death is caused. The difference between the ordinary fatal dose of the glucoside and the quantity used in the test represents the amount of strophanthin to which the digitalis being tested is equivalent; that is, the larger the amount of strophanthin which has been used, the weaker is the preparation. Other test-animals which have been suggested are gold-fish (Pittenger) and turtles (Zeigler, *J. A. Ph. A.*, 1916, v, 1188).

Among the most important objections to the frog methods of standardizing are the facts that not only is there great difference in susceptibility between different species of frogs, but also in the same species at different seasons of the year. Focke, for instance, has found that the frog in the spring was twice as resistant to digitalis as in the fall. (*A. Pharm.*, 1907.) This variation is due in part to the difference in temperature at various seasons of the year but also in part to the nutritional condition of the batrachian. For this reason the U. S. P. recommends that the frogs be standardized by testing their resistance against crystalline strophanthin. It is doubtful, however, whether this standardization of a frog is of any great usefulness for the reason that the relative toxicity of various members of the digitalis series to the cold-blooded animal bears little correspondence to their relative power in man. The question of whether or not the guinea-pigs show seasonal variation in susceptibility to digitalis is still open for difference of opinion. See Haskell (*A. J. P.*, 1914, lxxvi, p. 7).

There has been a good deal of difference of opinion as to which one of the methods of assay is to be preferred. Colson (*J. A. Ph. A.*, 1918, vii, 13) prefers the cat method as being more accurate and less time consuming; Kruse (*J. P. Ex. T.*, 1923, xxi, 216), on the other hand, condemns the intravenous injection, as the factor of rapidity of absorption influences clinical activity. It should be noted that, as shown by Rowe (*J. A. Ph. A.*, 1919, viii, 900), there is no close relation between the results on different animals. Gottlieb (*A. E. P. P.*, 1918, lxxxiii, 117) pointed out that there will be a difference in the one-hour and twelve-hour frog methods, depending on the variations in rapidity and elimination of the various principles; thus sample A by the one-hour method might be more active than sample B, but by the twelve-hour method the relationship be reversed.

After all none of these methods of biological standardization of digitalis and its congeners can be regarded as an accurate method for the assay in the same sense that chemical standardization is; their chief utility is in preventing inert preparations of digitalis from being placed upon the market. In a comparative test by a number of experienced pharmacologists carried out under the auspices of a committee of the American Drug Manufacturers' Association, neither the Hatcher's method on the cat nor the one-hour frog test gave satisfactory results; not only was there wide variance in the results by different workers, but the results did not correspond with the known values of the tinctures tested.

For a discussion of the various details of the methods for the assay of digitalis, see also Edmunds and Hale (*U. S. Hygienic Laboratory Bulletin* No. 48, 1909); Hamilton and Rowe (*J. A. Ph. A.*, 1915, iv, p. 108); Vanderkleed and Pittenger (*J. A. Ph. A.*, 1914, iii, 815).

No simple and satisfactory *chemical assay* process has yet been devised for digitalis and hence the U. S. P. contains no process. The amount of digitoxin present in digitalis has been proposed by several investigators as a means of standardizing it, but it is by no means clear that this is a reliable criterion. Several attempts have been made to estimate the practical usefulness of the assay for digitoxin by comparing the results with the physiological tests of digitalis. While some experimenters have found a fairly close agreement between them, the great majority of those who have studied the question incline to the opinion that the two methods of assay do not run at all parallel. There are three possible reasons for this variation and each one of them seems to be operative. These are, first, inaccuracies in the chemical method for assaying digitalis; second, the unavoidable inaccuracy of the biological assay; third the fact that the relative quantity of digitoxin to the other constituents of digitalis may vary from one sample to another. While digitoxin is the most important constituent of digitalis it is by no means the only important one. The experiments of Lutzkaga (*A. I. P. T.*, 1908, xviii) and those of Barger and Shaw demonstrate that between 60 and 70 per cent. of the activity of digitalis leaf is due to its digitoxin, and that the proportion in digitalis cannot be relied upon as a criterion of the quality of the drug. (See *B. Chem. G.*, 1897; *Ph. Rev.*, 1901, 514; *D. C.*, 1902, 223; *P. J.*, 1902, 358; *Chem. News*, 1903, 123; *A. Pharm.*, 1903, 358.) J. Gordon Sharp proposed a test for digitalis based upon the fact that the leaves contain an enzyme, which acts on amygdalin producing an odor like that of bitter almond with hydrocyanic acid. (*P. J.*, 1902, 236.)

Knudson and Dresbach (*J. P. Ex. T.*, 1922, xx, p. 205) report on quantitative assay of digitalis based upon the *Baljet reaction* (*Schweiz. Ap. Ztg.*, 1918, lvi, p. 84). This is an orange-red color produced by the salts of picric acid with digitalis and strophanthus glucosides. The quantitative method as applied by the authors is as follows: A quantity of the liquid preparation, representing 0.5 Gm. of digitalis, diluted with water to 15 cc. To this add 2.5 cc. of a 10 per cent. solution of neutral lead acetate. After standing one minute filter and to 12.5 cc. of the filtrate add 1.25 cc. of a 10 per cent. solution of dibasic sodium phosphate. Add water up to 25 cc. Filter. The filtrate should be clear and almost colorless. Take 5 cc. of this filtrate and add to it 5 cc. of picrate solution, at the same time using for standard a solution of ouabain containing 0.266 milligm. in 5 cc. of water. These two solutions are allowed to stand 20 minutes and then compared in a colorimeter. Instead of the ouabain solution a permanent standard made with potassium dichromate can be used. In camparative experiments with 25 galenical preparations by this color reaction and the Hatcher cat assay, there was a very obvious similarity in the results by the two methods; in two preparations, however, there was considerable discrepancy.

Uses.—Although digitalis appears to have been used by the inhabitants of Britain as far back as the tenth century of the Christian Era, it was introduced into regular medical practice by William Withering in 1775, who obtained his knowledge of the value of foxglove in dropsy from an old woman of Shropshire.

The opinion of the medical profession as to the mode of action of digitalis and the class of cases in which it is useful has undergone many changes. Recent studies have led to another one of these revisions of the accepted belief concerning the effects of this drug upon the system, especially upon the circulation.

When given in small dose, that is, in quantities barely sufficient to cause any visible change, the only marked effect of digitalis upon the circulation is a slowing of the pulse, which is due to a stimulation of the inhibitory mechanism of the heart. After somewhat larger quantities the heart-beat becomes extremely slow, the size of the wave very large, and the vigor of the contraction of the heart perhaps a little increased, but the blood pressure is not materially affected because of the great reduction in pulse rate. The slowing of the pulse is due partly to a delayed conduction of the cardiac muscles, but also in part to a reduction in the impulses arising in the node. In the normal animal these effects are apparently produced entirely through the inhibitory mechanism unless toxic doses have been given. According to Cushny (*J. P. Ex. T.*, 1918, xi, 103), however, when the nutritional condition of the heart muscles is poor, as seen in certain cardiac diseases, conduction across the auriculo-ventricular bundle may be greatly impeded or entirely blocked through an action directly upon the muscle tissue.

Despite the fact that there is no increase in arterial pressure it is probable that even at this stage of the action of the drug there is more or less stimulant effect upon the vasomotor mechanism, the pressor effect of the vascular constriction being overcome by the great reduction in the pulse rate. When toxic doses are administered the blood pressure is distinctly, and sometimes greatly, elevated. This is brought about partially by an increased vigor of the heart's contraction, but probably in greatest part by constriction of the blood vessels. Often at this stage there appear various forms of cardiac irregularities, the most common of which is that which is known as an "extra-systole"; the irritability of the heart muscle is so greatly increased that before the completion of the diastolic period a new contraction interrupts the relaxation. Sometimes these extra-systoles occur regularly with every alternate beat of the pulse, producing the so-called *pulsus bigeminus* (sometimes incorrectly called a dicrotic pulse). Later on in the poisoning the cardiac contractions become extremely rapid, more or less irregular, and the diastole never complete. Eventually in the frog the ventricle passes into a condition of permanent contraction, or, as it is more frequently called, systolic spasm. In the warm-blooded animal, however, the heart relaxes immediately before death and passes into a state of fibrillation.

Under certain conditions digitalis produces a marked increase in the flow of urine. Apparently in normal health it has little or no diuretic action. Its effect upon the kidney appears to be the result of the reaction of the renal artery. Joseph (*A. E. P. P.*, 1913, lxxiii, p. 81) has shown that the contraction of the renal artery by digitalis is less than that in the rest of the body and that after small doses there may even be an actual dilation of the blood vessels of the kidney. This, of course, means that a larger proportion of the blood is driven to these organs and consequently there will be a freer secretion. Although both Gottlieb (*A. E. P. P.*, 1917, lxxxii, p. 1) and Hatcher and Eggleston (*J. P. Ex. T.*, 1919, xii, 405) have found 90 per cent. of digitalis glucoside, injected intravenously, disappear from the blood within ten to fifteen minutes, the physiological effects of digitalis last for a long period of time. Robinson (*J. A. M. A.*, 1919, lxxiii, 716) states that the maximum effects from a single dose of digitalis by the mouth appear within from 15 to 26 hours and last for several days, the average of his observations being nine days; but Pardee (*J. A. M. A.*, 1920, lxxv, 1258) finds the effect of single doses begins in 3 to 4 hours and reach their maximum usually by the 6th or 7th hour. The average elimination under continuous administration ordinarily is about 22 minims of the tincture per day, and the continued administration of 10 minims three times per day if continued will generally lead eventually to toxic symptoms.

Digitalis is used in practical medicine for three purposes, as a stimulant in acute circulatory failure, as a diuretic, and as a cardiac tonic in chronic heart disease.

As a circulatory stimulant digitalis is a remedy of only secondary importance. In the first place, in the acuter forms of *circulatory failure*, such as *surgical shock*, when given by the mouth it is so slow in its action that the condition will have terminated one way or the other before it begins to influence the circulation. When given hypodermically it is intensely irritant and even by this channel its effects are too slow to be of much service, and although certain proprietary preparations are upon the market which are suitable for intravenous injection, there is no reason to believe them superior for this purpose to stophanthin. In *infectious fevers* the weakness of the heart manifests itself sufficiently gradually that there is usually time enough for the action of the drug, but unfortunately clinical experience has shown that in this condition its power is much diminished.

As a diuretic digitalis is of service whenever there is *dropsical accumulation*. How far the beneficial effects are the result of improvement in the circulation and how far from a direct action upon the kidney is somewhat doubtful.

The most important use of this drug is in the treatment of various forms of *chronic heart disease*, including those due to *valvular lesions*, various types of *myocarditis*, and the *cardiac neuroses*. Its beneficial influence in these states is probably the result of several factors: the stimulation of inhibition gives the heart more time to rest, the increased force of the contraction improves the nutrition of the heart muscle, the diuresis, which occurs if there be edema, lessens the burden upon the diseased heart. Although this drug is, in a large number of cardiac conditions, the most important remedy we possess it must not be regarded as a panacea for all forms of chronic heart disease. A discussion of the various forms of cardiac weakness in which this drug is indicated or contraindicated can scarcely be undertaken in this place, and the interested reader is referred to H. C. Wood, Jr.'s *Text-book of Pharmacology* for further information.

The active principles of digitalis are absorbable through the skin and the external application of digitalis poultices was formerly used to a considerable extent in the treatment of dropsies.

Two methods for the administration of digitalis have been advocated. The older and more frequently used is to begin with moderate doses —5 to 10 minims of the tincture three times a day—gradually increasing until some definite effect is obtained. The second method advocated by Eggleston (*J. A. M. A.*, 1920, lxxiv, 733) is to rapidly digitalize the patient. The principle of the Eggleston method is that it requires 0.15 cc. (approximately 2½ minims) of a standard tincture per pound body weight to produce maximum therapeutic results. From ¼ to ½ of this quantity may be given at once and followed by 1/10 of the dose every 6 hours, until the occurrence of either nausea, slowing of the pulse or cardiac irregularity; evidences of digitalis action. The method is not safe in patients who have previously received any drug of the digitalis group, and for its successful application requires a preparation that meets the physiological standard advocated by Doctor Eggleston, as well as continuous observation, and is therefore more suitable for hospital practice than ordinary clinical conditions.

Preparations of digitalis vary so much in their potency, and the conditions in which it is used so frequently demand the full actions of the drug, that the therapeutist should be guided in his dosage only by the degree of effect. The two most important symptoms indicating that the patient is taking as much as he can stand are great reduction in the rate of the pulse—say below sixty per minute—or the occurrence of nausea.

The symptoms of digitalis poisoning are nausea and vomiting, with muscular weakness, the pulse is at first very slow, may fall to thirty or forty a minute, and in severe cases later becomes very rapid and irregular. Visual disturbances, especially of the color sense, have been reported in several cases (see Sprague, *J. A. M. A.*, 1925, lxxxv). In some instances the pulse may be slow as long as the patient remains in a recumbent posture but becomes rapid if he assumes an upright position. Outside of the evacuation of the stomach and keeping the patient lying down there is no treatment of the poisoning which is known to be efficacious, although Zugsmith has reported favorable results from the external application of heat.

Preparations.—Because of the variability of the official preparation of digitalis and of their liability to produce gastric disturbances, a large number of proprietary preparations of the drug have been placed upon the market. It may be pointed out in connection with these substances that Hatcher and Weiss (*A. I. M.*, 1922, xxix, 690) have shown that the nauseating action of digitalis is due chiefly to a reflex from the heart to the vomiting center in the medulla, and that any preparation, therefore, which does not nauseate is therapeutically useless. In the second place, it is not probable that any single principle of the drug has exactly the same influence upon the circulation as the whole leaf. The following are some of the more important preparations of digitalis.

Digitalinum Gallicum, French digitaline, also known as *digitaline chloroformique* and as *Homolle's digitaline.* This is almost insoluble in water, and is said to consist largely of a glucoside allied to, or identical with, Kiliani's digitalin. The dose of the commercial article may be put down as about one two-hundred and sixtieth of a grain (0.00025 Gm.), to be repeated several times per day, the maximum daily dose being one-fortieth of a grain (0.0016 Gm.).

Digitoxin has been used to a certain extent clinically. According to the experiments of Fraenkel, however, it is more liable to give rise to cumulative effects than is the crude drug. It is almost insoluble in water and is locally irritant. *Dose,* one two-hundredth to one one-hundredth of a grain (0.0003–0.0006 Gm.).

Digitalinum Germanicum, also known as *Merck's digitalin* or *German digitalin.* This is practically a concentrated extract of the digitalis seeds. It probably contains true digitalin, and digitalein, as well as digitonin. The dose is from one-tenth to one-half a grain (0.005–0.03 Gm.).

Digalen is claimed to be a *soluble digitoxin,* but such a statement is manifestly impossible. The claim of its discoverer Cloetta that it is isomeric with digitoxin but has twice the molecular weight of digitoxin, would seem to disprove its identity. According to Kiliani (*M. M. W.*, 1907), it is identical with digitalein.

Digipuratum is a yellowish powder which is asserted to contain all the active glucosides of digitalis leaves in the form of tannates without various objectionable constituents. It is physiologically standardized by tests upon frogs. The dose is the same as that of the leaves.

Digifolin is asserted to contain the cardiac principles without the saponins of digitalis. It is marketed in the form of tablets and of ampoulæ, each of which represents one and one-half of a grain (0.1 Gm.) of digitalis leaves. *Digipan* is a preparation of the same nature which is issued both in tablets and in solution, the dose of the tablets being one or two and of the solution fifteen drops (0.9 cc.). *Adigan* is also a saponin free preparation but does not seem to have been proven clinically. *Digitol* is standardized tincture made from leaves freed of their fatty matter by treating with benzin. The *dose* is the same as of the official tincture.

Of the various pure principles of digitalis the doses are as follows: *Digitalein,* one-sixtieth to one-thirtieth of a grain (0.0011–0.002 Gm.); *digitoxin,* one two-hundredth to one one-hundredth of a grain (0.0003–0.0006 Gm.); *Kiliani's digitalinum verum* has not been used enough clinically to determine the proper dose. *Verodigen,* which is stated to be the same as gitalin, is given in doses of one-eightieth of a grain 0.0008 Gm.).

There are two substances known as *crystallized digitalin,* one of which, the *digitaline crystallisée* of the French Codex also known as *Nativelle's digitalin,* is probably identical with digitoxin. Merck's *crystallized digitalin* appears to be largely composed of digitonin and does not therefore represent the physiological properties of digitalis.

Dose, of digitalis leaves, one to two grains (0.065–0.13 Gm.).

Off. Prep.—Fluidextractum Digitalis, *U. S.;* Infusum Digitalis, *U. S., Br.;* Tinctura Digitalis, *U. S., Br.;* Pilulæ Digitalis, Scillæ et Hydrargyri, *N. F.*

DIOSCOREA. N. F.

DIOSCOREA Dioscor. [Wild Yam Root]

"Dioscorea consists of the dried rhizome of *Dioscorea villosa* Linné (Fam. *Dioscoreaceæ*). Dioscorea contains not more than 2 per cent. of foreign organic matter." *N. F.*

Wild Yam Root, Colic Root, Rheumatism Root.

The genus *Dioscorea* is represented by over 200 species which are native to tropical and temperate countries. They are all herbs with tuberous roots and twining herbaceous stems. Their leaves are broad, petiolate, frequently cordate, reticulately veined, and vary from simple, alternate or opposite to compound. Their flowers are small, greenish-yellow and diœcious and their fruits are 3-winged capsules enclosing winged seeds.

While *Dioscorea villosa* L. has long been considered the species yielding the drug, Bartlett finds this name no longer tenable on account of the confusion attending its use. He recognizes 5 species passing as *D. villosa,* namely *D. quaternata* Gmel., *D. Glauca* Muhl., *D. paniculata* Michx., *D. Lirticaulis* Bartlett and *D. floridana* Bartlett. For a detailed description of these see Bull. 189, *Bur. Pl. Ind., U. S. Dept. Agric.,* 1910. The species yielding the drug are all native to North America. The commercial supplies of the drug are obtained from Virginia, North Carolina, Indiana and Michigan.

Description and Physical Properties.—"*Unground Dioscorea.*—Knotted and woody, elongated, 6 to 20 mm. thick, often compressed, bent and branched, bearing scattered nodular projections, slender tough roots or thorn-like root-remains in circular depressions on the sides and underneath, and stem-scars on the upper surface; externally pale brown, surface more or less scaly from the partly detached, thin outer layer; fracture short but tough, the fractured surface whitish or pale-yellowish, with numerous small, scattered, yellowish wood-bundles. Odorless; taste starchy, insipid, afterwards acrid.

"*Structure.*—Rhizome: epidermis thin-walled, more or less detached; an outer layer composed of several rows of parenchyma cells with yellowish walls occasionally developing as a thin cork layer; a few rows of tangentially elongated thin-walled parenchyma, remaining tissue consisting chiefly of longitudinally elongated, thick-walled porous, partially lignified parenchyma containing starch, with numerous collateral fibrovascular bundles scattered throughout; raphides of calcium oxalate occasionally present in the parenchyma cells. Root; epidermal cells with yellowish thin walls; cortex composed of thin-walled, porous, slightly lignified parenchyma; endodermis distinct, the inner and radial walls being heavily thickened and slightly lignified; stele with a continuous zone of heavily lignified fibers, alternating small groups of tracheæ and sieve tissue and a pith composed of thick-walled, slightly lignified parenchyma. Sections of the root made close to the rhizome do not exhibit an endodermis.

"*Powdered Dioscorea.* — Whitish; exhibits numerous fragments of thick-walled, lignified parenchyma cells many of which contain spherical or ovoid starch grains up to 0.035 mm. in diameter; numerous isolated starch grains and a very few raphides of calcium oxalate; few fragments of thin-walled parenchyma cells; fragments of fibro-vascular bundles with tracheæ and tracheids which have minute border pores; yellowish or brownish fragments of epidermal tissue; few isolated lignified fibers." *N. F.*

W. C. Kalteyer found abundant saponin in the roots. (*A. J. P.,* 1888; see also *M. R.,* 1913, 311.) A substance, improperly called *dioscorein,* obtained by precipitating the tincture with water, is used in the *dose* of from one to four grains (0.0065–0.26 Gm.).

Dioscorea hirsuta Bl. grows in the island of Java, where it is known as *Gadoeng.* In 1894 W. G. Boorsma separated from it an alkaloid to which he gave the name of *dioscorine.* Plugge and Schutte (*A. J. P.,* 1897) assigned to it the formula $C_{13}H_{19}O_2N$, and found it to be a convulsant poison, resembling closely in its action picrotoxin, but much less active. Heckel and Schlagdenhauffen found a glucoside in the tuber of the *D. bulbifera* L. which grows in tropical Africa.

The *D. sativa* L., probably a native of Asia, is widely cultivated in the West Indies, its tuber being the popular amylaceous food called *yam.* The *D. alata* L. or *winged yam* yields a tuber which is popular in the southern states as a substitute for potatoes. The *D. Batatas* Decne. (*Chinese yam* or *cinnamon vine*) is also extentively used as a food in Asia.

From the *D. Tokoro,* a Japanese plant which is used as a fish poison, Honda (*A. E. P. P.,* 1904, li, p. 213) has separated several saponin substances. One of these, *dioscin,* is extraordinary for the strength of its hemolytic action, 1 part in 400,000 dissolving the coloring matter from the red cells in a 1 per cent. blood solution. It possesses also a strong toxic effect on fish and ameba. The root of *Dioscorea rhipogonoides* Oliver, under the names of *Cunao, Shu-Lang, faux gambier,* is exported in enormous quantities from Indo-China to Southern China for use as a dye-stuff.

Uses.—In large doses dioscorea exercises a nauseating effect and therefore may be expectorant and diuretic. By that group of practitioners who call themselves eclectics it was supposed to have antispasmodic powers and was regarded as a specific in *biliary colic,* whence its popular name of "colic root." It is very doubtful, however, whether this drug possesses any real therapeutic virtues.

Dose, one-half to one drachm (1.9–3.75 Gm.).

Off. Prep.—Fluidextractum Dioscoreæ, *N. F.;* Tinctura Viburni Opuli Composita, *N. F.*

DROSERA. N. F.

DROSERA Droser. [Sundew]

"Drosera is the air-dried flowering plant of *Drosera rotundifolia* Linné, frequently mixed with the closely allied species *Drosera anglica* Hudson and *Drosera longifolia* Linné, or at times wholly replaced by these (Fam. *Droseraceæ*). Drosera contains not more than 5 per cent. of foreign organic matter and yields not more than 10 per cent. of acid-insoluble ash." *N. F.*

Herba Rorellæ; Herba Roris Solio; Rosollis, Rosée du Soleil, *Fr.;* Sonnen-thau, *G.*

The Droseras or Sundews comprise about 90 species of small carnivorous plants common to peat bogs of both hemispheres but most abundant in Australia. They are characterized by possessing a much reduced fibrous root system from which springs a rosette of modified leaves, the upper surfaces of which possess numerous irritable, glandular hairs which secrete a viscid fluid that ensnares and catches insects. The hairs then bend over the insect and hold it in place while an acid fluid containing a protease is excreted by the glands that digest the animal tissues, the soluble nitrogenous products then being absorbed for the plant's nutrition. One or more scapes arise from the center of the leaf-rosette and terminate in scorpioid cymes of white, pink or crimson flowers. The N. F. recognizes 3 species of *Drosera,* all of which occur in bogs and moist sandy soil of Europe and North America. The leaf blades of *D. rotundifolia* L. are suborbicular, those of *D. Anglica* Huds. (*D. intermedia* Hayne) are spatulate, 2 to 3 times as long as wide, while those of *D. longifolia* L. are elongated spatulate-obovate 6 to 8 times as long as wide.

Description and Physical Properties.—"*Unground Drosera.*—Matted or broken leaves, stems and fibrous black rootlets; of a reddish color throughout; leaves mostly basal, petiolate. *Drosera rotundifolia;* blade orbicular, about 15 mm. in diameter, abruptly contracted into a slender pubescent petiole, upper surface covered with prominent pinkish red glandular tentacles, the latter up to 4 mm. in length; petiole slender, 2 to 4 cm. in length, 0.5 to 2 mm. in diameter, flattened and pubescent; scape filiform, smooth, from 10 to 30 cm. long, bearing a few five-parted, small, white fugacious flowers in a curved one-sided raceme. *Drosera anglica;* leaves linear—to obovate spatulate with blades 1.5–5 cm. long, 3–7 mm. wide, and glabrous or sparsely hairy petioles. *Drosera longifolia;* leaves spatulate with blades 2 to 3 times as long as they are wide, slender smooth petioles and scape, declinate at base. Odorless; taste faintly bitter and acidulous.

"*Powdered Drosera.*—Reddish brown; elements of diagnostic value; multicellular, oval heads of tentacles from 0.100 to 0.200 mm. in diameter; fragments of the multiseriate tentacle stalks; few glandular hairs with two-celled heads, the apical cells spreading and up to 0.095 mm. in width at the top; fragments of epidermal tissue with stomata, the latter up to 0.045 mm. in length; few fragments of fibro-vascular bundles with spiral tracheæ; fragments of parenchyma containing a reddish brown amorphous substance; a few rounded or ellipsoidal starch grains up to 0.012 mm. in diameter." *N. F.*

Chemists have failed to find in this plant any constituent more active than the vegetable acid which is probably citric or malic acid.

Uses.—Drosera was thought by the eclectic physicians to be useful in *whooping cough* and other pectoral complaints but probably is inert.

The *dose* of the crude drug is one drachm (4 Gm.).

Off. Prep.—Fluidextractum Droseræ, *N. F.*

DULCAMARA. N. F.

DULCAMARA Dulcam. [Bittersweet]

"Dulcamara is the dried stem of *Solanum Dulcamara* Linné (Fam. *Solanaceæ*). Dulcamara contains not more than 2 per cent of foreign organic matter." *N. F.*

Woody Nightshade; Stipites Dulcamaræ; Caulis Dulcamaræ; Tiges de Douceamère, (de Morelle grimpante), Douce amère, *Fr.;* Bittersüss, Bittersüss-Stengel, Hindischkraut, Alpranken, *G.;* Tallo de Dulcamara.

Dulcamara is a climbing shrub with a woody branching stem and purplish, cymose flowers, with lemon-yellow anthers. The bright scarlet berries remain after the falling of the leaves. The plant grows in wet places and around dwellings and is common to Europe and North

America, and in the United States grows from New England to Ohio. All portions of the plant are active. Fatal results from the eating of the berries by a child have been recorded. (*P. J.*, 1861.) For medicinal purposes the plant should be gathered in the autumn after the fall of the leaf, and the extreme twigs should be selected. That grown in high and dry situations is said to be the best.

Description and Physical Properties.—"*Unground Dulcamara.*—In short sections about 5 mm. or less in thickness, cylindraceous, outline of transverse section somewhat angular, longitudinally striate, more or less warty; bark thin, externally pale greenish, or light greenish brown, glabrous, marked with alternate leaf scars, internally green, the greenish or yellowish wood occurring in 1 to 2 concentric rings, usually hollow in the center. Odor slight; taste bitter, afterwards sweet.

"*Structure.*—Epidermis with a rather thick outer cuticle; several rows of cork composed of thin-walled cells and in the older stems entirely replacing the epidermis; phellogen composed of a number of rows of tangentially elongated cells; about six rows of collenchyma; a pericycle containing non-lignified fibers which are mostly in an interrupted single row; inner bark of parenchyma containing starch grains or sphenoidal micro-crystals of calcium oxalate, or groups of sieve cells; a continuous zone of cambium; a narrow zone of wood composed of numerous tracheæ, tracheids, wood fibers and lignified, porous parenchyma, the latter forming medullary rays one cell in width; within the wood a narrow zone of pith parenchyma with groups of sieve cells; pith surrounding a central hollow.

"*Powdered Dulcamara.* — Greenish yellow; exhibits tracheæ up to 0.112 mm. in diameter and with bordered pores or with spiral markings; tracheæ-like cells having pointed ends, slightly lignified walls and delicate spiral or reticulate markings; lignified wood fibers with few pores; non-lignified bast-fibers with walls up to 0.015 mm. thick; fragments composed of cork cells; very few, simple, unicellular hairs up to 0.800 mm. long, and with the lumina usually distinct in the lower portions only; starch grains, spheroidal, up to 0.012 mm. in diameter; sphenoidal micro-crystals numerous, up to 0.007 mm. long." *N. F.*

The dried twigs are inodorous, though the stalk in the recent state emits, when bruised, a peculiar, rather nauseous odor. Their taste, which is at first bitter and afterwards sweetish, have given origin to the name of the plant.

According to Davis (*P. J.*, 1902, xv), dulcamara contains the glucosidal alkaloids *solanine* (see Part II) and *solaneine*, besides *solanidine*, which is a non-glucosidal alkaloid and is the hydrolytic product from solanine, and a bitter principle *dulcamarin.*

The *picroglycion* of Pfaff seems to be identical with dulcamarin. This was obtained by Blitz, in the following manner: The aqueous extract was treated with alcohol, the tincture evaporated, the residue dissolved in water, the solution precipitated with lead subacetate, the excess of this salt decomposed by hydrogen sulphide, the liquor then evaporated to dryness, and the residue treated with acetic ether, which yielded the principle in small isolated crystals by spontaneous evaporation.

Uses.—In large doses dulcamara causes burning in the throat with nausea and vomiting and dizziness; the pulse temporarily accelerated becomes slow, the pupils dilated and there often occurs general weakness with convulsive muscular movements.

Formerly this drug was used in the treatment of *chronic rheumatism*, in *chronic bronchitis*, especially with an asthmatic tendency and in *whooping cough.* It was also attributed with anaphrodisiac properties. Today it is used almost solely in the treatment of scaly skin diseases such as *lepra, psoriasis*, and *pityriasis.*

Dose, thirty to sixty grains (2–4 Gm.).

Off. Prep.—Fluidextractum Dulcamaræ, *N. F.*

ECHINACEA. N. F.

ECHINACEA Echin.

"Echinacea consists of the dried rhizome and roots of *Brauneria pallida* (Nuttall) Britton or *Brauneria angustifolia* (De Candolle) Heller (Fam. *Compositæ*). Echinacea contains not more than 3 per cent. of foreign organic matter. Echinacea must not be used after it has lost its characteristic odor and taste." *N. F.*

Nigger-head; Pale Purple Coneflower.

This composite perennial herb, a native of the prairie region of America west of Ohio, has been introduced by the so-called eclectic physicians as a remedy in divers dissimilar diseases. It possesses lanceolate, three- to five-nerved leaves and slender stems terminating in single, large, conical, purplish heads of ligulate and tubular flowers. Its fruits are 4-sided achenes, each with a short-tootheed pappus. The drug is collected in autumn, the commercial supplies coming from Kansas. Kraemer and Sollenberger (*A. J. P.*, 1911, p. 315) have described the physical characteristics of the drug.

Description and Physical Properties.—"*Unground Echinacea.*—Nearly entire, cylindrical, very slightly tapering and sometimes spirally twisted, from 10 to 20 cm. long and from 4 to 15 mm. in diameter; externally grayish brown, light brown or purplish brown; slightly annulate in the upper portion, with occasional stem scars somewhat longitudinally wrinkled, or furrowed; fracture short, fibrous; bark less than 1 mm. thick, wood composed of alternate light yellowish and black wedges; the rhizome with a circular or angular pith. Odor faint, aromatic; taste sweetish, followed by a tingling sensation suggesting aconite, but lacking the persistent and benumbing effect produced by that drug.

"*Structure.*—An outer cork composed of several layers of tabular cells with yellowish walls and containing oil globules or granular masses; about 8 rows of tangentially elongated rather thick-walled parenchyma cells among which are oil or resin canals; in the rhizome portion are a few strongly lignified bast fibers with thick walls and simple pores; a thick layer of parenchyma with numerous stone cells and oil or resin canals; characteristic carbon-like masses occur around the stone cells and fibers; sieve tissue in radial rows the latter separated by parenchyma containing inulin and extending to the middle bark; a distinct cambium zone of several rows of thin-walled cells; central portion made up of radially arranged groups of tracheæ, separated by broad wedges of parenchyma, the latter with secretion canals and characteristic stone cells.

"*Powdered Echinacea.*—Grayish; numerous stone cells, strongly lignified, from 0.018 to 0.042 mm. in diameter, many being very much elongated and carrying the characteristic carbon-like deposits; numerous tracheæ from 0.025 to 0.075 mm. in diameter and with simple pores, annular or reticulate markings, occasionally with bordered pores or double spiral markings; fragments of inulin-bearing parenchyma tissue, the latter showing oil or resin canals from 0.080 to 0.145 mm. in diameter and filled with a reddish brown or yellowish content; few fragments of cork and a few fibers." *N. F.*

Heyl and Hart (*J. Am. C. S.*, 1915, xxxvii, p. 1769) found the drug to contain inulin, 5.9 per cent.; inuloid, 6; sucrose, 7; vulose, 4; betaine, 0.1, and resins, 1.9 per cent.; the latter consisting of two isomeric phytosterols, phytosterolin, and the following fatty acids, oleic, linolic, cerotic and palmitic, but could find no physiologically active substance.

Brauneria purpurea, DC., Britton (*Rudbeckia purpurea* L., *Echinacea purpurea* Moench), *Black Sampson, Purple Cone-flower* (Virginia to Illinois and southward to Louisiana), is similarly used.

Uses.—Echinacea has been attributed with the property of increasing the resistance of the body to infection and is consequently used in *boils, septicemia,* and other infective conditions. Couch and Giltner (*J. Agricult. Research,* 1920, xx, 63) in a study on guinea-pigs failed to obtain any evidence of a beneficial effect in a variety of experimental infections. It is also attributed with aphrodisiac and analgesic powers, but is probably without therapeutic value. Hale (*Lancet Clinic,* March, 1901) injects an extract into the rectum in the treatment of *hemorrhoids.*

Dose, of the fluidextract, fifteen to thirty minims (1–2 cc.).

Off. Prep.—Fluidextractum Echinaceæ, *N. F.*

ELATERINUM. U. S.

ELATERIN Elaterin.

"A substance obtained from the juice of the fruit of *Ecballium Elaterium* (Linné) A. Richard (Fam. *Cucurbitaceæ*)." *U. S.*

Elaterine, Elatine, *Fr.;* Elaterin, *G.;* Elaterina, *Sp.*

Elaterin was introduced into the U. S. Pharmacopœia on account of the well-known variability in quality of commercial elaterium. (See *Elaterium,* Part II.) Care must be taken to examine the elaterin, which is itself liable to be adulterated. It may be procured by evaporating an alcoholic tincture of elaterium to the consistence of thin oil, and throwing the residue while yet warm into a weak boiling solution of potassium hydroxide; this holds the green resin in solution, and the elaterin crystallizes as the liquor cools. Hennell obtained it by treating with ether the alcoholic extract procured by the spontaneous evaporation of the tincture. This consists of elaterin and the green resin, the latter of which, being much more soluble in ether than the former, is completely extracted by this fluid, leaving the elaterin pure. Flückiger prefers to exhaust elaterium with chloroform, and add to the percolate ether, which precipitates elaterin. The precipitate may be dissolved in chloroform and recrystallized. This process was adopted by the Br. Pharm., 1885. The yield of elaterin from elaterium is usually from 10 to 25 per cent.; the British Pharmacopœia 1898 required not less than 20 per cent.

According to Power and Moore (*Tr. Ch. Soc.*, xcvii, p. 99), elaterin consists of two isomeric substances, one lævorotary and physiologically inert, the active compound being dextrorotary. These they designate respectively as *alpha-* and *beta-elaterin.*

Description and Physical Properties.—"Minute white scales or prismatic crystals. It is odorless, and is stable in the air. Elaterin is insoluble in water. One Gm. is soluble in 325 cc. of alcohol, 310 cc. of benzene, 15.5 cc. of chloroform, and in 450 cc. of ether, at 25° C. One Gm. is soluble in 100 cc. of boiling alcohol.

"Its alcoholic solution is neutral to moistened litmus paper. To a solution of about 0.01 Gm. of Elaterin in 5 Gm. of melted phenol, add a few drops of sulphuric acid; the mixture becomes crimson, the color rapidly changing to scarlet. The ash from 0.1 Gm. is negligible. Shake 0.1 Gm. of Elaterin with a mixture of 9 cc. of distilled water and 1 cc. of diluted hydrochloric acid, and filter; separate portions of the filtrate yield no turbidity with 0.5 cc. of mercuric potassium iodide T.S. or iodine T.S. (*alkaloids*)." *U. S.*

Ernst Johannson (*In. Dis.*, Dorpat, 1884) gives the following reactions for elaterin besides those mentioned in the Pharmacopœia. In all of them elaterin is held in alcoholic solution. Froehde's reagent gives a green color passing into brown which fades away. Vanadin-sulphuric acid with the fortieth of a milligramme produced a splendid blue color passing into a clear green, finally into reddish-brown. After mixing with selenic acid and an addition of sulphuric acid, in a few minutes a red-brown color develops, which is not so deep as that which is produced by sulphuric acid. Kohler's reaction is produced by dissolving elaterin in a few drops of concentrated hydrochloric acid, evaporating the acid in a water bath, washing the white, amorphous residue with boiling water, and adding some concentrated sulphuric acid, when an amaranth-red color develops. By means of these reactions Johannson has been able to find elaterin in large quantities in the feces of animals poisoned by it, but no trace in the blood or urine or any part of the organism.

Uses.—Elaterin is a powerful hydragogue cathartic, frequently employed for the evacuation of *dropsy* especially in nephritic patients. Its too bold or frequent use is likely to prove debilitating and it should be employed only with great caution in persons of feeble constitution.

Dose, one-twentieth to one-tenth of a grain (0.003–0.006 Gm.).

Off. Prep.—Trituratio Elaterini, *U. S.*

ELIXIR AROMATICUM. U. S.

AROMATIC ELIXIR Elix. Arom. [Simple Elixir]

Elixir aromatique, *Fr.;* Aromatisches Elixir, *G.*

"Compound spirit of orange, 12 cc.; syrup, 375 cc.; purified talc, 30 Gm.; alcohol, distilled water, each, a sufficient quantity to make 1000 cc. To the compound spirit of orange add enough alcohol to make 250 cc. To this solution add the syrup in several portions, agitating after each addition, and afterwards add, in the same manner 375 cc. of distilled water. Mix the purified talc intimately with the liquid, and filter through a wetted filter, returning the first portions of the filtrate until a clear liquid is obtained. Lastly, wash the filter with a mixture of 1 volume of alcohol and 3 volumes of distilled water until the product measures 1000 cc.

"Alcohol content, by volume, 22 to 24 per cent." *U. S.*

This is justly one of the most popular vehicles of the Pharmacopœia. The flavor which is agreeable to nearly all palates is enhanced by its sweetness. If desired it can be colored with cochineal or caramel.

Off. Prep.—Elixir Aromaticum Rubrum, *N. F.*

ELIXIR GLYCYRRHIZÆ. U. S.

ELIXIR OF GLYCYRRHIZA Elix. Glycyrrh. [Elixir Adjuvans, Elixir of Licorice]

Adjuvant Elixir, Elixir adjuvant, *Fr.;* Gewürzhaftes Lakritzenelixir, *G.*

"Fluidextract of glycyrrhiza, 125 cc.; aromatic elixir, 875 cc.; to make 1000 cc. Mix and filter.

"Alcohol content, by volume, 21 to 23 per cent." *U. S.*

Uses.—This elixir is used as a vehicle for the administration of various medicinal preparations; it was introduced into the U. S. Pharmacopœia (8th Rev.) mainly to furnish an alternative elixir to aromatic elixir which is similarly used. The presence of the glycyrrhiza aids in disguising or obtunding the taste of bitter or disagreeable substance and the proportion might advantageously be increased.

ELIXIRIA

ELIXIRS

Cordials; Elixirs, *Fr.;* Elixire, *G.*

Elixirs as they are known in modern American pharmacy are aromatic, sweetened, spirituous preparations, containing small quantities of active medicinal substances. They differ greatly from the liquids formerly termed elixirs, from the fact that the first object sought for in the modern elixir is an agreeable taste, and sometimes this is attained only by such sacrifices as to render the effect of the medicine almost *nil,* while the principal activity is due to the alcohol, which has proved in many cases very injurious. These considerations have prevented an extensive official recognition of elixirs, and the U. S. recognizes but two, which are used merely as vehicles. A number are, however, included in the N. F.

EMBELIA. Br.

EMBELIA

"*Embelia* is the dried fruit of Embelia Ribes, *Burm. fil.,* and also of Embelia robusta, *Roxb.*" *Br.*

The genus *Embelia* (Fam. *Myrsinaceæ*) includes a large number of creeping or almost climbing tropical shrubs. They possess petiolate leaves, small white flowers and are especially abundant in tropical Asia, *Embelia Ribes* extending as far as southern China. The fruits of this plant somewhat resemble black pepper and have been used as an adulterant of it.

Most of the drug is collected in India from *Embelia robusta.* The fruits of this plant are longitudinally striate whereas those of *E. Ribes* are wrinkled or warty.

It is officially described as "globular, about four millimetres in diameter, varying in color from dull red to nearly black; warty or striated longitudinally; superior, minutely beaked and often attached to a 5-partite calyx and slender pedicel. Pericarp brittle, enclosing a single seed surrounded by a delicate membrane. Seed reddish, marked with lighter spots. Endosperm horny and slightly ruminated. Taste slightly astringent and aromatic." *Br.*

If the powdered drug be shaken with ether and the resultant ethereal extract treated with diluted ammonia water a violet blue color is produced.

Embelia contains 2.5 per cent. of *embelic acid,* $C_9H_{14}O_2$, which occurs in golden yellow crystals, which are insoluble in water and soluble in alcohol, ether, chloroform and benzene; in alkaline solutions it dissolves with red coloration. There is present also small amounts of an alkaloid *christembine.*

Uses.—Embelia, under the names of *viranga, vayvirang* or *birang-i-kabuli,* has long been employed in India as an anthelmintic and has found its way into European commerce. It has but slight laxative properties, so that it is better to follow it by a purgative. It is especially tenicidal, the *tape worm* being expelled dead. The powdered drug may be given in milk early in the morning. Warden has found that *ammonium embelate* is an effective tenicide in dose of three grains (0.2 Gm.) for children and six grains (0.4 Gm.) or more for adults. As it is nearly tasteless and soluble it may be readily administered in syrup.

Dose, of embelia, one to four drachms (3.9–15.5 Gm.).

EMETINÆ HYDROCHLORIDUM. U. S.

EMETINE HYDROCHLORIDE Emet. Hydrochl.

"The hydrochloride [$C_{30}H_{44}O_4N_2.2HCl$] of an alkaloid obtained from ipecac or prepared synthetically. It contains variable amounts of water of crystallization." *U. S.*

This alkaloidal salt is made by dissolving emetine in diluted hydrochloric acid, concentrating the solution and separating the crystals. It should be free from cephaëline.

J. L. Ague (*Bol. Farm.,* Lima, through *C. D.,* 1920, 93) states that the emetine hydrochloride of commerce is not always pure but contains considerable amounts of cephaëline and psychotrine.

Description and Physical Properties.—"A white or very slightly yellowish, odorless, crystalline powder. Emetine Hydrochloride is freely soluble in water and in alcohol.

"An aqueous solution of the salt (1 in 100) yields precipitates with iodine T.S., with mercuric potassium iodide T.S., or with platinic chloride T.S. Sulphuric Acid, containing in each cc. about 0.005 Gm. of molybdic acid, when added to Emetine Hydrochloride produces a bright green color. Silver nitrate T.S. produces in an aqueous solution of the salt (1 in 2) a white precipitate insoluble in nitric acid.

"The ash from 0.2 Gm. is negligible. Emetine Hydrochloride dried to constant weight at 100° C. loses not more than 19 per cent (*water*). A solution of 0.1 Gm. of Emetine Hydrochloride in 10 cc. of distilled water requires for neutralization not more than 0.5 cc. of fiftieth-normal sodium hydroxide, using 1 drop of methyl red T.S. as indicator. One-tenth of 1 Gm. of the salt dissolves in 2 cc. of sulphuric acid without producing more than a faint yellow color (*readily carbonizable substances*). Dissolve 0.2 Gm. of Emetine Hydrochloride in 10 cc. of water, add 5 cc. of sodium hydroxide T.S., and shake, successively, with 20 cc. of ether, and then with 10 cc. portions of ether, until the residue obtained by evaporating 2 cc. of the last ether extraction, when dissolved in 1 drop of diluted hydrochloric acid and 1 cc. of water, no longer yields a distinct turbidity with iodine T.S. Discard the ether solutions, acidulate the aqueous liquid with diluted sulphuric acid, add ammonia T.S. until alkaline, and shake with four successive 10 cc. portions of ether. Evaporate the combined ether solutions to dryness on a water bath, and dry the residue at 100° C. Its weight does not exceed 0.004 Gm. (*cephaëline*).

"Preserve in dark amber-colored vials, protected from light." *U. S.*

A. Lahiele reports the following color reactions for emetine: calcium chloride, yellow; concentrated sulphuric acid and ammonium molybdate green, followed by blue; concentrated sulphuric acid and potassium dichromate, green, followed by blue; concentrated nitric acid, yellow.

For further discussion of the properties of emetine and other alkaloids of this drug see *Ipecacuanha.*

Uses.—The observations of Vedder indicating that the antidysenteric effect of Ipecac (see article on *Ipecacuanha*), was due chiefly to its emetine, led Rodgers to the hypodermic administration of emetine in the treatment of amebic *dysentery.* Since the publication of his paper (*B. M. J.,* 1912) this has become the standard treatment. In his original communication, Vedder asserted that a 1/1000 solution of emetine was sufficient to destroy the vitality of ameba. More recent experiments have thrown great doubt upon his optimism. Allen (*J. P. Ex. T.,* 1920, xii, p. 21) from his own experiments and study of the literature, reaches the conclusion that in some instances, one part of emetine in 15,000 would destroy the ameba in dysenteric stools but in other cases these parasites resisted a solution of 1/150 after two hours' exposure. Dale and Dobell (*J. P. Ex. T.,* 1917, x, 399), as the result of somewhat similar observations, believe "that the therapeutic efficacy of emetine is a result of its action upon the host rather than upon the parasite." Sellards and Leiva (*J. P. Ex. T.,* 1924, xxii, 467) conclude that although therapeutic doses do not directly kill the entamebæ, they so lessen their resistance that the natural bodily defences can destroy them.

The most important use of emetine in clinical medicine is in the treatment of *amebic dysentery.* For this purpose the hydrochloride may be given hypodermically or one of the insoluble salts (see *Emetine-Bismuth Iodid,* Part II) may be administered by mouth. While in nearly all cases of amebic dysentery the drug will cause a prompt amelioration of symptoms, in chronic cases even its continued use may fail to produce permanent cure. Whether the therapeutic results of emetine are superior to those of ipecac, in this disease, is at present open to difference of opinion although the ease of administration has made the alkaloid almost universally the choice. It appears to be of value also in amebic *abscess of the liver,* which is so common a sequela of chronic dysentery: Pontano (*Il Policlinico,* 1920, xxcii, p. 607) reports ten cases of apparent cure of hepatic abscess. Emetine has also been highly lauded by Tsykalas (*W. K. W.,* 1921, xxxiv, 579) and others in the tropical infection known variously as *bilharziasis* or *schistosomiasis.*

There is strong clinical evidence that emetine has a marked action on the coagulation of the blood. Blasco (Abst., *J. A. M. A.,* March, 1919) and others have reported most favorable results from its use in *hemoptysis* and Monroe (*Pract.,* 1918, ci, p. 167) has found it useful in *hemophilia.* The changes seen in the lungs after toxic doses of emetine would suggest that the drug has some other effect upon the pulmonary structures than that of a simple nauseant. Le Clair (*B. Hôp. Par.,* 1920, xliv, p. 802) has employed it with asserted great benefit in the treatment of *asthmatic emphysema.* Lewissohn (*J. A. M. A.,* 1918, lxxx, p. 9) has found that the injection of solutions of emetine into *cancer* will cause a complete microscopic disappearance of the growth but these effects seem to be purely those of a caustic and not due to any specific action of the drug upon the tumor.

Large doses of emetine, when injected subcutaneously or intravenously, cause death by a depressant action upon the heart muscle but this effect probably does not come into consideration in its therapeutic employment. Pellini and Wallace (*A. J. M. S.,* 1916, xvii, 420) have found that the administration of large doses of emetine causes a profound disturbance of metabolism—characterized by an increase in the output of nitrogen and the appearance of acidosis accompanied by a marked irritation of the alimentary canal. Kilgore and Liu (*A. In. M.,* 1917, xx, 178) have found uniformly that in dogs toxic doses of emetine lead to hemorhagic enteritis and also hemorrhages in the liver, spleen and kidney. A number of observers have noted that toxic effects will follow from the daily exhibition of comparatively small doses if continued for a long enough period of time. Dalimier (*Press. Med.,* 1917, xxv, 33) concludes that it is dangerous to give a total dose of more than 1 Gm. (16 grains) within a period of two weeks. According to Mappai (*B. Hôp. Par.,* 1920, xliv, 531), this accumulative toxicity of emetine is due to the fact that it is eliminated in an irregular or intermittent manner. The elimination of emetine—as has been shown by Guglielmetti (*Prensa Medica,* Argentina, 1917, iv, p. 20) is entirely through the alimentary canal and the liver.

A large number of cases of poisoning by emetine have been observed in human beings. The most constant symptom has been a bloody diarrhea. Levy and Rowntree (*A. I. M.,* 1916, xvii, 420) have reported acute kidney failure with acidosis; Johnson and Murphy (*P. J.,* 1917, xcviii, p. 139), two cases of pneumonic consolidation of the lung, apparently caused by emetine. Although we do not know of any fatality from a single dose several deaths from its repeated use have been reported; the smallest lethal amount with which we are familiar is 1.74 Gm. given in 19 days.

In the administration of emetine in dysentery it seems to be a matter of no great difference, either from the therapeutic or toxicological standpoint, whether the daily dose be administered in one, two, or three portions. To give it more frequently, however, exposes the patient to unnecessary discomfort, as the injections are quite painful.

The ordinary *dose* for the adult is from ½ to 1 grain daily (0.03 to 0.065 Gm.), but its use should not be continued for more than two weeks without interruption.

EMPLASTRA.

PLASTERS

Emplâtres, *Fr.;* Pflaster, *G.;* Empiastri, *It.;* Emplastos, *Sp.*

Plasters are solid preparations intended for external application, adhesive to the skin at the temperature of the human body, and of such a consistence as to render the aid of heat necessary in spreading them Spread plasters are known as *sparadraps* (*Emplastra Extensa,* Fr. Cod.). Of recent years those having rubber in their composition are most largely used; they are usually perforated. Some plasters have as their basis a compound of olive oil and litharge. Others owe their consistence and adhesiveness to resinous substances, or to a mixture of these with wax and fats.

In the preparation of the plasters, care is requisite that the heat employed be not sufficiently elevated to produce decomposition, nor so long continued as to drive off any volatile ingredient upon which the virtues of the preparation may in any degree depend. After having been prepared, they are usually shaped into cylindrical rolls, and wrapped in paper to exclude the air. Plasters should be firm at ordinary temperatures, should spread easily when heated, and, after being spread, should remain soft, pliable, and adhesive, without melting, at the heat of the human body. When long kept, they are apt to change color and to become hard and brittle, and, as this alteration is most observable upon their surface, it must depend chiefly upon the action of the air, which should therefore be excluded as much as possible. The defect may usually be remedied by melting the plaster with a moderate heat and adding a sufficient quantity of oil to give it the proper consistence.

The spreading of plasters has become to a great extent a lost art to the pharmacists of this country, owing to the introduction of machine-spread plasters, which contain India-rubber in the adhesive composition. These are reasonably permanent, and do not require the application of heat. The perforation, or "porousing," of plasters is usually accomplished on a large scale by expensive apparatus.

Edmondson read a paper before the Pennsylvania Pharmaceutical Association in 1887 giving the process for manufacturing rubber-mass plasters on the large scale as follows: The principal ingredients employed are rubber, Burgundy pitch, gum olibanum, galbanum and orris root, with waxes or fats as excipients. The crude rubber is at first steeped in hot water, to cleanse and soften it, then the rubber is passed through the washer and crusher, where it is subjected to severe pressure between two corrugated rolls, eight inches in diameter and one foot wide, while a stream of water falling continually washes it thoroughly, and it comes out in sheets somewhat softened. After these sheets are dried, which requires a number of days, they are passed through the grinder, where they are crushed between two smooth rollers, fourteen inches in diameter and thirty-six inches across. This thoroughly softens the rubber and makes it plastic, so that it can be readily worked up with the other ingredients. The principal operation, the mixing, then takes place. The medication must be carefully combined, and the whole manipulation so managed that the plaster will be uniform, so that age or varying temperature shall not affect it. This operation is performed by means of rollers, sixteen inches in diameter, arranged so that one revolves at twice the speed of the other. Between these large rollers the mass is passed with whatever medication is required: *e. g.*, when a belladonna mass is to be made, a certain amount of the stock mass is taken and extract of belladonna in the proportions corresponding to the formula in the Pharmacopœia. These are repeatedly passed through the rollers until the extract of belladonna is thoroughly mixed with the mass, care being taken to keep the temperature from rising high enough to decompose or affect the alkaloids. The spreading is also done by rollers, into which the thoroughly mixed mass is fed at the same time that the cloth is fed, the thickness of the plasters being governed by the adjusting of screws on the side of the machine.

The rubber base is pliable, adhesive, it will not become too hard or too soft, but will yield up the medication to the absorbents of the skin, and its properties will be retained indefinitely. For formulas for plasters of former Pharmacopœias, see *U. S. D.*, 19th edition, p. 436 and for information concerning the extemporaneous spreading of plasters see *U. S. D.*, 20th edition, p. 413. The removal of plasters, either plain or medicated from the skin my be readily accomplished by moistening the back of the plaster slightly with ether, benzin or some other immiscible solvent, or by the use of a small amount of alcohol (medicated or denatured) which is allowed to flow under the plaster a few drops at a time beginning at one corner or edge of the plaster which may be slightly raised before applying the solvent.

Plasters which have lost their adhesiveness and have become brittle may be restored, according to K. Dieterich, by exposing them to the vapors of petroleum benzin for several days.

EMPLASTRUM ADHÆSIVUM. U. S.

ADHESIVE PLASTER Emp. Adhæs. [Emplastrum Elasticum, U. S. P. IX, Rubber Adhesive Plaster]

"A mixture of rubber, resins, and waxes, with a filler of an absorbent powder, such as zinc oxide, orris root, or starch, mechanically mixed and spread upon cotton cloth." *U. S.*

The term adhesive plaster was originally applied to the lead-base type of plaster (see *Emplastrum Resinæ*) which is still sold in several proprietary forms.

Sparadrapum Adhæsivum; Emplastrum Gummi Elastici; Emplatre Caoutchoute Simple, *Fr. Cod.;* Collemplastrum, *P. G.;* Esparadrapo Adhesivo de Caucho, *Sp.*

"The plaster mass should contain about 30 per cent. of pure rubber. When zinc oxide is used, it should represent at least 20 per cent. of the plaster mass. The mass must be free from nodules and spread evenly on a cotton fabric backing, having not less than 62 threads to each square cm., each piece of 100 square cm. weighing not less than 1.18 Gm. One hundred square cm. of the plaster should contain not less than 1.50 Gm. of the plaster mass. A strip of the plaster 5 cm. by 6.5 cm., applied to a hard wood surface for thirty minutes at a constant temperature of 37° C., should resist a tension of not less than 40 pounds when applied by a tensile strength machine or other suitable device, the pull being exerted parallel with the warp and with the longer dimension of the plaster." *U. S.*

Adhesive plaster should be applied at the body temperature. If properly preserved it will retain its adhesiveness for long periods. It should be protected from the effects of atmosphere by being wrapped in tin-foil or waxed paper; in the modern spools, or rolls, the outer layer affords a considerable degree of protection to the deeper ones.

Uses.—The uses of this popular substance are so numerous and various as to defy classification. Thus the surgeon utilizes it to immobilize various parts of the body, as in *sprains* and *strains;* to approximate the lips of *wounds;* to afford support in certain types of relaxations; to hold dressings in place; to make temporary repairs to various instruments and appliances, etc. In acute *pleurisy* or *pneumonia,* strapping the chest will often greatly assuage the pain, by preventing movement between the inflamed pleural surfaces. There is a general preference for those plasters which contain zinc oxide because of a common belief that they are less likely to irritate the skin, but even these, in sensitive individuals, may cause a very troublesome dermatitis.

Distinctive types of adhesive plaster—differing usually in the kind of cloth on which they are spread—intended for special uses by athletes, chiropodists, etc., are extensively employed.

EMPLASTRUM BELLADONNÆ. U. S., Br.

BELLADONNA PLASTER Emp. Bellad.

"Belladonna Plaster contains extract of belladonna corresponding to not less than 0.25 per cent. and not more than 0.30 per cent. of the alkaloids of belladonna leaves." *U. S.*

Emplâtre de Belladone, *Fr.;* Belladonna-Pflaster, *G.;* Emplasto de belladonna, *Sp.*

"Liquid Extract of Belladonna, 50.0 *millilitres;* Resin Plaster, 137.5 *grammes.* Concentrate the Liquid Extract of Belladonna by evaporation at a low temperature until it is reduced in weight to *twelve and a half grammes;* add the Resin Plaster, previously melted; mix. This Plaster contains 0.25 per cent. of the alkaloids of Belladonna Root, and is of one-half the strength of the Emplastrum Belladonnæ of the British Pharmacopœia, 1898," *Br.*

No process is given in the U. S. P. for making belladonna plaster. It is now made almost exclusively with a rubber base by manufacturers on a large scale.

Assay.—"Introduce 10 Gm. of Belladonna Plaster into a 100 cc. flask. (If the plaster is spread on fabric, cut the portion to be assayed into strips, weigh accurately, and introduce it into the flask.) Now add 50 cc. of chloroform, and shake the mixture until the plaster is dissolved. Pour the chloroform solution into a 250 cc. beaker, and wash the cloth upon which the plaster was spread with two successive portion of 25 cc. each of chloroform, adding the washings to the chloroform solution in the beaker. Then wash this cloth with 80 cc. of alcohol containing 1 cc. of ammonia T.S., and pour the washings into the chloroform solution in the beaker. Stir the mixture gently, and allow it to stand until the rubber has separated into a compact mass. Dry the cloth upon which the plaster was spread, weigh it, and subtract its weight from the first weight of the plaster. Pour the chloroform-alcohol solution into a 250 cc. separator, rinse the beaker and rubber with 10 cc. of alcohol, and add the rinsing to the separator. Completely extract the alkaloids from the chloroform-alcohol solution by shaking out repeatedly with weak sulphuric acid. Collect the acid washings in a separator, and add ammonia T.S. until the solution is decidedly alkaline to litmus paper, and completely extract the alkaloids by shaking out repeatedly with chloroform. Filter the chloroform solution through a pledget of purified cotton, evaporate it to dryness and dissolve the alkaloids from the residue in exactly 5 cc. of tenth-normal sulphuric acid, and titrate the excess of acid with fiftieth-normal potassium hydroxide. Each cc. of tenth-normal sulphuric acid corresponds to 0.02893 Gm. of the alkaloids of belladonna leaves (Proximate Assays)." *U. S.*

Uses.—Although belladonna plaster is a very widely used preparation it is essentially an irrational one. At times, sufficient of the active principle will be absorbed through the skin to produce constitutional symptoms. It is manifestly an uncertain and unsatisfactory mode of obtaining the general effects of belladonna and is never employed for this purpose. It is used purely as a local anodyne in *lumbago* and other *myalgias.* But atropine has comparatively feeble effects upon the sensory nerves. Moreover, in this type of inflammations the tissues involved are too deep-seated to expect to reach them directly by external applications. Such benefit as has followed the employment of belladonna plaster is due rather to the fixation to the parts of the plaster than to any action of the belladonna. A very popular type of belladonna plaster is one in which capsicum is also present. *Extract* of scopola was formerly largely used by manufacturers in making rubber-base belladonna plaster.

EMPLASTRUM CALEFACIENS. Br.

WARMING PLASTER

Emplastrum Picis Cantharidatum, *U. S.* 1890; Warm Plaster; Emplâtre de Poix cantharide, *Fr.;* Pechpflaster mit Canthariden, *G.*

"Cantharidin, 0.2 *gramme;* Chloroform, 20.0 *millilitres;* Olive Oil, 40.0 *millilitres;* Resin Plaster, 940.0 *grammes.* Dissolve the Cantharidin in the Chloroform, add the Olive Oil, and mix with the Resin Plaster, previously melted on a water bath. This Plaster contains 0.02 per cent. of Cantharidin, which is approximately the proportion contained in the Emplastrum Calefaciens of the British Pharmacopœia, 1898." *Br.*

Cantharidal pitch plaster or warming plaster is not official in the U. S. P. IX; the process of the U. S. P., 1890, will be found on p. 439, *U. S. D.,* 19th edition. The use of the blistering principle cantharidin dissolved in chloroform and olive oil will undoubtedly prove to be an improvement over the older process.

This plaster is an excellent rubefacient, more active than Burgundy pitch, yet in general not sufficiently so to produce vesication.

Warming plaster is employed in *chronic rheumatism,* and in chronic internal diseases attended with inflammation, such as *catarrh, asthma, pertussis, phthisis, hepatitis,* and the sequelæ of *pleurisy* and *pneumonia.*

EMPLASTRUM CANTHARIDIS. U. S.

CANTHARIDES PLASTER Emp. Canthar.

Fly Blister; Sparadrapum Cantharidis; Emplastrum Vesicans Extensum, Sparadrape Vesicant, *Fr. Cod.*

"Cantharides Cerate, Adhesive Plaster, spread on fabric, each, a sufficient quantity. Spread cantharides cerate upon the plaster, leaving a margin around the edges. It may also be spread on muslin, paper, or other suitable material. Each square cm. of spread plaster should contain 0.1 Gm. of cantharides cerate." *U. S.*

For formula of the British *Emplastrum Cantharidini* see under *Ceratum Cantharidis.*

Uses.—Cantharides plaster is used for the purpose of producing vesication in various deep-seated inflammations (see under *Cantharis*). It is at once the most certain and most convenient mode of obtaining the effects of Cantharides. In adults, when the full action of the flies is desired, and the object is to produce a permanent effect, the applications should be continued for eight hours. In very delicate persons, however, or those subject to strangury, or upon parts of a loose texture, or when the object is merely to produce a blister to be healed as quickly as possible, the plaster should remain no longer than is necessary for the production of full redness of the skin, which generally occurs in five or six hours, or even in a shorter time. It should then be removed, and followed by a flaxseed poultice, or some other emollient dressing, under which the cuticle rises, and a full blister is usually produced. By this management the patient will generally escape strangury, and the blister will very quickly heal after the discharge of the serum. In young children, cantharides sometimes produce alarming and even fatal ulceration, if too long applied, and from two to four hours are usually sufficient for any desirable purpose. When the head, or other hairy part, is to be blistered, an interval of ten or twelve hours should, if possible, be allowed between the shaving of the part and the application of the plaster, so that the abrasions may heal, and some impediment be offered to the absorption of the cantharidin. After the blister has been formed, it should be opened at the most depending parts, the cuticle being allowed to remain, and should be dressed with simple cerate; but, if it be desirable to maintain the discharge for a short time, rosin cerate should be used, and the cuticle removed if it can be done without inconvenience. When it is wished that the blistered surface should heal as soon as possible, the application of an antiseptic desiccant powder, as iodoform or thymol iodide, is advantageous.

Various preparations of cantharides have been proposed and employed as substitutes for the cerate. They consist for the most part of cantharidin, more or less pure, either dissolved in olive oil, and applied to the skin by means of a piece of paper saturated with it, or incorporated with wax and spread in a very thin layer upon fine waxed cloth, silk, or paper, constituting *blistering cloth, blistering paper, vesicating taffeta,* etc. Since the recognition of an official spread plaster these preparations have been largely abandoned. For some of the formulas employed see *U. S. D.,* 20th ed., p. 314.

EMPLASTRUM CAPSICI. U. S.

CAPSICUM PLASTER Emp. Capsic.

"Capsicum Plaster contains not less than 0.25 Gm. of oleoresin of capsicum in each 15 square cm." *U. S.*

Sparadrapum Capsici; Sparadrap de Capsique, *Fr.;* Capsicumpflaster, *G.*

The present pharmacopœia gives no process for this plaster as it is usually made by machinery. The formula of the U. S. IX was as follows: "Oleoresin of Capsicum, Rubber Plaster—spread on fabric—of each, a sufficient quantity. Apply Oleoresin of Capsicum to the surface of the rubber plaster so as to leave a margin around the edges. Each fifteen square centimeters of spread plaster contains 0.25 Gm. of oleoresin of capsicum." *U. S. IX.*

The oleoresin should be laid on very evenly with a camel's-hair brush.

EMPLASTRUM HYDRARGYRI. Br.

MERCURIAL PLASTER

Emplastrum Mercuriale; Emplâtre mercuriel, *Fr. Cod.;* Emplastrum Hydrargyri, *P. G.;* Quecksilberpflaster, *G.;* Empiastro mercuriale, *It.;* Emplasto Mercurial Simple, *Sp.*

"Mercury, 328 *grammes;* Olive Oil, 18 *grammes;* Sublimed Sulphur, 2 *grammes;* Lead Plaster, 652 *grammes.* Heat the Olive Oil with the Sulphur until a reddish-brown liquid is obtained; with this solution triturate the Mercury until metallic globules are no longer visible; add the Lead Plaster, previously melted; mix." *Br.*

Mercurial plaster is no longer official in the U. S. P. The U. S. Pharm. VIII employed oleate of mercury and hydrous wool-fat for the purpose of extinguishing the mercury; this it does effectually, and at the same time increases the efficiency of the mercurial constituent. The quantity of mercury was 30 per cent. The British preparation is stronger, containing 32.8 per cent. For methods of assaying this plaster, see *A. J. P.,* 1911, p. 314; *C. D.,* 1911, p. 631; *P. J.,* 1911, p. 654.

Uses.—This plaster is employed to produce the local effects of mercury upon *syphilitic* lesions of the skin and other chronic tumefactions of the bones or soft parts, dependent on a syphilitic taint. It occasionally affects the gums.

It has been asserted by Serres and others that the mercurial plaster of the Codex (*Emplastrum* (*Emplâtre*) *de Vigo cum Mercurio,* see *U. S. D.,* 19th edition, p. 440) has the power, when applied over the eruption of *small pox,* before the end of the third day from its first appearance, to check its progress and prevent suppuration and pitting. This operation of the plaster, so far from being attended with an increase of the general symptoms, seems to relieve them in proportion to the diminution of the local affection. It is probable that other mercurial preparations would answer the same purpose.

EMPLASTRUM MENTHOL. Br.

MENTHOL PLASTER

Emplâtre de Menthol, *Fr.;* Mentholpflaster, *G.*

"Menthol, 150 *grammes;* Yellow Beeswax, 100 *grammes;* Resin, 750 *grammes.* Melt the Beeswax and Resin together; when the mixture has cooled to about 70° C., add the Menthol, and stir until dissolved." *Br.*

This plaster is a mild counter-irritant, intended especially for relief in localized *neuralgia* and *rheumatic pains.*

EMPLASTRUM PLUMBI OLEATIS.

U. S. (Br.)

LEAD OLEATE PLASTER Emp. Plumb. Oleat. [Emplastrum Plumbi, U. S. P. IX, Lead Plaster, Diachylon Plaster]

Emplastrum Plumbi, *Br.;* Emplastrum Lithargyri, *Br.* 1864; Emplastrum Diachylon Simplex, Emplastrum Album Coctum; Litharge Plaster; Emplâtre simple, *Fr. Cod.;* Emplâtre de Plomb (de Litharge), Emplastrum simplex, *Fr.;* Emplastrum Lithargyri (simplex), *P. G.;* Emplastrum Cerusæ, Froschlaichpflaster; Bleipflaster, Diachylonpflaster, Gummipflaster, *G.;* Empiastro diachilon, *It.;* Emplasto de plomo simple, Emplasto simple, *Sp.*

"Lead Monoxide, 1000 Gm.; Olive Oil, 1000 Gm.; Lard, 1000 Gm.; Boiling Water, a sufficient quantity. Heat the olive oil and lard by a gentle heat until liquefied, in a bright copper or other suitable vessel of a capacity of not less than four times the bulk of the ingredients, sift the lead monoxide through a fine sieve, upon the surface of the hot liquid, and mix thoroughly. Then gradually add 350 cc. of boiling water, and boil the mixture, constantly stirring with a wooden spatula, and adding sufficient boiling water from time to time to replace that lost by evaporation, until the mass is homogeneous and a small portion removed and dipped into cold water is found to be pliable and tenacious. Then remove it from the fire, and wash several times with warm water to remove the glycerin. Finally knead the mass until it is free from water, roll it into cylinders of suitable size, and krap them in paper." *U. S.*

"Lead Oxide, 400 *grammes;* Olive Oil, 800 *grammes;* Distilled Water, 400 *millilitres,* or a *sufficient quantity.* Boil gently together in a steam-bath, stirring constantly until combination has been effected. When cool remove the plaster-like mass produced; knead it thoroughly with hot water, and allow it to dry." *Br.*

In the U. S. VIII an innovation in the preparation of this plaster was introduced. It was directed to be made by the precipitation produced between solutions of soap (sodium oleate) and lead acetate instead of by the time-honored method of boiling litharge, olive oil, and water together. The resulting product was chemically nearly identical with that made by the boiling process and much whiter in color, but experience proved that the precipitation method produced a plaster which does not keep as well as did the plaster made in the old way, hence the U. S. has returned to the former process, although the olive oil is partially replaced by lard.

The reaction in the U. S. P. VIII process, disregarding the palmitin present, was as follows:

$$\underset{\text{Sodium oleate}}{2NaC_{18}H_{33}O_2} + \underset{\text{Lead acetate}}{Pb(C_2H_3O_2)_2} = \underset{\text{Lead oleate}}{Pb(C_{18}H_{33}O_2)_2} + \underset{\text{Sodium acetate}}{2NaC_2H_3O_2}$$

In the U. S. X and the British process a reaction takes place expressed approximately by the following reaction:

$$\underset{\text{Olein}}{2C_3H_5(C_{18}H_{33}O_2)_3} + \underset{\text{Litharge}}{3PbO} + \underset{\text{Water}}{3H_2O} = \underset{\text{Lead oleate}}{3Pb(C_{18}H_{33}O_2)_2} + \underset{\text{Glycerin}}{2C_3H_5(OH)_3}$$

Other oleaginous substances and other metallic oxides are susceptible of the same combination, and some of them form compounds having the consistence of a plaster; but, according to Henry, of Paris, no oily matter except animal fat can properly be substituted for olive oil, and no metallic oxide, not even one of the other oxides of lead, for litharge. The British process does not provide for the separation of the glycerin and the plaster is not kneaded to separate the water, both of which, in our opinion, are necessary to produce the best result and which form part of the U. S. P. process.

The following description gives an outline of the method used in the large-scale manufacture: The vessel in which the lead plaster is prepared should be of such a size that the materials will not occupy more than two-thirds of its capacity. The oil should be first introduced, and the litharge then sprinkled in by means of a sieve, the mixture being constantly stirred with a spatula. The particles of the oxide are thus prevented from coalescing in small masses, which the oil would not easily penetrate, and which would, therefore, delay the process. While the water exerts an important chemical agency in the changes which occur, it is also useful by preventing too high a temperature, which would decompose the oil, and cause the reduction of the oxide. The waste must, therefore, be supplied by fresh additions as directed in the process, and the water added for this purpose should be previously heated, as otherwise it would not only delay the operation, but by producing explosion might endanger the operator.

During the continuance of the boiling, the material should be constantly stirred, and the spatula should be repeatedly passed along the bottom of the vessel, from side to side so as to prevent any of the oxide, which is disposed by its greater density to sink to the bottom, from remaining in that situation. The materials swell up considerably, in consequence partly of the vaporization of the water, partly of the escape of carbon dioxide, which is liberated by the fatty acids from traces of lead carbonate sometimes contained in the litharge. The process should not be continued longer than is sufficient to produce complete union of the ingredients, and this may be known by the color and consistence of the mass. The color of the litharge gradually becomes paler, and at length almost white when the plaster is fully formed. The consistence increases with the progress of the boiling, and is sufficiently thick when a portion of the plaster, taken out and allowed to cool upon the end of a spatula, or thrown into cold water, becomes solid, without adhering in this state to the fingers. The portion thus solidified should not present, when broken, any red spots, which would indicate the presence of a portion of uncombined litharge. When the plaster is formed, it should be removed from the fire, and after a short time cold water should be poured upon it. Portions should then be detached from the mass, and, having been well kneaded under water, in order to separate the viscid solution of glycerin contained in the interior, should be formed into cylindrical rolls, and wrapped in paper. Such, at least, has been the course of proceeding usually recommended. But Davallon maintains that the presence of glycerin in the plaster is useful by keeping it in a plastic state, and that washing and kneading are injurious, the former by removing the glycerin, the latter by introducing particles of air and moisture into the mass, which is thus rendered more disposed to rancidity. By employing steam heat in the preparation of this plaster, the risk of burning it is avoided. Bernbeck found that lead plaster could be preserved from hardening and oxidation if kept in air tight canisters. (*Ph. Ztg.*, 1881, p. 589.)

Zinc Plaster.—De Mussey, having witnessed inconveniences from lead plaster in consequence of the absorption of the lead, substituted for it a plaster with a basis of zinc oxide, which he has found to answer very well in practice. It cannot be made by direct combination of the oxide, and it is necessary to have recourse to the method of double decomposition. Solutions of white olive oil soap and of zinc sulphate being mixed, a copious precipitate takes place of zinc oleopalmitate, which, after being washed and dried, may be combined with resins, oil, and wax, to give it the necessary consistence.

Uses.—This plaster, which has long been known under the name of *diachylon,* is used as an application to excoriated surfaces and to slight wounds, which it serves to protect from the action of the air. It may also be beneficial by the sedative influence of the lead which enters into its composition. A case is on record in which lead colic resulted from its long continued application to a large ulcer of the leg. (*Am. J. M. S.*, xxiii, 246.) Its chief use is in the preparation of other plasters. See *Logan's Plaster, Mahy's Plaster, U. S. D.*, 19th edition, p. 443.

Off. Prep.—Emplastrum Resinæ, *U. S., Br.;* Emplastrum Hydrargyri, *Br.;* Emplastrum Saponis, *N. F., Br.;* Unguentum Diachylon, *U. S.*

EMPLASTRUM RESINÆ. Br.

ROSIN PLASTER Emp. Res. [Rosin Adhesive Plaster, Adhesive Plaster]

Resin Plaster, *Br.;* Resin Adhesive Plaster; Emplâtre Adhésif, Emplâtre Résineux, *Fr.;* Emplastrum adhæsivum, *P. G.;* Heftpflaster, *G.;* Emplastro adesivo, *It.*

"Resin, 100 *grammes;* Lead Plaster, 850 *grammes;* Hard Soap, 50 *grammes.* Melt each ingredient separately at as low a temperature as possible; mix." *Br.*

Resin plaster was dropped at the Tenth Revision of the U. S. Pharmacopœia. It differs from lead plaster in being more adhesive and somewhat more stimulating. The soap is added to give it greater pliability, and render it less liable to crack in cold weather, without impairing its adhesiveness. It is usually spread upon muslin, and the spreading is best accomplished, on a large scale, by means of a machine, as described in the general observations upon plasters. It is kept ready spread by the pharmacist; but, as the plaster becomes less adhesive by long exposure to the air, the supply should be frequently renewed.

As an adhesive plaster this has been almost completely displaced by plasters made with a rubber base. (See *Emplastrum adhæsivum.*) It is used only as a base for applying more active drugs to the skin.

EMPLASTRUM SAPONIS. Br.

SOAP PLASTER

Emplâtre de Savon, *Fr. Cod.;* Emplastrum cum Sapone, *Fr.;* Emplastrum Saponatum, *P. G.;* Seifenpflaster, *G.;* Emplasto de jabon, *Sp.*

"Hard Soap, 140 *grammes;* Lead Plaster, 835 *grammes;* Resin, 25 *grammes.* Melt each ingredient separately at a low temperature; mix; evaporate, with constant stirring, to a proper consistence." *Br.*

Soap plaster is not recognized by the U. S.; a preparation similar to, but not identical with, the British is in the National Formulary.

Soap plaster is considered discutient, and is sometimes used as an application to tumors, where a dressing is required. Somewhat softer in its character, the *soap cerate,* formerly official, may be found useful. This was made as follows: *Ceratum Saponis.* "Take of Soap Plaster *two troyounces;* White Wax *two troyounces and a half;* Olive Oil *four troyounces.* Melt together the Plaster and Wax, add the Oil, and, after continuing the heat a short time, stir the mixture until cool." *U. S.*, 1870.

EMPLASTRUM SINAPIS. U. S.

MUSTARD PLASTER Emp. Sinap. [Mustard Paper]

"A uniform mixture of powdered black mustard (deprived of its fixed oils), and a solution of rubber, spread on paper, cotton cloth or other fabric. Each 100 square centimeters contains not less than 2.5 Gm. of black mustard deprived of its fixed oil." *U. S.*

Charta Sinapis, *U. S. VIII;* Mustard Paper; Mustard Leaves; Sinapisme en feuille, *Fr. Cod.;* Papier Moutarde, Papier Sinapisé, *Fr.;* Charta sinapisata, *P. G.;* Senf-papier, *G.;* Carta senapata, *It.;* Papel sinapico, Charta sinapica, *Sp.*

The present Pharmacopœia gives no process for this plaster. That formerly official was as follows:

"Black Mustard, in No. 60 powder, *one hundred grammes;* Rubber, *ten grammes;* Petroleum Benzin, Carbon Disulphide, each, a *sufficient quantity.* Pack the Black Mustard in a conical percolator, and gradually pour Petroleum Benzin upon it until the percolate ceases to produce a permanent, greasy stain upon blotting paper. Remove the powder from the percolator, and dry it by exposure to the air. Having meanwhile dissolved the Rubber in a mixture of *one hundred cubic centimeters,* each, of Petroleum Benzin and Carbon Disulphide, mix the purified Mustard with a sufficient quantity of the solution to produce a semi-liquid magma, and apply this, by means of a suitable brush, to one side of a piece of rather thick, well-sized paper, so as to cover it completely, and then allow the surface to dry. A surface of sixty square centimeters should contain about 4 Gm. of Black Mustard deprived of oil. Before it is applied to the skin, Mustard Paper should be dipped in warm water for about fifteen seconds." *U. S. VIII.*

"When moistened thoroughly with tepid water and applied to the skin, the Plaster produces a decided warmth and reddening of the skin within five minutes. Preserve in tightly-closed containers.

"Before Mustard Plaster is applied, moisten it thoroughly with tepid water." *U. S.*

Solution of gutta-percha is unsuited for use in this preparation, on account of want of adhesiveness, and the tendency of the mixture, when dry, to crack and peel off. We have used instead a solution of 1 part of pure rubber in 30 of equal parts of carbon disulphide and petroleum benzin. On the large scale, by means of a plaster spreading apparatus a uniform coat of this solution may be applied to paper. As the latter passes out from under the apparatus, a sieve containing the powdered mustard is shaken over it; this is fixed by the adhesive coat and firmly retained after the evaporation of the volatile liquids in a warm place. The application of the powdered mustard must be properly regulated according to the speed with which the machine delivers the coated paper. The paper is cut into pieces of convenient size, and needs only to be wetted with tepid water to be ready for use. Owing to the fact that the large manufacturers can put mustard paper upon the market at such low rates that it pays the apothecary better to buy than to prepare it, and it is rarely made in the retail stores.

Mustard plaster is especially subject to deteriorating influences. It should never be exposed to a damp atmosphere for any length of time before using. Commercial mustard plasters are available spread either upon cloth or upon paper. They should be kept in well-closed containers.

Uses.—For the uses of the mustard plaster, see *Sinapis.*

Experience has shown that the ready-made mustard papers err rather from too much than from too little activity. Moreover, their action cannot be regulated with the same nicety as can that of the mustard poultice. Unless in the case of travellers, and of others who must wait upon themselves, the domestic application is preferable. The *mustard leaves* can rarely be borne for more than fifteen minutes.

EMULSA.

EMULSIONS

Emulsions, *Fr.;* Emulsiones, *G.;* Emulsiones, *It., Sp.*

Under this head are included in the U. S. Pharmacopœia liquid preparations in which oleaginous substances are suspended in aqueous fluids by the intervention of gum or other viscid matter. The preparations forming the present class of emulsions were termed Mixtures in earlier pharmacopœias, and it is to be regretted that under this indefinite term are still grouped liquids of many kinds; the separation of these into proper classes is only a question of time, and the introduction of this new class into the Pharmacopœia of 1890 marked the first step in the direction of greater accuracy in defining pharmaceutical preparations, and more system in classification. The object of emulsions is usually to facilitate the administration, to conceal the taste, or to obviate the nauseating effects of unpleasant medicines, and their perfection depends upon the intimacy with which the ingredients are blended. Some skill and care are requisite for the production of uniform and perfect emulsions. As a rule, the body to be suspended should be thoroughly mixed by trituration with the substance intended to act as the intermedium, before the aqueous vehicle is added. In the case of the liquid balsams and oils, if gum arabic is employed as the intermedium it should be previously brought to the state of mucilage of the consistence directed in the U. S. Pharmacopœia. When a fixed oil, oleoresin, or balsam is to be made into an emulsion, the method most employed abroad is to add one part of gum to two or three of the oil, in a mortar, triturate until the mixture is complete, and then add at once twice as much water as gum used, and triturate rapidly until the oil is completely emulsified, then gradually add the remainder of the vehicle with constant trituration. Agitation in a bottle is sometimes substituted for trituration. Another plan which is frequently used, especially in the preparation of emulsions extemporaneously is to make the emulsion with mucilage. Having a broad flat pestle and a mortar perfectly free from grease, put in a little mucilage, rub it around the mortar, add about half as much oil, triturate from the center so as to emulsify this, then add more mucilage, then oil, and so on until the operation is completed. Care is required never to get the oil in excess of the mucilage. This plan seems to accord with the principle laid down by R. Rother, that the most perfect and rapid emulsifier is a perfect emulsion.

The proportion of gum and water necessary to make a good emulsion with the fixed oils varies with the oil. Thus, while castor oil requires only two drachms of the gum and three drachms of water to the ounce, most other fixed oils require half their weight of gum, and a weight of water equal to half that of the oil and gum united. These quantities being well rubbed together, any desirable amount of water may afterwards be gradually added, and will readily incorporate with the other ingredients. The white of egg has been sometimes used as the suspending substance, but it is inferior for this purpose to the yolk, or to gum arabic. When volatile oils are to be emulsified it is an advantage to mix them with an equal volume of inert fixed oil to promote stability. Soap is valuable as an emulsifying agent for some purposes. Quillaja, saponin, and other substances having similar properties have been proposed as emulsifying agents, but they are objectionable on account of their medicinal activity. Emulsifying agents should be inert.

Leo Roon (*J. A. Ph. A.*, 1916, v, 496) gives an extensive review of the literature on emulsification and Roon and Oesper have made an important contribution to the theory of emulsification (*J. I. E. C.*, 1917, p. 156). The authors agree with Fischer (*Science*, 1916, p. 468) that emulsification is due to, or accompanied by, the formation of a hydrated colloid compound. Both the English and Continental methods of emulsification were studied carefully. The unsatisfactory results obtained by the majority of workers with the English method, are alleged to be due to the fact that the hydration of the emulsifying agent occurs progressively and not all at one time and for the greater part is not accomplished in the presence of the internal phase (oil). In the Continental method all of the emulsifying agent (colloid) is hydrated at one time and in the presence of the internal phase (oil). After experimenting with various proportions of materials, it is stated by the authors that the best and quickest results are obtained by the use of the following proportions in the preparation of the original nucleus: oil 4, water 3, gum 2.

Experimental emulsions were produced of the following substances: hexane, sp. gr. 0.691; chloroform, sp. gr. 1.526; carbon tetrachloride, sp. gr. 1.597; benzene, sp. gr. 0.877; oil of turpentine, sp. gr. 0.85; mineral oil, sp. gr. 0.853; cottonseed oil, sp. gr. 0.921. Gum emulsions and soap emulsions were made of all these and the conclusions, in part, were as follows: 1. The presence of a hydrated colloid is necessary for emulsification. 2. This hydration compound is most efficiently used if formed at the moment of dispersion of the internal phase—in other words, the three constituents, internal phase, emulsifier and water, in critical proportions, must all be mixed at one time in order to form a properly hydrated nucleus. 3. Slight variations from the proper procedure or from the critical proportions yield either less stable emulsions or none at all. 4. No emulsion results if the emulsifier is diluted before the dispersion of the internal phase.

When two liquids are emulsified together the question often arises which is the internal phase, which the dispersion medium. It is usually the case that when one liquid is in considerable excess, it becomes the dispersion medium, but this does not always follow. In the nomenclature of emulsions the first term in the compound title always indicates the dispersed (internal) phase. Thus a water-oil emulsion is one in which oil is suspended in water, an oil-water emulsion is one in which the reverse condition obtains. Carron oil is an example of the oil-water type of emulsion and cod liver oil emulsion of the water-oil type.

An excellent review of the theories of emulsification is given by W. Clayton in *J. Soc. Chem. Ind.*, 1919.

EMULSUM ASAFŒTIDÆ. U. S.

EMULSION OF ASAFETIDA Emuls. Asafœt. [Milk of Asafœtida]

Asafetida Mixture; Mistura (Lac) Asafœtidæ, Mistura Asafœtida, *U. S. P.* 1880; Mixture (Lait) d'Asafœtida, *Fr.;* Asafœtidaemulsion, Stinkasantmilch, *G.*

"Asafetida, in tears or selected masses, 40 Gm.; Water, a sufficient quantity of make 1000 cc. Rub the asafetida in a mortar with 900 cc. of water, at first very gradually added, until a uniform emulsion results. Then strain the mixture into a graduated vessel, and rinse the mortar and strainer with enough water to make the product measure 1000 cc. Mix thoroughly." *U. S.*

This emulsion is less stimulant than the tincture, and more prompt in its action than the pill. Its excessively disagreeable odor and taste are, however, objections, which induce a frequent preference for the last mentioned preparation. It is very often employed as an enema. From two to four fluidounces (60–120 cc.) may be given by the rectum. D. Ackerman prepares a concentrated *emulsion of asafetida,* which will keep if excluded from the light, by using a mixture of three-fourths of pure water and one-fourth of diluted acetic acid as the menstruum. For cleaning mortars in which asafetida has been rubbed, he recommends solution of potassium hydroxide, followed by soap and water. The use of an oily meal, like linseed meal or almond meal, has been recommended for the same purpose.

Dose, one-half to one fluidounce (15–30 cc.).

EMULSUM OLEI MORRHUÆ. U. S.

EMULSION OF COD LIVER OIL Emuls. Ol. Morrh.

Emulsion de Huile de Foie de Morue, *Fr. Cod.;* Leberthranemulsion, *G.* Emulsio Olei Jecoris Aselli, *P. G.;* Emulsion de Accite ce Higado de Bacalao, *Sp.*

"Cod Liver Oil, 500 cc.; Acacia, in very fine powder, 125 Gm.; Syrup, 100 cc.; Methyl Salicylate, 4 cc; Water, a sufficient quantity, to make 1000 cc. Thoroughly mix the acacia with the cod liver oil in a dry mortar or other suitable vessel, then add at once 250 cc. of water, and complete the emulsification by trituration or by the aid of a suitable mechanical device. When a thick, white, homogeneous mixture is obtained, add the methyl salicylate and the syrup with sufficient water to make the product measure 1000 cc., and mix thoroughly. [NOTE.—The methyl salicylate may be replaced by a suitable quantity of any other flavoring.] This emulsion is intended to be freshly prepared as required. If it is to be kept for any length of time, 70 cc. of alcohol should be added, replacing a corresponding volume of water. The alcohol should be added last and in small portions, shaking after each addition." *U. S.*

This emulsion was introduced into the U. S. P. for the purpose of affording a simple process for making a reasonably palatable and permanent preparation of cod liver oil. The Continental method is best adapted for stock emulsions; to those who object to the taste of a combination of syrup and an oil with a fishy taste, the emulsion may be flavored with bruised celery seed and salt and then strained. A very palatable preparation of this type has been prepared in which the flavoring agents used were Worcestershire sauce and mustard. (See *Emulsum Olei Morrhuæ cum Hypophosphitibus,* N. F.) A comparison of various flavors for this emulsion was made by G. M. Beringer, Jr. (*Proc. N. J. Ph. A.,* 1914, p. 81), in which it is asserted that the best disguising flavors are those of coriander and geranium; next came anise and cardamom, then bitter almond, clove, pimenta and vanilla. Of inferior value in this respect were peppermint, spearmint, lemon, orange and cinnamon and least valuable of all were caraway, sassafras, wintergreen and nutmeg. An excellent emulsion is made with malt extract as the emulsifying agent (see *Emulsum Olei Morrhuæ cum Malto,* N. F., Part III). The N. F. includes a number of other emulsions of cod liver oil.

Under the name of *Black Bottle,* there has long been used in New England an emulsion of cod liver oil flavored with licorice and aromatic oils, the following formula for which was contributed to the *Apothecary,* 1913, p. 24, by R. A. Newton: Powdered Acacia, 13 dr.; cod liver oil, 6½ fl. oz.; flavoring oils, 15 min.; pure extract of licorice, 5 dr.; glycerin, 2½ fl. oz.; water, to make 1 pint. Prepare an emulsion.

The flavoring oil mixture is made as follows: Oil of cassia, 1 fl. oz.; oil of lavender, ½ fl. oz.; oil of clove, 1 fl. dr.; oil of peppermint, ½ fl. dr.; mix.

Dose, two to four fluidrachms (7.5–15 cc.).

EMULSUM OLEI TEREBINTHINÆ. U. S.

EMULSION OF OIL OF TURPENTINE
Emuls. Ol. Tereb.

Emulsion d'Essence de Térébenthine, *Fr.;* Terpentinölemulsion, *G.*

"Rectified Oil of Turpentine, 15 cc.; Acacia, in very fine powder, 5 Gm.; Water, a sufficient quantity, to make 100 cc. Place the powdered acacia in a dry bottle, add the oil of turpentine, mix thoroughly, add exactly 10 cc. of water, and agitate briskly until an emulsion forms. Then add sufficient water to make the product measure 100 cc. and mix thoroughly." *U. S.*

The present formula differs from that of the previous Pharmacopœia in the omission of the expressed oil of almond. This we believe to be unfortunate as the presence of the fixed oil not only tends to stabilize the emulsion but also renders the turpentine less irritant to the stomach. It might advantageously be reduced in strength much like the one recommended by J. Winchell Forbes, and a mortar and pestle are not needed to produce a perfect emulsion.

Dose, twenty to sixty minims (1.2–3.7 cc.).

EPINEPHRINA. U. S. (Br.)

EPINEPHRINE Epineph. [Lævo-Methylaminoethanolcatechol]

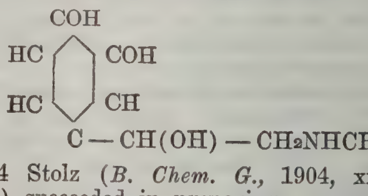
"$C_9H_{13}O_3N$." *U. S.*

"Adrenalin, or lævo-methylamino-ethanolcatechol, $C_9H_{13}NO_3$, may be obtained from the suprarenal glands of animals." *Br.*

Adrenalinum, *Br.;* Adrenalin, Suprarenalin, Suprarenin.

In 1897 Dr. John Abel (*J. H. H. B.,* July, 1897) separated from the suprarenal capsule the benzoyl-chloride of a base to which he gave the name epinephrine. The pure base was isolated in 1901 almost simultaneously by von Furth, who named it *suprarenin,* and Takamine, who named it *adrenalin,* the latter of whom patented the name and product. For description of suprarenal glands, which were formerly official see under *Organotherapy,* Part II.

As the result of much investigation into the nature of this substance it has been determined to be ortho-dioxyphenyl-ethanol-methyl-amine with the following structural formula:



In 1904 Stolz (*B. Chem. G.,* 1904, xxxvii, p. 4149) succeeded in preparing a compound synthetically which differed from the natural alkaloid only in being optically inert and much weaker physiologically. Flacher (*Z. P. C.,* 1908, lviii, p. 189) showed that the synthetic alkaloid was really the optically inactive racemic form and consisted of two principles, one dextro- and the other lævo-rotatory, and Abderhalden and Mueller (*Z. P. C.*, lviii, p. 185, and lxii, p. 484) and Cushny (*J. P.*, 1908, xxxvii and xxxviii) have shown that the lævo-rotatory form was nearly fifteen times as active as the dextro-rotatory.

The following method for separating this principle is given by Takamine (*A. J. P.*, 1901, p. 523): The comminuted suprarenal capsules are steeped in acidulated water for five hours at a temperature of from 50° to 80° C. with frequent agitation. At the end of this time the temperature is raised to 95° C. for a period of an hour to coagulate albuminous matters. As the adrenalin is prone to absorb oxygen from the air it is necessary to avoid exposure of the liquid as much as possible; a layer of fat floating on the surface acts well for this purpose and at the same time has the effect of retarding evaporation of the water. The liquid portion is separated by straining and the precipitate expressed and afterwards steeped for several hours in a fresh quantity of acidulated water in order to extract any residual alkaloid. The two liquid portions are united and allowed to separate from the oil and then partially evaporated in a vacuum pan. To this concentrated solution about two or three times its own volume of strong ethyl or methyl alcohol is added which precipitates various inert substances which may be removed by filtration. The alcoholic solution is then partially evaporated and ammonia added until distinct alkalinity. After standing several hours a yellow brownish precipitate is formed which is an impure basic form of adrenalin. This precipitate is washed with water and dried and further purified by dissolving in dilute acid and adding alcohol and ether which precipitate the coloring matter and inorganic impurities. To the filtrate from this precipitation ammonia is added which precipitates the adrenalin as almost colorless crystals. They may be further purified by repetition of the same process.

There are a number of processes for preparing this principle synthetically. The following is an outline of the most important of these methods: Pyrocatechol, $C_6H_4(OH)_2$ 1 : 2, is acted upon with chloracetyl chloride $CHCl_2COCl$ which unites to form a condensation product known as chloracetocatechol, $C_6H_3(OH)_2COCH_2Cl$. This product is then acted upon with methylamine, CH_3NH_2 which produces a compound known as *adrenalone* (amino-methyl-aceto-catechol) $C_6H_3(OH)_2COCH_2NHCH_3$. This is then reduced by nascent hydrogen to yield r-adrenalin, $C_6H_3(OH)_2CHOHCH_2NHCH_3$. This racemic, or optically inactive, adrenalin is then acted upon with an alcoholic solution of dextro-tartaric acid which dissolves the dextro and leaves behind the lævo modification.

Description and Physical Properties.—"A white or light brownish, microcrystalline, odorless powder, gradually darkening on exposure to the air. Epinephrine is very slightly soluble in water and in alcohol. It is insoluble in ether, chloroform, acetone, and in fixed or volatile oils.

"Epinephrine combines with acids, forming salts which are readily soluble in water, and from these solutions the base may be precipitated by ammonia or alkali carbonates. The acid solution is not affected by solutions of trinitrophenol, tannic acid, phosphomolybdic acid, mercuric potassium iodide, or platinic chloride. A saturated aqueous solution of Epinephrine is slightly alkaline to litmus paper. A slightly acid, aqueous solution of Epinephrine (1 in 1000) gives with ferric chloride T.S. an emerald-green color, turning to cherry-red and finally to brown on standing. Other oxidizing agents produce red, pink or violet colors which change to brown. Fixed alkali hydroxides cause the solution to darken on standing, but do not precipitate the Epinephrine. The ash from 0.1 Gm. is negligible.

"Preserve in well-closed containers, protected from light." *U. S.*

It is described by the British Pharmacopœia as "a light-brown, or nearly white, microcrystalline powder. Very slightly soluble in *water;* almost insoluble in *alcohol* (90 per cent.), in *ether,* and in *chloroform.* Combines with acids to form salts which are readily soluble in *water* and in *alcohol* (90 per cent.). Melts, with partial decomposition, between 205° and 212° C. Alkaline to moistened *litmus paper.* A diluted, slightly acid solution gives with a trace of *ferric chloride* an emerald-green color which is changed to purple or carmine by the cautious addition of a dilute solution of *sodium hydroxide;* readily reduces *solution of auric chloride;* gradually develops a characteristic unpleasant odor when a small quantity is mixed with five times its volume of *solution of sodium hydroxide;* yields no precipitate with *solution of potassio-mercuric iodide* (absence of most alkaloids). No appreciable ash." *Br.*

It has a slightly bitter taste and leaves a numb feeling on the tongue where it has been applied. Although its solutions readily undergo oxidation, in the dry form it is stable. It is easily soluble by dilute acids and by alkali hydroxides, forming salts, although not dissolved by ammonia or the carbonates. The alkaline solution absorbs oxygen very readily, in proportion to its alkalinity.

The following are some of the characteristic reactions: Ferric chloride colors epinephrine solution emerald green. A careful addition of caustic alkali to the green solution produced by ferric chloride, gives rise to the various shades of hue ranging from purple to carmine red, which are destroyed by careful neutralization with acids, restoring its original green color. Iodine as well as oxidizing agents, such as nitric acid, potassium bichromate and ferricyanide, etc., give a vivid pink.

A sensitive color test for epinephrine has been proposed by Moreschi (*Gaz. Med. Ital.*, 1913, 41), as follows: A small amount of tincture of iodine is cautiously floated upon the suspected liquid. In the presence of epinephrine a pink ring will be formed at the zone of contact, which gradually spreads into the lower liquid and then rapidly disappears. On then adding a few cc. of 1/1000 aqueous solution of sodium persulphate, a reddish or violet color will appear. This test will detect 1 part of epinephrine in two million of solution.

Gold chloride is very energetically reduced by epinephrine and a complete separation of the metal follows, from acid solution, by application of gentle heat; resultant liquid is colored pink or carmine red according to the strength of the solution used, as is the case with different oxidizing agents.

These color reactions, while satisfactory for identification tests, have not been found to be applicable for quantitative determinations. (See *Liquor Epinephrinæ Hydrochloride.*)

None of the following alkaloidal reagents produce precipitation: Mercuro-potassium iodide, picric acid, tannic acid, phosphomolybdic acid, phospho-tungstic acid, mercuric chloride, lead acetate, potassium bichromate, and platinum chloride.

Epinephrine is a substance of extreme chemical sensitiveness especially easily affected by oxidizing agents, but also being destroyed by alkalies, free halogens, and the salts of easily reducible metals such as iron. Beckwith (*J. A. Ph. A.*, 1914, iii, p. 1547) has shown that if protected from light, heat, and air, solutions of epinephrine will retain their activity for long periods of time. He found that the presence of slight excesses of non-oxidizing acids had a preservative effect. Formaldehyde, he states, if present in as small amounts as one-tenth of 1 per cent. will destroy the activity of epinephrine in a few hours. According to Rowe (*A. J. P.*, 1914, p. 145), boiling for a period of five minutes produces only an imperceptible amount of change in epinephrine solutions. After three boilings of five minutes each, however, there was a distinct loss of physiological activity.

Solutions of epinephrine are incompatible with oxidizing agents, such as ferric salts, hydrogen peroxide, free alkalies and free halogens. Most reducing agents, such as sulphites, have a preservative effect, but formaldehyde destroys its activity very quickly.

Uses.—Epinephrine stimulates the peripheral endings of the sympathetic nerves. As these nerves carry impulses to practically all of the vital organs it is evident that the injection of the alkaloid into the circulation will cause most wide-spread changes in function. In some cases the sympathetic nerves carry augmentor (motor) impulses, in others they carry inhibitory impulses. In the first case it is manifest that stimulation of these nerves by the epinephrine leads to an exaltation in the function of the organs supplied by them, while in the second instance the stimulation of the inhibitory mechanism will retard function. Hence we find that although epinephrine increases, for example, the contraction of the arterial muscles, it causes relaxation of the intestinal muscles.

It is impossible to consider all the results of this sympathetic stimulation upon the system and the interested reader is referred to H. C. Wood, Jr.'s *Text-book of Pharmacology* for further details. The effects resulting from this action which are of clinical interest are upon the circulation, the uterus and the bronchial musculature.

Because of the stimulation of the sympathetic nerves supplying them, epinephrine causes a violent contraction of the arterial muscles which in turn leads to a great increase in the intra-arterial blood pressure. Accompanying this rise in blood pressure there is usually a marked slowing of the pulse which, however, is probably due largely to the cardio-inhibitory reflex which ordinarily accompanies high blood pressure whatever be its cause.

The injection of large, and especially repeated, doses of epinephrine often causes an increase of the blood sugar and consequent appearance of glucose in the urine. This effect is probably due to an increased liberation of the glycogen in the liver which by some is attributed to the effects of the drug upon the sympathetic nerves.

In 1903, Josué (*C. B. S. B.*, 1903, lv, p. 30) announced that the repeated injection of adrenalin into the rabbit produced a degeneration of the walls of the aorta more or less similar to that seen clinically in atheroma. This effect appears to be due largely to a direct irritant action on the internal coat of the artery, although it is possible that the extremely high blood pressure may be an adjuvant factor. The practical importance of this observation is made questionable by the fact that the arterial changes do not seem to occur in either the dog or cat.

Epinephrine is used in medicine for five distinct purposes: (1) For overcoming local congestions; (2) to check local hemorrhages; (3) as a general circulatory stimulant; (4) for the relief of asthmatic paroxysms, and (5) to cause contraction of the uterus. Each of these requires separate consideration.

While the local application of moderately concentrated solutions of epinephrine in acute inflammatory conditions, such as *conjunctivitis, rhinitis* and the like, will cause an immediate blanching of the part, and often a temporary cessation of the symptoms, it is very questionable if the method of treatment in any way shortens the duration or lessens the real severity of the disease. Sollmann and Brody (*Proc. Soc. for Ex. Biol. and Med.*, 1922, xix, 400) have shown that the local application of adrenalin greatly reduces local resistance to infection by pyogenic organisms in the rabbit. On the other hand in passive congestions—the so-called *chronic inflammations*—it is often a remedy of much service. Thus, in *hay fever,* it produces temporary relief, at least in a very large proportion of cases. In this connection also might be mentioned the use of epinephrine in prolonging and enhancing the action of the local anesthetics. This effect is probably the result of the stoppage in the local circulation.

For *hemorrhages* from regions to which it can be directly applied to the bleeding point, epinephrine is one of the most valuable remedies that we possess. Its action differs essentially from that of the true styptics, in that the latter act chiefly by coagulating the albumen of the blood, and thus leave behind a hard clot, which is often an objectionable feature, while the hemostasis after epinephrine is due solely to its contraction of the blood vessels. When the torn vessel is of large caliber, epinephrine is a less certain remedy than the older styptics. Although it has been largely used internally in the treatment of non-accessible hemorrhages, it is not demonstrated that its influence in these conditions is beneficial. Some ground is afforded for its use in internal hemorrhages by the findings of Cannon and Grey (*A. J. Phys.,* 1914, xxxiv) that small doses accelerate the coagulation of blood. This has been confirmed by Grabfield (*A. J. Phys.,* 1916, xlii).

As a general circulatory stimulant the fugaciousness of the action of epinephrine limits its usefulness to the very acute forms of *circulatory failure,* such as *surgical shock, collapse* during anesthesia, and similar conditions. Although when injected hypodermically its effects are very slight, if thrown into the substance of a muscle (intramuscular injection) a very considerable degree of activity is obtained. Greuel (*B. K. W.,* 1921, lxiii, 1381) recommends that in very alarming conditions the epinephrine be injected directly into the heart and reports 13 cases, including 2 of his own, in which there was complete recovery, after apparent cessation of the heart beat, from this intracardiac injection. Donaldson (*B. M. J.,* 1914, i, p. 476) has shown that five minims of a one to one-thousand solution so injected will produce in normal men a rise in the blood pressure of from 15 to 45 millimeters, and according to Miller (*J. A. M. A.,* 1908) the rise lasts from one-half to three-quarters of an hour. In cases of degeneration of the heart muscle the drug must be used with great caution as the strong vascular constriction throws an intense strain upon the heart. Ulrich and Ripins (*J. P. Ex. T.,* 1922, xix, p. 217) have observed in an apparently healthy man, from the intravenous injection of 5 minims (0.3 cc.) of a one to 1000 solution of epinephrine symptoms so severe that death seemed imminent for several minutes.

In bronchial *asthma* the intramuscular injection of epinephrine will nearly always cause an immediate arrest of the paroxysm. Unfortunately in many instances the relief is only temporary, lasting perhaps an hour or two. According to Ephrain (*D. M. W.,* 1912), however, if the solution is applied directly to the bronchial mucous membrane the effects are much more lasting. When the asthma is dependent upon heart disease it should never be used because the sudden increase in arterial resistance may be sufficient to overcome the resistance of the enfeebled heart; Fredericia (*J. A. M. A.,* Feb. 5, 1916) has reported two deaths following the use of epinephrine for the relief of asthma which had been mistakenly diagnosed as bronchial when really of cardiac origin. In cases where evil effects are feared from the arterial spasm, it is well to guard the drug with nitroglycerin.

When applied either locally or injected internally, epinephrine causes a violent spasm of the uterus. Although, according to Neu (*Archiv. f. Gynekol.,* 1909, lxxv, p. 618), this occurs in the human being either in the pregnant or non-pregnant condition, the drug is not to be recommended for general uterine hemorrhages, but is of great value in the treatment of *post-partum hemorrhages.*

Various preparations containing epinephrine, as well as the alkaloid itself, have been used, with apparent benefit, in the treatment of *osteomalacia* and also *rickets.*

In 1918 Goetsch found that in patients suffering with exophthalmic goiter the hypodermic injection of 0.5 cc. of epinephrine solution (8 minims) caused a series of marked changes in the color of the skin. This has since been used as a diagnostic test for *hyperthyroidism.* It has been shown, however, that although the reaction occurs in the great majority of patients with over-acting thyroid glands it is by no means limited to this condition. For description of the test see Part II under *Diagnostic Tests.*

To obtain its systemic effects epinephrine must be given either intravenously or intramuscularly; ordinary hypodermic injections will not serve the purpose.

The number of proprietary brands of epinephrine on the market is very large. The more important of these include: *Adnephrin, adrenaline, adrenamine, epirenan, hemisine, hemostatin, paranephrin, renalina, supracapsulin, suprarenalin, supranephrane,* and *suprarenin.*

The *dose* of epinephrine is from one two-hundredth to three two-hundredths of a grain (0.0003–0.0009 Gm.) or as commonly expressed from 5 to 15 minims (0.3–1.0 cc.) of the one to one thousand solution.

As a local application, epinephrine may be used in strengths of from 1 in 10,000 up to 1 in 1000.

ERGOTA. U. S., Br.

ERGOT Ergot. [Secale Cornutum, P. I., Ergot of Rye]

"Ergot is the dried sclerotium of *Claviceps purpurea* (Fries) Tulasne (Fam. *Hypocreaceæ*), developed on rye plants. Ergot, in the form of the fluidextract, administered by intramuscular injection to single-comb, white Leghorn cocks, in doses not exceeding 0.5 cc. for each kilogram of body weight of cock, produces a darkening of the comb, corresponding in intensity to that caused by the same dose of a standard fluidextract of ergot, prepared as directed below. It contains not more than 5 per cent. of seeds, fruits or other foreign organic matter. Ergot should be dried at a low temperature. It deteriorates with age and should not be kept longer than one year." *U. S.*

"Ergot is the sclerotium of Claviceps purpurea, *Tulasne,* originating in the ovary of Secale cereale, *Linn.* Ergot should be thoroughly dried and kept entire in air-tight containers; it should not be used if more than one year old." *Br.*

Secale Clavatum, Mater Secalis, Clavus Secalinus; Rye Smut, Mother of Rye, Cockspur Rye; Ergot de Seigle, *Fr. Cod.;* Ergot, Seigle Ergoté (noir), Blé Cornu, *Fr.;* Secale Cornutum, *P. G.;* Mutterkorn, Kornmutter, Rogenmutter, Zapfenkorn, Hungkorn, *G.;* Segala cornuta, Grano speronato, *It.;* Cornezuelo de centeno, *Sp.*

In all the *Gramineæ,* or grass family, and in some of the *Cyperaceæ,* the place of the grains or fruits is sometimes occupied by a morbid growth which, from its resemblance to the spur of a cock, has received the name of *ergot,* adapted from the French. This product is most frequent in the rye, *Secale cereale,* and from that grain was adopted in the first edition of the U. S. Pharmacopœia, under the name of *secale cornutum,* or *spurred rye.* In the edition of 1840 the name was changed to *ergota.*

It is probable that this morbid growth has similar properties from whatever plant derived, and the fact has been proved in relation to the ergot of wheat. Tulasne found that dissimilar sclerotia collected from twelve species of grasses, produced fructification identical with that of the ergot of rye, so that it is probable that many apparently dissimilar ergots are specifically identical, their appearance being modified by the species of grass which they inhabit. It is further probable that all ergots have medicinal properties which agree in character though not in intensity. The short thick ergot which gathers upon the wild rice of Minnesota, *Zizania aquatica* L., has long been used as an abortifacient and oxytocic by the Indian women, and it is said that the wild ergot growing on various species of *Agropyron* and *Elymus* in the western United States, is fully equal medicinally to the official plant. The *Claviceps Paspali,* a fungus growing on a South African grass, has, according to Nutchell (*J. Dept. Agricul.,* South Africa, 1920), given rise to typical ergotism. M. Leperdriel, Jr., affirms that the *ergot of wheat* is destitute of the poisonous properties of that of rye, and is less liable to change. Ergot is rarer in wheat than in rye, and in the head of the former there is generally but one and very rarely more than two of the diseased grains. It is produced usually in wheat in wet seasons, and on that side of the head most exposed to the dampness. It is shorter and much thicker than the ergot of rye, being about half an inch long and three-quarters of an inch or more in circumference, and cleft into two or three divisions. In color and odor it resembles spurred rye.

The *ergot of oats* is said to be of a black color, measuring from ten to twelve millimeters in length and three to four in thickness, and to have been used in Algeria as a substitute for rye ergot. (*L. M. R.,* March, 1888.) Warburton (*Bot. Gaz.,* 1911, p. 64) reports the occurrence of ergot on oats grown in the oat breeding nursery at Ames, Iowa. The *ergot of diss* (an Algerian reed, *Ampelodesma tenax*) has appeared in commerce to some extent. It is, when small, slightly curved, but when long (6 to 9 centimeters) it takes a spiral turn from right to left, the longitudinal furrows being present on the inner face. It is thinner, dryer, and more brittle than the ergot of rye, and has been used for the preparation of an ergotine or extract closely resembling the official one, but said to be of a more translucent red or brown color. Lallemand asserts that the ergot of diss is twice as strong as the ergot of rye, and states that it is abundant and readily collected. It is also stated to be less hygroscopic and less apt to be attacked by acari than is the official article. (*P. J.,* xvi, 684, 1886.)

Investigations of Tulasne have shown that ergot represents the *sclerotium* of a fungus, *Claviceps purpurea* Tulasne. This fungus has three stages in its life history which is as follows:

In the spring or early summer the spores of this fungus are conveyed by insects or air-currents to the young developing ovaries of the rye. At the base of each ovary—where moisture occurs during damp weather—they germinate into filamentous hyphæ which penetrate the tissues by enzymic action. From here the hyphal filaments spread over the pistil enveloping it except at the summit and penetrating its outer coat. During all this time the hyphæ secrete enzymes which decompose the outer tissues of the ovary into a white, caseous mass called the sphacelia. The ovary enlarges and its upper end takes on a spongy appearance. This is due to the projection of twisted strands of hyphæ which here abstrict off chains of oval conidiospores. A yellow mucoid, saccharine exudate, issuing from the hyphæ and called *honey dew,* now envelops the conidiospores. The honey dew attracts ants, flies, weevils, etc., which carry the spores to the ovaries of other spikes of grain, so disseminating the disease. This terminates the sphacelia stage. At the base of the sphacelia and later extending upward through the ovarian substance, the hyphal threads penetrate deeper and deeper into the interior of the ovary consuming its substance until there ultimately forms a dense, compact tissue (pseudoparenchyma), violet black without and whitish within, that eventually replaces the developing grain with a violet or purplish curved body known as the sclerotium. This structure represents the resting or sclerotial stage in the life history of *Claviceps* and is collected as the official ergot.

The ergot which is not collected falls to the ground where, the following spring, it absorbs moisture and sprouts into several stalked projections terminated by globular heads which are called ascocarps or stromata. Each head develops in its peripheral parts flask-shaped invaginations called *perithecia.* From the base of each perithecium several sacs or asci develop. Within each of the latter there originate eight thread-like spores called ascospores. When these are mature the ascus ruptures and the ascospores are discharged. They are carried by air-currents to fields of gain, there to infect young ovaries and begin new life cycles.

Ergot has absolutely nothing in common with normal grain. The anatomical structure and all the physical characters of ergot are those of a sclerotic mycelium. The pseudoparenchyma, which is whitish, dry, and brittle, consists in all its parts of irregular, globular, or polyhedric thick-walled cells, intimately united, and filled with a limpid oil, but feebly colored by iodine. The superficial utricles, which alone are colored, have an outer wall thicker than the inner, and the color of these is what gives its characteristic hue to ergot. Not the least trace of starch is to be detected. If ergot is planted in a suitable soil, evidences of germination are seen in about three months. L. Hecke has recently produced artificial infection of rye flowers by spreading them with a suspension of conidiospores in water. The ergot grains (sclerotia), which were sown in autumn in boxes of earth and exposed to the frosts of winter, germinated in the spring, producing ascocarps which liberated ascospores. These were found to quickly germinate on nutritive gelatin and when transferred to suitable media produced large numbers of conidiospores (conidia). (*Schweiz. Apoth. Ztg.,* 1921, lix, 277.) The ergot usually projects out of the glume or husk beyond the ordinary outline of the spike or ear. In some spikes the place of the seeds is wholly occupied by the ergot, in others only two or three spurs are observed. It is said to be much more energetic when collected before than after harvest. Rye has generally been thought to be most subject to the disease in poor and wet soils, and in rainy seasons, and intense heat succeeding continued rains has been said to favor its development, especially if these circumstances occur at the time the flower is forming. It is now, however, asserted that moisture has little or nothing to do with its production.

Ergot is gathered in Spain, Galicia, Russia, Austria and Germany, being either picked by hand or thrashed and separated from the rye by special machinery. It enters commerce chiefly from Russia, Germany, and Spain. Of the three varieties the Spanish ergot is considered the best, yielding usually from 13 to 15, sometimes as high as 18, per cent. of extractive. It is somewhat darker colored, rather shorter, and more uniform than is the German ergot. An ergot of excellent quality has been sent from the Canary Islands to England.

Description and Physical Properties.—"*Unground Ergot*—Cylindraceous, obscurely 3-angled, tapering towards both ends, obtuse, somewhat curved, from 1 to 4.5 cm. in length and from 3 to 5 mm. thick, longitudinally furrowed; extremely dark purple or dark reddish-brown; fracture short; internally white, tinged with purple or gray; odor characteristic but free from mustiness or rancidity; taste oily, somewhat acrid, disagreeable.

"*Structure.*—A thin outer portion of small compact cells generally deep violet in color, turning red with 50 per cent sulphuric acid or with chloral hydrate T.S.; the inner portion, simulating parenchyma tissue, of thin-walled, colorless cells usually less than 0.015 mm. wide, but slightly elongated and containing numerous globules of fixed oil.

"*Powdered Ergot*—Grayish to purplish-brown; containing purplish and whitish fragments of the outer tissue and of the thin-walled cells.

"Shake 1 Gm. of powdered Ergot in a closed flask for about five minutes with 20 cc. of ether and about 15 drops of 20 per cent. sulphuric acid. Filter, and shake the filtrate thoroughly with 15 drops of a cold, saturated sodium bicarbonate solution. The separated lower aqueous layer is red or violet (*sclererythrin*). When crushed or powdered, Ergot does not develop a rancid or ammoniacal odor upon the addition of hot water." *U. S.*

"Subcylindrical or somewhat triangular, tapering towards the ends, generally curved; from one and a half to four centimetres long; longitudinally furrowed on each side, but more especially on that which is concave; often irregularly cracked; very dark violet-black externally, whitish or pinkish-white within; fracture short. Odor characteristic and disagreeable, especially when triturated with *solution of sodium hydroxide;* taste disagreeable." *Br.*

The aqueous infusion or decoction is claret-colored, and has an acid reaction. It is precipitated by lead acetate and subacetate, silver nitrate, and tincture of galls, but affords with iodine no evidence of the presence of starch.

The U. S. and the British Pharmacopœias state that ergot should not be kept for more than a year. While there is not sufficient data to allow of positive conclusions, Wood and Hofer (*A. In. M.,* 1910, vi, 388) found that in a sample carefully dried and sealed the activity was not perceptibly diminished after six months, and Eberhardt and Eldred (*J. A. Ph. A.,* 1914, iii, 38) quote Moss as having shown that, freed from its oil, ergot will retain its virtues unimpaired for two and even five years. (For discussion of the deterioration of the *Fluidextract of Ergot,* see p. 496.) The germinating test has been utilized in determining a good quality of ergot and Zimmermann (*Ztschr. f. Pflanzen-*

krankheiten, 1907, p. 129) concludes that the sclerotium of *Claviceps purpurea* is capable of germinating even after keeping for two years. Ergot sometimes contains small stones and cereal grains, implying that it has not been carefully garbled. Many samples are "wormy," some really being alive with insects. Old ergot is sometimes brightened by the use of a fixed oil; the revisers of Vienna Pharmacies (*Pharm. Prax.,* 1905, p. 38) reported finding one sample of powdered ergot which contained flour as an adulterant.

Ergot, when perfectly dry and kept in well-stoppered bottles, will retain its virtues for a considerable time, but exposed to air and moisture it speedily undergoes chemical change and deteriorates. It is, moreover, apt to be attacked by a minute worm, which consumes the interior of the grain, leaving the exterior shell and an excrementitious powder. This insect is sometimes found in the ergot before removal from the plant. Camphor and powdered benzoin are said to prevent injury from worms. Aymoiner immerses fresh ergot in an ethereal solution of tolu, dries it, and preserves in tightly closed bottles.

Constituents.—Ergot is an extremely complexed body containing a number of bases—to which its physiological properties are due—, a peculiar semi-cellulose called mannan, which yields on hydrolysis mannose, and probably one or more resinous acids.

Tschirch classifies the basic substances of ergot into three groups: "(A) *Initial* bases, *Ergotine, ergotoxine* (hydroergotinine), vernine and *ergothioneine.* (B) *Intermediate* bases, (1) acyclic: (Arginine, not isolated), agmatine, leucine, isoamylamine, choline, betaine; (2) with cyclic nucleus: (Tyrosine, not isolated), tyramine, uracil; (histidine, not isolated), histamine; (3) of unknown constitution; cornutine, clavine, sphacelic acid, ergotic acid. (C) *Decomposition end products of B,* among these cadaverine, putrescine, aniline, trimethylamine and methylamine."

Of the above named bases *cornutine,* which was first described by Kobert (*Ph. Centralh.,* 1884, p. 607) is regarded as an artefact not occurring naturally in ergot. Although a poisonous substance, it is improbable that ergot in any part owes its activity to this alkaloid. The cornutine of Keller is a very different substance and appears to represent all of the alkaloidal bodies present in the crude drug.

Ergotinine, $C_{35}H_{39}O_5N_5$, which was first described by Tanret (*P. J.,* 1885, p. 889), is a crystallizable, colorless alkaloid, and is probably identical with Wenzell's *ergotine.* The solutions of ergotinine turn greenish and red very soon; they are fluorescent. Sulphuric acid imparts to it a red, violet, and finally blue, hue. It is physiologically inert. A second alkaloid was discovered almost simultaneously by Barger and Carr, and by Kraft (*A. Pharm.,* 1906), the former calling it *ergotoxine,* and the latter *hydro-ergotinine.* Barger and Carr (*Tr. Chem. Soc.,* 1907, xci, 337) have shown that ergotoxine has the formula $C_{35}H_{41}O_6N_5$, and agree with Kraft that it is the anhydride of ergotoxine. Ergotoxine may be changed into ergotinine by boiling with methyl alcohol or acetic anhydride. *Sphacelotoxin,* described by Jacoby, is a substance having acid properties contaminated with ergotoxin; Wood and Hofer believe that the acid and the alkaloid are in chemical combination. The activity of ergot seems to be due chiefly to the alkaloid ergotoxine, but the effect of this is more or less modified by the putrefactive amines which are present. Of these amines there have been so far separated *para-phenylhydroxylamine* (also known as *tyramine* or *uteramine*), and *beta-iminazolethylamine* (*histamine, ergamine, imidazol*).

Aminosecalo-sulphonic acid, $NH_2.C_{15}H_{27}O_{15}$-SO_3H, is identical with *ergotic* acid of Kobert and is physiologically inert. *Clavine* has been shown by Barger and Dale to be a mixture of leucine and aspartic acid. Ewins (*Biochem. J.,* 1914, viii, p. 44) has shown the occurrence in certain specimens of ergot of *acetyl-choline* which is a powerful circulatory depressant, and more or less antagonistic to the other principles of ergot.

In 1921 Spiro and Stoll (*Schweiz. Apoth. Zeit.,* 1922, lx, 341) isolated what they believe to be a new alkaloid which they called ergotamine and assign the formula $C_{35}H_{35}O_5N_5$. Dale and Spiro (*A. E. P. P.,* 1922, xcv, 337), however, showed that the actions of this alkaloid are identical with those of ergotoxine.

Carr and Dale (*W. Br. Ph. Conf.,* 1913, 505) state that as *ergotoxine* is the recognized active principle of ergot the value of ergot and its preparations should be judged by the content of that principle. They also recognize the supplementary value of the amines, such as *ergamine,* and state that, given equal ergotoxine values, the sample which is higher in amines will be therapeutically superior. They commend the U. S. P. fluidextract as being a preparation of great value.

According to T. R. Baker, the ergot oil has a taste and odor similar to those of castor oil, with which it also agrees in ultimate composition, and yields analagous results in saponification. T. C. Herrmann investigated specially the chemical constitution of the oil of ergot. As obtained by means of ether, it was brownish-yellow, of an aromatic odor and acrid taste, viscid, of the sp. gr. 0.9249, and without any drying property. It consists of 22.703 per cent. of palmitic acid, 69.205 of oleic acid, and 8.091 of glycerin. (*N. R.,* 1872, p. 238.) The *sugar of ergot* was found by Mitscherlich to be *mycose,* $C_{12}H_{22}O_{11}$.

Assay.—The great variation in the potency of different samples of ergot, as well as its practical importance, has led to a number of attempts to develop means of determining the quality of the drug. These efforts have included both the chemical and the biological assay.

The earliest systematic use of the biological reaction for determining the quality of ergot were the experiments of Grünfeld in 1895. His method was based upon the quantity of the sample which was necessary to cause gangrene in the combs and wattles of roosters, and is commonly spoken of as the *cock's comb method*. This test was later utilized by Houghton (*T. G.*, 1898) on a commercial scale and is now official.

"Use single-comb, white Leghorn cocks, which are less than eighteen months of age, and weigh approximately 2 kilograms. Injections are made deeply into the breast muscles, and the effects are observed within one hour to one hour and a half after the administration of the drug. The same cock must not be used for testing purposes at shorter intervals than two weeks." *U. S.*

The criterion of the cock's comb method is the dose of a sample of ergot which is required to cause a bluing of the comb. It is important that the same breed of chickens be used throughout any series of experiments; white Leghorns are generally preferred. The method is carried out as follows: A rooster is weighed, and then a dose of the fluidextract to be tested, equivalent to about 1 cc. (16 minims) per kilogramme of body weight, is injected into the muscle of the breast. An hour later the bird is examined. If the specimen has been an active one, there will be a bluish or cyanotic appearance around the edge of the comb. The extent and degree of this discoloration is compared with that caused by a standard preparation in the same chicken on another day. The same rooster may be used over and over again, and the experimenter soon learns the degree of bluing which is the characteristic reaction of that individual chicken for a standard dose of active drug. If no bluing occurs the drug is below the standard.

In order to have some standard of comparison for this test the U. S. has recognized a *Standard Fluidextract of Ergot* which is prepared as follows:

"Prepare a composite fluidextract, representing at least ten different lots of Ergot, conforming to the official botanical description. This standard fluidextract, which must be aged for at least six months before being standardized by the method described in the preceding paragraph, and must be preserved in a vacuum, when administered by intramuscular injection in doses not exceeding 0.5 cc. per kilogram of body weight of cock, produces darkening of the comb of a single-comb, white Leghorn cock which is less than eighteen months of age, and which weighs approximately 2 kilograms.

"Preserve in air-tight containers." *U. S.*

The U. S. Bureau of Chemistry will furnish such a standard to manufacturers.

The idea of using the elevation of blood pressure for the assay of ergot seems to have been first suggested by Dixon (*P. J.*, 1905), and was elaborated by Wood and Hofer. (*A. In. M.*, 1910, vi, 388.) The method as employed by the latter is as follows: A dog is anesthetized with morphine and ether, and the carotid artery connected with a mercurial manometer. The normal blood pressure is observed, and then a dose of the sample equivalent to 0.15 Gm. of ergot for each kilo of body weight is injected intravenously, and the blood pressure noted (1) at its highest point after the injection, (2) five minutes after, and (3) ten minutes after the injection, the average elevation above the norm of these three observations represents the physiological activity of the specimen. In order to obviate peculiar susceptibility in individual dogs, it is necessary that experiments be made upon three animals with each sample. Edmunds and Hale modified the method by previously administering atropine for the purpose of avoiding the stimulant action upon the vagus, but their results were less consistent than those who have worked on the normal animal. The two objections which have been urged against this method are, in the first place, the assertion that because the drug is used chiefly as a uterine stimulant, a blood pressure test does not give satisfactory criterion of the therapeutic activity of the drug, and secondly, the possibility of a market abnormality in the reaction of one of the experimental animals creating a false idea of the activity of the drug. An attempt has been made to obviate this last objection by comparing the effects of a standard specimen upon the same animal.

The objection that since the drug is used chiefly as a uterine stimulant, the blood pressure test is not a satisfactory criterion of its therapeutic activity, must not be given too great stress. Stewart and Pittinger (*Trans. of the Amer. Therap. Soc.*, 1914) have shown that there is a close parallelism between the degree of action of various samples of ergot upon the blood pressure and upon the uterus.

Two methods in which the uterine muscle is used as an indicator of ergot have been suggested, that of Kehrer (*A. E. P. P.*, 1908, lviii) in which the uterus is removed from the body and either strips of the isolated muscle or the whole organ are employed, and that of Edmunds in which the uterus *in situ* furnishes the test reaction.

The first of these methods is the same as that now official for standardizing of pituitary solution (see *Liquor Pituitarii*) except that the drug should be compared with a standard fluidextract of ergot.

Pittinger and Vanderkleed (*J. A. Ph. A.*, 1914, iii, p. 925) have modified this method by adding weights until the uterus is barely able to move the lever and testing the strength of the muscle against this added resistance.

The method employed by Edmunds (*Hygienic Lab. Bul.*, No. 76, July, 1911) is most satisfactorily performed upon cats. The anesthetized animal, which is kept alive by artificial respiration throughout the experiment, is immersed in a bath of physiological salt solution at a temperature of 39° C., the abdomen is then opened by a medium incision, the bladder and intestines drawn aside; one horn of the exposed uterus freed by tearing away the peritoneal attachments and two fine silk threads passed through this horn at a distance of about two centimeters apart. These threads are then connected to a light muscle lever. To obtain the proper degree of tension weights may be added to the muscle lever. The ergot to be tested is then injected intravenously alternating with a standard solution. As in this method there is no definite end reaction it is often difficult to judge of the relative potency of the two preparations. Edmunds and Hale themselves say of it: "It is not an unusual experience to carry on such an experiment for two or three hours and . . . . to know very little more about the relative strengths of the two specimens at the end than at the beginning of the experiment."

There are several practical objections to all the uterine methods of assay. In the first place, they require a greater degree of technical skill in carrying out than either the blood pressure or cock's comb methods; in the second place, there is no definite end-point of the reaction so that it is difficult to make quantitative comparisons; and in the third place, the uteri of different species of animals do not respond in the same way to the drug, and even in the same species the effect may vary. Thus Dale finds that isolated strips of uterine muscle from the guinea-pig respond to ergotoxine but similar strips from the cat do not, although the intact uterus from the latter animal is excited by this alkaloid; tyramine causes contraction of the uterus in the pregnant and relaxation in the virgin cat. Brown and Clark (*J. P. Ex. T.,* 1923, xxi, p. 59) criticize the Edmunds method on the ground that it is in large degree a measure of the amine content which is of small therapeutic importance. They suggest another test based on the fact that the ergot alkaloids when applied to isolated strips of uterine muscle in sufficient concentration destroys the response of the muscle to epinephrine.

There has been much discussion as to which method is the most useful for standardizing ergot. For commercial purposes at least the choice lies between the cock's comb and the blood pressure method. The former has the great advantage of its simplicity, but it has the disadvantage of the absence of a sharp end reaction, for the change in the color of the comb may vary anywhere from an almost imperceptible darkening of the tip to a deep cyanotic color of the whole appendage—and hence leaves a wider range for possible personal error. As the different principles of ergot produce different physiological effects, it is evident that the two tests may give very different results for the same specimen of ergot; thus ergotoxine causes both bluing of the comb and rise in blood pressure; while tyramine causes rise in blood pressure but no bluing, while histamine causes no rise in blood pressure but, according to Crawford and Crawford (*J. A. M. A.,* 1913, lxi), it does cause bluing of the comb. For reasons pointed out by Crawford and Crawford, it is improbable that the fluidextract of ergot, prepared according to the U. S. P., will contain any considerable proportion of histamine, and it would seem, therefore, that a blood pressure method would furnish more accurate information concerning the American fluidextract than the test upon the rooster. But it must be remembered that the proper performance of the blood pressure test requires more technical skill than that upon the rooster, and in the hands of the unpractised it is probable that the cock's comb method would yield more favorable results.

The reader who is interested in this subject may find extensive references to the literature in the paper of Wood and Hofer (*A. In. M.,* 1910, iv, p. 388) and of Edmunds and Hale (*U. S. Hygienic Laboratory Bull.,* No. 76, 1911).

Pearson (*J. A. Ph. A.,* 1913, ii, p. 1453) reports upon the tests of the activity of ergot by the blood pressure method. Heated on a water bath for thirty minutes the fluidextract of ergot loses almost completely its power of raising the blood pressure. Evaporating at room temperature by a current of air does not destroy its activity. Extract of ergot (U. S. P.) had practically no effect on blood pressure. Bonjean's ergotin produced no rise and usually a decided fall in pressure. A powdered extract (method of manufacture not given) produced a temporary rise but the increased pressure was not sustained.

Uses.—The three bases of ergot, while differing in their physiological actions, unite in increasing the contractions of the pregnant uterus. Ergotoxine is a stimulant to all the involuntary muscles including the heart, the arteries and the intestines, as well as the uterus; it, therefore, increases blood pressure and intestinal peristalsis. Histamine has a similar effect to ergotoxine upon muscle fibers but differs in that it has a specific action upon the vasomotor center and tends to dilate instead of contracting the arterial muscles and also in the fugaciousness of its effects; it tends to lower rather than increase blood pressure. Tyramine is a stimulant to the sympathetic nerve endings closely resembling epinephrine in its actions; the involuntary muscles are either excited or inhibited according to the character of impulses conveyed by the sympathetic nerves. Like ergotoxine it tends to increase the blood pressure but its action is much quicker and of comparatively short duration.

When a dose of ergot is injected intravenously there occurs a rise in the blood pressure, sometimes preceded by a transient fall, and accompanied with a reduction in the rate of the pulse. The elevation of the pressure is due in part to a contraction of the blood vessels, the result of a direct stimulant action upon their muscular coats, but also in part to a stimulating effect upon the cardiac muscle. The effect of a small dose of ergot upon the uterus is to increase both the vigor of its contraction, and its muscular tone. If the dose is larger, the increase in muscle tone becomes relatively more and more pronounced, until eventually the organ may be thrown into a permanent spasmodic contraction.

On the continent of Europe ergot has long been empirically employed by midwives for promoting contraction of the uterus, and its German name "Mutterkorn" implies the popular acceptance of its peculiar powers, but it was first introduced to the regular medical profession as the result of the writings of Stearns. (*N. Y. Medical Repository,* 1807.) While a remedy of undoubted utility in properly selected cases of *labor,* its injudicious use may do much harm, and even prove fatal to either the mother or the child. When used freely, ergot is liable to transform the normal intermittent contractions of the parturient uterus into one violent spasm. If this spasmodic contraction occurs too early in the course of the birth process it may lead to asphyxiation of the child, to wide lacerations of the birth canal, or even to rupture of the uterus. In the third stage of labor, however, no such accidents can occur, and many obstetricians recommend the routine use of ergot at this time, as a prophylactic against *post partum hemorrhage.* Ergot is also used as a stimulant to the non-pregnant uterus to check bleeding in *menorrhagias* and *metrorrhagias.*

As a circulatory stimulant, ergot deserves more popularity than it has received. Although certain authors have found it a serviceable remedy in acute circulatory failure, such as *surgical shock,* the slowness of its action interferes with its utility in this condition, and its most important field of usefulness is in chronic vasomotor relaxations. Thus, it is useful in cerebral or *spinal congestion,* in *colliquative sweats,* in relaxing *diarrhea,* and similar conditions in which there are local passive congestions. Because of its success in hemorrhage from the uterus, ergot has been widely employed in various other internal *hemorrhages,* but its value under these circumstances is doubtful. Probably because of the effects of ergot on the circulation it is a very valuable remedy in the treatment of *delirium tremens.* (See Ransom and Scott, *A. J. M. S.,* 1911, cxli, p. 673.) Osborne (*N. Y. M. R.,* July 14, 1906) says that it has a powerful sedative effect upon the central nervous system and is useful in certain types of *asthma,* in *Graves's disease, hysteria,* and especially for the nervousness in the withdrawal of morphine.

Under the name of "ergotin," usually with the name of the maker attached, a number of more or less purified extracts of ergot are upon the market. The doses of these range from one to ten grains according to their purity. *Bonjean's ergotin* is made by exhausting ergot with water, evaporating to the consistency of syrup, precipitating the albumen, gum, etc., with alcohol, decanting the clear liquid and evaporating to the consistency of the soft extract. It is to be remembered in this connection that no aqueous extract of ergot can thoroughly represent the crude drug. *Ergotoxine* is marketed in the form of a crystalline phosphate, the dose of which is from one one-hundredth to one-fiftieth of a grain (0.0006–0.0013 Gm.). The hydrochloride of para-hydroxyphenylethylamine is sold under the trade name of *tyramine.* Hewlett (*A. I. M.,* 1918, xxi, 411) has found that it causes a rise of blood pressure and increased output of the heart, in human beings, in doses of 0.030–0.080 Gm. (½ to 1¼ grains).

The most widely used unofficial preparations of ergot are as follows:

Ergotin Bonjean (see *Extractum Ergotæ Aquosum,* Part III).—*Dose,* three to eight grains (0.2–0.5 Gm.).

Ergotin Wernich Merck.—Purified, dried, dialyzed aqueous extract of ergot. *Dose,* twenty grains (1.3 Gm.).

Ergotin Wiggers.—Dose, ten to fifteen minims (0.6–0.9 cc.).

Ergotole.—Dose, five to twenty minims (0.3–1.3 cc.).

Ernutin.—Dose, five to ten minims (0.3–0.6 cc.).

Ergone.—Dose, fifteen to thirty minims (0.9–1.8 cc.).

Cornutol (*Liquid Extractum Ergotæ*).—*Dose,* ten to thirty minims (0.6–1.8 cc.).

Clavin.—Dose, one-third of a grain (0.02 Gm.).

Femergen is asserted to be ergotamine tartrate.

Toxicology.—Ergot can scarcely be considered as a poison, since an ounce of the fluidextract rarely produces, except in the pregnant, any obvious symptoms unless it be nausea. Large doses are liable, it is true, to produce abortion in pregnant women, but even this result is uncertain. We know of but one instance of fatal poisoning by it, unless the death was produced by the abortion. The symptoms of the recorded cases of poisoning have been paleness, and, as most characteristic, an especial coldness of the surface, partial paralysis with numbness and tingling in the limbs, feebleness of the pulse, restlessness, and finally stupor or delirium.

On the other hand, the long continued and free use of ergot is highly dangerous, even when no immediate effects are perceptible. Fatal epidemics in different parts of the continent of Europe, particularly in certain provinces of France, have long been ascribed to the use of bread made from rye contaminated with this fungus. Dry gangrene, and disorder of the nervous system attended with convulsions, are the forms of disease which have followed the use of this unwholesome food. It is true that ergot has been denied to be the cause, but accurate investigations made by competent men upon the spot where the epidemics have prevailed, together with experiments upon inferior animals, leave no room for reasonable doubt that at least the gangrenous affection alluded to has resulted from it.

Dose, of ergot, fifteen to sixty grains (1–3.9 Gm.).

Off. Prep.—Extractum Ergotæ, *U. S., Br.;* Extractum Ergotæ Aquosum, *N. F.;* Fluidextractum Ergotæ, *U. S.* (*Br.*)*;* Infusum Ergotæ, *Br.;* Injectio Ergotæ Hypodermica (from Extract), *Br.;* Tinctura Ergotæ Ammoniata, *Br., N. F.*

ERIODICTYON. U. S.

ERIODICTYON Eriodict. [Yerba Santa]

"Eriodictyon is the dried leaf of *Eriodictyon californicum* (Hooker et Arnott) Greene (Fam. *Hydrophyllaceæ*). Eriodictyon contains not more than 5 per cent. of its stems or more than 2 per cent. of other foreign organic matter." *U. S.*

Mountain Balm, Consumptive's Weed, Bear's Weed, Gum Bush; Eriodictyon, *G.;* Feuilles d'Eriodictyon, *Fr.*

Eriodictyon californicum is a low evergreen shrub growing abundantly upon dry hills in California. It is glabrous, resinous, having alternate, short petiolate, long lanceolate leaves, irregularly more or less serrate, whitened beneath, between the reticulations, by a minute and close tomentum, above glabrous. The corolla is tubular funnel-form, violet or white in color; the calyx being sparsely hirsute. The fruit is a 2-celled capsule. The leaf structure has been studied by F. W. Ritter. (See *A. J. P.*, 1895, 565.) The commercial supplies of Eriodictyon come from California.

E. tomentosum, which grows often along with *E. californicum,* especially in the southern part of California, is readily distinguished by its dense coat of short villous hairs, whitish or rusty-colored with age. It is also a larger shrub than *E. californicum,* has its corolla somewhat salver-form, and its leaves oblong or oval, and obtuse.

Description and Physical Properties.—"*Unground Eriodictyon.*—Usually in fragments; when entire, lanceolate, from 5 to 15 cm. in length and from 1 to 3 cm. in breadth; apex acute; base slightly tapering into a short petiole; margin irregularly serrate or crenate-dentate; upper surface yellowish-brown, covered with a more or less glistening resin; under surface grayish- or yellowish- white, conspicuously reticulate with greenish-yellow veins and minutely tomentose between the reticulations; thick, brittle, odor aromatic; taste balsamic, bitter, becoming sweetish.

"*Structure.*—Upper epidermis with large cells, the outer walls very uneven, owing to indentations which appear as striations in surface view, glandular hairs numerous; palisade cells very narrow, from 2 to 6 rows deep; cells of loose mesophyll forming but a few layers; vascular tissues not strongly developed except in the midrib and more prominent veins; numerous non-glandular hairs occurring on the lower surface between the veins.

"*Powdered Eriodictyon.* — Greenish; non-glandular hairs 1-celled, undulate and with thick walls; glandular hairs with 1-celled stalk and 6- to 8-celled heads, the latter up to 0.075 mm. in diameter; tracheæ with spiral thickenings or simple pores and associated with lignified fibers; starch grains few, from 0.003 to 0.020 mm. in diameter; calcium oxalate crystals numerous, in rosette aggregates from 0.005 to 0.030 mm. in diameter." *U. S.*

Tunmann (*Ph. Centralh.,* 1908, p. 159) describes and illustrates the pharmacognostic and microscopic characteristics of *Eriodictyon californicum,* and discusses the morphological importance of the oil glands of eriodictyon.

According to the analysis of Chas. Mohr (*A. J. P.*, 1879, 549), it contains tannic acid and 8 per cent. of an acrid, bitter resin, upon which its activity is believed to depend, also a minute quantity of volatile oil. Thal (*Ph. Z. R.*, 1883, p. 209) affirmed the presence of *ericolin,* $C_{34}H_{56}O_{21}$. Power and Tutin (*Proc. A. Ph. A.*, 1906) deny that ericolin is present but find besides volatile oil and resin, *triacontane,* $C_{30}H_{62}$, *penta triacontane,* $C_{35}H_{72}$, *eriodictyol,* $C_{15}H_{12}O_6$, *homoeriodictyol,* $C_{16}H_{14}O_6$, and an unidentified phenol, $C_{16}H_{41}O_6$. (See also Tutin, *Tr. Chem. Soc.*, 1910, xcvii, 2054.)

Uses.—Eriodictyon has long been used in California as a bitter tonic, and also as a stimulant balsamic expectorant. There is considerable testimony to its usefulness in *asthma, chronic bronchitis,* and allied conditions; also in chronic inflammation of the genito-urinary tract. Attention has been called by Kier to its remarkable power of disguising the taste of quinine, and Meyer (*Ph. Ztg.*, 1905) found that it will also mitigate the unpleasantness of hydrastis or aspidium. It is best exhibited in the form of the official fluidextract, the dose of which is one-half to one fluidrachm (1.8–3.75 cc.); a solid extract has been made, which may be given in doses of from five to fifteen grains (0.32–1.0 Gm.). In cases of asthma, eriodictyon is often used by smoking. The aromatic syrup is well adapted as a vehicle for quinine.

Dose, fifteen to sixty grains (1.0–3.9 Gm.).

Off. Prep.—Fluidextractum Eriodictyi, *U. S.;* Elixir Eriodictyi Aromaticum (from Fluidextract), *N. F.;* Syrupus Eriodictyi Aromaticus (from Fluidextract), *N. F.*

EUCAINÆ HYDROCHLORIDUM. U. S.

EUCAINE HYDROCHLORIDE Eucain. Hydrochl. [Betaeucainæ Hydrochloridum, U. S. P. IX]

"Eucaine Hydrochloride, when dried to constant weight at 100° C., contains not less than 99 per cent. of $C_5H_7N(CH_3)_3O(C_6H_5CO).HCl$." *U. S.*

This derivative of piperidine is made by acting on diacetonamine with paraldehyde and metallic sodium. The product is treated with benzoyl chloride and the trimethyl-benzoxypiperidine, which is formed, is neutralized with hydrochloric acid and the resulting crystals are purified.

Description and Physical Properties.—"A white, odorless, crystalline powder. It is stable in the air. One Gm. of Eucaine Hydrochloride is soluble in 30 cc. of water, 35 cc. of alcohol, and in 6 cc. of chloroform, at 25° C. It is more soluble in boiling water and in boiling alcohol.

"Dissolve about 0.1 Gm. of the salt in 1 cc. of sulphuric acid. Keep the solution at 100° C. for five minutes, and then mix it cautiously with 2 cc. of water; the aromatic odor of methyl benzoate becomes noticeable and on cooling crystals of benzoic acid form. Ten cc. portions of its saturated aqueous solution yield a white, curdy precipitate on the addition of mercuric chloride T.S., and a yellowish, curdy precipitate with a few drops of a mixture of equal volumes of potassium chromate T.S. and diluted sulphuric acid. Silver nitrate T.S. produces in an aqueous solution of the salt (1 in 100) a white precipitate which is insoluble in nitric acid.

"An aqueous solution of Eucaine Hydrochloride (1 in 50) is neutral to litmus paper. The ash from 0.5 Gm. is negligible. A solution of 0.1 Gm. of Eucaine Hydrochloride in 1 cc. of sulphuric acid is colorless (*readily carbonizable substances*). Triturate about 0.05 Gm. of the salt with about five times its weight of mild mercurous chloride, and moisten the mixture with a few drops of water; no black color is produced (*difference from cocaine hydrochloride*). No permanent precipitate is produced by the addition of 5 cc. of mercuric chloride T.S. to 5 cc. of an aqueous solution of the salt (1 in 100) (*cocaine and alphaeucaine*)." *U. S.*

Assay.—"Dissolve about 0.5 Gm. of Eucaine Hydrochloride, previously dried to constant weight at 100° C. and accurately weighed, in 100 cc. of neutral alcohol. Titrate this alcoholic solution with tenth-normal sodium hydroxide, using phenolphthalein T.S. as indicator. Each cc. of tenth-normal sodium hydroxide corresponds to 0.02837 Gm. of $C_5H_7N(CH_3)_3O$-$(C_6H_5CO).HCl$." *U. S.*

Uses.—Eucaine is used solely as a local anesthetic. It differs from cocaine in that it is not stimulant to the central nervous system, that it does not dilate the pupil nor contract the blood vessels. Moreover, it is free from the danger of habit formation which is always such an imminent evil with cocaine; and, although at first included in the Harrison Anti-narcotic Law as a restricted drug, the Department has ruled that it is no longer subject to the provisions of the Act.

Although according to the experiments of Eggleston and Hatcher (*J. P. Ex. T.*, 1919, xiii, p. 433) by intravenous injection eucaine has approximately the same toxicity as that of cocaine, when given hypodermically it is very much less poisonous. According to Closson (*J. Mich. State Med. Soc.*, 1914, xiii, 587) the lethal dose for the guinea-pig, by subcutaneous injection, is about eight times as large as that of cocaine, but other experimenters have estimated its toxicity at from one-fourth to one-sixth that of cocaine. It is, however, distinctly less powerful in its anesthetizing action. According to Sollmann (*J. A. M. A.*, 1918, lxx, p. 216), it requires double the strength of eucaine to produce the same degree of anesthetizing effect as of cocaine. Compared to procaine, which it more closely resembles, Sollmann finds that eucaine is inferior in power for injection anesthesia but is superior when applied over mucous membranes. As a local anesthetic it may be used in strengths of from 1 to 5 per cent. It is not used internally except for its anesthetic action upon the stomach in cases of *gastric ulcer*, or other painful conditions of the stomach. For this purpose from one-half to two grains (0.032–0.13 Gm.) may be given at a *dose*.

EUCALYPTI GUMMI. N. F. (Br.)

EUCALYPTUS GUM Eucalypt. Gum. [Red Gum]

"Eucalyptus Gum is a dried gummy exudation from *Eucalyptus rostrata* Schlecht. and other species of *Eucalyptus* (Fam. *Myrtaceæ*)." *N. F.*

"Eucalyptus Kino is an exudation from the stem of various species of Eucalyptus." *Br.*

Kino Eucalypti, *Br.*; Eucalyptus Kino; Australian Kino.

McGookin and Heilbron (*J. P. Ex. T.*, 1926, xxvi, 421 give a list of over 50 species of Eucalypts which yield kino, but most of the commercial article is prepared from *E. rostrata* Schlecht., a common tree in western Australia. This tree received its name from the rostrate character of the opercula. Masses of kino are sometimes found in cavities between the wood and the bark, this being due to the evaporation of the sap in these places. It is usually obtained by incising the trees and collecting the exuding liquid; this, on boiling, yields a solid dark mass which, being friable, breaks up into small dark fragments. The drug is shipped from Melbourne and Victoria to England from which small amounts are imported into the United States. Occasionally the juice reaches England unevaporated. *Kino juice* has a fine deep red color, a slightly aromatic odor, and a decidedly astringent taste, and on evaporation yields a genuine kino in varying amount. It must not be confounded with the so-called *Liquid Kino*, which is obtained from incisions in the *Angophora intermedia* DC. (Fam. *Myrtaceæ*) or kino gum-myrtle of Australia. This varies from the consistency and colorlessness of water to an orange brown or reddish-brown liquid as thick as molasses. It contains catechin and tannic acid, and is said to be especially employed for the purposes of tanning nets.

Description and Physical Properties.—"*Unground Eucalyptus Gum.*—In dark reddish brown grains or angular masses which in thin layers are of a transparent ruby-red color; brittle, the older surfaces sometimes dusty; forming a plastic mass and adhering to the teeth when chewed, coloring the saliva red; taste very astringent; odor slight.

"*Powdered Eucalyptus Gum.*—Dark reddish brown; in angular fragments with a conchoidal fracture, the thinner pieces light yellow or light reddish brown; upon mounting in water the fragments gradually disintegrate, leaving colorless granular particles and a few cellular fragments. An aqueous solution of Eucalyptus Gum is faintly acid to litmus, and has reddish color, the color being intensified by an aqueous solution of an alkali. A very dilute solution gives a dark green color with ferric chloride T.S., while a more concentrated one yields a dark green precipitate. Almost completely soluble in alcohol without becoming plastic." *N. F.*

"In very dark reddish-brown grains or small masses. Thin fragments transparent and ruby-red, or garnet-red. Inodorous; taste astringent. Tough and adhering to the teeth when chewed. Not less than 80 per cent. soluble in *water.* Almost entirely soluble in *alcohol* (90 per cent.)." *Br.*

Eucalyptus kino contains about 47 per cent. of kino-tannic acid besides small amounts of catechin, pyrocatechin and kinoin, and in some specimens a volatile oil, giving a slightly aromatic odor to the drug, which is especially developed by hydrochloric acid. J. H. Maiden (*A. J. P.,* 1895, 575) states that Australian kino contains *eudesmin* and *aromadendrin.* The former of these when purified exists as a pure mass with a luster resembling spermaceti. It is soluble in hot water, but crystallizes out again on cooling. It is soluble in alcohol, ether, acetic ether, and chloroform, but not in benzene, petroleum spirit, or carbon disulphide. It is dissolved by sulphuric acid with a dark color changing to purple, by nitric acid with a beautiful yellow color. Its formula is given as $C_{26}H_{30}O_8$, and its melting point as 99° C. The second substance was also obtained crystallized from boiling water, and melted at 162° C. No analysis has been made of it.

Botany Bay kino is the inspissated juice of *Eucalyptus calophylla* R. Brown and some other Australian species of Eucalyptus. It occurs in irregular dark red pieces and contains a tannin which will not gelatinize in solution.

Uses.—Red gum does not equal kino in astringency. It is used for *diarrheas of relaxation,* and other affections for which kino has been employed, and is also largely employed as the basis of lozenges and gargles for the relief of relaxed conditions of the pharynx.

Dose, from five to twenty grains (0.3–1.3 Gm.).

Off. Prep.—Trochiscus Kino Eucalypti, *Br.* Trochisci Eucalypti Gummi, *N. F.*

EUCALYPTOL. U. S.

EUCALYPTOL [Cineol]

"A substance [$C_{10}H_{18}O$] obtained from oil of eucalyptus and from other sources." *U. S.*

Cajuputol Eucalyptolum, *Fr. Cod.;* Cinéol, Terpane, Cajeputol, *Fr.;* Terpan, *G.;* Eucaliptol, *Sp.*

In the distillation of eucalyptus leaves, the portion which comes over between 170° C. and 178° C. is set aside as crude eucalyptol. To obtain it pure a redistillation from potassium hydroxide or calcium chloride is necessary. It is very liquid, nearly colorless, with a strong, aromatic, camphoraceous odor, is slightly soluble in water, but very freely soluble in alcohol. Nitric acid produces with it a crystallizable acid; by the action of phosphoric anhydride (*J. P. C.,* 4e sér., xii, 204) it is converted into *eucalyptene,* $C_{10}H_{16}$, a substance allied to cymene, and *eucalyptolen.*

C. Jahns (*A. J. P.,* 1885, p. 237) gave the formula $C_{10}H_{18}O$ to eucalyptol, and showed it to be identical with cajuputol, or, as it is now generally known, *cineol.* Wallach (*Ann. Ch. Ph.,* 248, pp. 278 to 283) showed that the oil from *E. Globulus* contained cineol (eucalyptol) and dextro-pinene, while that from *E. amygdalina* Labill., contained cineol and lævo-phellandrene. (For the nearer study of oil of eucalyptus and for consideration of other eucalyptol bearing oils, see under *Oleum Eucalypti.*)

Eucalyptol forms condensation compounds with a number of phenols in equimolecular proportions. These have been studied and classified by Belluci and Grassi (*Chem. Zentral.,* 1914, 884).

Description and Physical Properties.—"A colorless liquid, having a characteristic aromatic, distinctly camphoraceous odor, and a pungent, spicy taste. Eucalyptol is very slightly soluble in water. It is miscible with alcohol, chloroform, ether, glacial acetic acid, and with fixed or volatile oils.

"Specific gravity: 0.921 to 0.923 at 25° C. It boils between 174° and 177° C. Congealing point: not below 0° C. Place 1 cc. of Eucalyptol in a freezing mixture and gradually add an equal volume of phosphoric acid; a solid, white, crystalline mass of eucalyptol-phosphoric acid forms, and upon the addition of warm water, the Eucalyptol separates.

"Its alcoholic solution (1 in 10) is neutral to moistened litmus paper. Eucalyptol is optically inactive (*difference from oil of eucalyptus and many other volatile oils*). Shake 5 cc. of Eucalyptol with 5 cc. of sodium hydroxide T.S.; the volume of the Eucalyptol is not diminished (*phenols, etc.*). Shake 1 cc. of Eucalyptol with 20 cc. of distilled water, and allow the liquids to separate. To 10 cc. of the acueous layer, separated from the Eucalyptol, add 1 drop of ferric chloride T.S.; no violet color is produced (*phenols*). *U. S.*

Uses.—Eucalyptol has to a considerable extent replaced the oil of eucalyptus especially as a stimulant expectorant in *chronic bronchitis* and *bronchorrhea,* etc. Berliner (*B. K. W.,* 1913, p. 1703) injected hypodermically an oily solution of menthol and eucalyptol in the treatment of *tuberculosis of the lungs* with asserted great benefit. Eucalyptol has been also used to a considerable extent as a vermifuge, especially against the ankylostoma, but has largely been abandoned for remedies more efficient for this purpose. Locally it possesses mildly anesthetic and antiseptic powers and is widely used in the treatment of inflammatory conditions of the nose and throat in strengths of from ½ to 2 per cent. According to the investigations of Martindale its germicidal powers are about equal to those of phenol. Grieg-Smith (*Bot. Abst.*, 1921, vii, p. 189) finds that eucalyptol is germicidal in more dilute solution than phenol, but is decidedly slower in action, so that the phenol coefficient depends upon the length of exposure; at five minutes' exposure eucalyptol and phenol are about of equal potency. Recently it has come into wide-spread use as a solvent for Dichloramine-T. Brownscomb (*Chemist and Druggist,* 1910), however, asserts that eucalyptol is a less powerful antiseptic than the other ingredients of the oil of eucalyptus. For information on the poisonous properties of this principle see *Oleum Eucalypti.*

Dose, five to ten minims (0.3–0.6 cc.), four to six times a day.

Off. Prep.—Liquor Antisepticus, *N. F.;* Liquor Antisepticus Alkalinus, *N. F.;* Liquor Pepsini Antisepticus, *N. F.;* Nebula Aromatica, *N. F.;* Nebula Eucalyptolis, *N. F.;* Nebula Mentholis Composita, *N. F.;* Petroxolinum Eucalyptolis, *N. F.;* Petroxolinum Iodoformi, *N. F.;* Petroxolinum Sulphuratum Compositum, *N. F.;* Pulvis Antisepticus, *N. F.*

EUCALYPTUS. U. S.

EUCALYPTUS Eucalypt.

"Eucalyptus is the dried, scythe-shaped leaf of *Eucalyptus Globulus* Labillardière (Fam. *Myrtaceæ*). Eucalyptus contains not more than 3 per cent. of stems, fruits, or other foreign organic matter." *U. S.*

Blue Gum-tree Leaves, Australian Fever-tree Leaves, Eucalyptus Leaves; Eucalyptus, *Fr. Cod.;* Feuilles d'Eucalyptus, *Fr.;* Eucalyptusblätter, *G.;* Eucalitto, *It.;* Eucalipto (Hoja de), *Sp.*

The genus *Eucalyptus* was named by L'Heritier in 1788, from the two Greek words, *εὐ,* well and *καλύπτω*, I cover, in allusion to the operculum formed of the fused petals and calyx lobes, which covers the flower until the stamens have matured and then separates from the calyx-tube by transverse dehiscence. This genus comprises about 300 plants, mostly trees, all natives of Australia, Tasmania and Malayan regions. The leaves are simple and entire on young shoots and seedlings, dorso-ventral, opposite, sessile, with cordate bases, on older parts; usually bifacial, alternate, with twisted petioles and lanceolate to falcate in outline, the leaf parenchyma containing numerous oil-glands. The flowers vary from white through yellow to red and are arranged in corymbs or panicles of umbels. Each has an obconic, bell-shaped or oblong calyx tube adnate to the base of the ovary, the petals and calyx lobes connate, forming a lid which separates from the calyx-tube by transverse dehiscence, numerous stamens and a compound pistil with an undivided style. The fruit is a 3- to 6-celled woody pyxis containing numerous small seeds, many of which are sterile.

Some of the species, according to Kerner, attain a height of 140 to 152 meters and so become close rivals of the giant sequoias of California which have been recorded as the tallest trees known.

Most of the species do not require excessive heat for their perfecting, and some of them are able to resist moderate frosts. Over forty species are being grown successfully in the United States, chiefly in California, where volatile oil has been produced on an experimental scale and leaves collected in commercial amounts. On account of the rapidity of their growth and the hardness and indestructibility of their timber, many of the species are very valuable for economic purposes. A number of the species are cultivated in the southwest as a source of honey. (For methods of cultivation of *Eucalyptus globulus* and other species see *Bulletin No. 35 of the U. S. Bureau of Forestry* and *Univ. of Calif. Agr. Exp. Sta., Bull.* 196).

With a genus of so many species and numerous varieties it was to be expected that there would be considerable confusion in regard to the accurate determination of its species. Tate and Luehman give prominence to the fruit for purposes of classification. Maiden, however, says that all of its characters display a puzzling amount of variation, and concludes that for herbarium work the best characters are afforded by the anthers and fruits; whereas the scientific forester will be largely guided by the nature of the bark and timber. Baker and Smith, in addition to morphological characters, base their deductions on the chemical properties and physical characters of oils, dyes, kinos, etc. (*A Research on the Eucalypts,* Sydney, 1902.) Up to the present no satisfactory natural classification has yet been devised for this large genus. For purposes of identification of herbarium specimens it is necessary to have mature fruits, adult leaves, buds and flowers. By far the most extensive treatise on the genus Eucalyptus is that entitled *"A Critical Revision of the Genus Eucalyptus"* by J. H. Maiden now (1925) appearing in parts. It is stated that the leaves of the *E. rebaudianum,* of Paraguay, are used in that country in place of sugar, which they exceed in sweetening power.

Eucalyptus globulus is a large evergreen tree, attaining a height of 300 or even 350 feet, with a smooth, ash-colored bark. The leaves attain a foot in length, and vary, according to age, from a glaucous white to a bluish-green color. The flowers are large, pinkish-white, axillary, occurring singly, or in clusters. Although its wood is very resinous, hard, and durable, the tree is remarkable for the rapidity of its growth, reaching, under favorable circumstances, fifty feet of height in five or six years. It flourishes best in valleys having a rich, moist soil, and has very largely been naturalized in semi-tropical countries, partly on account of its economic value, but chiefly because of the reputation it enjoys as a means of overcoming malaria. Its sanitary powers appear to be established, numerous notoriously miasmatic stations and districts having been rendered healthful by its growth. It is probable that the destruction of the miasma is due not so much to emanations from the tree as to the fact that it evaporates water so rapidly from its innumerable large leaves as to drain the swamps and marshes in which it is planted. It is possible, however, that the large amount of volatile oil which must escape from it has some effect, and it is even affirmed (*A. J. P.*, 1875, p. 423) that the parasitic phylloxera will not attack grapevines growing near it.

Eucalyptus globulus is cultivated in Spain, Portugal, Italy, France, Algeria, California and other warm countries. The leaves should be collected from older parts of the tree, for such contain the maximum quantity of volatile oil. The drug used in America is collected chiefly from trees grown in southern Europe. It is exported from Spain, France and Belgium to the United States. Small amounts of the drug have been obtained from California but are not at present (1925) commercially available.

Burke and Scalione (*J. I. E. C.*, 1915, 206) made an investigation of oil distilled from *Eucalyptus globulus* in California and found the oil to have the same qualitative composition as the Australian oil but to vary widely in the proportions of the various constituents from the average content of the Australian oil. They found the California oil to be insoluble in 70 per cent. alcohol and to contain 47 per cent. of cineol and 22 per cent. of pinene. *Eudesmol*, *globulol* and aldehydes of butyric, capronic and isovaleric acids were also found.

Description and Physical Properties.—"*Unground Eucalyptus.*—Blades lanceolate, curved, from 8 to 30 cm. in length and from 2 to 7.5 cm. in breadth; apex acute or acuminate; base unequal, obtuse or rounded; petiole twisted, from 5 to 35 mm. in length; margin uneven, revolute; coriaceous; both surfaces varying from pale yellowish-green to grayish-green and more or less glaucous, glaborous, glandular-punctuate and with numerous small, circular brown dots of cork; veins of the first order anastomosing to form a vein nearly parallel with the margin; odor aromatic; taste aromatic, bitter and cooling.

"*Structure.*—The epidermis of both surfaces composed of polygonal cells with rather thickened, straight walls, sunken stomata and strongly thickened cuticle; palisade of 3 to 4 rows beneath each epidermis; loose mesophyll of but a few rows of cells; large oil reservoirs with yellowish or orange-colored contents; collenchyma strands at the edges of the blade and at the ribs; rosette aggregates or mono-clinic prisms of calcium oxalate abundant in the parenchyma; occasional brown corky lenticels deeply depressed into the palisade.

"*Powdered Eucalyptus.*—Light green; containing fragments of epidermis with stomata nearly invisible because of the thickened cuticle; fragments of chlorenchyma with broken oil reservoirs; fragments of brownish cork; long, slightly lignified bast-fibers associated with small dotted tracheæ; calcium oxalate in rosette aggregates or prisms, from 0.015 to 0.025 mm. in diameter." *U. S.*

Hans Kramer (*B. P. G.*, 1907, p. 319) presents an anatomical study of Eucalyptus with the characteristics of the drug in a powdered form.

Eucalyptus owes its medicinal value to a volatile oil of which the fresh leaves afforded 2.75 per cent., the recently dried leaves 6 parts; leaves which had been kept some time yielded a much smaller percentage. (Cloez, *J. P. C.*, 1870; Broughton, *P. J.*, 1873.) In the distillation, the oil for a time comes over freely at from 170° C. to 178° C.; subsequently another portion of oil distils at 188° C. to 190° C., and finally a very minute portion does not volatilize until the temperature reaches 200° C. The bulk of the oil yielded is the portion first distilled; to this Cloez gave the name of *eucalyptol.* (See previous article.)

The oils distilled from the leaves and from the twigs or wood of the various species of this very large genus, are so dissimilar in composition and properties in many cases that the generic term "eucalyptus oil" is without definite meaning unless the species is known. Gildemeister and Hoffmann (*Aetherische Oele*, 1899, p. 690) divide the eucalyptus oils into 5 groups according to their constituents, viz.: Group 1, Cineol- (or Eucalyptol-) containing oils, of which group *Eucalyptus Globulus* is the most important; Group 2, Citronellal-containing oils, of which group *Eucalyptus maculata* is the most important; Group 3, Citral-containing oils, of which *E. staigeriana* F. von Muell. is the typical example; Group 4, Peppermint smelling oils, of which *Eucalyptus piperita* is an example; and Group 5, Less known oils of varying odor. See also *Oleum Eucalypti.*

Schimmel & Co. (*Semi-Annual Report,* April, 1897) gave a list of some fifteen varieties of eucalyptus oils from the different Eucalyptus species. In their report for October, 1904, they give the sources and state the properties and components of 109 different eucalyptus oils obtained by them from Baker and Smith, Curators of the Technological Museum of Sydney, N. S. W.

The *E. purpureum* L. (*Joe-Pye Weed*) and the *E. verbenæfolium* Michx. (*wild horehound*) have been used as folk remedies for the same purposes as the official drug. *E. incarnatum* Walt. and *E. aromaticum* L. are said to contain an aromatic principle similar to, if not identical with, coumarin. (See *P. J., Oct.*, 1874, 303.) The *E. ageratoides* L.f., commonly known as *white* *snake-root,* has been popularly supposed to give rise to a disease of cattle known as the "trembles," but Crawford (*Bureau of Plant Industry,* Bull. 121, 1908, U. S. Dept. of Agriculture) was unable to find any evidence of toxicity in the plant. *E. Rebaudianum* contains a principle, *rebaudin,* which is stated to have 180 times the sweetening power of sugar and has been suggested as a substitute for saccharine.

For account of other species of Eupatorium see *U. S. D.,* 20th ed., p. 1380.

Uses.—Whatever medicinal virtue eucalyptus possesses—beyond a slight astringency—is due to its volatile oil. Preparations of the crude drug are rarely used in this country. The leaves are occasionally rolled into cigarettes to be smoked for the relief of *bronchitis* or *asthma.* Certain French authors have reported a beneficial effect from infusion of eucalyptus in diabetes but John (*J. Metabol. Research,* 1922, i, 489) made a careful test in twenty patients with entirely negative results. For therapeutic properties see *Oleum Eucalypti.*

Dose, of eucalyptus, ten to thirty grains (0.65–2.0 Gm.); of the oil, five to ten minims (0.3–0.6 cc.).

Off. Prep.—Fluidextractum Eucalypti, *U. S.*

EUGENOL. U. S.

EUGENOL

"A phenol [$C_6H_3.C_3H_5.OCH_3.OH$ 1:3:4] obtained from clove and other sources." *U. S.*

Ollylguaiacol, Allylmethylpyrocatechol; Eugenol, *Fr.;* Aleum Caryophyllorum, ***P.*** *G.;* Eugenol, *G.*

Eugenol is extracted on a large scale from oil of cloves and utilized as the starting point in the manufacture of artificial vanillin. (See *Vanillinum.*) It is also found in pimenta, cinnamon leaves, sassafras, canella, bay and other plants. It has been shown to be the methyl ether of allyl-dioxybenzene. One of its most important reactions is its conversion into vanillin. It yields a characteristic benzoyl derivative which melts at 69° to 70° C. Methyl eugenol is also known. For the manufacture of vanillin it is first converted into an isomeric compound which has a different side chain arrangement. This *iso-eugenol* is found naturally in certain volatile oils, as nutmeg and ylang-ylang.

Description and Physical Properties.—"A colorless or pale yellow, thin liquid, having a strongly aromatic odor of clove, and a pungent, spicy taste. Exposure to air causes it to become darker and thicker. Eugenol is slightly soluble in water, but is miscible with alcohol, chloroform, ether, and with fixed oils. It is soluble in twice its volume of 70 per cent. alcohol.

Specific gravity: 1.0 4 to 1.070 at 25° C. Eugenol boils between 250° and 255° C. It is optically inactive and strongly refractive. A mixture of 1 cc. of Eugenol and 20 cc. of hot distilled water is only very slightly acid to litmus paper. Dissolve 1 cc. of Eugenol in 12 cc. of sodium hydroxide T.S., and add 18 cc. of distilled water; a clear solution results which becomes turbid when exposed to air (*hydrocarbons*). Shake 1 cc. of Eugenol with 20 cc. of distilled water, filter, and add 1 drop of ferric chloride T.S. to 5 cc. of the clear filtrate; a transient grayish-green color, but not a blue or violet color, is produced (*phenol*).

Preserve in well-stoppered containers, in a cool place, protected from light." *U. S.*

Uses.—The medicinal properties of eugenol are practically the same as those of Oil of Cloves. Our own experiments, as well as those of Martindale, indicate, however, that it is slightly less active as an antiseptic than natural oil. It is much used by dentists for disinfecting root-canals.

Dose, two to five minims (0.12–0.3 cc.).

Off. Prep.—Mistura Olea Balsamica, *N. F.*

EUONYMUS. N. F. (Br.)

EUONYMUS Euonym. [Wahoo Bark]

"Euonymus is the dried bark of the root of *Evonymus atropurpureus* Jacquin (Fam. *Celastraceæ*). Euonymus contains not more than 5 per cent. of adhering wood or more than 2 per cent. of other foreign organic matter and yields not more than 4 per cent. of acid-insoluble ash." *N. F.*

"The dried root bark of Euonymus atropurpureus, *Jacq.*" *Br.*

Euonymi Cortex, *Br.;* Cortex Euonymi; American Indian Arrow-wood; Ecorce d'Evonymus, *Fr. Cod.;* Spindlebaum, Pfaffenhütchen, Spillbaumrinde, *G.*

Euonymus (more properly *Evonymus*) *atropurpureus,* named variously *wahoo, spindle-tree,* and *burning-bush,* is a tall, erect shrub or rarely (frequently, west of the Mississippi) a slender tree with quadrangular branchlets, and opposite, petiolate, oval-oblong, pointed, serrulate, membranous leaves. The flowers, which stand in loose cymes on axillary peduncles, are small and dark purple, with sepals and petals commonly in fours. The fruit is a deeply 3- to 4-lobed crimson-purple capsule, each lobe dehiscing to expose a seed which is covered by a succulent crimson aril. The plant is native to eastern North America, west to Montana, Arkansas and Indian territory.

The plants belonging to the *Euonymus* genus are shrubs or small trees, presenting in the autumn a striking appearance from the rich red color of their fruit, which has obtained for them the name of *burning-bush. E. americanus* L. and *E. europæus* L. have been cultivated in gardens as ornamental plants. Several species have been used in medicine. Their properties are probably similar, if not identical. An oil expressed from the seeds of *E. europæus* was formerly used in Europe for the destruction of vermin in the hair, and sometimes also as an application to old sores. The seeds of a number of this and other species are purgative and emetic and of some the leaves are poisonous to sheep and other animals feeding on them. It is probable that much of the wahoo of our drug stores has been obtained from *E. americanus,* which is distinguished from *E. atropurpureus* by its rough, warty, depressed capsules, and almost sessile, thicker leaves.

Description and Physical Properties.—"*Unground Euonymus.*—Usually in transversely curved pieces, occasionally in single quills from 2 to 7 cm. long; bark from 1 to 4 mm. thick; very light in weight; outer surface grayish or light brown, somewhat wrinkled, with soft scaly cork and transverse lenticels, the latter occasionally forming fissures; inner surface grayish white, longitudinally striate and somewhat porous; fracture short with projecting, silky, elastic fibers of a caoutchouc-like substance. Odor distinct; taste bitter and acrid.

"*Structure.*—Cork cells with thin, nearly colorless, lignified walls, the outer layers somewhat collapsed, a zone of isodiametric cortical parenchyma; sieve separated by bast parenchyma and wavy secondary medullary rays, the latter, one cell in width; the medullary ray cells and parenchyma contain starch or rosettes of calcium oxalate; elongated secretory cells with a brownish or yellowish amorphous content distributed throughout the middle and inner bark.

"*Powdered Euonymus.* — Light brown; numerous starch grains, nearly spherical, from 0.003 to 0.012 mm. in diameter; fragments of cork; elongated fragments of secretion cells; numerous fragments of starch-bearing parenchyma; calcium oxalate in rosettes from 0.015 to 0.060 mm. in diameter, the amount in different specimens showing some variation. Prisms of calcium oxalate are wanting." *N. F.*

"In quilled or curved pieces, from two to four millimetres thick. Outer layer a soft, friable, greyish cork, marked with dark patches. Inner surface pale tawny-white and smooth. Fracture short, the fractured surface yellowish in color. Transverse section free from sclerenchymatous cells and fibres, and exhibiting, in the secondary bast, laticiferous cells filled with a granular, elastic substance. Faint but characteristic odor; taste somewhat mucilaginous, afterwards bitter and slightly acrid." *Br.*

The chief adulterant of Euonymus within recent years has been the bark of the *Wafer Ash, Ptelea trifoliata* L. (Fam. *Rutaceæ*). The latter may readily be distinguished from Euonymus, upon fracture, by its absence of caoutchouc threads extending between the broken surfaces, the latter appearing waxy and pale yellow. It can be identified microscopically by the layer of stone cells beneath the cork, the presence of prismatic and rosette crystals of calcium oxalate, the former in the outer parenchyma of the cortex, the numerous oleoresin cells scattered throughout the parenchyma and the absence of secretory cells containing a caoutchouc-like material. For detailed anatomical distinctions between these barks see paper by H. W. Youngken in *A. J. P.,* 1918, p. 160.

The bark frequently has had as much as 25 per cent. of adhering wood. The amount of the latter with other foreign matter should not exceed 3 per cent. Holm (*Merck's Rep.,* 1909, p. 169) illustrates the structural characteristics of *E. atropurpureus* and *E. americanus.* Holmes (*P. J.,* 1905) describes the bark of *Alstonia scholaris* R. Br., which has been used as an adulterant of Euonymus. The name of Wahoo (pronounced *Wawhoo*) was given to it by the Indians who employed a decoction of the inner bark of the *E. atropurpureus* in uterine troubles. The same name has also been applied to *Ulmus alata* Michx. of the southern States, and has thus led to mistakes.

The term *euonymin* has been applied (1) to the resinous matter which is precipitated by adding water to an alcoholic tincture of the drug; (2) to a crystallizable bitter principle isolated by Wenzell in 1862 and (3) to a glucoside found by Meyer and Romin (*Ph. Central.,* 1885), although the term *euonymo-toxin* has been suggested for this glucoside. This glucoside is stated to exercise a digitalis-like effect on the heart. Frank V. Cassaday (*A. J. P.,* 1889, p. 284) found 1.30 per cent. of volatile oil and resin, 1.48 per cent. of *euonic acid* and resin, 2.10 per cent. of euonymin and resin, together with the usual plant constituents. Kubel has discovered in the fresh inner bark of *E. europæus* a saccharine, crystallizable substance, closely resembling mannite, but differing in its crystalline form and in its melting point. He calls it *euonymite.* (*J. P. C.,* Dec., 1862, 523.)

H. Rogerson (*P. J.,* 1912, p. 687) has made a complete chemical examination of this bark with the result that the following definite constituents are reported present: dulcitol; *furan—β—carboxylic acid,* $C_5H_4O_3$; *euonymol,* $C_{21}H_{30}O_4$ (a new crystalline alcohol, having a melting point of 248° C.); a sugar which yielded *d-phenyl glucozazone; euonosteryl,* $C_{31}H_{51}O.OH$; *homoeuonosteryl,* $C_{40}H_{69}O.OH$; *atropurol,* $C_{27}H_{44}(OH)_2$; *citrullol,* $C_{22}H_{36}O_2(OH)_2$; and a mixture of palmitic, cerotic, oleic and linoleic acids. No glucoside was found.

Uses.—This bark was introduced many years ago as a remedy for *dropsy,* but has been used chiefly for its cathartic action. By the eclectics it was supposed to exert an especial effect on the liver and was used in cases of *chronic constipation, dyspepsia,* etc. Its use, however, is not to be recommended because of the possibility of an undesirable effect upon the circulation.

Dose, of euonymus, five to fifteen grains (0.32–1.0 Gm.).

"*Caution.*—It has been stated that the absorption of Euonymus in the gastro-intestinal tract is uncertain and irregular. To avoid possible toxic or cumulative action of the drug the physician should determine in each case the tolerance of the patient and regulate the dosage accordingly." *N. F.*

Off. Prep.—Extractum Euonymi, *Br., N. F.;* Fluidextractum Euonymi, *N. F.*

EUPATORIUM. N. F.

EUPATORIUM Eupator. [Thoroughwort, Boneset]

"Eupatorium consists of the dried leaves and flowering tops of *Eupatorium perfoliatum* Linné (Fam. *Compositæ*). Eupatorium contains not more than 10 per cent. of its stems and not more than 2 per cent. of foreign organic matter." *N. F.*

Boneset; Thoroughwort; Herba Eupatorii Perfoliati, Indian Sage; Thorough-stem; Cross-wort; Thorough-wax; Sweating Plant; Herbe d'Eupatoire perfoliée, Herbe à fièvre, Herbe parfaite, *Fr.;* Durchwachsener Wasserhanf or Wasserdost, *G.*

This is an indigenous perennial plant, with numerous, herbaceous stems, which are erect, round, hairy, from two to five feet high, simple below, and trichotomously branched near the summit. The leaves serve to distinguish the species at the first glance. They are connate-perfoliate and decussate at regular distances upon the stem. They are narrow in proportion to their length, broadest at the base where the two opposite, sessile leaves have coalesced, gradually tapering to a point, serrate, much wrinkled, paler on the under than on the upper surface, and beset with whitish hairs, which give them a grayish-green color. The uppermost pairs are sessile, not joined at the base. The flowers are all tubular and white, being arranged in corymbs of numerous heads, with hairy peduncles. The involucre, which is cylindrical and composed of imbricated, lanceolate, hairy bracts, encloses from twelve to fifteen tubular florets, having their border divided into five spreading segments. The anthers are five, black, and united into a tube, through which the bifid filiform style projects. This species of *Eupatorium* inhabits meadows, the banks of streams, and other moist places, growing generally in bunches, and abounding in almost all parts of the United States. It flowers from the middle of summer to the end of October. The leaves and flowering tops are collected from wild plants during late summer and dried in the shade. The commercial supplies are obtained chiefly from the central and southern United States. It has a faint odor, and a strongly bitter, somewhat peculiar taste.

Description and Physical Properties.—"*Unground Eupatorium.*—Usually more or less broken; leaves opposite, the pair united at the base, from 8 to 20 cm. long and from 1.5 to 5 cm. in width, tapering regularly from near the base to an acute apex, crenate-serrate, rugosely veined, rough and bright green above, yellowish gray-green, tomentose and resinous-dotted beneath; flower-heads small, numerous, corymbed, with a campanulate involucre of lance-linear, imbricated scales and with from 10 to 15 tubular yellowish white florets having a bristly pappus in a single row. Odor faintly aromatic; taste strongly bitter.

"*Powdered Eupatorium.*—Dark green; multicellular, non-glandular hairs with thin finely striate walls and end cells pointed or somewhat rounded; glandular hairs, short-stalked with 2-celled heads, the latter from 0.045 to 0.080 mm. in diameter or with a 6- to 8-celled stalk, the cells arranged in a double row and a 4- to 12-celled head; ellipsoidal pollen grains up to 0.025 mm. in diameter, with numerous spiny centrifugal projections; hairs of the pappus, in the form of a multicellular axis with numerous, short, unicellular, alternate branches; tracheæ spiral, annular or with bordered pores; numerous fragments of leaf epidermis showing elliptical stomata from 0.018 to 0.036 mm. in length; many fragments of achene pericarp composed of cells with thick characteristic brownish walls; fragments of stem tissue showing epidermal cells, parenchyma associated with non-lignified, thin-walled porous fibers, tracheæ, and pith parenchyma; numerous fragments of corolla tissue." *N. F.*

George Latin (*A. J. P.,* Aug., 1880) found a glucoside, *eupatorin,* and a crystallizable body of the nature of wax. Shamel (*Am. Chem. J.,* 1892, p. 224) published an analysis of the nitrate of the crystalline principle giving the formula $C_{20}H_{25}O_{36}HNO_3$.

Uses.—In large doses eupatorium is emetic and aperient. It has long been a popular household remedy in a variety of disorders. It probably, however, possesses no therapeutic virtues which are not explicable on the ground of its nauseating properties. Because of this effect the warm infusion tends to increase perspiration and it may be useful as a diaphoretic in the formative stages of colds, muscular rheumatism and similar disorders. Probably through the same action it has been applied in various types of *bronchitis,* and by some is believed to have established virtues when there is a tendency towards asthma.

Dose, thirty to sixty grains (2–4 Gm.).

Off. Prep.—Fluidextractum Eupatorii, *N. F.*

EUPHORBIA. N. F.

EUPHORBIA Euphorb. [Euphorbia Pilulifera, Pill Bearing Spurge]

"Euphorbia is the dried herb of *Euphorbia hirta* Linné (Fam. *Euphorbiaceæ*). Euphorbia contains not more than 5 per cent. of foreign organic matter and yields not more than 3 per cent. of acid-insoluble ash." *N. F.*

Pill-bearing Spurge; Snakeweed; Queensland Asthma Weed; Cat's-hair.

This plant is a prostrate or ascending branched annual indigenous to India, but naturalized in other tropical countries. It is characterized by its slender, cylindrical, hairy stems; the leaves are opposite, oblong-lanceolate, shortly petiolate, denticulate or serrulate, hairy and unequal at the base, they vary from 2 to 4 cm. in length and are often blotched with red. Minute linear stipules are present. The flower-heads are small, numerous, crowded in head-like cymes, globular, and are borne on a short stalk in one axil, only, of each pair of opposite leaves. The involucre is small, entire, and without petal-like appendages. The fruits are small, yellow, 3-celled capsules, each component carpel of which is keeled. The seeds are minute, triangular-ovoid and of a pale brown color. It is to be distinguished from E. *parviflora* (L.), which is sometimes substituted for it, by the head-like cymes of the latter having but few flowers, by the glands of the involucre being furnished with a white, obovate-orbicular appendage, and by the seeds being minutely papillose.

The commercial supplies come chiefly from India. For description of other species see *Euphorbia,* Part II.

Description and Physical Properties.—"*Unground Euphorbia.*—Roots usually present, small, branched, and reddish; stems slender, cylindrical, obliquely erect, dichotomously branched from near the base, branches recurved at apices; branches and stem only sparsely leafed at base, pale greenish brown, rough or hairy, rather densely on the upper parts but sparsely on the lower; leaves opposite, obliquely oblong, acute, serrulate, rusty pale green, pubescent especially on the prominent veins on the lower surface, becoming brittle on drying and usually much broken in the drug; flowers small, numerous, in short peduncled axillary clusters; fruits about 2 mm. in diameter, three-celled capsules; seeds about 0.9 mm. in diameter, triangular-ovoid, pale brown. Odor aromatic and characteristic, taste faintly bitter, aromatic and acrid.

"*Powdered Euphorbia.*—Light yellowish; numerous fragments of lignified tissue composed of wood fibers, wood parenchyma, medullary ray and pith parenchyma, associated with tracheids and tracheæ, the latter from 0.020 to 0.060 mm. in diameter and with bordered pores, spiral or scalariform markings; fragments composed of cork cells containing a reddish brown amorphous content and having walls which are sometimes lignified; numerous spherical to ovoid starch grains, simple to 3-compound, the individual grains from 0.005 to 0.025 mm. in diameter; numerous, thick-walled, lignified fibers from 0.020 to 0.070 mm. in diameter, either isolated or associated with thick-walled, starch containing parenchyma, the latter and latex tubes, the latter with a grayish, amorphous content, few fragments of epidermis from leaf or upper part of stem showing multicellular, yellowish, non-glandular hairs, up to about 0.090 mm. in diameter at the base and up to 0.850 mm. in length, and colorless, curved multicellular, non-glandular hairs up to 0.040 mm. in diameter at the base and up to 0.400 mm. in length." *N. F.*

Levison found in it (*A. J. P.,* 1885, 147) several glucoside resins, wax, and volatile matter. Dr. F. B. Power (*C. D.,* 1913, 544) examined *E. pilulifera* from the Fiji Islands and found a monohydric alcohol, *euphosterol,* among other constituents, none of which seem to possess value therapeutically.

Uses.—A physiological study of *Euphorbia pilulifera* led A. Marsset (*T. G.,* 1885) to the conclusion that the active principle acts directly upon the heart and respiration; that it is not an irritant to the skin, but in large dose it is to the gastric mucous membrane. It has been used by Dujardin-Beaumetz and a number of other clinicians with asserted excellent results in the treatment of *asthma* and *bronchitis.*

Dose of the fluidextract, from a half to one fluidrachm (1.8–3.75 cc.) three or four times a day.

Off. Prep.—Fluidextractum Euphorbiæ Piluliferæ, *N. F.;* Elixir Euphorbiæ Compositum, *N. F.*

EXTRACTA. U. S.

EXTRACTS

"Extracts are either pasty or semi-solid masses, or dry, solid or powdered products, prepared by exhausting drugs with appropriate solvents, carefully evaporating the solutions so obtained to the prescribed consistence and adjusting the products to the fixed standards. An extract is intended to preserve the useful constituents of the drug in a concentrated, relatively uniform, permanent condition and in a form suitable for medication." *U. S.*

Extraits, *Fr.;* Extrakte, *G.;* Estratti, *It.;* Extractos, *Sp.*

Extracts, as the term is employed in the Pharmacopœias, are solid preparations, resulting from the evaporation of the solutions of vegetable principles, obtained either by exposing a dried drug to the action of a solvent, or by expressing the juice from a fresh plant. A distinction was formerly made between those prepared from the infusions, decoctions, or tinctures, and those from the expressed juices of plants, the former being called *Extracta,* the latter *Succi Spissati,* but the distinction has been generally abandoned.

The composition of extracts varies with the composition of the plant, the character of the solvent, and the mode of preparation. The object is generally to obtain as much of the active principle of the plant with as little of the inert matter as possible, though sometimes it may be desirable to separate two active ingredients from each other when their effects upon the system are materially different; this may be accomplished by employing a menstruum which, while it dissolves one, leaves the other untouched. The proximate principles most commonly present in extracts are gum, sugar, starch, tannin, extractive, coloring matter, salts, and the peculiar principles of plants, to which, when an alcoholic solvent is employed, may usually be added resinous substances, fatty matter, and frequently more or less essential oil, gum and starch being excluded when the menstruum is pure alcohol. Of these substances, as well as of others which, being soluble, are sometimes necessarily present in extracts, we have taken occasion to treat under various heads in this commentary. There is one, however, which from its supposed almost uniform presence in this class of preparations, and from the influence it is thought to exert upon their character, deserves particular consideration in this place. We allude to *extractive,* or, as it is sometimes called, *extractive matter.*

It has long been observed that in most plant tissues there is a substance, soluble both in water and alcohol, which, in the preparation of extracts, undergoes characteristic changes during the process of evaporation, imparting to the liquid even if originally limpid, first a greenish, then a yellowish-brown, and ultimately a deep brown color, and becoming itself insoluble. This substance, originally called *saponaceous matter* by Scheele, afterwards received the more expressive name of *extractive,* derived from its frequent presence in extracts. The most important property of extractive is its disposition to pass, by the influence of atmospheric air at a high temperature, into an insoluble substance. If a vegetable infusion or decoction be evaporated in the open air to the consistence of an extract, then diluted, filtered, and again evaporated, and the process repeated so long as any insoluble matter is formed, the whole of the extractive will ultimately be separated from the liquid, while the other ingredients may remain. The name of oxidized extractive which has been given to it is incorrect, and Berzelius proposed to substitute for it that of *apothem,* synonymous with deposit. According to Berzelius, apothem is not completely insoluble in water, but imparts a slight color to that liquid when cold, and is rather more soluble in boiling water, which becomes turbid upon cooling. It is still more soluble in alcohol, and is freely dissolved by solutions of the alkalies and alkaline carbonates, from which it is precipitated by acids. It has a great tendency, when precipitated from solutions, to unite with other principles, probably on account of its colloidal absorptive properties, and to carry them along with it, thus acquiring properties somewhat different according to the source from which it is obtained. In this way also, even when the extractive of a plant is itself medicinally inert, its conversion into apothem may be injurious by causing a precipitation of a portion of the active principle, and in practical pharmaceutical operations this change should always, if possible, be avoided.

We shall treat of the subject under the several heads of (1) the extraction of the soluble principles from the plant; (2) the method of conducting the evaporation; (3) the proper condition of extracts, the changes they are liable to undergo, and the best method of preserving them.

1. *Extraction of the Soluble Principles.*

There are two distinct modes of obtaining, in a liquid state, the principles which we wish to extract: (1) by expression alone; (2) by the agency of a solvent, with or without expression.

1. By Expression.—This method is applicable to fresh vegetable tissues when they are very succulent and when other conditions are favorable. It is not recognized by the U. S. but there are four preparations in the Br. in which expression of juice is employed. All plants cannot be usefully treated in this way, as many have too little juice to afford an appreciable quantity upon pressure, and of the succulent a considerable portion do not yield all their active principles with their juice. Succulent fruits, and various acrid and narcotic plants, are proper subjects for this treatment. The plants should be operated upon, if possible, immediately after collection. Battley, of London, recommended that, if not entirely fresh, they should be revived by the immersion of the stalks in water for twelve or eighteen hours, and those only used which recover their freshness by this management. They should then be cut into pieces, and bruised in a stone mortar till brought to a pulpy consistence. When the plant is not very succulent, it is necessary to add a little water during this part of the process, in order to dilute the juice. After sufficient contusion, the pulp is introduced into a linen or canvas bag, and the liquid parts expressed. Brande states that light pressure only should be employed, as the extract is thus procured greener, of a less glutinous or viscid consistence, and, in his opinion, more active than when considerable force is used in the expression. The juice thus obtained is opaque, and usually green, in consequence of the presence of chlorophyll, and of a portion of the undissolved vegetable tissues in minute division. By heating the juice to about 71.1° C. the albumen contained in it coagulates, and, involving the chlorophyll and vegetable fiber, forms a greenish precipitate. If the liquid be now filtered, it becomes limpid and nearly colorless, and is prepared for evaporation. The clarification, however, is not absolutely necessary, and is generally neglected. Sometimes the precipitate carries with it a considerable portion of the active principle, in which case it should be subsequently incorporated with the juice, when the latter is reduced by evaporation to the consistence of syrup. Chloroform or ether added to the expressed juices of plants enables them to be kept long without injurious change. Lepage, of Gisors, France, has kept the juice of belladonna preserved with ether more than ten years, and found it, at the end of that time, to yield an extract identical in physical, chemical, and physiological properties with that obtained from the fresh juice.

2. By Solution.—"The solvent or menstruum to be employed in the preparation of an extract is dependent upon the physical characteristics of the drug and the nature of its constituents. The solvents commonly adopted are water or alcohol, or mixtures of these, in the proportions directed in the formulas. For the extraction of a few drugs, the addition of an acid or an alkali to the solvent is required. When alcohol is used as a solvent, it may be recovered by distillation. When a drug contains an oily constituent that is extracted by the menstruum, it becomes necessary to adopt in the process of manufacture some method for the separation of this oil so that a permanent product of the proper consistence, dryness, or pulverulent form may be obtained." *U. S.*

The active principles of dried vegetable substances can be extracted only by means of a liquid solvent. The menstruum usually employed is either water or alcohol, or a mixture of the two. Water, on account of its cheapness, is always preferred, when circumstances do not strongly call for the use of alcohol. It has the advantage, moreover, that it may be assisted in its action if necessary by a higher degree of heat than the latter. Tap water is often unfit for the purpose, in consequence of the quantity of its saline matter, which in some instances may exert an unfavorable influence on the active principle, and must always be left in the extract. Distilled water is preferred. Alcohol is employed when the principles to be extracted are insoluble or but slightly soluble in water, as in the case of the resins; when it is desirable to avoid in the extract inert substances, such as gum and starch, which are dissolved by water and not by alcohol; when the heat required to evaporate the aqueous solution would dissipate or decompose the active ingredients of the plant, as the volatile oils; when the reaction of the water itself upon the vegetable principles is injurious; and, finally, when the nature of the substance to be exhausted requires so long a maceration in water as to endanger spontaneous decomposition. The aqueous solution requires to be quickly evaporated, as this fluid rather promotes than counteracts chemical changes, while an alcoholic tincture may be preserved unaltered for an indefinite period. An addition of alcohol to water is sufficient to answer some of the purposes for which the former is preferable, and the employment of both fluids is essential, when the virtues of the plant reside in two or more principles, all of which are not soluble in either of these menstrua. In this case it is usually better to submit the vegetable to the action of the two fluids successively than of both united. Extracts obtained by the agency of water are called *aqueous extracts;* those by means of alcohol, undiluted or diluted, *alcoholic* or *spirituous extracts.* Sometimes the term *hydro-alcoholic* is applied to extracts obtained by the joint agency of alcohol and water. The methods of extraction are by infusion, decoction, maceration or percolation.

Chloroform is frequently used to saturate the water used in making aqueous extracts to prevent fermentation during percolation.

It is always desirable to obtain the solution in the first place as concentrated as possible, so as to prevent the necessity of long continued evaporation, which injures the extract. It is better, therefore, to incur the risk, both when decoction and infusion are employed, of leaving a portion of the active matter behind, than to obtain a very weak solution. When successive portions of water are employed, those which are least impregnated should be brought by evaporation to the strength of that first obtained before being mixed with it.

Acetic acid has been introduced into use as a menstruum in the preparation of extracts. It is supposed to be a better solvent of the active principles of certain substances than either water or alcohol alone. Experiments have shown that strong acetic acid (60 per cent.) is a powerful solvent for the active properties of various drugs, particularly those which contain volatile oils, and in many cases a 10 per cent. acetic acid is an excellent menstruum for making extracts; for these the name *acetract* has been proposed. (*Proc. A. Ph. A.,* 1897, 416.) E. R. Squibb has used acetic acid largely for extracts. (*West. Drug.,* 1897, 123.)

Ether also is now used to a considerable extent in the preparation of oleoresins which are a class of extracts. Having the property of dissolving volatile oil and resin, and of evaporating at a temperature insufficient to volatilize the oil, it is admirably adapted for the extraction of drugs the virtues of which reside in the two principles referred to. An ethereal tincture is first prepared by the process of percolation, and the ether is then allowed to escape by spontaneous evaporation, or distilled off at a very moderate heat. The oleoresinous extracts thus obtained are usually of a thick fluid or semifluid consistence. Several of them now rank among the official preparations, in the U. S. P., under *Oleoresinæ.* Acetone is another solvent used much for the same purpose as ether.

"**Powders—Fineness.**—The fineness of vegetable drugs is expressed in this Pharmacopœia by the following terms: (1) *coarse powder* (No. 20), (2) *moderately coarse powder* (No. 40), (3) *fine powder* (No. 60), (4) *very fine powder* (No. 80). A powder to conform to any one of these specified terms must meet the requirements given below. In the preparation of ground or powdered drugs, no portion of the drug shall be rejected during milling or sifting unless specifically permitted under the official description of the drug. It is permissible, however, to withhold *final tailings* not exceeding 5 per cent. of the drug being powdered, which may be added in no greater percentage to other lots of the same drug in subsequent millings.

"STANDARDS FOR UNIFORMITY OF FINENESS.—A *coarse powder* (No. 20) is one in which all of the particles will pass through a No. 20 standard mesh sieve and not more than 40 per cent. through a No. 60 standard mesh sieve. A *moderately coarse powder* (No. 40) is one in which all of the particles will pass through a No. 40 standard mesh sieve and not more than 40 per cent. through a No. 80 standard mesh sieve. A *fine powder* (No. 60) is one in which all of the particles will pass through a No. 60 standard mesh sieve and not more than 40 per cent. through a No. 100 standard mesh sieve. A *very fine powder* (No. 80) is one in which all of the particles will pass through a No. 80 standard mesh sieve."

The "standard *sieves*" referred to in the official description is intended to mean those that meet the standards of the U. S. Department of Commerce (*Circular* LC, 74, April 15, 1924). This circular describes in detail the size of the opening, diameter of the wire and shape of sieve necessary to conform to Federal regulations; manufacturers may have their sieves certified by the Bureau of Standards by payment of a small fee. The meaning of the numbers adopted can be most readily explained by the following quotation from this Circular:

"Because of the wide range of openings in sieves now manufactured which is possible with a given number of meshes per unit length by the use of wires of different diameters, and the consequent confusion and uncertainty which arises in designating sieves by the number of meshes per unit length, it is recommended that all reference to mesh be avoided in the designation of the sieves, but that for convenience each sieve be given an abstract number which will indicate the approximate position of the sieve in the series. The proper designation of a sieve is the size of the opening, supplemented by the wire diameter, but it is well recognized that few users of sieves will be able to carry the sizes of the various openings in mind without reference to a printed table. All that the users of sieves desire to know in general is that the sieves are 'standard,' that is, that they conform to established specifications, and therefore the only designation required is a simple one which will suggest the degree of fineness or coarseness of the material passing or retained upon any given sieve. Such a designation is an abstract number which is approximately the number of meshes per linear inch. The advantage of such a designation is readily apparent. Thus the sieve, which has a 0.105 mm. opening, is given the number 140, which may be regarded simply as a fixed arbitrary number indicating that the sieve has approximately 140 meshes per inch. The fact that a sieve of nominal opening and wire diameter has actually 141.9 meshes per inch or 55.9 meshes per centimeter is of no importance; the number 140 merely indicates to those who are familiar with the old sieves what order of separation this sieve would give in testing any graded material. It is urgently recommended that all users of sieves in the future designate these standard sieves by these arbitrary numbers approximately the mesh per inch, and that the manufacturers mark and list the sieves in this manner, together with the size of the openings and the wire diameters in both millimeters and inches." *Circular,* U. S. Bureau of Standards.

"METHOD FOR DETERMINING UNIFORMITY OF FINENESS.—For determining uniformity of degree of fineness of a powdered vegetable drug, the following process shall be used, employing standard testing sieves which meet the requirements of the Bureau of Standards, U. S. Department of Commerce. For *coarse* and *moderately coarse powders,* place from 25 to 100 Gm. of the powder to be tested upon the proper standard testing sieve with a tightly fitting receiving pan and cover. Shake the sieve in a rotary horizontal direction and vertically by tapping on a hard surface for not less than twenty minutes or until no appreciable number of particles pass through the sieve. Weigh accurately the amount remaining on the sieve and in the receiving pan and calculate to per cent. In the case of *fine* or *very fine powders,* proceed as for *coarse* or for *moderately coarse powders,* but shake the sieve for at least thirty minutes or until no appreciable number of particles pass through the sieve. In the case of oily or other powders which tend to clog the openings, the screen should be carefully brushed at intervals during the test. In the case of powders which tend to form lumps, such lumps should be carefully disintegrated during the sifting test. In all cases care must be taken not to increase the fineness of the powder during the process of sieve testing.

"Mechanical testing machines which impart a rotating and tapping effect to the testing sieves may be employed for making the tests. In all cases care must be taken to see that the separation is complete before the weighings are made.

"**Percolation and Maceration.**—*Percolation,* as directed in this Pharmacopœia, consists in subjecting a comminuted substance or a mixture of substances, contained in a vessel called a percolator, to the solvent action of successive portions of a liquid termed the menstruum in such a manner that the liquid, as it traverses the powder in its descent to the receiver, shall extract the soluble constituents, and pass from the percolator free from insoluble matter. When the process is successfully conducted, the first portion of the liquid, or percolate, passing through the percolator will be nearly saturated with the soluble constituents of the substance treated; and, if the quantity of menstruum be sufficient for its exhaustion, the last portion of the percolate will be nearly free from color, odor, and taste, other than those of the menstruum itself. In preparations which direct the process of percolation, wherever the expression 'until the drug is exhausted' or a similar phrase occurs, it is to be understood that the term 'exhausted' means that point at which the valuable constituents have been as completely extracted as is practicable, and this must be determined by the judgment and experience of the operator.

"*Percolators.*—The following statement with regard to percolators and the process of percolation is given in order to illustrate a method of percolation. It is not intended to be compulsory and it is permissible for manufacturers and others to modify the process to suit their needs. The percolator most suitable for the quantities contemplated by this Pharmacopœia should be nearly cylindrical, or slightly conical, with a funnel-shaped termination at the smaller end. The neck of this funnel-end should be rather short, and should gradually and regularly become wider toward the orifice, so that a perforated cork, bearing a short glass tube, may be tightly wedged into it. The glass tube, which must not project above the inner surface of the cork, should extend from 3 to 4 cm. beyond the outer surface of the cork, and should be provided with a closely fitting rubber tube, at least one-fourth longer than the percolator itself, and ending in another short glass tube, whereby (when it is desired to interrupt the percolation) the rubber tube may be so suspended that its orifice shall be above the surface of the menstruum in the percolator, a rubber band or wire loop holding the tube in position. The shape of the percolator should be adapted to the nature of the drug to be operated upon. For drugs which are apt to swell, particularly when a weak alcoholic or an aqueous menstruum is employed, a *conical* percolator is preferable. A *cylindrical* or only slightly tapering percolator may be used for drugs which are not likely to swell, particularly if difficult to exhaust, also when the menstruum is strongly alcoholic, or when ether or some other volatile liquid is used for extraction. The size of the percolator selected should be in proportion to the quantity of drug extracted. When properly packed, the drug should not occupy more than two-thirds of the height of the percolator. The percolator is best constructed of glass, but, unless otherwise directed, may be made of any suitable material not affected by the drug or menstruum. Metallic percolators are required for hot percolation. The percolator is prepared for percolation by gently pressing a small tuft of purified cotton into the neck, and this may then be moistened by pouring a few drops of menstruum upon the cotton, to facilitate the passage of the first portion of percolate, which is often very dense.

"*The Process.*—The substance to be percolated, of the fineness directed in the formula, and thoroughly air-dried before it is weighed, is put into a suitable dish, sufficient menstruum is poured on, and the powder stirred until it is uniformly moistened. The moist powder is then passed through a sieve. Coarse powders usually do not require this additional treatment after the moistening. The moist powder is now transferred to a sheet of thick paper and the whole quantity poured from this into the percolator. It is then shaken down lightly and allowed to remain in that condition for a period varying from fifteen minutes to several hours, unless otherwise directed. After maceration, the moist powder is removed from the percolator, and then returned in suitable portions, pressing each portion, with the aid of a plunger of suitable dimensions, more or less firmly, in proportion to the character of the powdered substance and the alcoholic strength of the menstruum. Strongly alcoholic menstrua, as a rule, permit firmer packing of the powder than weaker menstrua. The percolator is now placed in position for percolation, and, the rubber tube having been fastened at a suitable height, the surface of the powder is covered by an accurately fitting disc of filter paper, held in place by a layer of washed sand or a glass stopper or percolator weight, and a sufficient quantity of the menstruum is poured on through a funnel reaching nearly to the surface of the paper. If these conditions are accurately observed, the menstruum will penetrate the powder equally until it has passed into the rubber tube and has reached, in this, a height corresponding to its level in the percolator, which is now closely covered to prevent evaporation. The apparatus is then allowed to stand at rest for the time for maceration specified in the formula.

"To begin percolation, the rubber tube is lowered and its glass end introduced into the neck of a bottle, previously marked for the quantity of liquid to be received, if the percolate is to be measured, or tared, if the percolate is to be weighed. By raising or lowering this receiver the rapidity of percolation may be increased or decreased as may be desirable. A layer of menstruum must constantly be maintained above the powder, to prevent the access of air to its interstices, until all has been added, or the requisite quantity of percolate has been obtained. This is conveniently accomplished, if the space above the powder will admit of it, by inverting a bottle containing the entire quantity of menstruum over the percolator in such a manner that its mouth may dip beneath the surface of the liquid, the bottle being of such shape that its shoulder will serve as a cover for the percolator.

"When the dregs of a tincture, or of a similar preparation, are to be subjected to percolation, after maceration with all or with the greater portion of the menstruum, the liquid portion should be drained off as completely as possible, the solid portion packed in a percolator, as described, and the liquid poured on until all has passed from the surface, when immediately a sufficient quantity of the directed menstruum should be poured on to displace the retained liquid and obtain the prescribed quantity.

"*Repercolation or Fractional Percolation.*—Authority is given to employ, where it may be applicable, the process of repercolation, without change of the initial menstruum or the process of fractional percolation, described in Type Process C for fluidextracts.

"*Rate of Flow.*—The success of the process of percolation largely depends upon the regulation of the flow of the percolate; if this is too rapid, incomplete exhaustion will result, but if too slow, valuable time is wasted and considerable loss of menstruum occurs from evaporation. For fluidextracts using 1000 Gm. of powder, the rate of flow should not exceed ten drops a minute; for official quantities of tinctures and preparations of about the same strength, twenty drops a minute, and the word "slowly" throughout the text is understood to mean a rate of flow corresponding to this. The proper rate of flow should vary with the quantity and character of the drug employed and the density of the menstruum.

"*Maceration.*—Percolation is not suitable for exhausting some drugs, and for such the process of maceration is employed. The tinctures of asafetida, sweet orange, and tolu are illustrations. Maceration should be conducted preferably at a temperature of from 15° to 20° C. Specific directions will be found in the monographs." *U. S.*

For an account of E. R. Squibb's process of repercolation, see *Fluidextracta.*

Large scale production enables the pharmaceutical manufacturer to employ vacuum stills for recovering the solvents and enabling concentration to be effected at temperatures which are not injurious to the principles involved.

2. *Mode of Conducting the Evaporation.*

"In the preparation of extracts, the concentration of the liquid extractions is to be completed without delay, and undue exposure to heat must be avoided. The limit of temperature for the evaporation, as stated in the formulas, should not be exceeded. In the manufacture of extracts on a large scale, apparatus for distilling and evaporating under reduced pressure should be used. It is also important that the residue be frequently stirred in order to hasten the evaporation and to obtain a uniformly smooth product. In the preparation of powdered extracts, it is necessary to use solvents that will extract the active principles of the drug and only a minimum amount of inert substance. The drying of the soft extract can be greatly facilitated by spreading it upon plates of glass or tinned metal and exposing it to currents of warm dry air. Powdered extracts must be thoroughly dried, powdered, intimately mixed with the diluent, and carefully preserved as directed below." *U. S.*

In evaporating the solutions, attention should always be paid to the fact that the extractive matter is constantly becoming insoluble at high temperatures with the access of air, and that other chemical changes are going on, sometimes not less injurious than this, while the volatile principles are expelled with the vapor. The operator should, therefore, observe two rules: (1) to conduct the evaporation at as low a temperature as is consistent with other objects; (2) to exclude atmospheric air as much as possible, and, when this cannot be accomplished, to expose the liquid the shortest possible time to its action. The injurious influence of atmospheric air is much greater at the boiling point of water than at a less heat, even allowing for the longer exposure in the latter case, and therefore a slow evaporation at a moderate heat is preferable to the more rapid effects of ebullition. First, however, it is proper to observe that decoctions generally let fall, upon cooling, a portion of insoluble matter, and it is a question whether this should be rejected, or retained so as to form a part of the extract. Though it is undoubtedly in many instances inert, as in that of the insoluble substance formed during the decoction of certain vegetable substances, yet, as it frequently also contains a portion of the active principle which a boiling saturated solution necessarily deposits on cooling, and as it is difficult to decide with certainty when it is active and when otherwise, the safest plan, as a rule, is to allow it to remain.

The method of evaporation formerly resorted to in the case of aqueous solutions is rapid boiling over a fire. This method has been entirely superseded by the use of steam in connection with reduced pressure.

The use of the vacuum kettle or evaporator has become very general in this country, as it requires a smaller consumption of fuel, and the heat imparted to the liquid, while sufficient to evaporate it, may be considerably less than 100° C.

A former plan of evaporation, though slow, was to place the liquid in a broad, shallow vessel, exposed in a stove or drying room to a temperature of about 37.8° C., or a little higher, taking care that the air have free access in order to facilitate the evaporation.

In the concentration of alcoholic solutions, distillation should always be performed, as not only is the atmospheric air thus excluded, but the alcohol is recovered, if not absolutely pure, certainly fit for the purpose to which it was originally applied. When the decoction or infusion and the tincture of the same vegetable have been made separately, they should be separately evaporated to the consistence of syrup, and then mixed together while they are of such a consistence as to incorporate without difficulty. The object of this separate evaporation is that the spirituous extract may not be exposed to the degree of heat, or lengthened action of the air, which is necessary in the ordinary mode of concentrating the infusion or decoction.

In every instance, care should be taken to prevent any portion of the extract from becoming dry and hard on the sides of the evaporating vessel, as in this state it will not readily incorporate with the remaining mass. The heat, therefore, should be applied to the bottom and not to the sides of the vessel.

"Alkaloidal standards have been adopted for those extracts that can be reliably assayed. Assay methods are directed for the determination of their strengths and to provide for their standardization. When necessary, an inert diluent is directed to reduce the product to the standard. In the official formulas, glucose is directed in most instances as the diluent for the pilular extracts, and dried starch for the powdered extracts. It is permissible, however, for the manufacturer to use as inert diluents, for the former, a sub-standard extract of the same drug; for the latter, sucrose, lactose, powdered glycyrrhiza, magnesium carbonate, or the finely powdered, dried drug or marc from which the respective extract was made. Before admixture the diluent may be colored by the addition of chlorophyll, caramel or other harmless coloring to simulate the color of the extracts. For the convenience of the prescriber, the standards of strength for the extracts have been adjusted wherever possible, so that each bears a definite relation to that of the respective drug of average strength. A statement of the standard adopted accompanies each formula." *U. S.*

C. H. LaWall has prepared a valuable table giving the yield of extract by various drugs. (*Proc. A. Ph. A.*, 1897, 414.) For methods of assay, see various official processes.

"The pasty or semi-solid extracts are designated '*pilular extracts*' because they are extensively used in pill masses. They are also used in ointments, and to facilitate their use in these preparations, the degree of concentration is directed to be that of a 'pilular consistence.' In these, an excess of moisture is to be avoided and the proper pliability and consistence may be maintained by the addition of a small amount of glycerin. Pilular extracts should be protected from exposure to sunlight, air, and moisture, by being kept in tightly-covered glass or earthenware containers, and should be stored in a cool, dark place.

"*Powdered extracts* differ from pilular extracts in that they are dry and prepared either as fine or granular powders. They are more generally used than pilular extracts because they can be more accurately weighed, more easily dispensed, and more conveniently preserved. These should be preserved in tightly-stoppered, small, wide-mouthed, amber-colored bottles, and stored in a cool, dry place." *U. S.*

Extracts of the pilular character, in order that they may keep well, should be placed in glazed earthenware, glass, or porcelain jars, and completely protected from the access of the air. This may be effected by covering their surface with a layer of melted wax, or with a piece of paper moistened with strong spirit, then closing the mouth of the vessel with a cork, spreading wax or rosin over this, and covering the whole with leather or a piece of bladder. The application of alcohol to the surface has a tendency to prevent mouldiness. Should the extract become too moist, it may be dried by means of a water bath; should it, on the contrary, be too dry, the proper consistence may be restored by softening it in the same manner and incorporating with it a little distilled water.

When extracts which are too soft are subjected to a moderate temperature, fermentation or molding may set in; E. Cocardas describes the various forms of micro-organisms which are found in such extracts, and concludes that the ferment causes them to undergo changes similar to those effected by heat—*viz.*, the absorption of oxygen and the disengagement of carbon dioxide. (*P. J.*, 1886, p. 590.)

The addition of a little glycerin has been suggested to prevent the hardening of extracts; the U. S. directs the addition of glucose in the pilular extracts which will have a like effect. The U. S. VIII officially recommended the addition of glycerin. It is preferable to add a definite weight of the glycerin to the percolate. If it were added to the menstruum, owing to the variation in the yield of extracts from plants, some would be too soft, and at another time, in the case of a large yield of extract, the quantity of glycerin would be insignificant.

Extracts from recent plants should be prepared at the season when the plant is medicinally most active; a good rule is to prepare them once a year; but the demand for extracts from fresh drugs has almost entirely ceased, as it has been found that properly dried drugs yield extracts of uniform strength.

Powdered extracts are always prepared by vacuum evaporation and they are stabilized by incorporating some inert material as starch, lactose or magnesium carbonate to prevent absorption of moisture and caking. They must be kept in tightly stoppered containers.

A. B. Lyons, of Detroit (1898), has introduced *scale extracts.* These do not, as a class, bear a definite relation to the drug; they are assayed, however, and acacia is used as a means of preserving their dry condition; they are easily pulverized, and are very convenient for dispensing.

EXTRACTUM ALOES. Br.

EXTRACT OF ALOES

Extrait d'Aloès, *Fr.;* Extractum Aloës, *P. G.;* Aloeextract, *G.;* Estratto di aloe acquoso, *It.*

"Aloes, in small fragments, 1000 *grammes;* Distilled Water, boiling, 10,000 *millilitres.* Add the Aloes to the Distilled Water and stir well until they are thoroughly mixed; set aside the mixture for twenty-four hours; decant; strain; evaporate the strained liquid to dryness at a temperature not exceeding 60° C." *Br.*

The object of this preparation is to afford an aloes purified from mechanical impurities. The process is based upon the British formulas for extracts of Barbados aloes and Socotrine aloes, formerly official. With an official purified aloes, the necessity for this preparation is not obvious. The U. S. P. IX dismissed Extract of Aloes and *Aloe Purificata,* but added tests for aloe which exclude inorganic impurities, gum, etc. (See *Aloe.*) An extract made with cold distilled water was formerly official in the German Pharmacopœia, as was also the vitriolated extract, "*Extractum Aloes Acido Sulfurico Correctum,*" made by suspending eight parts of extract of aloes in thirty-two parts of distilled water, adding drop by drop one part of pure sulphuric acid, and evaporating in a porcelain vessel to dryness.

Dose, one to five grains (0.06–0.3 Gm.).

Off. Prep.—Decoctum Aloes Compositum, *Br.;* Extractum Colocynthidis Compositum, *Br.;* Pilulæ Antiperiodicæ, *N. F.;* Tinctura Antiperiodica, *N. F.*

EXTRACTUM BELLADONNÆ. U. S. (Br.)

EXTRACT OF BELLADONNA Ext. Bellad. [Extractum Belladonnæ Foliorum U. S. IX.]

"Extract of Belladonna yields not less than 1.18 per cent. and not more than 1.32 per cent. of the alkaloids of belladonna leaves. One Gm. of the Extract represents about 4 Gm. of belladonna leaves." *U. S.* "Dry Extract of Belladonna contains in 100 grammes 1 gramme of the alkaloids of Belladonna Leaves." *Br.*

Extractum Belladonnæ Siccum, *Br.;* Dry Extract of Belladonna; Extractum Belladonnæ Alcoholicum; Extractum Belladonnæ; Extrait de Belladone (Racine), *Fr. Cod.;* Spirituöses Tollkirschenextrakt, *G.;* Estratto di belladonna idroalcoolico, *It.;* Extracto alcoholico de belladona, *Sp.*

The U. S. directs this extract in two forms, Pilular Extract and Powdered Extract, so that the pharmacist might select the form that was best suited for dispensing. The pilular extract is used officially in the ointment. Both forms of the extract, however, are of the same strength.

"*Pilular Extract of Belladonna.*—Belladonna Leaves, in moderately coarse powder, 1000 Gm.; Glucose, Alcohol, Water, each, a sufficient quantity. Moisten the drug with sufficient of a mixture of 3 volumes of alcohol and 1 volume of water, and pack it firmly in a cylindrical percolator, then add enough menstruum, using the same proportion of alcohol and water as before, to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding menstruum of the same strength, until the percolate measures 3000 cc. or until the drug is exhausted. Recover the alcohol from the percolate by distillation, and evaporate the residue with frequent stirring at a temperature not exceeding 70° C. to a pilular consistence. Mix the mass thoroughly and weigh it. Assay a portion of this extract as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloids in the remainder of the mass, and to this add sufficient glucose to make the finished Extract contain 1.25 per cent. of the alkaloids of belladonna leaves. Mix thoroughly.

"**Assay.**—Proceed by Type Process D, taking 2 Gm. of Extract of Belladonna, using chloroform as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal acid corresponds to 0.02893 Gm. of the alkaloids of belladonna (Proximate Assays)." *U. S.*

"*Powdered Extract of Belladonna.*—Belladonna Leaves, in moderately coarse powder, 1000 Gm.; Starch, dried at 100° C., Alcohol, each, a sufficient quantity. Moisten the drug with sufficient alcohol, and pack it in a cylindrical percolator, then add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed very slowly, adding alcohol as required. Reserve the first 1000 cc. of percolate, and continue the percolation until the second percolate measures 1000 cc. or until the drug is exhausted. Transfer the second percolate to a suitable apparatus, and distil the alcohol at as low a temperature as practicable, until a residue measuring about 100 cc. remains, then add the reserved percolate, and continue distillation until the residue in the still is of syrupy consistence. Transfer this syrupy residue to a shallow evaporating dish, rinse the flask or still with small portions of warm alcohol, adding the rinsings to the residue in the dish. Evaporate this to a soft extract, with frequent stirring, at a temperature not exceeding 70° C. Then add 50 Gm. of the dried starch, and continue the heating at the same temperature, with frequent stirring until the mass is nearly dry. Now thoroughly incorporate an additional 20 Gm. of dried starch, and set the product aside in a current of warm air until thoroughly dry. Reduce the product to a fine powder and weigh it. Assay a portion of this product as directed below, and from the alkaloidal content thus determined ascertain by calculation the amount of alkaloids in the remainder of the powder, and add to this sufficient of the dried starch to make the finished Extract contain 1.25 per cent. of the alkaloids of belladonna leaves. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles, and stopper them tightly.

"**Assay.**—Proceed as directed under the *Pilular Extract of Belladonna.*" *U. S.*

"Belladonna Leaves, in No. 40 powder, Alcohol (70 per cent.), of each, *a sufficient quantity.* Reduce ten grammes of the Belladonna Leaves to No. 60 powder and determine the proportion of alkaloids present by the process described under 'Belladonnæ Folia.' Moisten one thousand grammes of the Belladonna Leaves with two hundred and fifty millilitres of the Alcohol, pack firmly in a percolator and percolate with more of the Alcohol until four thousand millilitres of percolate have been obtained. Determine the proportion of total solids in the percolate by evaporating twenty millilitres, drying the residue at 80° C., and weighing. Determine also the proportion of alkaloids in the percolate, by the process described under 'Tinctura Belladonnæ,' employing forty millilitres of the percolate in the place of one hundred millilitres of the Tincture. Having thus determined the proportion of total solids and of alkaloids in the percolate, calculate the amount of each the remainder of the percolate will yield, and also the amount of the powdered Belladonna Leaves, the alkaloidal strength of which has also been determined, that must be added to afford a dry extract containing 1 per cent. of alkaloids. Add to the percolate a somewhat smaller amount of the powdered Leaves than calculation has shown to be necessary, recover the alcohol by distillation, and dry the residue in a shallow, flat, tared dish, first on a water-bath, and finally in a current of air at 60° to 80° C. Weigh the dish with its contents, calculate the additional amount of powdered Leaves that will be necessary, add this to the product of evaporation, transfer the whole to a dry, slightly warmed mortar and triturate carefully until thoroughly mixed. Pass the powdered Extract through a No. 20 sieve, transfer to a bottle which can be securely closed, and preserve in a cool dry place. Slightly moisten 5 grammes of the Extract with a mixture of 1 volume of *acetic acid* and 9 volumes of *alcohol* (70 per cent.), pack in a small percolator and percolate with the same menstruum, if necessary under increased air-pressure, until 50 millilitres of percolate have been collected. Then proceed as described under 'Tinctura Belladonnæ,' using 50 millilitres of percolate in the place of 100 millilitres of the Tincture. Examined by the foregoing process, Dry Extract of Belladonna is found to contain in 100 grammes 1 gramme of the alkaloids of Belladonna Leaves. *Limit of error* 0.05 gramme in excess or defect. This Dry Extract contains 1 per cent. of the alkaloids of Belladonna Leaves." *Br.*

Uses.—There is no physiological difference between the pilular and powdered extracts of belladonna. The former may be used in the preparation of pills or ointments, the latter wherever the action of belladonna is wished in the form of a powder or compressed tablet. For the conditions in which these extracts are useful, see under *Atropina.*

Dose, internally, from one-sixth to one-third of a grain (0.010–0.021 Gm.).

Off. Prep.—Emplastrum Belladonnæ, *U. S.; Br.;* Suppositoria Belladonnæ, *Br.;* Unguentum Belladonnæ, *U. S.;* Pilulæ Aloes et Podophylli Compositæ (from Pilular Extract), *N. F.;* Pilulæ Aloini Compositæ (from Pilular Extract), *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ (from Pilular Extract), *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ (from Pilular Extract), *N. F.;* Pilulæ Antidyspepticæ (from Pilular Extract), *N. F.;* Pilulæ Laxativæ Compositæ (from Pilular Extract), *N. F.*

EXTRACTUM CANNABIS. U. S. (Br.)

EXTRACT OF CANNABIS Ext. Cannab. [Extractum Cannabis Indicæ, U. S. P. VIII]

"Extract of Cannabis, administered by the mouth to dogs, in doses not exceeding 0.004 Gm. for each kilogram of body weight of dog, produces a degree of incoördination equivalent to that caused by 0.03 cc., for each kilogram of body weight of dog, of the standard fluidextract of cannabis prepared as directed under *Cannabis.*" *U. S.*

Extractum Cannabis Indicæ, *Br.;* Extract of Indian Hemp, *Br.;* Extrait de Chanvre de l'Inde, *Fr. Cod.;* Indischer Hanfextrakt, *G.*

"Cannabis, in moderately coarse powder, 1000 Gm.; Alcohol, a sufficient quantity. Moisten the drug with sufficient alcohol, pack it firmly in a cylindrical percolator, and add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding alcohol until the drug is exhausted. Recover the alcohol from the percolate by distillation, and evaporate the residue with frequent stirring, at a temperature not exceeding 70° C., to a pilular consistence. Mix the mass thoroughly, and weigh it. Assay a portion of this extract as directed under *Cannabis,* and from the result thus obtained adjust the weight of the finished Extract by the addition of either storax or a substandard Extract of Cannabis to conform to the required biological standard.

"**Assay.**—Administer the Extract in gelatin capsules, proceeding as directed under *Cannabis.*" *U. S.* (See under *Cannabis* and Part III.)

"Exhaust Indian Hemp, in coarse powder, with Alcohol (90 per cent.) by the *percolation process;* recover the alcohol by distillation, and evaporate the residue to a soft extract." *Br.*

The continuation in the Br. Pharm. of the name of Indian Hemp is unfortunate because of the possibility of its being mistaken for the root of *Apocynum cannabinum,* which is also called Indian Hemp. Several mistakes have occurred through this unfortunate confusion of nomenclature.

Although there is some difference in the details of the two processes, the preparations of the U. S. and Br. Pharmacopœias are practically identical.

The preparation varies considerably in strength, so that it is wisest to begin with a small dose, one-quarter of a grain (0.016 Gm.), and rapidly increase the amount given until some effect is produced.

Dose, one-fourth to three-fourths of a grain (0.015–0.045 Gm.).

Off. Prep.—Tinctura Cannabis Indicæ, *Br.;* Mistura Chlorali et Potassii Bromidi Composita, *N. F.*

EXTRACTUM CARNIS. N. F.

EXTRACT OF BEEF Ext. Carnis [Beef Extract]

"The residue obtained from fresh beef broth by evaporation at a low temperature." *N. F.*

In its preparation the sound fresh meat is usually cut into small pieces, the appropriate amount of water is added, and the mixture placed in a vessel which may be closed to prevent the escape of any aqueous vapor and permit the application of slight pressure. After digestion for several hours in this apparatus, with occasional stirring, the liquid portion is poured off, the solid material gently pressed to separate any remaining liquid, then cooled to remove fat, and afterward strained. The clear liquid is afterwards evaporated in vacuo to the consistence of a pasty mass. Bones and tendons are not used as they introduce gelatin which is looked upon as an adulterant. It is usually spoken of as the *Liebig type of beef extract.*

Description and Physical Properties.—" A yellowish brown to dark-brown, slightly acid, pasty mass, having an agreeable meat-like odor and taste.

" Twenty-five Gm. of Extract of Beef, diluted with 250 cc. with distilled water, yields a nearly clear solution, free from sediment. Separate portions of this solution respond to the following tests: Boil 10 cc. of the solution for one minute with 1.5 Gm. of purified animal charcoal, add distilled water to replace that lost by evaporation and filter; the filtrate produces no blue coloration when one drop is added to three drops of a solution of diphenylamine (1 in 100) in concentrated sulphuric acid (*nitrate*). Distribute 10 cc. of the solution over dry sand or asbestos, and dry to constant weight in a flat-bottomed porcelain dish in an oven at a temperature of 105° C.; it yields a residue of not less than 0.75 Gm., equivalent to 75 per cent. of solids in the original Extract. Incinerate the residue from 10 cc. of the solution obtained in the preceding test; the ash does not exceed 30 per cent. of the residue, nor does the sodium chloride in the ash exceed 10 per cent. of the residue when determined as directed under the Assay for chlorides. To 100 cc. of the solution contained in a 500 cc. Kjeldahl flask, add 5 Gm. of barium carbonate and 100 cc. distilled water and, using a connecting bulb, distil 100 cc. into 10 cc. of half-normal hydrochloric acid. Titrate the excess of acid, using cochineal T.S. as indicator, and from the acid consumed by the distillate, calculate the percentage of nitrogen as ammonia. This does not exceed 0.35 per cent. of the total solids. Transfer 25 cc. of the solution to a 100 cc. Erlenmeyer flask, add 50 cc. of alcohol and shake the mixture thoroughly. When the precipitate has subsided, filter, collect the precipitate upon a 9 cm., counterpoised filter, wash the precipitate three times with a mixture of two volumes of alcohol and one volume of distilled water and then dry it to constant weight at 105° C. The weight of this precipitate does not exceed 10 per cent. of the total solids. (Reserve the filtrate and washing for the following determination of nitrogen.) To an aliquot portion of the alcoholic filtrate from the preceding test corresponding to 1 Gm. of the alcohol soluble solids, add 4 cc. of sulphuric acid and evaporate to dryness in a 500 cc. Kjeldahl flask. Determine the nitrogen by the Gunning-Kjeldahl method. The amount of nitrogen thus found is not less than 0.06 Gm." *N. F.*

The chief constituents present from the meat are *creatin, creatinin, xanthin, carnin,* and *carnic acid.* Under the name of *extract of beef* or *meat extract* products are found upon the market which probably are made by boiling down the liquor in which corned beef has been "cured" or "pickled." This is evidenced by the high proportion of salt and saltpeter which is found in some of these commercial products.

Uses.—As most of the protein of meat is precipitated by boiling and as the fat is deliberately rejected by the cold filtration of meat extract it is manifest that the final preparation can contain very little of the nutritional value of the meat. It is possible that the xanthin derivatives contained in this product may have a slight stimulating effect upon the system but the chief value of this preparation lies in its flavor which tends to excite appetite and thereby improve digestion.

Off. Prep.—Elixir Carnis et Ferri, *N. F.*

EXTRACTUM CASCARÆ SAGRADÆ.
U. S. (Br.)

EXTRACT OF CASCARA SAGRADA Ext. Casc. Sagr.
[Extractum Rhamni Purshianæ, U. S. VIII, Powdered Extract of Cascara Sagrada]

" *One gramme* of the Extract represents *three grammes* of cascara sagrada." *U. S.*

Extractum Cascaræ Sagradæ Siccum, *Br.;* Dry Extract of Cascara Sagrada; Extrait de Cascara Sagrada, *Fr. Cod.;* Cascara Sagrada-Extrakt, Amerikanisches Faulbaumrinden-extrakt, *G.;* Extracto alcoholico de cascara sagrada, *Sp.*

" Cascara Sagrada, in coarse powder, 900 Gm.; Starch, dried at 100° C., Boiling Water, each, a sufficient quantity, to make 300 Gm. Mix the cascara sagrada with 4000 cc. of boiling water, and macerate the mixture during three hours. Then transfer it to a metallic percolator, allow it to drain, and pour on boiling water until the percolate measures 5000 cc. or the drug is exhausted. Evaporate the percolate to dryness on a water or steam bath, reduce the extract to a fine powder, weigh it, and add sufficient of the dried starch to make the product weigh 300 Gm. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles, and stopper them tightly." *U. S.*

" Exhaust Cascara Sagrada, in No. 20 powder, with Distilled Water by the *percolation process;* evaporate the percolate to dryness on a water-bath." *Br.*

The U. S. preparation is made to represent a definite proportion of the drug (4 to 1), by adding magnesium oxide, and is slightly weaker than that of the Br.

It well represents the virtues of the bark, and furnishes a good means of administering this purgative in pilular form.

Dose, from two to eight grains (0.13–0.5 Gm.).

Off. Prep.—Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ, *N. F.*

EXTRACTUM COLCHICI. U. S., Br.

EXTRACT OF COLCHICUM Ext. Colch. [Extractum Colchici Cormi, U. S. IX. Powdered Extract of Colchicum Corm]

"Extract of Colchicum yields not less than 1.25 per cent. and not more than 1.55 per cent. of colchicine. One Gm. of the Extract represents about 4 Gm. of colchicum corm." *U. S.*

Extractum Colchici Radicis, *U. S.*, 1890; Extrait de Colchique acetique, *Fr.;* Zeitlosen Essigextrakt, *G.*

"Colchicum Corm, in fine powder, 1000 Gm.; Alcohol, Purified Petroleum Benzin, Starch, dried at 100° C., each, a sufficient quantity. Moisten the colchicum corm with sufficient alcohol, pack it in a cylindrical percolator, and add enough alcohol to saturate the drug and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, adding alcohol as required, until the percolate measures 2000 cc. or until the drug is exhausted. Recover the alcohol from the percolate by distillation at as low a temperature as practicable until a residue measuring about 150 cc. remains in the still. Transfer this residue to a flask or separator, using small portions of warm alcohol to rinse the still, and add the rinsings to the residue in the flask. When it has cooled, add 250 cc. of purified petroleum benzin, and shake the mixture thoroughly for several minutes. Allow the liquids to separate, and decant the benzin layer as closely as possible, again add to the residue 150 cc. of purified petroleum benzin, agitate, decant the benzin layer as before, repeat the washing with 100 cc. of purified petroleum benzin, and reject the benzin washings. Transfer the fat-free residue to a shallow evaporating dish, rinse the flask with small portions of warm alcohol, add the rinsings to the residue in the dish, and evaporate on a water bath to a thick extract. To this add 50 Gm. of the dried starch, mix well, spread the mixture on glass plates, and continue the drying in a current of warm air at a temperature not exceeding 70° C. until thoroughly dry. Reduce the product to a fine powder, and weigh it. Assay a portion of this product as directed below, and from the alkaloidal content thus determined ascertain by calculation the amount of alkaloid in the remainder of the powder, and add to this sufficient of the dried starch to make the finished Extract contain 1.4 per cent. of colchicine. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles, and stopper them tightly.

"**Assay.**—Place 6 Gm. of Extract of Colchicum in a 500 cc. flask containing 290 cc. of distilled water, mix well, add 10 cc. of solution of lead subacetate, and agitate the mixture frequently during one hour. Filter off 200 cc. and proceed as directed under *Colchici Semen* assay, beginning with the word 'Add.'" *U. S.*

"Crush fresh Colchicum Corms, deprived of their coats; press out the juice; allow the feculence to subside, decant; heat the clear liquid to 100° C.; strain through flannel, and evaporate at a temperature not exceeding 70° C. to a soft extract." *Br.*

The U. S. VIII extract was an acetic extract of the corm, but in the present process the acetic acid is omitted. The British extract is made by evaporating the juice of fresh corms.

In Great Britain a preparation called *preserved juice of colchicum* is given in the dose of five minims (0.3 cc.) or more. It is made by expressing the fresh corm, allowing the juice to stand for forty-eight hours that the starchy matter may subside, then adding one-fourth of its bulk of alcohol, allowing it again to stand for a short period, and ultimately filtering.

As the fresh colchicum corm is rarely to be had in this country, the U. S. Pharmacopœia employs the dried corm; its process, if properly conducted, will afford a very efficient extract. In preparing this extract according to the British process, by expression from the recent corm, there will be experienced some inconveniences, which would seem to render the U. S. process under all circumstances preferable. (*P. J.*, xiii, 62.)

Dose, from one-fourth to one grain (0.016–0.065 Gm.).

EXTRACTUM COLOCYNTHIDIS. U. S.

EXTRACT OF COLOCYNTH Ext. Colocynth. [Powdered Extract of Colocynth]

"One Gm. of the Extract represents 4 Gm. of colocynth." *U. S.*

Extractum Colocynthidis Alcoholicum; Extrait de Coloquinte, *Fr. Cod.;* Extractum Colocynthidis, *P. G.;* Koloquintenextrakt, *G.;* Estratto di coloquintide idroalcoolico, *It.*

"Colocynth, in coarse powder, 1000 Gm.; Diluted Alcohol, Starch, dried at 100° C., each, a sufficient quantity, to make 250 Gm. Moisten the drug with 2000 cc. of diluted alcohol, and macerate it in a closed vessel for twenty-four hours, then transfer the moist drug to a cylindrical percolator, shake it down evenly without packing, and gradually pour diluted alcohol upon it, allowing the percolation to proceed slowly until the percolate measures 5000 cc. or until the drug is practically exhausted. Recover the alcohol from the percolate by distillation, and evaporate the residue to dryness on a water or steam bath. Reduce the product to a fine powder, weigh it, and add sufficient of the dried starch to make the product weigh 250 Gm. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles, and stopper them tightly." *U. S.*

The colocynth should always be deprived of its seeds, following the directions of the U. S. Pharmacopœia, before being submitted to the action of the menstruum. Boiling water extracts such a large amount of pectin and mucilage from colocynth that either the decoction or the hot infusion gelatinizes on cooling, and the extract made by means of it is therefore loaded with inert matter, and, besides, is liable to become mouldy, or so tough and hard as to resist trituration and formation into pills. Hence many years ago the London College, following in this respect the old French Codex, directed, in the last edition of its Pharmacopœia, maceration with cold water; but diluted alcohol has been found to be a much better menstruum, and has accordingly been adopted in the U. S. Pharmacopœia process, while in the British Pharmacopœia the simple extract has been discarded altogether. The chief, if not exclusive, use of the alcoholic extract is in the preparation of the compound extract.

This is an active, but harsh purgative and is rarely employed except in combination with other cathartics.

Dose, one-half grain (0.032 Gm.).

Off. Prep.—Extractum Colocynthidis Compositum, *U. S.*

EXTRACTUM COLOCYNTHIDIS COMPOSITUM. U. S., Br.

COMPOUND EXTRACT OF COLOCYNTH Ext. Colocynth. Co. [Powdered Compound Extract of Colocynth]

Extrait de Coloquinte composé, *Fr.;* Zusammengesetzten Koloquintenextrakt, *G.*

"Extract of Colocynth, 160 Gm.; Aloe, 500 Gm.; Cardamom Seed, in fine powder, 50 Gm.; Resin of Ipomœa, in fine powder, 140 Gm.; Soap, dried and in powder, 150 Gm.; to make 1000 Gm. Triturate the ingredients until the product is reduced to a fine powder. Pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles, and stopper them tightly." *U. S.*

"Colocynth Pulp, 150 *grammes;* Extract of Aloes, 300 *grammes;* Scammony Resin, 100 *grammes;* Curd Soap, in powder, 75 *grammes;* Cardamom Seeds, in powder, 25 *grammes;* Alcohol (60 per cent.), 4000 *millilitres.* Macerate the Colocynth Pulp in the Alcohol for four days; press out the tincture; recover the alcohol by distillation; evaporate to dryness; add the Extract of Aloes, Scammony Resin, and powdered Cardamom Seeds; powder; mix the powder with the Curd Soap." *Br.*

The U. S. X preparation differs from the former in that Ipomea resin has been substituted for Scammony. The Br. Pharm. (1914) directs Extract of Aloes instead of Barbados Aloes, and decreased the proportion of soap from four to three ounces. The object of the soap is to improve the consistence of the mass, which, when hardened by time, it renders more soluble in the gastric juices. It may possibly also serve the purpose of modifying the action of the aloes. In the U. S. process the extract is in the form of powder, which is very convenient for admixture with other substances; while if given uncombined, it may be readily made into pills by suitable additions. The plan of having the powders simply mixed was liable to the objection that the mixture was not likely to be so thoroughly effected as to obtain a uniform result, and hence the U. S. Pharm., 1880, adopted Squibb's suggestion, to melt together all the ingredients unpowdered, except the cardamom, add a little alcohol, and, when the mixture is thoroughly made, to stir in the powdered aromatic, and finally to reduce the whole to a fine powder. The U. S. P. X, however, relies upon trituration as an assurance of thorough commingling.

This extract is an energetic cathartic, possessing the activity of its three purgative ingredients, with comparatively little of the drastic character of the colocynth and scammony. It may be still further and advantageously modified by combination with rhubarb, calomel, etc., with one or more of which it is often united in prescription.

Dose, as a laxative, one to two grains (0.065–0.13 Gm.); as a purgative, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Pilulæ Hydrargyri Chloridi Mitis Compositæ, *U. S.;* Pilulæ Catharticæ Vegetabiles, *N. F.;* Pilulæ Antidyspepticæ, *N. F.;* Pilulæ Laxativæ Post Partum, *N. F.*

EXTRACTUM ERGOTÆ. Br.

EXTRACT OF ERGOT Ext. Ergot.

Extractum Hæmostaticum; Ergotin, *Br.*, 1898; Extrait d'Ergot de Seigle, *Fr. Cod.;* Extractum Secalis cornuti, *P. G.;* Mutterkornextrakt, *G.;* Estratto di segala cornutta, *It.;* Extracto Acuoso de Cornezuelo de Centeno, *Sp.*

"Ergot, crushed, 1000 *grammes;* Distilled Water, 7500 *millilitres;* Alcohol (90 per cent.), 650 *millilitres.* Macerate the Ergot with *five thousand millilitres* of the Distilled Water for twelve hours; strain; repeat the maceration with the remainder of the Distilled Water; strain; press; evaporate the mixed liquids to *five hundred millilitres;* add the Alcohol; set aside for three days, stirring occasionally; filter; evaporate the filtrate to a soft extract." *Br.*

Because of the injurious effect of heat on the active principles of ergot, it is almost impossible to concentrate the percolates to an extract consistency without largely destroying their physiological properties, and at the last revision of the Pharmacopœia this preparation was very properly omitted. The British extract being made with an aqueous menstruum, cannot contain all the active principles of the drug as some are insoluble in water (see *Ergota*).

Dose, from two to eight grains (0.12–0.5 Gm.).

Off. Prep.—Injectio Ergotæ Hypodermica, *Br.*

EXTRACTUM EUONYMI. Br.

EXTRACT OF EUONYMUS

Dry Extract of Euonymus; Extract of Wahoo; Extrait d'Evonymus atropurpureus, *Fr. Cod.;* Extrait de Fusain Américaine, *Fr.;* Spindelbaumextrakt, Spillbaumrindenextrakt, *G.*

"Exhaust Euonymus Bark in No. 20 powder with Alcohol (45 per cent.) by the *percolation process.* Evaporate the percolate and thoroughly dry the residue. Powder the product as far as possible and mix it with one-fourth of its weight of Calcium Phosphate, continuing the drying and powdering until a sufficiently dry preparation is obtained; transfer this to a well-closed bottle." *Br.*

The N. F. preparation (see Part III) is diluted with starch and made to represent four times its weight of crude drug, whereas the Br. is mixed with an amount of calcium phosphate proportional to the extract.

This extract was not admitted to the U. S. P. IX, but was retained in the Br. Pharm. (1914) and introduced into the National Formulary (see Part III) which directs the percolation of euonymus in No. 40 powder with alcohol 4 volumes and water 1 volume. The percolate is evaporated or distilled and the residue dried and mixed with dried starch so that 1 Gm. of the extract represents 4 Gm. of euonymus. On account of the reports of physicians of cumulative effects the following note was inserted: "CAUTION—It has been stated that the absorption of Euonymus in the gastro-intestinal tract is uncertain and irregular. To avoid an accumulation of the drug or toxic action, the physician should carefully guard the dosage and determine in each case the tolerance of the patient." *N. F. IV.* Dry and powdered extract of euonymus is frequently but erroneously termed "*euonymin*" (see under *Euonymus*).

Dose, one to three grains (0.065 to 0.2 Gm.).

EXTRACTUM FELLIS BOVIS. U. S. (Br.)

EXTRACT OF OXGALL Ext. Fel. Bov. [Powdered Extract of Oxgall]

"One Gm. of the Extract represents 8 Gm. of oxgall." *U. S.*

Fel Bovinum Purificatum, *Br.;* Purified Ox Bile; Fel Tauri Depuratum; Extractum Fellis Bovini; Extrait de Fiel de Bœuf, *Fr. Cod.;* Gereinigte Ochsengalle (Rindsgalle), *G.;* Bile cristallizzata di platner, *It.;* Hiel de toro preparada, *Sp.*

"*Oxgall,* 800 Gm.; Alcohol, 1500 cc.; Starch dried at 100° C., a sufficient quantity, to make 100 Gm. Add 1000 cc. of alcohol slowly and with agitation to the oxgall contained in a bottle of sufficient size. Allow the mixture to stand for two days, and then decant the liquid portion. Wash the residue in the bottle with an additional 500 cc. of alcohol, decant the liquid portion, mix it with the liquid first separated, and filter. Recover the alcohol from the filtrate by distillation, transfer the residue to a shallow dish, and evaporate it to a thick extract at a temperature between 75° and 80° C. Spread this extract on glass plates, and continue the drying by exposure to warm air at a temperature not exceeding 70° C. until thoroughly dry. Reduce the product to a fine powder, weigh it, and add sufficient of the dried starch to make the product weigh 100 Gm. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles, and stopper them tightly. The use of copper apparatus in the preparation of this Extract should be avoided." *U. S.*

"Evaporate five hundred *millilitres* of fresh ox bile to one-fourth of its volume; shake this liquid with twice its volume of Alcohol (90 per cent.); set the mixture aside until the solid matter has subsided; decant the clear solution, and filter the remainder, washing the filter and contents with a little more Alcohol (90 per cent.). Distil off most of the alcohol from the mixed liquids, and evaporate the residue in a porcelain dish, on a water-bath, to the consistence of a firm extract." *Br.*

The object of this preparation is to furnish purified concentrated oxgall in a condition in which it can be satisfactorily prescribed for internal administration. The addition of alcohol to the concentrated liquid is made for the purpose of separating albuminous matter.

Properties.—"A yellowish-green hygroscopic substance, having a taste partly sweet and partly bitter, soluble in *water* and in *alcohol* (90 per cent.). 1 millilitre of an aqueous solution (1 in 100) in which 0.1 gramme of *refined sugar* has been dissolved, gradually acquires a deep violet color when mixed with 10 millilitres of *syrupy phosphoric acid* and heated in a water-bath. Its aqueous solution on the addition of twice its volume of *alcohol* (90 per cent.) gives no precipitate (absence of unpurified ox bile)." *Br.*

Refined oxgall, much used by painters, is prepared, according to Gray, in the following manner. Take of "fresh oxgall, one pint; boil, skim, and add one ounce of alum, and keep it on the fire for some time; to another pint, add one ounce of common salt in the same manner; keep them bottled up for three months; then decant off the clear; mix them in an equal proportion; a thick yellow coagulum is immediately formed, leaving the refined gall clear and colorless."

This extract represents practically a mixture of sodium glycocholate and sodium taurocholate contaminated with traces of fatty and soapy matters. (See *Fel Bovis.*) The direction to add starch in sufficient quantity in this extract is unfortunate. The therapeutic activity of bile resides in its solid matters and as the proportion of these varies greatly it is manifest that the extract should be standardized, not as it is at present, to represent a certain amount of fresh bile, but to represent a proportion of dried bile, *i.e.,* of the biliary solids.

Uses.—By the ancients bile was a very highly esteemed remedy and was used in a great variety of conditions. It, however, fell into desuetude and for many years was rarely employed. Recently it has again come largely into favor but for a very different class of disorders. Its most frequent use to-day is to replace or augment the hepatic secretions when these for any reason are lacking. While the exact rôle that the bile plays in the intestinal tract is not clearly understood, it is well established that it plays an important part in digestion, especially of the fatty foods.

When introduced into the circulation bile has a depressant effect upon the heart muscle leading to a reduction in the blood pressure and slowing of the pulse. Whether or not the slowing of the pulse is partly indicative of inhibitory stimulation is at present under dispute, but it seems well established that after large doses, at least, the slowing of the pulse is the result of a direct action upon the heart muscle. According to Meltzer and Salant (*J. Ex. M.*, viii), there are present in the bile both an excito-motor and depresso-motor principle. Bile has long been recognized as the most powerful stimulant to the secretory activity of the liver which we possess, but according to Shaffer (*A. J. Phys.*, 1907, xvii, p. 389), this is not indicative of a true excitation of the hepatic cells but is simply that, after its injection, the blood contains the preformed material for excretion and that the increase in the output of the bile solids does not exceed the dose which was injected. Hooper and Whipple (*J. A. M. A.*, 1917, lxix, 386) have found that taurocholic acid has a strong cholagogue action but that glycocholic acid, while causing a moderate increase in the flow of bile, lessens the output of the bile pigments. The presence of bile in the intestinal tract has by some been held to diminish the multiplication of bacteria, but there is no convincing evidence of such an action. It increases peristaltic movements in the large intestines but appears to diminish those of the upper bowel.

Oxgall has been found useful in a variety of conditions in which there is a diminution in the amount of bile in the intestinal tract, as for instance in *catarrhal cholangitis,* and *hepatic torpor.* In *gall stones* while it may improve the digestion by offering a necessary ferment there is no sufficient reason to believe that it will aid the solution of the stones. It is also a valuable agent in the treatment of certain forms of *chronic constipation,* not solely because of its own action in increasing the peristalsis of the colon, but because its presence in the intestines is essential for the action of many of the cathartics. Cholesterin, which is one of the ingredients of bile, has the power of neutralizing certain poisons such as tetanotoxin, sapotoxin, and snake venom, and may perhaps prove clinically useful for this purpose. It should be noted, however, that as cholesterin is scarcely soluble in cold alcohol, the extract will contain not more than traces of it.

The daily amount of bile secreted by an ordinary man varies between two hundred and four hundred cc. (6.7–13.3 fluidounces), containing from 1 to 3 per cent. of solids. If there is a marked reduction in the secretion of bile it is evident that the pharmacopœial dose is far too small to have any effect. Because of a supposed injurious action upon gastric digestion various recommendations have been made for administering bile in the form that it will pass through the stomach; among these may be mentioned the use of keratin coated or salol coated pills, and by mixing with spermaceti. We think, however, that the liability of disturbance of the stomach by this agent has been over-estimated.

Among the proprietary preparations of bile may be mentioned: *bilein,* which is marketed in pills ranging from one-twelfth to one-fourth of a grain (0.05–0.016 Gm.); *cholalin,* a yellow powder, dose one-fourth to one-half grain (0.016–0.032 Gm.); *glycotauro,* dose five to ten grains (0.32–0.65 Gm.); *ovogall,* a yellowish powder said to consist of a combination with egg albumen, dose eight to fifteen grains (0.5–1 Gm.); *sodium choleinate,* dose eight to fifteen grains (0.5–1 Gm.); *cholesterin* may be given in doses of fifteen to twenty-five grains (1.0–1.7 Gm.).

Dose, of extract of bile, two to eight grains (0.12–0.5 Gm.).

EXTRACTUM GENTIANÆ. Br.

EXTRACT OF GENTIAN Ext. Gentian.

Extrait de Gentiane, *Fr. Cod.;* Extractum Gentianæ, *P. G.;* Enzianextrakt, *G.;* Estratto di genzian acquoso, *It.;* Extracto acuoso de genciana, *Sp.*

"Infuse Gentian Root in ten times its weight of Distilled Water for two hours; boil for fifteen minutes; pour off; press; strain; evaporate the liquid to a soft extract." *Br.*

This preparation has been dismissed from the U. S. X.

As ordinarily procured, the extract of gentian has an agreeable odor, is very bitter, and of a dark brown color approaching to black, shining, and tenacious. It is frequently used as a tonic, in the form of pill, either alone or in connection with metallic preparations; but the practice of some pharmacists of using it indiscriminately as a pill excipient is deserving of severe censure.

Dose, from two to eight grains (0.12–0.5 Gm.).

Off. Prep.—Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Ferri, Quininæ, Aloes, et Nucis Vomicæ, *N. F.*

EXTRACTUM GLYCYRRHIZÆ. U. S.

EXTRACT OF GLYCYRRHIZA Ext. Glycyrrh.
[Extract of Licorice]

"The commercial Extract of Glycyrrhiza." *U. S.*

Extractum Liquiritiæ; Liquorice, Licorice; Extrait de Réghsse, *Fr. Cod.;* Suc de Réglisse, Sucre noir, *Fr.;* Succus Liquiritiæ, *P. G.;* Lakriz, Lakritzensaft, Süssholzsaft, *G.;* Estratto diliquirizia, Sugo di liquirizia, Legorizia, Regolizia, *It.;* Extracto acuoso de regaliz, Regaliza en ballos, *Sp.*

Licorice is an article of export from the north of Spain, particularly Catalonia, where it is obtained in the following manner. The roots of the *G. glabra,* having been dug up, thoroughly cleansed, and half dried by exposure to the air, are cut into small pieces, and boiled in water until the liquor is saturated. The decoction is then allowed to rest, and, after the dregs have subsided, is decanted, and evaporated to the proper consistence. The extract, thus prepared, is formed into rolls from five to six inches long by an inch in diameter, which are dried in the air, and wrapped in laurel leaves.

The British extract of licorice is nearly the same as the "pure extract" of the U. S.

Much licorice is prepared in Calabria, according to Fée, from the *G. echinata,* which abounds in that country. The process is essentially the same as that just described, but conducted with greater care, and the Italian licorice is purer and more valuable than the Spanish. It is in cylinders, generally somewhat smaller than the Spanish, and usually stamped with the manufacturer's brand. Most of the extract brought to this country comes from Messina and Catania in Sicily and Naples, from Seville and Saragossa in Spain, and from Smyrna in Turkey. Perhaps in no other part of the world is more licorice consumed than in the United States, from four to five thousand tons having been imported annually before 1860; but the article is now made on an extensive scale in this country, very successfully, with the best modern appliances, and of such good quality as to have almost driven the foreign article out of the market. The principal use of Extract of Licorice is in the manufacture of chewing tobacco, that in the form of rolls as sold by the druggist being a comparatively small portion of the whole amount consumed.

Crude Licorice, Licorice Paste, or *Licorice Mass,* as it is variously termed, is found in the market in cases ranging from two hundred and fifty to four hundred pounds, of a hard pilular consistence and, as its name implies, in a mass, which has been run into the case while hot and then allowed to cool.

Licorice is usually in cylindrical rolls, somewhat flattened, and usually packed in bayleaves. When good, it is black, dry, brittle, breaking with a shining fracture, of a peculiar sweet and slightly acrid or bitterish taste, and almost entirely soluble, when pure, in boiling water.

Description and Physical Properties.—"In flattened, cylindrical rolls or in masses, of a glossy black color externally; fracture brittle, sharp, smooth, conchoidal; taste characteristic and sweet. When pulverized it yields a brown powder.

"Not less than 60 per cent. of Extract of Glycyrrhiza is soluble in cold water. The yield of ash does not exceed 8 per cent." *U. S.*

Neumann obtained 460 parts of aqueous extract from 480 parts of Spanish licorice. It is, however, considerably less soluble in cold water. In different commercial specimens examined by Chevallier he found from 9 to 50 per cent. of insoluble matter. (*J. P. C.,* xxx, 429.) This is by no means, however, always impurity. In the preparation of the extract by decoction, a portion of matter originally insoluble, or rendered so by decoction, is taken up, and is, in fact, necessary to the proper constitution of the licorice. When this is prepared with cold water, or even with hot water by simple displacement, the extract attracts moisture from the air, becomes soft, and loses the characteristic brittleness of the drug. The additional substances taken up in decoction serve to protect the extract against this change. Delondre has obtained the same result by using steam as the solvent. He prepares from the root an excellent licorice, having all the requisite qualities of color, taste, and permanence, by passing steam, in suitable vessels, through the coarse powder of the root. The vapor thoroughly penetrates the powder, and is drawn off as it condenses. With about 500 lbs. of the root, this treatment is continued for twelve hours, and repeated at the end of five days. The liquors are collected, decanted, clarified with about 4 lbs. of gelatin, and quickly evaporated. After being put into the form of cylinders, the extract is kept for ten days in a drying room, at a temperature of 25° C. A bitter or empyreumatic taste is a sign of inferior quality in licorice. As ordinarily found in commerce, it requires to be purified. (See *Extractum Glycyrrhizæ Purum.*)

Licorice contains *glycyrrhizin,* a glucosidic acid, partly free and partly in combination with ammonia, to which combination the characteristic sweet taste of licorice is due. The glycyrrhizin, which is the acid ammonium salt of *glycyrrhizic acid,* $C_{44}H_{62}NO_{18}NH_4$, when boiled with dilute acids decomposes into *glycyrrhetin,* $C_{32}H_{47}NO_4$, and *parasaccharic acid,* $C_6H_{10}O_8$.

Mellor (*A. J. P.,* 1898, 23, 54, 136) examined twelve samples, of which the one highest in glycyrrhizin content was a Greek licorice with 27.78 per cent., and the lowest a Spanish with 5.28 per cent. of glycyrrhizin. Of insoluble matter, the highest was a Spanish with 36.52 per cent., and the lowest a Greek with 5.95 per cent. The average yield, however, was strongly in favor of American licorice.

Several methods have been suggested for determining the proportion of glycyrrhizin; one of these is as follows: 2 Gm. of the licorice are dissolved in 10 cc. of hot water and after cooling precipitated with 50 cc. of alcohol. The precipitate is allowed to settle, or separated by means of a centrifuge, then washed with 80 per cent. alcohol and the washings added to the alcoholic extract. This is then evaporated in vacuo on a water bath and the extract dissolved in 30 cc. of water, cooled to 15° C., the glycyrrhizin precipitated by adding 3 cc. of 10 per cent. sulphuric acid. The glycyrrhizin is dissolved in 95 per cent. alcohol, filtered and evaporated to dryness. (See Housemann, *A. J. P.,* 1921, xciii, 481). Some authorities recommend washing the glycyrrhizin with ice water, in which it is practically insoluble, before weighing. For other methods see Luiz, *A. Pharm.,* 1916, ccliv, 134 and Evans' Sons, Lescher and Webb method. (*Proc. A. Ph. A.,* 1911, 57.)

W. Zimmermann has studied various methods of glycyrrhizin assay and other factors for determining the quality of licorice extract (*Ap. Ztg.*, through *Chem. Abstr.*, 1919, xiii, 2962). He states that the water content of the extract should not exceed 17 per cent., ash not more than 11 per cent. and glycyrrhizin content not less than 10 per cent. The water insoluble portion should not exceed 25 per cent. and should be examined microscopically for specific adulterants. The *Pontefract cakes* are small lozenges of licorice made in the vicinity of Pontefract, England.

Uses.—Licorice has some demulcent property and is a popular addition to various lozenges. In large quantities it is somewhat laxative. Its most important rôle in medicine, however, is for the purpose of disguising the taste or covering the acrimony of various drugs such as quinine or ammonium chloride. It is also used to impart consistency to pills and troches.

Off. Prep.—Trochisci Ammonii Chloridi, *U. S.*

EXTRACTUM GLYCYRRHIZÆ PURUM.
U. S. (Br.)

PURE EXTRACT OF GLYCYRRHIZA
Ext. Glycyrrh. Pur.

Extractum Glycyrrhizæ, *Br.;* Extract of Liquorice; Extractum Glycyrrhizæ Depuratum, Succus Liquiritiæ Depuratus; Extrait de Réglisse, *Fr.;* Succus Liquiritiæ depuratus, *P. G.;* Gereinigter Süssholzsaft, Reines Lakriz, *G.;* Extracto Acuoso de Regliz, *Sp.*

"Glycyrrhiza, in coarse powder, 1000 Gm.; Boiling Water, a sufficient quantity. Moisten the drug with sufficient boiling water, transfer the moist drug to a metallic percolator, and percolate with boiling water until the glycyrrhiza is exhausted. Promptly evaporate the percolate to a pilular consistence on a water bath." *U. S.*

"Liquorice Root, in No. 20 powder, 1000 *grammes;* Chloroform Water, 5000 *millilitres.* Mix the Liquorice Root with one-half of the Chloroform Water; set aside for twenty-four hours; strain; press; to the pressed marc add the remainder of the Chloroform Water and set aside for six hours; strain; press; mix the strained liquids; heat to 100° C.; strain through flannel; evaporate to a soft extract." *Br.*

The necessity for a pure extract of licorice must be apparent to every pharmacist; the very variable quality of the commercial extract has frequently led to disappointment. The official process affords a preparation which is unexceptionable, the ammonia rendering the glycyrrhizin soluble, yet care must be taken in its evaporation, as it is very easily injured by too much heat, which gives it an empyreumatic taste, destroying at once its usefulness as an agreeable adjuvant. Extract of licorice is incompatible with acids of all kinds which precipitate the glycyrrhizin.

Off. Prep.—Mistura Glycyrrhizæ Composita, *U. S.;* Mistura Ammonii Chloridi, *N. F.*

EXTRACTUM HYOSCYAMI. U. S., Br.

EXTRACT OF HYOSCYAMUS Ext. Hyosc.

"Extract of Hyoscyamus yields not less than 0.22 per cent. and not more than 0.28 per cent. of the alkaloids of hyoscyamus. One Gm. of the extract represents about 4 gm. of hyoscyamus." *U. S.* "Extract of Hyoscyamus contains in 100 grammes 0.3 gramme of the alkaloids of Hyoscyamus Leaves." *Br.*

Extract of Henbane; Extrait de Jusquiame, *Fr. Cod.;* Extractum Hyoscyami, *P. G.;* Bilsenkrautextrakt, *G.;* Estratto di giusquiamo idroalcoolico, *It.;* Extracto alcoholico de beleno, *Sp.*

"*Pilular Extract of Hyoscyamus.*—Hyoscyamus, in moderately coarse powder, 1000 Gm.; Glucose, Alcohol, Water, each, a sufficient quantity. Moisten the drug with sufficient of a mixture of 3 volumes of alcohol and 1 volume of water, pack it firmly in a cylindrical percolator, and add enough menstruum, using the same proportion of alcohol and water as before, to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding more of the same menstruum until the drug is exhausted. Recover the alcohol by distillation, and evaporate the residue, with frequent stirring, at a temperature not exceeding 70° C., until it is reduced to a pilular consistence. Mix the mass thoroughly, and weigh it. Assay a portion of this extract as directed below, and from the alkaloidal content thus determined ascertain by calculation the amount of alkaloids in the remainder of the mass, and to this add sufficient glucose to make the finished Extract contain 0.25 per cent. of the alkaloids of hyoscyamus. Mix thoroughly." *U. S.*

Assay.—"Proceed by Type Process D, taking 5 Gm. of Extract of Hyoscyamus, using chloroform as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal acid corresponds to 0.02893 Gm. of the alkaloids of hyoscyamus (Proximate Assays)." *U. S.*

"*Powdered Extract of Hyoscyamus.*—Hyoscyamus, in moderately coarse powder, 1000 Gm.; Starch, dried at 100° C.; Alcohol, each, a sufficient quantity. Moisten the drug with sufficient alcohol, and pack it in a cylindrical percolator; then add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed very slowly, adding alcohol as required. Reserve the first 1000 cc. of percolate, and continue the percolation until the drug is exhausted. Transfer the weaker percolate to a suitable apparatus, and distil the alcohol at as low a temperature as practicable until a residue measuring about 100 cc. remains, then add the reserved percolate and continue distillation until the residue in the still is of syrupy consistence. Transfer this syrupy residue to a shallow evaporating dish, and rinse the flask or still with small portions of warm alcohol, adding the rinsings to the residue in the dish. Evaporate this to a soft extract, with frequent stirring, at a temperature not exceeding 70° C. Then add 50 Gm. of the dried starch, and continue the heating at the same temperature, with frequent stirring, until the mass is nearly dry. Now thoroughly incorporate an additional 20 Gm. of the dried starch, and set the product aside in a current of warm air, until thoroughly dry. Reduce the product to a fine powder, and weigh it. Assay a portion of this product as directed below, and from the alkaloidal content thus determined ascertain by calculation the amount of alkaloids in the remainder of the powder, and add to this sufficient of the dried starch to make the finished Extract contain 0.25 per cent. of the alkaloids of hyoscyamus. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles, and stopper them tightly.

" **Assay.**—Proceed as directed under *Pilular Extract of Hyoscyamus.*" *U. S.*

" Hyoscyamus Leaves, in No. 40 powder, Alcohol (70 per cent.), of each, *a sufficient quantity*. Reduce ten grammes of the Hyoscyamus Leaves to No. 60 powder, and determine the proportion of alkaloids present by the process described under 'Belladonnæ Folia.' Moisten one thousand grammes of the Hyoscyamus Leaves with two hundred and fifty millilitres of the Alcohol, pack firmly in a percolator, and percolate with more of the Alcohol until four thousand millilitres of percolate have been obtained. Determine the proportion of total solids in the percolate by evaporating twenty millilitres, drying the residue at 80° C., and weighing. Determine also the proportion of alkaloids in the percolate by the process described under 'Tinctura Belladonnæ.' Having thus determined the proportion of total solids and of alkaloids in the percolate, proceed as directed under 'Extractum Belladonnæ Siccum' to prepare a dry Extract of Hyoscyamus containing 0.3 per cent. of alkaloids. Examined by the process described under 'Extractum Belladonnæ Siccum,' Extract of Hyoscyamus is found to contain in 100 grammes 0.3 gramme of the alkaloids of Hyoscyamus Leaves. *Limit of error* 0.015 gramme in excess or defect." *Br.*

" This Extract may be used when the Extractum Hyoscyami of the International Agreement is required. It contains 0.3 per cent. of the alkaloids of Hyoscyamus Leaves." *Br.*

The strength is not quite the same, the U. S. P. requires not less than 0.22 per cent. nor more than 0.28 per cent. of alkaloids while the Br. Pharm., 1914, requires not less than 0.3 per cent. of alkaloids. For an account of the disadvantages of the extract from the fresh leaves see *U. S. Dispensatory,* 19th ed., p. 478.

Dose, from one-half to two grains (0.03–0.13 Gm.).

Off. Prep.—Pilulæ Carthartieæ Vegetabiles, *N. F.;* Pilula Colocynthidis et Hyoscyami, *Br.* (*N. F.*)*;* Pilulæ Laxativæ Post Partum, *N. F.*

EXTRACTUM KRAMERIÆ. Br.

EXTRACT OF KRAMERIA

Extract of Rhatany; Extractum Ratanhæ; Extrait d Ratanhia, *Fr. Cod.;* Ratanhaextrakt, *G.;* Estratto di ratania acquoso, *It.;* Extracto acuoso de ratania, *Sp.*

" Exhaust Krameria Root, in No. 10 powder, with Distilled Water by the *percolation process;* evaporate the percolate to dryness." *Br.*

A powdered extract of krameria is recognized by the N. F. (see Part III).

Extract of krameria should have a reddish-brown color, a smooth shining fracture, and a very astringent taste, and should be almost entirely soluble in water. Its virtues may be considered as in proportion to its solubility. It is much used for all the purposes for which the astringent extracts are employed.

Dose, from five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Trochiscus Krameriæ, *Br.;* Trochiscus Krameriæ et Cocainæ, *Br.*

EXTRACTUM MALTI. U. S.

EXTRACT OF MALT Ext. Malt.

Essence (Extrait) de Malt, *Fr.;* Malzextrakt, *G.*

" Extract of Malt is obtained by infusing malt with water at 60° C., concentrating the expressed liquid at a temperature not exceeding 60° C., and adding 10 per cent., by weight, of glycerin. It contains dextrin, maltose, a small amount of glucose, and an amylolytic enzyme. Extract of Malt is capable of converting not less than five times its weight of starch into water-soluble sugars." *U. S.*

Description and Physical Properties.—" A sweet, viscous, light brown, liquid extract having an agreeable, characteristic odor. It is soluble in cold water, more readily soluble in warm water. Specific gravity: not less than 1.350 and not more than 1.430 at 25° C.

" **Assay.**—Mix a quantity of potato starch, purified as directed under *Pancreatinum,* equivalent to 5 Gm. of dried starch, in a beaker with 10 cc. of cold, distilled water. Add 140 cc. of boiling distilled water, and heat on a water bath with constant stirring for two minutes, or until a translucent, uniform paste is obtained. Cool to 40° C. in a suitable bath previously adjusted to this temperature. Add 20 cc. of a fresh solution of Extract of Malt at 40° C., prepared by dissolving 5 Gm. of Extract of Malt in sufficient distilled water to make 100 cc. of solution at 40° C., mix well, and maintain the same temperature for exactly thirty minutes, stirring frequently. A thin, nearly clear liquid is produced. Add at once 0.1 cc. of this liquid to a previously made mixture of 0.2 cc. of tenth-normal iodine and 60 cc. of distilled water. No blue or reddish color is produced." *U. S.*

Under the name of extract of malt, two distinct preparations were formerly found upon the market, the one being a liquid similar to beer, the other, the official extract prepared from malt, composed chiefly of dextrin and glucose, with some albumen and phosphates. The object of the U. S. process is to obtain all of the soluble principles of malt in a permanent form. To secure this, strict attention to the details of the process is necessary. Good extract of malt should contain no starch, have the consistence of thick honey, a brown color, and should be free from empyreumatic taste. A great deal of commercial extract of malt is said to be adulterated with glucose. A *dry extract of malt* has come into extensive use as an infant's food, made by artificially drying the thick syrupy extract. It is in the form of a straw-colored, coarse powder, and is given dissolved in milk or water.

Extract of malt is a viscid brown liquid with a characteristic empyreumatic flavor and sweet taste. It consists of from 45 to 55 per cent. of maltose, with smaller quantities of dextrin and protein, and contains in addition a characteristic enzyme, *diastase.* This ferment appears to act very much like the ptyalin of the saliva, converting starch into maltose; it differs from that enzyme, however, in that whereas ptyalin acts most rapidly at the body temperature (37° C.) the malt is most active at a temperature of about 55° C. Chittenden and Cummins have shown that the presence of either free acid or free alkalies interferes with the amylolytic properties of diastase.

Under the name of *Diastasum,* the U. S. IX recognized a mixture containing the active ferments of malt. It was capable of digesting 50 times its weight of starch and was officially described as follows: "Diastase occurs as a yellowish-white, amorphous powder or in translucent scales; odorless and tasteless. It converts starch into dextrin and maltose. Diastase gradually loses its amylolytic power on keeping; this power is destroyed by heating its solutions above 85° C., or by the addition of much acid and is diminished by the presence of acids or alkalies. Diastase is soluble in water, the solutions being more or less turbid; almost insoluble in alcohol.

"*Assay.*—Mix a quantity of potato starch, purified as directed under *Pancreatinum,* equivalent to 5 Gm. of dry starch, in a beaker with 10 mils of cold distilled water. Add 140 mils of boiling distilled water, and heat the mixture on a water bath with constant stirring for two minutes, or until a translucent, uniform paste is obtained. Cool the paste to 40° C. in a water bath previously adjusted to this temperature. Prepare a fresh solution of 0.1 Gm. of Diastase in 10 mils of distilled water at 40° C. and add it to the paste. Mix them well and maintain the same temperature for exactly thirty minutes, stirring frequently; a thin, nearly clear liquid is produced. Add at once 0.1 mil of this liquid to a previously made mixture of 0.2 mil of tenth-normal iodine V.S. and 60 mils of distilled water; no blue or reddish color is produced." *U. S. IX.*

Diastase is frequently found upon the market in an impure or adulterated condition, samples having been observed containing as much as 60 per cent. of starch. Much of the commercial diastase is variable in strength and frequently it is almost inert. *Takadiastase* is the name of a proprietary form of diastase which is not produced from malt but is produced by the growth of certain species of *Aspergillus* upon rice hulls or bran. In Japan takadiastase is used in the brewing industry as malt is used in other countries. Wahl has shown that malt contains a proteolytic as wel as an amylolytic ferment.

Uses.—The extract of malt is used in medicine for three purposes, first, as a highly nutritious and easily assimilable food in various states of *malnutrition;* secondly, for the purpose of increasing the digestion of starches in certain types of *dyspepsia.* In those rare cases where there is an organic deficiency of saliva, or in the more frequent condition where the patient is too lazy to masticate his food, it may be of service, but as its action upon starch like that of ptyalin is inhibited by the rising acidity of the stomach at mealtime, its range of usefulness as a digestant is certainly not very wide. The third use of the extract of malt is as a vehicle. It is an excellent emulsifying agent and possesses also considerable power in covering unpleasant flavors. For both of these reasons as well as its own nutritive value, it is frequently used in conjunction with cod liver oil. It is also employed widely as a vehicle for cascara sagrada, creosote, and other drugs.

Dose, from one to four fluidrachms (3.75 to 15 cc.).

Off. Prep.—Emulsum Olei Morrhuæ cum Malto, *N. F.*

EXTRACTUM NUCIS VOMICÆ.
U. S. (Br.)

EXTRACT OF NUX VOMICA Ext. Nuc. Vom.
[Powdered Extract of Nux Vomica, Nucis Vomicæ Extractum, P. I.]

"Extract of Nux Vomica yields not less than 15.2 per cent. and not more than 16.8 per cent. of the alkaloids of nux vomica." *U. S.*

"Dry Extract of Nux Vomica contains in 100 grammes 5 grammes of strychnine." *Br.*

Extractum Nucis Vomicæ Siccum, *Br.;* Dry Extract of Nux Vomica; Extractum Nucum Vomicarum Spirituosum (vel Alcoholicum); Extrait de Noix Vomique, *Fr. Cod.;* Extractum Strychni, *P. G.;* Weingeistiges Krähenaugenextrakt, Brechnussextrakt, Strychnossamenextrakt, *G.;* Estratto di noce vomica alcoolico, *It.;* Extracto alcoholico de nuez vomica, *Sp.*

"Nux Vomica, in moderately coarse powder, 1000 Gm.; Alcohol; Water; Acetic Acid; Purified Petroleum Benzin; Starch, dried at 100° C., each, a sufficient quantity. Moisten the drug with a sufficient quantity of a mixture of 75 volumes of alcohol, 1 volume of acetic acid, and 24 volumes of water, pack it firmly in a cylindrical percolator, and add enough of this menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, adding more of the same menstruum as required until the drug is practically exhausted. Recover the alcohol from the percolate by distillation at as low a temperature as practicable, and concentrate the liquid until the residue measures about 200 cc. Transfer this residue to a flask or separator, add 150 cc. of water and 200 cc. of purified petroleum benzin, and shake the mixture thoroughly for several minutes. Allow the liquids to separate, and decant the benzin layer as closely as possible, again add to the residue 100 cc. of purified petroleum benzin, agitate, and decant the benzin as before, and then reject the benzin solutions. Evaporate the fat-free residue to dryness on a water bath with frequent stirring. Assay a portion of this product as directed below, and from the alkaloidal content thus determined ascertain by calculation the amount of alkaloids in the remainder of the product, and add sufficient of the dried starch to make the finished Extract contain 16 per cent. of the alkaloids of nux vomica. Reduce the mixture to a fine powder, mix thoroughly, pass the extract through a fine sieve, transfer it to small, wide-mouthed bottles, and stopper them tightly." *U. S.*

"Liquid Extract of Nux Vomica, Calcium Phosphate, of each, *a sufficient quantity.* Evaporate ten millilitres of the Liquid Extract in a flat-bottomed dish and dry at 100° C. The weight of the dry extract thus obtained deducted from three grammes gives the weight of Calcium Phosphate to be added to each ten millilitres of the Liquid Extract. Take one hundred parts by volume of the Liquid Extract; recover the alcohol by distillation; add sufficient of the Calcium Phosphate, as indicated by the above determination, to produce, when dried at 100° C., and reduced to a fine powder, thirty parts by weight of the Dry Extract." *Br.*

Assay.—"Proceed by Type Process D, taking 1 Gm. of Extract of Nux Vomica, using chloroform as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal acid corresponds to 0.0364 Gm. of the alkaloids of nux vomica (Proximate Assays)." *U. S.*

"3 grammes of Dry Extract of Nux Vomica, when exhausted with *alcohol* (70 per cent.), afford a liquid which when tested by the process described under 'Extractum Nucis Vomicæ Liquidum' yield 0.15 gramme of strychnine, representing in 100 grammes of the Dry Extract 5 grammes of strychnine. *Limit of error* 0.2 gramme in excess or defect. This Dry Extract contains 5 per cent. of strychnine." *Br.*

Extract of Nux Vomica, U. S. P., is a powdered extract containing 16 per cent. of total alkaloids. This alkaloidal strength is the standard adopted by The Brussels Protocol. The U. S. P. VIII standard was 5 per cent. of strychnine and the British Pharm. (1914) retained its former standard of 5 per cent. of strychnine and directed the evaporation of the standardized liquid extract of nux vomica.

The U. S. IX used sulphuric, instead of acetic, acid in this extract. Acetic acid is the most effective menstruum for nux vomica, but has the disadvantage of also extracting inert constituents; it leaves the fixed oil in the marc and this is a great point in its favor.

Dose, one-fourth to one-half of a grain (0.016–0.032 Gm.).

Off. Prep.—Pilulæ Aloes et Podophylli Compositæ, *N. F.;* Pilulæ Ferri, Quininæ Aloes et Nucis Vomicæ, *N. F.;* Pilulæ Laxativæ Post Partum, *N. F.*

EXTRACTUM OPII SICCUM. Br.

DRY EXTRACT OF OPIUM [Opii Extractum, P. I.]

"Dry Extract of Opium contains in 100 grammes 20 grammes of morphine, calculated as anhydrous." *Br.*

Extractum Opii, *U. S. IX.;* Extract of Opium; Extractum Thebaicum; Extrait d'Opium, *Fr. Cod.;* Extrait Thébaique, *Fr.;* Extractum Opii, *P. G.;* Opiumextrakt, *G.;* Estratto di opio acquoso, *It.;* Extracto acuoso de opio, *Sp.*

"Exhaust sliced Opium with about five times its weight of Distilled Water; strain the liquid through flannel; cool and ascertain its volume. Determine the percentage of morphine present in forty millilitres of this liquid by the process described under 'Tinctura Opii,' and determine also the percentage of total solids dried at 100° C. Add to the remainder of the liquid sufficient Calcium Phosphate to yield an extract which, when dried at 100° C., contains 20 per cent. of morphine; evaporate to dryness, powder, and finally dry at 100° C. Examined by the process described under 'Opium,' Dry Extract of Opium is found to contain in 100 grammes 20 grammes of morphine, calculated as anhydrous. *Limit of error* 1 gramme in excess or defect. This Dry Extract contains 20 per cent. of morphine." *Br.*

This extract has been omitted from the U. S. X, but a similar preparation is recognized by the N. F. (see Part III).

As purely aqueous preparations of opium have been found to agree better with certain individuals than opium alone or its alcoholic preparations, there is reason to believe that there are in the crude drug one or more principles, which are capable of causing nausea, headache, nervous disturbances, etc., and which are insoluble in water, though extracted by alcohol or ether. (See *Opium Deodoratum.*)

Dose, one-sixth to one grain (0.01–0.06 Gm.).

Off. Prep.—Extractum Opii Liquidum, *Br.*

EXTRACTUM RHEI. U. S., Br.

EXTRACT OF RHUBARB Ext. Rhei. [Powdered Extract of Rhubarb]

"One Gm. of the Extract represents 2 Gm. of rhubarb." *U. S.*

Extractum Rhei Alcoholicum; Extrait de Rhubarbe, *Fr. Cod.;* Extractum Rhei, *P. G.;* Rhabarberextrakt, *G.;* Estratto di rabarbaro acquoso, *It.;* Extracto acuoso de ruibarbo, *Sp.*

"Rhubarb, in moderately coarse powder, 1000 Gm.; Starch, dried at 100° C.; Alcohol; Water; each, a sufficient quantity to make 500 Gm. Moisten the drug with sufficient of a mixture of 4 volumes of alcohol and 1 volume of water, pack it in a cylindrical percolator, and add enough of this menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding menstruum of the same proportion of alcohol and water as before until the drug is exhausted. Recover the alcohol from the percolate by distillation at as low a temperature as practicable, and continue distillation until a residue of syrupy consistence remains in the still. Transfer this to a shallow dish, rinse the still with small portions of warm menstruum, add the rinsings to the residue in the dish, and evaporate the mixture to dryness, with frequent stirring, at a temperature not exceeding 70° C. Weigh the dry product, and add sufficient of the dried starch to make the weight 500 Gm. Reduce the mixture to a fine powder, mix thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles, and stopper them tightly." *U. S.*

"Exhaust Rhubarb, in No. 20 powder, with Alcohol (60 per cent.) by the *percolation process.* Recover most of the alcohol from the percolate by distillation, and evaporate the residual liquid to dryness." *Br.*

The British extract (1914) is now nearly identical with the U. S. preparation—except that the U. S. is made to bear a definite relation to the whole drug by adding magnesium oxide—the menstruum used for the former is, however, slightly more aqueous. Rhubarb yields all its active matter to water and alcohol; but, unless the evaporation be performed with great care and with a moderate heat, it is certain that the purgative principle is to a greater or less extent injured or dissipated in the process, and the extract may thus become even less efficient than the root. When properly prepared, the extract has decidedly the peculiar odor of rhubarb.

Dose, from two to ten grains (0.13–0.65 Gm.).

EXTRACTUM STRAMONII. U. S.

EXTRACT OF STRAMONIUM Ext. Stramon.

"Extract of Stramonium yields not less than 0.9 per cent. nor more than 1.1 per cent. of the alkaloids of Stramonium. One gramme of the Extract represents about *four grammes* of stramonium." *U. S.*

Extrait de Stramoine (feuille), *Fr. Cod.;* Stechapfelblätterextrakt, *G.*

"*Pilular Extract of Stramonium.*—Stramonium, in moderately coarse powder, 1000 Gm.; Glucose, Alcohol, Water, each, a sufficient quantity. Moisten the drug with sufficient of a mixture of 3 volumes of alcohol and 1 volume of water, and pack it in a cylindrical percolator; then add enough of this menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding menstruum of the same strength until the drug is exhausted. Recover the alcohol from the percolate by distillation, and evaporate the residue with frequent stirring at a temperature not exceeding 70° C. to a pilular consistence. Mix the mass thoroughly and weigh it. Assay a portion of this Extract as directed below, and from the alkaloidal content thus determined ascertain by calculation the amount of alkaloids in the remainder of the mass, and to this add sufficient glucose to make the finished Extract contain 1 per cent of the alkaloids of stramonium. Mix thoroughly.

"**Assay.**—Proceed by Type Process D, taking 2 Gm. of Extract of Stramonium, using chloroform as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal acid corresponds to 0.02893 Gm. of the alkaloids of stramonium (Proximate Assays)." *U. S.*

"*Powdered Extract of Stramonium.*—Stramonium, in moderately coarse powder, 1000 Gm.; Starch, dried at 100° C.; Alcohol; each, a sufficient quantity. Moisten the drug with sufficient alcohol, and pack it in a cylindrical percolator; then add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed very slowly, adding alcohol as required. Reserve the first 1000 cc. of percolate and continue the percolation until the second percolate measures 1000 cc. or until the drug is exhausted. Transfer the second percolate to a suitable apparatus and distil the alcohol at as low a temperature as practicable until a residue measuring about 100 cc. remains, then add the reserved percolate, and continue distillation until the residue in the still is of syrupy consistence. Transfer this syrupy residue to a shallow evaporating dish, rinse the flask or still with small portions of warm alcohol, and add the rinsings to the contents of the dish. Evaporate this to a soft extract, with frequent stirring, at a temperature not exceeding 70° C. Then add 50 Gm. of the dried starch, and continue the heating at the same temperature, with frequent stirring, until the mass is nearly dry. Now thoroughly incorporate an additional 20 Gm. of dried starch, and set the product aside in a current of warm air until thoroughly dry. Reduce the product to a fine powder, and weigh it. Assay a portion of this product as directed below, and from the alkaloidal content thus determined ascertain by calculation the amount of alkaloids in the remainder of the powder, and add to this sufficient of the dried starch to make the finished Extract contain 1 per cent. of the alkaloids of stramonium. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles, and stopper them tightly.

" **Assay.**—Proceed as directed under *Pilular Extract of Stramonium.*" *U. S.*

E'we and Vanderkleed report specimens of extract of stramonium which contain a green coal tar color to simulate the chlorophyll present in extracts made from high grade leaf. This coloring matter interferes with the alkaloidal assay and must be removed by shaking out with chloroform in the acid solution. (*J. A. P. A.*, 1914, 1683.)

Dose, from one-eighth to one-fourth of a grain (0.008–0.016 Gm.).

Off. Prep.—Unguentum Stramonii (from Pilular Extract), *U. S.*

EXTRACTUM STROPHANTHI. Br.

EXTRACT OF STROPHANTHUS

Extrait de Strophanthus Kombé (Semence), *Fr.;* Strophantusextrakt, *G.*

" Strophanthus Seeds, reduced to No. 30 powder, and dried at 45° C., 25 *grammes;* Ether, Alcohol (90 per cent.), Milk Sugar, in powder, of each, *a sufficient quantity.* Pack the Strophanthus Seeds in a percolator; moisten with the Ether, and macerate for twenty-four hours; then allow percolation to proceed, continuing the addition of the Ether until the liquid passes through colorless. Remove the marc from the percolator, and dry it, gradually heating it to 50° C. Again reduce it to powder, repack in the percolator, and moisten with the Alcohol. Macerate for forty-eight hours, then pour on successive quantities of the Alcohol, percolating slowly, until two hundred and fifty *millilitres* of liquid are obtained. Evaporate most of the alcohol; transfer the residual liquid to a tared dish; concentrate until the liquid begins to thicken; then add sufficient of the Milk Sugar to produce fifty *grammes* of Extract, in powder." *Br.*

This preparation of the British Pharmacopœia closely resembles an "abstract" of the U. S. P., 1880; an important detail, in our opinion, has been neglected in not washing the fatty matter extracted by the ether with diluted alcohol to remove active constituents held by the fatty substances, then evaporating the solution and incorporating the residue with the extract.

This extract fills a very decided want of a solid preparation of strophanthus that can be administered in pill and capsule. A grain of it may be considered to represent five minims of the U. S. tincture of strophanthus.

Dose, as given in the British Pharmacopœia, from one-fourth to one grain (0.016–0.065 Gm.).

EXTRACTUM TARAXACI. Br.

EXTRACT OF TARAXACUM Ext. Tarax.

Extract of Dandelion; Extrait de Pissenlit, *Fr.;* Extrait de Dent-de-lion, *Fr. Cod.;* Löwenzahnextrakt, *G.;* Estratto di tarassaco acquoso, *It.*

" Crush Taraxacum Root; press out the juice; allow the starchy matter to subside; decant; heat the liquid to 100° C., and maintain the temperature for ten minutes; strain; evaporate to a soft extract." *Br.*

This extract represents whatever therapeutic value dandelion root may possess, in a relatively concentrated form.

Dose, from five to fifteen grains (0.3–1 Gm.) three times a day.

FARFARA. N. F.

COLTSFOOT [Coltsfoot Leaves, Tussilâgo Leaves]

"Coltsfoot is the dried leaf of *Tussilago Farfara* Linné (Fam. *Compositæ*). Coltsfoot contains not more than 3 per cent. of foreign organic matter and yields not more than 4 per cent. of acid-insoluble ash." *N. F.*

Folia Farfaræ, *P. G.;* Tussilage, Pas d'âne, *Fr.;* Huflattig, Rosshuf, *G.*

Coltsfoot is a low perennial, woolly herb, indigenous to Europe and growing in scattered wet places from Quebec to Pennsylvania and westward to Minnesota. It possesses a horizontal rhizome from which, early in the spring, arise several leaflets, erect, simple scapes or flower-stems bearing yellow, terminal flower-heads surrounded by an involucre of appressed scale-like bracts of a brownish-pink color. The leaves, which appear after the flowers, are all radical, vary in outline from cordate to ovate-reniform and possess white-tomentose lower surfaces. The flowers have an agreeable odor, which they retain after desiccation. The dried root and leaves are inodorous, but have a bitter, mucilaginous taste. The leaves are gathered in June and July and carefully dried. The commercial supply used in the United States comes from Europe.

Description and Physical Properties.—"*Unground Coltsfoot.*—Petiole long, pubescent; blade very brittle, nearly orbicular or broadly ovate-reniform, from 8 to 15 cm. long and nearly as wide, deeply cordate at the base, angular and dentate with red-brown teeth, palmately 5- to 9-nerved; glabrous above, slightly wrinkled, dark green to brownish green or yellowish green. The younger leaves densely white, floccose beneath, the older nearly or often quite glabrous below. Odor indistinct; taste mucilaginous, faintly herbaceous, bitter.

"*Powdered Coltsfoot.*—Yellowish green; numerous multi-cellular, non-branching hairs, usually curved and twisted together, the lower cells up to 0.040 mm. wide, the terminal cells much elongated, 0.010 to 0.024 mm. in width and at times with spiral bands; broadly elliptical stomata up to 0.054 mm. in length and associated with finely striated epidermal cells, the latter having wavy vertical walls; non-porous fibers few with walls from 0.006 to 0.012 mm. in thickness; parenchyma cells containing chloroplastids; tracheæ few, spiral, annular or with simple pores." *N. F.*

C. S. Bondurant (*A. J. P.*, 1887, 340) examined coltsfoot chemically. He found, besides mucilage and tannin, evidences of a bitter glucoside. Klobb isolated two phytosterols from coltsfoot flowers. (*P. J.*, 1909, 999.)

Uses.—The leaves were smoked by the ancients in *pulmonary complaints,* and in Germany they are said to be substituted for tobacco. The only therapeutic value they possess is a demulcent effect due to their mucilage. In the N. F. they are used in a pectoral tea (see *Species Pectorales,* Part III).

Dose, of the dried leaves, one to two drachms (3.9–7.5 Gm.), which may be conveniently given in decoction.

Off. Prep.—Species Pectorales, *N. F.*

FEL BOVIS. U. S.

OXGALL

"Oxgall is the fresh bile of the ox, *Bos taurus* Linné (Fam. *Bovidæ*)." *U. S.*

Fel Bovinum, Fel Tauri, Bilis Bubula, Ox Bile; Bile de Bœuf, *Fr. Cod.;* Ochsengalle, Rindsgalle, *G.;* Hiel de toro, *Sp*

Bile is a viscid fluid varying in color from a golden yellow to a greenish brown. It contains —besides mucin and other proteins, inorganic salts, cholesterin, traces of lecithin and fatty acids—the salts of two peculiar acids known as *glycocholic* and *taurocholic;* the salts of these are sometimes spoken of collectively as the *cholates.* In carnivorous animals the taurocholates predominate but in most herbivors and in man glycocholic salts are the more abundant. *Glycocholic acid,* $C_{26}H_{43}O_6N$, is a white monobasic acid, sparingly soluble in cold water, easily soluble in alcohol, its sodium salt being soluble in either water or alcohol. It is dextro-rotatory. Taurocholic acid, $C_{26}H_{45}SO_7N$, is similar in its general physical properties. The color of bile is due to the presence of two peculiar pigments known as *bilirubin* and *biliverdin* which are apparently derived from the hemoglobin of the blood. Biliverdin can be produced from bilirubin by oxidation. The customary tests for the presence of these bile pigments is to oxidize them, for example with nitric acid, which produces a play of colors passing from red to green, to purple and eventually to yellow (see under *Diagnostic Reagents,* Part II). The bile obtained from the gall-bladder is much more concentrated than that directly secreted by the liver. The commercial oxgall represents largely the bile stored in the gall-bladder.

The following table gives the approximate composition of human bile—in parts per hundred—from the liver and from the gall-bladder.

COMPOSITION OF BILE.

	From the Liver.	From the Gall-bladder.
Total Solids............	1.0 –2.0	10.0–17.0
Sodium Glycocholate ...	0.1 –0.6	6.0–10.0
Sodium Taurocholate ...	0.03–0.06	0.7– 0.9
Fats and Soaps.........	0.1 –0.2	1.0– 3.0
Mucin, etc.	0.2 –0.4	1.4– 3.0
Inorganic Salts..........	0.5 –0.8	0.6– 1.0

The *sodium glycocholate* and *taurocholate* may be separated in the following manner. Dry ox bile is treated with absolute alcohol, and the tincture precipitated by ether in excess. Both salts are deposited, and the glycocholate crystallizes upon standing, the taurocholate remaining in an amorphous form, resembling oily or resinous matter. They may be separated more completely by taking advantage of their different relations to lead acetate and subacetate. Both the acids are precipitated by the subacetate, the glycocholate only by the acetate. If the deposit above referred to be dissolved in water, solution of lead acetate will throw down a lead glycocholate, while the addition of the lead subacetate to the remainder will precipitate the taurocholate. The acids may be separated from the salts of lead by sulphuric acid, and then recombined with soda.

Description and Physical Properties.—"A brownish-green or dark green, somewhat viscid liquid, having a characteristic odor, and a disagreeable, bitter taste.

"Mix two drops of Oxgall with 10 cc. of water and a drop of a freshly prepared solution of 1 part of sucrose in 4 parts of water, and cautiously add sulphuric acid until the precipitate first formed is redissolved. The mixture gradually acquires a brownish-red color, changing successively to carmine, purple, and violet. A frothy mixture is produced when Oxgall is shaken with water.

"Specific gravity: 1.015 to 1.025 at 25° C. Oxgall is neutral or faintly alkaline to litmus paper." *U. S.*

Crude oxgall is rarely used for medical purposes. It is, however, frequently employed for various technical purposes, especially for cleaning cloth. For medicinal properties see *Extractum Fellis Bovis.*

Off. Prep.—Extractum Fellis Bovis, *U. S.;* Fel Bovinum Purificatum, *Br.*

FERRI CARBONAS SACCHARATUS. U. S., Br.

SACCHARATED FERROUS CARBONATE

Ferr. Carb. Sacch.

"Saccharated Ferrous Carbonate contains not less than 15 per cent. of $FeCO_3$." *U. S.* "Saccharated Iron Carbonate is ferrous carbonate, more or less oxidised, mixed with glucose. Contains not less than 50 per cent. of ferrous salts calculated as ferrous carbonate, $FeCO_3$." *Br.*

Saccharated Iron Carbonate; Saccharated Carbonate of Iron; Carbonas Ferrosus Saccharatus; Saccharure de Carbonate Ferreux, *Fr.;* Ferrum Carbonicum Saccharatum, *P. G.;* Zuckerhaltiges Kohlensaures Eisen, Zuckerhaltiges Ferrocarbonat, *G.*

"Ferrous Sulphate, 50 Gm.; Sodium Bicarbonate, 35 Gm.; Lactose, 10 Gm; Sucrose, in fine powder; Diluted Sulphuric Acid; Distilled Water; each, a sufficient quantity to make 100 Gm. Dissolve 8.5 Gm. of sucrose in 200 cc. of hot distilled water, and then dissolve the ferrous sulphate in that solution. Add from 3 to 5 drops of diluted sulphuric acid, and filter. Dissolve the sodium bicarbonate in 500 cc. of distilled water at a temperature not exceeding 50° C., and filter. To the solution of sodium bicarbonate contained in a flask having a capacity of about 1000 cc. gradually add the solution of ferrous sulphate and mix thoroughly by rotating the flask. Fill the flask with boiling distilled water, cork it loosely, and set the mixture aside. When the precipitate has subsided, draw off the clear supernatant liquid by means of a siphon, fill the flask again with hot distilled water, and shake it. Again draw off the liquid, and repeat the washing with hot distilled water in the same manner until the decanted liquid gives merely a slight cloudiness with barium chloride T.S. Drain the precipitate, transfer it to a porcelain dish containing 61.5 Gm. of sucrose and 10 Gm. of lactose, and mix intimately. Evaporate the mixture to dryness on a water bath, reduce it to a powder, weigh, and mix intimately with it, if necessary, enough well-dried sucrose to make the product weigh 100 Gm. To minimize oxidation make this preparation in the shortest possible time." *U. S.*

"Ferrous Sulphate, 97.5 *grammes;* Glucose, 30.0 *grammes;* Sodium Carbonate, 105.0 *grammes;* Distilled Water, boiling, *a sufficient quantity.* Dissolve fifteen *grammes* of the Glucose in three hundred *millilitres* of the Distilled Water, and dissolve the Ferrous Sulphate in the solution. Dissolve the Sodium Carbonate in one hundred and fifty *millilitres* of the Distilled Water, and to this add the solution of the Ferrous Sulphate, stirring constantly. Then add four hundred *millilitres* of the Distilled Water, mix thoroughly, and allow the precipitate to subside. Decant the supernatant liquid, and wash the precipitate with two successive quantities, each of four hundred *millilitres,* of the Distilled Water. Mix the washed precipitate with the remainder of the Glucose, and dry at a temperature not exceeding 100° C. Powder the product, and preserve it in a stoppered bottle." *Br.*

When solutions of ferrous sulphate and sodium carbonate are mixed together, there are formed, by double decomposition, sodium sulphate which remains in solution, and ferrous carbonate which falls as a pale-blue precipitate. This precipitate begins immediately to alter in nature by the absorption of oxygen, and, if washed and dried in the ordinary way, becomes ferric oxide, associated with a small quantity of the ferrous carbonate, which has escaped change. As the preparations of ferrous iron are the most esteemed, the change which this precipitate undergoes has always been a matter of regret, and various attempts have been made to prevent it. Saccharine matter has been ascertained to possess the required preservative properties, and in the preparation under consideration it is used to prevent the ferrous carbonate as first precipitated from passing into the ferric hydroxide.

Becker, a German physician, was the first to suggest the use of sugar as a means of protection against the absorption of oxygen, and the idea was carried out by Klauer, a German chemist, who first made the saccharated ferrous carbonate. The use of boiling distilled water in the process is to avoid the action of the air contained in unboiled water. The washed precipitate is pressed so as to free it from water as far as possible, and then incorporated with the sugar in fine powder. The mode of treating the precipitate unnecessarily exposes it to the action of the air, and the late London method of incorporating it with the sugar immediately after washing was on this account preferable. The final drying temperature should not exceed 54.5° C.

Description and Physical Properties.—"A greenish-brown, odorless powder, which gradually becomes oxidized by contact with air. Saccharated Ferrous Carbonate is only partially soluble in water.

"When treated with hydrochloric acid, it dissolves with copious evolution of carbon dioxide, a clear greenish-yellow liquid resulting. Dissolve 1 Gm. of Saccharated Ferrous Carbonate in 5 cc. of hydrochloric acid, and dilute the solution with distilled water until it measures 100 cc.: this solution responds to the reactions for ferrous salts.

"A 10 cc. portion of the solution prepared as above, when diluted with distilled water to 50 cc., shows no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid.

"Preserve in well stoppered bottles, exposed to light." *U. S.*

"A greenish-brown powder, with a feebly chalybeate taste. Soluble with effervescence in *hydrochloric acid* diluted with half its volume of *water.* 1 gramme, dissolved in excess of warm *concentrated phosphoric acid* and diluted with *water,* does not cease to yield a blue precipitate with *solution of potassium ferricyanide* until 43.1 millilitres of *N/10 solution of potassium bichromate* have been added. *Arsenic limit* 5 parts per million." *Br.*

Assay.—"Dissolve about 2 Gm. of Saccharated Ferrous Carbonate, accurately weighed, in 15 cc. of diluted sulphuric acid, and dilute the solution with distilled water to about 100 cc. Titrate immediately with tenth-normal potassium dichromate, potassium ferricyanide T.S. being used as indicator. Each cc. of tenth-normal potassium dichromate corresponds to 0.01159 Gm. of $FeCO_3$." *U. S.*

Saccharated ferrous carbonate is sometimes seen in small coherent lumps, usually of a grayish-brown color, permanent in the air, having a sweet, styptic taste, and wholly and readily soluble in warm hydrochloric acid, diluted with half its volume of water, with effervescence. The presence of ferric oxide is a defect, which is avoided in Vallet's ferruginous mass.

Uses.—The ferrous carbonate has for many years been one of the most highly esteemed chalybeates in the treatment of *chlorosis.* Its great advantage is the complete lack of astringency and consequent acceptability to the stomach. On exposure to the air it absorbs oxygen and is changed to the ferric state, which is apparently a less efficacious remedy. This absorption of oxygen is delayed by the presence of sugar, but the protection is not a complete one. The saccharated ferrous carbonate is inferior to Vallet's mass because in the latter the anti-oxidizing influence of sugar is more fully applied.

Dose, of the saccharated ferrous carbonate, from five to fifteen grains (0.32–1.0 Gm.), given in pills.

FERRI CHLORIDUM. U. S.

FERRIC CHLORIDE Ferr. Chlor. [Iron Perchloride, Sesquichloride of Iron]

" Ferric Chloride contains $FeCl_3$ in a hydrated form, corresponding to not less than 20 per cent. of Fe." *U. S.*

Perchloride of Iron, Chloride of Iron; Ferrum Muriaticum Oxydatum, Chlorum Ferricum; Chloretum Ferricum, Ferri Perchloridum; Chlorure ferrique, Perchlorure de Fer, *Fr.;* Ferrum Sesquichloratum, *P. G.;* Eisenchlorid, *G.;* Cloruro ferrico, *Sp.*

The U. S. P. X does not give a process for preparing ferric chloride; the U. S. P. VIII process is appended.

" Solution of Ferric Chloride, *one hundred grammes,* to make *forty grammes.* Evaporate the Solution of Ferric Chloride on a water-bath until it weighs *forty grammes;* then set it aside in a glass-covered vessel, until it forms a crystalline mass. Lastly, break the salt into pieces, and keep it in glass-stoppered bottles, protected from light." *U. S. VIII.*

For further information concerning the manufacture of this salt, see under *Liquor Ferri Chloridi.*

It contains a variable proportion of water according to the crystalline forms it is made to assume, having about 40 per cent., or six molecules, when in fine acicular crystals, and only 22 per cent., or two and a half molecules, when in the form of larger tables.

Tasteless Iron Chloride is made by adding an alkaline citrate in solution to a solution of iron sesquichloride, in such proportion that there shall be two molecules of the former and three molecules of chlorine. Usually from 150 to 175 grains of potassium or sodium citrate are required for the preparation of an ounce of a tincture of corresponding strength to the official tincture. The addition should be made to the liquor, and the final solution must not contain more than 40 per cent. of alcohol. R. Rother affirms that these so-called salts are mere mixtures of iron citrate and iodide or chloride of the alkali used. (See *Tinctura Ferri Citro-Chloridi,* N. F., Part III.)

Description and Physical Properties.—" Orange-yellow, or brown-yellow, crystalline pieces. It is odorless, or has a faint odor of hydrochloric acid, and a strongly styptic taste. It is very deliquescent. One Gm. of Ferric Chloride is soluble in 0.2 cc. of water at 25° C. It is freely soluble in alcohol, and is soluble in glycerin and in ether. At about 35.5° C. the salt fuses to a reddish-brown liquid. When strongly heated, it is decomposed, leaving a residue of ferric oxide.

" Ferric Chloride responds to the reactions for ferric iron, and for chlorides. An aqueous solution of Ferric Chloride, made by dissolving 10 Gm. of the salt in 15 cc. of distilled water, complies with the tests for purity under *Liquor Ferri Chloridi,* omitting the test for hydrochloric acid.

" Preserve in well closed glass containers protected from light.

" **Assay.**—Dissolve about 1 Gm. of Ferric Chloride, accurately weighed in a stoppered weighing-bottle, in 25 cc. of distilled water, transfer to a glass-stoppered flask or bottle, add 3 cc. of hydrochloric acid with 4 Gm. of potassium iodide, stopper the container securely, and allow the mixture to stand for thirty minutes at a temperature of 40° C. Cool this solution, then dilute it with 100 cc. of distilled water, and titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of Fe." *U. S.*

Ferric chloride is incompatible with alkalies and with iodides and bromides from which it liberates the halogen elements; also with tannic acid and most vegetable tinctures.

Uses.—Ferric chloride is used almost exclusively in the form of the tincture or solution, and in reference to its effect and application we refer to *Tinctura Ferri Chloridi* and *Liquor Ferri Chloridi.* Excepting deliquescence, it keeps without change. When used, it may be dissolved in water in such proportions as may be required. Six, three, two, and one and a half drachms to a fluidounce of water have been recommended, the stronger solutions being used in the treatment of *varices,* the weaker for application to *bleeding surfaces,* etc. J. Z. Lawrence, of England, has used it as a styptic in a semi-deliquescent state, and found it extremely efficient. He keeps it in a bottle, in which it gradually deliquesces, and applies the thick liquid portion, with a brush of spun glass, to the bleeding surface.

Dose, one grain (0.065 Gm.).

FERRI ET AMMONII CITRAS. U. S., Br.

IRON AND AMMONIUM CITRATE Ferr. et Ammon. Cit. [Ammonio-Ferric Citrate, Soluble Ferric Citrate]

"Iron and Ammonium Citrate is ferric citrate rendered more readily soluble by the presence of ammonium citrate and contains not less than 16 per cent. and not more than 18 per cent. of Fe." *U. S.*

Citrate of Iron and Ammonia; Ferri et Ammoniæ Citras, *Br.*, 1867; Ferrum Citricum Ammoniatum, Ferri Ammonio-Citras, Ferro-Ammonium Citricum; Ammonio-Citrate of Iron, Soluble Citrate of Iron; Citras Ferri Ammoniacalis; Ferrum Ammonio-Citricum, *Fr. Cod.;* Citrate de Fer et d'Ammoniaque, Citrate Ferrique Ammoniacal, *Fr.;* Citronensaures Eisenoxyd-Ammonium (Ammoniak), Ferriammoniumcitrat, *G.;* Citrato ferricoammonico, *Sp.*

No process is given in the U. S. P. X for Iron and Ammonium Citrate. The British Pharm., 1914, process is as follows: "Solution of Ferric Sulphate, 200 *millilitres;* Solution of Ammonia, 460 *millilitres,* or *a sufficient quantity;* Citric Acid, 80 *grammes;* Distilled Water, *a sufficient quantity.* Prepare ferric hydroxide as follows:—Mix three hundred and twenty millilitres of the Solution of Ammonia with eight hundred millilitres of Distilled Water; gradually add to this the Solution of Ferric Sulphate, previously diluted with eight hundred millilitres of Distilled Water; stir constantly and briskly, taking care that ammonia is, finally, in slight excess as indicated by the odor; set aside the mixture for two hours, stirring it occasionally; pour it on a calico filter; when the liquid has drained away, wash the precipitated ferric hydroxide with Distilled Water until free from sulphates. Dissolve the Citric Acid in its own weight of Distilled Water; warm the mixture on a water-bath; add the ferric hydroxide, previously well drained; stir them together until nearly the whole of the hydroxide has dissolved, or until the Citric Acid is saturated with ferric hydroxide (prepared, if necessary, from more of the Solution of Ferric Sulphate); let the solution cool; add one hundred and ten millilitres of Solution of Ammonia; filter through flannel, adding some Distilled Water if necessary, evaporate to the consistence of syrup, the presence of a very slight excess of ammonia being maintained; dry in thin layers on flat porcelain or glass plates at a temperature not exceeding 40° C.; remove the dry flakes of Iron and Ammonium Citrate." *Br.*

In the U. S. Pharmacopœia, 1890, the process consisted simply in evaporating a mixture of solution of ferric citrate and ammonia water. In the British, ferric hydroxide is first precipitated from a solution of the ferric sulphate, then digested at a moderate heat with a solution of citric acid, and lastly neutralized by ammonia. It has, however, been found by E. R. Squibb that a heat above 82.1° C. acts injuriously in the preparation of the ferric citrate, and the present Br. Pharmacopœia directs that the salt should be dried at a heat not above 40° C. In the U. S., 1890, formula the ferric citrate was used already prepared, in the British it is prepared in the process. The solution should be concentrated to a syrupy consistence before being poured out on porcelain or glass to dry, and it is important that the heat employed in the concentration should not exceed that indicated. Like most of the scaled iron salts, this preparation is not a true chemical compound, the ammonia not being in the proportion to form a double salt.

Iron and ammonium citrate has come into use recently for subcutaneous or intramuscular injection. It has been discovered that certain forms of this compound produce much more irritation or pain than others, when thus administered upon investigation it was learned that when less than 8 per cent. of ammonia (in the form of ammonium) is present, severe systemic reactions are likely to occur, while an ammonia content that is much over 8 per cent. is likely to cause severe local irritation.

A form of special *iron and ammonium citrate, green,* has been recognized by the *N. N. R.*, containing ferric citrate equivalent to 16 per cent. of iron (Fe) and ammonium citrate equivalent to 8.1 per cent. of ammonium (NH_3). This product is of U. S. P. quality as regards the iron content, but is specifically standardized as to ammonia content.

Description and Physical Properties.—"Thin, transparent, garnet-red scales or granules. It is odorless, and has a saline, mildly ferruginous taste. It is deliquescent in moist air. Iron and Ammonium Citrate is readily soluble in water. It is insoluble in alcohol.

"When strongly heated, it chars, and finally leaves a residue of ferric oxide. An aqueous solution of Iron and Ammonium Citrate (1 in 20) is neutral or but slightly acid or alkaline to litmus paper. Heat about 0.1 Gm. of Iron and Ammonium Citrate with about 5 cc. of potassium hydroxide T.S.: a brownish-red precipitate is produced and ammonia is evolved. Ammonia T.S. added to an aqueous solution of Iron and Ammonium Citrate (1 in 100) produces no precipitate, but darkens the solution.

"Remove the iron from 10 cc. of an aqueous solution of Iron and Ammonium Citrate (1 in 10) by boiling it with an excess of potassium hydroxide T.S., filter, and then slightly acidulate 4 cc. of the filtrate with acetic acid: a portion of the cooled filtrate, when mixed with 2 cc. of calcium chloride T.S., and again heated to boiling, gradually deposits a white, crystalline precipitate. The remainder of the filtrate, when acidulated more strongly with acetic acid and allowed to stand for twenty-four hours, does not yield a white, crystalline precipitate (*tartrate*). An aqueous solution of Iron and Ammonium Citrate (1 in 100) does not yield a blue precipitate with potassium ferrocyanide T.S. unless it is previously acidulated with hydrochloric acid (*ferric citrate*).

"Preserve in well-closed containers, protected from light." *U. S.*

"In thin, dark red, transparent scales. Taste slightly sweet and astringent. Soluble in 0.5 part of *water;* almost insoluble in *alcohol* (90 per cent.). Aqueous solution slightly acid to *litmus.* Yields from 31 to 32 per cent. of ash, which, when moistened with *water,* is not alkaline to *litmus* (absence of fixed alkali). When a solution of 1 gramme in 10 millilitres of *water* is heated with a slight excess of *solution of potassium hydroxide,* ammonia is evolved and ferric hydroxide is precipitated; the filtrate from this, acidified with *acetic acid,* does not yield any crystalline precipitate (absence of tartrates). Yields not more than the slightest characteristic *reaction* for sulphates. *Arsenic limit* 5 parts per million." *Br.*

"**Assay.**—Dissolve about 1 Gm. of Iron and Ammonium Citrate, accurately weighed, in 25 cc. of distilled water and 7 cc. of hydrochloric acid, in a glass-stoppered flask or bottle, add 4 Gm. of potassium iodide, stopper the container securely, and keep it at a temperature of 40° C. for thirty minutes. Then cool, dilute with 100 cc. of distilled water, and titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of Fe." *U. S.*

Uses.—This salt is a pleasant chalybeate, being practically free from astringency or local irritant action. It should be prescribed only in solution, as it is not suited for administration in the form of pills, owing to the presence of ammonia, which renders it too soluble, and causes the pills to flatten after they have been made, and frequently to cohere in one solid mass. The plain ferric citrate should always be used for pills, as it is less hygroscopic and makes more stable pills.

Dose, from three to eight grains (0.2–0.5 Gm.).

Off. Prep.—Vinum Ferri Citratis, *Br.;* Elixir Carnis et Ferri, *N. F.*

FERRI ET POTASSII TARTRAS. Br.

IRON AND POTASSIUM TARTRATE

Ferrum Tartaratum; Tartarated Iron; Potassio-ferric Tartrate; Ferri Potassio-Tartras, Ferrum Tartarizatum, Tartras Ferrico-Potassicus, s. Potassico-Ferricus, s. Ferrico-Kalicus, Ferri-Kalium Tartaricum; Tartarated (tartarized) Iron, Ferro-Tartrate of Potassium; Tartrate Ferrico-potassique, Tartrate de Fer et de Potasse, Tartre martial, *Fr.;* Ferritartrate de Potassium, *Fr. Cod.;* Kaliumferritartrat, Weinsäures Eisenoxyd-Kali, Eisenweinstein, *G.;* Tartrato ferrico-potassico, *It.;* Tartrato ferrico-potasico, *Sp.*

The U. S. no longer recognizes this salt, which represents about 15 per cent. of iron.

The British process is as follows: "Solution of Ferric Sulphate, 200.0 *millilitres;* Solution of Ammonia, 320.0 *millilitres,* or *a sufficient quantity;* Acid Potassium Tartrate in powder, 66.5 *grammes;* Distilled Water, *a sufficient quantity.* From the Solution of Ferric Sulphate prepare ferric hydroxide as directed under 'Ferri et Ammonii Citras.' Mix the ferric hydroxide intimately with the Acid Potassium Tartrate in a porcelain dish; let the mixture stand for twenty-four hours; heat to a temperature not exceeding 60° C., add gradually six hundred *millilitres* of Distilled Water; stir constantly until nothing more will dissolve; filter; evaporate at a temperature not exceeding 60° C. to the consistence of syrup; dry in thin layers on flat porcelain or glass plates at a temperature not exceeding 40° C.; remove the dry flakes of Iron and Potassium Tartrate." *Br.*

The object of this process was to combine the excess of acid in the potassium bitartrate with ferric hydroxide. The plan of Soubeiran in the main was adopted—namely, that of dissolving the moist ferric hydroxide to saturation in a mixture of the bitartrate and water, aided by a moderate heat. The oxide is obtained from the solution of ferric sulphate, which is precipitated by ammonia. Potassium hydroxide, which was used in the former British process, is not a good precipitant, because the alkali adheres obstinately to the precipitated oxide, and cannot be completely separated even by repeated washings. The oxide should be gradually added to the bitartrate and water, heated to 60° C., at which temperature the oxide dissolves more readily and in larger quantity than when a higher temperature is employed. Besides, in the latter case, a portion of the ferric oxide is converted into ferrous oxide. W. Lyon (*P. J.,* 1902, 530) proposes to substitute potassium and sodium tartrate for the acid potassium tartrate used in the British Pharm. process, believing that the resulting scaled salt will retain its ready solubility for a much longer time than will the official preparation; he uses the following proportions: Solution of ferric sulphate 300 cc.; solution of ammonia 480 cc. or a sufficient quantity; potassium and sodium tartrate 176 Gm. The official process and directions are otherwise followed. For Roger's process for this salt and the manufacture of *Boules de Mars* (balls of iron and potassium tartrate), see *U. S. D.,* 17th ed., 611.

Ure proposed *ferrous tartrate* for medicinal use. He made it by acting on clean iron filings, or bits of iron wire, with a solution of tartaric acid. It is a pulverulent salt, insoluble in water, and possessing a mild chalybeate taste.

Properties.—Iron and potassium tartrate is in "thin, transparent scales of a deep garnet color; taste somewhat sweetish and astringent. Soluble in *water,* sparingly soluble in *alcohol* (90 per cent.). *Arsenic limit* 5 parts per million. The aqueous solution, acidified with *hydrochloric acid,* yields a copious blue precipitate with *solution of potassium ferrocyanide.* When a solution of 1 gramme in 10 millilitres of *water* is boiled with a slight excess of *solution of potassium hydroxide,* a reddish-brown precipitate separates, and the filtered solution, slightly acidified with *acetic acid,* yields, as it cools, a crystalline deposit. Yields not less than 30 per cent. of ferric oxide when incinerated with free access of air, the ash being washed with *water* and again incinerated." *Br.*

According to the view of its nature taken in the U. S. Pharmacopœia VIII, it is a double salt, consisting of one molecule of ferric tartrate and one of potassium tartrate:

$$Fe_2(C_4H_4O_6)_3 + K_2C_4H_4O_6 + H_2O$$

Flückiger (*Pharmaceutische Chemie,* 2d ed., 573, 188), on the other hand, considers the salt formed to be one in which Fe_2O_2 is present as a bivalent group, and gives it the formula:

$$C_4H_4O_6K_2 + C_4H_4O_6(Fe_2O_2) + 4H_2O$$

The salt is incompatible with astringent vegetable infusions, which give rise to a dark-colored precipitate.

Uses.—Iron and potassium tartrate is a mild, agreeable chalybeate, with but little astringency. It is well borne by the stomach, taken fasting or with the food. Its slight taste and ready solubility make it one of the best ferruginous preparations for children.

Dose, for an adult, five to ten grains (0.32–0.65 Gm.), given preferably in solution.

FERRI ET QUININÆ CITRAS. Br.

IRON AND QUININE CITRATE

Ferri et Quininæ Citras, Solubilis, *U. S. VIII;* Soluble Iron and Quinine Citrate; Citrate of Iron and Quinia; Citras Ferricus cum Chinina; Citrate de Fer et de Quinine, *Fr.;* Chininum Ferro-Citricum, *P. G.;* Eisenchinincitrat, Citronensaures Eisen-Chinin, *G.*

This mixture has been very properly omitted from the U. S. X.

"Solution of Ferric Sulphate, 180 *millilitres;* Quinine Sulphate, 40 *grammes;* Diluted Sulphuric Acid, 60 *millilitres;* Citric Acid, 123 *grammes;* Solution of Ammonia, Distilled Water, of each, *a sufficient quantity.* From the Solution of Ferric Sulphate prepare ferric hydroxide as directed under 'Ferri et Ammonii Citras.' Mix the Quinine Sulphate with eight times its weight of Distilled Water; add the Diluted Sulphuric Acid; when the salt is dissolved precipitate the quinine with a slight excess of Solution of Ammonia; collect the precipitate on a filter; wash it with twelve hundred *millilitres* of Distilled Water. Dissolve the Citric Acid in its own weight of Distilled Water; warm the solution on a water-bath; add the ferric hydroxide, previously well drained; stir them together; when the hydroxide has dissolved, add the precipitated quinine; continue the stirring until this also has dissolved; let the solution cool; add, in small quantities at a time, sixty *millilitres* of Solution of Ammonia, diluted with eighty *millilitres* of Distilled Water; stir briskly, allowing the quinine which separates with each addition of ammonia to dissolve before the next addition is made; filter the solution; evaporate it to the consistence of a thin syrup; dry the latter in thin layers on flat porcelain or glass plates at a temperature not exceeding 40° C.; remove the dry flakes of Iron and Quinine Citrate." *Br.*

The final addition of ammonia is in order to render the iron and quinine citrate more soluble by the agency of a portion of ammonium citrate. It is important that the ammonia should not be added in excess; on the contrary, the solution should retain a slight acid reaction. After evaporation, the salt is dried, as in the other process, on glass or porcelain, so as to be obtained in thin scales.

No analysis has been made that determines precisely the chemical composition of this "scaled salt." It is undoubtedly a mere mixture of the iron and quinine citrates, containing ammonium citrate.

According to C. H. Wood (*P. J.,* 2d ser., x, 644), this salt undergoes a rapid change of composition when exposed to the influence of the direct rays of the sun.

Properties.—The British Pharm., 1914, describes it as "in thin scales of a greenish-yellow color, somewhat deliquescent; taste bitter, chalybeate. Soluble in 0.5 part of *water.* The solution is very slightly acid, and yields precipitates which are reddish-brown with *solution of potassium hydroxide,* white with *solution of ammonia,* blue with *solution of potassium ferrocyanide,* and with *solution of potassium ferricyanide. Arsenic limit* 5 parts per million. Ash, when moistened with *water,* not alkaline to *litmus* (absence of fixed alkali). 5 grammes, dissolved in 45 millilitres of *water* and treated with excess of *solution of ammonia,* yield a white precipitate, which, when dissolved out by repeated treatment of the liquid with chloroform, the latter evaporated, and the residue dried at 110° C., weighs not less than 0.75 gramme. This precipitate is almost entirely soluble in a little *ether;* on incineration it leaves not more than a minute residue; neutralised with *diluted sulphuric acid* and crystallised, it possesses the characters of and responds to the tests described under 'Quininæ Sulphas.'" *Br.*

See modification of process by F. A. Sieker (*Ph. Rund.,* 1895, 36).

The U. S. IX gave the following methods for determining the amount of quinine and iron respectively.

"**Assay for Quinine.**—Dissolve about 1 Gm. of Iron and Quinine Citrate, accurately weighed, in 20 mils of distilled water in a separator, add 5 mils of ammonia water and 10 mils of chloroform, and shake the separator for one minute. Allow the liquids to separate, draw off the chloroform layer through a small filter moistened with chloroform, into a tared dish, and shake the residuary liquid a second and a third time with portions of 10 mils each of chloroform, passing the chloroform through the filter each time and finally washing the filter with 5 mils of chloroform. Evaporate the combined chloroform solutions, redissolve the residue in 3 mils of alcohol, again evaporate and then dry the residue to constant weight at 100° C. This residue corresponds to not less than 11.5 per cent. of the amount of Iron and Quinine Citrate taken for the assay and conforms to the identity tests under *Quinina*." *U. S. IX.*

The quinine in this assay is undoubtedly contaminated with traces of the strychnine present. There is no reliable method for the separate determination of the two alkaloids in this compound.

"**Assay for Iron.**—Heat the aqueous liquid from which the quinine has been removed in the manner just described, on a water bath, until the odors of chloroform and of ammonia have disappeared, allow to cool and dilute with distilled water to a volume of 25 mils. Transfer the liquid to a glass-stoppered bottle, add 15 mils of hydrochloric acid and 3 Gm. of potassium iodide, and, after securely closing the bottle, allow the mixture to stand for thirty minutes at 40° C. Then cool and titrate with sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 13 per cent. of Fe.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Iron and Quinine Citrate corresponds to not less than 23.3 mils of tenth-normal sodium thiosulphate V.S." *U. S. IX.*

Uses.—Preparations of this character are therapeutically irrational; if the hematinic effects of iron and the tonic action of quinine are desired simultaneously, it is far better to compose an extemporaneous mixture in which the proportion of each shall be regulated to the needs of the individual patient than resort to a fixed combination. Each five grains (0.3 Gm.) of the salt represents approximately one-half grain (0.032 Gm.) of quinine and two-thirds of a grain (0.036 Gm.) of iron.

Dose, five to ten grains (0.32–0.65 Gm.).

FERRI GLYCEROPHOSPHAS. N. F.

FERRIC GLYCEROPHOSPHATE Ferr. Glycerophos. [Ferric Glycerinophosphate]

"Ferric Glycerophosphate contains a variable quantity of $Fe_2(C_3H_7O_6P)_3$(622.02) corresponding to not less than 14 per cent. and not more than 16 per cent. of Fe." *N. F.*

Ferrum Glycerinophosphoricum; Iron Glycerophosphate; Glycerinphosphorsaures Eisen, *G.*

Description and Physical Properties.—"Ferric Glycerophosphate occurs as yellowish green, transparent, amorphous scales or as a greenish yellow powder; odorless and nearly tasteless. One Gm. dissolves slowly in about 2 cc. of water at 25° C.; insoluble in alcohol. An aqueous solution is acid to litmus and becomes turbid when heated.

An aqueous solution of the salt (1 in 20) is colored dark blue by potassium ferrocyanide T.S.; on the subsequent addition of hydrochloric acid a dark blue precipitate is produced. Heat a powdered mixture of about 0.1 Gm. of the salt with about 0.5 Gm. of potassium bisulphate; the pungent vapors of acrolein are evolved.

"Not more than a slight yellow turbidity is produced at once on mixing 5 cc. of an aqueous solution of the salt (1 in 50) with 10 cc. of ammonium molybdate T.S. (*phosphate*), but on standing or on warming, a yellow precipitate is formed. An aqueous solution of the salt (1 in 50), acidulated with hydrochloric acid, does not become more than slightly turbid on the addition of barium chloride T.S. (*sulphate*). Another portion of this aqueous solution, acidulated with nitric acid, does not become more than slightly turbid on the addition of silver nitrate T.S. (*chloride*).

"**Assay.**—Dissolve about 0.5 Gm. of Ferric Glycerophosphate, accurately weighed, in 50 cc. of distilled water, in a 100 cc. glass-stoppered flask, add 5 cc. of hydrochloric acid and about 3 Gm. of potassium iodide. Warm to 40° C., and allow the mixture to stand one-half hour at this temperature in the stoppered flask, cool, and then titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of Fe. Each gram of Ferric Glycerophosphate corresponds to not less than 25.07 cc. nor more than 28.65 cc. of tenth-normal sodium thiosulphate.

"Preserve it in well-closed containers, protected from light." *N. F.*

This is made by dissolving freshly precipitated ferric hydroxide in glycerophosphoric acid, evaporating the solution *in vacuo* and scaling it upon glass plates.

The salt is used as a tonic and nervine in *doses* of from five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Elixir Glycerophosphatum Compositum, *N. F.*

FERRI HYPOPHOSPHIS. N. F.

FERRIC HYPOPHOSPHITE Ferr. Hypophos.

"Ferric Hypophosphite contains not less than 98 per cent. of $Fe(PH_2O_2)_3$(251.01), corresponding to not less than 21.8 per cent. of Fe." *N. F.*

Ferric Hypophosphite, *N. F. IV;* Iron Hypophosphite; Hypophosphite of Iron; Ferrum Hypophosphorosum; Hypophosphis Ferricus; Hypophosphite de Fer, *Fr.;* Unterphosphorigsaures Eisenoxyd, Ferrihypophosphit, *G.*

This salt may be made by the action of hypophosphorous acid on ferrous carbonate formed by precipitation from the sulphate.

Description and Physical Properties.—"Ferric Hypophosphite occurs as a white, or grayish white powder, odorless and nearly tasteless; permanent in the air. One Gm. dissolves in 2300 cc. of water at 25° C. and in 1200 cc. of boiling water; more readily soluble in the presence of hypophosphorous acid or in a warm, concentrated solution of an alkali citrate, forming with the latter a green solution.

"When strongly heated in a dry test tube, the salt evolves spontaneously inflammable hydrogen phosphide gas, and finally leaves a residue of ferric pyrophosphate. Ferric Hypophosphite is readily oxidized by nitric acid or other oxidizing agents.

"Add 15 cc. of acetic acid to 1 Gm. of the salt; no effervescence occurs (*carbonate*). Heat the mixture to boiling and filter; the filtrate responds to the following tests. Add to a portion of the filtrate a few drops of silver nitrate T.S. and warm; a brown to black coloration or precipitate is produced. To another portion of the filtrate add, drop by drop, an excess of mercuric chloride T.S.; a white precipitate of mercurous chloride is formed upon gently heating. Another 5 cc. portion of the filtrate shows no turbidity with ammonium oxalate T.S. within one minute (*calcium*). Dissolve 1 Gm. of the salt in 20 cc. of diluted hydrochloric acid, with the aid of heat, and add 1 cc. of barium chloride T.S.; not more than a slight turbidity is produced (*sulphate*). Boil 0.5 Gm. of the salt with 10 cc. of sodium hydroxide T.S.; a reddish brown precipitate is produced. Filter this mixture, slightly acidulate the filtrate with hydrochloric acid, add magnesia mixture T.S. and then an excess of ammonia water; no crystalline precipitate is produced (*phosphate*). Dissolve 1 Gm. of the salt in about 25 cc. of boiling distilled water by the aid of sufficient hydrochloric acid, added drop by drop, then add 2 cc. of nitric acid, boil and add a slight excess of ammonia water; the filtrate is colorless, and after acidulating with hydrochloric acid does not respond to the Test for heavy metals.

"**Assay.**—To 1 Gm. of Ferric Hypophosphite accurately weighed, add 10 cc. of nitrohydrochloric acid and evaporate to dryness on a water-bath. Dissolve the residue in 25 cc. of distilled water and 10 cc. of hydrochloric acid, transfer the solution to a glass-stoppered flask, add 3 Gm. of potassium iodide, keep it at 40° C. for thirty minutes, cool and titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of Fe, and 0.025101 Gm. of $Fe(PH_2O_2)_3$. Each gram of Ferric Hypophosphite requires not less than 39.04 cc. of tenth-normal sodium thiosulphate.

"Preserve it in well-closed containers." *N. F.*

Syrup of ferrous hypophosphite may be prepared by simply adding syrup to the solution of the hypophosphite.

Ferric hypophosphite is a feeble chalybeate, but has no advantages over the other official salts of iron. It enters into that therapeutic hodge-podge, the *Compound Syrup of Hypophosphites*. It may be administered in the form of pill or powder, but the syrup is more elegant.

Dose, from five to ten grains (0.32 to 0.65 Gm.).

Off. Prep.—Syrupus Hypophosphitus Compositus, *N. F.;* Liquor Hypophosphitum Compositum, *N. F.*

FERRI HYDROXIDUM CUM MAGNESII OXIDO. U. S.

FERRIC HYDROXIDE WITH MAGNESIUM OXIDE

Ferr. Hydrox. cum Mag. Oxid. [Arsenic Antidote, Ferric Hydrate with Magnesia]

Ferri Oxidum Hydratum cum Magnesia, *U. S.* 1890; Antidotum Arsenici; Antidote to Arsenious Acid; Hydrated Oxide of Iron with Magnesia; Contre-poison de l'arsenic, *Fr.;* Gegengift des Arseniks, Gegengift der Arsenigensaure, *G.;* Hidrato ferrico magnesico, *Sp.*

"Solution of Ferric Sulphate, 40 cc.; Magnesium Oxide, 10 Gm.; Water, a sufficient quantity. Mix the solution of ferric sulphate with 125 cc. of water, and keep the liquid in a large, well-stoppered bottle. Rub the magnesium oxide with cold water to a smooth, thin mixture, transfer this to a bottle capable of holding about 1000 cc., fill it with water to about three-fourths of its capacity, and keep it tightly stoppered. When the preparation is needed, shake the magnesium oxide mixture until of a thin, creamy consistence, slowly add to it the diluted solution of ferric sulphate, and shake them together until a uniformly smooth mixture results. Note—In this process the 10 Gm. of magnesium oxide may be replaced by 300 cc. of magnesia magma, diluting it with sufficient water to make the required volume.

"The diluted solution of ferric sulphate and the magnesia mixture should be kept on hand in separate bottles ready for immediate use so that the antidote may be quickly prepared." *U. S.*

Ferric hydroxide was dropped from the U. S. P. IX and ferric hydroxide with magnesium oxide retained. This is a preparation which has been introduced for the purpose of furnishing a ready and efficient antidote against arsenic trioxide or arsenous acid. It is almost identical with the *Antidotum Arsenici* of the German Pharmacopœia. Ferric hydroxide is produced when to the mixture of magnesia is added the diluted solution of ferric sulphate, and, as the magnesia is in excess and acidity thus prevented, no harm can result from not separating the by-products of the reaction. When mixed as officially directed, and ready for use, it contains ferric hydroxide with magnesium sulphate and hydroxide.

Uses.—The sesquioxide of iron was brought forward as an antidote in arsenical poisoning by Bunsen and Berthold in 1834. According to Wormley its antidotal effect is due to the ferric oxide yielding oxygen and thereby converting the arsenious acid into the arsenic state, the latter then uniting with the iron to form an insoluble arsenate. In the early part of the last century there waged a vigorous discussion as to the comparative usefulness of this antidote, as the result of which for more than half a century it became recognized as the standard antidote for arsenic. This position it held for more than half a century almost undisputed. Its efficacy, however, was attacked by Busscher in 1902. McGuigan reinvestigated the question (*J. A. Ph. A.*, 1923, xii, 327) and reached the conclusion that what little antidotal effect it exerted was purely physical. As pointed out, however, by H. C. Wood (*J. A. Ph. A.*, xii, 482) their experimental evidence scarcely justifies so sweeping a condemnation of a widely used remedy. (See *Arseni Trioxidum.*)

Dose, four fluidounces (120 cc.).

FERRI LACTAS. N. F.

FERROUS LACTATE Ferr. Lact. [Iron Lactate]

"Ferrous Lactate contains not less than 97 per cent of $Fe(C_3H_5O_3)_2.3H_2O$ (288.00)." *N. F.*

Iron Lactate; Ferrum Lacticum, *P. G.;* Lactas Ferrosus, Lactate de Fer, *Fr.;* Milchsaures Eisenoxydul, Eisenlactat, *G.;* Lactato Ferroso, *Sp.*

The U. S. P. V gave a process for preparing ferrous lactate through the direct action of lactic acid on iron wire.

It may be more cheaply prepared, on the large scale, by digesting the impure acid, with iron filings, or by reaction between ferrous sulphate and the calcium lactate prepared as a step in obtaining lactic acid.

Description and Physical Properties.—"Ferrous Lactate occurs as a greenish white crystalline powder, or in crystalline masses, having a slight, characteristic odor, and a mild, sweet and ferruginous taste. One Gm. dissolves slowly but almost completely in 40 cc. of water at 25° C., and in 12 cc. of boiling water; freely soluble in solutions of the alkali citrates yielding a green-colored solution; almost insoluble in alcohol.

"When strongly heated, the salt froths, gives out dense, white, acrid fumes, then chars and finally leaves a brownish red residue. An aqueous solution of the salt is greenish yellow, slightly acid to litmus, and separate portions give a deep blue precipitate with potassium ferricyanide T.S., and a light blue precipitate with potassium ferrocyanide T.S.

"Separate portions of an aqueous solution of the salt (1 in 20), acidulated with nitric acid, do not give more than a slight opalescence with barium chloride T.S. (*sulphate*), or with silver nitrate T.S. (*chloride*). Mix 25 cc. of an aqueous solution of the salt (1 in 50) with 5 cc. of diluted sulphuric acid, boil the mixture for a few minutes, then precipitate the iron by an excess of sodium hydroxide T.S., and filter; the filtrate, mixed with a few drops of alkaline cupric tartrate solution and heated to boiling, does not give a red precipitate (*sugar*). A portion of the salt triturated with sulphuric acid does not develop an offensive odor (*butyric acid*); this mixture, after standing for five minutes, does not assume more than a pale brown color (*readily carbonizable impurities*). Ignite 1 Gm. of the salt and triturate the residue with 10 cc. of distilled water, the liquid is not alkaline to moistened litmus paper. Filter, wash the filter with about 10 cc. of distilled water, evaporate the filtrate and washings to dryness, and ignite gently; the weight of the residue does not exceed 0.003 Gm.

"**Assay.**—Dissolve, in a glass-stoppered flask, about 0.5 Gm. of Ferrous Lactate, accurately weighed, in 15 cc. of solution of hydrogen dioxide and 5 cc. of hydrochloric acid, and evaporate this solution on a water-bath to 5 cc. Add 3 cc. of hydrochloric acid, boil the mixture for two minutes, cool to 40° C. and add 25 cc. of distilled water and 1 Gm. of potassium iodide. Allow this mixture to stand for one-half hour at 40° C., cool, and then titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.0288 Gm. of $Fe(C_3H_5O_3)_2 + 3H_2O$. Each gram of Ferrous Lactate requires not less than 33.7 cc. of tenth-normal sodium thiosulphate.

"Preserve it in well-closed containers." *N. F.*

Ferrous lactate has the general medicinal properties of the ferruginous preparations, and has been especially used in *chlorosis.* As much as twelve or even twenty grains (0.78–1.3 Gm.) may be given in the course of a day. It may be administered in pill, or syrup; the *pill,* of one grain (0.065 Gm.) of the salt, with an equal weight of some inert powder free from astringent matter, and sufficient honey.

Dose, three to six grains (0.2–0.4 Gm.).

Off. Prep.—Syrupus Calcii Lactophosphatis et Ferri, *N. F.*

FERRI PHOSPHAS SOLUBILIS. U. S.

SOLUBLE FERRIC PHOSPHATE Ferr. Phos. Sol. [Ferri Phosphas, U. S. P. IX, Ferric Phosphate with Sodium Citrate]

"Soluble Ferric Phosphate is ferric phosphate rendered soluble by the presence of sodium citrate and contains not less than 12 per cent. of Fe." *U. S.*

Ferri et Sodii Citro-phosphas; Ferrum Phosphoricum cum Natrio Citrico; Soluble Phosphate of Iron, Sodio-ferric Citrophosphate; Citro-phosphate de Fer et de Soude, *Fr.;* Natriumeisencitro-phosphat, *G.*

The word "solubilis" has been reinserted in the title of the U. S. P. X, in order to distinguish this preparation from the normal ferric phosphate. The latter which was at one time official is an insoluble yellowish powder. The present is in thin bright green scales.

No process is given for this preparation in the U. S. P. X. That of the U. S. P., 1890, is as follows: "Ferric Citrate, *fifty grammes;* Sodium Phosphate, uneffloresced, *fifty-five grammes;* Distilled Water, *one hundred cubic centimeters.* Dissolve the ferric Citrate in the Distilled Water by heating on a water-bath. To this solution add the Sodium Phosphate, and stir constantly until it is dissolved. Evaporate the solution on a water-bath, at a temperature not exceeding 60° C., to the consistence of thick syrup, and spread it on plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in dark amber-colored, well-stoppered bottles." *U. S.*, 1890.

Description and Physical Properties.—"Thin, bright green, transparent scales or granules. It is without odor, and has an acidulous, slightly saline taste. The salt is stable in dry air when protected from light, but when unprotected soon becomes discolored. Soluble Ferric Phosphate is freely soluble in water. It is insoluble in alcohol.

"An aqueous solution of Soluble Ferric Phosphate (1 in 10) is slightly acid to litmus paper. The addition of an excess of ammonia T.S. to an aqueous solution of Soluble Ferric Phosphate produces a reddish-brown color but no precipitate. Boil about 0.1 Gm. of Soluble Ferric Phosphate with 5 cc. of sodium hydroxide T.S.: a brownish-red precipitate is produced without the evolution of ammonia (*ammonium salts*). Remove the iron from 10 cc. of an aqueous solution of Soluble Ferric Phosphate (1 in 10) by boiling it with an excess of sodium hydroxide T.S., filter out the precipitate, and strongly acidulate the filtrate with hydrochloric acid: a cooled portion of this liquid mixed with an equal volume of magnesia mixture T.S. and treated with a slight excess of ammonia T.S. produces an abundant white, crystalline precipitate. This precipitate, after washing, turns yellow when treated with a few drops of silver nitrate T.S. (*distinction from pyrophosphate*).

"Preserve in amber-colored, well-stoppered bottles, protected from light.

"**Assay.**—Dissolve about 1 Gm. of Soluble Ferric Phosphate, accurately weighed, in 25 cc. of distilled water and 15 cc. of hydrochloric acid, in a glass-stoppered bottle, then add 3 Gm. of potassium iodide, securely stopper the bottle, and keep it at a temperature of 40° C. for thirty minutes. Then cool, and titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of Fe." *U. S.*

Uses.—Ferric phosphate is one of the best preparations to use when it is desired to exhibit iron in solution. It is as free from astringency as any of the official salts of iron, has little tendency to disturb the digestion and is an active chalybeate.

The *dose* is from five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Elixir Cinchonæ Alkaloidorum et Ferri, *N. F.;* Elixir Ferri Phosphatis, *N. F.;* Elixir Gentianæ et Ferri Phosphatum, *N. F.;* Liquor Phosphatum Compositus, *N. F.;* Syrupus Ferri, Quininæ et Strychninæ Phosphatum, *N. F.*

FERRI PHOSPHAS SACCHARATUS. Br.

SACCHARATED IRON PHOSPHATE

"Saccharated Iron Phosphate is ferrous phosphate, more or less oxidised, mixed with glucose. It contains not less than 60 per cent. of ferrous salts calculated as ferrous phosphate, $Fe_3(PO_4)_2,8H_2O$." *Br.*

This preparation was introduced into the British Pharmacopœia, 1914, to replace the former "Ferri Phosphas" which was an insoluble slate-colored powder. The process is as follows: "Ferrous Sulphate, 120 *grammes;* Sodium Phosphate, 110 *grammes;* Sodium Carbonate, 50 *grammes;* Glucose, 40 *grammes;* Distilled Water, boiling, *a sufficient quantity.* Dissolve twenty *grammes* of the Glucose in four hundred *millilitres* of the Distilled Water, and dissolve the Ferrous Sulphate in the solution. Dissolve the Sodium Phosphate in four hundred *millilitres* of the Distilled Water, and to this add the solution of the Ferrous Sulphate, stirring constantly. Then add the Sodium Carbonate previously dissolved in four hundred *millilitres* of the Distilled Water. Mix thoroughly, and allow the precipitate to subside. Decant the supernatant liquid, wash the precipitate with two successive quantities, each of two thousand *millilitres* of the Distilled Water, mix it with the remainder of the Glucose, and dry at a temperature not exceeding 100° C. Powder the product and preserve it in a stoppered bottle. A slate-blue, amorphous powder. Taste sweetish, chalybeate. Partially soluble in *water,* soluble in *hydrochloric acid.* The acid solution yields blue precipitates with *solution of potassium ferrocyanide* and *solution of potassium ferricyanide;* when treated with *tartaric acid* and excess of *solution of ammonia,* and subsequently with *solution of magnesium ammonio-sulphate,* it yields a white granular precipitate. 1 gramme dissolved in excess of warm *concentrated phosphoric acid* does not cease to yield a blue precipitate with *solution of potassium ferricyanide* until 35.9 millilitres of *N/10 solution of potassium bichromate* have been added. *Arsenic limit* 5 parts per million." *Br.*

Glucose is used to protect the ferrous phosphate from oxidation, which it does only partially. This iron phosphate must not be confounded with the soluble ferric phosphate of the U. S. P.

The British iron phosphate, 1898, was a very different salt. By double decomposition ferrous phosphate and sodium sulphate are produced, the former precipitating as a white bulky powder, which soon changes on exposure to a greenish-blue, and ultimately to a slate color; since the sodium phosphate is chemically an acid salt (Na_2HPO_4) a portion of phosphoric acid is liberated during the reaction, and this, retaining in solution some of the ferrous phosphate, requires the addition of the solution of sodium bicarbonate to neutralize it and set free the remainder of the ferrous phosphate. This salt, when first formed, is represented by the formula $Fe_3(PO_4)_2$; but its strong affinity for oxygen causes the gradual production of a sesquisalt, which, therefore, to a certain extent, always exists in the preparation.

Uses.—Ferric phosphate possesses the general properties of the ferruginous preparations, and has been given with advantage in *amenorrhea* and *dyspepsia.*

Dose, from five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Syrupus Ferri Phosphatis, *Br.;* Syrupus Ferri Phosphatis cum Quinina et Strychnina, *Br.;* Elixir Cinchonæ Alkaloidorum et Ferri, *N. F.;* Elixir Gentianæ et Ferri Phosphatis, *N. F.;* Liquor Phosphatum Compositus, *N. F.;* Syrupus Ferri, Quininæ et Strychninæ Phosphatum, *N. F.*

FERRI PYROPHOSPHAS SOLUBILIS. N. F.

FERRIC PYROPHOSPHATE Ferr. Pyrophos. Sol. [Soluble Ferric Pyrophosphate]

"Ferric Pyrophosphate, rendered soluble by the presence of sodium citrate, corresponding to not less than 10 per cent. of Fe." *N. F.*

Ferri Pyrophosphas; Soluble Ferric Pyrophosphate; Ferri Pyrophosphas Solubilis, *U. S. P. VIII;* Iron Pyrophosphate; Pyrophosphate of Iron; Ferri et Sodii Citro-pyrophosphas; Ferrum Pyrophosphoricum cum Sodio Citrico; Pyrophosphate of Iron with Sodium Citrate; Sodio-ferric Citro-pyrophosphate; Pyrophosphate de Fer et de Soude, *Fr.;* Pyrophosphorsaures Eisenoxyd mit Citronensaurem Natron, *G.*

The process formerly official for this salt was: "Ferric Citrate, *fifty grammes;* Sodium Pyrophosphate, uneffloresced, *fifty grammes;* Distilled Water, *one hundred cc.* Dissolve the Ferric Citrate in the Distilled Water, by heating on a water-bath. To this solution add the Sodium Pyrophosphate, and stir constantly, until it is dissolved. Evaporate the solution, on a water-bath, at a temperature not exceeding 60° C., to the consistence of thick syrup, and spread it on plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in dark amber-colored, well-stoppered bottles." *U. S.*, 1890.

Ferric pyrophosphate consists probably of sodio-ferric pyrophosphate, sodio-ferric citrate, and free ferric citrate. Sodio-ferric pyrophosphate, dried at 100° C., is considered by Flückiger (*Pharm. Chem.*, 2d ed., p. 607, 1888) to have the following composition: $Fe_4(P_2O_7)_3 + 3Na_4P_2O_7 + 14H_2O$.

Description and Physical Properties.—"Soluble Ferric Pyrophosphate occurs in thin, apple-green, transparent scales, without odor, and having an acidulous, slightly saline taste. The salt is permanent in dry air, when protected from light, but when unprotected soon becomes discolored. It is freely and completely soluble in water; insoluble in alcohol. An aqueous solution of the salt is slightly acid to litmus.

"Ferric Pyrophosphate, when warmed with sodium hydroxide T.S., produces a brownish red precipitate without evolving ammonia. Fuse 0.1 Gm. of the salt with 0.1 Gm. each of potassium nitrate and sodium carbonate, boil the residue with 10 cc. of distilled water and filter. The filtrate, after being rendered nearly, but not quite neutral with highly dilute nitric acid, yields a yellow precipitate on the addition of silver nitrate T.S.

"Boil an aqueous solution of the salt (1 in 10) with an excess of sodium hydroxide T.S. until the iron is precipitated, filter, strongly acidulate the filtrate with hydrochloric acid and cool. This liquid when mixed with an equal volume of magnesia mixture T.S., followed by a slight excess of ammonia water, yields a finely divided white precipitate, which, after collecting on a filter and washing, does not turn yellow when treated with a few drops of silver nitrate T.S. (*phosphate*).

"**Assay.**—Dissolve about 1 Gm. of Soluble Ferric Pyrophosphate, accurately weighed, in 25 cc. of distilled water and 15 cc. of hydrochloric acid, in a glass-stoppered bottle, add 2 Gm. of potassium iodide, securely stopper the bottle, keep it at a temperature of 40° C. for thirty minutes, cool and then titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of Fe.

"Preserve it in well-closed containers, protected from light." *N. F.*

Iron pyrophosphate is a good chalybeate, without disagreeable taste or astringency, and, from its solubility, readily administered in any form that may be desirable, whether that of pill, simple solution in water or syrup.

Dose, two to ten grains (0.13 to 0.65 Gm.).

Off. Prep.—Elixir Ferri Pyrophosphatis, Quininæ et Strychninæ, *N. F.*

FERRI SULPHAS. U. S., Br.

FERROUS SULPHATE Ferr. Sulph. [Iron Protosulphate]

"Ferrous Sulphate contains not less than 54.36 and not more than 57.07 per cent. of anhydrous ferrous sulphate, corresponding to about 99.5 per cent. of the crystallized salt [$FeSO_4.7H_2O$]." *U. S.* "Ferrous Sulphate may be prepared by the interaction of diluted sulphuric acid and iron. It contains not less than 97.5 per cent. of pure ferrous sulphate, $FeSO_4,7H_2O$." *Br.*

Sulphate of Iron, Green Vitriol, Iron Vitriol, Sulfas Ferrosus, Ferrum Vitriolatum Purum, Vitriolum Martis Purum; Sulphas Ferri; Sulfate Ferreux, Sulfate (protosulfate) de Fer, *Fr.;* Sulfate de Protoxyde de Fer, *Fr. Cod.;* Ferrum Sulfuricum, *P. G.;* Ferrosulfat, Schwefelsaures Eisenoxydul, *G.;* Solfato ferroso, *It.;* Sulfato ferroso, *Sp.*

A process for this salt was given in the U. S. P., 1870, which was based upon the method of Bonsdorff. This chemist found that, when a ferrous sulphate was formed in solution by heating diluted sulphuric acid with an excess of iron, it might be crystallized free from sesquioxide, provided a little excess of sulphuric acid were added to the liquid before filtration, in order to prevent the formation of any sesquioxide during the process, at the same time avoiding, as much as possible, contact with the air. Hence the directions in the former U. S. Pharmacopœia formula to acidulate with sulphuric acid; to cause the funnel to touch the bottom of the receiving vessel, which avoids the dropping of the liquid through the air; and to cover the vessel containing the concentrated liquid when it is set aside to crystallize.

As prepared by Bonsdorff's method, ferrous sulphate is blue, verging upon green. When it becomes more green than blue, or entirely green, an indication is afforded that it contains some sesquioxide. By exposure to the air the crystals absorb oxygen, and become first green, and ultimately covered with a yellow efflorescence of subsulphate, insoluble in water. Sometimes the crystals are quite permanent when made by Bonsdorff's method, owing to the slight excess of acid which they contain. The aqueous solution is bluish-green, but by standing it attracts oxygen, and becomes first green and then reddish depositing in the meantime a portion of sesquisulphate, having the composition:

$$Fe_2(SO_4)_3 + Fe_2O_3 + 8H_2O$$

At a red heat it loses its acid, and is converted into the anhydrous ferric oxide called *colcothar.*

Commercial Ferrous Sulphate, or *Copperas,* is manufactured on a large scale for the purposes of the arts, from the native ferric sulphide or iron pyrites, by roasting, oxidation by exposure to air and moisture, and lixiviation. The constituents of the mineral become sulphuric acid and ferrous and ferric oxides, which, by their union, form the salt. Ferrous sulphate is also obtained in many chemical processes as a collateral or by-product, as in the manufacture of alum, in the precipitation of copper from solutions of copper sulphate by scraps of iron, in the manufacture of hydrogen, etc.

Commercial ferrous sulphate is far from being pure. Besides containing some ferric sulphate, it is generally contaminated with metallic and earthy salts, such as those of copper, zinc, aluminum, and magnesium. Two principal kinds occur in the market, one in large grass-green crystals, the surface of which is studded with yellow spots; the other of a bluish-green color, and ordinarily mixed with the powder of the effloresced salt.

Description and Physical Properties.—"Pale, bluish-green, monoclinic prisms. It is odorless, and has a saline, styptic taste. The salt is efflorescent in dry air, but on exposure to moist air, the crystals rapidly oxidize and become coated with brownish-yellow, basic ferric sulphate. When it has thus deteriorated, the salt must not be used for any official or medicinal purpose. One Gm. of Ferrous Sulphate is soluble in 1.4 cc. of water at 25° C. and in 0.4 cc. of boiling water. It is insoluble in alcohol. When slowly heated to 115° C., the crystals disintegrate and the salt loses the greater part of its water of crystallization.

"An aqueous solution of the salt (1 in 20) is acid to litmus paper. Ferrous Sulphate responds to the reactions for ferrous salts, and for sulphates. Dissolve 1 Gm. of the salt in about 50 cc. of distilled water containing 1 cc. of diluted sulphuric acid, heat the solution to boiling, oxidize it with nitric acid, mix it with a slight excess of ammonia T.S., and filter: the filtrate is colorless and after acidulating with hydrochloric acid meets the requirements of the test for *heavy metals.* Agitate 1 Gm. of Ferrous Sulphate, in small fragments, during four or five minutes with 10 cc. of alcohol, and filter the mixture: the filtrate does **not** immediately redden moistened blue litmus paper (*free acid*).

"Preserve in well-closed containers.

"**Assay.**—Dissolve about 1 Gm. of Ferrous Sulphate, accurately weighed, in 25 cc. of diluted sulphuric acid, and titrate with tenth-normal potassium permanganate until a permanent pink color is produced. Each cc. of tenth-normal potassium permanganate corresponds to 0.01519 Gm. of $FeSO_4$." *U. S.*

"Oblique rhombic prisms of a greenish color, or a crystalline powder of a pale bluish-green color; taste astringent. Insoluble in *alcohol* (90 per cent.), soluble in less than 2 parts of *water* previously boiled and cooled, giving a clear solution (absence of oxysulphate). Yields the *reactions* characteristic of ferrous salts and of sulphates. 1 gramme dissolved in 20 millilitres of *diluted sulphuric acid* decolorises not less than 35 millilitres of *N/10 solution of potassium permanganate.* Yields no characteristic *reactions* for copper or zinc. *Arsenic limit* 2 parts per million." *Br.*

Ferrous sulphate is incompatible with alkalies and their carbonates, soaps, lime water, calcium and barium chlorides, sodium borate and phosphate, silver nitrate, and lead acetate and subacetate. It is decomposed also by astringent vegetable infusions, the tannic and gallic acids of which form, if any sesqui-oxide be present, a black compound of the nature of ink. The extent to which this change lessens the activity of the salt is not well ascertained. It is incompatible also with even feeble oxidizing agents which quickly convert it into ferric sulphate or subsulphate.

Uses.—Ferrous sulphate is an active local irritant and astringent. In overdoses it produces nausea, vomiting, griping, and purging, and other evidences of gastro-enteric irritation. Because of this action it is not to be recommended as an internal remedy. Externally, the solution has been used in chronic *ophthalmia, leucorrhea,* and *gleet,* made of various strengths, from one or two to eight or ten grains of the salt to the fluidounce of water. Velpeau has recommended in *erysipelas* the local use of a three per cent. solution applied by compresses kept constantly wet. An ointment made of one or two parts of the sulphate to sixty of lard was found by Devergie to be particularly efficacious in certain skin diseases, especially in *eczema.* In scaly affections it had no effect. (See *Ferri Sulphas Exsiccatus.*)

Ferrous sulphate, usually in the impure form known commercially as copperas, has been used extensively as a disinfectant and deodorant. Its germicidal value is certainly low, Sternberg having found that a 20 per cent. solution was not certainly fatal to bacteria after two hours' exposure, and Leitz, that a 5 per cent. solution required three days for the destruction of typhoid bacilli. Its deodorant properties, however, are quite marked, due probably to its power of combining either with hydrogen sulphide or ammonia. It is asserted that ferric sulphate unites with organic substances to form definite stable compounds, and that animal substances kept in a 3 per cent. solution of neutral ferric sulphate for some time and then removed, mummify without decomposition. (*N. R.,* Dec., 1883, 685.)

Dose, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Ferri Carbonas Saccharatus, *U. S., Br.;* Ferri Phosphas Saccharatus, *Br.;* Ferri Sulphas Exsiccatus, *U. S., Br.;* Ferri Sulphas Granulatus, *U. S.;* Liquor Ferri Subsulphatis, *N. F.;* Liquor Ferri Tersulphatis, *U. S., Br.;* Massa Ferri Carbonatis, *U. S.;* Mistura Ferri Composita, *Br., N. F.*

FERRI SULPHAS EXSICCATUS. U. S., Br.

EXSICCATED FERROUS SULPHATE Ferr. Sulph. Exsic. [Dried Ferrous Sulphate]

"Exsiccated Ferrous Sulphate contains the equivalent of not less than 80 per cent. of anhydrous ferrous sulphate [$FeSO_4$]." *U. S.* "Exsiccated Ferrous Sulphate is Ferrous Sulphate deprived of part of its water of crystallization. It contains not less than 77 per cent. of pure anhydrous ferrous sulphate, $FeSO_4$." *Br.*

Ferri Sulphas Exsiccata, *Br.*, 1885; Dried Sulphate of Iron; Sulfate Ferreux desséché, *Fr.;* Ferrum Sulfuricum Siccum, *P. G.;* Getrochnetes Ferrosulfat, Entwässertes Schwefelsaures Eisenoxydul, *G.;* Sulfato ferroso desecado, *Sp.*

"Ferrous Sulphate, in coarse powder, 100 Gm. Allow the salt to effloresce at a temperature of about 40° C. in dry air, and then heat it in a tared porcelain dish on a water bath, constantly stirring, until the product weighs from 64 to 65 Gm. Reduce the residue to a fine powder, and transfer it at once to dry bottles, which should be stoppered immediately." *U. S.*

The reason for the preliminary drying at a lower temperature than is subsequently employed is to prevent the melting of the salt in its full water of crystallization which greatly retards the process when it occurs.

In this process about six molecules out of seven, of the water of crystallization of the salt, are driven off. The heat in the earlier stages should be gentle to avoid liquefaction of the salt and subsequent difficulty in exsiccation, and in the latter stages of the process should not exceed 149° C., otherwise the salt itself would suffer decomposition. If the heat has been excessive, the color of the salt will be brownish instead of grayish-white.

No process is given in the British Pharmacopœia, 1914.

Description and Physical Properties.—"A grayish-white powder, slowly soluble in water. A solution of the salt (1 in 20) in recently boiled distilled water is not more than slightly turbid, and when taken in proportionate amount, conforms to the reactions and tests under *Ferri Sulphas,* except the test for free acid.

"Preserve in tightly-stoppered bottles." *U. S.*

"A nearly white powder, slowly but entirely soluble in *water.* 0.5 gramme dissolved in *water* and acidified with *sulphuric acid* decolorises not less than 25.3 millilitres of *N/10 solution of potassium permanganate. Arsenic limit* 5 parts per million." *Br.*

Assay.—"Dissolve about 0.8 Gm. of Exsiccated Ferrous Sulphate, accurately weighed, in 25 cc. of diluted sulphuric acid, and titrate with tenth-normal potassium permanganate until a permanent pink color is produced. Each cc. of tenth-normal potassium permanganate corresponds to 0.01519 Gm. of $FeSO_4$.

"Each cc. of tenth-normal potassium permanganate V.S. used corresponds to 0.015191 Gm. of $FeSO_4$. Each gramme of Exsiccated Ferrous Sulphate corresponds to not less than 52.7 cc. of tenth-normal potassium permanganate V.S." *U. S.*

Dried ferrous sulphate is used for making pills, the crystallized sulphate not being adapted to that purpose. In prescribing the dried sulphate it is necessary to recollect that about three grains of it are equivalent to five grains of the crystallized salt.

Dose, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Pilulæ Aloes et Ferri, *Br., N. F.;* Pilula Ferri, *Br.;* Pilulæ Ferri, Quininæ, Aloes et Nucis Vomicæ, *N. F.*

FERRI SULPHAS GRANULATUS U. S.

GRANULATED FERROUS SULPHATE Ferr. Sulph. Gran. [Precipitated Ferrous Sulphate]

Granulated Sulphate of Iron; Ferri Sulphas Præcipitatus, *U. S. P.*, 1880; Precipitated Sulphate of Iron; Sulfate Ferreux précipite, *Fr.;* Prăcipitirtes Ferrosulfat, *G.*

"Ferrous Sulphate, 100 Gm.; Distilled Water, 100 cc.; Diluted Sulphuric Acid, 5 cc.; Alcohol, 25 cc. Add the diluted sulphuric acid to the distilled water, heat to boiling, dissolve the ferrous sulphate in the liquid, and filter the solution while hot. Evaporate the solution immediately in a tared porcelain dish on a sand bath until it weighs 150 Gm., and cool it quickly with constant stirring. Transfer the product to a glass funnel fitted with a pledget of purified cotton, and when it has thoroughly drained pour the alcohol upon it. When this has also drained, spread the crystalline powder on bibulous paper, dry it quickly at room temperature, and transfer it at once to dry bottles, which should be stoppered immediately." *U. S.*

The process of the U. S. P. (1890), retained by the U. S. P., differs radically in manipulation from that of 1880; instead of pouring the filtered solution of ferrous sulphate into alcohol and collecting the precipitate which falls, the solution is granulated by heat with constant stirring (not quite to dryness), and this salt is then washed with alcohol, which displaces impurities and facilitates the rapid drying of the granular powder.

Description and Physical Properties.—"A pale bluish-green, crystalline powder, which meets the requirements of the tests for identity and purity and the assay under *Ferri Sulphas.*

"Preserve in tightly-stoppered bottles." *U. S.*

This salt is less liable to oxidation on exposure than is the sulphate in its ordinary form, and experience has shown that it is admirably adapted for dispensing.

Dose, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Pilulæ Ferri Carbonatis, *U. S.*

FERRUM. U. S., Br.

IRON Ferr.

"Metallic iron in the form of fine, bright wire." *U. S.* "Iron is annealed iron wire, having a diameter of about 0.1 millimetre (about No. 35 wire gauge), or wrought-iron nails, free from oxide. *Arsenic limit* 200 parts per million." *Br.*

Fer métallique, *Fr. Cod.;* Fil de Fer, *Fr.;* Eisen, Eisendraht, *G.;* Ferro, Limatura di ferro, *It.;* Hierro, *Sp.*

In the U. S. Pharmacopœia, this metal is employed in different preparations in the form of wire; it was official in 1850 as *Ferri Ramenta, Iron Filings.* See *U. S. Dispensatory,* 19th edition, p. 514.

Iron is one of the most abundant and useful of the metals, and so interwoven with the wants of mankind that the extent of its consumption by a nation may be taken as an index of progress in civilization. It is universally diffused in nature, not only in the mineral but also in the vegetable and animal kingdoms. There are very few minerals in which traces of it are not to be found, and it is an essential constituent in many parts of animals, but particularly in the blood. It is one of the few metals which are not deleterious to the animal economy. Iron occurs: (1) native (almost exclusively, however, of meteoric origin); (2) as a sulphide, in the minerals *pyrites, pyrrhotite,* or *magnetic pyrites,* and *arsenopyrite* or *mispickel* (a sulpharsenide of iron); (3) oxidized, embracing the magnetic, specular, red, brown, and argillaceous iron oxides which include *hæmtite, limonite,* etc., also *chromite* (mixed iron, chromium, and magnesium oxides), *siderite,* a ferrous carbonate, and *franklinite* (mixed iron, manganese and zinc oxides); (4) in saline combination, forming ferrous carbonate, sulphate, phosphate and arsenate. Those minerals of iron which admit of being worked to advantage are called *iron ores.* These include the different native oxides and the carbonate (spathic iron). The best iron is obtained from the ferroso-ferric oxide usually called magnetic iron ore, and the anhydrous sesquioxide, known as specular iron ore. These occur abundantly in Sweden, and furnish the superior iron of that country. The upper peninsula of Michigan and the borders of Lake Champlain in New York yield similar ores. As a rule, those ores which occur in primitive formations yield the best iron.

Extraction.—The mode of extracting iron from its ores varies somewhat with the nature of the ore; but the general principles of the operation are the same for all. The ore, previously broken into small pieces and roasted, is exposed to the action of an intense heat, urged by an air blast, in contact with carbonaceous matter, such as charcoal, coke, or anthracite, and in connection with some flux capable of fusing with the impurities of the ore. The flux varies with the nature of the ore, and is generally limestone. Fluorspar is occasionally used, but is not often found in sufficiently large deposits to be available. The flux, whatever it may be, enters into fusion with the impurities, and forms what is called the slag, which is a fusible lime silicate chiefly, while the carbon monoxide formed from the carbonaceous matter, acting on the ferric oxide, reduces it to the metallic state. The reduced metal, from its density, occupies the lower part of the furnace, and is protected from the action of the air by the melted slag which floats on its surface. When the reduction is completed, the slag is allowed to run out by a hole in the side of the furnace, and the melted metal by an aperture at the bottom, the latter being received into a series of sand moulds, where it solidifies in masses, known in commerce by the name of *pig* or *cast iron.* In this state the metal is brittle and far from being pure, as it contains from 3 to 6 per cent. of carbon, with silicon, phosphorus, sulphur, and manganese. It is purified, and brought to the state of *malleable iron,* by being fused and subjected, while stirred, to the action of a current of air on its surface. By these means the carbon is nearly burnt out, and the other impurities are oxidized and made to rise to the surface as a slag. Instead of this process, called "refining," usage in this country and in England substitutes what is called "pig boiling"—that is, the pig iron is at once submitted to the operation of puddling without previous refining. The "puddling" process consists in heating the charge of pig iron on the hearth of a reverberatory furnace in contact with ferric oxide and in a reducing flame. The silicon is first burnt out, and then the carbon gradually disappears; the phosphorus goes into the "tap cinder" as phosphide and phosphate; the sulphur in part disappears as sulphur dioxide and in part remains in the cinder as ferrous sulphide. As the metal approaches to purity, it becomes tough and less liquid, and its particles agglutinate so as to form semi-fused lumps, though the temperature of the furnace continues the same. These lumps are then taken out of the furnace, and their particles, by means of ponderous hammers moved by steam or water power, or by great pressure, are forced together so as to form one tenacious mass. The metal is finally rolled out into bars of a convenient size, when it constitutes *wrought iron* of commerce.

The third form of commercial iron, known as "steel," is made either by the *cementation* process, the *Bessemer* process, the *open hearth* process, or by *electrical* processes. In the first case, wrought iron is packed with charcoal and heated until combination takes place, and the resulting steel is cast into ingots. In the second case, cast iron is melted in large vessels called converters, when a blast of air is blown through the mass, burning out the requisite amount of carbon, and then, after addition of a small amount of *spiegeleisen,* or manganiferous cast iron, the finished product is run into moulds; while in the third or open hearth process, a mixture of pig iron and ore is heated with a reverberatory flame, as in the puddling process, or bars and blooms of wrought iron are heated with the pig iron, and steel is made by the combination of the two. Steel contains from ½ to 1 per cent. of carbon.

Iron mines occur in most countries, but more particularly in northern ones. In Spain the principal mines furnish spathic iron and the red oxide. The chief iron ores of France are the spathic iron, and the specular, brown, and argillaceous oxides; of Germany, the spathic iron and brown oxide. The island of Elba is celebrated for its rich and abundant specular iron ore. In the United States iron is abundant. The principal ores that are worked are the magnetic, red, and brown oxides. The magnetic oxide is found in large beds in Essex County, N. Y., on the borders of Lake Champlain, and in the Lake Superior district; the red oxide in New York, New Jersey, Pennsylvania, Alabama, and especially in a very pure state in Missouri, at Iron Mountain and Pilot Knob.

Properties.—Iron is a hard, malleable, ductile, and tenacious metal, of a grayish-white color and fibrous texture, a characteristic taste, and a sensible odor when rubbed. In tenacity it yields only to nickel and cobalt. (Deville.) Its sp. gr. is about 7.7, and its fusing point very high, about 1510° C. It possesses magnetic properties and is very malleable. It is combustible, and, when heated to whiteness, burns in atmospheric air, and with brilliant scintillations in oxygen gas. At a red heat, its surface is converted into black oxide, and at common temperatures, by the combined agency of air and moisture, it becomes covered with a yellowish-brown matter, called *rust,* which is a complex hydrated oxide of iron. It combines with all the non-metallic elements, except hydrogen and nitrogen, and with most of the metals. It forms three compounds with oxygen, a ferrous oxide and a ferric oxide, which by their union form the native magnetic oxide, hence often termed ferroso-ferric oxide, and a trioxide, which forms an acid called ferric acid. The *monoxide,* or ferrous oxide, is of a dark blue color, attracted by the magnet, and spontaneously combustible in the air, being converted into sesquioxide or ferric oxide. It is the base of ferrous sulphate, and the green salts of iron generally. It is very prone to absorb oxygen, and hence the salts which contain it are soon partially converted, when in solution, into ferric salts. Its formula is FeO. The *sesquioxide,* or *ferric oxide,* is readily obtained by dissolving iron in nitrohydrochloric acid, precipitating by ammonia, and igniting the precipitate. It is of a red color, not attracted by the magnet, and forms salts which for the most part have a reddish color. Its formula is Fe_2O_3. The *native black oxide,* the magnetic oxide of mineralogists, consists of one molecule of FeO and one molecule of Fe_2O_3.

Under the name of *Ferri Oxidum Magneticum,* the British Pharmacopœia formerly had a preparation consisting of this oxide with three molecules of water. *Ferric acid,* discovered by Frémy, may be obtained, in union with potassium hydroxide, by passing chlorine through a very concentrated solution of the alkali, holding the hydrated ferric oxide in suspension, or by fusing iron filings with potassium nitrate. Iron forms a number of important salts.

Iron is readily detected, even in minute quantities, by oxidation to the ferric condition, and adding potassium ferrocyanide or tincture of galls, the former of which will produce a deep blue, the latter a black color. In an interesting series of articles published in the *Scientific American,* Suppl. 2192 and 2193 (1918) the experiences of an iron atom are described, which brings in the entire history of the manufacture and uses of iron.

The so-called *stainless-steel* or *rustless-iron* is one of the alloys of iron, usually one containing chromium. Silicon is also used to the extent of about 15 per cent. in making a form of iron which is resistant to the action of acids. *Tantiron* and *Duriron* are ferro-silicon alloys of this character.

Uses.—The only condition in which the value of iron, as an internal remedy, has been proven beyond cavil is in certain types of *anemia.* The conditions of the blood which are characterized by a reduction in the percentage of hemoglobin may be divided into three groups, those in which the number of corpuscles is reduced to a greater extent than the percentage of hemoglobin—each individual corpuscle, therefore, being richer than normal in coloring matter—secondly, those in which the reduction in the number of corpuscles and the quantity of hemoglobin is approximately equal, and thirdly, those in which the number of corpuscles is not reduced as much as the percentage of hemoglobin—each corpuscle being poor in coloring matter. The first condition is seen typically in cases of pernicious anemia; the second in the so-called accidental anemias, those which are due to hemorrhage, wasting diseases, etc.; and the third is seen in chlorosis. The value of iron in any individual case of impoverishment of the blood is in proportion as the condition approaches the chlorotic type. In true *pernicious anemia,* iron is probably of no value at all, in the accidental or secondary anemia, it is often of considerable service, provided the cause of the blood impoverishment can be removed, and in true *chlorosis* it almost reaches the height of a specific.

Some years ago, certain chemists, failing to find any increase in the amount of iron in the urine after the administration of the inorganic salts of iron by the mouth, were led to believe that these forms of iron were not absorbable from the intestinal tract, and the theory had at one time a considerable number of adherents. It would carry us beyond the proper bounds of an article for the Dispensatory to go into all the evidence for and against the absorbability of iron, and the reader interested in the details is referred to H. C. Wood, Jr.'s *Pharmacology*. The subject may be summed up for the present purposes with the statement that it has been as firmly established as any fact in pharmacology, that the inorganic salts of iron are absorbed through the intestinal walls, and exercise a direct influence upon the blood making organs. That the amount of iron in the urine is not increased is owing to the fact that the great bulk of the metal is eliminated through the intestinal glands; this is true whether the drug be given by the mouth or hypodermically. Because of the former vogue for the theory of the non-absorption of iron, various chemists were led to place upon the market preparations in which the iron is bound up with organic matter in a non-ionizing form; these are spoken of as "organic iron" or "masked iron," and supposed to be more assimilable than the pharmacopœial salts. There is no convincing evidence that any of these preparations has any advantage over the inorganic salts, except, perhaps, a little less liability to disturb digestion. Indeed, the experiments of Abderhalden (*Z. B.*, 1900, xxxix) indicate that the iron in organic combination is of less value for the treatment of anemia than when in the inorganic form. Because iron is an essential constituent of the hemoglobin, it was formerly almost universally believed, and still is to a considerable extent, that it acted in anemia as a food-stuff. This belief has for its base mere assumption; and the infinitesimal amount of iron which is consumed in the human body, as well as the fact that patients with chlorosis are not cured by feeding upon the food rich in iron, throws great doubt upon this ancient legend, and the experiments of Abderhalden, quoted above, furnish almost conclusive proof of its error. It is far more probable that the action of iron is due to a stimulating effect upon the blood making organs analogous to the stimulant action of caffeine upon the kidneys, or strychnine upon the spinal cord.

The question of the selection of a preparation of iron for an individual case is often one of great importance. If it be simply desired to combat anemia, a preparation should be selected which is free as may be from astringency. Most of the liquid preparations of iron are more or less injurious to the teeth, so that commonly it is preferable to give a solid salt in pill or capsule rather than one of the liquid forms, unless the latter be especially indicated.

Certain salts of iron are extremely astringent and more or less irritant. The most important of these are the sulphates and the chlorides. These salts should never be employed as chalybeates, except in those cases in which, for some reason, astringency is desired. In some cases some laxative should be combined with iron to overcome its constipating influence.

The hypodermic use of iron suggested a number of years ago by Kobert of Dorpat has in the past decade come into a very wide popularity. When large quantities of iron—corresponding to twenty or thirty grains for a man—are injected hypodermically, it causes toxic symptoms and may even prove fatal. Although after large doses a considerable proportion is eliminated through the kidney and may exercise an irritating effect on this organ, the observations of Quincke (*A. E. P. P.*, 1896, xxxvii) and others show that after therapeutic quantities, the greater proportion is eliminated through the intestinal glands, and there is, therefore, relatively little danger of renal irritation. The favorite preparation of iron for hypodermic use is some form of ferric citrate. Sometimes the local reactions have been so severe as to entirely preclude the use of the drug. According to Stieglitz (*Am. J. Anat.*, 1921, xxix, p. 33), these reactions are due to a deficiency in ammonium, and he recommends the use of a ferric and ammonium citrate, representing not less than 8.1 per cent. of ammonia. Such a salt under the name of *green iron citrate* has been recognized by the N. N. R.

When used subcutaneously the dose must be much smaller than that ordinarily given by mouth (see under *Ferri et Ammonii Citras*). It is stated that after the hypodermic injection of large doses the irritation of the alimentary canal is more severe than when the drug is given by the mouth—a statement which finds confirmation in the experiments of Gottlieb, who found that when he injected iron subcutaneously into a dog he was able to obtain nearly 97 per cent. of it from the feces. The effort at intestinal elimination is evidently accompanied by irritation if the amount of iron to be eliminated is large.

Off. Prep.—Liquor Ferri Chloridi, *U. S.* (*Br.*); Liquor Ferri Pernitratis, *Br.*; Syrupus Ferri Iodidi, *U. S.*, *Br.*; Syrupus Ferri Phosphatis, *Br.*; Syrupus Ferri Phosphatis cum Quinina et Strychnina, *Br.*; Vinum Ferri, *Br.*; Liquor Ferri Protochloridi, *N. F.*; Syrupus Ferri et Mangani Iodidi, *N. F.*

FERRUM ALBUMINATUM. N. F.

ALBUMINIZED IRON Ferr. Album. [Iron Albuminate]

"Albuminized Iron is a compound of iron oxide and albumin, rendered soluble by the presence of sodium citrate. It contains not less than 17 per cent. and not more than 19 per cent. of Fe." *N. F.*

Under the name of "albuminate of iron" there have been used in medicine a variety of preparations made from egg albumen and either the chloride or oxychloride of iron. The exact form in which the iron exists in these compounds is not known; indeed, it probably differs according to the divergent methods of manufacture. The solution in the process of the German Pharmacopœia, 35 parts of dried albumen is dissolved in 1000 parts of water, to this is added 120 parts of the solution of iron oxychloride (*Liquor Ferri Oxychloratum,* P. G.)—previously diluted with 1000 parts of water; the resulting precipitate is washed and dissolved in dilute solution of sodium hydroxide, or it may be rendered soluble by means of sodium citrate as required by the N. F.

Description and Physical Properties.—"Reddish brown, lustrous granules, or a brown powder. It is odorless, or has not more than a slight odor. Albuminized Iron is freely soluble in water yielding dark solutions. It is almost insoluble in alcohol.

"The addition of acids to an aqueous solution of Albuminized Iron produces a precipitate which dissolves by warming with an excess of hydrochloric acid. The resulting solution yields the reactions characteristic of ferric iron. An aqueous solution of Albuminized Iron (1 in 20) is neutral or slightly alkaline to litmus paper. An aqueous solution (1 in 50) yields no blue color upon the addition of potassium ferrocyanide T.S. (absence of *ionic iron*).

"Dissolve 1 Gm. of Albuminized Iron in 50 cc. of distilled water. Render the solution slightly alkaline, if necessary, by the addition of sodium hydroxide T.S., and precipitate the iron from the solution with hydrogen sulphide. Filter, add to the filtrate 5 cc. of diluted hydrochloric acid and evaporate almost to dryness on the water bath. Dissolve the residue in 10 cc. of distilled water, and to 5 cc. of the solution, rendered slightly alkaline with sodium hydroxide, add 2 cc. of alkaline cupric tartrate solution and heat. No red precipitate is produced (*sugar*).

"**Assay.**—Weigh accurately about 0.5 Gm. of Albuminized Iron and ignite it in a crucible to destroy the organic matter. Allow to cool, transfer the residue completely into a beaker, add 10 cc. of hydrochloric acid, heat until all the iron is dissolved, then add 10 cc. of hydrogen dioxide T.S., and evaporate almost to dryness on the water bath. Dissolve the residue by warming with 5 cc. of hydrochloric acid and 10 cc. of water and transfer the solution completely into a glass-stoppered flask, filtering if necessary, and washing the residue, and filter with small quantities of hot water until free from iron. Now add to the solution 3 Gm. of potassium iodide, allow to stand for one-half hour at about 40° C., cool and titrate the liberated iodine with tenth-normal sodium thiosulphate. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of iron (Fe)." *N. F.*

Uses.—While this preparation is an eligible chalybeate there is no evidence that it possesses any real advantage over some of the older salts of the metal.

Dose, from five to ten grains (0.3–0.6 Gm.).

Off. Prep.—Liquor Ferri Albuminati, *N. F.*

FERRUM PEPTONATUM. N. F.

PEPTONIZED IRON Ferr. Pepton. [Iron Peptonate]

"Peptonized Iron is a compound of iron oxide and peptone, rendered soluble by the presence of sodium citrate. It contains not less than 16 per cent. and not more than 18 per cent. of Fe." *N. F.*

Several formulas for preparing compounds of iron with peptone have been suggested. Dieterich's is made by treating a 10 per cent. aqueous solution of peptone (100 parts) with *Liquor Ferri Oxychlorati,* P. G. (120 parts), exactly neutralize with sodium hydroxide solution; the resulting precipitate decomposed with hydroxide may be dissolved by means of sodium hydroxide citrate and the solution evaporated, forming brownish yellow granules. In the original method the precipitated peptonate was dissolved with the aid of hydrochloric acid.

Description and Physical Properties.—"Dark brown, lustrous granules, or a brown powder. It has a slight characteristic odor. Peptonized Iron is freely soluble in water yielding dark solutions. It is almost insoluble in alcohol.

"The addition of acids to an aqueous solution of Peptonized Iron produces a precipitate which dissolves upon warming with an excess of hydrochloric acid. The resulting solution yields the reactions characteristic of ferric iron. An aqueous solution of Peptonized Iron (1 in 20) is neutral or slightly alkaline to litmus paper. An aqueous solution (1 in 50) yields no blue color upon the addition of potassium ferrocyanide T.S. (absence of *ionic iron*).

"Dissolve 1 Gm. of Peptonized Iron in 50 cc. of distilled water, render the solution slightly alkaline, if necessary, by the addition of sodium hydroxide T.S., and precipitate the iron from the solution with hydrogen sulphide. Filter, add to the filtrate 5 cc. of diluted hydrochloric acid and evaporate almost to dryness on the water bath. Dissolve the residue in 10 cc. of distilled water, and to 5 cc. of the solution, rendered slightly alkaline with sodium hydroxide, add 2 cc. of alkaline cupric tartrate solution and heat. No red precipitate is produced (*sugar*).

"**Assay.**—Weigh accurately about 0.5 Gm. of Peptonized Iron and ignite it in a crucible to destroy the organic matter. Allow to cool, transfer the residue completely into a beaker, add 10 cc. of hydrochloric acid, heat until all the iron is dissolved, then add 10 cc. of hydrogen dioxide T.S., and evaporate almost to dryness on the water bath. Dissolve the residue by warming with 5 cc. of hydrochloric acid and 10 cc. of water, and transfer the solution completely into a glass-stoppered flask, filtering, if necessary, and washing the residue and filter with small quantities of hot water until free from iron. Now add to the solution 3 Gm. of potassium iodide, allow to stand for one-half hour at about 40° C., cool and titrate the liberated iodine with tenth-normal sodium thiosulphate. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of iron (Fe)." *N. F.*

Uses.—This preparation of iron is nearly free from astringency or tendency to disturb digestion but it is doubtful whether it possesses any real advantage over the citrate or soluble phosphate.

Dose, three to eight grains (0.2–0.5 Gm.).

Off. Prep.—Liquor Ferri Peptonati, *N. F.;* Liquor Ferri Peptonati et Mangani, *N. F.*

FERRUM REDUCTUM. U. S. (Br.)

REDUCED IRON Ferr. Reduct. [Iron by Hydrogen, Quevenne's Iron]

"Reduced Iron is obtained by the action of hydrogen upon ferric oxide and contains not less than 90 per cent. of metallic iron [Fe]." *U. S.* "Reduced Iron may be obtained by reducing ferric hydroxide, heated to dull redness, by means of a stream of dry hydrogen. It contains not less than 80 per cent. of metallic iron, with a variable amount of iron oxide." *Br.*

Ferrum Redactum, *Br., U. S.* 1870; Ferri Pulvis, *U. S.* 1850; Powder of Iron; Ferrum Hydrogenio Reductum, Ferrum Ope Hydrogenii Paratum; Iron Reduced by Hydrogen; Fer réduit par l'Hydrogène, *Fr. Cod.;* Ferrum reductum, *P. G.;* Reduzirtes Eisen, *G.;* Ferro ridotto dall' idrogeno, *It.;* Hierro reducido por el hidrogeno, *Sp.*

A process for this form of iron is no longer given in the United States Pharmacopœia. (See *U. S. Dispensatory,* 19th edition, page 518.)

This preparation consists of metallic iron in fine powder, obtained by reducing the ferric oxide by hydrogen at a dull red heat. The compound of iron formerly called the subcarbonate which is essentially the ferric oxide, is deprived of water by calcination, and then subjected to the reducing influence of a stream of hydrogen, purified from hydrogen sulphide and acid compounds by passing successively through a solution of lead subacetate and milk of lime. The hydrogen unites with the oxygen of the ferric oxide to form water, and leaves the iron in the metallic state. The ferric oxide should be perfectly free from sodium sulphate, which it is likely to contain when imperfectly washed. If this salt be present, it will be reduced by the hydrogen to the state of sodium sulphide, which will contaminate and spoil the metallic iron formed, and cause the preparation, when taken internally to give rise to unpleasant eructations. The heat should be carefully regulated, for if it fall below dull redness, part of the oxide will escape reduction, and if it exceed that point considerably, the particles of reduced iron will agglutinate, and the preparation will be heavy and not readily pulverizable.

Under the name of *"alcoholized iron,"* a powdered iron was at one time sold in this country, said to be prepared, in the eastern parts of Germany, by attrition of iron filings with honey, by some cheap method, as by attachment to a saw mill or steam machinery. It had the appearance of powdered plumbago, but under the magnifying glass was seen to contain particles with metallic luster and rounded as if by friction. It was soluble in diluted sulphuric acid, with the escape of hydrogen, free, or nearly so, from sulphur, but a small quantity of black powder remained undissolved. The relation of the epithet "alcoholized" to this powder is an example of an unusual use of the word alcohol, which in the Arabic means "very finely divided." The word alcoholize, therefore, simply means to reduce to an impalpable powder and has been so used since its first use by Phillips in 1706.

Other forms of finely divided iron which have been produced by mechanical or electrical processes and not by the reduction method, have been offered at various times to take the place of reduced iron or even under the name of the latter substance, but are therapeutically inferior to the official form.

Description and Physical Properties.—"An odorless, grayish-black, lusterless powder, all of which must pass through a No. 100 sieve. When viewed under a lens having a magnifying power of one hundred diameters, Reduced Iron appears as an amorphous powder, free from crystalline particles. It is stable in dry air. Reduced Iron is insoluble in water and in alcohol.

"Heat about 1 Gm. of Reduced Iron in a porcelain crucible with a small Bunsen flame until it assumes a bluish-black color without glowing. Then quickly pour it from the crucible: the particles of iron will glow brightly as they fall through the air. Shake 1 Gm. of Reduced Iron with 5 cc. of distilled water, and filter: the filtrate does not change the color of litmus paper. Treat 1 Gm. of Reduced Iron with 20 cc. of diluted sulphuric acid and when the reaction subsides, heat gently until no more gas is evolved. Filter, wash the residue with distilled water until the washings cease to react for sulphate, dry at 110° C. to constant weight, and weigh. The weight of the residue should not exceed 0.010 Gm. One Gm. of Reduced Iron mixed with 20 cc. of diluted sulphuric acid in a flask causes the evolution of nearly odorless hydrogen gas, which does not affect paper moistened with lead acetate T.S. within two minutes (*sulphide*). Add 20 cc. of diluted sulphuric acid to 0.5 Gm. of Reduced Iron contained in a small, covered beaker, and after the reaction has subsided somewhat warm the liquid on a water bath until the reaction ceases. Pass the solution through a small filter to collect any undissolved residue, rinse the beaker with distilled water, add the rinsings to the filter, and then wash the residue with distilled water until free from acid reaction. Transfer the residue to the beaker by rinsing it back, and after adding about 0.25 Gm. of potassium chlorate and 5 cc. of hydrochloric acid, slowly evaporate the solution to dryness on a water bath. Dissolve the residue in sufficient distilled water to measure 50 cc., add 5 cc. of this solution to 5 cc. of a saturated solution of sulphurous acid, and heat the liquid on a water bath for fifteen minutes, or until all traces of sulphurous acid have been removed: the resulting solution meets the requirements of the test for *arsenic*.

"Preserve in well-closed containers." *U. S.*

"A fine greyish-black powder, strongly attracted by the magnet, and producing metallic streaks when rubbed with firm pressure in a mortar. Dissolves in *hydrochloric acid* with evolution of hydrogen, and without any odor of hydrogen sulphide, the solution giving a light-blue precipitate with *solution of potassium ferrocyanide.* When 0.25 gramme, in very fine powder, is added to a hot solution of 1.25 grammes of *copper sulphate* in 20 millilitres of *water,* the mixture kept hot and occasionally well shaken during ten minutes, and then rapidly filtered with the minimum of exposure to air, the filtrate decolorises not less than 35.8 millilitres of *N/10 solution of potassium permanganate.* Not more than 1 per cent. is insoluble in *hydrochloric acid. Arsenic limit* 200 parts per million." *Br.*

Assay.—"Triturate thoroughly about 1 Gm. of Reduced Iron, weigh accurately, place it in a 100 cc. flask, and add 10 Gm. of finely powdered corrosive mercuric chloride and 50 cc. of boiling distilled water. Boil the mixture for five minutes, shaking it frequently, then fill the flask to the 100 cc. mark with distilled water, recently boiled and cooled, and cool the mixture to room temperature. Again fill the flask to the mark with distilled water, stopper, agitate the contents well, and allow to stand for a few minutes. Now filter the contents of the flask, and immediately titrate 20 cc. of the filtrate to which has been added 20 cc. of diluted sulphuric acid, with tenth-normal potassium permanganate, until a permanent pink color is produced. Each cc. of tenth-normal potassium permanganate corresponds to 0.005584 Gm. of Fe." *U. S.*

O. E. Winter (*J. A. P. A.*, 1913, p. 296) presents a critical review of the methods and requirements in all existing pharmacopœias and compares the efficiency of the various official methods for the determination of the iron. He favors the mercuric chloride method adopted in the U. S. P., when accompanied by a limiting test for sulphides, which when present in large amounts, interferes with the accuracy of the method.

Uses.—Powder of iron, reduced from the oxide by hydrogen, was first prepared for medicinal purposes by Quevenne and Miquelard, of Paris. When of official quality it is an excellent chalybeate, being especially serviceable for administration in pills because of its concentrated condition and lack of astringency. A mechanically powdered iron, made from factory waste, is sometimes fraudulently substituted for the official form, but is greatly inferior in its therapeutic action; the value of the official form is due to the very fine division of the particles of iron by virtue of which it can be dissolved in the fluids of the alimentary tract.

Dose, one to three grains (0.065–0.20 Gm.) several times a day, given in powder or in pill.

Off. Prep.—Pilulæ Ferri Iodidi, *N. F.;* Trochiscus Ferri Redacti, *Br.;* Extractum Ferri Pomatum, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arsenii Fortiores, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arsenii Mites, *N. F.*

FICUS. N. F.

FIG

"Ficus is the clean, sound, partially dried fruit of *Ficus Carica* Linné (Fam. *Moraceæ*)." *N. F.*

Caricæ; Ficus Passa; Fructus Caricæ; Figue, *Fr. Cod.* Feigen, *G.;* Fichi, *It.;* Higos, *Sp.*

The genus *Ficus* yields a number of economic products. Many species possess a milky juice containing caoutchouc (see *Elastica*); some possess anthelmintic properties, as *F. anthelmintica* Mart.; some yield shellac (see *Lac*); and some are esteemed for their fruits, as *F. Carica* L., *F. religiosa* L., etc.

Ficus Carica, or fig tree, though often not more than twelve feet high, sometimes rises in warm climates twenty-five or even thirty feet. Its trunk, which seldom exceeds seven inches in diameter, is divided into numerous spreading branches, covered with a brown or ash-colored bark. Its large, palmate leaves, usually divided into five obtuse lobes, are deep green and shining above, pale green and downy beneath, and stand alternately on strong, round petioles. The flowers are situated within a common receptacle, placed upon a short peduncle in the axils of the upper leaves. This receptacle, the walls of which become thick and fleshy, constitutes what is commonly called the fruit; though this term is, strictly speaking, applicable to the small seed-like bodies found in great numbers on the internal surface of the receptacle, to which they are attached by fleshy pedicles. Cultivation has produced in the fig, as in the apple and peach, a great diversity in shape, size, color, and taste. It is usually, however, turbinate, or top-shaped, umbilicate at the large extremity, of the size of a small pear, of a whitish, yellowish, or reddish color, and of a mild, mucilaginous, saccharine taste. The dried figs can be partially restored to their original shape by soaking. The fig tree is native to Western Asia. It was introduced at a very early period into various parts of the south of Europe, and is now very common throughout the whole basin of the Mediterranean, particularly in Italy and France. Large numbers of Syrian fig cuttings were planted in the Pomona Valley, California, in 1882, and California figs are now commercial articles. Many varieties of figs are now being cultivated throughout the coastal plain from Texas to the Carolinas chiefly for home consumption, canning and preserving. For details of fig culture see *Bull. 732 U. S. Dept. Agric., 1918.* To hasten the ripening of the fruit, it is customary to puncture it with a sharp pointed instrument covered with olive oil. *Caprification* consists in attaching branches of the wild fig tree—or caprifig—to the cultivated plant. The fruit of the former contains great numbers of the eggs of a small wasp, *Blastophaga glossorum,* the larvæ of which, as soon as they are hatched, spread themselves over the unripened receptacle of the cultivated fig, enter its hollowed interior through a narrow terminal aperture, and, by conveying the pollen to the inclosed female florets, hasten the impregnation of the latter, and cause to quickly come to perfection the fig which might otherwise ripen very slowly, or wither and drop off before maturity.

The chief commercial sources of the figs used in this country are Smyrna and California. They are gathered when fully ripe and dried in the sun or in ovens. Smyrna figs are imported in boxes or drums containing from ½ to 20 kilos, in which they are carefully packed, and also, in string clusters packed in sacks. The individual figs are more or less compressed, and are usually covered in cold weather with a whitish saccharine efflorescence, which softens in the middle of summer and renders them moist. The best or Suzini grade are yellowish or brownish, somewhat translucent when held to the light, and filled with a sweet viscid pulp, in which are lodged numerous small yellow achenes. They are much more saccharine than is the fresh fruit. Their chief constituents are grape sugar, and gum or mucilage.

Description and Physical Properties.—"*Whole Fig.*—Usually compressed, of irregularly rounded shape, from 2.5 to 5 cm. in diameter, fleshy, light brown to yellow, frequently with an efflorescence of sugar; apex with a small, scaly orifice; base with a scar or short stalk; internally hollow, with numerous small, brownish yellow, glossy, hard achenes. Odor distinctive, fruity; taste sweet, pleasant.

"*Structure.*—Epidermal cells of receptacle thick-walled up to 0.020 mm. in diameter, some being modified into tapering, unicellular epidermal hairs with a rounded base up to 0.060 mm. in diameter and 0.300 mm. in length, others modified into broadly elliptical stomata up to 0.035 mm. in length; hypodermis consisting of several layers of small cells with thick walls frequently containing rosettes of calcium oxalate, the latter up to 0.020 mm. in diameter; remaining tissue of receptacle chiefly of large parenchyma cells containing sugar, branching latex cells and tracheæ having spiral or reticulate markings. Achenes yellowish; broadly rounded at one end and rounded or straight pointed at the other, up to 1.550 mm. in length and 1.400 mm. in width; pericarp characterized by outer layer of thin-walled cells and an inner layer of stone cells, the latter rounded or angular; seed-coat thin, yellowish; endosperm composed of thick-walled cells containing fixed oil, aleurone grains and few starch grains; embryo curved." *N. F.*

An average of several analyses of dried figs as quoted by Königs (*Nahrungs und Genussmittel,* 3te Aufl., Bd. i, 781) gives—water, 31.20; nitrogenous material, 4.01; sugar, 49.79; ash, 2.86. Reckoned on the weight of absolutely dry material, the nitrogenous matter amounted to 5.75 per cent. and the sugar to 72.26 per cent. According to Landerer, the unripe fig contains an irritant juice, which inflames the skin, and may even disorganize it. (See *A. J. P.,* xxxiii, 215.) They are officially described as

Uses.—Figs are nutritious, laxative, and demulcent. In the fresh state they are considered, in the countries where they grow, a wholesome and agreeable aliment, and have been employed from time immemorial. They are prone, however, when eaten freely, to produce flatulence, pain in the bowels, and diarrhea. The latex of the fig has been used as an anthelmintic against intestinal parasites. Their chief medicinal use is as a laxative article of diet in *constipation.* They occasionally enter into demulcent decoctions, and, roasted or boiled, and split open, are sometimes applied as a cataplasm to inflamed gums.

Off. Prep.—Confectio Sennæ, *N. F.;* Syrupus Ficorum Compositus, *N. F.*

FLUIDEXTRACTA. U. S. (Br.)

FLUIDEXTRACTS

"Fluidextracts are concentrated liquid preparations of vegetable drugs, containing alcohol either as a solvent or as a preservative, and bearing a uniform relation to the drugs used so that 1 cc. of the fluidextract closely represents the useful constituents of 1 Gm. of the air dried and powdered drug of standard quality." *U. S.*

Extracta Liquida, *Br.;* **Fluid Extracts; Extraits liquides,** *Fr;* Extracta fluida, *P. G.;* Fluidextrakte, Flüssige Extrakt, *G.*

The Latin title Extractum —— Fluidum formerly used for fluidextracts was dropped by the U. S. P. VIII because of the confusion which resulted from the necessary bringing together of the extracts and fluid extracts due to a strict alphabetical arrangement; the name "fluidextractum" is now used for "fluidextract" and the latter made one word.

Fluidextracts were first introduced into the U. S. P. of 1850. They are now perhaps the most important class of liquid preparations in use. Their distinctive character is the concentration of the active ingredients of medicinal substances into a small bulk, in the liquid form, a cubic centimeter of any one of them representing a gramme of the crude drug.

It has been repeatedly proposed to make 50 per cent. tinctures or half-strength fluidextracts, the main object being to secure more representative preparations when made on the small scale. Experiments by Sayre, Gregory, Patch, and others prove that half-strength fluidextracts possess no advantages over those of official strength. (*D. C.*, 1897, 119, 147.)

Fluidextracts U. S. P. X.

"The fluidextracts of this Pharmacopœia, with few exceptions, may be classified according to the menstruum used in the extraction of the drugs and the processes of manufacture employed. Several drugs require special manipulation to obtain satisfactory fluidextracts, and for these appropriate formulas have been devised and are printed in full in the text. In the preparation of fluidextracts by the appended type processes A, B, or C, the rate of percolation must be carefully controlled and, for the quantities directed in the formulas of the Pharmacopœia, the flow should not exceed ten drops per minute until the percolate to be reserved is collected, and twenty drops per minute thereafter. One thousand Gm. of powdered drug may frequently be exhausted by percolation with sufficient menstruum to yield 3000 cc. of percolate, but, in all cases the percolation should be continued until the drug is practically exhausted. Fluidextracts should be kept in tightly-stoppered, amber-colored bottles, protected from sunlight and extremes of temperature. After keeping for one month, the clear portion should be decanted from any sediment, the remainder filtered, and the liquids thoroughly mixed before storing.

"The percentage of alcohol in fluidextracts made by type processes A, B, or C, is variable and always less than that in the menstruum employed, due, among other causes, to loss of alcohol by evaporation during manufacture, the presence of a variable proportion of water in the air-dried drug, and to the extraction from the drug of its soluble constituents, which also often vary greatly in different lots of the same drug. The percentage of alcohol in the finished product can therefore only be ascertained by an actual determination." *U. S.* (See *Alcohol Determination*, Part III.)

"*Type Process A.*—This process is recommended for fluidextracts that are made with a menstruum of alcohol, or a mixture of alcohol and water, by the usual process of percolation. Moisten 1000 Gm. of the powdered drug directed with a sufficient quantity of the prescribed menstruum to render it evenly and distinctly damp and to so maintain it during maceration for six hours in a tightly-covered container. Then pack it in a cylindrical percolator, and add enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding more menstruum until the drug is exhausted. Reserve the first 850 cc. of the percolate (unless otherwise specified in the formula), recover the alcohol from the remainder of the percolate, and concentrate the residue to a soft extract at a temperature not exceeding 60° C. Dissolve the extract in the reserved portion, mix thoroughly, and finally add a sufficient quantity of the menstruum to make the fluidextract measure 1000 cc., or the volume determined by calculation from the assay.

"*Type Process B.*—This process is recommended for fluidextracts in which glycerin or an acid is used in the extraction and two menstrua are successively employed. Moisten 1000 Gm. of the powdered drug directed with a sufficient quantity of the prescribed Menstruum I to render it evenly and distinctly damp and to so maintain it during maceration for six hours in a tightly-covered container. Then pack it in a cylindrical percolator, add the remainder of Menstruum I, and when this has just disappeared from the surface, gradually add Menstruum II, constantly maintaining a stratum of liquid above the drug. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours, and then allow the percolation to proceed slowly, gradually adding Menstruum II until the drug is exhausted. Reserve the first 850 cc. of the percolate (unless otherwise specified in the formula), recover the alcohol from the remainder of the percolate, and concentrate the residue to a soft extract at a temperature not exceeding 60° C. Dissolve the extract in the reserved portion, mix thoroughly, and finally add a sufficient quantity of Menstruum II to make the fluidextract measure 1000 cc. or the volume determined by calculation from the assay.

"*Type Process C—Fractional or Divided Percolation.*—This process is especially recommended for drugs containing volatile constituents or constituents which are injured by exposure to heat. This process may also be used as an alternative process in the formulas in which Type Process A is directed. Divide 1000 Gm. of the powdered drug directed into three portions of 500 Gm., 300 Gm., and 200 Gm., respectively. Moisten the first portion of the drug (500 Gm.) with a sufficient quantity of the prescribed menstruum to render it evenly and distinctly damp and to so maintain it during maceration for six hours in a tightly-covered container. Then pack it in a cylindrical percolator, and add enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours, and then allow the percolation to proceed slowly, gradually adding more of the menstruum. Reserve the first 200 cc. of percolate, and continue the process until the additional percolate measures 1500 cc., the latter being collected in successive portions of 300 cc. Moisten the second portion of the powdered drug (300 Gm.) with a sufficient quantity of the percolate collected in the preceding operation, immediately after the reserved portion, to render it evenly and distinctly damp and to so maintain it during maceration for six hours in a tightly-covered container. Then pack it in a cylindrical percolator, macerate, and percolate as directed for the first portion of the drug, using as menstruum the several portions of percolate from the preceding operation in the order in which they were collected, and, if this is insufficient, follow with more of the original menstruum. Reserve the first 300 cc. of percolate, and continue the process until the additional percolate measures 800 cc., the latter being collected in successive portions of 200 cc. each. Moisten the third portion of the powdered drug (200 Gm.), with a sufficient quantity of the percolate collected in the preceding operation, immediately after the reserved portion, to render it evenly and distinctly damp and to so maintain it during maceration for six hours in a tightly-covered container. Then pack it in a cylindrical percolator, macerate, and percolate as before, using as menstruum the several portions of percolate from the preceding operation in the order in which they were collected, and, if this is insufficient, follow with more of the original menstruum. Collect 500 cc. of percolate, and mix this with the two portions previously reserved to make 1000 cc. of finished fluidextract. When Type Process C is directed for fluidextracts which are adjusted by assay to a definite alkaloidal standard, collect only 420 cc. of percolate from the third portion of drug instead of the 500 cc. directed above. Mix this percolate with the two portions previously reserved, assay a portion of the mixture and adjust its volume by the addition of the menstruum directed so that each 100 cc. of finished fluidextract will contain the prescribed amount of alkaloid.

"*Type Process D.*—This process is recommended for those fluidextracts in which extraction is effected by infusion and percolation with boiling water, alcohol being added to the concentrated liquid as a preservative. To 1000 Gm. of the ground drug add 5000 cc. of boiling water, mix thoroughly, and allow it to macerate in a covered container in a warm place for two hours. Then transfer the moist drug to a tinned or enameled metallic percolator, and allow percolation to proceed, gradually adding boiling water until the drug is exhausted. Evaporate the percolate on a water bath or steam bath to the volume specified, and when cold add the alcohol directed, and mix thoroughly. Allow the product to stand for seven days in a stoppered container, then decant the clear liquid, filter the remainder, and wash the residue on the filter with sufficient of a mixture of alcohol and water in the proportion used to make the fluidextract measure 1000 cc." *U. S.*

The precipitation experienced when the evaporated weak percolate was added to the reserved portion, is considerably diminished by causing the former to be evaporated to a soft extract. This precipitation, formerly noticed more particularly in alcoholic fluidextracts, was due to the greater volatility of the alcohol in the weak percolates, which, when evaporated, left the residue to a great extent aqueous; when this was added to the strongly alcoholic reserved portion, a precipitation of resinous, and frequently of active matter, took place, which necessitated the storing of the fluidextract until precipitation ceased, and subsequent filtration. This is not altogether avoided by evaporating to a soft extract, but the loss of activity through precipitation is thus greatly diminished. Fluidextracts invariably deposit insoluble matter upon standing, and those made in warm weather, owing to the greater solvent powers of the menstrua (due to the elevated temperature) are found to deposit more freely than the same kind of fluidextracts if made in the winter time with menstrua correspondingly reduced in temperature.

The reason for the apparent stability of the fluidextracts furnished by the large scale manufacturer, is that sufficient reserve stock is kept on hand to permit this precipitation to take place before marketing the products.

In the earlier formulas for fluidextracts in the U. S. P. glycerin was used too lavishly in the menstrua and many of the preparations were loaded with inert extractive matter. Scoville (*J. A. Ph. A.*, 1920, ix, 868) has completed a study of the function of glycerin in the menstrua of fluidextracts and tinctures and points out the fact that glycerin in some cases must be considered as a solvent, and in others as a stabilizer. In some cases, as in a few of the alkaloidal and astringent drugs, it is a distinct disadvantage, as it retards extraction.

A useful distillatory apparatus has been contrived by Joseph P. Remington for recovering alcohol from weak percolates, and for general pharmaceutical uses. (See *Practice of Pharmacy.*)

Fluidextracts are mostly prepared by percolation (see under *Extracta*) but in a few instances maceration yields satisfactory results.

Several methods have been suggested for preparing fluidextracts more economically. The use of acetic acid as a menstruum to replace alcohol or diluted alcohol has the merit of economy. (See *Extracta,* also *A. J. P.*, 1899, 1, 67; *Proc. Pennsylvania Pharm. Assoc.,* 1898, 116; *Ph. Era,* 1898, 796; *Proc. Minnesota Pharm. Assoc.,* 1902, 103; *West. Drug.,* 1903, 652.)

The most important modification is the plan of *repercolation,* as proposed by E. R. Squibb, for this class of preparations as well as the dry extracts.

This process consists in the successive application of the same percolating menstruum to fresh portions of the substances to be percolated. The result is that the same menstruum, acting repeatedly on unexhausted portions of the substance, becomes concentrated to the greatest possible extent, so that much of the menstruum is saved, while subsequent evaporation is avoided. Repercolation is officially permitted, by the U. S., as an alternative process, and is generally employed by wholesale manufacturers.

H. Biroth (*Pharm.*, April, 1877) proposed the method which he termed *"insuccation,"* for making non-alcoholic fluidextracts; the advantages claimed for it are simplicity and economy. Colaz prepared fluidextracts from fresh plants by bruising and crushing them, and placing the mass in a dialyzer suspended in 90 per cent. alcohol; when the dialysis is completed, the liquid is evaporated to free it from alcohol, the remaining aqueous liquid retaining the active constituents in the proportions in which they are found in the plant. (*Ph. Post,* xxix, 271.)

For other methods which have been suggested for economizing alcohol—most of which have been abandoned—see *U. S. D.,* 20th ed., p. 482.

Assaying Fluidextracts.—The U. S. gives assay processes for the fluidextracts of alkaloidal drugs; these differ but slightly from the process used for the corresponding drug; they will be found in the succeeding pages under their appropriate headings.

A new method of assay for alkaloidal fluidextracts, especially adapted to the mydriatic leaf drugs in that the interfering chlorophyll is removed, making only one shaking out operation necessary, was proposed by LaWall (*J. A. Ph. A.*, 1912, 29), as follows: Place 25 Gm. of sodium chloride in a 100 cc. graduated cylinder, with water sufficient to make 85 cc. Add 5 cc. of the fluidextract and 5 cc. of 10 per cent. ammonia water. Agitate well for 1 minute, then pour upon a dry filter and collect 50 cc. of clear filtrate, which can be shaken out as directed in the final shake out of the ordinary assay process, using the solvent directed for the particular drug which is being assayed. The method does not work with cinchona, guarana or other drugs containing large amounts of alkaloids in the form of cinchotannates.

The keeping quality of fluidextracts, judged from the alkaloidal content of those which are assayable, has been greatly overestimated. Scoville (*J. A. Ph. A.,* 1919, viii, 799) made an exhaustive study of the keeping qualities of about fifty fluidextracts and tinctures. He found that deterioration is largely due to the unstable nature of the alkaloids in many cases and to the precipitation of secondary constituents that also carry down alkaloids. In general, he says that any large amount of precipitation is accompanied by a loss of strength. Haussmann (*A. J. P.,* 1895, 291,) after examining a large number of commercial fluidextracts, finds great variation in the quality, due to deviation from pharmacopœial processes.

EXTRACTUM AGROPYRI FLUIDUM. Br.

LIQUID EXTRACT OF COUCH GRASS

Fluidextractum Tritici, *U. S. IX.;* Fluidextract of Triticum; Liquid Extract of Couch Grass; Liquid Extract of Triticum; Fluidextract of Couch-grass Root; Extrait liquide de petit Chiendent, *Fr.;* Flüssiges Queckenwurzelextrakt, *G.*

"Couch Grass, cut small, 1000 *grammes;* Distilled Water, boiling, 10,000 *millilitres;* Alcohol (90 per cent.), sufficient to product 1000 *millilitres.* Boil the Couch Grass with the Distilled Water for thirty minutes; strain; evaporate to seven hundred and fifty *millilitres;* cool and add sufficient of the Alcohol to produce the required volume; filter." *Br.*

This fluidextract is no longer recognized by the U. S., but is official in the N. F. (see *Fluidextractum Tritici,* Part III).

In making this fluidextract in warm weather, it is advisable to commence evaporating the percolate before the drug is exhausted, or fermentation may set in; triticum contains fermentable sugars, and diluted aqueous solutions do not keep well.

This fluidextract represents whatever virtues triticum possesses. The German Pharmacopœia formerly directed an *Extractum Graminis,* by digesting 1 part of Triticum with 6 parts of hot water, for six hours, straining, evaporating to a syrup, mixing 1 part of this extract with 4 parts of cold distilled water, filtering, and evaporating to an extract. The fluidextract is preferable, as the excessive use of heat is avoided.

Dose, from one to four fluidrachms (3.75–15 cc.).

EXTRACTUM BELÆ LIQUIDUM. Br.

LIQUID EXTRACT OF BAEL

"Bael Fruit, bruised, 1000 *grammes;* Chloroform Water, 15,000 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Macerate the bruised Bael Fruit for twelve hours in five thousand *millilitres* of the Chloroform Water; pour off and reserve the clear liquid; repeat the maceration a second and a third time for one hour in each case, using for each maceration five thousand *millilitres* of the Chloroform Water; press the marc; strain the mixed liquids through flannel. Evaporate to seven hundred and fifty *millilitres;* cool; add sufficient of the Alcohol to produce the required volume; filter." *Br.*

This represents whatever therapeutic virtues may reside in Bael Fruit. (See *Belæ Fructus.*)

Dose, one to two fluidrachms (3.75–7.5 cc.).

FLUIDEXTRACTUM BELLADONNÆ FOLIORUM. U. S.

FLUIDEXTRACT OF BELLADONNA LEAVES

Fldext. Bellad. Fol.

"Fluidextract of Belladonna Leaves yields, from each 100 cc., not less than 0.27 Gm. and not more than 0.33 Gm. of the total alkaloids of belladonna leaves." *U. S.*

"Belladonna Leaves, in moderately coarse powder, 1000 Gm. Prepare a fluidextract by Type Process A, using a mixture of 3 volumes of alcohol and 1 volume of water as the menstruum, and reserving the first 800 cc. of percolate. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and from the result thus obtained ascertain by calculation the amount of alkaloids in the remainder of the liquid, and dilute this with sufficient menstruum to make each 100 cc. of the finished Fluidextract contain 0.3 Gm. of the alkaloids of belladonna leaves." *U. S.*

Assay.—"Proceed by Type Process D, taking 10 cc. of Fluidextract of Belladonna Leaves, using chloroform as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal acid corresponds to 0.02893 Gm. of the alkaloids of belladonna (Proximate Assays)." *U. S.*

Alcohol content, by volume, 58 to 63 per cent.

The need for a fluidextract of belladonna leaves in addition to that of the root is not obvious. Its admission, in our opinion, is unfortunate as tempting careless pharmacists to make the tincture by dilution of the fluidextract instead of by the official method.

Dose, one to two minims (0.06–0.12 cc.).

FLUIDEXTRACTUM BELLADONNÆ RADICIS. U. S. (Br.)

FLUIDEXTRACT OF BELLADONNA ROOT
Fldext. Bellad. Rad.

"Fluidextract of Belladonna Root yields, from each 100 cc., not less than 0.405 Gm. and not more than 0.495 Gm. of the alkaloids of belladonna root." *U. S.* "Liquid Extract of Belladonna contains in 100 millilitres, 0.75 gramme of the alkaloids of Belladonna Root." *Br.*

Extractum Belladonnæ Liquidum, *Br.;* Liquid Extract of Belladonna; Extrait liquide de Racine de Belladonne, *Fr.;* Flüssiges Tollkirschenwurzelextrakt, *G.*

"Belladonna Root, in moderately coarse powder, 100 Gm. Prepare a Fluidextract by Type Process A, using a mixture of 5 volumes of alcohol and 1 volume of water as the menstruum, and reserving the first 800 cc. of the percolate. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and from the result thus obtained ascertain by calculation the amount of alkaloids in the remainder of the liquid, and dilute this with enough menstruum to make each 100 cc. of the finished Fluidextract contain 0.45 Gm. of the alkaloids of belladonna root." *U. S.*

"Belladonna Root, in No. 20 powder, 1000 *grammes;* Alcohol (90 per cent.), Distilled Water, of each, *a sufficient quantity.* Exhaust the Belladonna Root with a mixture of seven volumes of the Alcohol and one volume of Distilled Water by the *repercolation process* until from every three *grammes* of the Root one *millilitre* of strong percolate has been obtained." *Br.*

Assay.—"Proceed by Type Process D, taking 10 cc. of Fluidextract of Belladonna Root, using chloroform as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal acid corresponds to 0.02893 Gm. of the alkaloids of belladonna (Proximate Assays).

"Alcohol content, by volume, 69 to 73 per cent." *U. S.*

"Determine the proportion of alkaloids in this strong percolate by the following process: Introduce into a separator 10 *millilitres* of the strong percolate, 50 *millilitres* of *water,* 2 *millilitres* of *diluted sulphuric acid,* and 10 *millilitres* of *chloroform.* Shake vigorously, set aside until complete separation has taken place, draw off the lower layer, and wash it with two successive portions, each of 10 *millilitres,* of *water* acidified with *diluted sulphuric acid.* Add the washings to the upper layer left in the separator. Make the mixture distinctly alkaline with *solution of ammonia,* and extract the alkaloids by shaking with three successive portions, each of 10 *millilitres* of *chloroform.* Mix the chloroformic solutions, shake with 10 *millilitres* of *water,* allow separation to take place, draw off the lower layer into a beaker, and set aside for the chloroform to evaporate. Heat the residue on a water-bath for thirty minutes, add 10 *millilitres* of *N/20 solution of sulphuric acid,* warm gently until dissolved, and titrate back with *N/20 solution of sodium hydroxide, tincture of cochineal* being used as indicator. Deduct the number of *millilitres* of alkaline solution required from 10; the remainder, multiplied by 0.01446, gives the number of *grammes* of the alkaloids contained in 10 *millilitres* of the strong percolate. To the remainder of the strong percolate add sufficient of the alcoholic menstruum to produce a Liquid Extract of Belladonna containing 0.75 *gramme* of the alkaloids of Belladonna Root in 100 *millilitres.* Examined by the foregoing process, Liquid Extract of Belladonna is found to contain in 100 millilitres 0.75 gramme of the alkaloids of Belladonna Root. *Limit of error* 0.05 gramme in excess or defect. This Liquid Extract contains 0.75 gramme of the alkaloids of Belladonna Root in 100 millilitres; 110 minims contain ¾ grain." *Br.*

The British liquid extract, 1914, represented several radical improvements in British pharmacy,—*i.e.,* the use of repercolation with absence of heat in the process, and standardization, thus making the end product bear a definite relation towards the quantity of active constituents found in the root (0.75 per cent.). It is based upon the formula proposed by R. A. Cripps. (*P. J.,* 1895, 795.) It will be observed that the alkaloidal standards of the U. S. and Br. Pharmacopœias are not identical; the U. S. fluidextract is made from the standardized drug (belladonna root) (0.45 per cent.); the British liquid extract is made from the *unstandardized* drug and hence the standard for the liquid extract can be made stronger (0.75 per cent.).

The fluidextract of the root is a good preparation, of reddish-brown color, very different in appearance from the deep-green fluidextract of the leaves.

Dose, from one to two minims (0.06–0.12 cc.) of the British liquid extract, not more than one minim (0.06 cc.).

Off. Prep.—Emplastrum Belladonnæ, *Br.;* Extractum Belladonnæ Siccum, *Br.;* Linimentum Belladonnæ, *N. F., Br.;* Unguentum Belladonnæ, *Br.*

FLUIDEXTRACTUM BUCHU. U. S.

FLUIDEXTRACT OF BUCHU Fldext. Buchu.

"Buchu, in moderately coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process A, using alcohol as the menstruum.

"Alcohol content, by volume, 78 to 84 per cent." *U. S.*

The menstruum selected for this fluidextract has been alcohol, although experience has shown that with the weaker alcohol used in the U. S. P. VIII formula it was possible to percolate buchu leaves satisfactorily. We prefer as a menstruum that of the U. S. P. VIII, *i.e.,* alcohol 3, water 1.

This fluidextract is of a dark green color, and shows in a high degree the sensible properties of the leaves. It acquires the odor of mint when long kept, showing that some change takes place in its volatile oil. This fluidextract affords the best means at our command for the exhibition of buchu.

Dose, thirty minims to a fluidrachm (1.8–3.75 cc.), three to five times a day.

Off. Prep.—Elixir Buchu, *N. F.;* Elixir Buchu et Potassii Acetatis, *N. F.;* Elixir Buchu, Juniperi et Potassii Acetatis, *N. F.*

FLUIDEXTRACTUM CANNABIS. U. S.

FLUIDEXTRACT OF CANNABIS Fldext. Cannab. [Fluidextractum Cannabis Indicæ, U. S. P. VIII]

"Fluidextract of Cannabis, administered by the mouth to dogs in doses not exceeding 0.1 cc. for each kilogram of body weight of dog, produces the same degree of incoördination as that produced by an equivalent dose of the standard fluidextract of cannabis, prepared as directed under *Cannabis.*" *U. S.*

Extrait liquide de Chanvre Indien, *Fr.;* Flüssiges Indisch-Hanfextrakt, *G.*

"Cannabis, in moderately coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process A, using alcohol as the menstruum. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and from the result thus obtained adjust the volume of the finished Fluidextract by the addition of alcohol to conform to the above biological standard.

"**Assay.**—Proceed as directed under *Cannabis.* Alcohol content, by volume, 75 to 85 per cent." *U. S.*

Uses.—The fluidextract of cannabis represents the therapeutic virtues of that drug in a convenient form. The smallness of the dose is an advantage over the tincture and many believe that the extract is injured by the evaporation. It has been generally asserted that fluidextract of cannabis is subject to rapid deterioration but this view has not been scientifically confirmed by recent investigators. Hamilton (*J. A. Ph. A.,* 1918, vii, p. 117) tested a fluidextract seventeen years old and found a value of 70 per cent. of standard. But, whatever be the reason, commercial samples vary so greatly in power that it is impossible to assign the proper dose. The only satisfactory way to use it is to start in with doses of one or two minims, increasing each day until some effect is obtained.

Dose, one to four minims (0.06–0.25 cc.).

Off. Prep.—Collodium Salicylici Compositum, *N. F.*

FLUIDEXTRACTUM CASCARÆ SAGRADÆ. U. S. (Br.)

FLUIDEXTRACT OF CASCARA SAGRADA Fldext. Casc. Sagr. [Fluidextract of Rhamnus Purshiana]

Extractum Cascaræ Sagradæ Liquidum, *Br.;* Liquid Extract of Cascara Sagrada; Fluidextractum Rhamni Purshianæ, *U. S. VIII.;* Extrait liquide de Cascara Sagrada, *Fr.;* Flüssiges Cascara-Sagrada-extrakt, *G.*

"Cascara Sagrada, in coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process D. Evaporate the aqueous percolate to 750 cc., and when cold gradually add 250 cc. of alcohol and if necessary, sufficient water to make the product measure 1000 cc. Alcohol content, by volume, 20 to 24 per cent." *U. S.*

"Cascara Sagrada, in No. 20 powder, 1000 *grammes;* Alcohol (90 per cent.), 250 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Exhaust the Cascara Sagrada with the Distilled Water by the *percolation process;* evaporate the percolate to six hundred *millilitres;* add the Alcohol previously mixed with one hundred and fifty *millilitres* of the Distilled Water, or with sufficient to produce the required volume." *Br.*

The emodin strength of this and similar preparations of cascara, which has been arbitrarily set by most manufacturers at 1.50 grammes in each 100 cc. of the fluidextract, may be estimated by the method of Vanderkleed and E'we (*Proc. Pa. Pharm. Assoc.,* 1913, p. 325).

A comprehensive study of the market fluidextracts of cascara was made by Westman and Rowat (*Bull. Lab. Int. Rev. Dept. of Canada* through *C. D.,* 1918, xc, 978). They give data on the examination of numerous samples and conclusions and recommendations based upon these data.

This preparation thoroughly represents the medicinal virtues of cascara sagrada. It is less pleasant but more efficient than the aromatic fluidextract.

Dose, fifteen minims to one fluidrachm (0.9–3.75 cc.).

Off. Prep.—Extractum Cascaræ Sagradæ Siccum, *Br.;* Syrupus Cascaræ Aromaticus, *Br.*

FLUIDEXTRACTUM CASCARÆ SAGRADÆ AROMATICUM. U. S.

AROMATIC FLUIDEXTRACT OF CASCARA SAGRADA Fldext. Casc. Sagr. Arom. [Aromatic Fluidextract of Rhamnus Purshiana]

Tasteless Fluidextract of Cascara Sagrada; Extrait liquid Aromatique de Cascara Sagrada, *Fr.;* Bitterloses flüssiges Cascara-Sagradaextrakt, *G.*

"Cascara Sagrada, in coarse powder, 1000.0 Gm.; Magnesium Oxide, 60.0 Gm.; Lime, 60.0 Gm.; Pure Extract of Glycyrrhiza, 40.0 Gm.; Glycerin, 200.0 cc.; Alcohol, 200.0 cc.; Gluside, 1.0 Gm.; Oil of Anise, 2.5 cc.; Oil of Cinnamon, 0.2 cc.; Oil of Coriander, 0.1 cc.; Methyl Salicylate, 0.2 cc.; Boiling Water, a sufficient quantity to make 1000 cc. Slake the lime by the gradual addition of water, mix it thoroughly with the cascara sagrada and the magnesium oxide, moisten uniformly with 2000 cc. of boiling water, set aside in a shallow dish for forty-eight hours, stirring occasionally, and then pack in a percolator. Now pour on boiling water and allow the percolation to proceed until the drug is exhausted. Evaporate the percolate to 500 cc., and while yet warm dissolve in it the pure extract of glycyrrhiza. When cold, add the glycerin, then the alcohol in which the gluside and the oils have been dissolved, and finally sufficient water to make the Fluidextract measure 1000 cc. Alcohol content, by volume, 17 to 19 per cent." *U. S.*

An aromatic fluidextract was introduced into the U. S. P. VIII for the first time. The object of the addition of magnesium and calcium oxides is to destroy the bitter taste of the cascara sagrada. It is not quite so actively cathartic as the plain fluidextract.

Dose, fifteen minims to one fluidrachm (0.9–3.75 cc.).

Off. Prep.—Elixir Cascaræ Sagradæ, *N. F.;* Elixir Cascaræ Sagradæ Compositum, *N. F.*

FLUIDEXTRACTUM CIMICIFUGÆ. U. S.

FLUIDEXTRACT OF CIMICIFUGA Fldext. Cimicif. [Fluidextract of Black Cohosh, Fluidextract of Black Snakeroot]

Extractum Cimicifugæ Liquidum, *Br.*, 1898; Liquid Extract of Cimicifuga; Liquid Extract of Actæa Racemosa; Extrait liquide d'Actée à Grappes, *Fr.;* Flüssiges Cimicifügaextrakt, *G.*

"Cimicifuga, in moderately coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process A, using alcohol as the menstruum. Alcohol content, by volume, 79 to 85 per cent." *U. S.*

There probably cannot be two opinions about the menstruum, although it has been asserted that a good fluidextract can be made with a menstruum of three parts alcohol and one part water. The probabilities are, however, that a portion of the resinous principle would precipitate on standing. This fluidextract is of a deep reddish-brown color, and thoroughly represents the drug.

Dose, from ten to thirty minims (0.6–1.8 cc.).

Off. Prep.—Elixir Sodii Salicylatis Compositum, *N. F.*

FLUIDEXTRACTUM CINCHONÆ. U. S. (Br.)

FLUIDEXTRACT OF CINCHONA Fldext. Cinchon.

"Fluidextract of Cinchona yields, from each 100 cc., not less than 4 Gm. and not more than 5 Gm. of the total alkaloids of cinchona." *U. S.* "Liquid Extract of Cinchona contains in 100 millilitres 5 grammes of the alkaloids of Red Cinchona Bark." *Br.*

Extractum Cinchonæ Liquidum, *Br.*, Liquid Extract of Cinchona; Extractum Chinæ Calisayæ Fluidum; Fluidextract of Calisaya Bark; Extrait liquide de Quinquina jaune, *Fr.;* Flüssiges Kalisayarinden extrakt, Flüssiges Chinaextrakt, *G.*

"Cinchona, in moderately coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process B (page 160), using a mixture of 100 cc. of glycerin, 100 cc. of diluted hydrochloric acid, and 800 cc. of alcohol as Menstruum I, and a mixture of 4 volumes of alcohol and 1 volume of water as Menstruum II. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and from the result thus obtained ascertain by calculation the amount of alkaloids in the remainder of the liquid and dilute this with enough of Menstruum II to make each 100 cc. of the finished Fluidextract contain 4.5 Gm. of the total alkaloids of cinchona." *U. S.*

"Red Cinchona Bark, in No. 60 powder, 1000 *grammes;* Hydrochloric Acid, 31 *millilitres;* Glycerin, 125 *millilitres;* Alcohol (90 per cent.), Distilled Water, of each *a sufficient quantity.* Mix the Red Cinchona Bark with five thousand *millilitres* of the Distilled Water, to which the Hydrochloric Acid and Glycerin have been added; set aside in a covered vessel for forty-eight hours, stirring frequently; transfer to a percolator; when the liquid ceases to pass continue the percolation with Distilled Water until the percolate ceases to give a precipitate with excess of *solution of sodium hydroxide.* Evaporate the percolate in a porcelain or enamelled iron vessel at a temperature not exceeding 85° C., until it is reduced to one thousand *millilitres.*" *Br.*

Assay.—"Proceed by Type Process C, taking 5 cc. of Fluidextract of Cinchona, using 200 cc. of ether-chloroform mixture for maceration. Decant an aliquot portion of 160 cc., representing 4 cc. of Fluidextract of Cinchona, using chloroform for the final extraction, and determine the alkaloids gravimetrically (Proximate Assays).

"Alcohol content, by volume, 56 to 62 per cent." *U. S.*

"Determine the proportion of alkaloids in the liquid product by the following process: Transfer 5 *millilitres* to a stoppered glass separator; add 15 *millilitres* of *benzolated amylic alcohol* and 10 *millilitres of N/1 alcoholic solution of potassium hydroxide;* shake well, set aside in a warm place for a few minutes, shaking occasionally, and then allow the liquids to separate; pour off the clear upper layer into a second separator and repeat the shaking with two further portions of 15 and 10 *millilitres* of *benzolated amylic alcohol.* Shake the mixed alcoholic liquids with two portions, each of 5 *millilitres,* of *water,* and reject the aqueous liquid; then shake vigorously with a warm mixture of 12 *millilitres* of *diluted hydrochloric acid* and 60 *millilitres* of *water,* using three successive portions of 30, 30, and 12 *millilitres,* and drawing off the acid liquids into a separator. To this acid liquid add 15 *millilitres* of *chloroform* and distinct excess of *solution of ammonia,* shake vigorously, allow the liquids to separate and draw off the chloroformic layer into a tared dish; repeat the shaking and separating with further portions, each of 10 *millilitres,* of *chloroform* until the aqueous liquid, after acidification with *diluted sulphuric acid,* gives no further precipitate with *solution of potassio-mercuric iodide.* Add the chloroformic solutions to that in the dish, allow the chloroform to evaporate slowly; dry the residue in the dish at a temperature of about 110° C. and weigh. The weight of the residue is that of the total alkaloids in 5 *millilitres* of the liquid product. Having thus ascertained the alkaloidal strength of the liquid product, bring every volume of it containing 5 *grammes* of total alkaloids to eighty-five *millilitres,* either by evaporation or by dilution with Distilled Water as may be necessary, add twelve and a half *millilitres* of the Alcohol, and finally sufficient Distilled Water to produce one hundred *millilitres* of the Liquid Extract. Examined by the foregoing process, Liquid Extract of Cinchona is found to contain in 100 *millilitres* 5 grammes of the alkaloids of Red Cinchona Bark. *Limit of error* 0.2 gramme in excess or defect. This Liquid Extract contains 5 grammes of the alkaloids of Red Cinchona Bark in 100 millilitres; 110 minims contain 5 grains." *Br.*

The U. S. and Br. preparations are not made from the same variety of cinchona bark, the U. S. preparation being made from either the red or the yellow cinchona, while the Br. P. preparation is made from the red variety. The latter bark is much more difficult to extract.

Dose, five to twenty minims (0.3–1.3 cc.).

FLUIDEXTRACTUM COLCHICI. U. S.

FLUIDEXTRACT OF COLCHICUM Fldext. Colch. [Fluidextractum Colchici Seminis, U. S. P. IX]

"Fluidextract of Colchicum yields, from each 100 cc., not less than 0.36 Gm. and not more than 0.44 Gm. of colchicine." *U. S.*

Extrait liquide de Semences de Colchique, *Fr.;* Flüssiges Zeitlosensamenextrakt, *G.*

"Colchicum Seed, in moderately coarse powder, 1000 Gm.; Purified Petroleum Benzin, a sufficient quantity. Pack the colchicum seed in a cylindrical percolator, and slowly percolate with purified petroleum benzin until a few drops of the percolate leave no greasy stain when evaporated from filter paper. Reject the benzin solution, remove the powder from the percolator, and dry it by exposure to the air. Then proceed to make the Fluidextract by Type Process A, using a mixture of 2 volumes of alcohol and 1 volume of water as the menstruum. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and from the result thus obtained ascertain by calculation the amount of alkaloids in the remainder of the liquid, and dilute this with enough menstruum to make each 100 cc. of the finished Fluidextract contain 0.4 Gm. of colchicine." *U. S.*

Assay.—"Place 15 cc. of Fluidextract of Colchicum in a 500 cc. flask containing 275 cc. of distilled water, mix well, add 10 cc. of solution of lead subacetate, and agitate the mixture frequently during one hour. Filter off 200 cc. and proceed as directed under *Colchici Semen Assay,* beginning with the word 'Add.'

"Alcohol content, by volume, 53 to 58 per cent." *U. S.*

The present formula is an improvement over the older method, as the fixed oil is removed by the benzin treatment. L. I. Morris (*A. J. P.,* 1881, 7) believes that it is unnecessary to grind the colchicum seeds, and that if the whole seeds are digested with diluted alcohol at 80° C. the colchicine is easily extracted. It well represents the therapeutic virtues of colchicum seed.

Dose, two to eight minims (0.12–0.5 cc.).

FLUIDEXTRACTUM ERGOTÆ. U. S. (Br.)

FLUIDEXTRACT OF ERGOT Fldext. Ergot. [Secalis Cornuti Extractum Fluidum P. I.]

"Fluidextract of Ergot, administered by intramuscular injection to single-comb, white Leghorn cocks, in doses not exceeding 0.5 cc. for each kilogram of body weight of cock, produces a darkening of the comb, corresponding in intensity to that caused by the same dose of the standard fluidextract of ergot prepared as directed under *Ergota.*" *U. S.*

Extractum Ergotæ Liquidum, *Br.;* Liquid Extract of Ergot; Extrait liquide de Seigle ergoté, *Fr.;* Extractum Secalis Cornuti fluidum, *P. G.;* Mutterkorn-Fluidextrakt, Flüssiges Mutterkornextrakt, *G.*

"Ergot, recently ground and in coarse powder, 1000 Gm.; Purified Petroleum Benzin, a sufficient quantity. Pack the Ergot in a cylindrical percolator, and slowly percolate with purified petroleum benzin until a few drops of the percolate leave no greasy stain when evaporated from filter paper. Reject the benzin solution, remove the drug from the percolator, and dry it by exposure to the air. Then proceed to make the Fluidextract by Type Process B (page 160), using a menstruum of 20 cc. of hydrochloric acid and 980 cc. of diluted alcohol as Menstruum I, and diluted alcohol as Menstruum II. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and from the result thus obtained adjust the volume of the finished Fluidextract by the addition of enough Menstruum II to make it conform to the required biological standard.

"**Assay.**—Proceed as directed under *Ergota.*

Alcohol content, by volume, 37 to 42 per cent." *U. S.*

"Ergot, crushed, 1000 *grammes;* Distilled Water, 7500 *millilitres;* Alcohol (90 per cent.), 375 *millilitres.* Macerate the crushed Ergot with five thousand *millilitres* of the Distilled Water for twelve hours; strain; repeat the maceration with the remainder of the Distilled Water; press; strain; evaporate the mixed liquids to seven hundred *millilitres;* when cold, add the Alcohol; set aside for an hour; filter. The product measures about one thousand *millilitres.*" *Br.*

The Br. preparation is greatly inferior to the U. S. because of the use of an aqueous menstruum. It has been shown by Barger and Dale (*Biochem. J.*, 1907, ii, p. 286) and by Brown and Clark (*J. P. Ex. T.*, 1923, xxii, 59) that the Br. liquid extract is almost completely lacking in the characteristic alkaloid, ergotoxin.

An increase in the percentage of alcohol used in this fluidextract would have been an advantage, as some of the active principles of ergot are practically insoluble in water. Great care should be observed in the evaporation of the second portion of the percolate not to exceed the official temperature, 60° C. as the activity of ergot is seriously lessened by heating.

The U. S. fluidextract, when fresh, well represents the activity of ergot and is probably the best preparation of ergot on the market. Unfortunately, however, as shown by H. C. Wood, Jr. (*A. J. P.*, 1911, 172), it is subject to rapid deterioration. (For literature on this subject, see Eberhardt and Eldred, *J. A. Ph. A.*, 1914, iii, 38.) This loss of potency is accelerated by exposure to the air and the preparation should be stored in small containers which are kept tightly corked until used. Pittenger and Vanderkleed assert that by keeping the fluidextract in hermetically sealed vacuum tubes it will retain its activity almost indefinitely; but the figures they give do not entirely confirm their claim. Certainly the common custom of buying fluidextract of ergot, for retail dispensing, and pouring out a little now and then as it may be called for on prescriptions, can not be too severely condemned. Under such conditions the preparation may lose 50 per cent. of its power in less than six months.

Dose, from half a fluidrachm to two fluidrachms (1.8–8.0 cc.).

FLUIDEXTRACTUM ERIODICTYI. U. S.

FLUIDEXTRACT OF ERIODICTYON Fldext. Eriodict. [Fluidextract of Yerba Santa]

Extrait liquide d'Eriodictyon, *Fr.;* Flüssiges Eriodictyonextrakt, *G.*

"Eriodictyon, in moderately coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process A, using a mixture of 4 volumes of alcohol and 1 volume of water as the menstruum, and reserving the first 800 cc. of percolate.

"Alcohol content, by volume, 57 to 62 per cent." *U. S.*

For a process for Aromatic Fluidextract of Yerba Santa, see *U. S. D.*, 19th ed., p. 539.

This fluidextract has a dark brownish-green color, and has proven a valuable addition.

Dose, from fifteen minims to a fluidrachm (0.9–3.75 cc.).

Off. Prep.—Elixir Eriodictyi Aromaticum, *N. F.;* Syrupus Eriodictyi Aromaticus, *N. F.*

FLUIDEXTRACTUM EUCALYPTI. U. S.

FLUIDEXTRACT OF EUCALYPTUS
Fldext. Eucalypt.

Extrait liquide d'Eucalyptus, *Fr.;* Flüssiges Eucalyptusextrakt, *G.*

"Eucalyptus, in coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process A, using a mixture of 3 volumes of alcohol and 1 volume of water as the menstruum, and reserving the first 800 cc. of percolate.

"Alcohol content, by volume, 58 to 63 per cent." *U. S.*

This fluidextract well represents the drug, and is of a dark greenish-brown color, having the peculiar odor and taste of eucalyptus very strongly developed, but in effectiveness it is much inferior to the volatile oil.

Dose, from ten to thirty minims (0.6–1.8 cc.).

FLUIDEXTRACTUM GLYCYRRHIZÆ. U. S. (Br.)

FLUIDEXTRACT OF GLYCYRRHIZA
Fldext. Glycyrrh.

Extractum Glycyrrhizæ Liquidum, *Br.;* Liquid Extract of Liquorice; Fluidextract of Licorice or Liquorice; Extrait liquide de Réglisse, *Fr.;* Flüssiges Süssholzwurzelextrakt, *G.*

"Glycyrrhiza, in coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process D. Promptly evaporate the aqueous percolate to 750 cc., allow this to cool, and gradually add 250 cc. of alcohol and, if necessary, sufficient water to make the product measure 1000 cc.

"Alcohol content, by volume, 20 to 24 per cent." *U. S.*

"Liquorice Root, in No. 20 powder, 1000 *grammes;* Chloroform Water, 5000 *millilitres;* Alcohol (90 per cent.), *a sufficient quantity.* Mix the Liquorice Root with one-half of the Chloroform Water; set aside for twenty-four hours; strain; press; to the pressed marc add the remainder of the Chloroform Water, and set aside for six hours; strain; press; mix the strained liquids; heat to 100° C.; strain through flannel; evaporate until the liquid has acquired, when cold, a specific gravity of 1.200; add to this one-fourth of its volume of the Alcohol; let the mixture stand for twelve hours; filter." *Br.*

The process of the U. S. P. IX in which ammonia water was used in the original macerating liquid and the drug was subsequently exhausted with chloroform water has been superseded by a process in which the ammonia water has been omitted and the extraction is accomplished by percolation with boiling water, alcohol being subsequently added to stabilize and preserve the preparation. This change was made in the interests of both flavor and of stability. The former preparation was somewhat acrid and was frequently subject to precipitation. The use of boiling water as a menstruum and the subsequent concentration of this percolate by evaporation causes the precipitation of albuminous matter and other objectionable extractives which are thus renewed before the preparation is completed. The object of the use of chloroform water in the Br. process is to avoid fermentation during the extracting process. The British formula for the liquid extract has several inconvenient manipulative features, such as the repeated macerations and expressions, evaporating to a certain specific gravity, etc. (See *Mont. Pharm. Journ.*, 1893, 147; *P. J.*, 1898, 188.)

This preparation is now very largely used as an adjuvant, and for disguising the bitter taste of quinine, which should be added to the preparation of licorice just before the dose is taken. It is a very convenient form for using licorice. It is a dark brown liquid, having the sweet taste of licorice, and froths when shaken with water. A *syrup of licorice* may be made by adding two parts of fluidextract to fourteen parts of simple syrup. (See also *N. F.*, Part III.)

Used as a vehicle only.

Off. Prep.—Elixir Glycyrrhizæ, *U. S.;* Mistura Sennæ Composita, *Br.;* Syrupus Sarsaparillæ Compositus, *U. S.;* Elixir Glycyrrhizæ Aquosum, *N. F.;* Elixir Taraxaci Compositum, *N. F.*

EXTRACTUM GOSSYPII RADICIS CORTICIS LIQUIDUM. Br.

LIQUID EXTRACT OF COTTON ROOT BARK

"Cotton Root Bark, in No. 30 powder, 1000 *grammes;* Glycerin, 250 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Mix the Glycerin with seven hundred and fifty *millilitres* of the Alcohol; moisten the Cotton Root Bark with this mixture and continue the *percolation process,* using as menstruum first the remainder of the mixture of Glycerin and Alcohol, and afterwards sufficient of the Alcohol to produce the required volume." *Br.*

The fluidextract of cotton root bark was not retained in the U. S. but the National Formulary has introduced a fluidextract made from the recently gathered air-dried bark of the root, using alcohol for the menstruum. (See Part III.) The British process requires the use of glycerin which may have a tendency to prevent gelatinization.

Uses.—There is reason to believe that cotton-root bark loses some of its activity in drying. For this reason the preparation of the N. F. is to be preferred to the Br. For therapeutic properties of cotton root, see *Gossypii Radicis Cortex.*

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

FLUIDEXTRACTUM GRANATI. U. S.

FLUIDEXTRACT OF POMEGRANATE

Fldext. Granat.

Fluidextract of Pomegranate Root Bark; Extrait liquide d'Ecorce de Balaustier, Extrait liquide d'Ecorce de Grenadier, *Fr.;* Flüssiges Granatwurzelrindenextrakt, *G.*

"Pomegranate, in coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process B (page 160), using a mixture of 100 cc. of glycerin, 500 cc. of alcohol and 400 cc. of water as Menstruum I, and diluted alcohol as Menstruum II.

"Alcohol content, by volume, 34 to 40 per cent." *U. S.*

This fluidextract well represents the virtues of pomegranate but is less used than the alkaloids.

Dose, from one-half to one fluidrachm (1.8–3.75 cc.).

EXTRACTUM GRINDELIÆ LIQUIDUM. Br.

LIQUID EXTRACT OF GRINDELIA

Fluidextractum Grindeliæ, *U. S. IX.;* Liquid Extract of Grindelia; Extrait liquide de Grindélia, *Fr.;* Flüssiges Grindelienextrakt, *G.*

"Grindelia, in No. 40 powder, 1000 *grammes;* Sodium Bicarbonate, 100 *grammes;* Distilled Water, 500 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Exhaust the Grindelia by *percolation* with the Alcohol. Recover the alcohol from the percolate by distillation, and dissolve the residue in the Distilled Water, to which the Sodium Bicarbonate has previously been added; after effervescence has ceased, add sufficient Distilled Water to produce seven hundred and fifty *millilitres,* and then sufficient of the Alcohol to produce the required volume." *Br.*

A fluidextract of Grindelia is recognized by the N. F. (see Part III).

This is a fluidextract which well represents the drug; owing to the large quantity of resinous matter present, it does not mix well with aqueous liquids. The so-called *"alkaline fluid extract of grindelia"* may be made by evaporating one pint of official fluidextract until reduced to twelve fluidounces, making a solution of 180 grains of sodium bicarbonate in four fluidounces of water, adding it slowly to the evaporated fluidextract, and filtering; the British liquid extract is made upon this principle. The fluidextract is a dark brown liquid having the peculiar odor of grindelia.

For medical properties and uses, see *Grindelia.*

Dose, ten to thirty minims (0.6–1.8 cc.).

EXTRACTUM HAMAMELIDIS LIQUIDUM. Br.

LIQUIDEXTRACT OF HAMAMELIS

Fluidextractum Hamamelis Foliorum, *N. F.;* Fluidextract of Hamamelis Leaves; Fluidextract of Witch-hazel Leaves; Extrait liquide de Hamamélis, *Fr.;* Flüssiges Hamamelis-extrakt, *G.;* Extracto fluido de hamamelis, *Sp.*

"Hamamelis Leaves, dried, in No. 40 powder, 1000 *grammes;* Alcohol (45 per cent.), sufficient to produce 1000 *millilitres.* Exhaust the

Hamamelis Leaves by *percolation* with the Alcohol. Reserve the first eight hundred and fifty *millilitres* of the percolate; recover the alcohol from the remainder by distillation; evaporate the residue to a soft extract; dissolve this in the reserved portion; add sufficient of the Alcohol to produce the required volume." *Br.*

This liquid extract well represents the virtues of witchhazel. The fluidextract of hamamelis leaves is not recognized by the U. S., but will be found in the N. F. (See Part III.) It has a dark reddish-brown color.

Dose, ten to thirty minims (0.6–1.8 cc.).

Off. Prep.—Unguentum Hamamelidis, *Br.*

FLUIDEXTRACTUM HYDRASTIS. U. S. (Br.)

FLUIDEXTRACT OF HYDRASTIS Fldext. Hydrast. [Fluidextract of Golden Seal]

"Fluidextract of Hydrastis yields, from each 100 cc., not less than 1.8 Gm. and not more than 2.2 Gm. of the ether-soluble alkaloids of hydrastis." *U. S.* "Liquid Extract of Hydrastis contains in 100 millilitres 2 grammes of hydrastine." *Br.*

Extractum Hydrastis Liquidum, *Br.;* Liquid Extract of Hydrastis; Extrait liquide de Hydrastis, *Fr.;* Extractum Hydrastis fluidum, *P. G.;* Hydrastis-Fluidextrakt; Flüssiges Hydrastisextrakt, *G.;* Estratto di idraste liquido, *It.;* Extracto fluido de hidrastis, *Sp.*

"Hydrastis, in moderately coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process B (page 160), using a mixture of 100 cc. of glycerin, 600 cc. of alcohol, and 200 cc. of water as Menstruum I, and a mixture of 2 volumes of alcohol and 1 volume of water as Menstruum II. Reserve the first 750 cc. of percolate. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and from the result thus obtained ascertain by calculation the amount of alkaloids in the remainder of the liquid, and dilute this with enough of Menstruum II to make each 100 cc. of the finished Fluidextract contain 2 Gm. of the ether-soluble alkaloids of hydrastis." *U. S.*

Assay.—"Proceed by Type Process D, taking 5 cc. of Fluidextract of Hydrastis, using ether as the solvent, and determine the alkaloids gravimetrically (Proximate Assays).

"Alcohol content, by volume, 47 to 52 per cent." *U. S.*

"Determine the proportion of hydrastine in the liquid extract thus obtained by the following process: Transfer 10 millilitres of the liquid extract to a 100 millilitre graduated flask, add 20 millilitres of *solution of potassium iodide* diluted with 60 millilitres of *water,* and then sufficient *water* to produce 100 millilitres. Shake the mixture for several minutes and filter. Transfer 50 millilitres of the filtrate to a separator, render alkaline with *solution of ammonia,* add 30 millilitres of *ether,* and shake at intervals during several minutes. Allow the liquids to separate, draw off the aqueous solution into a beaker and the ethereal solution into a tared beaker. Return the aqueous solution to the separator and repeat the operation with two successive portions, each of 20 millilitres, of *ether* for one minute. Draw off and reject the aqueous layer; transfer the ethereal solutions to the tared beaker and evaporate at a gentle heat; dry the residue on a water-bath and weigh. The weight is that of the hydrastine in 5 millilitres of the liquid extract examined. To the remainder of the liquid extract add sufficient of the menstruum to produce a Liquid Extract of Hydrastis containing 2 grammes of hydrastine in 100 millilitres. Examined by the foregoing process Liquid Extract of Hydrastis is found to contain in 100 millilitres 2 grammes of hydrastine. *Limit of error* 0.1 gramme in excess or defect. This Liquid Extract contains 2 grammes of hydrastine in 100 millilitres; 110 minims contain 2 grains." *Br.*

The Holland Pharmacopœia Commission have proposed a ratio of alkaloidal matter to total extractive in this preparation of 1 to 8.5.

The fluidextract thoroughly represents the drug. It is of a deep brownish-yellow color.

Dose, from fifteen minims to one fluidrachm (0.9–3.75 cc.).

Off. Prep.—Tinctura Hydrastis, *Br.;* Mistura Rhei Alkalina, *N. F.;* Elixir Hydrastis Compositum, *N. F.*

FLUIDEXTRACTUM HYOSCYAMI. U. S.

FLUIDEXTRACT OF HYOSCYAMUS Fldext. Hyosc. [Fluidextract of Henbane]

"Fluidextract of Hyoscyamus yields, from each 100 cc., not less than 0.055 Gm. and not more than 0.075 Gm. of the alkaloids of hyoscyamus." *U. S.*

Extrait liquide de Jusquiame, *Fr.;* Flüssiges Bilsenkrautextrakt, *G.*

"Hyoscyamus, in moderately coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process A, using a mixture of 3 volumes of alcohol and 1 volume of water as the menstruum. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and from the result thus obtained ascertain by calculation the amount of alkaloids in the remainder of the liquid, and dilute this with enough menstruum to make each 100 cc. of the finished Fluidextract contain 0.065 Gm. of the alkaloids of hyoscyamus.

"**Assay.**—Proceed by Type Process D, taking 25 cc. of Fluidextract of Hyoscyamus, using chloroform as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal acid corresponds to 0.02893 Gm. of the alkaloids of hyoscyamus (Proximate Assays).

"Alcohol content, by volume, 58 to 63 per cent." *U. S.*

Dose, from three to ten minims (0.2–0.6 cc.).

FLUIDEXTRACTUM IPECACUANHÆ. U. S. (Br.)

FLUIDEXTRACT OF IPECAC Fldext. Ipecac.

"Fluidextract of Ipecac yields, from each 100 cc., not less than 1.35 Gm. and not more than 1.65 Gm. of the ether-soluble alkaloids of ipecac." *U. S.* "Liquid Extract of Ipecacuanha contains in 100 millilitres 2 grammes of the alkaloids of Ipecacuanha Root." *Br.*

Extractum Ipecacuanhæ Liquidum, *Br.;* Liquid Extract of Ipecacuanha; Extrait liquide d'Ipécacuanha, *Fr.;* Flüssiges Ipecacuanhaextrakt, *G.*

"Ipecac, in fine powder, 1000 Gm.; Diluted Hydrochloric Acid, a sufficient quantity. Prepare a Fluidextract by Type Process B, using a mixture of 150 cc. of diluted hydrochloric acid, 300 cc. of alcohol, and 300 cc. of water as Menstruum I, and a mixture of 2 volumes of alcohol and 3 volumes of water as Menstruum II. Reserve the first 800 cc. of percolate. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and from the result thus obtained ascertain by calculation the amount of alkaloids in the remainder of the liquid. Test a small portion for miscibility by adding 7 cc. to a mixture of 10 cc. of glycerin and sufficient syrup to make 100 cc. If this does not produce a clear mixture, gradually add diluted hydrochloric acid, drop by drop, until a clear mixture is obtained which will remain clear for four days. Add to the remainder of the Fluidextract the amount of diluted hydrochloric acid determined as necessary by this test and sufficient of Menstruum II to make each 100 cc. of the finished Fluidextract contain 1.5 Gm. of the ether-soluble alkaloids of ipecac." *U. S.*

"Ipecacuanha Root, in No. 120 powder, 1000 *grammes;* Alcohol (90 per cent.), *a sufficient quantity.* Pack the Ipecacuanha Root uniformly in a conical percolator, add two hundred *millilitres* of the Alcohol, and set aside for twelve hours; then percolate with successive portions, each of two hundred *millilitres,* of the Alcohol, added at intervals of twelve hours, until the liquid begins to drop from the orifice of the percolator. Continue the percolation with more of the Alcohol until seven hundred and fifty *millilitres* of percolate have been collected. Reserve this portion. Then percolate until exhaustion is complete; recover the alcohol from this percolate by distillation, and dissolve the residual extract in the reserved portion." *Br.*

The menstruum for the U. S. fluidextract contains hydrochloric acid, which combines with the alkaloids and more thoroughly exhausts the ipecac. It was proved by J. U. Lloyd that when alcohol alone is used a portion of emetine escapes solution. On the other hand, it is known that when the menstruum is more aqueous large amounts of the pectinous principles are taken up, and it is very desirable to separate these in order to prevent their appearance as a flocculent precipitate in syrup of ipecac; but efficiency is to be sought for as the first desideratum, and hence a menstruum which will extract the activity and make a fluidextract that will not let fall a bulky precipitate of inert matter has been secured; usually this will not mix with syrup without slight precipitation, but the improved official process for syrup of ipecac should effectually separate any precipitate resulting from the presence of apotheme in the fluidextract. An *acetic extract of ipecac* (dry) is used in Great Britain; it has been shown that the heating necessary to dry it is injurious to its emetic properties. (*P. J.,* 1895, 158.)

Assay.—"Proceed by Type Process D, taking 5 cc. of Fluidextract of Ipecac, using ether as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal acid corresponds to 0.024 Gm. of the alkaloids of ipecac (Proximate Assays).

"Alcohol content, by volume, 28 to 33 per cent." *U. S.*

Victor O. Mattson (*D. C.,* 1925, p. 224) points out that while the ipecac assay method of the U. S. P. IX for the root itself gives very satisfactory results, the method of the U. S. P. IX for the assay of the fluidextract of ipecac gives discordant results, probably due to the fact that alkaloidal isomers are formed when the fluidextract is evaporated upon sawdust as directed at or below 80° C. They find that evaporation in a vacuum gives satisfactory results. In the U. S. P. X, the method of assay for ipecac root has not been changed from that of the U. S. P. IX, but the method for the fluidextract has been materially changed in that no evaporation whatever is required, and chances of injury by heat are therefore entirely eliminated.

"Determine the proportion of alkaloids in the liquid extract thus obtained by the following process: Introduce 5 *millilitres* of the liquid extract into a separator and add 4 *millilitres* of *water,* 1 *millilitre* of *diluted sulphuric acid,* and 10 *millilitres* of *ether.* Shake, and separate the ethereal solution. Repeat the shaking with 5 *millilitres* of *ether* and again separate. Wash the mixed ethereal solutions in a second separator with two successive portions, each of 5 *millilitres,* of *water,* and add the washings to the contents of the first separator. Shake this aqueous liquid with 10 *millilitres* of *chloroform* and excess of *solution of ammonia.* Separate the chloroformic solution and filter it through a small filter-paper into a tared dish. Repeat the shaking with *chloroform,* separation, and filtration, twice, finally washing the filter-paper with a little *chloroform.* Evaporate the mixed chloroformic solutions to about 2 *millilitres,* add 5 *millilitres* of *ether,* evaporate, dry at a temperature not exceeding 80° C. and weigh the residual alkaloids. To the remainder of the liquid extract add sufficient of the Alcohol to produce a Liquid Extract of Ipecacuanha containing in 100 *millilitres* 2 grammes of the alkaloids of Ipecacuanha Root. Examined by the foregoing process Liquid Extract of Ipecacuanha is found to contain in 100 millilitres 2 grammes of the alkaloids of Ipecacuanha Root. *Limit of error* 0.1 gramme in excess or defect. This Liquid Extract contains 2 grammes of the alkaloids of Ipecacuanha Root in 100 millilitres; 110 minims contains 2 grains." *Br.*

This fluidextract is a thin, dark reddish-

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brown, transparent liquid, of a bitterish, slightly acrid taste, but without the nauseous flavor of the root. It is a convenient preparation for adding to expectorant and diaphoretic mixtures.

Dose, as emetic, fifteen to thirty minims (0.9–1.8 cc); as an expectorant, one to two minims (0.06–0.12 cc.).

Off. Prep.—Syrupus Ipecacuanhæ, *U. S.;* Tinctura Ipecacuanhæ et Opii, *N. F.;* Vinum Ipecacuanhæ, *Br.;* Mistura Rhei Composita, *N. F.;* Syrupus Asari Compositus, *N. F.*

EXTRACTUM KAVÆ LIQUIDUM. Br.

LIQUID EXTRACT OF KAVA

"Kava Rhizome, in No. 20 powder, 1000 *grammes;* Alcohol (90 per cent.), *a sufficient quantity;* Alcohol (45 per cent.), *a sufficient quantity.* Mix the powdered Kava Rhizome with two thousand *millilitres* of the Alcohol (90 per cent.); set aside in a closed vessel for forty-eight hours; transfer to a percolator and percolate slowly, reserving the first seven hundred and fifty *millilitres* of the percolate. Continue the percolation, adding the Alcohol (45 per cent.) until the powder is exhausted; recover most of the alcohol from this percolate by distillation; evaporate the residue at a temperature below 80° C. to a soft extract, and dissolve this in the reserved percolate; add sufficient of the Alcohol (90 per cent.) to produce one thousand *millilitres* of the Liquid Extract." *Br.*

This fluidextract is also official in the N. F. (See Part III.)

Dose, thirty minims to one fluidrachm (1.8–3.75 cc.).

EXTRACTUM NUCIS VOMICÆ LIQUIDUM. Br.

FLUIDEXTRACT OF NUX VOMICA Fldext. Nuc. Vom.

"*One hundred cc.* of Fluidextract of Nux Vomica yields not less than 2.37 Gm. nor more than 2.63 Gm. of the alkaloids of nux vomica." *U. S.* "Liquid Extract of Nux Vomica contains in 100 millilitres 1.5 grammes of strychnine." *Br.*

Fluidextractum Nucis Vomicæ, *N. F.;* Fluidextract of Nux Vomica; Extrait liquide de Noix-Vomique, *Fr.;* Flüssiges Kräbenaugen-Extrakt, Brechnussextrakt, Strychnossamenextrakt, *G.*

"Nux Vomica, in No. 20 powder, 1000 *grammes;* Alcohol (70 per cent.), *a sufficient quantity.* Exhaust the Nux Vomica with the Alcohol by the *repercolation process* until five hundred millilitres of percolate have been obtained. Place this percolate in a closed vessel with fifteen grammes of Hard Paraffin and heat to 60° C. for a few minutes, shaking vigorously. Allow the contents of the vessel to cool and the layer of paraffin which will have separated to solidify. Pour off the percolate thus freed from fat; filter." *Br.*

"Determine the proportion of strychnine in it by the following process: Evaporate 10 *millilitres* on a water-bath to a syrupy extract; dissolve the residue in 10 *millilitres* of warm *water* and transfer to a separator, washing the dish with a further 10 *millilitres* of *water.* Add 10 *millilitres* of *chloroform* and a solution of 5 *grammes* of *sodium carbonate* in 25 *millilitres* of *water.* Shake vigorously; set aside and separate the chloroformic solution. Repeat the extraction with *chloroform* twice. Mix the three chloroformic solutions, and extract the alkaloids by shaking with three successive portions, each of 10 *millilitres,* of *N/1 solution of sulphuric acid,* transferring the acid solutions to a second separator. Make the acid solutions alkaline with *solution of ammonia,* and again extract the alkaloids by shaking successively with 10, 5, and 5 *millilitres* of *chloroform,* drawing off the chloroformic solutions into a small flask. Remove the chloroform by distillation, dissolve the residue in 15 *millilitres* of *water* containing 3 per cent. by weight of *sulphuric acid,* heat the solution to 50° C., add 3 *millilitres* of a mixture of equal volumes of *nitric acid* and *water,* and set aside for ten minutes. Transfer the solution to a separator, rinsing the flask with a little *water,* make alkaline with *solution of sodium hydroxide,* and extract the alkaloid by shaking successively with 10, 5, and 5 *millilitres* of *chloroform.* Wash the mixed chloroformic solutions in a separator with 5 *millilitres* of *water,* transfer to a tared dish and allow the chloroform to evaporate, adding towards the end 5 *millilitres* of *alcohol* (90 per cent.). Evaporate to dryness, dry the residue at 100° C. and weigh. The weight is the weight in *grammes* of the strychnine contained in 10 *millilitres* of percolate. To the remainder of the percolate add sufficient Alcohol (70 per cent.) to produce a Liquid Extract of Nux Vomica containing in 100 *millilitres* 1.5 *grammes* of strychnine. Examined by the foregoing process Liquid Extract of Nux Vomica is found to contain in 100 *millilitres* 1.5 *grammes* of strychnine. *Limit of error* 0.05 *gramme* in excess or defect. This Liquid Extract contains 1.5 grammes of strychnine in 100 *millilitres;* 110 minims contain 1.5 grains." *Br.*

For *Fluidextractum Nucis Vomicæ,* N. F., see Part III.

Dose, one to three minims (0.06–0.2 cc.).

Off. Prep.—Tinctura Nucis Vomicæ, *Br.;* Extractum Nucis Vomicæ Siccum, *Br.*

EXTRACTUM OPII LIQUIDUM. Br.

LIQUID EXTRACT OF OPIUM

"Liquid Extract of Opium contains in 100 millilitres 0.75 gramme of morphine, calculated as anhydrous." *Br.*

"Dry Extract of Opium, 37.5 *grammes;* Alcohol (90 per cent.), 200.0 *millilitres;* Distilled Water sufficient to produce 1000.0 *millilitres.* Mix the Extract with seven hundred *millilitres* of the Distilled Water; set aside in a cool place for twenty-four hours, stirring frequently; add the Alcohol; set aside again for twenty-four hours; filter; wash the filter with sufficient Distilled Water to produce the required volume." *Br.*

"Examined by the process described under 'Tinctura Opii,' Liquid Extract of Opium is found to contain in 100 millilitres 0.75 gramme of morphine, calculated as anhydrous. *Limit of error* 0.05 gramme in excess or defect. This Liquid Extract contains 0.75 gramme of morphine in 100 millilitres; 110 minims contains 3/4 grain." *Br.*

It is well known that in opium there are principles soluble in alcohol but not in water, which often produce various disagreeable effects not experienced from the aqueous extract; what was wanted was a liquid preparation meeting this demand. All that was required was to make an aqueous solution of solid extract, and to add something to preserve it. The British Pharmacopœia uses alcohol for the purpose, but the spirit constitutes only one-fifth, which is considerably short of the proportion recommended by Squire. In the *Deodorized Tincture of Opium* of the U. S. Pharmacopœia the advantages of the preparation have, we think, been still better secured.

Dose, five to thirty minims (0.3–1.8 cc.).

EXTRACTUM PICRORHIZÆ LIQUIDUM. Br.

LIQUID EXTRACT OF PICRORHIZA

"Picrorhiza, in No. 60 powder, 1000 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Exhaust the Picrorhiza with the Alcohol by the *percolation process.* Reserve the first eight hundred and fifty *millilitres* of the percolate; recover the alcohol from the remainder by distillation; evaporate the residue to a soft extract; dissolve this in the reserved portion; add sufficient of the Alcohol to produce the required volume." *Br.*

This fluidextract was transferred from the British and Colonial Addendum to the British Pharm. (1914). (See *Picrorhiza.*)

Dose, fifteen to sixty minims (0.9–3.75 cc.).

FLUIDEXTRACTUM RHOIS GLABRÆ. U. S.

FLUIDEXTRACT OF RHUS GLABRA Fldext. Rhois. Glab.

Fluidextract of Sumach Berries.

"Rhus Glabra, in coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process B (page 160), using a mixture of 100 cc. of glycerin, 500 cc. of alcohol, and 400 cc. of water as Menstruum I, and diluted alcohol as Menstruum II.

"Alcohol content, by volume, 37 to 43 per cent." *U. S.*

This astringent is most popular as a gargle because of its not unpleasant flavor; it should be diluted with 2 or 3 times its volume of water for this purpose. It is also sometimes employed in diarrhea.

Dose, one to two fluidrachms (4–8 cc.).

FLUIDEXTRACTUM RHEI. U. S.

FLUIDEXTRACT OF RHUBARB Fldext. Rhei

Extrait liquide de Rhubarbe, *Fr.;* Flüssiges Rhabarberextrakt, *G.*

"Rhubarb, in moderately coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process A, using a mixture of 4 volumes of alcohol and 1 volume of water as the menstruum.

"Alcohol content, by volume, 55 to 63 per cent." *U. S.*

The present process affords a fluidextract which thoroughly represents the root, but when mixed with syrups and water, it loses its transparency. An alkali or an alkaline carbonate dissolves this precipitate, but the use of the fluidextract is limited. The British Pharm. (1898) "Liquor Rhei Concentratus" is made with alcohol (20 per cent.) as a menstruum and is one-half the strength of the U. S. fluidextract of rhubarb.

Dose, for an adult, as a purgative, twenty to thirty minims (1.3–1.8 cc.); as a laxative, from five to ten minims (0.3–0.6 cc.).

Off. Prep.—Syrupus Rhei, *U. S.;* Mistura Rhei Alkalina, *N. F.;* Mistura Rhei Composita, *N. F.;* Elixir Catharticæ Compositum; *N. F.*

FLUIDEXTRACTUM ROSÆ. U. S.

FLUIDEXTRACT OF ROSE Fldext. Rosæ

Fluidextract of Red Rose; Extrait liquide de Rose rouge, *Fr.;* Flüssiges Essigrosenblumenblätterextrakt, *G.*

"Red Rose, in moderately coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process B, using a mixture of 100 cc. of glycerin, 500 cc. of alcohol, and 400 cc. of water as Menstruum I, and diluted alcohol as Menstruum II.

"Alcohol content, by volume, 35 to 40 per cent." *U. S.*

This fluidextract is a useful adjuvant and an excellent astringent. It is of a deep red color, with the agreeable flavor of rose. Wm. C. Alpers prefers repercolation for this fluidextract, stating that even a moderate heat imparts an unpleasant odor to the finished product. (*Proc. A. Ph. A.,* 1897, 425.)

Dose, from one to two fluidrachms (3.75–7.5 cc.).

Off. Prep.—Mel Rosæ, *U. S.;* Syrupus Rosæ, *N. F.*

FLUIDEXTRACTUM SARSAPARILLÆ. U. S.

FLUIDEXTRACT OF SARSAPARILLA Fldext. Sarsap.

Extractum Sarsæ Liquidum, *Br.* 1898; Liquid Extract of Sarsaparilla; Liquor Sarsæ; Extrait liquide de Salsepareille, *Fr.;* Flüssiges Sarsaparillaextrakt, *G.*

"Sarsaparilla, in coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process A, using diluted alcohol as the menstruum.

"Alcohol content, by volume, 37 to 42 per cent." *U. S.*

Dose, thirty to sixty minims (1.8–3.75 cc.).

Off. Prep.—Syrupus Sarsaparillæ Compositus, *U. S.*

FLUIDEXTRACTUM SCILLÆ. U. S.

FLUIDEXTRACT OF SQUILL Fldext. Scil.

"Fluidextract of Squill, properly diluted and injected into the ventral lymph sac of a frog, has a minimum systolic dose of not less than 0.00,055 cc. and not more than 0.00,065 cc. of Fluidextract, or the equivalent in Fluidextract of not less than 0.00,000,046 Gm. and not more than 0.00,000,054 Gm. of ouabain, for each gram of body weight of frog." *U. S.*

Extrait liquide de Scille, *Fr.;* Flüssiges Meerzwiebelextrakt, *G.*

"Squill, in coarse powder, 1000 Gm.; Diluted Alcohol; Alcohol; Water; each, a sufficient quantity to make about 1000 cc. Mix 2000 cc. of alcohol with 1000 cc. of water, moisten the squill thoroughly with a sufficient quantity of the mixture, and allow it to macerate for two hours in a tightly-covered container. Then transfer to a percolator, shake it down evenly without packing, and pour on enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding more menstruum composed of 2 volumes of alcohol and 1 volume of water. When the percolate measures 1000 cc., close the lower orifice, and macerate the drug for twelve hours before continuing the percolation. Then collect a second 1000 cc. of percolate, again interrupt the percolation, macerate for twelve hours, and then continue the percolation until the total percolate measures 5000 cc. Recover the alcohol from the percolate at as low a temperature as possible, and then concentrate the residue to a volume measuring 800 cc. When the residue is cold, add slowly, with continuous agitation, 2000 cc. of alcohol, and set the mixture aside in a tightly-stoppered container for twelve hours. Decant the supernatant liquid from the syrupy layer, filter the decanted liquid, and wash the syrupy residue with two portions of 300 cc. each of a mixture of 4 volumes of alcohol and 1 volume of water, passing the washings through the filter into the previously collected alcoholic liquid. Reduce the combined alcoholic liquids to 800 cc. by distillation, assay a portion as directed below, and from the result thus obtained adjust the volume of the finished Fluidextract by the addition of diluted alcohol to conform to the above biological standard.

"**Assay.**—Proceed as directed under *Scilla.* Alcohol content, by volume, 47 to 52 per cent." *U. S.*

Dose, from one to three minims (0.06–0.2 cc.).

Off. Prep.—Syrupus Scillæ Compositus, *U. S.;* Mistura Pectoralis, Stokes, *N. F.*

FLUIDEXTRACTUM SENEGÆ. U. S.

FLUIDEXTRACT OF SENEGA Fldext. Seneg.

Extrait liquide de Polygale de Virginie, Extrait liquide de Sénéca, *Fr.;* Flüssiges Senegaextrakt, *G.*

"Senega, in moderately coarse powder, 1000 Gm.; Ammonia Water; Alcohol; Water; each, a sufficient quantity to make 1000 cc. Moisten the drug with a sufficient quantity of a mixture of 2 volumes of alcohol and 1 volume of water, pack it in a cylindrical percolator and add more of the menstruum to saturate the drug and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding more of the same menstruum until the drug is exhausted. Reserve the first 800 cc. of the percolate, and evaporate the remainder to a soft extract; dissolve this in the reserved portion, and then gradually add ammonia water until the product is faintly alkaline and has a slight odor of ammonia. Finally add enough of the menstruum to make the Fluidextract measure 1000 cc.

"Alcohol content, by volume, 45 to 50 per cent." *U. S.*

Formerly, Fluidextract of Senega was very frequently the cause of annoyance to the pharmacist through gelatinization. This was due to the presence of pectinous bodies in the root. The addition of an alkali to the menstruum effectually prevents this, and in this respect the present preparation is a great improvement over the 1890 fluidextract.

For other processes, see *N. R.,* 1883, pp. 195, 196. The British Pharm. (1898) "Liquor Senegæ Concentratus" was made half the strength of the U. S. fluidextract with a menstruum composed of 2 parts of 20 per cent. alcohol and 1 part of 45 per cent. alcohol.

Dose, five to twenty minims (0.3–1.3 cc.).

Off. Prep.—Syrupus Scillæ Compositus, *U. S.;* Syrupus Senegæ, *U. S.;* Mistura Pectoralis, Stokes, *N. F.;* Syrupus Cimicifugæ Compositus, *N. F.*

FLUIDEXTRACTUM SENNÆ. U. S.

FLUIDEXTRACT OF SENNA Fldext. Senn.

Extrait liquide de Séné, *Fr.;* Flüssiges Sennaextrakt, *G.*

"Senna, in coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process A, using a mixture of 1 volume of alcohol and 2 volumes of water as the menstruum, and reserving the first 800 cc. of percolate.

"Alcohol content, by volume, 23 to 27 per cent." *U. S.*

The U. S. P. VIII process provided for the elimination of the griping principles by the previous percolation of the powdered senna with alcohol; diluted alcohol was then used to exhaust the drug of the purgative principles.

This previous treatment of the senna is omitted from the U. S. P. X process and the menstruum was made less alcoholic. The fluidextract is a dark, blackish, thick, and somewhat turbid liquid, with a strong flavor of senna. It is well adapted for exhibition with saline cathartics, such as Epsom salt or cream of tartar, which also obviate its griping. In this case not more than one-half of the full dose of the fluidextract should be given at once.

The British Pharm. (1898) "Liquor Sennæ Concentratus" was more like a concentrated infusion than a fluidextract, but had the same strength of the latter, the menstruum is distilled water; tincture of ginger and alcohol being added.

Dose, from one-half to two fluidrachms (1.8–7.5 cc.), for an adult.

Off. Prep.—Syrupus Sennæ, *U. S.;* Elixir Cascaræ Compositum, *N. F.;* Elixir Catharticum Compositum, *N. F.;* Syrupus Ficorum Compositus, *N. F.;* Syrupus Sennæ Aromaticus, *N. F.*

FLUIDEXTRACTUM UVÆ URSI. U. S.

FLUIDEXTRACT OF UVA URSI Fldext. Uvæ Ursi

Extrait liquide de Busserole, *Fr.;* Flüssiges Bärentraubenblätterextrakt, *G.*

"Uva Ursi, in moderately coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process B, using a mixture of 100 cc. of glycerin, 300 cc. of alcohol, and 500 cc. of water as Menstruum I, and a mixture of 1 volume of alcohol and 2 volumes of water as Menstruum II. Reserve the first 800 cc. of percolate.

"Alcohol content, by volume, 18 to 25 per cent." *U. S.*

This preparation is a dense, almost black, liquid, of a sweet, bitterish, astringent, but not very disagreeable taste.

Dose, from thirty minims to a fluidrachm (1.8–3.75 cc.).

EXTRACTUM VIBURNI PRUNIFOLII LIQUIDUM. Br.

LIQUID EXTRACT OF BLACK HAW

Fluidextractum Viburni Prunifolii, *U. S. IX;* Fluidextract of Viburnum Prunifolium; Black Haw; Extrait liquide de Viburne, *Fr.;* Flüssiges Viburnumextrakt, *G.*

"Black Haw, in No. 60 powder, 1000 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Exhaust the Black Haw with the Alcohol by the *percolation process.* Reserve the first eight hundred and fifty *millilitres* of the percolate; recover the alcohol from the remainder by distillation; evaporate the residue to a soft extract; dissolve this in the reserved portion; add sufficient of the Alcohol to produce the required volume." *Br.*

This is a fluidextract which well represents the drug. It is of a dark reddish-brown color.

Dose, from one-half to one fluidrachm (1.8–3.75 cc.).

FLUIDEXTRACTUM ZINGIBERIS. U. S.

FLUIDEXTRACT OF GINGER Fldext. Zingib.

Extrait liquide de Gingembre, *Fr.;* Flüssiges Ingwerextrakt, *G.*

"Ginger, in moderately coarse powder, 1000 Gm. Prepare a Fluidextract by Type Process A, using alcohol as the menstruum.

"Alcohol content, by volume, 78 to 83 per cent." *U. S.*

This fluidextract is a highly concentrated alcoholic solution of the active principles of ginger. It is transparent, and of a reddish color.

Dose, from five to fifteen minims (0.3–1.0 cc.).

Off. Prep.—Syrupus Zingiberis, *U. S.;* Elixir Hydrastis Compositum, *N. F.*

FŒNICULUM. N. F. (Br.)

FENNEL Fœnic. [Fennel Seed]

"Fennell is the dried, ripe fruit of cultivated varieties of *Foeniculum vulgare* Miller (Fam. *Umbelliferæ*). Fennel contains not more than 4 per cent. of foreign organic matter." *N. F.*

"Fennel Fruit is the ripe fruit of Fœniculum vulgare, *Mill.*, collected from cultivated plants, and dried." *Br.*

Fœniculi Fructus, *Br.;* Semen Fœniculi, Fennel Fruit (Seed), Sweet Fennel Fruit; Fenouil doux (Fruit), *Fr. Cod.;* Fruits (Semences) de Fenouil, *Fr.;* Fructus Fœniculi, *P. G.;* Fenchel, Fenchelsamen, *G.;* Finocchio, *It.;* Hinojo, *Sp.*

The plant producing fennel seed was attached by Linnæus to the genus *Anethum,* but was separated from it by De Candolle, and placed, with three or four others, in a new genus styled *Fœniculum,* which has been generally adopted by botanists. The *Anethum Fœniculum* of Linnæus embraced two varieties, the *common* or *wild fennel,* and the *sweet fennel,* the latter being the plant usually cultivated in the gardens of Europe. These are considered by De Candolle as distinct species, and named respectively *Fœniculum vulgare* and *Fœniculum dulce,* but the correctness of the opinion of the great Swedish botanist is now generally admitted.

Fœniculum vulgare is a stout, glabrous biennial or perennial, aromatic herb 3 to 5 feet tall with pinnately decompound leaves having numerous filiform terminal segments. The small yellow flowers are in large, flat, terminal compound umbels, with from thirteen to twenty rays, and destitute both of general and partial involucres. The corolla consists of five petals, which, as well as the stamens, are golden yellow. The fruit is ovate, and of a dark color, especially in the grooves. The plant is a native of Southern Europe, growing wild upon sandy and chalky ground throughout the continent, and is also abundant in Asia, possibly extending as far as China. It is extensively cultivated in Europe as well as in this country. It has escaped from gardens and is somewhat naturalized in Maryland and Virginia. In India, fennel is said to be obtained from *F. panmorium* DC., which is probably, however, only a variety of the official plant. Sicilian fennel or *Carosella* is the fruit of *F. piperitum* DC. (*F. vulgare* var. *piperitum* Hart.). Its young tender stems enclosed in the sheathing leaf stalks are eaten raw by the natives of Southern Italy and Sicily.

F. dulce De Cand., *Sweet Fennel,* bears a general resemblance to *F. vulgare,* but differs in having its stem somewhat compressed at the base, its radical leaves somewhat distichous, and the number of rays in the umbel only from 6 to 8. It is also a much smaller plant, being only about a foot high; its flowers appear earlier, and its young sweet shoots, or turions, are eaten in Italy boiled or as a salad.

Most of our supply comes from Hamburg, Germany, although Leghorn, Italy and Marseilles, France were also important shipping centers. The drug is imported in bags. German fennel is shipped mostly from Hamburg, Roumanian fennel from Hamburg and Trieste, French fennel mostly from Marseilles, Levant fennel from Trieste, Indian fennel from Bombay and London. The German large fennel is green in color and is the variety usually preferred. The French, Levant, Italian and Indian fennels are yellow. The Roumanian variety is small and green and not highly prized.

The roots of fennel were formerly employed in medicine, but are generally inferior in virtues to the fruit, which is now the only portion recognized by any of the pharmacopœias. It is stated that manufacturers of the oil usually distil the whole plant.

Description and Physical Properties.—"*Unground Fennel.*—Mericarps usually separate, each being broadly elliptical with the commissural surface flattened, more or less curved, from 4 to 15 mm. in length and from 1 to 3.5 mm. in breadth, some having a slender stalk from 2 to 10 mm. in length; dorsal surface convex, yellowish green to grayish brown, with five prominent longitudinal primary ribs and at the summit a short, conical stylopodium; commissural surface with three narrow, light brown longitudinal areas separated by two dark brown or brownish black areas containing oil-tubes. Odor and taste aromatic and characteristic.

"*Structure.*—A pentagonal mericarp, four of the sides being nearly equal and slightly concave, the other or commissural surface being much broader and more or less undulate; cells of the seed-coat closely united with those of the mericarp giving the transverse section two very distinct areas, the inner and larger portion (endosperm) more or less rounded-pentagonal and somewhat reniform, composed of polygonal cells, filled with aleurone grains and a thin protoplasmic layer enclosing a fixed oil; the outer or pericarp layer distinguished by large elliptical oil-tubes with thick, brown walls, the latter occurring singly and alternating with the primary ribs, and two oil-tubes on the dorsal surface, making usually six oil-tubes in all, there sometimes being, however, one or two oil-tubes additional; in the central portion of each of the ribs occurs a nearly circular, fibro-vascular bundle with a few tracheæ and numerous thin-walled, strongly lignified fibers.

"*Powdered Fennel.*—Yellowish brown; colorless, irregular, angular fragments of endosperm, the cells filled with aleurone grains, each containing a rosette of calcium oxalate, 0.002 mm. to 0.005 mm. in diameter; fragments containing yellowish brown oil-tubes, the latter from 0.100 to 0.200 mm. in width; fibers few, strongly lignified and with numerous, oblique, simple pores and occasionally reticulately thickened; tracheæ few, with spiral or annular thickenings; in mounts made with chloral hydrate T.S., numerous globules of a fixed oil separate." *N. F.*

Fennel seeds (half fruits) are officially described in the Br. Pharm. as follows:

"Small, oblong, straight or slightly curved, from three to ten millimetres long, and from two to four millimetres in diameter. Greenish or greenish-brown. Each of the two mericarps with five prominent principal ridges and six large vittæ. Aromatic odor; taste strong, sweet and camphoraceous. Ash not more than 11 per cent." *Br.*

There are ten chief varieties of fennel known in commerce, the fruits differing very much in size and considerably in taste. They are as follows: French (sweet); French (bitter); German; Roumanian; Indian; Russian; Levant; Italian; Persian and Japanese. For histological differences of the different commercial varieties see monograph by Hartwich and Jama in *B. P. G.*, 1909, p. 306. Rosenthaler (*B. P. G.*, 1913, p. 570) has made a pharmacognostical study of a Chinese fennel.

Commercial fennel varies greatly in quality, this being either due to lack of care in harvesting or deliberate adulteration. It may contain sand, dirt, stem tissues, weed seeds, or other material to an extent that amounts to adulteration. The fruits, especially the powder, may be deficient in volatile oil, inferring that they have been partly exhausted. Exhausted or otherwise inferior fennel has been occasionally improved in appearance by the use of a factitious coloring. (See Spaeth, in *Ph. Zentralh.*, 1908, p. 545; and 1913, p. 736.) Bitter fennel (*F. piperitum*) has in some instances been substituted for the true article. It may be distinguished from the latter by its smaller size and bitter taste.

The odor of fennel seed is fragrant, its taste warm, sweet, and agreeably aromatic. It yields its virtues to hot water, but more freely to alcohol. The essential oil may be separated by distillation with water. (See *Oleum Fœniculi.*) From 960 parts of the seed Neumann obtained 20 parts of volatile and 120 of fixed oil.

Uses.—Fennel seed was used by the ancients. It is one of our most grateful aromatics, and in this country is much employed as a carminative, and as a corrigent of other less pleasant medicine, particularly senna and rhubarb. It is recommended for these purposes by the absence of any highly excitant property. An infusion may be prepared by introducing two or three drachms of the seeds into a pint of boiling water. In infants the infusion is frequently employed as an enema for the expulsion of flatus.

Dose, of the bruised or powdered seeds, twenty grains to half a drachm (1.3–2.0 Gm.).

Off. Prep.—Aqua Fœniculi, *U. S.* (from Oil), *Br.;* Infusum Sennæ Compositum, *N. F.;* Pulvis Glycyrrhizæ Compositus, *Br.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloes, *N. F.;* Species Laxativæ, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.*

FRANGULA. N. F.

FRANGULA Frang. [Buckthorn Bark]

"Frangula is the dried bark of *Rhamnus Frangula* Linné (Fam. *Rhamnaceæ*). Frangula contains not more than 2 per cent. of foreign organic matter." *N. F.*

Rhamni Frangulæ Cortex, *Br.* (1865); Frangula Bark; Alder Buckthorn; Ecorce de Bourdaine, Bourgène, *Fr.;* Cortex Frangulæ, *P. G.;* Faulbaumrinde, *G.;* Corteccia di frangola, *It.*

R. Frangula or *Alder Buckthorn* is an erect glabrous shrub from ten to fifteen feet high, without thorns, with broadly ovate, obtuse leaves, the margins being entire or slightly sinuate, the underside sometimes slightly downy, and the rather numerous lateral veins diverging equally almost from the whole length of the midrib. Flowers all hermaphrodite, two or three together in each axil, with the calyx teeth, petals, and stamens in fives. Fruit a dark purple drupe the size of a pea. This plant grows in hedges and bushy places throughout Europe and Russian Asia, except in the far north. It has become established on Long Island, northern New Jersey and in Ontario.

Frangula is collected in the spring and either heated at 37.7° C. for 48 hours or kept one year before being used, so as to render inert the ferment present in the green bark which is claimed to act as a gastro-intestinal irritant. It is packed in bags or bales averaging 100 to 200 lbs. and shipped to this country mainly from Hamburg and Trieste.

It is probable that most of the species of the genus *Rhamnus* have cathartic properties. Articles upon *R. Purshiana* and *R. cathartica* will be found elsewhere. (See *Cascara Sagrada* and *Rhamnus Cathartica.*)

Description and Physical Properties.—"*Unground Frangula.*—In quills varying in length, frequently flattened or crushed; from 0.5 to 1 mm. in thickness; outer surface grayish brown or purplish black, with numerous, prominent, lighter-colored, transverse lenticels and occasional patches of foliaceous lichens bearing small, blackish apothecia; inner surface smooth, orange-brown to dark brown with occasional purplish blotches, longitudinally striate, becoming red when moistened with solutions of the alkalies; fracture short, slightly fibrous in the inner layer. Odor distinctive; taste slightly bitter.

"*Structure.*—Corky layer of about 12 rows, distinctly undulate, the cells containing a reddish brown amorphous content; parenchyma cells of the middle bark, small with numerous rosettes of calcium oxalate and small starch grains; a few partially lignified fibers in the middle bark; inner bark with small groups of bast fibers in narrow tangential rows interrupted by the medullary rays, the latter one to three cells in width and containing starch grains; each group of bast fibers surrounded by a layer of crystal fibers.

"*Powdered Frangula.*—Yellowish brown; numerous fragments of cork tissue; fragments of parenchyma tissue, the cells containing rosettes of calcium oxalate, the latter from 0.010 to 0.025 mm. in diameter; bast fibers with thick yellowish, strongly lignified walls, mostly 0.010 to 0.020 mm. in diameter, a few slightly lignified and up to 0.040 mm. in diameter; crystal fibers with prismatic crystals of calcium oxalate, the latter from 0.007 to 0.015 mm. in length; starch grains from 0.003 to 0.010 mm. in diameter; stone cells absent (distinction from *Rhamnus Purshiana*).

"Add 0.1 Gm. of powdered Frangula to 10 cc. of hot distilled water, shake the mixture occasionally until cold and filter; on the addition of a few drops of ammonia water, the filtrate is colored deep red. Macerate 0.1 Gm. of powdered Frangula with 10 drops of alcohol, boil with 10 cc. of distilled water and filter when cold. Shake this filtrate with 10 cc. of ether; a yellow, ethereal solution separates, and 3 cc. of this ethereal solution, when shaken with 3 cc. of ammonia water, yields a red alkaline solution, which, on being diluted with 20 cc. of distilled water, still possesses a distinct cherry-red color." *N. F.*

As first pointed out by Schrenk (*Am. Drug.,* April, 1887), the bark of *Rhamnus Frangula* can be distinguished from that of *R. Purshiana* (*Cascara Sagrada*) by the absence of the irregular angular sclerenchymatous cells, which in *R. Purshiana* are wedged together in large compact groups, increasing in size and number towards the surface, and causing the short fracture of the outer bark.

Tschirch and Pool (*S. W. P.,* 1908, p. 665) have made a comparative pharmacognostical and chemical study of the barks of *R. Frangula* and *R. Purshiana.* Würffel (*Zeit. Oest. Apoth. Ver.,* 1907, p. 211) and Mitlacher (*Bull. sc. pharmacol.,* 1911, p. 10) report the substitution of Frangula by the bark of an alder (*Alnus glutinosa* Medic). The latter may be detected by not being reddened with solutions of the alkalies. Mitlacher (*Ph. Post,* 1905, p. 751) and Moser (*A. J. P.,* 1909, p. 580) have found that the official Frangula is either admixed with or entirely substituted by the bark of *R. carniolica* A. Kerw. Tunmann (*Ph. Era,* 1916, xlix, 113) has also reported on these substitutions. He states that the *R. carniolica* possesses similar constituents to Frangula and gives the important structural differences between the three barks. E'we (*Proc. A. Ph. A.,* 1914, p. 131) obtained a sample of Frangula which proved to be wild-cherry bark.

It is not certainly known which of the several bodies isolated from frangula bark is the purgative principle. The most important body, *frangulin,* the *rhamnoxanthin* ($C_{20}H_{20}O_{10}$) of Buchner and Binswanger, may be obtained by Phipson's process by macerating the bark for three or four days in carbon disulphide, then permitting the liquid to evaporate, exhausting the residue with alcohol, which leaves the fatty matter behind, evaporating the alcoholic liquid to dryness, and recrystallizing from ether. As thus obtained it is in fine yellow crystals, melting at about 229° C., and subliming in golden-yellow needles. It is insoluble in water, soluble in 160 parts of warm 80 per cent. alcohol, nearly insoluble in cold alcohol, soluble in hot fixed oils, petroleum benzin, and oil of turpentine. It communicates its color to cotton, silk, and wool. Faust (*A. Pharm.,* clxxxvii, 8) first proved the glucosidal character of frangulin by boiling it in alcoholic solution with hydrochloric acid, obtaining glucose and *frangulinic acid,* $C_{14}H_8O_4$ (according to Schwabe, $C_{21}H_{20}O_9$). This forms fine microscopic needles of reddish color, fusing at 248° to 250° C. Liebermann and Waldheim (*B. Chem. G.,* ix, p. 1775) obtained in this decomposition instead of frangulinic acid, emodin, which is a trioxymethyl—anthraquinone (see under *Rheum*); frangulinic acid, on the other hand, would be a dioxyanthraquinone and an isomer of alizarin. Gunton and Biehl (*J. A. Ph. A.,* 1922, xi, 669) have also found that emodin and rhamnose were the decomposition products of frangulin; they state that neither frangulin nor emodin are as actively cathartic as the crude drug. They also report the presence of free emodin and of chrysophanol both free and combined.

E. Amweg has devised a method of separating the glucosides from frangula, cascara and rhubarb by extraction with solvents; he uses, 1, benzene; 2, a mixture of two parts of benzene, and one part of absolute alcohol, and 3, alcohol (60 per cent.). (*Ap. Ztg.,* 1897, 747.) Kubly isolated a crude acid which, when purified, he termed *frangulic acid;* Amweg regards this acid as a decomposition product and calls it *pseudofrangulin,* this when hydrolyzed becomes *pseudoemodin.* The emetic action of green bark is attributed to a hydrolytic ferment, which is destroyed by heating. (*P. J.,* 1898, 24.)

Uses.—In its fresh state this drug is very irritant to the gastro-intestinal mucous membrane, producing, when taken in sufficient quantity, violent catharsis, accompanied by vomiting and much pain. During drying it is said to lose much of its irritant power, and the dried bark is affirmed to resemble rhubarb in its action.

Dose, of frangula, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Fluidextractum Frangulæ, *N. F.;* Elixir Catharticum Compositum (from Fluidextract), *N. F.*

FUCUS. N. F.

FUCUS [Bladderwrack]

"Fucus is the dried thallus of *Fucus vesiculosus* Linné, *Fucus serratus* Linné, *Fucus Nodosus* Linné or *Fucus siliquosus* Linné (Fam. *Fucaceæ*). Fucus contains not more than 3 per cent. of foreign organic matter and yields not more than 4 per cent. of acid-insoluble ash." *N. F.*

Sea-wrack; Kelp-ware; Black-tang; Cutweed; Quercus Marina; Fucus (Varech) vésiculeux, *Fr.;* Blasentang, Seetang, Meeriche, *G.*

This is a common brown alga of the Rockweed group found growing on the rocks in the North Atlantic Ocean or on the banks of inlets and bays thereof, between low and high tide marks. It attaches itself to the rocks or mussels by its expanded foot. On the coasts of Scotland and France it is much used in the preparations of kelp. It is also employed as a manure, and is mixed with the fodder of cattle.

Under the name of *Corsican moss* or *helminthochorton* there was formerly used, as a vermifuge, a mixture of various marine plants.

Bladder-wrack contains a gelatinous substance known as *algin* (*alginic acid*), about 0.1 per cent. of a volatile oil and a small quantity of combined iodine. According to Marchand (*P. J.,* 1884, p. 1011), the proportion of iodine is much smaller than that in various other seaweeds. It is said to contain mannitol in appreciable amounts. Tollens and Rovoir state that 0.8 per cent. of a sugar named *fucose,* $C_6H_{12}O_6$, exists in dried seaweed. Votocek and Potmesil obtained from fucose an alcohol which they named *fucitol.* (*B. P. G.,* 1913, 3653.)

Description and Physical Properties.—"*Unground Fucus.*—Sometimes a meter in length, but usually in shorter pieces, dichotomously branched, brownish black or slightly reddish, usually with a slight, whitish incrustation; flat, smooth, from 0.5 to 4 cm. in width, margin entire or serrate, with or without a stout midrib throughout, along which are irregularly disposed oval or oblong air-vesicles of varying length or which may be absent; apex of thallus occasionally swollen, ovate or elliptical, about 5 mm. in diameter and bearing numerous conceptacles. Odor strongly seaweed-like; taste saline and nauseous.

"*Structure.*—Epidermal cells polygonal in surface view, with colorless walls; hypodermis of about 4 rows of longitudinally elongated mucilaginous cells; remaining tissue consisting of pseudo-parenchyma loosely arranged, much elongated and with large intercellular spaces; sections bearing conceptacles of thallus show spherical cavities up to about 0.625 mm. in diameter, containing either antheriodiophores bearing pyriform antheridia from 0.030 to 0.043 mm. in length and sterile cells, or rounded oogonia up to 0.080 mm. in diameter separated by paraphyses.

"*Powdered Fucus.*—Reddish brown; numerous fragments of epidermal tissue with polygonal cells from 0.012 to 0.025 mm. in length; elongated cells of hypodermis from 0.045 to 0.080 mm. in length, inner tissue in irregular fragments composed of pseudo-parenchyma with thick mucilaginous walls." *N. F.*

Uses.—The charcoal derived from kelp was at one time used, under the name of *Æthiops vegetabilis* or *vegetable ethiops,* in the treatment of *goiter* and *scrofulous swellings.* Bladderwrack is an ingredient in certain nostrums used in the treatment of morbid *obesity.* A. T. Carson affirms, however, that the *Fucus vesiculosus* is largely used in Ireland for fattening pigs, and it is doubtful whether its preparations are capable of reducing human obesity unless given in such doses as to interfere with digestion and injure the health. A possible explanation of the action of bladderwrack in obesity, if it exercise any, is found in the experiments of Hunt and Seidell (*J. P. Ex. T.,* 1910, ii, p. 15), who present evidence indicating that the extract of this plant is a powerful stimulant to the thyroid gland.

Dose, ten to thirty grains (0.6–2 Gm.).

Off. Prep.—Fluidextractum Fuci, *N. F.*

GALANGA. N. F.

GALANGAL. Galang.

"Galangal is the dried rhizome of *Alpinia officinarum* Hance (Fam. *Zingiberaceæ*). Galangal contains not more than 2 per cent. of foreign organic matter and yields not more than 3 per cent. of acid-insoluble ash." *N. F.*

Chinese Ginger; China Root; India Root; Galangal; East India Catarrh Root; Rhizoma Galangæ, *P. G.;* Galgant, *G.*

The Galangas are related both botanically and therapeutically to ginger. Two varieties are described by authors, the *Galanga major* and *Galanga minor,* or *large* and *small galangal.* The large galangal is derived from *Alpinia Galanga* Willd. (*Maranta Galanga* L., *Galanga officinalis* Salisb.). The official drug, the smaller galangal, is the product of a distinct but closely allied plant, *Alpinia officinarum* Hance. This is a reed-like plant growing to a height of about 3 feet, a native of the Island of Hainan off the southern coast of China, where it is also widely cultivated. The rhizome is dug up in the fall, washed, cut into pieces and dried. Galangal has recently been shipped to the United States in burlap bags from Hamburg, Marseilles and London.

Description and Physical Properties.—"*Unground Galangal.*—Irregularly branched, from 2 to 10 cm. long and from 1 to 2 cm. thick, the branches thinner toward the base; marked with the fine annuli of the leaf bases, which are from 3 to 10 mm. apart and of lighter color than the general surface; externally reddish or rusty-brown; internally of a lighter orange-brown; cut ends of the branches circular and expanded; fracture fibrous. Odor aromatic and agreeable; taste hot and spicy, resembling ginger.

"*Structure.*—An epidermis of cells polygonal in surface view, with thin, nearly colorless walls, some of the cells containing a reddish brown amorphous substance; a wide cortical area composed chiefly of nearly isodiametric, starch-bearing parenchyma and many scattered oil and resin secretion cells, the latter with a yellowish or reddish brown amorphous content; a distinct, narrow endodermis of thin-walled cells, enclosing parenchyma and secretion cells similar to those of the cortex; concentric fibro-vascular bundles numerous, many collateral fibro-vascular bundles throughout the parenchyma and especially along the endodermis.

"*Powdered Galangal.*—Reddish brown; numerous simple starch grains from 0.010 to 0.060 mm. in length, the small grains few in number, the large grains narrow-ellipsoidal, often broadened at one end, truncate, frequently curved, occasionally with a lateral development, lamellæ mostly indistinct, hilum circular or a cleft in the larger end of the grain, sometimes inconspicuous; numerous yellowish oil cells and reddish resin cells; fragments of tracheæ with scalariform or reticulate thickenings or simple pores; thick-walled fibers with oblique pores; lignified tissue absent." *N. F.*

It contains a pungent oil-like principle, *galangol,* a tasteless concrete resin, *kaempferid, galangin* (*dioxyflavanol*) and a small quantity of cineol. The substance called *alpinin* appears to be a mixture of kaempferid and galangin.

Uses.—Galangal is a stimulant aromatic similar in its effects to ginger. It was known to the ancient Greeks and Arabians, and formerly entered into numerous compounds. (*A. J. P.,* xliii.)

Dose, from fifteen to thirty grains (1.0–2.0 Gm.) in substance, and twice as much in infusion.

Off. Prep.—Tinctura Aromatica, *N. F.*

GALEGA. N. F.

GALEGA. Galeg. [European Goat's Rue]

"Galega is the dried flowering herb, *Galega officinalis* Linné (Fam. *Leguminosæ*). Galega contains no stems over 4 mm. in diameter and not more than 3 per cent. of foreign organic matter." *N. F.*

Goat's Rue; Herba Rutæ Caprariæ; Rue de Chèvre, *Fr.;* Geisraute, Pestilenzkraut, *G.*

This is a hardy, bushy, perennial, leguminous herb indigenous to southern Europe and western Asia. It grows to the height of 2 to 3 feet and possesses odd-pinnate leaves with lanceolate leaflets and axillary racemes of small, pea-shaped flowers which vary from purplish-blue in the pure species, to white, rose-colored and lilac in the several varieties. It is native to the south of Europe, and sometimes cultivated in gardens. It is without odor unless bruised, when it emits a disagreeable odor. The crude drug is shipped to this country in burlap bags and bundles chiefly from Leghorn and Marseilles.

Description and Physical Properties.—"*Unground Galega.*—Stem smooth, erect, branched, when entire from 15 to 45 cm. long commonly cut and broken; leaves oddly-pinnate with from 6 to 8 pairs of leaflets; stipules lanceolate, sagittate on one side; leaflets bright green, smooth or slightly hairy, short petioled, lanceolate or ovate-lanceolate, obtuse, slightly mucronate, from 2 to 5 cm. long and from 2 to 6 mm. in width; flowers small, white to violet, in axillary racemes. Odor indistinct; taste mucilaginous, slightly bitter and astringent; it colors the saliva yellowish green.

"*Powdered Galega.*—Light green to yellowish green; many fragments of epidermal tissue of leaf and stem showing narrowly elliptical stomata up to 0.045 mm. in length; numerous somewhat curved or slightly undulate, simple, thick-walled, non-glandular hairs up to 0.600 mm. in length and about 0.018 mm. in diameter at the base; tracheæ with bordered pores, spiral or reticulate markings; numerous crystal fibers with monoclinic prisms of calcium oxalate, the latter from 0.010 to 0.025 mm. in length; numerous fibers with thick, strongly lignified walls and simple pores; fragments of cortical tissue with nearly isodiametric parenchyma, the latter occasionally containing prisms of calcium oxalate; pollen grains smooth spheroidal, from 0.015 to 0.020 mm. in diameter; starch grains somewhat rounded, few or wanting." *N. F.*

It contains a bitter principle and tannin. In 1914 Tanret separated from goat's rue an alkaloid *galegine*, $C_6H_{13}N_3$, which has been further studied by Barger and White (*Bio. Chem. J.*, 1923, xvii, p. 827). They showed it to be a derivative of glycocyanamine.

In medieval times goat's rue was used against the *plague* and other malignant fevers and in the treatment of *snake-bites*, etc. In 1873 Gillet-Damitte, in a communication to the French Academy, stated that this plant when fed to cows would increase the secretion of milk from 35 to 50 per cent.; since that time it has been employed as a galactague with more or less favorable results. Lewis and Carlson (*J. A. M. A.*, 1917, lxviii, 1570) as the result of experimentation on dogs and goats reached the conclusion that it had no effect on the secretion of milk. The root of the indigenous *Tephrosia virginiana* (L.) Pers. (*Galega virginiana* L.) is said to be diaphoretic and anthelmintic.

Dose, one drachm (4 Gm.).

Off. Prep.—Fluidextractum Galegae, *N. F.*

GALLA. U. S., Br.

NUTGALL. Gall.

"Nutgall is the gall from the young twigs of *Quercus infectoria* Olivier and other allied species of *Quercus* (Fam. *Fagaceæ*)." *U. S.* "Galls are excrescences on Quercus infectoria, *Olivier*, resulting from the deposition of the eggs of Cynips gallæ tinctoriæ, *Olivier*." *Br.*

Galls, Aleppo Galls, Smyrna Galls, Syrian Galls; Galla Tinctoria; Galla Quercina; Galle d'Alep, *Fr. Cod.;* Noix de Galle, *Fr.;* Gallæ, *P. G.;* Galläpfel, Gallen, *G.;* Noce di galla, *It.;* Agalla, *Sp.*

Most of the plant outgrowths or excrescences which are known as "galls" are occasioned through the agency of insects. Many of the smaller galls are caused by mites and a few are due to invasion by nematodes and fungi. It is now known that in the case of insect-produced galls two factors are essential to gall formation, *i.e.*, the deposition of an egg in or on a plant tissue capable of growth, and the response of the plant protoplasm to the stimulating action of a secretion exuded by the insect larva. Among insects, the gall-flies belonging to the genus *Cynips* (Fam. *Cynipidæ*, Order *Hymenoptera*) take leading rank as gall-makers. Many of the oaks are attacked by them and the resulting galls, possessing in high degree the astringent constituents of these plants, have been employed for various practical purposes. Galls may occur anywhere on a plant and their form is usually characteristic for each pair of biological agents involved. According to Olivier, the official article is produced mainly on *Quercus infectoria.*

Quercus infectoria, or the so-called *dyer's oak*, is a small tree or shrub, with a crooked stem, seldom exceeding six feet in height. The leaves are petiolate, obtusely toothed, smooth and of a bright-green color on both sides. The acorn is elongated, smooth, two or three times longer than the cup, which is sessile, somewhat downy and scaly. This species of *Quercus* grows, according to Olivier, throughout Asia Minor, from the Archipelago to the confines of Persia. M. Kinnier found it also in Armenia and Kurdistan; Hardwicke observed it growing in the neighborhood of Adwanie, and it probably pervades the middle latitudes of Asia.

The gall originates from the deposited egg of the *Cynips tinctoria* Olivier, a hymenopterous insect or fly, with a fawn-colored body, dark antennæ, and the upper part of its abdomen shining brown. The insect pierces the shoots and young boughs, and deposits its egg in the wound.

It was formerly believed that the tissues of the plant were irritated and their cells caused to proliferate through the puncture produced by the insect's ovipositor, but A. Cosens has thrown new light upon this subject which seems to disprove that theory. It now appears that the larva or young insect, after hatching from the egg, secretes a fluid (probably from its salivary glands) which contains an enzyme that changes the starch in the cells immediately surrounding it into sugar. By increasing the rate of change from starch to sugar, it makes more food available than usual to the growing cells and therefore stimulates the activity of the protoplasm toward greater cell-division. Accordingly, the gall as well as the larva withdraws food from the nutritive zone. As the starch disappears from the cells at the center of the tumor, shrinkage of the cells of this area takes place, resulting in a central cavity. The insect therein passes through the larval and pupal stages and finally, upon becoming an imago or adult fly, escapes by eating its way out, leaving a tubular canal communicating with the central cavity. At the time of development of the adult fly, most of the cells of the gall contain masses of tannin together with a small amount of gallic acid; they are then in the best condition for collection. When collected at this time, they are called, from their dark color, *blue, green* or *black galls.* If gathered after the imago has escaped, the galls are lighter in weight and color, more spongy in texture, and, since the tannin has undergone oxidation to form a water-insoluble product, are practically worthless. Such galls are called *white galls.*

Most of the official galls are collected by the peasants of Asia Minor and Persia, who pursue no systematic method in gathering them. They are then dried in the sun and lose about 50 per cent. in weight. After drying, the product is sold to dealers in the small villages or is bartered for articles of European manufacture. Owing to different degrees of maturity, the galls range in color from black, through green, to white. The black galls contain the greatest amount of tannin and the white contain the smallest quantity. The galls are graded by the exporter. They are exported mainly through Aleppo and Smyrna to Trieste, London, and the United States.

Description and Physical Properties.—"*Unground Nutgall.*—Nearly globular, from 0.8 to 2.5 cm. in diameter, heavy, mostly sinking in water; externally dark olive-green to dark grayish, tuberculated on upper portion; basal portion smooth and contracted into a short stalk; fracture short, horny; internally grayish to dark brown, with a central slightly radiate portion; occasionally with a central cavity connected by a narrow, radial canal to the external surface; odor slight; taste strongly and persistently astringent.

"*Structure.*—The external and largest part of the gall consists of thin-walled parenchyma cells, containing masses of tannin and occasionally rosettes and prisms of calcium oxalate; a middle layer of thick-walled stone cells and an inner layer of thick-walled parenchyma containing starch granules.

"*Powdered Nutgall.*—Brownish-yellow; showing numerous simple and compound starch grains, the simple grains up to 0.030 mm. in size and ellipsoidal, spheroidal, or polygonal in shape; few stone cells with narrow cavities and branched pore-canals; occasionally fragments of spiral and reticulate tracheæ; tannin masses, slowly dissolving in water mounts; monoclinic prisms and rosettes of calcium oxalate, the latter up to 0.040 mm. in diameter." *U. S.*

"Hard, heavy, subglobular, from twelve to eighteen millimeters or more in diameter, tuberculated on the surface, the tubercles and intervening spaces being smooth; dark bluish-green or dark olive-green externally, yellowish or brownish-white within, with a small central cavity. Galls sink in water and exhibit no perforation. No odor; taste intensely astringent." *Br.*

The best are externally of a dark bluish or lead color, sometimes with a greenish tinge, internally whitish or brownish, hard, solid, brittle, with a flinty fracture, a striated texture, and a small spot or cavity in the center, indicating the presence of the undeveloped or decayed insect. Their powder is of a light yellowish-gray. Those of inferior quality are of a lighter color, sometimes reddish or nearly white, of a loose texture, with a large cavity in the center, communicating externally by a small hole through which the fly has escaped.

Galls have a bitter, very astringent taste, and when whole are inodorous or nearly so, but bruised or in powder they have a decided and peculiar though not very strong odor.

Galls owe their medicinal virtues to a tannin, usually known as *gallo-tannic acid,* which appears to exist in the galls, in part, at least, as a glucoside, but one very easily broken up by ferments like pectase, into glucose and *di-gallic acid,* $C_{14}H_{10}O_9$, therefore, extractable from the galls. Galls yield, on an average, from 65 to 77 per cent. of tannin. (See *Acidum Tannicum* and *Acidum Gallicum.*) All the soluble matter of galls is taken up by forty times their weight of boiling water, and the residue is tasteless. Alcohol dissolves seven parts in ten, ether five parts. A saturated decoction deposits upon cooling a copious pale-yellow precipitate. The infusion or tincture affords precipitates with sulphuric and hydrochloric acids and the precipitants of tannic acid. The infusion of galls reddens litmus paper and is rendered orange by nitric acid. Infusion of galls is rendered more permanent by the addition of 10 per cent. of glycerin.

Galls are formed on a number of trees and shrubs, including oaks, rhus, rhododendron, juniper, eucalyptus and sage. Hartwich (*Arch. d. Pharm.,* 1905, p. 584) illustrates these several varieties and discusses their composition. Richter gives minute descriptions of the origin, structural characteristics and microscopical appearance of galls in *Ph. Zentralh.,* 1912, p. 533. Feist and Haun have published (*A. Pharm.,* 1913, ccli, 468) an article on the constitution of the tannin in Turkish and Chinese galls. *Chinese galls* are produced on the leaves of *Rhus semialata* Murray by the deposited ova of an aphis or plant louse. They are irregularly spindle-shaped, often more or less bent, with obtusely pointed protuberances, about two inches long by an inch in diameter at the central thickest part, of an ash color and a soft velvety feel, very light, hollow, with translucent walls about a line in thickness, of a slight odor recalling that of ipecac, and a bitter astringent taste. The Chinese make great use of this product both in dyeing and as a medicine. Chinese galls contain 65 per cent. of tannic acid identical with that of the official galls. An inferior kind of galls is produced in great quantities in England, by the attack of the *Cynips kollari* of Hartig, upon the common English oak; but they have been ascertained to contain little tannic acid, and are of little value.

Kraemer (*Bot. Gaz.,* 1900, p. 275) made a microchemical study of American galls. These closely resemble the Aleppo variety and are formed on *Quercus coccinea* Moench and *Q. imbricaria* Michx. by *Cynips aciculata.* Kraemer found the chemical constituents to vary with the development of the insects. At the chrysalis stage gallic acid is more abundant than when the winged insect is developed. Texas galls are formed on the live oak (*Q. vireus*), California oak balls are formed on *Q. lobata.*

From the so-called gall-wax of certain kinds of galls, M. Nierenstein obtained a nitrogenous constituent, $C_{13}H_{17}O_6N$, which is probably a lævorotatory *galloleucin.* (*Z. P. C.,* 92, 53.)

Uses.—Galls have a powerfully astringent action, but are no longer prescribed internally. Nutgalls may be used externally for the same purposes as tannic acid.

Dose, five to fifteen grains (0.3–0.9 Gm.).

Off. Prep.—Tinctura Gallæ, *N. F.;* Unguentum Gallæ, *U. S., Br.;* Unguentum Gallæ cum Opio, *Br.*

GAMBIR. U. S. (Br.)

GAMBIR [Pale Catechu]

"Gambir is the dried aqueous extract prepared from the leaves and twigs of *Ourouparia Gambir* (Hunter) Baillon (Fam. *Rubiaceæ*). Gambir yields not less than 70 per cent. of water-soluble extractive and not less than 60 per cent. of alcohol-soluble extractive." *U. S.* "Catechu is an extract of the leaves and young shoots of Uncaria Gambier, *Roxb.*" *Br.*

Catechu, *Br.;* Catechu Pallidum, Terra Japonica, Gambier, Cutch; Cachou Clair, Gambir Cubique, *Fr.;* Gelbes Katechu, Gambir-Catechu, *G.;* Catecu, *It., Sp.*

Ourouparia Gambir (Hunter) Baillon (*Uncaria Gambier* Roxb.) is a climbing shrub with slender stems somewhat thickened at the nodes; leaves opposite, stipulate, glabrous, ovate or oblong, entire, rounded at the base, but abruptly attenuated at the summit. The flowers are small and crowded into a dense globular head on a hairy receptacle; the flower heads are borne on long axillary peduncles which bear in the middle a whorl of bracts. At the point where these bracts occur the peduncle breaks after the falling of the inflorescence and the remainder of the peduncle becomes elongated and curved into hooks by means of which the plant climbs. Corolla gamopetalous, trumpet-shaped, tube slender; fruit one inch long, pericarp dry, dehiscing vertically into two valves; seeds very numerous.

It is a native of the Malay Archipelago and is largely cultivated in the islands of Bintang, Singapore, Prince of Wales and in British North Borneo. The gambir is prepared by lopping off the leaves, shoots, and twigs of the plant, chopping them into pieces, and throwing them into a pot filled with boiling water. Upon the exhaustion of the material, the decoction is poured into copper pans, evaporated to a syrupy consistency and cooled. During the cooling process, the liquor is induced to crystallize by the workman who rapidly works a wooden stick up and down in the extract, until a mass the consistency of soft clay is obtained. This mass is finally turned out, and cut into cubes, which are put upon trays and smoke-dried. (See also *P. J.,* 1892, 1003.) This extract, which is known by the native Malays as *pinang* or *siren* was first brought to the attention of the profession by Campbell.

Most of the commercial article is shipped from Singapore to London and Hamburg. The natives of Malay distinguish four different kinds: 1. *Gambir bulat* or *round Gambir,* which occurs in biscuit-like pieces and is mostly used for chewing. 2. *Gambir papan* or *table Gambir* which occurs in yellowish-brown thin tablets and is also used in chewing. 3. *Gambir paku* (*nail* or *finger Gambir*) which occurs in long black sticks resembling licorice extract. 4. *Gambir dutoor* or *cube Gambir.* The latter is the form in which it is usually employed in pharmacy. Gambir is also imported in large blocks, being used in this form for dyeing and tanning. Most of the drug is imported into this country in bags from London.

Good gambir should occur in a hard compact mass, breaking up, when the adhering mat is removed, into distinct cubes of a brownish-black color externally, and a deep mahogany-red with an occasional streak of yellow internally. It should not steam when the mat is opened. From this quality it grades down to a stuff which has been prepared by mixing the material obtained by reboiling the exhausted leaves with various mixtures. This lowest grade is not in cubes, steams when opened, frequently shows large patches of black or dirty blue color, and often has a sour fetid odor; its color varies from black to light-brown. None of the finest varieties of gambir, such as are used by the natives for chewing, occur to any extent in American commerce. Prebble records his examination of a cube gambir of fine appearance which contained a large percentage of starch. (*P. J.,* 1893, 21.)

Description and Physical Properties.—"*Unground Gambir.*—Masses approximately cubical or rectangular, from 20 to 30 mm. in diameter; externally pale grayish-brown to reddish-brown, more or less dull and porous; friable, internally of a light brown or dark gray color; inodorous; taste bitterish and very astringent.

"*Powdered Gambir.*—Light brown; mostly masses of acicular crystals which are branched or interlacing and somewhat refractive of polarized light; starch grains few, single or compound, of variable shapes, from 0.005 mm. to 0.030 mm. in diameter; epidermal fragments and thick-walled, wavy, non-glandular hairs up to 0.350 mm. in length, very few.

"Macerate 1 Gm. of Gambir with 50 cc. of water, and filter: separate portions of this filtrate should give an intense, green color with dilute ferric chloride T.S. and no precipitate with copper sulphate T.S.

"**Assay.**—Proceed as directed under water-soluble extractive, and alcohol-soluble extractive." *U. S.*

Catechu is described in the Br. as follows: "In cubes, sometimes more or less agglutinated, each side measuring about twenty-five millimetres. Dark reddish-brown externally, pale cinnamon-brown internally, porous and friable. When examined under the microscope they are found to consist chiefly of minute acicular crystals. No odor; taste at first bitter and very astringent, but subsequently sweetish. Almost entirely soluble in boiling *water*. Not less than 80 per cent. is soluble in *alcohol* (90 per cent.); the alcoholic solution made strongly alkaline with *solution of sodium hydroxide* and shaken with *petroleum spirit* imparts to the latter a brilliant green fluorescence (distinction from Black Catechu); the residue insoluble in *alcohol* (90 per cent.) exhibits no starch grains when examined under the microscope. Ash not more than 5 per cent.; ash of the powder not more than 8 per cent." *Br.*

The microscopical appearance of gambir is very characteristic and Brumwell (*J. Soc. Chem. Ind.*, 1911, p. 475) illustrates the appearance of commercial specimens. Gambir is light and porous, so that it floats when thrown in water. It is partially soluble in cold water, and almost wholly so in boiling water, which deposits a portion upon cooling.

Nees von Esenbeck found gambir to contain from 36 to 40 per cent. of *catechutannic acid,* also called *catechu red* or *mimotannic acid,* and also from 20 to 30 per cent. of a peculiar principle called *catechuin, catechin,* or *catechuic acid. Catechin,* when perfectly pure, is snow-white, of a silky appearance, crystallizable in fine needles, melting at 217° C., unalterable in the air if dry, fusible by heat, very slightly soluble in cold water, with which it softens and swells up, soluble in boiling water, which deposits it on cooling, and soluble also in alcohol and ether. It very slightly reddens litmus paper, and, though coloring solution of chloride of iron green, and producing with it a grayish-green precipitate, differs from tannic acid in not affecting a solution of gelatin. The very great discordance of different authors as to its formula seems to be explained by some experiments of Etti (*Ann. Ch. Ph.*, clxxxvi, p. 327), who showed that *catechin,* $C_{19}H_{18}O_8$, readily gives at 100° C., or even when kept for some time over sulphuric acid, an anhydride, $C_{38}H_{34}O_{15}$, and at 160° C. a second anhydride, $C_{38}H_{32}O_{14}$, which, mixed in varying proportions, explain the varying results. Gathercoal (*J. A. Ph. A.*, 1924, xiii, 103) reached the conclusion that catechutannic acid, which he found to be present from 45 to 55 per cent., is one of the anhydrides of catechin, which is present to the extent of 30 to 40 per cent. Catechin possesses no acid properties, when heated, however it is converted into catechutannic acid which is similar in its properties to kinotannic acid. *Rubinic* and *japonic* acid are names indefinitely applied to derivatives of catechutannic acid. *Protocatechuic acid,* $C_7H_6O_4$, does not exist in catechu or gambir but is produced when certain tannins, resins or gum resins are heated with potassium hydroxide. *Pyrocatechin* or *catechol,* $C_6H_6O_2$, is a product of the destructive distillation of many tannins or vegetable extracts.

Perkin and Yoshitako (*P. J.*, 1902, p. 530) have made an elaborate investigation of gambir and acacia catechus. They find three catechins, designated respectively as (*a*), (*b*), and (*c*). Catechin (*b*), $C_{15}H_{14}O_6 + 4H_2O$, occurs in air dried, colorless needles, melting at 175° to 177° C., and gives, on fusion with alkali, phloroglucinol, protocatechuic acid, and an acid resembling acetic acid. Catechin (*c*), $C_{15}H_{14}O_6$, air dried, contains no water of crystallization and forms colorless prisms, melting at 235° to 237° C. Catechin (*a*), $C_{15}H_{14}O_6 + 3H_2O$ (or less probably $C_{14}H_{14}O_6 + 3H_2O$), air dried, forms colorless needles, melting at 204° to 205° C.

Enormous quantities of gambir are used both in Europe and America in tanning, calico printing, dyeing, as an ingredient in boiler compounds for preventing the hard scaly incrustation caused by certain kinds of water, and other processes requiring tannic acid.

Vanderkleed and E'we call attention to the fact that the apparent alcohol soluble content of gambir may be unduly raised by the high moisture content of some of the commercial varieties, which they report as containing over 21 per cent. of moisture, all of which would be calculated in the alcohol soluble extractive by the ordinary methods in which no allowance is made for water. (*J. A. Ph. A.*, 1914, 1685.)

Uses.—Gambir is a serviceable remedy in those cases where astringents are indicated. The complaints to which it is best adapted are *diarrhea* dependent on debility or relaxation of the intestinal mucous membrane, and *passive hemorrhages,* particularly from the uterus. A small piece held in the mouth and allowed slowly to dissolve is an excellent remedy in *relaxation of the uvula* and the *troublesome cough* which depends upon it. Applied to *spongy gums,* in the state of powder, it sometimes proves useful.

Dose, from ten grains to half a drachm (0.65–2.0 Gm.).

Off. Prep.—Tinctura Gambir Composita, *U. S. (Br.)*; Tinctura Pectoralis (from Compound Tincture), *N. F.*

GELATINUM. U. S., Br.

GELATIN Gelat.

"A product obtained from animal tissues, such as skin, ligaments, and bones." *U. S.* "Gelatin is the air-dried product obtained by the action of boiling water on animal tissues such as skin, tendons, ligaments, and bones." *Br.*

Gélatine Officinale, *Fr. Cod.;* Grenatine, Colle de Flandre purifiée, *Fr.;* Gelatina alba, *P. G.;* Weisser Leim, Gallerte, *G.;* Gelatina, *Sp.*

The *collagens* are a class of albuminoids abundant in bones, skin, tendons, cartilage and similar tissues of animals. These collagens unite with water at high temperatures, producing the compounds known respectively as glue and gelatin which differ from each other mainly in the character of the raw stock from which they are manufactured and also in the relative amounts of *glutin* and *chondrin* which they contain; glutin being present in higher proportions in glue, to which it imparts its great adhesive power and chondrin giving to gelatin its greater gelatinizing power. The commercial stock from which much edible gelatin is produced is prepared from clean bones by treatment with hydrochloric acid to remove calcium phosphate and is known as *ossein.* Among the commercial varieties of these substances may be mentioned *hide glue* and *bone glue,* which are commercially the most important.

The bones and animal matter from which the best qualities of gelatin are prepared are carefully selected so as to be free from decomposed products and odorous substances. The hot solution of gelatin must be thoroughly clarified if the so-called sparkling gelatin is to be made.

On account of the tendency to decompose during the process of manufacture, it is sometimes the practice to employ preservatives such as sulphurous acid, which, being frequently used in excessive amounts, remain in the finished product as contaminating substances. Sometimes metallic impurities, as lead, copper, zinc, and arsenic, are present from the apparatus or substances used during the manufacture of the gelatin.

After the gelatin solution has been purified by the use of animal charcoal or other appropriate means, it is brought to the proper degree of concentration and is then allowed to solidify or gelatinize. It is now cut up into slabs which are rapidly dried in long, continuous mechanical drying machines where it is supported upon netting to allow free access of the warm, dry air currents which pass over it.

The surface of sheet gelatin is covered with lozenge-shaped marks, due to impressions left by the knotted netting upon which it is dried. Shred gelatin is made by cutting sheet gelatin into very narrow shreds by a shearing-machine. (See *Nat. Drug.,* 1894, 134.) Granulated gelatin is the form in which it usually appears upon the market in the best grades at the present time. *Gelatose* and *paragelatose* are terms used by Dastre and Floresco to define gelatin which has lost its power of "gelatinization" through the action of ferments or microbes, saline solutions, or the prolonged action of boiling water. (*P. J.,* 1895, 454.)

Description and Physical Properties.—"In sheets, flakes, shreds, or as a coarse or fine powder. It is colorless or yellowish, and has a very slight, characteristic odor and taste. When dry it is stable in the air, but when moist or in solution it decomposes. Gelatin is insoluble in cold water, but swells and softens when immersed in it, gradually absorbing from 5 to 10 times its own weight of water. It is soluble in hot water, acetic acid, and in a hot mixture of glycerin and water. It is insoluble in alcohol, chloroform, ether, benzene, carbon disulphide, and in fixed or volatile oils.

"An aqueous solution of Gelatin (1 in 100) yields no precipitate with copper sulphate T.S. or mercuric chloride T.S., but is precipitated by solution of chromium trioxide or trinitrophenol T.S. Even a very dilute solution of Gelatin (1 in 5000) is at once rendered turbid by the addition of tannic acid T.S.

"A hot solution of Gelatin in distilled water (1 in 40) is free from a putrid odor, and is not more than slightly acid to litmus paper. In a layer 2 cm. in thickness the solution is only slightly opalescent and on cooling to 6° C., and standing for several hours, it forms a firm, transparent or translucent jelly. Incinerate 0.5 Gm. of Gelatin: it yields not more than 2 per cent. of ash. Dissolve this ash with the aid of heat in a slight excess of hydrochloric acid and a few drops of nitric acid: the resulting solution diluted with distilled water to 25 cc. meets the requirements of the test for *heavy metals,* page 439. Heat 1.5 Gm. of Gelatin with 30 cc. of hydrochloric acid (1 in 4) in a 150 cc. Erlenmeyer flask on a water bath, and, when the Gelatin has dissolved, add 3 cc. of bromine T.S., and heat on a water bath for thirty minutes, shaking the flask occasionally. Then add 0.5 Gm. of potassium iodide and follow it with 0.5 cc. of a 25 per cent. solution of stannous chloride. Heat the solution for five minutes on a water bath, cool and subject it to the test for *arsenic,* page 428. The stain, if any, is not greater than that produced in a test made with the same quantities of the reagents and 2 cc. of the standard arsenic test solution. Dissolve 20 Gm. of Gelatin in 150 cc. of hot distilled water in a flask having a round bottom and a long neck, add 5 cc. of phosphoric acid and 1 Gm. of sodium bicarbonate, and at once connect the flask with a condenser. Distil 50 cc., receiving the distillate under the surface of 50 cc. of tenth-normal iodine. Acidulate the distillate with a few drops of hydrochloric acid, add 2 cc. of barium chloride T.S., and heat on a water bath until the liquid is nearly colorless. The precipitate of barium sulphate, if any, when filtered, washed and ignited, weighs not more than 0.003 Gm., corresponding to not more than 0.004 per cent. of sulphur dioxide, correction being made for any sulphate which may be present in 50 cc. of the tenth-normal iodine.

"NOTE.—Gelatin to be used for capsules for medicines may contain not more than 0.15 per cent. of sulphur dioxide." *U. S.*

"In almost colorless, translucent sheets or shreds. Insoluble in *alcohol* (90 per cent.) and in *ether;* soluble in *acetic acid.* A solution in hot *water* (1 in 50) is inodorous and solidifies to a jelly on cooling. An aqueous solution yields a precipitate with *solution of tannic acid,* but not with solutions of other acids, or with dilute solution of *alum, solution of lead acetate,* or *T. Sol. of ferric chloride.* Ash not more than 2 per cent." *Br.*

Gelatin is largely used for making *capsules.* Certain medicines are so offensive to the taste, and consequently so likely to cause nausea, that it is highly desirable to administer them in such a way as to prevent their contact with the tongue and palate. Capsules for enclosing dry powders are ovoid in shape and, after being filled with the powder by the pharmacist, are closed by putting upon the open end a rounded gelatin cap and pressing it down tightly. When so-called *soft capsules* are desired, a small quantity of glycerin is introduced into the gelatin mass; this makes the film elastic by preventing its drying completely. Gelatin capsules are now made in enormous quantities by machinery.

Formalized gelatin is but very slightly or not at all affected by the gastric juice, but is slowly dissolved in the intestines. Advantage has been taken of this fact to manufacture capsules for the administration of drugs which it is desirable should not come in contact with the gastric mucous membrane. A special brand of such capsules is on the market under the name of *glutoid capsules.* These are called *enteric capsules.* Scoville (*J. A. Ph. A.*, 1915, p. 1243) recommends that the sealed capsules be immersed in a 1 per cent. aqueous formaldehyde solution for thirty seconds, then dried quickly and allowed to stand two weeks before use. If stronger formaldehyde solutions are used or the time of treatment extended, the capsules become insoluble in the intestines.

Uses.—In 1896 Dastre and Floresco (*C. R. S. B.*, 1896, ii, iii), while engaged in a research of the physical properties of gelatin, made the observation that injection of gelatin greatly accelerated the coagulation of the blood. This observation led to a good deal of experimental study as well as clinical use of gelatin in the treatment of hemorrhage. Although it was abundantly demonstrated that the injection of gelatin, either hypodermically or intravenously, had a marked effect in controlling *hemorrhage* through its effect in hastening clot formation. It was soon found that the difficulty of sterilizing solutions of gelatin greatly limited the clinical value of the treatment. Because of its source, gelatin is very prone to be contaminated with tetanus spores which are, as is well known, highly resistant to heat; and a number of fatal cases of tetanus have followed the subcutaneous injections of gelatin solutions. Although there is some evidence that the use of gelatin by mouth has an effect on the coagulability of the blood, the question has never been definitely settled. The discovery of other clot-accelerating substances (see *Blood,* Part II) in more recent years has led to a great diminution in the use of gelatin for its effects on blood coagulation.

In the milder forms of internal hemorrhages such as certain cases of *hemoptysis* or of *menorrhagia* gelatin feedings may be tried, at least for a time. For this purpose from a half to two ounces (15.5–62 Gm.) of commercial gelatin may be dissolved in four or five times as much water, suitably flavored and seasoned, and allowed to cool; this is eaten in the same manner as ordinary table gelatin. In local hemorrhages, as *epistaxis,* a warm 10 per cent. solution may be applied directly to the bleeding point. It has also been employed in the treatment of *diarrhea* and *mucous colitis* with asserted benefit.

Gelatin chemically belongs to the group of proteins, and under the influence of digestion is converted into amino-acids, which are the form in which protein foods are utilized. It is not capable, however, of furnishing all the protein needs of the body because of the absence of the tyrosin and tryptophane groups in the products of its breaking down. Because of its ease of digestion it is a very valuable accessory food in various disease conditions when the digestive powers are reduced.

Dose, one-half to one ounce (15.5–31 Gm.).

Off. Prep.—Gelatinum Glycerinatum, *U. S.;* Suppositoria Glycerini, *Br.* (Vehicle for lamellæ in Br.)

GELATINUM GLYCERINATUM. U. S.

GLYCERINATED GELATIN Gelat. Glycerin.

Gelatina Glycerinata, Gelatinum Glycerini; Glycerin Jelly; Gelée Glycérinée, *Fr.;* Glycerinleim, *G.*

"Gelatin, 100 Gm.; Glycerin, 100 Gm.; Water, a sufficient quantity to make 200 Gm. Pour upon the gelatin sufficient water, which has been previously boiled and cooled, to cover it, allow it to stand one hour, pour off the water, and allow the gelatin to drain for a few minutes. Then transfer it to a dish, add the glycerin, and heat on a water bath until the gelatin is dissolved. Strain the solution while hot, transfer to a tared dish, and continue the heat on the water bath until the product weighs 200 Gm. When cold, cut the mass into pieces, and preserve in well-closed containers." *U. S.*

Uses.—Glycerinated gelatin is used as a vehicle in making gelatin suppositories, bougies, etc. The National Formulary IV introduced a class of preparations termed "*Glycerogelatins*," to be used in dermatological practice. (See Part III.)

GELSEMIUM. N. F. (Br.)

GELSEMIUM Gelsem. [Yellow Jasmine Root, Yellow Jessamine]

"Gelsemium consists of the dried rhizome and roots of *Gelsemium sempervirens* (Linné) Persoon (Fam. *Loganiaceæ*). Gelsemium contains not more than 2 per cent. of foreign organic matter." *N. F.*

"Gelsemium Root is the dried rhizome and root of Gelsemium nitidum, *Michaux*." *Br.*

Gelsemii Radix, *Br.;* Gelsemium Root, Yellow Jasmine, Yellow Jessamine, Carolina or American Yellow Jessamine, Yellow or Evening Trumpet Flower; Gelsemium, *Fr. Cod.;* Jasmin sauvage, *Fr.;* Gelsemie, Giftjasmin, *G.;* Gelsemio, *Sp*

The *yellow* or *Carolina Jessamine* (*Gelsemium sempervirens*) is one of the most beautiful climbing plants of our Southern States, ascending lofty trees, and forming festoons from one tree to another, and during its flowering season, in the early spring, scenting the atmosphere with its delicious odor. The stem is twining, smooth, and shining; the leaves opposite, nearly persistent, short, petiolate, lanceolate, entire, dark green above, and paler beneath; the flowers in axillary clusters, large, of a deep-yellow color, and fragrant, with a very small, five-leaved calyx, and a funnel-shaped corolla, having a spreading, five-lobed, nearly equal border. The fruit is a flat, 2-loculed, compressed capsule containing flattened seeds. The plant grows in rich, moist soils along the sea-coast from Virginia to the south of Florida and Texas. The flowers are said to be poisonous. The drug is collected in autumn, washed and dried. The commercial supplies come chiefly from Virginia, North and South Carolina and Tennessee. *Gelsemium elegans* Benth., of upper Burma, is an extremely poisonous creeper which contains gelsemine or an allied alkaloid.

This official plant must not be confounded with the true yellow jasmine of Madeira, often planted in the Southern States, which is the *Jasminum odoratissimum* L., which also has very fragrant yellow flowers.

Description and Physical Properties.—"*Unground Gelsemium.*—Rhizome cylindrical, usually in pieces from 3 to 20 cm. in length and from 3 to 30 mm. in diameter; externally light yellowish brown, longitudinally wrinkled, with purplish brown longitudinal lines and transverse fissures; the upper surface with a few stem-scars; fracture tough, splintery, internally light brown or pale yellow, bark thin, wood distinctly radiate, excentric, pith disintegrated. Roots light brown, fracture one-half transverse, the other oblique or splintery. Odor slight; taste bitter.

"*Structure.*—Rhizome with a strong development of cork, the walls being grayish or yellowish brown and more or less lignified; a cortex made up chiefly of parenchyma containing starch and having in the outer portion small scattered groups of stone cells or fibers, and in the inner portion in the region of the medullary rays prisms of calcium oxalate; woody portion made up of broad wedges consisting of large tracheæ and thick-walled tracheids and separated by medullary rays, the cells of which are usually strongly lignified in the xylum but non-lignified in the phlœm and contains starch or prisms of calcium oxalate; an internal phlœm, the cells forming distinct, more or less rounded groups, the latter being partly surrounded by a thin-walled starch-bearing pith.

"*Powdered Gelsemium.*—Dark yellow, tracheæ with bordered pores numerous and conspicuous; spiral tracheæ and bast-fibers few; thick-walled tracheids long and narrow, strongly lignified; starch grains spherical, from 0.004 to 0.012 mm. in diameter; calcium oxalate in monoclinic prisms from 0.015 to 0.032 mm. in length; occasional groups of stone cells or fibers, the walls being very thick, porous and strongly lignified." *N. F.*

"In nearly cylindrical pieces about fifteen centimetres or more long, and usually from six to eighteen millimetres thick; occasionally with fibrous rootlets attached. Fracture splintery. In transverse section, a thin cortex, and a porous, yellowish, distinctly radiate wood with numerous, conspicuous, straight medullary rays. Rhizome usually with a brown or dark brownish-violet cork, often much fissured; nearly straight, and exhibiting silky fibres in the bast. Root yellowish-brown, finely wrinkled, and somewhat tortuous. Slightly aromatic odor; taste bitter." *Br.*

The chief diagnostic feature of gelsemium rhizome is seen in its cross section which shows four masses of internal phloem on the inner face of the xylem zone. For studies of the structure of gelsemium, see *A. J. P.*, 1898, 398; *A. J. P.*, 1899, 422; *D. C.*, 1901, 244; *Merck's Rep.*, 1908, p. 86. Tunmann (*Ph. Zentralh.*, 1907, p. 679) has made a pharmacognostic study of gelsemium and has proposed its identification through the microsublimation of æsculin. Tutin (*P. J.*, Feb. 10, 1912) has shown that the sublimate obtained by Tunmann from gelsemium root must have consisted of scopoletin. Tutin further states that "The detection of scopoletin in gelsemium may prove to be a valuable means of distinguishing this drug from others of a similar appearance, such as that derived from *Gelsemium elegans* Benth., but it is doubtful whether the sublimation method is the most convenient one. If 0.5 gramme of ground gelsemium be heated in a test tube with chloroform, the mixture filtered, and the filtrate shaken with water to which a few drops of dilute ammonia have been added, the aqueous layer, on separation, will be found to show a distinct, blue fluorescence, thus indicating the presence of scopoletin."

Sayre (*A. J. P.*, 1897, 8) found specimens of the rhizome mixed with considerable proportions of the stem. The latter differs microscopically from the rhizome in possessing collenchyma-containing chloroplastids in the outer region of the cortex and sclerenchyma fibers in the pericycle. Ingham (*A. J. P.*, 1897, 234) found that there was not much difference between the root and rhizome in alkaloidal value, but the stem does not appear to contain either gelsemine or gelsemic acid. (See also *A. J. P.*, 1897, 140.) Gelsemium yields its virtues to water, and readily to diluted alcohol.

Constituents.—In 1855 Henry Kollock found in gelsemium gum, starch, pectic acid, albumen, gallic acid, fixed oil, a fatty resin, a dry acrid resin, yellow coloring matter, volatile oil, extractive, lignin, a peculiar alkaloid called *gelsemine*, and mineral salts. The alkaloid, however, was not obtained sufficiently pure to admit of a full investigation of its properties. Theo G. Wormley (*A. J. P.*, 1870) obtained pure gelsemine from the root and a peculiar acid, which he called *gelseminic* (*gelsemic*) *acid*.

Wormley obtained the acid by acidulating a concentrated aqueous solution of the drug and extracting with ether. (For details of his method, see *U. S. D.*, 19th ed., p. 578.) The acid, when pure, is colorless, inodorous, almost tasteless, and readily crystallizable, usually in groups or tufts of fine needles. The action of concentrated nitric acid upon gelsemic acid or any of its salts, produces a yellow, reddish, or red solution, which, if treated with ammonia in excess, becomes of a deep blood-red color, lasting for hours. The one-thousandth of a grain will exhibit these changes. Potassium, sodium, or ammonium hydroxide, added to the acid, cause it to become intensely yellow, and form with it highly fluorescent solutions. The acid is fusible, and, at a high heat, volatilizable without change. Robbins (*B. Chem. G.*, 1876, 1182) stated that it was identical with æsculin (the glucoside of the horse-chestnut), and gave it the formula $C_{15}H_{16}O_9 + 1\frac{1}{2}H_2O$. But Coblentz (*Proc. A. Ph. A.*, 1897, 225) showed that it differs from æsculin in several particulars, and gave for its formula $C_{13}H_{11}O_5$, which melts at 206° C. E. Schmidt believes that Wormley's gelsemic acid is identical with *scopoletin* derived from scopola root, and gives the name as *β-methylæsculin*, $C_9H_5(CH_3)O_4$.

Gelsemine as obtained by Wormley is a brittle, transparent solid, crystallizing with difficulty from alcohol. Boiling water sparingly dissolves it. It softens at 38° C., and fuses at 45° C. The pure base gives no color reaction with strong nitric acid, and the mixture is scarcely changed in color by heating. Strong sulphuric acid has no apparent action upon it; but if to the mixture a little manganic oxide be added and then rubbed with a glass rod, a deep crimson-red is obtained, passing to green. This reaction is so delicate that it can be demonstrated with a solution of 1 in 100,000. If this reaction be performed upon the pure alkaloid, the color may be sufficiently intense to cause it to be mistaken for strychnine, but if a parallel experiment be carried on with strychnine, the two alkaloids cannot be mistaken, for the strychnine gives an intense purple, passing to red. It was probably not a pure substance. Moore (*Tr. Chem. Soc.*, 1910, xcvii; 1911, xcix) gives the formula as $C_{20}H_{22}O_2N_2$. He also confirms the presence of a second alkaloid *gelseminine*, originally announced by F. A. Thompson (*Ph. Era*, 1887, p. 3).

Sayre (*J. A. Ph. A.*, 1912, p. 458; 1913, p. 436; 1914, p. 314, and 1915, p. 60) has found two alkaloids differing in physiological activity and color reactions, the one of which he called gelseminine (the former name for the combination of the two), and the other *gelsemoidine*, which was later changed to *sempervirine*. This latter alkaloid is similar in some of its properties to cinchonamine, particularly in the matter of the insolubility of its salts in water. Sayre also calls attention to the fact that the alkaloid commercially supplied under the name gelseminine is usually the crystalline alkaloid gelsemine. He states that the principles obtained by him show the following color reactions with sulphuric acid and manganic oxide: *Gelsemine*, at first crimson, then green, and finally yellow; *gelseminine*, at first brown, then pink, and finally yellow; *gelsemoidine*, at first purple and finally blue.

Uses.—According to the researches of Cushny (*A. E. P. P.*, 1892, xxxi, 49) gelseminine is so much more powerful than gelsemine that it is improbable that the latter alkaloid plays any part in the effect of the whole drug in mammals. Gelseminine is a depressant to the centers in the spinal cord and, in large doses, also paralyzes the peripheral motor nerves. Gelsemine acts, in the frog, much like strychnine, causing convulsions, by stimulating the spinal cord, which are followed by paralysis due to an effect on the motor nerves. In toxic quantities gelsemium lowers the blood pressure, probably by a direct action on the heart, but death is usually brought about through respiratory failure. When locally applied, or if given internally in poisonous dose, it causes dilatation of the pupil with loss of accommodation.

Formerly gelsemium was used as an arterial sedative and febrifuge in various sthenic *fevers*, but is probably useless for this purpose. Bartholow (*Pract.*, 1870) has recommended it in spasmodic disorders, as *asthma* and *whooping cough*. It is, at present, rarely used except in the treatment of *neuralgias*, especially those involving the facial nerves. The mode of its action in these cases is obscure, but there is considerable clinical evidence of its utility.

Toxicology.—The symptoms of gelsemium poisoning are: dizziness, dimness of vision, dilated pupil, general muscular debility, and universal prostration, reducing the frequency and force of the pulse, and the frequency of respiration. After very pronounced poisonous doses the symptoms which have just been enumerated are intensified: double or impaired vision, ptosis, dilated insensible pupils, falling of the lower jaw, loss of power of enunciation, and excessive muscular relaxation are associated with slow, labored breathing, which in some cases is interrupted by violent spells of dyspnea; consciousness is long unimpaired, but is apt to be lost before death, and in rare cases unconsciousness has been present, even although recovery followed. Of the various symptoms of gelsemium poisoning the most characteristic are the dropping of the jaw and the ocular manifestations, combined with general muscular relaxation. The effects usually begin in half an hour, but sometimes almost immediately. According to Wormley, death has occurred at periods which vary from one to seven and a half hours. Twelve minims of the fluidextract are said to have proved fatal to a boy three years old, and thirty-five drops of a tincture of the bark have caused death in one hour and a half. In several instances a drachm of the fluidextract has, under treatment, been recovered from.

The treatment of poisoning by gelsemium should consist in evacuating the stomach, maintaining absolute rest in the horizontal position, keeping up the bodily temperature, if required, by external warmth, and administering spinal and arterial stimulants. We have very little experimental data as to the physiological antidotes to gelsemium. Our general knowledge indicates that ammonia, strychnine, and digitalis given hypodermically should be of service in the treatment of the poisoning. Artificial respiration is of service.

Dose, of gelsemium, one-half to two grains (0.03–0.13 Gm.).

Off. Prep.—Tinctura Gelsemii, *Br., N. F.;* Elixir Sodii Salicylatis Compositum (from Fluidextract), *N. F.;* Fluidextractum Gelsemii, *N. F.*

GENTIANA. U. S. (Br.)

GENTIAN Gentian. [Gentian Root]

"Gentian is the dried rhizome and roots of *Gentiana lutea* Linné (Fam. *Gentianaceæ*). Gentian yields not less than 30 per cent. of water-soluble extractive." *U. S.* "Gentian Root is the dried rhizome and root of Gentiana lutea, *Linn.*" *Br.*

Gentianæ Radix, *Br.;* Yellow Gentian Root, Bitter Root, Fel Root; Gentiane (Racine), *Fr. Cod.;* Racine de Gentiane, Gentiane jaune, *Fr.;* Radix Gentianæ, *P. G.;* Enzianwurzel, Bitterwurzel, Rother Enzian, *G.;* Genziana, *It.;* Genciana (Raiz de), *Sp.*

Gentiana lutea or *Yellow Gentian* is among the most remarkable of the species which compose this genus, both for its beauty and large size. From its perennial rhizome—which is thick, long and branching—an erect, round stem rises to the height of three or four feet, bearing opposite, sessile, ovate, acute, five- to seven-nerved leaves of a bright-green color, and somewhat glaucous. The lower leaves, which spring from the root, are narrowed at their base into the form of a petiole. The flowers are large and beautiful, of a yellow color, and arranged in axillary cymes along the upper part of the stem. The calyx is gamosepalous, membranous, yellowish, and semi-transparent, splitting when the flower opens, and reflected when it is fully expanded; the corolla is rotate, and deeply divided into five or six lanceolate, acute segments; the stamens are five or six, and shorter than the corolla. The fruit is an ovate capsule containing winged seeds. The plant grows among the Apennines, the Alps, the Pyrenees, and in other mountainous or elevated regions of Europe and Asia Minor. It is stated by Bourquelot and Hérissey that in order to develop the deep colored fracture preferred by many druggists the root is frequently submitted to fermentation by heaping it up into a mass which becomes heated. Gentian root which has thus been treated is said to yield 27 per cent. less extractive than does that which has been properly dried.

The crude drug comes to the United States in burlap bags and bales chiefly from Marseilles, Bordeaux and Paris, France and Antwerp and Brussels, Belgium. Hamburg, Trieste and Budapest also ship this drug.

Several other species possess analogous virtues, and are used for similar purposes. The roots of *G. purpurea* L. and *G. punctata* L., inhabiting the same regions as *G. lutea,* and of *G. pannonica* Scopoli, growing in Austria, are said to be often mingled with the official. All of these are usually smaller than the official article, the *G. purpurea* rhizomes, which occasionally are admixed with the official, being crowned with a number of aerial stem bases with scaly remains of leaves attached. The German Pharmacopœia permits the use of the rhizome and roots of these three species. The *G. macrophylla* of Pallas is used in Siberia.

G. quinquefolia L. (*G. quinqueflora* Lam.), growing throughout the northern and northwestern States, is said to be much used in domestic practice. In Europe the rhizome of *G. asclepiadea* L. has been admixed with the official rhizome. According to Vogl, it can be detected by the abundance of lignified prosenchymatous elements and stone cells, the genuine powder containing scarcely any lignified elements other than large reticulated vessels. (*O. Z.,* 1903, 141.)

One indigenous species, *G. Catesbæi* (now *G. Elliottii* Chapm.), growing in the southern States, formerly had a place in the secondary list of the U. S. Pharmacopœia, and is reputed to be but little inferior to the official species. This plant, popularly called *blue gentian,* has a perennial, branching, somewhat fleshy root, and a simple, erect, rough stem, rising eight or ten inches in height, and bearing opposite ovate-lanceolate leaves and pale blue flowers, crowded, nearly sessile, and axillary or terminal. It grows in the grassy swamps from Virginia to Florida, where it flowers from September to December. It may be given in powder in the dose of from fifteen to thirty grains, or in the form of extract, infusion, wine or tincture.

Powdered gentian has been adulterated with ground olive stones, ground peanut shells, and even quassia root. These are all readily detected by means of their lignified tissues, which may be seen through the use of the microscope. Gadd and Gadd assert (*P. J.*, 1905, xxi, p. 439) that adulterations of gentian are most readily detected by means of the microscope, but that good evidence of quality is also furnished by the yield of extract, which should be about 40 per cent.

As found in commerce, gentian is in pieces of various dimensions and shapes, usually of considerable length, consisting sometimes of longitudinal slices, sometimes of the rhizome and root cut transversely.

Description and Physical Properties.—"*Unground Gentian.*—In pieces nearly cylindrical, sometimes branched, from 5 to 40 mm. in thickness; the rhizome portions annulate and the roots longitudinally wrinkled; externally yellowish-brown; brittle when dry, tough and flexible when damp; internally yellowish-brown, with a cortex from 0.5 to 2 mm. in thickness, separated from a spongy wood by a dark brown cambium zone and distinctly radiate in appearance, especially in the region of the cambium; odor strong and characteristic; taste slightly sweetish at first, then strongly and persistently bitter.

"*Structure.*—Cork of 4 to 6 rows of thin-walled cells; secondary cortex of several rows of thick-walled cells; inner bark of many layers of more or less tangentially collapsed parenchyma and numerous sieve bundles and separated from the wood by a distinct cambium ring; medullary rays indistinct; wood rays consisting of a few large tracheæ scattered through an abundance of brown, thin-walled parenchyma.

"*Powdered Gentian.*—Light brown or yellowish-brown and consists chiefly of parenchymatous cells with fragments of scalariform or reticulate tracheæ. Starch grains and calcium oxalate crystals are few or absent. Stone cells and bast- or wood-fibers are absent.

"**Assay.**—Proceed as directed under water-soluble extractive." *U. S.*

"Parenchymatous tissue of rhizome and root abundant, containing small oil globules and minute crystals of calcium oxalate but not more than an occasional starch grain; vessels reticulated; no sclerenchymatous cells or fibres. Characteristic odor; taste at first slightly sweet but afterwards bitter. When 5 grammes of the powdered Root are macerated with 100 millilitres of *water* for twenty-four hours, shaken occasionally and filtered, 10 millilitres of the filtrate yield on evaporation in a flat-bottomed dish not less than 0.165 gramme of residue dried at 100° C. Ash not more than 6 per cent." *Br.*

Constituents.—Kromayer, in 1862, first obtained the bitter principle of gentian in a state of purity, and gave it the name of *gentiopicrin*, and the formula $C_{20}H_{30}O_{12}$. This principle has been found in many other species of the genus *Gentiana* and seems to be a characteristic principle of the genus. It is a glucoside, crystallizing in colorless needles, which readily dissolve in water. It is soluble in 95 per cent. alcohol, but in absolute alcohol only when aided by heat; it does not dissolve in ether. A solution of sodium hydroxide forms with it a yellow solution. Under the influence of diluted acids, gentiopicrin is resolved into glucose and an amorphous yellowish-brown neutral substance named *gentiogenin*. Fresh gentian roots yield about one-tenth per cent. of gentiopicrin. Another constituent is *gentianin* or *gentisin*, $C_{14}H_{10}O_5$. It forms tasteless, yellowish prisms, subliming with partial decomposition at a temperature over 300° C. sparingly soluble in alcohol, and with alkalies yields intensely yellow, crystallizable compounds, easily decomposed by carbon dioxide. Von Kostanecki (*A. J. P.*, 1891, p. 192), by boiling gentisin with hydriodic acid, succeeded in demethylating it, and so obtained *gentisein*, $C_{13}H_8O_5$, which crystallizes with $2H_2O$ in fine straw-colored needles; these become anhydrous at 100° C.

There is a small quantity of tannin in gentian root. (See Patch, *Proc. A. Ph. A.*, 1881.)

Louis Magnes found in the root, when perfectly dried at 100° C., 15 per cent. of reducing sugar. When gentian is macerated in cold water, it undergoes the vinous fermentation, in consequence of the presence of this saccharine principle. From the fermented infusion a spirituous liquor is obtained by distillation, which, though bitter, and having an unpleasant odor, is said to be relished by the Swiss and Tyrolese. A. Meyer (*Ph. Cb.*, May, 1882) obtained a sweet principle, which he called *gentianose*, $C_{16}H_{66}O_{31}$, by precipitation of the filtered juice with alcohol, treatment with ether, and crystallization from alcohol. It does not reduce Fehling's solution. Infusion of gentian is precipitated by tannic acid and the soluble salts of lead, but is compatible with the salts of iron. Pectin, so frequently found in fleshy roots, exists in gentian. (Bourquelot and Hérissey, *Répert de Pharm.*, 1898.) The yellow coloring matter of the root was investigated by E. V. Howell, who concludes that it is quercitrin. Tanret (*P. J.*, lxxvi, p. 87) found two glucosides, *gentiamarin* and *gentiin*. He also states (*B. G. T.*, 1905, p. 730) that in fresh roots the amount of gentiopicrin is about 1.5 per cent., but that it is destroyed in the process of drying so that dried roots contain only 0.1 per cent. Bridel (*J. P. C.*, 1920, xxii, 411) reports that the amount of the principle grows less on keeping.

Uses.—Gentian has been known from the highest antiquity and is said to have derived its name from Gentius, a king of Illyria. Many of the complex preparations handed down from the Greeks and Arabians contain it among their ingredients. The ordinary preparations of gentian are, however, almost without physiological properties except their local effects on the mucous membrane of the alimentary tract. Moorhead (*J. P. Ex. T.*, 1915, vii) has given a scientific rationale for the ancient empirical belief in the bitters, by showing that gentian markedly increased the gastric secretions in cachectic dogs. As a stimulant to gastric digestion gentian is perhaps the most popular of all bitters in the treatment of *atonic dyspepsia, anorexia,* and similar complaints. In overdose it acts as a local irritant and may occasion nausea or vomiting. The porous property of the root causes it to expand with moisture and it has been employed as a substitute for the sponge tent to enlarge strictured passages. According to Tanret (*B. G. T.*, 1905, p. 730) gentiopicrin is highly poisonous to the plasmodium and in doses of twenty to thirty grains (1.3–2.0 Gm.) is a useful remedy in *malarial fevers;* it might be pointed out in this connection that it would require between four and five pounds of dried gentian root to produce one dose of gentiopicrin.

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Extractum Gentianæ, *N. F., Br.;* Fluidextractum Gentianæ, *N. F.;* Infusum Gentianæ Compositum, *Br.;* Tinctura Gentianæ Composita, *U. S., Br.;* Elixir Gentianæ (from Fluidextract), *N. F.;* Elixir Gentianæ et Ferri (from Fluidextract), *N. F.;* Elixir Gentianæ et Ferri Phosphatis (from Fluidextract), *N. F.;* Elixir Gentianæ Glycerinatum (from Fluidextract), *N. F.;* Infusum Gentianæ Compositum, *N. F.;* Pilulæ Antiperiodicæ (from Extract), *N. F.;* Pilulæ Ferri, Quininæ, Aloes et Nucis Vomicæ (from Extract), *N. F.;* Pilulæ Antiperiodicæ sine Aloe (from Extract), *N. F.;* Tinctura Amara, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.;* Tinctura Rhei et Gentianæ, *N. F.*

GERANIUM. N. F.

GERANIUM Geran. [Cranesbill]

"Geranium is the dried rhizome of *Geranium maculatum* Linné (Fam. *Geraniaceæ*). Geranium yields not more than 2 per cent of foreign organic matter." *N. F.*

Spotted or Wild Cranesbill, Storksbill; Alum Root; Racine de Bec-de-Grue tacheté, Racine de Pied-de-Corneille, *Fr;* Fleckstorchschnabelwurzel, *G.*

This indigenous herb differs from the other native species of geranium in having a perennial root stock and also in that its flowers are much larger, being from 1 to 1½ inches in diameter. The petals, which are five in number, are of a rose-purplish color and bearded at their base; the leaves are deeply five parted, the wedge-shaped lobes being irregularly notched. The fruit is a five-celled regma, the persistent 5-cleft style forming a beak-like appendage, whence the popular name of cranesbill. The plant is found throughout the United States in moist woods, thickets, and hedges, and generally in low grounds. It flowers from May to July. The rhizome should be collected in autumn. The commercial supplies of Geranium come mostly from Virginia, North Carolina, Indiana and Michigan.

Description and Physical Properties.—"*Unground Geranium.*—Rhizome cylindraceous, somewhat branched, bent, flattened and strongly tuberculated, from 2.5 to 10 cm. long and from 3 to 15 mm. in diameter; surface marked with root scars and remnant of slender roots, longitudinally wrinkled; externally dark purple-brown; internally light purple-brown; fracture short, non-fibrous, the section shows a thin bark, a distinct cambium, irregular in outline, large central pith, wood indistinct, the fibrovascular bundles few and at unequal distances. Odorless; taste strongly astringent.

"*Structure.*—A more or less irregular cork layer consisting of about 10 rows of tangentially elongated cells, the outer layers with brownish walls and a brownish amorphous content, the inner layers with colorless walls; a layer of about 5 rows of tangentially elongated oval cells; a wide layer of nearly isodiametric parenchyma containing either starch, rosettes of calcium oxalate, or tannin; distinct groups of sieve separated from the central cylinder by a broad, continuous zone of cambium; fibrovascular bundles few, radially arranged with tracheæ and tracheids and narrow medullary rays; very large pith, the cells containing starch or in a few instances rosettes of calcium oxalate.

"*Powdered Geranium.*—Purplish brown; fragments composed of cortical or pith parenchyma containing numerous, smooth, simple, ovate or ellipsoidal starch grains up to 0.035 mm. in length, with the hilum near the larger end, the inner lamellæ concentric about it, the outer excentric, rosettes of calcium oxalate up to 0.120 mm. in diameter, occasionally up to 0.145 mm. either isolated or contained within the parenchyma; fragment composed of cork cells having brownish walls and a brownish amorphous content; numerous fragments colored bluish black by ammonio-ferric alum T.S.; tracheæ small with spiral or reticulate markings; tracheids with reticulate markings or simple pores; with the exception of the tracheæ and tracheids, lignified tissue is wanting." *N. F.*

The medicinal properties of geranium are due solely to the tannic and gallic acids it contains. Henry Trimble and J. C. Peacock (*A. J. P.*, 1891, p. 265) collected the plant at periods of the year ranging from January to October, and determined the percentage of tannin as calculated for the perfectly dry drug to vary from 9.72 to 27.85 per cent. They also determined that it belonged to the class of tannins analogous to gallo-tannic acid, yielding pyrogallol on heating. They decomposed the tannin by the action of hydrochloric acid, obtaining gallic acid, glucose, and geranium red as products.

Uses.—Geranium is one of our best indigenous astringents, and may be employed for all the purposes to which these medicines are applicable. The absence of unpleasant taste and of other offensive qualities renders it peculiarly serviceable in the case of infants and of persons of very delicate stomach. *Diarrhea, chronic dysentery, cholera infantum* in the later stages, and the various hemorrhages, are the forms of disease in which it is most commonly used and with greatest advantage. As an application to *indolent ulcers,* an injection in *gleet* and *leucorrhea,* and a gargle in *relaxation of the uvula* and *aphthous ulcerations of the throat,* it answers the same purpose as kino, catechu, and other medicines of the same class. It is a popular domestic remedy in various parts of the United States, and is said to have been employed by the Indians.

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Fluidextractum Geranii, *N. F.*

GLUCOSUM. U. S., Br.

GLUCOSE Glucos. [Syrupy Glucose, Liquid Glucose]

"A product obtained by the incomplete hydrolysis of starch, consisting chiefly of dextrose (d-glucose) [$C_6H_{12}O_6$], dextrins and water." *U. S.* "Glucose is a mixture of dextrose and other analogous substances, and is obtained by the hydrolysis of starch." *Br.*

Saccharum amylaceum; Saccharum uveum; Grape-sugar; Starch-sugar; Stärkezucker, Traubenzucker, Glykose, *G.*

The term "glucose" has been rather loosely applied either to chemically pure grape sugar or to a syrupy mixture containing varying amounts of dextrose. In view of the fact that the present Pharmacopœia recognizes a chemically pure sugar under the name of dextrose and the rather indefinite syrupy mixture under the name of glucose and that the medicinal properties of the two substances are quite different, it is very important that a distinction be made in the use of these words. We shall use the term "Glucose" in the Pharmacopœia sense. *Fruit sugar,* or *levulose,* is an isomeric form of glucose, found in honey and in the juice of fruits; an uncrystallizable mixture of dextrose and levulose, called *invert sugar,* is generated from cane sugar by solution in water or weak acids, and boiling. Hence it is present in molasses. An aqueous solution of this sugar, like grape sugar, is susceptible of the vinous fermentation without an intermediate change. In consequence of its effect on polarized light, which is the opposite of that of the cane sugar from which it is prepared, it has been named by the French chemists *invert sugar* (*sucre interverti*). A solution of cane sugar, like that of grape sugar, has a rotating power to the right. When it ferments, it is first changed into uncrystallizable sugar by the invertase of the yeast, according to the reaction:

$$C_{12}H_{22}O_{11} + H_2O = (C_6H_{12}O_6)_2$$

and, as the change proceeds, the rotating power to the right of the cane sugar gradually lessens and disappears, and is replaced by the rotating power to the left of the levulose which remains behind on account of its fermenting more slowly than the dextrose which is simultaneously formed in the process of inversion.

Glucose is the liquid product of the hydrolysis of starch by diluted acids in the presence of moisture and heat. Formerly the conversion was accomplished by the use of sulphuric acid, the excess of which was subsequently removed by neutralization with milk of lime and crystallizing out the difficultly soluble calcium sulphate, enough of which remained in solution, however, to render the detection of glucose in honey or cane sugar syrup indirectly possible by testing for calcium sulphate. (For details, see *U. S. D.,* 19th ed., p. 1071.) The conversion at the present time is accomplished by the use of hydrochloric acid which is ultimately volatilized by raising the temperature in open vessels, so that modern glucose contains no calcium sulphate and the older tests for its detection therefore are not applicable. The straw or amber color of the crude product was formerly removed by bleaching with sulphur dioxide, which sometimes was allowed to remain in the finished product in appreciable amounts. As many state food laws specifically prohibit sulphur dioxide or sulphites in most food products in which glucose was largely used as an ingredient, the modern method of decolorizing it is analogous to that for cane sugar and consists in the use of animal charcoal filters. The composition of commercial glucose varies. Theoretically the reaction is as follows:

$$\underset{\text{Starch}}{C_6H_{10}O_5} + H_2O = \underset{\text{Dextrose}}{C_6H_{12}O_6}.$$

In practice, however, the reaction is much more complex. In the commercial glucose there is present, besides the dextrose which is the predominating constituent, maltose, and dextrin; the latter is the constituent that prevents glucose from crystallizing. Another carbohydrate, which is unfermentable, named *gallisin,* $C_{12}H_{24}O_{10}$, is also present in varying amounts.

Syrupy glucose is also known commercially as *corn syrup,* although a better name would be *starch syrup,* as it is only in the United States, where corn is the cheapest raw material, that it is made exclusively from corn starch. In Germany it is made from potato starch and it certainly would not be proper to term such a product "corn syrup."

On account of the preponderance of dextrose which is a powerful reducing sugar and directly capable of alcoholic fermentation glucose is much used in the industries where these properties are desirable as in brewing and in reducing indigo to its leuco derivative, indigo-white, in the dye vat. It is extensively used as an adulterant in dyewood extracts, sole leather, etc. It is a frequent ingredient in the manufacture of confectionery, jellies, etc. Formerly some discredit attached to its use in food products under the mistaken popular belief that its manufacture was in some way connected with that of glue. The question of its healthfulness is no longer in doubt for when properly made and free from impurities it may be considered as a predigested form of starch.

It is theoretically possible, but not economically practicable at present, to make glucose not only from starch but also from any carbohydrate having the same formula, as cellulose (saw-dust).

Glucose is not so sweet as cane sugar and is more slowly soluble in cold water. Paul (*Chem. Ztg.*, 1921, xlv, 705) gives the sweetening power, as compared to sucrose as unity, of dextrose 0.52, levulose 1.03, lactose 0.28.

Description and Physical Properties.—"A colorless or yellowish, thick, syrupy liquid. It is odorless, or nearly so, and has a sweet taste. Glucose is very soluble in water, but is sparingly soluble in alcohol. Add a few drops of an aqueous solution of Glucose (1 in 20) to 5 cc. of hot alkaline cupric tartrate T.S.; a copious red precipitate of cuprous oxide is produced (*distinction from sucrose*).

"Introduce about 0.5 Gm. of Glucose into a wide-mouthed, tared weighing-bottle, weigh accurately, add 2 cc. of distilled water, evaporate at about 70° C., and dry the residue to constant weight at 90° C.; the loss in weight of the Glucose does not exceed 21 per cent (*water*). Ash: not more than 0.5 per cent. A solution of 5 Gm. of Glucose in 15 cc. of distilled water, mixed with 5 drops of phenolphthalein T.S., requires not more than 0.6 cc. of tenth-normal sodium hydroxide to produce a pink color (*free acid*). Dissolve about 2 Gm. of Glucose in 50 cc. of distilled water, boil the solution for one minute, and cool; the addition of one drop of tenth-normal iodine to this solution produces no blue color (*starch*). On now adding a few drops of starch T.S. to the solution, a blue color is produced (*limit of sulphur dioxide*). An aqueous solution of Glucose meets the requirements of the test for *heavy metals*. If the solution of Glucose is not colorless, comparison must be made with 10 cc. of the same solution, to which a volume of distilled water, equal to that of the hydrogen sulphide T.S. has been added. Dissolve 1.5 Gm. of Glucose in 5 cc. of distilled water, add 5 cc. of diluted sulphuric acid and 1 cc. of bromine T.S., and heat for five minutes on a water bath. Then add 0.5 Gm. of potassium iodide and 5 drops of stannous chloride T.S., cool and test the solution for *arsenic*. The stain, if any, is not greater than that produced in a test made with the same quantities of the reagents and 2 cc. of the standard arsenic test solution." *U. S.*

"A very viscous syrup, almost colorless. No odor; taste sweetish. Freely soluble in *water*, the solution being dextrorotatory and yielding a red precipitate when warmed with *solution of potassio-cupric tartrate.* 2 grammes dried at 100° C. in a thin film in a flat-bottomed dish do not lose more than 0.4 gramme (limit of moisture). When 10 grammes are dissolved in 100 millilitres of *water,* to which 10 millilitres of *N/10 solution of iodine* have previously been added, on shaking the mixture and immediately titrating with *N/10 solution of sodium thiosulphate,* not less than 6.8 millilitres of the latter solution are required for decolorisation (limit of sulphites). *Arsenic limit* 2 parts per million. Ash not more than 0.5 per cent." *Br.*

Uses.—For description of the intravenous uses of glucose see under *Dextrose.* The syrupy glucose is used in medicine for three purposes: First, as a cheap substitute for dextrose for oral or rectal administration; secondly, for its local dehydrating effect, and thirdly, as a pharmaceutical agent. In cases of *gastric ulcer* or other conditions in which it is undesirable to administer food by the stomach, rectal enemata of six to eight fluidounces (180–240 cc.) of a ten per cent. solution of glucose, every four hours, is often of assistance in aiding the maintenance of the nutritive condition. In *acidosis,* especially that type seen after prolonged *anesthesia,* the administration of large amounts of carbohydrates usually exercises a most beneficial action. The administration of glucose immediately before the production of anesthesia has been highly recommended as a preventative for vomiting, especially in children. (See *B. M. J.*, 1911, ii, p. 505.)

According to S. Meslach, glucose, when given in doses of from six to six and a half ounces per day in the form of the concentrated syrup, acts as a powerful diuretic, and is very useful in the treatment of *cardiac dropsy.* If the kidneys be healthy, the glucose is said not to appear in the urine. The celebrated grape cure of Europe is said to act by virtue of the dextrose in the grape.

Locally glucose has been used for its dehydrating effect, especially in the treatment of gun-shot wounds. For this purpose gauze may be saturated with solutions of glucose, either with or without the addition of some antiseptic, and placed over the wounds. It is claimed that this treatment encourages the flow of lymph and thereby tends to diminish the severity of infection. (See *L. L.*, 1915, i, p. 851.) Pharmaceutically glucose is used in solid extracts and other preparations where a uniform, moist consistence is desired, and as a diluent.

Off. Prep.—Used in making extracts U. S. P. and N. F., and in Br. Pharm. for pill masses. Ferri Carbonas Saccharatus, *Br.;* Ferri Phosphas Saccharatus, *Br.;* Mistura Ferri Composita, *Br.;* Syrupus Ferri Iodidi, *Br.;* Syrupus Glucosi, *Br.*

GLUSIDUM. U. S., Br.

GLUSIDE Glusid. [Benzosulphinidum, U. S. P. IX, Saccharin]

"The anhydride [$C_6H_4.CO.SO_2.NH$ 1:2] of ortho-sulphamide-benzoic acid." *U. S.* "Gluside, or benzoic sulphinide, $C_7H_5NSO_3$, the anhydride of orthosulphamidobenzoic acid, may be prepared from toluene." *Br.*

Neo-Saccharin; Glucusimide; Benzoyl-Sulphonicimide; Glukusin; Saccharine, *Fr. Cod.*; Sulfimide Benzoique, Sucre d'Houille, *Fr.*; Saccharinum, *P. G.*; Benzoesauresulfimid, Saccharol, Toluolsuss, Zuckerin, *G.*; Saccarina, *Sp.*

Preparation.—This artificial sweetening substance, which is known commonly as "saccharin," is made from toluene by first forming the ortho-sulphonic acid $C_6H_4\left\{\begin{matrix}SO_3H\\CH_3\end{matrix}\right.$; from this the sulphamide $C_6H_4\left\{\begin{matrix}SO_2NH_2\\CH_3\end{matrix}\right.$; from this, by oxidation, the sulphamide-benzoic acid $C_6H_4\left\{\begin{matrix}SO_2NH_2\\COOH\end{matrix}\right.$, of which the anhydride is the official compound. When dissolved in alkaline hydroxide solutions the salt of the sulphamide-benzoic acid is formed as $C_6H_4\left\{\begin{matrix}SO_2NH_2\\COONa\end{matrix}\right.$. (See *Sodii Benzosulphinidum.*)

Saccharin may be detected in sugar solutions by extracting with ether, evaporating and fusing the residue, which, if saccharin, will melt at about 220° C., and fused with potassium nitrate and sodium carbonate will show sulphuric acid. The weight of $BaSO_4$ obtained in this way from 100 Gm. of material multiplied by 0.785 will give the weight of saccharin extracted.

The aqueous solution of saccharin has a distinctly acid reaction and forms salts. Its most remarkable property is its sweet taste, which is approximately three hundred times more intense than that of sugar. (See Paul, *A. J. P.*, April, 1921.) The commercial product, according to Pope, frequently contains para-sulphamide-benzoic acid, from which impurity it can be freed by recrystallization, acetone being used as the solvent. Hefelman has furnished a process for assaying saccharin. (See *Proc. A. Ph. A.*, 1895, 701.) The difference in melting points of pure saccharin and para-sulphamide-benzoic acid is also used for distinguishing them; the former melts at 220° C. and the latter at 286.5° C. (*Ph. Cb.*, 1896, 279.)

Description and Physical Properties.—"White crystals, or a white, crystalline powder. It is odorless, or has a faint, aromatic odor. Gluside in aqueous solution is from 300 to 500 times sweeter than sucrose. One Gm. of Gluside is soluble in 290 cc. of water and in 31 cc. of alcohol, at 25° C. One Gm. is soluble in about 25 cc. of boiling water. It is slightly soluble in chloroform and in ether, and is easily dissolved by ammonia water, by solutions of alkali hydroxides, and by solutions of alkali bicarbonates with the evolution of carbon dioxide.

"The melting point of Gluside is not below 222° C. Pure Gluside melts at about 228° C. A saturated aqueous solution of Gluside is acid to litmus paper. Dissolve about 0.1 Gm. of Gluside in 5 cc. of an aqueous solution of sodium hydroxide (1 in 10), evaporate the solution to dryness, and gently fuse the residue over a small flame until ammonia is no longer evolved. Allow the residue to cool, dissolve in 20 cc. of distilled water, neutralize the solution with diluted hydrochloric acid, and filter; the addition of a drop of ferric chloride T.S. to the filtrate produces a violet color. Mix about 0.02 Gm. of Gluside with about twice its weight of resorcinol, add 10 drops of sulphuric acid, and heat the mixture over a small flame until it acquires a dark green color. Allow it to cool, add 10 cc. of distilled water, and an excess of sodium hydroxide T.S.; a fluorescent-green liquid results.

"Ash: not more than 0.5 per cent. A solution of 0.2 Gm. of Gluside in 10 cc. of sulphuric acid, kept at a temperature of from 48° to 50° C. on a water bath, develops no darker color than light brown within ten minutes (*readily carbonizable substances*). A solution of 0.2 Gm. of Gluside in 5 cc. of sodium hydroxide T.S. is clear, and, when mixed with 5 cc. of alkaline cupric tartrate T.S., does not deposit cuprous oxide on heating (*glucose, lactose*). Add ferric chloride T.S., drop by drop, to 10 cc. of a hot, saturated aqueous solution of Gluside; no precipitate or violet color appears (*benzoic or salicylic acid*). No odor of ammonia is noticeable on warming 0.5 Gm. of Gluside with about 1 Gm. of magnesium oxide and 10 cc. of distilled water (*ammonium compounds*)." *U. S.*

"A white crystalline powder. Taste in dilute solution, intensely sweet. Soluble in 400 parts of *water*, and in 38 parts of *alcohol* (90 per cent.); soluble also in solutions of alkalies and of alkaline carbonates, the neutral sodium salt being known as 'soluble gluside.' Completely soluble in 12 parts of *acetone*. 1 gramme heated for four hours on a water-bath with 10 millilitres of a mixture of 4 volumes of *sulphuric acid* and 3 volumes of *water* completely dissolves, and when the solution is diluted with an equal volume of *water* and allowed to stand for twenty-four hours no crystals separate. Gently warmed for a short time with *sulphuric acid* no blackening occurs. Ash not more than 0.5 per cent." *Br.*

Commercial saccharin sometimes contains impurities derived from the manufacture. Among these may be found sulphamido-benzoic acids, toluene sulphonamides, etc. P. V. McKil (*J. Soc. Chem. Ind.*, 1921, xl, 150-T) discusses these impurities and the methods for their detection.

Saccharin may be readily estimated in food products, etc., with no danger of emulsification, by the following method: 100 cc. of the liquid under examination are added to 10 to 15 cc. of a 10 per cent. solution of tannic acid, and then lead subacetate solution is added. Filter and acidify an aliquot portion of the filtrate with phosphoric acid and extract by shaking out with a mixture of ether and petroleum ether.

Upon evaporating the ethereal mixture the saccharin is left in a pure state.

Saccharin may be determined quantitatively by the method of Richmond and Hill (*C. D.,* 1918, xc, 851 and 913) which depends upon the liberation of ammonia under specified conditions.

Uses.—Taken internally saccharin is rapidly absorbed and eliminated unchanged through the kidneys. It is almost free from general physiological activities. Mosso and Aducco have given seventy-five grains to a man without sensible effect, and 600 grains to a dog within ten days without any change in the weight, general health or metabolism as indicated by urinalysis. On the other hand it has a slight local irritant action and according to the referee board of the U. S. Bureau of Chemistry, doses of more than 0.3 Gm. per day are liable, if used over periods of time, to impair digestion. The statement sometimes made that it is irritant to the kidneys seems to lack positive confirmation. Its use in medicine is purely as a sweetening agent in those diseases such as *diabetes* and *obesity* where sugar is contraindicated. The assertion that saccharin increases the catalase of the blood has been disproven by Stehle (*J. Bi. Chem.,* 1919, xxxix, 39) and by Becht (*J. P. Ex. T.,* 1920, xvi, 155).

The sweetening power of gluside as compared to sugar has been shown by Paul (*J. Soc. Chem. Ind.,* 1921, xl, 33-R) to vary with the degree of concentration; thus in relatively strong solutions —corresponding to about 10 per cent. of sugar— the sweetening effect of the sodium salt of gluside is about 200 times that of sugar, on dilution the gluside solution retains its sweetness better, so that when compared to a 2 per cent. solution of sugar the soluble gluside has approximately 700 times the sweetening power of sugar. It has also been widely employed in preserves, canned foods, and beverages for the same purpose, but this latter act, according to the decision of the U. S. Department of Agriculture, constitutes adulteration of the food, as it allows the omission of cane sugar.

Dose, three to five grains (0.2–0.32 Gm.).

GLUSIDUM SOLUBILE. U. S.

SOLUBLE GLUSIDE Glusid. Sol. [Sodii Benzosulphinidum, U. S. P. IX, Soluble Saccharin]

“ $C_6H_4.CO.SO_2.NNa.2H_2O$.” *U. S.*

For the chemistry of benzosulphinide, see under *Glusidum.*

This salt may be prepared by the careful neutralization of sodium carbonate solution with benzosulphinide or so-called insoluble saccharin, and subsequent concentration of the solution and crystallization of the salt.

Description and Physical Properties.— “ Colorless crystals or a white, crystalline powder. It is odorless or has a faint, aromatic odor, and an intensely sweet taste even in dilute solutions, being from 300 to 500 times sweeter than sucrose. It is somewhat efflorescent. One Gm. of Soluble Gluside is soluble in 1.2 cc. of water, and in about 50 cc. of alcohol at 25° C.

“ Soluble Gluside responds to the identity tests with ferric chloride and with resorcinol under *Glusidum.* When Soluble Gluside is incinerated, a residue remains consisting chiefly of sodium sulphate, which imparts a yellowish color to a non-luminous flame. On mixing 10 cc. of its aqueous solution (1 in 10) with 1 cc. of hydrochloric acid, a crystalline precipitate of gluside is produced.

“An aqueous solution of Soluble Gluside (1 in 10) is neutral or only slightly alkaline to litmus paper, but produces no red color with phenolphthalein T.S. Add 3 drops of ferric chloride T.S. to 10 cc. of an aqueous solution of Soluble Gluside (1 in 20) previously acidulated with 5 drops of acetic acid; no precipitate or violet color is produced (*benzoate* or *salicylate*). Soluble Gluside complies with the tests for *ammonium compounds, readily carbonizable substances, and for glucose and lactose,* under *Glusidum.*” *U. S.*

Uses.—Sodium benzosulphinide is useful solely as a sweetening agent in those conditions, such as *diabetes, gout, obesity,* etc., in which sugar is objectionable. It has the advantage over the anhydride (see *Benzosulphinidum*) of being more freely soluble.

Dose, one-fourth to three grains (0.016–0.2 Gm.).

GLYCERINUM. U. S., Br.

GLYCERIN Glycerin. [Glycerol]

“ Glycerin contains not less than 95 per cent. of $CH_2OH.CHOH.CH_2OH$.” *U. S.* “ Glycerin, or glycerol, is a trihydric alcohol, $C_3H_5(OH)_3$, associated with a small percentage of water; it is obtained by the hydrolysis of fats and fixed oils by means of alkalies or of superheated steam.” *Br.*

Glycerina, *U. S.* 1870; Glycerine; Glycerine officinale, *Fr. Cod.;* Glycerinum, *P. G.;* Glycerin, Glyceryloxyhydrat, Oelsüss, Scheelesches Süss, *G.;* Glicerina, *It., Sp.*

Glycerin was discovered in 1789 by Scheele, by whom it was called the *sweet principle of oils.* It is produced not only during the saponification of the fats and oils by lead oxide in forming lead plaster, but also during the same process when affected by potassium and sodium hydroxides in the manufacture of soap, the alkalies uniting with the fatty acids and setting the glycerin free. Soap-maker’s waste is an abundant source of glycerin; but when thus obtained it is apt to have more or less odor, which even percolation through animal charcoal does not always remove.

The recovery of glycerin from spent soap lyes is accomplished by treatment with lime or ferrous sulphate and subsequent acidulation, clarification with aluminum sulphate, filtration and concentration in a vacuum still. The crude glycerin thus obtained represents about 90 per cent. of glycerin; it is used for industrial purposes in its crude form or may be purified by distillation.

Glycerin is also prepared by the direct hydrolysis of fat. In the so-called "autoclave method" this is accomplished by heating with zinc oxide and zinc dust under pressure of 6 atmospheres. The "Twitchell method" employs a "reactive" which is formed by treating a mixture of an aromatic compound (such as benzol or naphthalene) and a fatty acid (as stearic) with concentrated sulphuric acid. The compound formed is soluble in both water and oil and possesses marked emulsifying and hydrolizing power. The fat to be decomposed is first treated with sulphuric acid to remove albuminous and pectinous substances, and is then boiled for some time with from 0.4 to 0.5 per cent. of the "reactive." The resulting solution of glycerin in water is treated in succession with barium carbonate, barium hydroxide and ammonium sulphate filtered and evaporated to 28° Baumé. The crude glycerin is purified by distillation (see *Ap. Ztg.*, 1915, p. 500).

In America the purification of glycerin by distillation is frequently accomplished according to Scott's patent in a high vacuum with superheated steam. A new method called "multiple-effect distillation" uses the same current of steam for several stills and condensers. In this method the glycerin is first warmed and then sprayed through steam; the mixed glycerin and water vapors pass into a condenser whose temperature is so regulated that only the glycerin vapor condenses while the water vapor passes to the next still to be again mixed with glycerin. Glycerin is now being made by synthetic processes. A recent English patent starts with propylene which is first converted into dichlor-propane, which subsequently is converted into allyl chloride and then into trichlor-propane, $CH_2Cl.CHCl.CH_2Cl$, which when heated with water to 150° C. splits up into glycerin and water according to the following reaction:

$$\underset{\text{Trichlor-propane}}{CH_2Cl.CHCl.CH_2Cl} + 3H_2O = \underset{\text{Glycerin}}{CH_2OH.CHOH.CH_2OH} + 3HCl.$$

Glycerin is always produced to a limited extent during alcoholic fermentation, the amount of glycerin present in certain liquids produced originally by alcoholic fermentation—as wine, vinegar, etc.—being so constant as to constitute a valuable aid in proving identification or freedom from adulteration. Various attempts have been made to economically recover the glycerin from the waste liquors of distilleries but without practical results as yet, although there is little doubt of its ultimate accomplishment. During the World War the high price of glycerin led to further researches along this line and special methods of controlling and augmenting the glycerin yield during alcoholic fermentation resulted in obtaining yields as high as 21.3 grammes of glycerin for each 100 grammes of sugar taken. It is said that the Germans used one of these fermentation methods for their supply of glycerin at that time. (See *J. I. E. C.*, 1919, xi, 842 and *J. Soc. Chem. Ind.*, 1919.)

Description and Physical Properties.—"A clear, colorless, syrupy liquid, having a sweet taste. It has not more than a slight, characteristic odor which is neither harsh nor disagreeable. When exposed to the air, it absorbs moisture. Glycerin is miscible with water and with alcohol. It is insoluble in chloroform, ether, benzene, petroleum benzin, carbon disulphide, and in fixed or volatile oils. Heat a few drops of Glycerin with about 0.5 Gm. of potassium bisulphate: pungent vapors of acrolein are evolved.

"Glycerin is colorless when viewed transversely in a tube of colorless glass about 30 mm. in diameter, held in a vertical position. Specific gravity: not below 1.249 at 25° C. An aqueous solution of Glycerin (1 in 20) is neutral to litmus paper. Heat 50 Gm. of Glycerin in an open, shallow, 100 cc. porcelain dish until it ignites, and allow it to burn without further application of heat in a place free from draught: not more than 0.015 per cent. of carbonaceous and mineral residue remains. Ignite this residue at a low red heat, until combustion is complete: not more than 0.007 per cent. of mineral residue remains. Place 5 cc. of Glycerin in a 50 cc. glass-stoppered cylinder, add 5 cc. of sulphuric acid, and shake vigorously for one minute: the liquid does not become darker than yellow on standing for one hour (*readily carbonizable substances*). Mix 50 Gm. of Glycerin with 50 cc. of freshly boiled distilled water and 5 cc. of half-normal sodium hydroxide, boil the mixture for five minutes, cool, and titrate the excess of alkali with half-normal hydrochloric acid, using phenolphthalein T.S. as indicator: not less than 4 cc. of half-normal hydrochloric acid is required (*fatty acids and esters*). Ten cc. portions of an aqueous solution of Glycerin (1 in 10) remain clear on the addition of 0.5 cc. of calcium chloride T.S. (*oxalate*), or of 0.5 cc. of silver nitrate T.S. (*chloride*), and no turbidity is produced in 10 cc. of the solution, previously treated with three drops of dilute hydrochloric acid, by the addition of five drops of barium chloride T.S. (*sulphate*). An aqueous solution of Glycerin meets the requirements of the test for *heavy metals,* and the test for *arsenic.* A mixture of 5 cc. of Glycerin and 5 cc. of an aqueous solution of potassium hydroxide (1 in 10) does not become yellow when kept for five minutes at 60° C. (*acrolein, glucose*) or emit an odor of ammonia (*ammonium compounds*).

"Preserve in well-closed containers." *U. S.*

"A clear, colorless, hygroscopic, syrupy liquid. No odor; taste sweet, followed by a sensation of warmth. Miscible with *water,* and with *alcohol* (90 per cent.). Insoluble in *ether,* in *chloroform,* and in fixed oils. Specific gravity 1.260. When strongly heated decomposes with evolution of irritating vapors. Neutral to *litmus.* An aqueous solution (1 in 10) yields no characteristic *reactions* for ammonium, chlorides, or sulphates. Assumes, when heated, not more than a faint yellow but no pink coloration, and yields not more than a very slight charred residue and no odor of burnt sugar (absence of sugar). Undergoes no darkening in color when mixed with an equal volume of *solution of ammonia* and a few drops of *solution of silver nitrate,* the mixture being kept protected from light and the observation being made after a lapse of five minutes (absence of formic acid, acrolein). Gently warmed with an equal volume of *diluted sulphuric acid,* the mixture being vigorously shaken, not more than a faint odor is noticeable (absence of fatty acids). Shaken with an equal volume of *sulphuric acid,* the mixture being kept cool, not more than a very slight straw coloration is produced (absence of extraneous organic matter). A mixture of 10 millilitres of Glycerin with 40 millilitres of *water,* 1 drop of *solution of ammonia,* and 1 drop of *solution of tannic acid,* assumes not more than a faint and transient pink or purple coloration (limit of iron). When tested for lead according to the quantitative test described in Appendix V, but using 10 grammes in each Nessler glass, no difference is observed upon the addition of the *solution of sodium sulphide* to one of the solutions (absence of lead). When the foregoing test is repeated, but omitting the addition of *solution of ammonia* and of *solution of potassium cyanide,* and adding to each solution 1 millilitre of *diluted hydrochloric acid,* no difference in color is observed upon the addition of *solution of hydrogen sulphide* to one of the solutions (absence of copper). *Arsenic limit* 4 parts per million. No appreciable ash." *Br.*

When exposed to the air glycerin gradually absorbs moisture. As already stated, though decomposed by a high heat in its unmixed state, yet with water under pressure it is volatilizable unchanged at a temperature between 204.4° and 260° C. Cooled down rapidly, it only becomes more viscid, without congealing, even when a temperature of –40° C. is attained; but, if kept for some time at a temperature of about 0° C., it gradually forms hard but deliquescent crystals, which melt only at about 22° C. This fact is now utilized as a means of concentrating and purifying glycerin.

According to G. F. Wilson, glycerin, when of the density 1.24, contains 94 per cent. of anhydrous glycerin; when of the density 1.26, 98 per cent. A table by Wilhelm Lenz (*Zeit. An. Chem.,* 1880), showing the percentage of absolute glycerin in mixtures of glycerin and water, which was obtained by a quantitative determination of the carbon in the various dilutions by ultimate analysis, will be found in the U. S. D., 15th ed., p. 712. The table below, by W. W. J. Nicol of England, has been constructed after careful determinations, aided by A. B. Lyons's data on expansion of glycerin solutions. (*Ph. Era,* 1888.)

Per cent. Glycerin.	Sp. Gr. at 15° C.=59° F.	Per cent. Glycerin.	Sp. Gr. at 15° C.=59° F.	Per cent. Glycerin.	Sp. Gr. at 15° C.=59° F.	Per cent. Glycerin.	Sp. Gr. at 15° C.=59° F.
1	1.00236	26	1.06500	51	1.13265	76	1.20131
2	1.00473	27	1.06765	52	1.13539	77	1.20404
3	1.00711	28	1.07031	53	1.13814	78	1.20677
4	1.00949	29	1.07297	54	1.14088	79	1.20949
5	1.01189	30	1.07564	55	1.14362	80	1.21221
6	1.01430	31	1.07832	56	1.14637	81	1.21493
7	1.01673	32	1.08100	57	1.14912	82	1.21766
8	1.01917	33	1.08370	58	1.15187	83	1.22038
9	1.02163	34	1.08639	59	1.15462	84	1.22310
10	1.02409	35	1.08908	60	1.15737	85	1.22583
11	1.02656	36	1.09176	61	1.16011	86	1.22855
12	1.02904	37	1.09445	62	1.16286	87	1.23128
13	1.03153	38	1.09713	63	1.16561	88	1.23400
14	1.03403	39	1.09983	64	1.16837	89	1.23673
15	1.03653	40	1.10253	65	1.17113	90	1.23945
16	1.03905	41	1.10525	66	1.17387	91	1.24217
17	1.04160	42	1.10798	67	1.17662	92	1.24487
18	1.04416	43	1.11071	68	1.17937	93	1.24756
19	1.04672	44	1.11345	69	1.18212	94	1.25021
20	1.04930	45	1.11618	70	1.18487	95	1.25285
21	1.05189	46	1.11893	71	1.18761	96	1.25547
22	1.05449	47	1.12167	72	1.19035	97	1.25809
23	1.05712	48	1.12441	73	1.19309	98	1.26072
24	1.05973	49	1.12716	74	1.19583	99	1.26335
25	1.06236	50	1.12990	75	1.19857	100	1.26596

Glycerin has been formed artificially from tribromallyl, by Wurtz, and from trichlorhydrin, by Friedel and Silva.

Glycerin possesses extensive powers as a solvent, and is an excellent excipient for many medicinal substances. It dissolves bromine and iodine, sulphur iodide, potassium and sodium chlorides, the fixed alkalies, some of the alkaline earths (it increases the solubility of lime in water), and a large number of neutral salts. It is a good solvent of pepsin, and is used for the extraction of this principle from the mucus of the stomach. Glycerin, next to alcohol, is the best solvent of iodine. Iodine and potassium iodide, when dissolved in it, form *iodized glycerin,* the medicinal applications of which are given under iodine. (See *Iodum.*) It combines with a number of alkalies, and also with sulphuric acid.

Glycerin does not evaporate rapidly when exposed to the air, although it vaporizes to such an extent as to make it necessary to avoid a water-bath temperature to the concentrated article during its quantitative estimation. It can not be distilled without decomposition, unless in the presence of water or steam. When decomposed by heat, it emits extremely irritating vapors of acrolein. At a full red heat it takes fire, and burns with a blue flame. In consequence of the high temperature required for its volatilization, it has been proposed to use it for an evaporating bath, in which a heat beyond that of boiling water is required.

The solvent properties as well as agreeable taste and permanent consistence of glycerin render it very useful as a menstruum in pharmacy, and a class of preparations consisting of medicinal substances dissolved in it has come into extensive use. The British Pharm. (1885) adopted such a class, under the name of *Glycerina,* or *glycerins.* The title "glycerines" is not now available because the termination "ine" is reserved for alkaloids, while the term *glyceroles,* adopted from the French, is objectionable, as the termination "ole" has been used to designate certain proximate principles; but the U. S. Pharmacopœia title, *Glycerita,* or *glycerites,* is satisfactory. (See *Glycerita.*) G. M. Beringer proposed a class of preparations made with glycerin. (See *Fluidglycerates,* in the National Formulary.)

Impurities and Tests.—Glycerin is occasionally deficient in density and consistency. According to Dalpiaz, it is sometimes perfectly colorless from being bleached by chlorine, when it is apt to contain calcium chloride, as well as free chlorine. The latter may be detected by rendering the suspected sample slightly blue by a few drops of an acid solution of indigo in sulphuric acid, when, if free chlorine be present the blue color will disappear. Starch paste containing a little potassium iodide is a better test, however; if a blue color appears when this is added to glycerin, free chlorine is indicated. (See U. S. P. and Br. tests.)

Glycerin, on account of its high price during the World War, was substituted industrially by a number of cheaper products, among which was a commercial invert sugar of about the same consistency as glycerin, but slightly higher in specific gravity. (Jos. Feil, *J. A. Ph. A.,* 1914, 1648.)

One of the more recent substitutes for glycerin is ethylene glycol, $(CH_2OH)_2$, which resembles glycerin more closely than any other substance that has been proposed. *Glycol* is prepared from acetylene. It is more volatile and less viscous than glycerin; boiling point, 197°; density at 0° C., 1.125; index of refraction at 20° C., 1.4723. The solubility in water, alcohol, and ether is perfectly analogous to that of glycerin. The Denigès reaction (heating with bromine water, addition, after cooling, of condensed sulphuric acid and a 50 per cent. guaiacol solution, blue coloration, violet in heating) gives a positive result with glycerin and glycol, but the latter does not give the Neuberg-Mendel reaction (boiling with a slightly alkaline hypochlorite solution, addition of olein and hydrochloric acid, boiling to violet or green coloration). The two substances can also be distinguished by the index of refraction. When this constant is less than 1.428 the material is surely glycol, and when more than 1.464, glycerin. (*Chem. News,* 1921, cxxii, 239.)

In the quantitative determination of glycerin when in a state of purity, the specific gravity test is important. In crude glycerin and in other products where it may only exist in small amounts, various processes are in use. One of the best known of these is the Hehner, Richardson, Jaffe, method, which depends upon the oxidation of potassium dichromate; or it may be determined by its acetylization with acetic anhydride, the so-called acetin method.

The official method of the A. O. A. C. given in Bulletin No. 107, of the Bureau of Chemistry of the U. S. Department of Agriculture, is used for the determination of glycerin in wines, etc. Leroy Forman (*J. A. Ph. A.,* 1914, 1644) shows this method to give low results when applied to the analysis of tablets, confections, etc. He overcomes this difficulty by the use of milk of lime during the evaporation.

Uses.—Glycerin is valuable as a vehicle not only because of the solvent properties, but because of its sweetness, having the great advantage over syrup of non-fermentability. It has been recommended as a preservative for galenicals in which alcohol is undesirable, but its antiseptic action is so slight that its usefulness for this purpose is very questionable. Ruediger (*J. A. M. A.,* 1915, lxiv, 1529) has found that although certain bacteria are more susceptible, it requires four days' exposure for 50 per cent. glycerin to destroy non-sporulating organisms and that the spore-forming bacteria are not destroyed by fifteen days' exposure. Goodrich (*P. J.,* 1917, xcviii, 453) states that 50 per cent. glycerin is scarcely more disinfectant than pure water. When injected intravenously in large doses it is capable of causing severe and even fatal poisoning, but the amount required to produce this effect is so large as to suggest that it acts rather by altering the physical condition of the blood than by any true physiological properties. Faust and Tallquist (*A. E. P. P.,* 1907, lvii, p. 366), on the theory that the hemolytic poison in *pernicious anemia* is oleic acid, suggested the use of glycerin as a remedy and the theory has received some clinical confirmation. Aside from its pharmaceutical use, the most important medical value of glycerin is as a local remedy. Pure glycerin because of its hygroscopic properties is locally irritating to mucous membranes. It is serviceable, however, probably through dehydrating influence as a local application over *furuncles* and similar local inflammatory conditions and has even been recommended in burns and wounds. In a diluted form it is often of great value for its emollient properties in various forms of *skin diseases.*

It is extensively employed in habitual *constipation* in the form of suppositories. (See *Suppositoria Glycerini*).

To collodion it gives a valuable plasticity. Incorporated in very small proportion with extracts and pills, it keeps them soft and free from mouldiness. Glycerin may be used in the form of an ointment, and is also used in the menstruum of official extracts, fluidextracts, glycerites, infusions, syrups, tinctures, etc., and in making pills.

Dose, one fluidrachm (3.75 cc.).

Off. Prep.—Gelatinum Glycerinatum, *U. S.;* Suppositoria Glycerini, *U. S., Br.;* Cataplasma Kaolini, *N. F.;* Glyceritum Amyli, *U. S.;* Glyceritum Boroglycerini, *U. S.;* Suppositoria Boroglycerini, *N. F.;* and as solvent and preservative in Glycerites, Fluidglycerates, Fluidextracts and Tinctures.

GLYCERINUM ALUMINIS. Br.

GLYCERIN OF ALUM

Glycéré d'Alun, *Fr.;* Alaun-Glycerit, *G.*

"Purified Alum, 20.0 *grammes;* Distilled Water, 7.5 *millilitres;* Glycerin sufficient to produce 120.0 *millilitres.* Powder the Alum, triturate with the Distilled Water and Glycerin until solution is effected, warming slightly if necessary; set aside; pour off the clear liquid from any deposit that may be formed." *Br.*

This has an astringency similar to glycerite of tannin without the tendency to soil the linen or blacken in contact with iron, but it is much more irritating.

GLYCERINUM BORACIS. Br.

GLYCERIN OF BORAX

Glycéré de Borax, *Fr.;* Borax-Glycerit, *G.*

"Purified Borax, 20 *grammes;* Glycerin, 120 *millilitres.* Powder the Borax, and triturate with the Glycerin in a warmed mortar until solution is effected." *Br.*

The demulcent properties and sweet taste of this preparation render it a useful and convenient method of applying borax to the infantile *thrush* and other forms of sore mouth in children.

GLYCERINUM PEPSINI. Br.

GLYCERIN OF PEPSIN

Glycéré de Pepsine, *Fr.;* Pepsin-Glycerit, *G.*

"Pepsin, 100.0 *grammes;* Hydrochloric Acid, 11.5 *millilitres;* Glycerin, 600.0 *millilitres;* Distilled Water, sufficient to produce 1000.0 *millilitres.* Mix the Hydrochloric Acid, Glycerin, and two hundred and sixty *millilitres* of the Distilled Water; add the Pepsin; dissolve; add sufficient Distilled Water to produce the required volume; set aside for twenty minutes; filter. Ten cc. of this preparation contain 1 gramme of Pepsin; 1 fluidrachm contains about 5.5 grains." *Br.*

This preparation is practically identical with the glycerite of pepsin of the National Formulary. (See Part III.)

Dose, one fluidrachm (3.75 cc.), equivalent to five grains of pepsin.

GLYCERINUM PLUMBI SUBACETATIS. Br.

GLYCERIN OF SUBACETATE OF LEAD

Glycéré de Sousacétate de Plomb, *Fr.;* Bleiessigglycerit, *G.*

"Strong Solution of Lead Subacetate, 500 *millilitres;* Glycerin, 500 *millilitres;* Distilled Water, a sufficient quantity. Evaporate the Strong Solution of Lead Subacetate to dryness on a water-bath; add the Glycerin; warm gently until dissolved; cool; add Distilled Water till the specific gravity of the mixture is 1.48; filter, if necessary." *Br.*

This glycerite originated with Balmanno Squire of London, but the process made official in the Br. Pharm. (1898) was that recommended by R. W. Parker. (See *A. J. P.,* 1886, 296.) The official process (1914) is a simpler one and more convenient for the pharmacist. It is a powerful sedative astringent, and may be employed as a local application in external inflammation.

GLYCERINUM TRAGACANTHÆ. Br.

GLYCERIN OF TRAGACANTH

Glycéré de Gomme Adragante, *Fr.;* Traganth-Glycerit, *G.*

"Tragacanth, in powder, 10 *grammes;* Glycerin, 30 *millilitres;* Distilled Water, 10 *millilitres.* Mix the Glycerin with the Tragacanth; add the Distilled Water; triturate until a homogeneous paste is produced." *Br.*

This preparation has been introduced into the British Pharmacopœia mainly to serve as an excipient for pills.

GLYCERITA.

GLYCERITES

Glycerina, *Br.;* Glycerins; Glycerata, Glycerolata, Glycerols; Glycérés, *Fr. Cod.;* Glycérats, Glycérolés, *Fr.;* Glycerit, Glycerolat, *G.*

These are solutions of medicinal substances in glycerin. The U. S. name is certainly much better than the British name glycerin (*Glycerinum*) for this does not distinguish a *class* of preparations from the *solvent* used in making them. (See under *Glycerinum.*)

Glycerin has valuable properties as a solvent and vehicle for medicinal substances. Such are its not unpleasant taste and bland character, its wide range of solvent power, which adapts it sometimes as a menstruum where neither water nor alcohol could be advantageously used, and enables it to retain in solution otherwise insoluble substances so frequently found in infusions and decoctions, and its preservative influence, which often protects against oxidation, and, by a destructive agency upon all of the lowest forms of vegetable and animal life, prevents the various fermentative processes so destructive to organic bodies. Another important property, as a vehicle for external remedies, is the permanence of its liquid character, so that it does not, like water and alcohol, dry up when applied to the skin, resembling in this respect, as well as in its demulcent quality, the fixed oils, without their tendency to rancidity. Its hygroscopic quality, however, gives it irritating properties under certain conditions.

GLYCERITUM ACIDI TANNICI. U. S. (Br.)

GLYCERITE OF TANNIC ACID Glycer. Acid. Tann.
[Glycerite of Tannin]

Glycerinum Acidi Tannici, *Br.;* Glycerin of Tannic Acid (of Tannin); Glycéré de Tanin, *Fr. Cod.;* Glycérole de Tannin; Glycérine tannique, *Fr.;* Tannin-Glycerit, Tannin-Glycerol, *G.*

"Tannic Acid, 20 Gm.; Sodium Citrate, 1 Gm.; Glycerin, 79 Gm.; to make 100 Gm. Weigh the glycerin into a tared, wide-mouthed bottle, having a capacity of 125 cc. Suspend the tannic acid and sodium citrate, in a gauze bag, in the glycerin, place the bottle and contents in a water bath containing boiling water and continue the heat, stirring the mixture occasionally until solution results." *U. S.*

"Tannic Acid, 20 *grammes;* Glycerin, sufficient to produce 100 *millilitres.* Triturate the Tannic Acid with the Glycerin in a warmed mortar until solution is effected." *Br.*

The U. S. preparation is a 20 per cent. solution by weight; the strength of the British preparation is somewhat weaker, being a 20 per cent. solution by measure. Glycerin is the only solvent that will enable a stable solution of tannic acid to be made, that may be readily diluted with water to any desired strength.

This preparation may be used, both internally and externally, for most of the purposes to which tannic acid is applied. On the whole, it is the most useful preparation of tannic acid for external use; as circumstances require the official strength may be altered by direction of the physician; a very concentrated solution, two parts of glycerin to one of tannin, may be made by the aid of a moderate heat. This applied daily to nipples, during the later months of pregnancy, will usually prevent the occurrence of *sore nipples* during suckling.

Dose, from ten to forty minims (0.65–2.6 cc.). (See *Acidum Tannicum.*)

GLYCERITUM AMYLI. U. S. (Br.)

GLYCERITE OF STARCH Glycer. Amyl.

Glycerinum Amyli, *Br.;* Glycerin of Starch, Glycamyl, Plasma; Glycéré d'Amidon, *Fr. Cod.;* Glycérate simple (d'Amidon), *Fr.;* Unguentum Glycerini, *P. G.;* Glycerinsalbe, Stärke-Glycerit, *G.;* Glicerolato di amido, *It.;* Glicerolado de almidon, *Sp.*

"Starch, 10 Gm.; Water, 20 cc.; Glycerin, 70 cc. Triturate the starch with the water until a homogeneous mixture is produced. Then gradually add this to the glycerin, contained in a porcelain dish, and heated to about 140° C. Continue the heat, keeping it below 144° C., constantly stirring the mixture until a translucent jelly is formed. Transfer the product to suitable vessels, provided with well-fitting covers." *U. S.*

"Starch, 20 *grammes;* Glycerin, 130 *millilitres;* Distilled Water, 30 *millilitres.* Mix; heat, stirring constantly, until a translucent jelly is formed." *Br.*

These preparations are used as a substitute for ointments, the emollient and demulcent properties of which they possess, without their inconvenience, whether used simply, or as a vehicle for other substances to be employed locally. J. H. Pearson (*P. J.*, 1897, 201) recommends the addition of one grain of powdered tragacanth to the ounce of finished product, to prevent the separation of the glycerin and water from the mass, on standing.

GLYCERITUM BOROGLYCERINI. U. S. (Br.)

GLYCERITE OF BOROGLYCERIN Glycer. Boroglyc.
[Solution of Boroglyceride]

Glycerinum Acidi Borici, *Br.;* Glycerin of Boric Acid; Glycerite of Glyceryl Borate; Glycéré de boroglycéride, *Fr.;* Boroglyceridlösung, *G.*

"Boric Acid, in fine powder, 310 Gm.; Glycerin, a sufficient quantity to make 1000 Gm. Heat 460 Gm. of glycerin in a tared porcelain dish on a sand bath to a temperature between 140° and 150° C., and add the boric acid in portions, constantly stirring. When all is added and dissolved, continue the heat at the same temperature, frequently stirring, and breaking up the film which forms on the surface until the mixture has been reduced to 500 Gm., then add 500 Gm. of glycerin, mix thoroughly, and immediately transfer the product to bottles and stopper them tightly." *U. S.*

"Boric Acid, 300 *grammes;* Glycerin, sufficient to produce 1000 *grammes.* Add the Boric Acid to four hundred and fifty *grammes* of the Glycerin, boil until dissolved, constantly stirring; evaporate at a temperature rising to but not exceeding 150° C. until the weight of the mixture has been reduced to five hundred grammes, the stirring being continued. Add sufficient Glycerin to produce the required weight; mix thoroughly." *Br.*

This solution was first introduced into the U. S. P. 1890 from the National Formulary. It is a thick, sweet, viscid, colorless liquid, and has the advantage of offering the antiseptic, boric acid, in a very soluble form as it is soluble in practically all proportions in water. It may be made more rapidly than by the above process if one ounce av. of boroglyceride be dissolved in one ounce av. of glycerin with the aid of a gentle heat. (See *Boroglyceride*, Part II.)

Off. Prep.—Suppositoria Boroglycerini, *N. F.*

GLYCERITUM PHENOLIS. U. S. (Br.)

GLYCERITE OF PHENOL Glycer. Phenol.
[Glycerite of Carbolic Acid]

Glycerinum Acidi Carbolici, *Br.;* Glycerin of Phenol; Glycérole d'Acide Phénique, Glycéré de Phenol, Glycérine Phénique, *Fr.;* Phenol-Glycerit, *G.;* Glycerina con acido fenico, *Sp.*

"Liquefied Phenol, 20 cc.; Sodium Citrate, 1 Gm.; Boiling Distilled Water, 1 cc.; Glycerin, 79 cc.; to make 100 cc. Dissolve the sodium citrate in 1 cc. of boiling distilled water, and add this solution to the mixture of glycerin and phenol, previously prepared." *U. S.*

"Phenol, 20 *grammes;* Glycerin, sufficient to produce 100 *millilitres.* Triturate the Phenol with the Glycerin in a warmed mortar until solution is effected." *Br.*

Uses.—For the uses of this preparation, see *Phenol.* The U. S. P. glycerite is a 20 per cent., by volume, solution of liquefied phenol; the British preparation is slightly stronger, being a 20 per cent., by volume, solution of crystallized phenol. It may be used internally or locally, and for both purposes should in general be diluted with water.

Dose, from five to ten minims (0.32–0.65 cc.).

GLYCYRRHIZA. U. S. (Br.)

GLYCYRRHIZA Glycyrrh. [Licorice Root]

"Glycyrrhiza is the dried rhizome and roots of *Glycyrrhiza glabra* Linné var. *typica* Regel et Herder, known in commerce as Spanish Licorice or of *Glycyrrhiza glabra* Linné var. *glandulifera* Regel et Herder known in commerce as Russian Licorice, or of other varieties of *Glycyrrhiza glabra* Linné yielding a yellow and sweet wood (Fam. *Leguminosæ*). Glycyrrhiza yields not more than 2.5 per cent. of acid-insoluble ash." *U. S.* "Liquorice Root is the peeled root and peeled subterranean stem of Glycyrrhiza glabra, *Linn.*, and other species of Glycyrrhiza." *Br.*

Glycyrrhizæ Radix, *Br.;* Radix Glycyrrhizæ Hispanicæ, Spanish Licorice Root; Liquiritiæ Radix, Réglisse, *Fr. Cod.;* Réglisse, Racine de Réglisse, Bois doux, Racine douce, *Fr.;* Radix Liquiritiæ, *P. G.;* Spanisches Süssholz, Spanische Süssholzwurzel, Süssholzwurzel, *G.;* Liquirizia, *It.;* Regaliz (Raiz de), Orozuz, Palo dulce, *Sp.*

Glycyrrhiza glabra, which yields Spanish Licorice, is a perennial herb whose underground portion consists of a slender branching rhizome bearing a number of delicate rootlets. The stems are herbaceous, erect, slightly branching, and usually four or five feet in height. The leaves are alternate, pinnate, consisting of several pairs of ovate, blunt, petiolate leaflets, with a single leaflet at the end, of a pale-green color, and clammy on their under surface. The flowers are violet or purple, formed like those of the pea, and arranged in axillary spikes supported on long peduncles. The calyx is tubular and persistent. The fruit is a compressed, smooth, acute, one-celled legume, containing from one to six small kidney-shaped seeds. This plant grows best on sandy soil near streams, usually not being found more than fifty meters from a body of water. It is indigenous to southern Europe and southwestern Asia, and is cultivated in England, Germany, Spain, Italy and Austria and has been grown on an experimental scale in the United States. *Glycyrrhiza echinata,* the source of "Russian Licorice," is a native of southern Russia and Hungary but also occurs in the wild state in Italy, Sicily and other Mediterranean countries where it is also cultivated. Its subterranean portion consists of a fleshy, fusiform root, from which stems spring that attain a height of 5 to 6 feet. These are several-branched, the branches being cylindrical toward the base and angled toward their ends. The leaves are smooth, imparipinnate, with oblong-mucronate leaflets. The flowers are violet-colored and occur in short-stalked, axillary heads in the leaf axils. The fruit is an oval, pointed, spiny, one-seeded legume.

A comparatively small portion of the licorice imported into the United States is used by the drug industry, the greater bulk of the huge supply which is annually coming into our ports being consumed by the tobacco and confectionery trades and in fire extinguisher compounds. The root is collected alike from wild and cultivated plants, cleaned and variously prepared for the market. The Spanish variety is the most esteemed and usually comes in segments of variable length, in bundles, and as cut root, the first two grades being packed in covered or uncovered bales, the last, in bags. This variety has been frequently named after the country in which it is collected, a practice which has often been confusing to the purchaser. Most of the licorice designated as Italian, Turkish, Levant, Persian or Arabian has been found to be yielded by geographical varieties of *G. glabra.* It is shipped commonly from Smyrna, Haifa, the Spanish ports of Alicante, Barcelona and Seville, from Leghorn, Italy, Constantinople and Marseilles. Russian Licorice is now being shipped chiefly through Hamburg and London to the United States. Importations of this variety have been comparatively small. It occurs on the market both in the peeled and unpeeled condition, the peeled roots often being split lengthwise. Licorice is often offered for entry that is poorly dried, mouldy, insect infested or partially decayed; such roots should be rejected. According to Rusby (*Ph. Era,* 1909, p. 634), ground licorice has been imported which apparently consisted of the peelings of Russian licorice. Asiatic licorice, known as "*Chuntschir,*" is obtained from *G. uralensis*

Fisch. The plant is found in Siberia, Turkestan and Mongolia, and it is claimed that the root is of better quality and is but little inferior if any to the best Russian licorice. (See Alsberg and Viehoever, *J. A. Ph. A.*, 1919, viii, 467 and also *P. J.*, 1908, lxxxi, 164.)

The U. S. Department of Agriculture has had Spanish licorice under cultivation in South Carolina and the plant thrives in various localities in this country. It is said that the soil and climatic conditions in the Coachella Valley of California are ideal for the growing of the licorice plant.

A species of *Glycyrrhiza, G. lepidota* Pursh., grows abundantly from Missouri, westward into Nevada and northern California and northward to Washington. It is probably the same as the licorice plant mentioned by Mackenzie as growing on the northern coast of this continent. Nuttall states that its root possesses in no inconsiderable degree the taste of licorice, and M. L. McCullough found it to contain 6.39 per cent. of crude glycyrrhizin, in contrast with 7.18 per cent. in the official species. (*A. J. P.*, 1890.) Schneider reports that *G. lepidota glutinosa* Pursh., a native of California, is much like *G. glabra* and can no doubt be substituted for the true licorice. (*Pacific Pharm.*, ii, p. 144.)

Description and Physical Properties.—"*Unground Spanish Licorice.*—Nearly cylindrical, the upper portion more or less knotty; usually in pieces from 14 to 20 cm. or more in length and from 5 to 20 mm. in thickness; externally yellowish-brown or dark brown, longitudinally wrinkled, the thinner rhizomes often having prominent alternate buds, the thicker rhizomes having distinct corky patches; fracture coarsely fibrous; internally yellow, radiate; odor distinctive; taste sweetish and slightly acrid.

"*Unground Russian Licorice.*—Nearly cylindrical, somewhat tapering, sometimes split longitudinally, from 15 to 30 cm. in length and from 1 to 5 cm. in diameter; when deprived of the outer corky layer, it is externally pale yellow; fracture coarsely fibrous; internally pale yellow; wood radially cleft; odor distinct; taste sweetish.

"*Structure.*—Rhizome with numerous layers of yellowish-brown cork cells, absent in the peeled drug; one or more rows of cells with a tendency to collenchymatous thickening; a middle bark of starch-bearing parenchyma and groups of bast-fibers surrounded with crystal-fibers; inner bark with radial arrangement of phloem and medullary rays, the phloem consisting of wedges of small groups of bast-fibers and parenchyma separated tangentially by sieve tissue, the cells of the latter with thick, highly refracting walls; medullary rays from 1 to 8 cells wide; wood bundles characterized by broad wedges consisting of large tracheæ with yellowish walls, small compact groups of wood-fibers and starch-bearing parenchyma; pith of large, more or less polygonal starch-bearing parenchyma or occasionally containing prisms of calcium oxalate. In roots the pith is absent.

"*Powdered Glycyrrhiza.*—Brownish-yellow (unpeeled Licorice) or pale yellow (peeled Licorice); starch grains numerous, mostly single and elliptical or oval, from 0.002 to 0.020 mm. in diameter; tracheæ mostly with bordered pores; wood- and bast-fibers numerous, very long, much attenuated at the ends and about 0.010 mm. in width; crystal-fibers with monoclinic prisms of calcium oxalate, the latter from 0.010 to 0.030 mm. in length; occasional fragments of reddish-brown cork cells which are practically absent in the powder prepared from peeled Licorice." *U. S.*

"When 5 grammes are macerated with 50 millilitres of *chloroform water* for twenty-four hours, shaken occasionally and filtered, 10 millilitres of the filtrate evaporated in a flat-bottomed dish yield not less than 0.200 gramme of residue dried at 100° C. Ash not more than 6 per cent." *Br.*

A character said by Rothrock (*A. J. P.*, 1884) to be diagnostic of Glycyrrhiza is the occurrence of crystal fibers adjoining the wood and bast fibers. These are recognized in the official description of the powdered drug. In the Russian root the parenchymatous wood-cells are larger than in the Spanish. The powder is of a grayish-yellow color, when the root is pulverized without being deprived of its epidermis; of a pale sulphur-yellow, when the epidermis has been removed.

Constituents.—Besides various ordinary matter such as starch, lignin, etc., glycyrrhiza contains a brown acrid resin, a crystallizable substance originally called agedoïte but now known to be asparagin, and a characteristic principle known as *glycyrrhizin.* This is in reality the acid ammonium salt of *glycyrrhizic acid,* $C_{44}H_{62}NO_{18}.NH_4$. It is a glucoside which, according to Kobert (*Ph. Ztg.*, 1915, 182) belongs to the group of saponins and yields upon hydrolysis a hemolitic product; he also states that there are present in the root other saponins. Glycyrrhizic acid does not possess the characteristic sweetness of licorice, but its salts, especially the ammonium compounds, are sweet. Roussin in 1875 showed that licorice root which has lost a portion of its sweetness through fermentation, could be restored by treating with ammonium and suggested the name of *ammonium glycyrrhizate* as proper for the sweetening principle.

Glycyrrhizic acid is practically insoluble in cold water and the method of precipitating it from infusions of licorice root by means of sulphuric acid has been used for the purpose of assaying licorice (see under *Extractum Glycyrrhiza*). Habermann (*An. Ch. Ph.*, cxcvii) studied the properties of glycyrrhizic acid. He found that it was insoluble in ether, slightly soluble in absolute alcohol but more soluble in alcohol of lower percentage. It was only sparingly soluble in water but formed with it a transparent yellowish jelly. Houseman who has done considerable work on glycyrrhiza (*A. J. P.*, 1916, lxxxviii, 97) states that the biologically active saponins of licorice are in the inner bark. He also confirms the nitrogen content of glycyrrhizin which had been questioned.

Under the name of *Glycyrrhizinum Ammoniatum* (*Ammoniated Glycyrrhizin, Glyzina*), the U. S. IX recognized a crude form of this substance which it defined as "A sweet principle combined with ammonia obtained from glycyrrhiza." *U. S. IX.*

The process for making this preparation was given in the U. S. P. VIII as follows:

"Glycyrrhiza, in No. 20 powder, *five hundred grammes.* Water, Ammonia Water, Sulphuric Acid, each, *a sufficient quantity.* Mix *four hundred and seventy-five cc.* of Water with *twenty-five cc.* of Ammonia Water, and, having moistened the powder with the mixture, macerate for twenty-four hours. Then pack it moderately in a conical glass percolator, and gradually pour water upon it until *five hundred cc.* of percolate are obtained. Add Sulphuric Acid slowly to the percolate, with constant stirring, so long as a precipitate is produced. Collect this on a strainer, wash it with cold Water until the washings no longer have an acid reaction, redissolve it in Water with the aid of Ammonia Water, filter, if necessary, and again add Sulphuric Acid so long as a precipitate is produced. Collect this, wash it, dissolve it in a sufficient quantity of Ammonia Water previously diluted with an equal volume of Water, and spread the clear solution upon plates of glass, so that, when dry, the product may be obtained in scales." *U. S. P. VIII.*

The U. S. P. IX described it as follows: "Ammoniated Glycyrrhizin occurs in dark brown or brownish-red scales, without odor, and having a very sweet taste. It is freely soluble in water and soluble in alcohol. Its aqueous solution when heated with potassium hydroxide T.S. evolves ammonia. Supersaturate an aqueous solution of Ammoniated Glycyrrhizin with an acid; a precipitate is produced (consisting essentially of *glycyrrhizin*), which, when dissolved in hot water, forms a jelly on cooling. This substance, after being washed with diluted alcohol and dried, appears as an amorphous, yellow powder, having a strong, bitter-sweet taste, and an acid reaction. Incinerate 0.5 Gm. of Ammoniated Glycyrrhizin; not more than 0.5 per cent. of ash remains." *U. S. IX.*

According to Habermann glycyrrhizin is decomposed, by boiling with diluted sulphuric acid, into *glycyrrhetin* and *parasaccharic acid*, according to the reaction:

$$C_{44}H_{63}NO_{18} + 2H_2O = C_{32}H_{47}NO_4 + 2C_6H_{10}O_8.$$

By fusing glycyrrhizin with potassium hydroxide, Weselsky and Benedikt (*B. Chem. G.*, 1876) obtained *paraoxybenzoic acid.*

For methods of quantitatively determining glycyrrhizin, see *Ext. Glycyrrh.*

Uses.—Powdered licorice root is used for various pharmaceutical purposes as in the preparation of pills, either to give due consistence or to cover their surface and prevent them from cohering, and as a diluent of powdered extracts, etc. As a remedial agent it has been almost entirely replaced by the extract.

Off. Prep.—Extractum Glycyrrhizæ, *Br.;* Extractum Glycyrrhizæ Purum, *U. S.;* Fluidextractum Glycyrrhizæ, *U. S.* (*Br.*)*;* Mistura Glycyrrhizæ Compositus (from Extract), *U. S.;* Pulvis Glycyrrhizæ Compositus, *U. S., Br.;* Species Pectoralis, *N. F.;* Fluidglyceratum Glycyrrhizæ, *N. F.;* Mistura Ammonii Chloridi (from Pure Extract), *N. F.;* Syrupus Glycyrrhizæ (from Fluidglycerate), *N. F.*

GOSSYPII CORTEX. N. F. (Br.)

COTTON ROOT BARK Gossyp. Cort.

"Cotton Root Bark is the recently gathered air-dried bark of the root of one or more of the cultivated varieties of *Gossypium herbaceum*, Linné, and of other species of *Gossypium* (Fam. *Malvaceæ*). Cotton Root Bark contains not more than 5 per cent. of wood or other foreign organic matter." *N. F.*

"Cotton Root Bark is the dried root-bark of Gossypium herbaceum, *Linn.*, and of other cultivated species of Gossypium." *Br.*

Gossypii Radicis Cortex, *Br.;* Ecorce de la Racine de Cottonnier, *Fr.;* Baumwoll-Wurzelrinde, *G.;* Corteza de la raiz d'algodon, *Sp.*

In consequence of changes produced in the plants of this genus by cultivation, botanists have found great difficulty in determining which are distinct species and which are merely varieties. By some taxonomists more than fifty species of *Gossypium* are recognized. There are only 5 or 6 species which yield useful products and the bulk of the cotton is the product of two species, *G. herbaceum* L., which furnishes the Upland or short staple cotton, and *G. Barbadense* L., the source of the Sea Island or long staple cotton. All of the species are of tropical origin. The Upland cotton has been cultivated in East India and Arabia since ancient times. The Sea Island cotton is indigenous to the West Indies and is the type observed by Columbus.

Gossypium herbaceum is a biennial or triennial plant, with a branching stem from two to six feet high and palmately-lobed hoary leaves, the lobes of which are somewhat lanceolate and acute. The flowers possess yellow petals, having a purple spot near the claw. The leaves of the involucre or outer calyx are serrate. The capsule opens when ripe, and displays a loose white tuft of long slender filaments, which surround the seeds and adhere firmly to the outer coating. The plant is a native of Asia, but is cultivated in most tropical countries. It requires a certain duration of warm weather to perfect its seeds, and, in the United States, does not ordinarily mature north of Virginia. It is cultivated widely in the Southern United States from Virginia to Texas.

Gossypium Barbadense (Sea Island cotton) differs from *G. herbaceum* in having smoother and more deeply lobed leaves, brighter yellow flowers, smaller, longer and more pointed bolls, and seed hairs with a finer and longer staple. It is cultivated chiefly in South Carolina, Georgia and Northern Florida.

The herbaceous part of the plant contains much mucilage, and has been used as a demulcent. The seeds yield by expression a fixed oil of the semi-drying kind, which is employed for making soap and for other purposes. (See *Oleum Gossypii.*) The portion, for which the plant is cultivated, is the filamentous substance surrounding the seeds. This, when separated, constitutes the cotton of commerce, and when purified, is official as *Gossypium Purificatum.* Cotton seeds have been employed in our Southern States in the treatment of intermittents, but are at present seldom, if ever used. (For details, see *U. S. D.,* 16th ed.)

Description and Physical Properties.—"*Unground Cotton Root Bark.*—In flexible bands or quilled pieces; attaining a length of 30 cm. and a thickness of about 1 mm.; outer surface orange-brown, sometimes smooth, but usually finely wrinkled and fissured longitudinally and roughened from the tendency of the corky layers to exfoliate the fibrous inner bark; inner surface light brown, longitudinally striate; fracture tough, fibrous, the inner bark readily separable into fibrous layers. Odor slight; taste very slightly acrid.

"*Structure.*—Cork composed of from 4 to 6 layers of tabular, yellowish brown cells with thin walls; a thin primary cortex consisting of starch-bearing parenchyma and occasional large secretion reservoirs with yellowish brown contents; inner bark with a nearly closed ring of V-shaped groups consisting of layers of strongly lignified bast fibers, sieve tissue, tannin-containing cells and traversed by medullary rays, the arrangement giving a deeply incised appearance to the outer edge of the bast ring when viewed in transverse section; medullary rays 1 to 6 cells in width, the cells usually containing starch grains; occasional cells containing rosette crystals of calcium oxalate.

"*Powdered Cotton Root Bark.*—Numerous bast fibers from 0.300 to 1.000 mm. in length and about 0.015 mm. in width, with strongly lignified walls, the latter about 0.005 mm. in thickness and with few pores, the ends of the fibers being acute and markedly attenuate; numerous fragments consisting of cortical parenchyma containing simple or compound starch grains, the latter up to 0.020 mm. in diameter, the tissue occasionally enclosing a secretory reservoir; fragments composed of medullary ray cells, the latter containing starch grains; rosette crystals of calcium oxalate from 0.009 to 0.025 cm. in diameter." *N. F.*

"In strips or quilled pieces; thin, tough and fibrous. Cork thin, pale brown, longitudinally striated; removed in places and then disclosing the orange-brown cortex. Inner surface whitish, silky and finely striated. Secondary bast readily separable into thin fibrous laminæ. No odor; taste slightly acrid and astringent." *Br.*

For an account of a microscopical and microchemical examination of cotton root bark by F. W. Morgan, see *A. J. P.,* 1898, p. 427. Farwell has made a histological study of the root and stem barks. (See *Merck's Rep.,* 1914, p. 133.) Stanford and Viehoever have made a detailed study of the glands of *Gossypium hirsutum* L. and their constituents. (See *J. Agric. Res.,* 1918, p. 419.) The drug of commerce frequently contains considerable woody material and many samples have been found to consist chiefly of segments of whole roots. It deteriorates with age and therefore only recently gathered bark should be used.

Power and Browning (*P. J.,* 1914, xciii, 420) found in an investigation of cotton root bark the following constituents: acetovanillone (in the steam distillate), a phenolic acid (probably 2:3 dihydroxybenzoic acid), salicylic acid, a new colorless phenolic substance, $C_9H_{10}O_8$, a new yellow phenolic substance, $C_{13}H_{18}O_5$, betaine, a fatty alcohol, $C_{20}H_{42}O$, a phytosterol, $C_{27}H_{46}O$, triacontane, ceryl alcohol, oleic and palmitic acids, and a sugar. Almost all of these constituents were separated from the resinous extractive which constituted between 10 and 11 per cent. of the air dried bark. No tannin was present and no alkaloids were detected.

Seeking the constituents of the Upland cotton plant, *Gossypium hirsutum,* that were attractive to the boll weevil, Viehoever, Chernoff and Johns studied the plant and found that the leaves and flowers (deprived of the petals) contained the glucoside, *quercimeritrin,* while the petals contained both quercimeritrin and *isoquercitrin.* These two glucosides are isomeric, having the formula $C_{21}H_{20}O_{12}$, and both hydrolyze to quercetin and dextrose. By distillation of 4000 pounds of fresh leaves of Upland cotton about 1 ounce of volatile oil, attractive to the boll weevil, was obtained. This oil on distillation was separated into 6 fractions passing over (*a*) below 200°, (*b*) 200–250°, (*c*) 250–270°, (*d*) 270–285°, (*e*) 285–300° and (*f*) 300–325°. Fraction "*d*" was the largest and consisted of a dark blue-green oil, which did not give any furol reaction nor deposit any crystals. (*J. Agr. Research,* 1918, xiii, 345.)

Uses.—The attention of the medical profession was called to cotton root bark by Bouchelle in 1840, who stated that it was a popular abortifacient among the negro slaves. Scott (*T. G.,* 1911) and Eckler (*Lilly Scientific Bull.,* 1920, p. 349) from studies on the lower animals, both reached the conclusion that it has a weak stimulating effect upon the uterus; while its action is similar in kind to that of ergot, it is scarcely to be compared because of its great inferiority in power.

Dose, thirty to sixty grains (2.0–3.9 Gm.).

Off. Prep.—Decoctum Gossypii Radicis Corticis, *Br.;* Extractum Gossypii Radicis Corticis Liquidum, *Br.;* Fluidextractum Gossypii Corticis, *N. F.*

GOSSYPIUM PURIFICATUM. U. S. (Br.)

PURIFIED COTTON Gossyp. Purif.
[Absorbent Cotton]

"The hairs of the seeds of cultivated varieties of *Gossypium herbaceum* Linné or other species of *Gossypium* (Fam. *Malvaceæ*) freed from adhering impurities and linters and deprived of fatty matter." *U. S.* "Cotton consists of the hairs of the seed of Gossypium herbaceum, *Linn.,* and of other cultivated species of Gossypium, freed from fatty matter." *Br.*

Gossypium, *Br.;* Cotton Wool; Lana (Lanugo, s. Pili) Gossypii; Coton Hydrophile, *Fr. Cod.;* Coton absorbant, Xylum præparatum, *Fr.;* Gossypium depuratum, *P. G.;* Gereinigte Baumwolle, Baumwolle, *G.;* Cotone assorbente, C. idrofilo, *It.;* Algodon hidrofilo, Algodon absorbente, *Sp.*

There is considerable difference in the capsules or so-called bolls, the seeds, as well as the lint of the several species of *Gossypium.* The bolls of Sea Island (*G. barbadense*) cotton are uniformly smaller, more sharply pointed, contain fewer and smaller seeds and longer lint than the Upland bolls. The Sea Island cotton has small black seeds from which the lint separates readily. The Upland cottons have large seeds which are greenish in color, and surrounded by a short dense hair beneath the longer and more valuable lint. The lint of the Sea Island cotton is from 3.5 to 6.5 cm. in length, while the Upland cotton seldom exceeds 3.5 cm. in length, usually being much shorter. There are numerous hybrids between these two types, *G. herbaceum* and *G. barbadense.* The long and extra long fiber produced in the United States are all obtained from varieties of *G. barbadense* and their hybrids, the shorter fibers being usually Upland cottons of the *G. herbaceum* type. The commercial grading of cotton by the New York Cotton Exchange is as follows: Samples the average fiber of which is under 25 mm. in length are called "short staple"; those between 25 to 30 mm. are called "medium" and from 30 to 40 mm. are called "long staple." What are known as "full grades" are designated by the words "fair," "middling fair," "good middling," "middling," "low middling," "good ordinary" and "ordinary."

The inadequacy of the former U. S. P. requirements for absorbent quality having been pointed out in several articles by Dr. F. B. Kilmer, the suggestions made by him for improvement of the standards have all been adopted in later U. S. P. texts.

In the process of purifying cotton a soap is formed through the union of the fatty matter with the alkali, and this is subsequently dissolved out by repeated washings. F. L. Slocum published in 1881 a process for preparing it as follows: Take of the best quality of carded cotton batting any desired quantity, and boil it with a 5 per cent. solution of potassium or sodium hydroxide for one-half hour, or until the cotton is entirely saturated with the solution, and the alkali has saponified all oily matter. Then wash thoroughly, to remove all soap, and nearly all alkali, press out the excess of water, and immerse in a 5 per cent. solution of chlorinated lime for 15 or 20 minutes; again wash, first with a little water, then dip in water acidulated with hydrochloric acid, and thoroughly wash with water; press out the excess of water, and again boil for 15 or 20 minutes in a 5 per cent. solution of potassium or sodium hydroxide; now wash well, dipping in the acidulated water and rinsing thoroughly with pure water. Afterwards press out and dry quickly.

The amount of loss by this process is practically 10 per cent. A sample of 360 gr. lost, on boiling with alkali and bleaching, 15 gr., or 4.17 per cent., and 270 gr. of this bleached sample lost, on again boiling with an alkali, 14 gr., or 518 per cent., a total loss of 9.35 per cent. (*A. J. P.,* 1881, 53; see also *Ph. Era,* 1890, p. 22).

Description and Physical Properties.—"White, soft, fine filaments, appearing under the microscope as hollow, flattened and twisted bands, spirally striate and slightly thickened at the edges. It is odorless and almost tasteless. Purified Cotton is insoluble in ordinary solvents, but is soluble in ammoniated cupric oxide T.S.

"Purified Cotton, previously compressed in the hand, when thrown on the surface of water at about 25° C., readily absorbs it and sinks. Ash: not more than 0.2 per cent. Thoroughly saturate about 10 Gm. of Purified Cotton with 100 cc. of distilled water, then with the aid of a glass rod press out two 25 cc. portions of the water into white porcelain dishes. Add to one portion 3 drops of phenolphthalein T.S. and to the other portion 1 drop of methyl orange T.S.: no pink color develops in either portion (*alkali or acid*). Pack 10 Gm. of Purified Cotton in a narrow percolator, extract with ether, until the percolate measures 200 cc., and evaporate to dryness: the residue does not exceed 0.6 per cent. (*fatty matter*). Pack 10 Gm. of Purified Cotton in a narrow percolator, and extract with alcohol until the percolate measures 50 cc.: when observed downward through a column 20 cm. in depth, the percolate may show a yellowish color, but no blue or green tint (*dyes*). Place 10 Gm. of Purified Cotton in 200 cc. of boiling distilled water in a porcelain dish; keep the water at about 100° C. for five minutes, holding the cotton under the surface with the aid of a glass rod. Then press out with the assistance of the rod, and decant 100 cc. of the water, filtering it if not clear. Now add 50 cc. of cold distilled water to the Purified Cotton, thoroughly working it through the Cotton with the glass rod, for ten minutes, and again decant 50 cc. of the water. Twice again wash the Cotton with 50 cc. portions of cold distilled water, in the manner described, and evaporate to dryness the combined washings so obtained in a porcelain or platinum dish on a water bath. The residue, dried to constant weight at 100° C., does not exceed 0.025 Gm. (*water-soluble substances*)." *U. S.*

"In long, white, soft filaments, each consisting of an elongated cell, appearing, when seen under the microscope, as a flattened, twisted band with slightly thickened rounded edges. Inodorous and tasteless. Soluble in *ammoniacal solution of copper oxide*. Readily wetted by *water*, and not imparting to it either an alkaline or an acid reaction. Ash not more than 0.5 per cent." *Br.*

It is without odor or taste, soluble in strong alkaline solutions, and decomposed by the concentrated mineral acids. In chemical character it is related to but not identical with lignin, the latter being called *lignocellulose*, whereas cotton is composed of *cellulose*, $(C_6H_{10}O_5)n$. By nitric acid it is converted into gun-cotton (see *Pyroxylinum*). *Mercerized cotton* is made by treating woven cotton fabrics with concentrated sodium hydroxide solution which so modifies the fiber that a sheen like silk is produced. This must not be confused, however, with *artificial silk* (*rayon*) which is made by several processes using cotton or cellulose is taken as the starting point. In one of these the cellulose is converted into a nitroderivative which, after dissolving in suitable solvents to make a thick solution, is drawn out into threads which are subsequently denitrated and made less inflammable by immersing them in alkaline sulphide solution. In another method the cellulose is treated with alkali and carbon disulphide which forms cellulose thiocarbonate or xanthate which when treated with water yields "*viscose*," a thick tenacious substance capable of being drawn into glossy threads. In another process the solvent powers of an ammoniated copper is utilized. *Acetylcellulose* or *cellulose acetate* is made by the action of acetic anhydride upon cotton. It is used for making non-inflammable moving picture films and for making the transparent thin sheets used for wrapping confectionery and for other purposes where an air-tight package is desirable.

A method of distinguishing between these four types of rayon is afforded by the use of a reagent called *ruthenium red*. This is an aqueous soultion of $Ru_2(OH)_2Cl_4(NH_3)_7.3H_2O$ in the proportion of 1 in 1000. If an unknown sample of rayon is treated with the reagent for a twelve hour period the following distinguishing results are observed: Viscose rayon shows a distinct pink color, which becomes more pronounced upon standing. Denitrate nitro-rayon is colored red, which becomes violet upon standing. Copper ammonium rayon is not colored even after twelve hours. Acetate rayon is colored irregularly but this variety is distinguished from the others by its ready solubility in glacial acetic acid, the other varieties being insoluble in this reagent.

The first U. S. P. IX test proves the absence of fatty matter, for if even a small quantity be present the cotton will float in water. Repeated experiments have proved that cotton will take fire spontaneously if impregnated with linseed oil, or some of the other fixed oils, and allowed to stand; the heat produced by the oxidation of the oil suffices to ignite the matted fibers of the cotton. For medicinal use it should be carded into thin sheets. Air passed through cotton becomes sterile on account of the microscopic organisms being strained out of it; and this fact has been utilized in preserving infusions by placing them in bottles containing corks armed with tubes loosely filled with cotton, and drawing the infusion from a stopcock near the bottom.

Wood Wool.—Under this name Bruns has introduced finely grained, purified wood fiber, such as is used in making paper. It may be medicated like cotton.

Uses.—The use of cotton as a filtering medium and in the preparation of medicated waters has already been alluded to. It is much used in surgery as a dressing for *burns* and *wounds*, in order to prevent the access of pathogenic germs and to absorb discharges. Cotton batting is often employed to maintain a uniform temperature in parts affected with *acute rheumatic inflammation*. Absorbent cotton has been medicated in various ways and come largely into use. (For *Iodized Cotton*, see *Iodum.*) *Picric Cotton* is prepared by dissolving 0.25 Gm. of picric acid in 25 Gm. of ether, or of 94 per cent. alcohol, and immersing in the solution 10 Gm. of clean cotton, and drying. *Salicylic Cotton* (5 per cent.) may be prepared by Brun's process, by saturating one kilogramme of cotton with 4 liters of a solution of 50 Gm. of salicylic acid, and 20 Gm. of castor oil in 3.930 liters of alcohol. England communicates in *A. J. P.*, 1887, p. 173, practical formulas for preparing the following medicated cottons and gauzes: *Borated Cotton, Benzoated Cotton, Salicylated Cotton, Naphthalinated Cotton, Iodoformized Cotton, Carbolized Cotton, Sublimated Cotton, Carbolized Gauze, Sublimated Gauze, Absorbent Canton Flannel.* For methods of assay of medicated cottons, gauzes, etc., see *Proc. A. Ph. A.*, 1897, 457. See also formulas for the extemporaneous preparation of medicated gauzes, by George M. Beringer, Jr., *A. J. P.*, 1911, p. 178.

Off. Prep.—Pyroxylinum, *Br.;* Gossypium Stypticum, *N. F.*

GRANATUM. U. S.

POMEGRANATE Granat. [Pomegranate Bark]

"Pomegranate is the dried bark of the stem or root of *Punica Granatum* Linné (Fam. *Granataceæ*). Pomegranate contains not more than 2 per cent. of wood or other foreign organic matter." *U. S.*

Granati Cortex, *Br.*, 1898; Pomegranate Bark; Cortex Mali Punici, Ecorce de Grenadier, *Fr. Cod.;* Ecorce deBalaustier, Ecorce de Granade, *Fr.;* Cortex Granati, *P. G.;* Granatrinde, Granatwurzelrinde, *G.;* Melogranato, Malicorio, Scorza del Melogranati, *It.;* Granado (Corteza de), *Sp.*

The *pomegranate* is a small tree, attaining in favorable situations the height of twenty feet, with a very unequal trunk, and numerous branches which sometimes bear thorns. The leaves are opposite, petiolate, entire, oblong or lance-shaped, pointed at each end, smooth, shining, and of a bright-green color. The flowers are large, of a rich scarlet color, and stand at the end of the young branches. The petals are wrinkled and inserted into the upper part of the tube of the calyx, which is red, thick, and fleshy. The fruit is a globular pome-like berry, about the size of an orange, crowned with the persistent calyx, covered with a reddish-yellow, thick, coriaceous rind, and divided internally into many loculi, which contain an acidulous pulp, and numerous oblong, angular seeds.

This tree grows wild upon both shores of the Mediterranean, in Arabia, Persia, Bengal, China, and Japan, has been introduced into the East and West Indies, and is cultivated in all civilized countries where the climate is sufficiently warm to allow the fruit to ripen. In higher latitudes, where it does not bear fruit, it is raised in gardens and hot-houses for the beauty of its flowers, which become double and acquire increased splendor of coloring by cultivation. Doubts have been entertained as to its original country. The name of *Punicum Malum*, applied by the ancients to its fruit, implies that it was abundant at an early age in the vicinity of Carthage. The fruit, for which the plant is cultivated, varies much in size and flavor. It is said to attain greater perfection in the West Indies than in its native country. The edible pulp is red, succulent, pleasantly acid, and sweetish. See a paper by J. U. Lloyd in *West. Drug.*, 1897, 202.

The pomegranate may be grown in the United States as far north as Maryland. It is cultivated to some extent in California, and the Gulf States as a garden and hedge plant. The seeds are utilized in the south in making cooling drinks. There are several varieties of the pomegranate, the typical having an acid pulp, and others having a sweet and sub-acid character. There is an East Indian variety which is seedless and is highly prized in India. There are several double-flowered varieties which do not bear fruit and are largely cultivated in the south and in green-houses for ornamental purposes.

The *rind of the fruit* is seen in commerce in the form of irregular fragments, hard, dry, brittle, of a yellowish or reddish-brown color externally, paler within, without odor, and of an astringent, slightly bitter taste. It contains a large proportion of tannin, and in countries where the tree abounds, has been employed for tanning leather.

The flowers, sometimes called *balaustines,* are inodorous, have a bitterish, astringent taste, and impart a violet-red color to the saliva. They contain tannic and gallic acids, and were used by the ancients in dyeing.

Description and Physical Properties.—"*Unground Pomegranate.*—Stem bark in pieces from 2 to 8 cm. in length; bark from 0.5 to 3.5 mm. in thickness; outer surface yellowish to grayish-brown, with patches of grayish lichens, broadly elliptical lenticels and yellow-brown furrows or abraded patches of cork; longitudinally wrinkled; inner surface light yellow or yellowish-brown, finely striate; fracture short; phelloderm dark green; inner bark yellowish-green.

"Root bark in transversely curved pieces; externally brownish-yellow with conchoidal depressions and dark brown irregular patches in the cork; internally dark yellow, the medullary rays extending nearly to the outer surface.

"In either root or stem bark, odor slight, taste astringent, somewhat bitter and nauseous.

"*Structure.*—Cork thin, of alternating rows of thin-walled suberized cells and lignified cells with greatly thickened inner walls; cortex of parenchyma with a few large stone cells isolated or in small groups; medullary rays mostly 1-cell wide; rosette aggregates of calcium oxalate very numerous in the parenchyma.

"*Powdered Pomegranate.*—Yellowish-brown to dark brown; calcium oxalate crystals in rosette aggregates or monoclinic prisms from 0.006 to 0.018 mm. in diameter; starch grains numerous, spherical, ellipsoidal, biconvex or irregular and single or compound, from 0.002 to 0.010 mm. in diameter; fragments of whitish cork with prominent, thickened, lignified walls; stone cells from 0.050 to 0.300 mm. in length, the walls being very thick and strongly lamellated; occasional long wood fibers from 0.015 to 0.020 mm. in thickness and associated with tracheæ possessing simple and bordered pores.

"Mix 1 Gm. of powdered Pomegranate with 100 cc. of distilled water, macerate it with occasional agitation for about an hour, and filter; a light yellow filtrate is obtained. Upon the addition of a drop of ferric chloride T.S. to 10 cc. of this filtrate, a bluish-black precipitate is produced. Upon the addition of from 40 to 50 cc. of calcium hydroxide T.S., to another 10 cc. portion of the filtrate, an orange-brown, flocculent precipitate is produced.

"Preserve in tightly closed containers." *U. S.*

The bark of the stem of the pomegranate differs from the root bark by the presence of a broader cortex whose outer cells contain chloroplastids and by possessing shorter medullary rays. The commercial supply of pomegranate bark is obtained chiefly through Marseilles, France.

The inner surface of the bark, steeped in water and then rubbed on paper, produces a yellow stain, which by the contact of ferrous sulphate is rendered blue, and by that of nitric acid acquires a slight rose tint, which soon vanishes. These properties serve to distinguish this bark from those of the box root and barberry. When used, it should be separated from the ligneous portion of the root, as the latter is inert.

Granatum is sometimes substituted by the barks of other plants. Among these are *Berberis vulgaris,* which is bitter and not astringent; *Buxus sempervirens,* which is also bitter and free from tannin; and *Strychnos Nux Vomica* or false Angostura bark which has a dark inner surface and a very bitter taste. None of these barks have the characteristic checkered appearance of the transverse surface of genuine Granatum.

Constituents.—Rembold (*Ann. Ch. Phys.,* cxliii, p. 285) found in the bark about 22 per cent. of a tannin which he thought was peculiar and called *punico-tannic acid* but which Trimble (*A. J. P.,* 1897, p. 636) has shown to be gallo-tannic acid.

Pomegranate bark also yields a considerable quantity of mannite, which was formerly described under the names of *punicin* or *granatin.* The medicinal value of the root, however, is due to the alkaloids discovered by Tanret in 1878 to 1880 (*C. R. A. S.,* lxxxvi, p. 1270 and lxxxviii, p. 716); the first of these he named *pelletierine,* $C_8H_{15}ON$. It is a dextrogyrate liquid boiling at 195° C., easily soluble in water, alcohol, and ether, and especially so in chloroform. It has strong basic properties and precipitates many metallic salts: 1000 parts of dry bark yielded 4 parts of it. In addition he has found three volatile bases in the bark, a liquid left-rotating one, a liquid optically inactive one, and a crystallizable inactive one, to which the names of *methylpelletierine,* $C_9H_{17}ON$, and *pseudopelletierine* (*granatonine*), $C_9H_{15}ON$, and *isopelletierine,* have been given. Carl J. Bender (*Ph. Centralh.,* 1885, p. 6) objects to the name pelletierine, and substitutes *punicine.*

Hess and Eichel (*B. Chem. G.,* 1917, l; 1919, lii, 1005) state that the alkaloid reported by Picinni as *methyl-isopelletierine* is identical with Tanret's methyl-pelletierine. They have also added two more to this list: *iso-pelletierine,* $C_8H_{15}ON$ and *alpha-N-methylpiperidyl-2-propanone,* $C_9H_{17}ON$. Flückiger stated that methylpelletierine predominates in the bark of the root and pelletierine in the bark of the overground portions of the plant.

The alkaloids are prepared by extracting a finely ground mixture of pomegranate and slacked lime with water and shaking out from this with chloroform; the alkaloids are then extracted from the chloroform by means of a weak aqueous solution of hydrochloric acid. The separation of the mixed chlorides is accomplished by fractional distillation.

The bark of the stem usually contains slightly less alkaloid than the bark of the root. The amount in the stem bark has been determined by various investigators to range from 0.35 to 0.6 per cent. and in the root, from 0.6 to 1.0 per cent. Stoeder (*Nederl. Tijd. Pharm.,* 1890) found that of the root bark of three varieties of the wild pomegranate recognized and used by the natives of Java, the red-flowered 'merah,' yielded 2.43 per cent.; the white-flowered, 'poetih,' yielded 3.75 per cent.; the black-flowered, 'hitam,' yielded 1.71 per cent. Wm. F. Junkunz believes that the alkaloid exists in the bark as a tannate. (*A. J. P.,* 1884.) The old idea that the bark loses activity when kept seems to be negatived by the analysis of De Vrij. (*P. J.,* xxi.)

For Leger's method of determining total alkaloids, see *P. J.,* 1904, 581. Assay processes for granatum are given in most of the foreign pharmacopœias and these were critically reviewed by Dichgans (*Ph. Ztg.,* 1914, 852), who finds the one in the Swiss Pharmacopœia to be the best.

Uses.—The bark of the root was used by the ancients as a vermifuge, and is recommended in the writings of Avicenna, but was unknown in modern practice until brought into notice by F. Buchanan, who learned its powers in India. The Mahometan physicians of Hindostan consider it a specific against *tænia.* One of these practitioners, having relieved an English gentleman in 1804, was induced to disclose his secret, which was then made public. The French writers prefer the product of the wild pomegranate, growing on the borders of the Mediterranean, to that of the plant cultivated in gardens for ornamental purposes. The bark may be administered in powder or decoction, but the latter form is usually preferred. The decoction is prepared by macerating two ounces of the bruised bark in two pints of water for twenty-four hours, and then boiling to a pint. Of this a wineglassful may be given every half hour, hour, or two hours, until the whole is taken. It often nauseates and vomits, and usually purges. Portions of the worm often come away soon after the last dose. It is recommended to give a dose of castor oil and to diet the patient strictly on the day preceding the administration of the remedy, and, if it should not operate on the bowels, to follow it by castor oil, or an enema. If not successful on the first trial, it should be repeated daily for three or four days, until the worm is discharged.

Although the value of pomegranate in the treatment of *tape-worm* was known to the ancients and commented on by Dioscorides, the drug fell into disuse in Europe for several centuries until revived by Buchanan in 1805. The efficacy of its alkaloids as tænicides has been abundantly confirmed, and it appears to be established that the tannate of the alkaloids is the most effective and the least dangerous form of the remedy,—probably because its insolubility prevents its rapid absorption and enables it to come in prolonged contact with the worm. (See *Pelletierinæ Tannas*).

The rind of the pomegranate fruit (*Granati Fructi Cortex*) was formerly recognized by the U. S. Pharmacopœia (1870). It is astringent, and in the form of decoction is sometimes employed in *diarrhea* and *colliquative sweats*, and, more frequently, as an injection in *leucorrhea*, and as a gargle in *sore throat* in the earlier stages, or after the inflammatory action has in some measure subsided. The powdered rind has also been recommended in *intermittent fever*. The flowers have the same medicinal properties and are used for the same purposes. The dose of pomegranate rind and flowers in powder is from twenty to thirty grains (1.3–2.0 Gm.). *Decoctum Granati Corticis* was formerly official in the British Pharm. (1898). The decoction may be prepared in the proportion of four ounces of the bark to twenty fluidounces of water, and given in the dose of half a fluidounce (15 cc.). The remedy should always be given after a twelve hours' fast, and be followed in two hours by a brisk cathartic. The seeds are demulcent.

Dose, of granatum, twenty to thirty grains (1.3–2.0 Gm.).

Off. Prep.—Fluidextractum Granati, *U. S.*

GRINDELIA. N. F., Br.

GRINDELIA Grindel.

"Grindelia consists of the dried leaves and flowering tops of *Grindelia camporum* Greene, or *Grindelia cuneifolia* Nuttal, or *Grindelia squarrosa* (Pursh) Dunal (Fam. *Compositæ*). Grindelia contains not more than 10 per cent. of stems of over 2 mm. in diameter, or more than 2 per cent. of other foreign organic matter." *N. F.*

"Grindelia consists of the dried leaves and flowering tops of Grindelia camporum, *Greene*." *Br.*

Gum Plant, Tar Weed; Herba Grindeliæ; Grindelie, G.

The genus *Grindelia* includes some twenty-five species, six or eight of which are found in South America and the remainder occurring in the United States west of the Mississippi. They are coarse perennial or biennial herbs, being occasionally shrub-like. Most, if not all, of the species produce a sticky resinous exudation on the stem and leaves and especially on the flower-heads, whence they are called "gum plants." The leaves are alternate, sessile or clasping and spinulose-dentate. The flowers occur in heads which are either solitary on the ends of branches, or in cymes or panicles. Both the outer ray florets and the central tubular florets are yellow in color. The ray flowers are pistillate and the involucre is bell-shaped or hemispherical, the bracts being imbricated, in several series, being usually subulate-tipped. The drug of the market appears to be derived in large part from *G. camporum* Greene, which is the common *"gum plant"* of California. It occurs abundantly in the inner coast ranges, where it has been collected in quantity in Lake and Napa Counties. It is also common in the foot hills of the Sierra Nevada and is almost the only plant found on the plains in certain regions of the Sacramento Valley. The leaves are oblong or spatulate, sessile or clasping, coarsely serrate and of a pale-green color. The flower-heads are yellow and the involucre consists of several rows of lanceolate acuminate recurved bracts. The achenes are distinctive in this species and are usually biauriculate or more rarely unidentate at the summit.

G. cuneifolia closely resembles *G. camporum.* The leaves are cuneate-oblong or linear-oblong and either sessile or amplexicaul. It is a marsh plant and is not as glutinous as *G. camporum.* The leaves of this species, in addition to their being cuneiform in shape, are darker green and not so thick as in *G. camporum.* The achenes are compressed and closely resemble those of *G. camporum.*

G. squarrosa is a common plant on the prairies and dry banks of the West. It is occasionally found in the East where it is hardy. It has been reported as occurring from the Saskatchewan to Minnesota, Texas, California and Mexico. It is a glabrous, erect, branching herb having linear-oblong or spatulate leaves, which are more or less clasping at the base and sharply spinulose-dentate. It is especially characterized by the bracts of the involucre being linear-lanceolate, subulate tipped and spreading or squarrose at the summit, giving the species its name. The achenes are truncate, those of the outer flowers being usually thicker. The pappus consists of two or three awns.

It was formerly supposed that the drug of commerce was derived from *G. robusta.* The studies of Perrédès (*Proc. A. Ph. A.*, 1906, 370) showed this not to be the case. *G. robusta* is apparently not a very common plant and is distinguished by having cordate-oblong, amplexicaul, coarsely serrate leaves. The involucre is squarrose and leafy at the base. The pappus consists of two awns. At one time both *G. cuneifolia* and *G. camporum* were considered merely as varieties of *G. robusta.* According to Jepson (*Flora of Western Middle California*), there is more divergence between the varieties of *G. robusta* than between the species *G. camporum* and *G. rubricaulis.*

According to Joseph Beauvais (*A. J. P.*, Feb., 1889), the resin of the leaf of *G. robusta* is contained in epidermal glands, and also in rather large resin-ducts situated in an interior collenchymatous layer.

The leafy tops of the Grindelia species are gathered in July and dried in the sun. Most of the commercial supplies come from California and other southwestern states.

Description and Physical Properties.—"*Unground Grindelia.*—Stems and branches cylindrical, light yellow or rose-colored, with alternate leaf scars, occasionally with basal portions of leaves, sometimes irregularly flexous and coated with resin, and terminating in resinous flower heads; leaves usually separate from the stem and broken, oblong to oblong-spatulate, from 1 to 7 cm. in length, mostly sessile or amplexicaul and sharply serrate or evenly spinosely toothed, pale yellow to yellowish green, very resinous, somewhat coriaceous and brittle; bracts of flowering branches almost entire and usually more or less spreading; flower-heads from 5 to 20 mm. in diameter, urn-shaped and conical when unexpanded but flattened or depressed when partly open and usually very resinous; involucre bracts numerous, imbricated, with recurved tips; ray florets yellow or brownish, ligulate and pistillate; disk florets yellow, tubular and perfect; pappus of two or three mostly unequal linear awns about the length of the disk florets; disk achenes ovoid or oblong; compressed, four-angled or triquetrous, and either biauriculate or broadly unidentate or with a broad truncate, corky, thickened summit. Odor balsamic; taste aromatic and bitter, resinous.

"*Powdered Grindelia.*—Yellowish brown; consisting of numerous fibrous fragments, bearing tracheæ with annual and spiral thickenings or marked with simple or bordered pores, associated with numerous, narrow, strongly lignified wood fibers; pith cells more or less tabular and containing a layer of protoplasm in which are embedded numerous spheroidal granules; fragments of leaf epidermis showing more or less polygonal areas containing cloroplastids and colorless, basal cells of the glandular hairs; the latter with compound heads up to 0.100 mm. in diameter each cell of which contains a rosette crystal from 0.005 to 0.008 mm. in diameter; pollen grains spherical, about 0.035 mm. in diameter, spinose, and in section showing three pores." *N. F.*

"Stems slender, yellow, smooth. Leaves three to five centimetres long, oblong or spatulate, sessile or amplexicaul, pale green, rigid, brittle, smooth, glabrous; surface minutely dotted; margin coarsely serrate. Flower-heads yellow, hard, resinous, with several rows of lanceolate-acuminate, recurved bracts. Fruits bi-auriculate or unidentate at the summit, with a pappus consisting of two thick, stiff bristles. All parts more or less resinous. Slightly aromatic odor; taste aromatic and bitter." *Br.*

As it occurs in commerce, grindelia is in the form of the whole dried herb; the stems are about eighteen inches in length, light brownish, very frequently stripped of their leaves, but with some of the floral heads adherent. The brittle leaves are much broken, and, with separate floral heads, are mixed with the stem. The taste is warm, peculiar, and very persistent. Tunmann (*Ph. Zentralh.*, 1908, p. 457) has made an excellent pharmacognostical study of *G. robusta.* Wohn (*Merck's Rep.*, 1910, p. 310) presents the results of a morphological study of *G. squarrosa.* Farwell (*D. C.*, 1907, p. 460) reports having received one of the California "tar weeds," *Hemizouella minima* Gray, for grindelia. The plant is very diminutive in size, but the inflorescence is very glutinous. Perrédès (*P. J.*, 1909, xxix, pp. 596 and 604) gives the results of some experiments in the cultivation of *G. camporum.*

The activity of the drug probably resides in the resinous exudation. Clark and Fischer (*A. J. P.*, 1888) reported the presence of an alkaloid, *grindeline,* and Schneegans (*A. J. P.*, 1892) the presence of a glucosidal saponin. Power and Tutin (*Proc. A. Ph. A.*, 1905 and 1907) were unable to confirm these results and attributed the value of the drug to the amorphous resins which compose over 21 per cent. of the drug. The greater portion of this resinous matter was a complex mixture of liquid acids which were chiefly unsaturated cyclic compounds and were optically active. They found also traces of a bright yellow volatile oil possessing to a high degree the characteristic odor of the drug. *Grindelia robusta* is said to contain 0.28 per cent. of a dark-brown essential oil, having a specific gravity of 0.9582 at 15° C., and the optical rotation in alcoholic solution of –8° 08′. It is soluble in ether, amyl alcohol, and chloroform. (*Ph. Ztg.*, 48, 574.)

Uses.—Grindelia is possessed of only feeble physiologic powers, but according to Buffington, when given to the lower animals in very large doses produces narcosis, with dilated pupils, slowing of the action of the heart from stimulation of the inhibitory nerves, and elevation of the blood pressure from stimulation of the vasomotor center. Dobroklowsky has found that it had a primary stimulating and later depressant effect on the isolated frog's heart. He further states that it acts chiefly upon the motor nerves and muscles, but Buffington asserts that it paralyzes first the sensory nerve-trunks, then the sensory side of the spinal cord, and afterwards involves the motor nerve-trunk and cord. Grindelia is used in the treatment of *bronchial catarrhs,* especially when there is a tendency to *asthma.* Its action is probably simply that of a stimulating expectorant, but some believe it exerts also an antispasmodic influence. It is frequently used in conjunction with stramonium leaves in the preparation of "Asthma powders" or cigarettes. It has been employed with asserted success in *whooping cough.* Its active principles appear to be excreted from the kidneys; hence, after large doses, there are sometimes evidences of renal irritation, and in chronic *catarrh of the bladder* good has been effected by its stimulant influence upon the mucous membrane of the viscus. As a local application, grindelia has been employed with asserted advantage in *burns, vaginitis, genito-urinary catarrh,* etc., applied either in the form of a poultice or in solution. It has considerable use also as a local application in the treatment of *rhus poisoning.* The fluidextract, diluted with water, is employed.

Dose, thirty to forty grains (2.0–2.6 Gm.).

Off. Prep.—Fluidextractum Grindeliæ, *N. F.* (*Br.*).

GUAIACI LIGNUM. Br.

GUAIACUM WOOD

"Guaiacum Wood is the heart-wood of Guaiacum officinale, *Linn.*, or of Guaiacum sanctum, *Linn.*" *Br.*

Lignum Sanctum (vel Benedictum); Lignum Vitæ; Gaïac, Bois de Gayac, *Fr.;* Lignum Guajaci, *P. G.;* Guajakholz, Franzosenholz, Pockholz, *G.;* Guajaco, Legno guajaco, *It.;* Guayaco (Leño de), *Sp.*

This drug is not official in the U. S., but the resin is recognized by the N. F.

Guaiacum officinale (Fam. *Zygophyllaceæ*) is a middle-sized or low evergreen tree indigenous to the West Indies and northern part of South America. The branches are knotted, and covered with an ash-colored striated bark. That of the stem is of a dark-gray color, variegated with greenish or purplish spots. The leaves are opposite, leathery, and abruptly pinnate, consisting of two, three, and sometimes four pairs of leaflets, which are obovate, smooth, shining, dark green, from an inch to an inch and a half long, and almost sessile. The flowers are of a rich blue color, stand on long peduncles, and grow to the number of eight or ten at the axils of the upper leaves. The seeds are solitary, hard, and of an oblong shape.

G. sanctum L. is distinguished from *G. officinale* by its five-celled fruit and its oblong or obliquely obovate or sometimes rhomboid-ovate leaflets, six to eight to each leaf. It grows in Cuba, Haiti, the Bahama Islands and Florida. Its wood is smaller than that of *G. officinale,* and is said by Fée to be paler and less dense.

The commercial supplies are shipped from Cuba, Haiti and the Dominican Republic to the United States and Europe.

As imported, guaiac wood is in the shape of logs or billets, covered with thick gray bark, which presents on its inner surface, and upon its edges, when broken, numerous shining crystalline particles. These were supposed by Guibourt to be benzoic acid, by others a resinous exudation from the vessels of the plant; but Otto Berg has determined that they are crystals of calcium sulphate. The billets are used by turners for the fabrication of various instruments and utensils, for which the wood is well adapted by its extreme hardness and density. The waste heartwood, consisting of raspings or shavings from turners, is usually alone employed in pharmacy and medicine. It is commonly called *lignum vitæ,* a name which obviously originated from its durable properties.

Properties.—Guaiacum wood is hard and heavy. The color of the sap-wood is yellow, that of the older and central layers greenish-brown, that of the shavings a mixture of the two. It is said that when the wood is brought into a state of minute division its color is rendered green by exposure to the air, and bluish-green by the action of nitric acid fumes, and the latter change may be considered as a test of its genuineness. (Duncan.) An easier test is a solution of corrosive sublimate, which, added to the shavings and slightly heated, causes a bluish-green color in the genuine wood. Guaiacum wood is almost without odor unless rubbed or heated, when it becomes odorous. When burned, it emits an agreeable odor. It is bitterish and slightly pungent, but requires to be chewed for some time before the taste is developed.

"Dark greenish-brown, dense, hard; heavier than water. In transverse section, abundant sclerenchymatous fibres, scattered, isolated vessels, and medullary rays one cell wide. Odor, on warming, somewhat aromatic; taste slightly acrid. An alcoholic tincture prepared from the Wood assumes a blue color in the addition of diluted *T. Sol. of ferric chloride.*" *Br.*

The N. F. IV described it as follows: "Usually in the form of shavings, chips or raspings of a greenish-brown color, heavier than water, entirely free from adhering bark and containing only a few chips or shavings of a whitish color (*sap wood*). Almost odorless except when heated; taste bitter and acrid when chewed for some time. The powder, when examined under the microscope, exhibits numerous fragments of more or less lignified, thick-walled wood fibers, up to 0.028 mm. in width, some with simple, oblique pores; tracheæ from 0.09 to 0.16 mm. in width, some filled with resin; numerous small masses of resin; wood parenchyma and medullary ray cells up to 0.02 mm. in width, with lignified, porous walls and usually containing resin; occasionally tangential views of the medullary rays show an elliptical group of from three to six cells; the resin masses and resinous tissue become bluish-green on the addition of iodine T.S. Place powdered Guaiac Wood in a solution of sodium chloride (1 in 3); the blackish-brown part only will sink and this does not exceed in amount the portion which floats. Shake 10 cc. of alcohol with 0.5 Gm. of ground Guaiac Wood for a few seconds and filter the mixture; the filtrate yields a deep blue color with one drop of a solution of ferric chloride (1 in 10). Guaiac Wood yields to alcohol not less than 15 per cent. of extractive. Guaiac Wood yields not more than 3 per cent. of ash." *N. F. IV.*

Guaiac wood contains, according to Trommsdorf, 26 per cent. of resin, and 0.8 of bitter pungent extractive, upon both of which, probably, though chiefly on the former, its medicinal virtues depend. (See *Guaiacum.*) Paetzold (*Schim. Rep.*, 1902, 43) states that the bark of the guaiac tree yields 1 per cent. of a volatile oil, having an exquisite odor. The wood yields its virtues but slightly to water. One pound of the wood afforded to Geiger two ounces of extract.

Uses.—Guaiacum wood possesses no therapeutic powers which are not contained in its resin and the latter is always to be preferred.

Dose, thirty to sixty grains (2.0–3.9 Gm.).

Off. Prep.—Decoctum Sarsaparillæ Compositum, *N. F.*

GUAIACUM. N. F. (Br.)

GUAIAC Guaiac. [Guaiac Resin]

"Guaiac is the resin of the wood of *Guajacum officinale* Linné or of *Guajacum sanctum* Linné (Fam. *Zygophyllaceæ*). Guaiac yields not more than 15 per cent. of residue insoluble in alcohol." *N. F.*

"Guaiacum Resin is the resin obtained from the stem of Guaiacum officinale, *Linn.*, or of Guaiacum sanctum, *Linn.*" *Br.*

Guaiaci Resina, *Br.;* Guaiac; Guaiacum Resin; Résine de Gaïac, *Fr. Cod.;* Resina Guajaci, *P. G.;* Guajak, Guajakharz, *G.;* Resina de guajaco, *It.;* Resina de guayaco, *Sp.*

For a description of *Guaiacum officinale,* see *Guaiaci Lignum.*

Guaiac resin was introduced into the London Pharmacopœia in 1677. It exists in the tree as a physiological product filling up the tissues of the wood. It is obtained in several different modes. The most simple is by spontaneous exudation, or by incisions made into the trunk. Another method is by sawing the wood into billets about three feet long, boring them longitudinally with an auger, then placing one end of the billet on the fire, and receiving in a calabash the melted guaiac, which flows out through the hole at the opposite extremity. But the plan probably most frequently pursued is to boil the wood, in the state of chips or sawdust, in a solution of common salt, and skim off the substance which arises to the surface. Guaiac resin is chiefly produced in the eastern portion of the Island of Haiti, being exported from Azua and Gonaïves in bags within cases. Formerly, the quality of the drug was often bad, being loaded with bark and wood. At present much of it is so clean that it appears to be strained. It is usually in large irregular pieces of various sizes, in which small fragments of bark, sand, and other impurities are mixed with the genuine guaiac, so as to give to the mass a diversified appearance. Sometimes it is found in small roundish homogeneous portions, separate or agglutinated; sometimes in homogeneous masses, prepared by melting and straining the drug in its impure state. It is probable that the guaiac obtained from the billets in the manner above described is of uniform consistence.

Description and Physical Properties.—"In irregular fragments or in large, nearly homogeneous masses, occasionally in more or less rounded or ovoid tears, enclosing fragments of vegetable tissues; externally brown, becoming greenish gray-brown on exposure, the fractured surface having a glassy luster, the thin pieces being translucent and varying in color from reddish to yellowish brown. The powder is grayish, becoming green on exposure to the air. Odor balsamic; taste slightly acrid.

"Guaiac melts between 85° and 90° C. It is readily soluble in alcohol, ether, chloroform, creosote, and in solutions of the alkalies or in chloral hydrate T.S. It is sparingly soluble in carbon disulphide or benzene; the alcoholic solution, on the addition of an excess of chlorine water or tincture of ferric chloride, becomes blue, changing quickly to green, the color being best seen when the solutions are diluted with an equal volume of water. A petroleum benzoin solution of Guaiac is colorless and yields no test for rosin with cupric acetate T.S." *N. F.*

"In masses, or sometimes in large more or less rounded tears. Brittle; fracture vitreous; thin splinters transparent, from yellowish-green to reddish-brown. Powdered Resin greyish, but becoming green on exposure to light and air. Odor, on warming, somewhat aromatic; taste slightly acrid. A solution in *alcohol* (90 per cent.) is colored blue by diluted *T. Sol. of ferric chloride.* 1 gramme of the powdered Resin, shaken for five minutes with 5 millilitres of *petroleum spirit,* yields a colorless filtrate which does not become green when shaken with an equal volume of *diluted solution of copper acetate* (absence of colophony). Not more than 10 per cent. insoluble in *alcohol* (90 per cent.). Ash not more than 4 per cent." *Br.*

The tincture is of a deep-brown color, is decomposed by water, and affords blue, green, and brown precipitates with the mineral acids. It is colored blue by nitric acid, by chlorine, and by tincture of ferric chloride, and usually by spirit of nitrous ether, and is similarly changed when treated successively by diluted hydrocyanic acid and solution of copper sulphate. Either in substance or tincture, guaiac gives a blue color to gluten and substances containing it, to mucilage of gum arabic, to milk, and to various freshly cut roots, as to the potato, carrot, and horseradish. This is on account of the fact that oxidizing enzymes, or oxidases, are present in all of these substances and guaiac resin is one of the most delicate reagents for detecting this class of enzymes. It is soluble also in ether, alkaline solutions, and sulphuric acid. The solution in sulphuric acid is of a rich claret color, deposits, when diluted with water, a lilac precipitate, and, when heated, carbonizes. Exposed to air and light, guaiac absorbs oxygen and becomes green, and the change takes place rapidly in the sunshine. Schaer states that a good natural guaiac resin is preferable to a resin purified by alcoholic treatment as a reagent, but a solution of resin extracted by chloroform from the wood is the most sensitive of all. Tincture of guaiac has been used for the detection of blood stains, which it does by the blue color produced by it, when in contact with the red coloring matter of blood, in connection with some ozonized substance, especially hydrogen dioxide.

Adulterations.—Guaiac resin is sometimes adulterated with the rosin of the pine. The fraud may be detected by the terebinthinate odor exhaled when the sophisticated guaiac is thrown upon burning coals, as well as by its partial solubility in hot oil of turpentine. This liquid dissolves rosin, but leaves pure guaiac untouched. Amber was said to be another adulterant at one time. Nitric acid affords an excellent test of guaiac. If paper moistened with the tincture be exposed to the fumes of this acid, it speedily becomes blue. Purgotti proposed guaiac resin as a test for copper. (See *A. J. P.*, June, 1880.)

Constituents.—Guaiac resin is made up chiefly of resin acids. (Lücker, *Proc. A. Ph. A.*, 1894.) Of these *guaiaconic acid,* $C_{20}H_{24}O_5$, which composes some 70 per cent. of the resin, occurs in two form known as alpha- and beta-guaiaconic acid. *Guaiaretic acid,* $C_{26}H_{24}O_4$, which is present in a little more than 11 per cent. is an optically inert, unsaturated acid. *Guaiac-betaresin* is present to the extent of about 15 per cent. Alpha-guaiaconic acid is colorless and amorphous, the beta variety, however, is crystalline. These acids are readily converted by oxidizing agents into a deep blue substance called *guaiac-blue,* which reaction is the bases of the guaiac test for blood (see under *diagnostic Tests,* Part II). There are present also small amounts of a coloring matter called *guaiac-yellow* and *guaiacic acid,* $C_{20}H_{24}O_4$, and traces of vanillin and a saponin. Guaiac beta-resin appears to be a decomposition product of guaiaconic acid and gives the blue reaction on oxidation.

On dry distillation guaiac resin yields *guaiacene,* C_5H_8O, guaiacol, creosol (see *Creosotum*), *guaiene* and finally *pyroguaiacin,* $C_{38}H_{44}O_6$ (according to Wiesner, $C_{18}H_{18}O_3$), in pearly scales, melting at 180° C. Guaiacene is the aldehyde of tiglic acid, $C_5H_8O_2$, and can be made synthetically from a mixture of acetaldehyde and propionaldehyde. Guaiene is 2:3-dimethyl naphthalene.

According to the experiments of W. Frieboes (*In. Dis.,* Rostock, 1903), the guaiac saponin (1 to 1000) forms a frothing solution which is persistent, is an excellent emulsifier, has the power to maintain in solution large proportions of sparingly soluble substances and is innocuous and non-irritant.

The mineral acids are incompatible with the solutions of guaiac.

Uses.—Guaiac, like many other resinous substances, is stimulant and alterative. If given to a patient when covered warm in bed, and accompanied with hot drinks, it may assist in exciting perspiration, and hence it has been ranked among the diaphoretics. In large doses it purges, and it has been especially commended as a laxative in *chronic rheumatism,* and it is thought by some practitioners to be possessed of emmenagogue powers. It has been given in *chronic rheumatism, gouty affections,* secondary *syphilis, scrofulous diseases,* and *cutaneous eruptions,* but is of doubtful service. The medicine is given in pill, emulsion or tincture.

An objection to the form of powder is that it quickly aggregates. Guaiac is sometimes administered in combination with alkalies, with which it readily unites. The ammoniated tincture of guaiac is a preparation of this kind. Several European Pharmacopœias direct a *soap of guaiac,* under the name of *sapo guaiacinus,* to be prepared by diluting solution of potassium hydroxide with twice its weight of water, boiling lightly, then adding guaiac gradually, with continued agitation, so long as it continues to be dissolved, and finally filtering, which is followed by evaporating to the pilular consistence.

T. C. Craig (*A. J. P.*, July, 1880) recommends a *Syrup of Guaiac* made as follows: Powd. Guaiac Resin, 640 grains; Caustic Potassa, 58 grains; White Sugar, 1 lb. (av.); Water, q. s. Dissolve the Potassa in 8 fluidounces of water; moisten the Guaiac with this solution; pack it in a percolator, and gradually pour on the remainder of the solution; when this ceases dropping, add sufficient water to make the percolate measure 8 fluidounces; add the sugar, and dissolve.

Dose, from ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Mistura Guaiaci, *Br.;* Pilula Hydrargyri Subchloridi Composita, *Br.;* Tinctura Guaiaci, *N. F.;* Tinctura Guaiaci Ammoniata, *N. F., Br.;* Trochiscus Guaiaci Resinæ, *Br.;* Gargarisma Guaiaci Compositum, *N. F.;* Tinctura Guaiaci Composita, *N. F.*

GUAIACOL. U. S., Br.

GUAIACOL

"A liquid consisting principally of $C_6H_4(OH)(OCH_3)$ 1 : 2, usually obtained from wood creosote, or a solid, consisting almost entirely of $C_6H_4(OH)(OCH_3)$ 1 : 2, usually prepared synthetically." *U. S.* "Guaiacol, $C_7H_8O_2$, may be prepared synthetically or obtained by the fractional distillation of beech tar creosote." *Br.*

Gaiacolum Methyl-orthodioxybenzene, Methyl-pyrocatechin, Catechol-monomethyl-ether; Gaïacol, *Fr. Cod.;* Guajacolum, *P. G.;* Guajakol, Brenzcatechin-monomethylester, *G.;* Guajocolo, *It.;* Guayacol, *Sp.*

Preparation.—Guaiacol is the monomethyl ester of the ortho-dioxybenzene known as catechol (pyrocatechin), and can be made from this diatomic phenol by methylating with the aid of methyl-sulphuric acid. It is, however, largely obtained from beechwood creosote, of which it constitutes from 60 to 90 per cent. The separation of the diatomic phenols and phenol-ethers from monatomic phenols in a mixture like creosote, is effected in several ways. The compounds formed by baryta with the former are much less soluble than those with the latter, and this is also true of magnesia compounds. Another method is to rub up the creosote with potassium carbonate. Guaiacol and creosol combine to form solid addition compounds, from which the other phenols are washed out with ether or petroleum benzin, when the crystalline mass is decomposed with water and the phenols separated. It is also prepared from ortho-nitrophenol by conversion into ortho-anisidine, a methylated derivative, as an intermediate step.

Description and Physical Properties.—"Liquid Guaiacol is colorless or yellowish. Solid Guaiacol is crystalline and is colorless or yellowish. Guaiacol becomes darker on exposure to light. When liquefied, the solid form may remain liquid for a long time even at a low temperature. Guaiacol has an agreeable, aromatic odor. One Gm. of Guaiacol is soluble in from 60 to 70 cc. of water and in 1 cc. of glycerin, at 25° C., but separates from the glycerin on the addition of water. It is miscible with alcohol, chloroform, ether, and with glacial acetic acid.

"Solid Guaiacol melts at about 28° C. The addition of a few drops of ferric chloride T.S. to 10 cc. of an alcoholic solution of Guaiacol (1 in 100) immediately produces a blue color, changing to emerald-green, and finally becoming yellowish.

"Specific gravity: liquid Guaiacol, not below 1.112 at 25° C.; melted solid Guaiacol, about 1.132 at 25° C. Not less than 85 per cent. of liquid Guaiacol distils between 200° and 210° C. when determined by Method II, page 000. Solid Guaiacol boils between 204° and 206° C. Ash: not more than 0.1 per cent. Shake 2 cc. of liquefied Guaiacol with 4 cc. of purified petroleum benzin; the mixture separates into two distinct, clear layers on standing. Permanent turbidity, or failure to separate into layers indicates the presence of impurities. One cc. of liquefied Guaiacol dissolves in 2 cc. of 15 per cent. potassium hydroxide solution when heated for one minute in boiling water; on cooling, the solution congeals to a nearly white mass. Much coloration or failure to congeal indicates the presence of impurities. The mass thus obtained forms a clear solution with 25 cc. of distilled water (*hydrocarbons*).

"Preserve in well-closed containers, protected from light." *U. S.*

"A colorless liquid, or colorless crystals melting at about 28° C. Characteristic, tarry odor; taste caustic, very pungent. Soluble in 80 parts of *water;* freely soluble in *alcohol* (90 per cent.), in *ether,* in *glycerin,* and in fixed oils. Liquid Guaiacol optically inactive; specific gravity 1.16 to 1.20. Distils between 200° and 205° C. A trace of *T. Sol. of ferric chloride* added to 25 millilitres of a solution (1 in 100) of Guaiacol in *alcohol* (90 per cent.) immediately produces a blue color which changes to emerald-green on the addition of more of the test-solution, and finally becomes yellowish. When liquid Guaiacol is shaken with twice its volume of *petroleum spirit* and allowed to stand, the mixture separates into well-defined layers which do not exhibit permanent turbidity. 1 millilitre of liquid Guaiacol dissolves when warmed with 2 millilitres of an aqueous solution (15 in 100) of *sodium hydroxide;* the nearly white mass which results on cooling yields a clear solution with 25 millilitres of *water* (absence of oily hydrocarbons)." *Br.*

S. Vreven (*Zeit. Oestr. Apoth. Ver.,* 1896, 711) recommended the following method for distinguishing between guaiacol and creosote: A drop of the liquid to be examined, 2 to 3 drops of ether, and 1 or 2 drops each of concentrated nitric and hydrochloric acids are well shaken together in a test tube. The mixture assumes at first a red-brown color, which is particularly evident in the ether layer; but upon spontaneous evaporation, well-formed needle-shaped crystals will separate out if guaiacol is present, the formation of these crystals being facilitated by occasional shaking, whereas in the presence of creosote oily globules only separate. While phenol gives a reaction similar to that of guaiacol, the crystals formed are easily distinguished from the needles produced by the latter.

Uses.—Guaiacol is locally irritant and somewhat anesthetic. Its germicidal power, although inferior to that of creosote, equals or perhaps surpasses phenol. It is absorbed readily, not only from the alimentary canal, but also through the skin. It is eliminated chiefly through the kidneys in combination with sulphuric and glycuronic acids. Although its general physiological action has not been carefully studied, it seems to resemble phenol, although less poisonous. Guaiacol is used internally chiefly as a stimulating expectorant in *phthisis* and *bronchitis.* It has been also largely used by endermic administration as an antipyretic in *pneumonia* and other *fevers,* but is liable to produce dangerous collapse. Locally it is employed for its anesthetic effects in various skin diseases as *herpes zoster, eczema, furunculosis,* and even minor operations in the nose and throat, and as an antiseptic in old *ulcers,* especially when *tubercular* or *leprous.*

For percutaneous administration from ten to twenty drops are gently rubbed on the abdomen and the surface covered with oiled silk.

Dose, from five to ten minims (0.3–0.6 cc.).

Off. Prep.—Petroxolinum Guaiacolis, *N. F.*

GUAIACOLIS CARBONAS. U. S. (Br.)

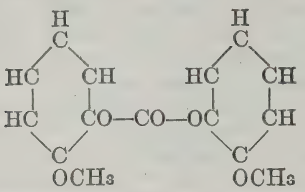
GUAIACOL CARBONATE Guaiacol. Carb.

"The guaiacol ester [$(C_6H_4(OCH_3)O)_2.CO$] of carbonic acid." *U. S.* "Guaiacol Carbonate, $(C_7H_7O)_2CO_3$, is the carbonic ester of guaiacol. It may be obtained by the interaction of carbonyl chloride with sodium guaiacolate." *Br.*

Guaiacol Carbonas, *Br.;* Duotal; Gaiacolum Carbonicum; Carbonas Guajacoli; Carbonate de Gaïacol, *Fr.;* Guajacolum Carbonicum, *P. G.;* Guajacolkarbonat, Kohlensaure-Gaujacyläther, *G.;* Carbonato de guayacol, *Sp.*

It is not a true carbonate in the sense that acids are capable of decomposing it with the evolution of CO_2. It is a carbonyl derivative and is prepared by the action of phosgene (carbonyl chloride) upon guaiacol in the presence of alkalies, or by combining guaiacol with methyl chloroformate.

The structural formula is:



Description and Physical Properties.—"Small, colorless crystals, or a white, crystalline powder. It is odorless and tasteless, or has a slight aromatic odor and taste. Guaiacol Carbonate is insoluble in water. One Gm. is soluble in 60 cc. of alcohol, 1 cc. of chloroform, and in 18 cc. of ether, at 25° C. It is freely soluble in boiling alcohol and benzene, and is slightly soluble in glycerin and in fixed oils.

"Guaiacol Carbonate melts between 85° and 88° C. Heat about 0.5 Gm. of Guaiacol Carbonate for a few minutes with 10 cc. of alcoholic potassium hydroxide T.S., cool, and decant the liquid from the precipitate; the addition of an acid to the precipitate produces effervescence. Evaporate the alcohol from the decanted liquid, strongly acidulate the residue with diluted sulphuric acid, and shake with chloroform; the separated chloroform layer upon evaporation leaves a residue which responds to the ferric chloride test for identity under *Guaiacol.*

"Ash: not more than 0.1 per cent. A saturated alcoholic solution of Guaiacol Carbonate is neutral to litmus paper, previously moistened with distilled water, and yields no bluish-green color on the addition of ferric chloride T.S. (*free guaiacol*). Dissolve 0.1 Gm. of Guaiacol Carbonate in 2 cc. of sulphuric acid; the solution is not darker than faint yellow (*readily carbonizable substances*)." *U. S.*

"A white crystalline powder, inodorous and almost tasteless. Insoluble in *water;* sparingly soluble in *alcohol* (90 per cent.), the solution being neutral to *litmus.* Melting point 85° to 88° C. When the liquid obtained by heating Guaiacol Carbonate with *N/20 solution of sodium hydroxide* is acidified, carbon dioxide is evolved and guaiacol is liberated. A saturated solution in *alcohol* (90 per cent.) does not assume a greenish or bluish color on the addition of *T. Sol. of ferric chloride* (absence of free guaiacol). No appreciable ash." *Br.*

Maue (*Ph. Ztg.,* 1918) proposes the following test for the identification of guaiacol carbonate: About 0.02 gramme of the sample is dissolved in 1 cc. of alcohol, 2 drops of ferric chloride solution and 1 drop of formaldehyde solution are added, and the mixture is poured on the surface of 2 cc. of sulphuric acid; a cherry-red coloration, due to the presence of guaiacol, develops at the junction of the two liquids. The sensitiveness of the reaction is about 1 : 300,000.

Uses.—Guaiacol carbonate is much used as a substitute for guaiacol on account of its comparative tastelessness and its lack of irritant properties. It is, however, much less effective than is guaiacol, both as a local and systemic drug. The experiments of W. Hesse (*D. M. W.,* 1898) indicate that when taken internally much of it passes through the alimentary canal unabsorbed.

Dose, from ten to twenty grains (0.65–1.3 Gm.).

GUARANA. N. F.

GUARANA

"Guarana is a dried paste consisting chiefly of the crushed seed of *Paullinia Cupana* Kunth (Fam. *Sapindaceæ*). Guarana yields not less than 4 per cent. of caffeine." *N. F.*

Paullinia, Brazilian Cocoa, Guarana Bread; Guarana, *Fr. Cod.;* Pasta Guaranæ; Guarana, *G., It.;* Paulinia, Pasta de Guarana, *Sp.*

There are described of the genus *Paullinia* 121 species, all of them confined in their geographical range to tropical and subtropical South America, except one, which has strayed to Eastern and Western Africa, and two others which are found in Mexico and in the gardens of the Sandwich Islands.

The *Paullinia Cupana* Kunth is a climbing shrub with alternate, imparipinnate leaves, which is native to the northwestern provinces of Brazil. The flowers are of yellowish color, growing in axillary spicate panicles. The leaves are long petioled, the leaflets being 5 to 6 inches long by 2 or 3 inches wide, and sinuate dentate on the margins. The fruit is ovoid or pyriform and about the size of a grape, and contains 1 to 3 seeds which resemble small horse chestnuts. They are lenticular and almost thorny and are invested with a flesh-colored arillus which is easily separable when dry.

It is probable that in the preparation of guarana the seeds of the allied species, *P. sorbilis* Martius, are used interchangeably with those of the official species.

Guarana is made exclusively by the Guaranis, a tribe of South America Indians, and probably varies in the details of its preparation, as it certainly does in appearance and quality. The drug appears to be produced almost exclusively from plants cultivated in the region of the lower Madeira and southward. After the seeds are shelled and thoroughly washed they are roasted for about six hours, and their external papery shells are then removed by placing them in sacks and beating them with clubs. The kernels are then broken in a mortar, the coarse powder is mixed with a little water, and then kneaded into a paste, which is shaped into cylindrical or globular masses; tapioca is sometimes added before kneading to increase plasticity. The lumps are dried, sometimes in the sun, or more usually by the heat of a slow fire so arranged as to avoid smoke. When finished, the masses are of a reddish-brown color, rugose on the surface, very hard, with an irregular fracture, and of a marble appearance when broken, due to the fragments of the seeds and their black testa embedded in the mass.

The present commercial supplies of guarana come to this country in cases from Para, Brazil.

Description and Physical Properties.—"*Unground Guarana.*—Usually in cylindrical sticks, about 3 to 5 cm. in diameter, externally dark reddish brown; hard and heavy, fracture uneven, often fissured in the center; internally pale reddish brown, showing more or less coarse fragments of seed and occasionally their blackish brown seed-coats. Odor slight; taste slightly astringent and bitter.

"*Powdered Guarana.*—Light pinkish brown; consisting mostly of irregular masses of parenchyma containing more or less altered starch grains; unaltered starch grains occasional, varying from spherical and polygonal to ellipsoidal and broadly ovoid, 0.010 to 0.025 mm. in diameter; occasional fragments with narrow, elongated sclerenchymatous cells; the walls being thick, yellowish and non-lignified.

"Place on a slide a drop of hydrochloric acid, add about 0.001 Gm. of powdered Guarana, then add a drop of gold chloride T.S. and allow the mixture to stand for a few minutes; beginning at the edge of the mount, crystals of caffeine and gold chloride separate in the form of orthorhombic plates and needles, the latter usually occurring in spheroidal aggregates and finally forming branching groups.

"**Assay.**—Place 6 Gm. of Guarana, in fine powder, in a suitable flask or bottle, add 120 cc. of chloroform and shake. Allow to stand five minutes, then add 6 cc. of ammonia water and shake the mixture continuously during one hour, or intermittently (see Proximate Assays, Type Process A) during two hours. Allow the mixture to stand overnight, again shake intermittently during one-half hour, then allow the drug to settle. Decant, or filter off through a pledget of purified cotton, 100 cc. of the chloroformic liquid, representing 5 Gm. of Guarana, and evaporate it to dryness. Treat the residue with 10 cc. of weak (about 1 per cent.) sulphuric acid with the aid of a gentle heat, allow to cool, filter through a small filter into a separator, wash the dish and filter with successive small portions of distilled water until no test for alkaloid is obtained by acidulating a few drops of the filtrate strongly with sulphuric acid and adding iodine T.S. Now add ammonia water until the liquid is distinctly alkaline to litmus, and completely extract the caffeine with successive portions of chloroform, as shown by testing with iodine T.S. Evaporate the combined chloroform solutions, and dry the residue at 80° C. to constant weight. The weight is the amount of caffeine from 5 Gm. of Guarana." *N. F.*

Guarana is of a somewhat astringent and bitterish taste, and in this, as well as in its odor, bears some resemblance to chocolate, though not oleaginous. It swells up and softens in water, which partially dissolves it. It is also partly soluble in alcohol.

Martius found in it a crystallizable principle, which he named *guaranine,* but which was later proved by Berthemot and Dechastelus to be identical with caffeine. Alexander Bennett, in an elaborate series of physiological experiments, confirmed this identity. According to Berthemot and Dechastelus, the caffeine exists in the seeds united with tannic acid, with which it appears to form two compounds, one crystallizable and soluble in water, the other of a resinoid appearance and insoluble.

M. I. Wilbert (*J. A. Ph. A.,* 1914, 1286) reported a compilation of analyses of guarana comprising 41 samples in which the caffeine content varied from 3.72 to 5.16 per cent.

Rochefontaine and Gusset prepared caffeine by mixing one part of calcined magnesia with five parts of powdered guarana, moistening with water, and, after standing twenty-four hours, exhausting the mass with boiling chloroform, evaporating the chloroform, treating the residue with boiling water, filtering, and evaporating over sulphuric acid. (*A. J. P.,* 1886, p. 248.) F. V. Greene prefers a process for obtaining caffeine from guarana similar to one proposed by Wayne for its extraction from tea and coffee. See *U. S. D.,* 19th ed., p. 606.

F. V. Greene has shown that the tannic acid from guarana has different properties from that found in other plants, and proposes to call it *paullinitannic acid.* (*A. J. P.,* 1877, 390.)

Uses.—The effects of guarana upon the system are chiefly those of its alkaloid, although it contains enough tannin to have an appreciable influence. It is habitually employed by the Indians, either mixed with articles of diet, as with cassava or chocolate, or in the form of drink, prepared by scraping it, and suspending the powder in sweetened water, precisely as other nations use teas, coffees, etc. It is also considered by the Indians useful in the prevention and cure of bowel complaints. It is now used in medicine almost exclusively to give relief during the paroxysm of *migraine,* and in atonic *chronic diarrhea,* taken three or four times a day.

Dose, of the powder, twenty to sixty grains (1.3–3.9 Gm.).

Off. Prep.—Fluidextractum Guaranæ, *N. F.;* Elixir Guaranæ (from Fluidextract), *N. F.;* Elixir Guaranæ et Apii (from Fluidextract), *N. F.*

GUMMI INDICUM. Br.

INDIAN GUM Ghatti Gum]

"Indian Gum is a gummy exudation from the stem of Anogeissus latifolia, *Wall.*" *Br.*

The genus *Anogeissus* (Fam. *Combretaceæ*) includes four or five different species of tropical trees. Of these *A. latifolia* is widely distributed in India and Ceylon. The tree is large and handsome, and one of the most useful of tropical India. The leaves are broadly elliptical, obtuse at the base and summit. They contain large amounts of tannin and are used in Bombay for tanning. The flowers are axillary and the fruit is 2-winged, being arranged horizontally into dense heads. The gum from this tree is collected in April and is used extensively in calico printing, especially in Lucknow. It may be distinguished from Acacia by its dull surface, uniform vitreous fracture and by the frequent presence of vermiform tears. Its mucilage is more viscid but less adhesive than Acacia and is usually used in connection with turmeric with which there is some specific combination.

The commercial supplies of this drug come from Bombay and London.

"In vermiform or rounded tears of varying size, colorless or pale yellow; surface dull, fracture vitreous. Slight odor; taste insipid and mucilaginous. Entirely soluble in *water,* forming a viscous, adhesive mucilage. Insoluble in *alcohol* (90 per cent.). The aqueous solution is gelatinised by the addition of *alcohol* (90 per cent.), or *solution of lead subacetate;* but it is unaffected by the addition of *T. Sol. of ferric chloride* or of *solution of lead acetate* (distinction from Amrad and certain other gums). It is not colored blue or brown by a small quantity of *N/10 solution of iodine* (absence of starch or commercial dextrin). Ash not more than 4 per cent. In India and the Eastern Divisions of the Empire, India Gum may be employed in making the official preparations for which Gum Acacia is directed to be used, one part of the former being taken for every two parts ordered of the latter (see 'Mucilago Gummi Indici')." *Br.*

Ghatti gum forms a nearly colorless mucilage with water which is more viscous than that made with a similar amount of acacia. Its aqueous solution gives a slight precipitate with solution of lead subacetate.

Uses.—Indian gum is used for the same purposes in pharmacy as acacia. It is well suited for pharmaceutical use, and is said to be specially valuable in the making of emulsions. It is insoluble in 90 per cent. alcohol.

The Br. Pharmacopœia allows of the substitution of India gum in official preparations in place of gum acacia, with the statement that one part of it should be substituted for two of the acacia. It must not be confounded with either Bassora or Gum Sterculin, each of which is sometimes referred to as "Indian Gum." (See Part II.)

Off. Prep.—Mucilago Gummi Indici, *Br.*

HÆMATOXYLON. N. F. (Br.)

HEMATOXYLON Hæmatox. [Logwood]

"Hematoxylon is the heart-wood of *Hæmatoxylon campechianum* Linné (Fam. *Leguminosæ*). Hematoxylon contains not more than 2 per cent. of foreign organic matter." *N. F.*

"Logwood is the heart-wood of Hæmatoxylon campechianum, *Linn.*" *Br.* "The heart-wood of *Hæmatoxylon campechianum* Linné (Fam. *Leguminosæ*) that has not undergone fermentation." *N. F.*

Hæmatoxyli Lignum, *Br.;* Lignum Campechianum, Lignum Cœruleum; Bois de Campêche ou Bois d'Inde, Bois de Sang, *Fr.;* Blauholz, Campecheholz, Blutholz, Kampeschenholz, *G.*

Hæmatoxylon campechianum is a tree of medium height with crooked trunk covered with dark rough bark. The branches are beset with sharp spines and show many white lenticels. The sap-wood is yellowish, but the interior layers are of a deep-red color. The leaves are alternate, abruptly pinnate, and composed of three or four pairs of sessile, nearly obcordate, obliquely nerved leaflets. The flowers, which are in axillary spikes or racemes near the ends of the branches, have a brownish-purple calyx and lemon-yellow petals. They exhale an agreeable odor, said to resemble that of the jonquil.

The tree is a native of Campeche, the shores of Honduras Bay, and other parts of tropical America, and has become naturalized in Jamaica. It is cultivated in tropical America and Asia. The heartwood, which is the part used in medicine, is a valuable article of commerce, and largely employed in dyeing. It comes to us in logs deprived of the sap-wood and having a purplish-red to blackish-brown color externally. Logwood is imported from Campeche, Honduras, from San Domingo and Jamaica. That from Campeche is considered the best, while Jamaica logwood is poorest in tinctorial properties. According to Louis Siebold, the ground or chipped logwood of commerce is unfit for use as a medicinal agent, because it has been prepared as a dyestuff by being exposed in large moist heaps until its hematoxylin has been converted by oxidation into hematein. As a coloring agent, for commercial purposes, this fermented logwood, according to Siebold, is much superior to the natural wood. An inferior variety of logwood which contains little or no hematoxylin, but a pure yellowish-gray dye is that known as *bastard logwood.* According to the researches of E. S. Earl this bastard logwood is produced by a variety of the species, which, when growing, cannot be distinguished from the ordinary form. (*B. D. A. J.*, i, 31.)

Logwood is hard, compact, heavy, of a deep-red color, becoming purplish-black by exposure, internally brown-red, and marked with irregular, concentric circles, and splitting irregularly.

Description and Physical Properties.—"*Unground Hematoxylon.*—Usually in small chips, occasionally in billets reddish brown, the freshly cut surface dark yellowish red. Odor faint, agreeable; taste sweetish, astringent.

"*Structure.*—Composed of irregular, concentric zones of yellowish, thick-walled wood fibers and crystal fibers alternating with porous wood parenchyma, the latter surrounding tracheæ either isolated or in groups of two, rarely three; the entire tissue radially traversed by parallel medullary rays, the latter 1 to 7 cells in width.

"*Powdered Hematoxylon.*—Reddish brown; numerous fragments of tissue composed of wood fibers and crystal fibers, the latter with monoclinic prisms of calcium oxalate from 0.010 to 0.030 mm. in length; tracheæ from 0.080 to 0.170 mm. in diameter with bordered or simple pores and containing a reddish brown amorphous content; fragments of tissue of medullary rays, the walls of the cells with simple pores." *N. F.*

"Hard, heavy, dull orange to purplish-red externally and reddish-brown internally. In transverse section, alternating yellowish-brown and dark brown wavy tangential lines. In the form of chips or coarse powder, it is free from signs of fermentation, and from green metallic lustre. Slight, agreeable odor; taste sweetish, astringent. Readily imparts a reddish-violet color to *water* made slightly alkaline with *solution of sodium hydroxide.*" *Br.*

Its solution affords precipitates with sulphuric, nitric, hydrochloric, and acetic acids, alum, copper sulphate, lead acetate, and ferrous sulphate, giving a bluish-black color with the last mentioned salt. Precipitates are also produced with it by lime water and gelatin.

Chevreul found in logwood, a volatile oil, an oleaginous or resinous matter, and a peculiar principle called *hematoxylin* or *hematin* (which must not be confused with the hæmatin of the blood), on which the coloring properties of the wood depend. This is obtained by digesting the aqueous extract in alcohol, evaporating the tincture until it thickens, then adding a little water, and submitting the liquid to a new but gentle evaporation. Upon allowing it to rest, hematoxylin is deposited in crystals, which may be purified by washing with alcohol and drying. Thus procured, the crystals are shining, of a yellowish-rose color, bitterish, acrid, and slightly astringent to the taste, readily soluble in boiling water, forming an orange-red solution which becomes yellow on cooling, and soluble also in alcohol and ether. According to Erdmann, who obtained hematoxylin by the process of Chevreul, substituting ether for alcohol, its crystals, when quite pure, are colorless, without a tinge of redness; its taste is sweet, like that of licorice, without bitterness or astringency; and it is not of itself a coloring substance, but affords beautiful red, blue, and purple colors, by the joint action of an alkaline base and the oxygen of the air. He obtained from logwood 9 to 12 per cent. of crystallized hematoxylin, to which he gave the formula $C_{16}H_{14}O_6$. It crystallizes with 1 or with 3 molecules of water, and is readily soluble in hot water or alcohol, but sparingly in cold water or in ether. (*J. Pr. Chem.*, xxxvi, p. 205.) Commercial extract of logwood extracted from the wood by boiling water contains both hematoxylin and *hematin*, as the former is changed to the latter by oxidation. The proportion of *hematin* is about one-fourth that of the *hematoxylin.* There are "hematin" pastes in the color trade in which the conversion is almost complete, about 90 per cent. hematin being present. Hematoxylin, in alcoholic solution, is used as an indicator in the U. S. P. X. (See *Hematoxylin Test-solution,* Part III.)

Uses.—Logwood is a mild astringent, devoid of irritating properties, and well adapted to the treatment of that relaxed condition of the bowels which is apt to succeed *cholera infantum.* It is also occasionally used with advantage in ordinary *chronic diarrhea* and *chronic dysentery. Hematoxylin* was found by Combemale (*B. M. N.*, xxxiii, 1894) to be very feebly antiseptic, but capable in large doses of producing fatal gastro-enteritis in the lower animals. It is used not only as a dye-stuff but also as a microscopical stain.

Dose, from ten to thirty grains (0.65–1.9 Gm.).

Off. Prep.—Decoctum Hæmatoxyli, *Br.;* Extractum Hæmatoxyli, *N. F.*

HAMAMELIDIS CORTEX. Br.

HAMAMELIS BARK [Witchhazel Bark]

"Hamamelis Bark is the dried bark of Hamamelis virginiana, *Linn.*" *Br.*

Hamamelidis Cortex, *U. S. VIII;* Witchhazel, Spotted Hazel, Striped Alder, Snapping Hazel, Winterbloom; Ecorce de Hamamelis, *Fr. Cod.;* Hamamelis, Zauberhasel, *G.;* Hamamelis (Corteza de), *Sp.*

This bark was deleted from the U. S. P. IX, but retained by the *Br.* and *N. F.*

Witchhazel is an indigenous shrub or a small tree, from five to fifteen feet high, growing in almost all sections of the United States, usually on hills or in stony places, and often on the banks of streams. It is the only species of the genus found in eastern North America, occurring from New Brunswick to Minnesota and southward to Florida and Texas. Schneider asserts that it has been introduced into California and that it is extensively cultivated in this locality. It is specifically characterized by its leaves being obovate or oval, wavy-toothed, and somewhat downy when young. The seeds are black and shining externally, white, oily, and farinaceous within, and edible like the hazelnut. It is remarkable for the late appearance of its yellow flowers, which expand in October and November and continue until the weather becomes very cold in winter. The fruit is a 2-beaked, 2-celled woody capsule, each cell containing a single black seed. It ripens in October and November at the same time the blossoms appear and is in each instance the product of a blossom of the previous year.

Properties.—The bark occurs "in curved or channelled pieces about one and a half millimetres thick, and from one-half to two decimetres long, sometimes covered with a silvery-grey or dark-grey scaly cork marked with transverse lenticels, but frequently freed from the cork, and then exhibiting a nearly smooth reddish-brown outer surface. Inner surface pale reddish-pink, and finely striated longitudinally; fracture laminated and coarsely fibrous. In transverse section, a cortex containing prismatic crystals of calcium oxalate, a complete ring of sclerenchymatous cells, and numerous tangentially elongated groups of bast fibres. No marked odor; taste astringent." *Br.*

Holm (*Merck's Rep.*, xxi, p. 5) has written an illustrated paper on the morphology of hamamelis.

Walter B. Cheney examined witchhazel bark, and found tannin, resin, extractive, but no indication of an alkaloid or other crystalline principle. (*A. J. P.*, 1886, p. 418.) It contains a trace of volatile oil however.

Uses.—The bark of the witchhazel is said to have first attracted attention on account of its use by the North American Indians as a sedative application to external inflammations. Professional attention was strongly directed to the remedy on account of the enormous sale of a much vaunted proprietary remedy said to be made by distilling the bark with very dilute alcohol (six per cent.), and used externally for *sprains* and *bruises*, and internally for most of the diseases to which flesh is heir. The large use of this preparation led to the recognition by both the British and American Pharmacopœias of a distillate of hamamelis bark; this has however been dropped by the U. S. P. (see *Liquor Hamamelidis*), as whatever slight therapeutic virtue as witchhazel possesses seems to depend on its tannin, it is obvious that this distillate cannot represent the drug.

Dose, of the bark, thirty grains (2 Gm.).

Off. Prep.—Tinctura Hamamelidis, *Br.*

HAMAMELIDIS FOLIA. N. F., Br.

HAMAMELIS LEAVES Hamamel. Fol. [Witchhazel Leaves]

"Hamamelis Leaves consists of the dried leaves of *Hamamelis virginiana* Linné (Fam. *Hamamelidaceæ*). Hamamelis Leaves contain not more than 5 per cent. of stems or other foreign organic matter." *N. F.*

"Hamamelis Leaves are the fresh or dried leaves of Hamamelis virginiana, *Linn.*" *Br.*

Hamamelis, *U. S. 1890;* Folia Hamamelidis; Hamamélis de Virgine, *Fr. Cod.;* Feuilles de Hamamelis, *Fr.;* Witchhazel, Witch Hazel Leaves; Hoja de Hamamelis, *Sp.*

For description of this plant see *Hamamelidis Cortex.*

Description and Physical Properties.—"*Unground Hamamelis Leaves.*—Petiole from 1 to 1.5 cm. long; lamina when entire broadly elliptical or rhomboid-ovate, usually inequilateral, mostly from 8 to 12 cm. long, apex usually acute, sometimes rounded or acuminate; base slightly heart-shaped and oblique; margin sinuate or sinuate-dentate; upper surface pale or brownish green, with a few stiff hairs; lower surface lighter in color, somewhat hairy, midrib and veins prominent, the secondary veins running straight to the margin. Odor slight; taste astringent, slightly aromatic and bitter.

"*Structure.*—Epidermal layer prominent; a palisade layer consisting of a single row of cells; a spongy parenchyma tissue made up of three to six rows of strongly branching cells; large collateral, fibro-vascular bundles in the midrib and petiole, the tracheæ narrow, mostly spiral and associated with numerous narrow, strongly lignified and porous wood fibers; around the phlœm a nearly continuous circle of bast fibers, the latter with strongly lignified walls and associated with crystal fibers.

"*Powdered Hamamelis Leaves.*—Numerous fragments of epidermal tissue showing narrowly elliptical stomata from 0.023 to 0.035 mm. in length and with 2 to 4 neighboring cells; numerous stellate hairs composed of from 4 to 12 cells united at the base, the individual cells usually curved, with thick walls, narrow lumina and from 0.050 to 0.500 mm. in length; numerous fragments of tracheæ associated with strongly lignified, porous wood fibers; calcium oxalate in monoclinic prisms from 0.010 to 0.035 mm. in length in cells of the mesophyll or in crystal fibers associated with bast fibers." *N. F.*

The British Pharm., 1914, describes the leaves as follows: "Broadly oval in outline, from seven to fifteen centimetres long. Upper surface dark green or brownish-green, under surface paler; apex obtuse, margin sinuate; narrowed towards the base, oblique, slightly cordate, and shortly petiolate. Veins pinnate and prominent on the under surface, where they are furnished with stellate hairs. No marked odor; taste astringent and slightly bitter." *Br.*

The microscopical characteristics of the hamamelis leaves have been described by Hans Kramer in *B. P. G.*, xvii, p. 323.

Uses.—Witchhazel leaves contain a small amount of tannin and probably also a bitter principle, although we know of no careful analysis. The fluidextract is used chiefly as an astringent local application in *varicose veins, hemorrhoids, sore throat* and *chronic catarrhs.*

Dose, fifteen to forty-five grains (1–3 Gm.).

Off. Prep.—Fluidextractum Hamamelidis Foliorum, *N. F.* (*Br.*); Liquor Hamamelidis, *Br.;* Unguentum Hamamelidis (from Liquid Extract), *Br.*

HELONIAS. N. F.

HELONIAS Helon. [False Unicorn]

"Helonias consists of the dried rhizome and roots of *Chamælirium luteum* (Linné) A. Gray (Fam. *Liliaceæ*). Helonias contains not more than 5 per cent. of foreign organic matter." *N. F.*

Starwort; False Unicorn Root; Devil's Bit; Blazing Star.

Because of the fact that the English name of "Unicorn Root" has been applied to this plant as well as to the Aletris, there has been considerable confusion and rhizomes and roots of these plants are often substituted one for the other, although they are neither botanically nor therapeutically closely related.

The *Chamælirium luteum* (L.) A. Gray (*C. carolinianum* Willd., *Helonias dioica* Pursh.) is a native diœcious herb with a smooth stem 1 to 4 feet in height terminating in a spiked raceme of white flowers. The stem leaves are lanceolate and the basal leaves spatulate.

The rhizome and roots are used in medicine. They somewhat resemble those of Aletris but all of the rootlets of Helonias are whitish or pale yellowish, none exhibiting a reddish-brown external color through abrasion, nearly straight, and of a bitter, slightly astringent taste. (See *Aletris.*)

Description and Physical Properties.—"*Unground Helonias.*—Rhizome upright, or oblique, sometimes nearly cylindrical, from 0.5 to 3 cm. long and about 1 cm. in diameter; externally grayish brown; annulate from scars of bud-scales; upper portion with leaf-bases enclosing a small bud; oblique rhizomes with a few stem-scars up to 7 mm. in diameter; lower portion with numerous whitish or pale yellowish, slightly curved, wiry roots, from 5 to 8 cm. long, arising from deep pits in the rhizome and with cortex usually detached; fracture hard and horny; internally grayish yellow, cortex from 3 to 4 mm. thick. Odor slight; taste bitter, slightly astringent.

"*Structure.*—Rhizome; cork cells with lignified walls and with a brownish amorphous content; a wide cortical parenchyma layer through which extend, outwardly from the central cylinder, numerous lateral roots emerging from the base of deep cylindrical pits which extend inwardly from the surface of the rhizome; central cylinder made up of three or four irregular circles of fibrovascular bundles, the latter separated by parenchyma cells and from 0.200 to 0.300 mm. in diameter. Root; cortex composed chiefly of more or less collapsed parenchyma cells containing starch grains; a distinct endodermis of radially elongated cells with lignified walls; a central cylinder usually composed of from 5 to 7 vascular bundles.

"*Powdered Helonias.*—Light yellowish; numerous fragments composed of parenchyma cells containing altered or unaltered starch grains, the latter being spheroidal or ellipsoidal and up to 0.015 mm. in diameter; raphides of calcium oxalate chiefly in bundles, the individual crystals from 0.025 to 0.040 mm. in length; fragments of lignified cork tissue; numerous fragments of tracheæ tissue assocated with more or less lignified fibers; tracheæ with simple pores, scalariform or reticulate markings." *N. F.*

The Helonias root contains approximately 9.5 per cent. of a saponin first separated by Kruskal (*Arbeiten d. Pharmacol. Inst. zu Dorpat.*, 1891, vi) and by him named *chamælirin.* This is one of the least toxic of the saponin bodies; according to Kruskal 0.427 Gm. per kilo of pure chamælirin injected intravenously is not sufficient to kill a cat.

Helonin is a term used by the eclectics to define the alcoholic extract found in commerce.

Uses.—Large doses of Helonias are nauseant, probably from the local irritant action of its characteristic saponin. It is by some supposed to have a tonic action upon the uterus and used in *amenorrhea, dysmenorrhea* and *leucorrhea.* It has also been used as an anthelmintic. Its value, however, is very doubtful.

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Fluidextractum Heloniadis, *N. F.;* Elixir Aletridis Compositum, *N. F.;* Elixir Heloniadis Compositum, *N. F.*

HIRUDO. Br.

LEECHES

"Leeches are (1) Hirudo medicinalis, *Linn.*, the Speckled Leech, and (2) Hirudo quinquestriata, *Schmarda,* the Five-striped or Australian Leech." *Br.*

Sangsue, *Fr. Cod.;* Hirudines, Blutegel, *G.;* Sanguisuga, Mignatta, *It.;* Sanguijuela, *Sp.*

Leeches are highly specialized fresh water, marine or terrestrial Annelids devoid of setæ or parapodia and possessing anterior and posterior suckers. They belong to the Class *Hirudinea,* a group of *Annelida* characterized by the possession of 33 body segments, 2 suckers, one of which is around the mouth and the other at the posterior end and the absence of bristle-like appendages (setæ) except in a single genus. All are hermaphroditic, but the eggs of one animal are fertilized by the spermatozoa of another. There are three groups of leeches, depending upon their habits. (1) Temporary parasites which include most of this group of animals and are found in cold seas. (2) A group of nearly permanent parasites which are found in both temperate and tropical regions. (3) A group of predatory hunters or scavengers which are confined to warm regions. These groups may change from one mode of life to another. Four families are usually distinguished and commonly designated as fish leeches; tortoise and snail leeches; worm leeches; and jawed leeches. The latter include the *Hirudinidæ,* which are distinguished in that they have no proboscis and generally possess three-toothed jaws. The true blood-sucking leeches, the medicinal leeches of Europe, belong to this group.

The leech is an aquatic worm with a flattened body, tapering towards each end, and terminating in circular flattened disks, the posterior one being the larger of the two. It swims with a vertical undulating motion, and moves when out of the water by means of these disks or suckers, fastening itself first by one and then by the other, and alternately stretching out and contracting its body. The mouth is placed in the center of the anterior disk, and is furnished with three cartilaginous jaws at the entrance of the alimentary canal. These jaws are lined at their edges with fine, sharp, chitinous teeth, and meet so as to make a triangular incision in the flesh. The head is furnished with small raised points, supposed by some to be eyes. Respiration is carried on through small apertures ranged along the ventral surface. The nervous system consists of a cord extending the whole length, furnished with numerous ganglia. The intestinal canal is straight, and terminates in the anus, near the posterior disk. The eggs, varying from six to fifteen, are contained in a sort of spongy, slimy cocoon, from half an inch to an inch in diameter. These are deposited near the edge of the water, and hatched by the heat of the sun. The leech is torpid during the winter, and casts off from time to time a thick slimy coating from its skin. It can live a considerable time in sphagnous moss or in moistened earth, and is frequently transported in this manner to great distances without injury.

Savigny has divided the genus *Hirudo* of Linnæus into several genera. The true leech is the *Sanguisuga* of this author, and is characterized by its three lenticular jaws, each armed with two rows of teeth, and by having ten ocular points. Several species are used for medicinal purposes, of which the most common are the gray and the green leech of Europe, both of which are varieties of the *Hirudo medicinalis* of Linnæus, and the *Hirudo decora* of this country.

1. *Hirudo medicinalis* Linn. (*Sanguisuga officinalis* Savigny. *The green* or *gray leech.*—This leech is marked with six longitudinal dorsal ferruginous stripes, the four lateral ones being interrupted or tessellated with black spots. The color of the back varies from a blackish to a grayish-green. The belly in the one variety is of a yellowish-green color, free from spots, and bordered with longitudinal black stripes. In the second variety it is of a green color, bordered and maculated with black. This leech varies from two to four inches in length. It inhabits marshes and running streams, and is abundant throughout Europe. A variety of the leech has come into use in Europe, called in commerce, *African leeches.* They are of a beautiful light green color, varying to a deep green, and often inclining to red, with black points on the back, and broad streaks of a bright orange yellow, which are black towards the abdomen. They correspond perfectly with the *Sanguisuga interrupta* of Moquin-Tandon. These leeches draw very well. (*P. J.*, x, 38.) The leeches from Algiers, called in French commerce, *dragons* (*Sanguisuga troctena* of Moquin-Tandon), of which considerable numbers have been taken to France, are said by M. A. de Quatrefages, contrary to former opinion, to be quite equal to the European. (*J. P. C.*, 3e sér., xxxiii.)

2. *Macrobdella* (*Hirudo*) *decora* Say, the medicinal leech of America, has a back of a deep pistachio-green color, with three longitudinal rows of square spots. These spots are placed on every fifth ring, and are twenty-two in number. The lateral rows of spots are black, and the middle range of a light brownish-orange color. The belly is of the latter color, variously and irregularly spotted with black. The American leech sometimes attains the length of four or five inches, although its usual length is from two to three. It does not make so large and deep an incision as the European leech, and draws less blood. *Hirudo quinquestriata* Schmarda (*Hirudo australis* Bosisto; *Limnobdella quinquestriata* R. Blanch), the *five-striped* or *Australian leech,* has a dorsal surface greenish-yellow-brown, with five longitudinal stripes, the ventral surface being greenish-yellow and not spotted. The jaws are large, with forty-eight to fifty teeth, the inner being the larger.

The great use formerly made of leeches in the practice of medicine, occasioned them to become a considerable article of commerce. They were collected in Spain, France, Italy, Germany, and Sweden, and carried in large numbers to London and Paris. They were also frequently brought to this country, as the practitioners in some of our large cities used only the foreign leeches, although our own waters furnish an inexhaustible supply.

The British Pharm. (1914) gives the following description: "Body soft, smooth, five centimetres or more long, tapering to each extremity, plano-convex, marked with from ninety to one hundred fine annulations. Anterior extremity terminated by a small sucker surrounding the tri-radiate jaws, the posterior extremity by a large sucker. (1) Speckled Leech: dorsal surface olive-green, with six longitudinal stripes; ventral surface greenish-yellow, with black spots. (2) Five-striped Leech: dorsal surface greenish-brown, with five longitudinal stripes; ventral surface greenish-yellow, not spotted." *Br.*

The proper preservation of leeches is an object of importance, as they are liable to a great and sudden mortality. They are usually kept in jars, in clear, soft water, which should be changed twice a week in winter and every other day in summer. The jar must be covered with a linen cloth, and placed in a situation not liable to sudden changes of temperature. They will live a long time and continue active and healthy without any other attention than that of frequently changing the water in which they are kept. Derheims has proposed the following excellent method of preserving them. In the bottom of a large basin or trough of marble he places a bed, six or seven inches deep, of a mixture of moss, turf, and fragments of wood. He strews pebbles above, so as to retain them in their place without compressing them too much or preventing the water from freely penetrating them. At one end of the trough, and about midway of its height, is placed a thin slab of marble or earthenware, pierced with numerous holes, and covered with a bed of moss, which is compressed by a thick layer of pebbles. The reservoir being thus disposed is half filled with water, so that the moss and pebbles on the shelf shall be kept constantly moist. The basin is protected from the light by a linen cover stretched over it. By this arrangement the natural habits of the leech are not counteracted. One of these habits, essential to its health, is that of drawing itself through the moss and roots to clear its body from the slimy coat which forms on its skin and is a principal cause of its disease and death. James Banes recommends that when kept in jars they should be cleansed by means of a whisk of very fine broom or willow, when the water is changed. Lahache, an apothecary at Bruyères, stongly recommends carrageen, or Irish moss (*Chondrus crispus*), as admirably adapted to the habits and wants of the leech, furnishing the animal, he supposes, with nutriment, as it does not die of inanition when thus kept. The water should be renewed in the jars daily. (*J. P. C.,* 4e sér., iii, 128.) Alfred Allchin keeps them in aquaria with growing water-plants and snails, which keep the water pure. For other methods of keeping leeches, also of raising them, see *U. S. D.,* 14th ed., 472.

Uses.—Leeches afford the least painful and in many instances the most effectual means for the local abstraction of blood. They are often applicable to parts which, either from their situation, or from their great tenderness when inflamed, do not admit of the use of cups. They are now used much less often than formerly.

In applying leeches to the skin, care should be taken to shave off the hair, if there be any, and to have the part well cleansed with soap and water, and afterwards with pure water. If the leech does not bite readily, the skin should be moistened with a little blood, or milk and water. Sometimes the leech is put into a large quill open at both ends, and applied with the head to the skin until it fastens itself, when the quill is withdrawn. If it be desirable that the leech shall bite in a particular spot, this end may be attained by cutting a small hole in a piece of blotting paper, and then applying this moistened to the skin, so that the hole shall be immediately over the spot from which the blood is to be taken. Leeches continue to draw blood until they are gorged, when they drop off. As a very efficient mode of applying leeches, it is recommended, after having moistened the skin with pure warm water, to put the leeches into a tumbler half full of cold water, and by an adroit movement invert it upon the part. The leeches are said to attach themselves so rapidly that it seems to the patient as though they made but a single bite. When they are all attached, the glass is to be carefully removed, the water being absorbed, as it runs off on one side, by a sponge or linen cloths. As a rule, our leeches apply six for every fluidounce of blood. A single European leech will draw from half an ounce to an ounce. The quantity may often be much increased by bathing the wound with warm water. They may be separated from the skin at any time by sprinkling a little salt upon them. After they drop off, the same application will make them disgorge the blood they have swallowed. The practice of using over again leeches which have been made to disgorge the blood they have sucked is to be condemned on account of the danger of carrying infection from one patient to another. In cases where the bleeding from leech bites continues longer than is desirable, it may be stopped by continued pressure, with the application of lint, by the use of collodion, or by touching the wounds with lunar caustic or other styptic.

In 1884 Haycraft showed that the saliva of the leech prevented the coagulation of the blood. This is due to the action of a secondary albumose known as *herudin* (*hirudin* is a commercial name for a preparation manufactured from leech heads the precise nature of which is not revealed, see Part II). Although Rimann and Wolff found that it required twenty milligrammes to render one hundred grammes of human blood non-coagulable, Satterlee and Hooker found that as small an amount as three and a half milligrammes per hundred grammes, caused perceptible retardation of clotting. The anticoagulant properties of leech extract, or its active principle, have been of much value in the physiological laboratory. Leech extract may be prepared according to the following method which is a modification of that suggested by Franz: cut off the leech heads, mince them, rub up with a very fine sand, add to the mass 5 cc. of physiological salt solution for each leech head and heat for 20 minutes at a temperaure of 100° C., allow to macerate for twelve hours, decant off the liquid, wash the sand several times with physiological salt solution, unite the liquids and filter through cheesecloth. This solution, which is suitable for some laboratory purposes, is not gauged by the quantity of solution, but by the number of leechheads represented. According to Franz, it requires three leeches per kilo body weight to prevent coagulation of the blood in the dog. Preference to-day, however, is generally given to hirudin. This has been used not only in the physiological laboratory, but in clinical medicine for the purpose of preventing clotting during transfusion of blood. Marshall (*J. P. Ex. T.,* 1915, vii, 157) has found that commercial samples of hirudin may be highly toxic, apparently from contamination with some product of putrefaction. (For details of technique and extensive literature on the whole subject see article of Satterlee and Hooker, *J. A. M. A.*, 1914, lxii, p. 1781.) On the theory that *eclampsia* was due to excessive fibrin content of the blood, hirudin has been suggested as a therapeutic measure in this condition.

HOMATROPINÆ HYDROBROMIDUM. U. S., Br.

HOMATROPINE HYDROBROMIDE Homatrop. Hydrobr. [Homatropine Bromide, Homatropine Hydrobromate]

"The hydrobromide [$C_{16}H_{21}O_3N.HBr$] of a synthetic alkaloid prepared from tropine and mandelic acid." *U. S.* "Homatropine Hydrobromide, $C_{16}H_{21}NO_3$,HBr, is the hydrobromide of an alkaloid prepared from tropine." *Br.*

Bromhydrate d'Homatropine, *Fr.;* Homatropinum hydrobromicum, *P. G.;* Homatropinhydrobromid, Bromwasserstoffsaures Homatropin, Bromwasserstoffsaures Oxytoluyltropein, *G.*

Preparation.—This alkaloidal salt was first admitted to the British Pharmacopœia in the additions of 1890. Homatropine, $C_{16}H_{21}NO_3$, is prepared by evaporating a mixture of tropine, $C_8H_{15}NO$ (obtained through the hydrolysis of hyoscyamine), and *mandelic acid* (phenylglycollic), $C_6H_5.CH(OH)COOH$, with diluted hydrochloric acid; mandelic acid may be produced by acting on amygdalin with hydrochloric acid, or synthetically from benzaldehyde and hydrogen cyanide.

Description and Physical Properties.—"White crystals or a white, crystalline powder. It is odorless. *Caution.—Homatropine Hydrobromide is extremely poisonous.* One Gm. of Homatropine Hydrobromide is soluble in 6 cc. of water, 40 cc. of alcohol, and in 420 cc. of chloroform, at 25° C. One Gm. is soluble in 12 cc. of alcohol at 60° C. It is insoluble in ether.

"It melts at about 212° C. with partial decomposition. Iodine T.S. produces in an aqueous solution of Homatropine Hydrobromide a brown precipitate; silver nitrate T.S. produces a yellowish-white precipitate, insoluble in nitric acid. Shake 2 cc. of chloroform with 1 cc. of an aqueous solution of the salt (1 in 10) to which a few drops of chlorine T.S. have been added: the chloroform acquires a brownish color. Add a slight excess of ammonia T.S. to 1 cc. of an aqueous solution of the salt (1 in 100), shake it with chloroform, and evaporate the chloroform solution to dryness on a water bath: the residue becomes yellow and finally brick-red when warmed with about 1.5 cc. of a solution made by dissolving 1 Gm. of mercuric chloride in 50 cc. of a mixture of 5 volumes of alcohol and 3 volumes of distilled water (*difference from most other alkaloids except atropine and hyoscyamine*).

"Its aqueous solution (1 in 20) is neutral to litmus paper. The ash from 0.1 Gm. is negligible. One cc. of an aqueous solution of the salt (1 in 20) is not precipitated by tannic acid T.S. Another 1 cc. portion acidulated with hydrochloric acid yields no precipitate with platinic chloride T.S. (*difference from most other alkaloids*). Add 5 drops of nitric acid to about 0.01 Gm. of Homatropine Hydrobromide, and evaporate to dryness in a porcelain dish on a water bath: the residue does not become violet on the addition of a few drops of alcoholic potassium hydroxide T.S. (*atropine, hyoscyamine or scopolamine*)." *U. S.*

"White crystalline powder, or aggregations of minute crystals. Soluble in about 6 parts of *water*, and in about 18 parts of *alcohol* (90 per cent.), the solutions being neutral to *litmus*. Yields the *reactions* characteristic of bromides. An aqueous solution (1 in 100) applied to the eye powerfully dilates the pupil. 1 millilitre of this solution made alkaline with *solution of ammonia*, shaken with *chloroform*, the chloroformic solution being then separated and evaporated, yields a residue which turns first yellow and then brick-red when warmed with 1.5 millilitres of a solution (2 in 100) of *mercuric chloride* in *alcohol* (60 per cent.). When treated with *nitric acid* and *alcoholic solution of potassium hydroxide* as described under 'Atropina,' a reddish-yellow color is produced, not changing to violet (distinction from atropine)." *Br.*

Uses.—Homatropine is used in medicine solely as a mydriatic and cycloplegic. Its effects upon the eye are, like those of atropine, due to a paralyzing action upon the peripheral ending of the oculo-motor nerve. It has the advantage over atropine in being relatively much less toxic to the general system and of being somewhat quicker in its action. It has in the past been stated that homatropine had no depressant effect upon the pneumogastric nerve, indeed that it slowed the pulse, but Zulick has shown (*J. P. Ex. T.*, 1915, vi, 473) that its effects upon cardiac inhibition are similar in kind to those of atropine, although it requires very large doses to affect the circulation. Occasionally unpleasant symptoms have followed the instillation of homatropine solutions into the eye, but we know of no fatal case of homatropine poisoning.

After the instillation of a 1 per cent. solution the pupil begins to dilate in from seven to twenty minutes and accommodation fails in forty to ninety minutes, while recovery is usually complete in three to four days. For simple dilatation of the pupil a 1 per cent. solution is sufficient, but when it is desired to paralyze accommodation completely a 2 per cent. solution may be employed.

Dose, internally, from one one-hundredth to one-fiftieth of a grain (0.0006–0.0013 Gm.).

Off. Prep.—Lamellæ Homatropinæ, *Br.*

HUMULUS. N. F.

HOP Humul.

"Hop is the carefully dried strobile of *Humulus Lupulus* Linné (Fam. *Moraceæ*) bearing its glandular trichomes. Hop contains not more than 2 per cent. of stems, leaves or other foreign matter, and yields not more than 5 per cent. of acid-insoluble ash." *N. F.*

Lupulus, *Br. Pharm.* 1898; Hop; Strobili Humuli, Fructus Lupuli; Houblon, *Fr. Cod.;* Hopfen, *G.;* Luppolo, *It.;* Lupulo (Fruto de), Hombrecillo, *Sp.*

The hop plant is a twining, rough perennial having angular, rough, flexible stems, which twine around neighboring objects in a spiral direction from left to right, and climb to a great height. The leaves are opposite, and long petioled. The smaller are sometimes cordate; the larger have three or five lobes; all are serrate, of a deep green color on the upper surface, and, together with the petioles, extremely rough, with minute prickles. At the base of the petioles are two to four smooth, ovate, reflexed stipules. The flowers are numerous, axillary, and bracteate. The staminate flowers are a yellowish-white, and arranged in panicles; the pistillate, which grow on a separate plant, are pale green, and disposed in solitary, peduncled aments, composed of membranous scales, ovate, acute, and tubular at the base. Each scale bears, near its base, on its inner surface, two flowers, consisting of a roundish compressed ovary, and two styles, with long filiform stigmas. The aments are converted into ovate membranous cones or strobiles, the scales of which contain, each, at its base, two small achenes, surrounded by a yellow, granular powder—so-called "lupulin. Only the pistillate plants are cultivated by the hop growers in Europe, and it is interesting to note that the unfertilized pistillate plants produce strobiles richer in aroma and more plenteous in lupulin. The plants flower in August and the fruits are harvested during September. The hops grown in this country contain a great many achenes, showing that the staminate plants are also cultivated. The strobiles are collected when the scales change from a light golden to a somewhat deeper hue.

The hop plant is a native of North America and Europe. In parts of New England, New York, Michigan and Indiana, it is extensively cultivated, and most of the hops consumed in the United States is supplied by those districts. Hops are also cultivated in Europe, Australia and South America. The part of the plant used is the fruit or strobiles. These, when fully ripe, are picked, dried by artificial heat, packed in bales or hemp bags, and sent into the market.

By separating the volatile oils and determining its acid and ester value, Rabak (*C. D.*, lxxxv, 376) is able to distinguish American grown from imported hops. He finds that the European hops always show a lower ester value in the volatile oil than do the American.

Hops consist of numerous thin, translucent, veined, leaf-like scales, which are of a pale greenish-yellow color, and contain near the base two small, round, black achenes. They are

Description and Physical Properties.—"*Unground Hop.*—Strobile ovoid-cylindrical, about 3 cm. in length, consisting of a narrow, hairy, flexuous rachis and numerous, imbricated, yellowish green, obliquely ovate, membranous scales, the base of each with numerous, yellowish brown glandular hairs, and frequently infolded on one side, enclosing a subglobular, light brown, very glandular achene. Odor strong and characteristic becoming disagreeable and valerian-like on aging; taste aromatic and bitter.

"*Powdered Hop.*—Light yellowish green; numerous fragments of wavy-walled lignified epidermal tissue; fragments of parenchyma tissue with many of the cells containing calcium oxalate in rosettes and associated with branching tracheæ, the latter having spiral markings; numerous unicellular, slightly curved non-lignified hairs with walls frequently silicified, occurring either isolated or attached to fragments of epidermal tissue; numerous rosettes of calcium oxalate up to 0.024 mm. in diameter; glandular hairs with multi-cellular heads filled with yellowish oil from 0.100 to 0.300 mm. in diameter or frequently broken (*lupulin*); few glandular hairs with nearly colorless multi-cellular heads; few spherical, spinose yellowish pollen grains up to about 0.024 mm. in diameter; a few lignified fibers; few fragments of parenchyma tissue with large cells containing cystoliths of calcium carbonate.

"Preserve Hop in tightly closed containers, protected from light." *N. F.*

Though brittle when quite dry, they are pulverized with great difficulty. Their odor is strong, peculiar and fragrant; their taste very bitter, aromatic, and slightly astringent. Their aroma, bitterness, and astringency are imparted to water by decoction, but the first mentioned property is dissipated by long boiling. The most active part of hops is the lupulin (see *Lupulinum*).

Hops are often subjected in Germany to the fumes of burning sulphur, because of the supposition that they keep better when thus treated. Besides, by being partially bleached by the process, old hops, which have suffered from time, having become darker, generally spotted, and weaker, assume a brighter appearance, as if fresher, and generally command a better price in the market. To detect the consequent presence of sulphurous acid, the brewers put a silver spoon in a mixture of hops and water, under the impression that it will produce a black stain upon the silver. But this test will answer only when applied within a fortnight after the use of the sulphur. A more delicate method is that of Heidenreich, who puts twenty or thirty strobiles of the hops in a flask with zinc and hydrochloric acid, and passes the hydrogen evolved through solution of lead acetate. If sulphurous acid be present, hydrogen sulphide will be produced, which will occasion a dark precipitate with the solution. But even this plan often fails when the hops have been kept more than three or four weeks. A modification of this test has been proposed by R. Wagner. For the solution of lead acetate used in Heidenreich's method there is to be substituted a solution of sodium nitroprusside, so weak as to have a very light brown color, to which have been added a few drops of solution of potassium hydroxide. If the gas evolved contain the minutest proportion of sulphur, a violet color will be produced when the first bubble passes into the solution; and this will, by a continuance of the process become a magnificent purple. The least trace of sulphurous acid may thus be found, but a few months after the sulphuring of hops none at all can be detected.

Hops are said to be sometimes threshed in order to separate the lupulin, which is sold separately. Their efficiency is thus, no doubt, greatly impaired. Hops thus treated have the scales more or less broken; and any parcel presenting this appearance is to be suspected. Hops often contain a variable quantity of lupulin in consequence of the granules of this substance separating, especially on agitation, and seeking the lower portion of the mass, which thus becomes richer, while the upper is poorer. They should always be examined in reference to the lupulin they contain, and, if nearly or quite destitute of it, should be deemed of inferior value and not be used medicinally.

Constituents.—Hops contain two crystallizable bitter substances of an acid character, and three resins, two of which are soft in character and bitter in taste and are present to the extent of over 10 per cent., and one of which is hard in character and tasteless and present to the extent of less than 5 per cent. The two soft resins probably contribute the most valuable properties of the hops, although the insoluble bitter acids, according to some authorities, are hydrolized in preparing the wort and become bitter and communicate foaming properties to the liquid by changing the surface tension. The investigation of the acids showed the *alpha acid* to have the composition $C_{15}H_{24}O_4$, and to contain a carboxyl group and a ketonic group. It is probable that this acid exists in the hops, condensed with a valeric acid residue. There is also present *humulone,* $C_{28}H_{32}O_5$, a lactone which is probably a product of the hydrolysis of the alpha acid. It is also probable that the alpha resin is a simple polymer of the alpha acid. The *beta acid,* $C_{25}H_{36}O_4$, is also called *lupulinic acid* and yields valeric acid on oxidation. The essential oil of hops contains *myrcene.*

Lupulite, a name formerly applied to the bitter substance of hops, is not a chemical individual. W. Wöllmer states that the bitter principles of hops, $C_{21}H_{30}O_4$ and $C_{26}H_{30}O_5$, are not true acids, but owe their acid character to their hydroxyl groups. He therefore prefers to call them *humulone* and *lupulone.* He split humulone into carbon dioxide, isopentane, and a body, $C_{16}H_{24}O_5$; while lupulone was broken into isopentane and a body, $C_{21}H_{34}O_4$. Both humulone and lupulone on boiling with alkali yield *humulinic acid,* $C_{15}H_{22}O_4$, and an unsaturated acid, $C_6H_{10}O_2$. (*Chem. Abstracts,* 1919, xiii, 495.) There is present also a peculiar tannin known as *humulo-tannic acid,* which is hydrolizable into glucose and a substance called *hop-red.* (See also *Lupulinum.*)

References to the literature of hops will be found in *Tr. Chem. Soc.,* 1913, ciii, p. 1267, Power and Tutin; in *Proc. Chem. Soc.,* 1913, xxix, p. 132, Chapman; in *Jour. of the Industry of Brewing,* 1913, xix, p. 261, Garrigues; in *Rep. Pharm.,* 1922, xxxii, p. 322, and in *J. Soc. Chem. Ind.,* 1920, xxxix, p. 498a.

Uses.—Hops is an aromatic bitter and hence may be useful in *atonic dyspepsia.* By many they are believed to have a sedative effect on the nervous system and are used in *hysteria, restlessness, insomnia,* and the like. Whether this latter action is due to anything more than an effect through the imagination is open to question.

An *infusion* prepared with half an ounce of hops and a pint of boiling water may be given in the dose of four fluidounces (120 cc.). The tincture was a British official preparation of hops, but the alcohol probably acts more decidedly upon the system than the hops. The fluidextract of hops of the N. F. is superior because of the relatively smaller amount of alcohol. A pillow of hops has proved useful in allaying restlessness and producing sleep in nervous disorders. They should be moistened with water, containing a trace of glycerin, previously to being placed under the head of the patient, in order to prevent rustling. Fomentations with hops, and cataplasms made by mixing them with some emollient substance, are often beneficial in local pains and tumefactions.

Dose, thirty to ninety grains (2.0–5.8 Gm.).

Off. Prep.—Fluidextractum Humuli, *N. F.;* Tinctura Humuli, *N. F.*

HYDRANGEA. N. F.

HYDRANGEA Hydrang. [Seven-Barks]

"Hydrangea consists of the dried rhizome and roots of *Hydrangea arborescens* Linné (Fam. *Saxifragaceæ*). Hydrangea contains not more than 3 per cent. of foreign organic matter." *N. F.*

Wild Hydrangea, Seven Barks. Hortensia, *Fr.;* Hortensie, *G.*

This showy native shrub is closely related to the familiar cultivated hydrangea. It is found throughout the eastern part of the United States on rocky banks, along streams or rivers. It reaches a height of from five to ten feet and bears large clusters of white flowers in compound cymes; the marginal flowers being usually conspicuous and sterile and the central ones small and fertile. A peculiar characteristic is that the bark peels off in separate layers of different colors which has given rise to the popular name of "seven barks."

The commercial supplies of hydrangea are obtained chiefly from North Carolina, Virginia, Michigan and Illinois.

Description and Physical Properties.—"*Unground Hydrangea.*—Rhizome cylindrical, usually cut into pieces from 3 to 10 cm. long and from 3 to 20 mm. in diameter; externally light brown to yellowish brown with a pinkish tinge, longitudinally wrinkled, the upper portion marked by few elliptical lenticels and occasional prominent buds, short branches or stem scars; from the lower surface arise a few coarse fibrous roots; fracture tough, splintery, internally yellowish white or light brown, bark thin, easily separable from the distinctly radiate wood which surrounds a prominent whitish pith. Roots attaining a length of 25 cm. and a thickness of 2 mm., irregularly bent and branching, otherwise resembling the rhizome with the exception of the pith being absent. Inodorous; taste sweetish, becoming slightly acrid.

"*Structure.*—Rhizome: a few rows of grayish, tabular cork cells; a cortex made up chiefly of parenchyma containing starch, large cells containing raphides of calcium oxalate and small isolated groups of fibers and stone cells; a wood cylinder composed of slender wedges of tracheæ and tracheids separated by medullary rays 1 to 3 cells in width, the cells of the latter containing starch grains; pith of large polygonal cells with prominent simple pores.

"*Powdered Hydrangea.*—Light yellowish; irregular fragments consisting of strongly lignified tracheæ with reticulate thickenings, tracheids and medullary ray cells; strongly lignified stone cells and fibers from 0.030 to 0.200 mm. in length, the walls marked with simple or branching pores; raphides of calcium oxalate numerous from 0.050 to 0.135 in length; starch grains mostly single, ellipsoidal, up to 0.010 mm. in diameter, occasionally with a prominent central cleft." *N. F.*

Bondurant (*A. J. P.*, 1887, 122) isolated a characteristic glucoside, *hydrangin*, crystallizing in stellate clusters, melting at 235° C., and subliming without decomposition. It is decomposed by dilute acids into a resin-like body and glucose. Its aqueous solution fluoresces strongly on addition of an alkali, resembling æsculin, but distinctly different in several particulars. Bondurant also obtained a fixed oil and a volatile oil, the latter containing sulphur. Two resins seemed also to be present, together with saponin and sugar. He found no tannin, however. Y. Asahina has isolated two crystalline substances from the alcoholic extract of the flowers of *H. Hortensia*, the Chinese plant which is widely cultivated as an ornamental shrub in this country, *hydragenol* and *hydrangeaic acid*.

Uses.—Hydrangea is said to have been used by the Cherokee Indians. It was at one time used in medicine in the treatment of *stone* in the bladder and *cystitis* but has been largely abandoned. In overdose it is said to cause vertigo and oppression of the chest.

Dose, thirty grains (2 Gm.).

Off. Prep.—Fluidextractum Hydrangea, *N. F.;* Elixir Hydrangeæ et Lithii, *N. F.*

HYDRARGYRI CHLORIDUM CORROSIVUM. U. S. (Br.)

CORROSIVE MERCURIC CHLORIDE Hydrarg. Chlor. Corr. [Bichloride of Mercury, Corrosive Sublimate, Mercuric Chloride]

"Corrosive Mercuric Chloride contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99.5 per cent. of $HgCl_2$." *U. S.* "Mercuric Chloride may be obtained as a sublimate by heating a mixture of mercuric sulphate, sodium chloride, and black oxide of manganese. It contains not less than 98.6 per cent. of pure mercuric chloride, $HgCl_2$." *Br.*

Hydrargyri Perchloridum, *Br.;* Perchloride of Mercury, Sublimatus Corrosivus, Chloruretum (Chloretum) Hydrargyricum, Hydrargyrum Sublimatum Corrosivum, Hydrargyri Bichloridum; Hydrargyrum Muriaticum Corrosivum, Sublimatus Corrosivus, Mercurius Sublimatus Corrosivus; Corrosive Chloride of Mercury, Sublimé Corrosif, Chlorure mercurique, *Fr.;* Bichlorure de Mercure, *Fr. Cod.;* Hydrargyrum Bichloratum, *P. G.;* Quecksilberchlorid, Aetzender Quecksilbersublimat, *G.;* Bicloruro di mercurio, *It.;* Cloruro mercurico, Soliman, *Sp.*

The names given in the two Pharmacopœias to this important chloride do not exactly correspond. It is called *Hydrargyri Chloridum Corrosivum* in the U. S. Pharmacopœia, and *Hydrargyri Perchloridum* in the British. We prefer the former, as indicating, beyond any possibility of mistake, the article intended, as well as its corrosive property. Perchloride and subchloride are hardly sufficiently distinctive, when a mistake may be so serious as that of confounding corrosive sublimate and calomel. Indeed, death has at least in one recorded instance occurred in consequence of this confusion of nomenclature, and our official guides should take especial care to guard against such mistakes. The British Pharmacopœia (1898) uses for the English names mercuric chloride for corrosive sublimate and mercurous chloride for calomel, but these names are not used in prescription writing.

Preparation.—Corrosive sublimate may be made by heating sulphuric acid and the metal together, in a chamber so arranged as to carry off the sulphurous oxide, to form mercuric sulphate; the dry salt obtained is then mixed with sodium chloride and a small quantity of manganese dioxide, and the mixture sublimed. This method, which was formerly official, may be found in the *U. S. D.*, 19th ed., p. 617. It is usually made on the large scale, by the direct combination of gaseous chlorine with mercury which is heated almost to the volatilizing point. It is also sometimes manufactured by dissolving mercuric oxide (red precipitate) in hydrochloric acid, evaporating the solution to dryness, dissolving the dry mass in water, and crystallizing. Here a double decomposition takes place, resulting in the formation of water and the chloride. This method may be used in emergencies for making small amounts.

Description and Physical Properties.—"Heavy, colorless, odorless, rhombic crystals, or crystalline masses, or a white powder. *Caution*

—*Corrosive Mercuric Chloride is extremely poisonous.* One Gm. of Corrosive Mercuric Chloride is soluble in 13.5 cc. of water, 3.8 cc. of alcohol, about 12 cc. of glycerin, and in 22 cc. of ether, at 25° C. One Gm. is soluble in 2.1 cc. of boiling water and in 1.6 cc. of boiling alcohol. The salt fuses to a colorless liquid at about 265° C. and at about 300° C. volatilizes as a dense, white vapor.

"An aqueous solution of Corrosive Mercuric Chloride (1 in 20) is acid to litmus paper, but becomes neutral upon the addition of sodium chloride. An aqueous solution of the salt (1 in 20) responds to the reactions for mercuric compounds, and for chlorides.

"When volatilized at about 300° C., Corrosive Mercuric Chloride leaves not more than 0.1 per cent. of residue. Not more than 0.5 per cent. of residue remains on dissolving finely powdered Corrosive Mercuric Chloride in ether or alcohol.

"**Assay.**—Dry about 0.5 Gm. of Corrosive Mercuric Chloride to constant weight over sulphuric acid, weigh accurately, and dissolve in 300 cc. of warm water to which 1 cc. of hydrochloric acid has been added. Pass hydrogen sulphide through the cold solution until saturated when the precipitate of mercuric sulphide readily subsides, leaving a clear supernatant liquid. Collect the precipitate on counterpoised filters or on a Gooch crucible, wash it well with cold distilled water, and finally with three portions of about 10 cc. each of alcohol. Then close the tip of the funnel with a cork stopper, add sufficient carbon tetrachloride to cover the precipitate, cover the funnel with a watch-glass, and allow it to stand for about half an hour. Then drain off the solvent, and wash the precipitate with further portions of carbon tetrachloride until, after evaporating about 1 cc. of the filtrate, no visible residue remains. Remove the adhering carbon tetrachloride by washing with several portions of 10 cc. each of alcohol, and, after drying in the air, transfer to an oven and dry to constant weight at about 110° C. The weight of mercuric sulphide obtained, when multiplied by 1.167, indicates its equivalent in $HgCl_2$. Each Gm. of Corrosive Mercuric Chloride, previously dried to constant weight, corresponds to not less than 0.8526 Gm. of mercuric sulphide. Corrosive Mercuric Chloride, previously dried to constant weight, may also be assayed by the electrolytic method.

"Preserve in well-closed containers." *U. S.*

"Heavy, colorless, crystalline masses, possessing a highly acrid, metallic taste. Soluble is 18 parts of *water,* and in 4 parts of *alcohol* (90 per cent.), or of *ether.* Yields the *reactions* characteristic of mercuric salts and of chlorides. When heated Mercuric Chloride sublimes without decomposition, leaving only a trace of fixed residue. Yields not less than 72.8 or more than 73.8 per cent. of metallic mercury, Hg, when tested by the following process:—Dissolve 0.5 gramme in 20 millilitres of *water* in a tared beaker-flask, add 10 millilitres of *hypophosphorous acid,* or sufficient to reduce the whole of the mercuric chloride present, and heat on a water-bath until the particles of mercury that separate collect at the bottom of the flask. Pour the contents of the flask on a tared filter-paper, wash both the flask and filter-paper successively with *water, alcohol* (90 per cent.), and *ether;* dry over *sulphuric acid,* and weigh the metallic precipitate." *Br.*

Ether is capable of removing corrosive sublimate, to a considerable extent, from its aqueous solution when agitated with it. According to Mialhe, ether will not dissolve it when accompanied by a considerable quantity of mercuric oxide and a chloride of an alkalifiable metal. Sulphuric, nitric, and hydrochloric acids dissolve it without alteration. When heated it melts, and readily sublimes in dense, white, acrid vapors, which condense on cool surfaces, in white, shining needles. It is precipitated brick-red, becoming yellow, by the fixed alkalies and alkaline earths, and white by ammonia. (See *Hydrargyrum Ammoniatum.*) The former precipitate is mercuric hydroxide, which has the property of evolving oxygen and of being reduced to metallic globules when exposed to heat. This hydroxide is formed in the process for preparing *aqua phagedænica,* called also *yellow wash.* (See *Lotio Hydrargyri Flava.*) Corrosive sublimate forms, with ammonium chloride, and sodium chloride, compounds which are more soluble than the uncombined mercurial salt. The combination of corrosive sublimate with ammonium chloride was formerly called *sal alembroth,* or *salt of wisdom.*

Corrosive sublimate is incompatible with many of the metals, the alkalies and their carbonates, soap, lime water, tartar emetic, silver nitrate, the lead acetates, the potassium and sodium sulphides, the soluble iodides, and all the sulphydrates. It is decomposed by many vegetable and some animal substances. According to A. T. Thomson, it produces precipitates in infusions or decoctions of chamomile, horseradish, calumba, cinchona, gambir, rhubarb, senna, simaruba, and oak bark. Mialhe and Lepage have shown that corrosive sublimate is slowly converted into calomel by syrup of sarsaparilla and syrup of honey, but is not changed by contact with pure syrup. Samuel Kennedy (*Ph. Rec.,* 1888, p. 201) proved conclusively that when corrosive sublimate was dissolved in compound syrup of sarsaparilla, as frequently prescribed, precipitation invariably occurred. He found that if sodium chloride in quantity equalling that of the mercurial used were added, precipitation was greatly retarded.

Uses.—Corrosive sublimate is a powerful mercurial and may be used for the various purposes for which the other preparations of this metal are employed. (See *Hydrargyrum.*) When administered in large doses it is prone to irritate the stomach and intestines and, therefore, such large quantities of mercury cannot be introduced into the system with this salt as with calomel. It is one of the best of all the preparations of mercury for hypodermic use in *syphilis*. From ten to twenty minims of an 0.5 per cent. solution in distilled water may be thrown deeply into the muscles preferably of the back. The pain of the injection may be obviated by the previous injection of procain. Most careful asepsis is necessary to avoid abscess formation.

It has been employed, especially by intravenous injection with asserted benefit in *septicemia*, especially following child-birth. Stowe (*Chicago Medical Recorder*, 1911, xxxiii, p. 461) injects one-fifth of a grain at a dose. Its value for this purpose is very questionable.

Externally employed, corrosive sublimate is stimulant, escharotic, and germicidal. The powdered chloride has been used as an escharotic, but is, in general, inferior to silver nitrate or potassium hydroxide. In *onychia maligna*, however, it is employed with great advantage, mixed with an equal weight of zinc sulphate, and sprinkled thickly upon the surface of the ulcer, which is then to be covered with a pledget of lint saturated with tincture of myrrh. The whole diseased surface is thus removed, and the ulcer heals. This practice originated, we believe, with Perkins, of Philadelphia, and was highly recommended by Physick. Geo. B. Wood often employed it with success. A solution of corrosive sublimate in collodion (four parts to thirty) has been used as a caustic, for the destruction of *nævi materni*, and for other purposes. It can be very accurately applied, but its use requires care, as fatal poisoning has followed a single application of the alcoholic solution of corrosive sublimate to a moderate surface of *ringworm*. (*L. L.*, 1871, ii, 413.) It is applied by means of a camel's-hair pencil.

Corrosive sublimate is one of the most powerful of known chemical germicides. Solutions containing one part in twenty thousand are sufficient to destroy the vitality of most nonsporulating bacteria while one in one thousand will kill the most resistant sporulating organisms. According to Koch, one part in three hundred thousand absolutely prevents the multiplication of the *Bacillus anthracis*, while Behring (*D. M. W.*, 1887) finds that as little as one part in a million has a distinctly inhibiting effect. The practical utility of mercuric chloride as a disinfectant is, however, greatly limited by its chemical instability. It has a strong affinity for albumen, and, although the precipitate formed is redissolved in an excess of albumen, the disinfectant power of mercury is very much reduced. Moreover, it attacks most metals which are used in surgery and is therefore unsuitable for disinfecting instruments. Nevertheless, because of its convenience as well as its powerful action it is very widely employed as a germicide for surgical purposes.

The solution of one in one thousand may be used for washing the hands, disinfecting furniture, etc., and is even employed in the disinfecting of *wounds;* usually, however, a much weaker solution than that just mentioned is employed by the surgeon. It is rarely if ever justifiable to use upon a mucous surface or a wound a solution stronger than one in two thousand, and if the solution is to be used freely and continuously, as in washing out the vagina, etc., one in ten thousand is as strong as should be employed; indeed, the employment of a vaginal wash of this strength has been followed by violent poisoning. (See H. C. Wood, Jr., *Am. Med.*, Dec., 1902, and Bland, *A. J. M. S.*, 1920, lxxiv, 1227.) In a number of cases a solution of one part in fifteen hundred used locally by the surgeon has produced death, preceded by constitutional symptoms.

It is essential that the tablets be colored or in some way marked so that the attention may be drawn to their nature, and accidental poisoning prevented. Mercuric chloride tablets are now officially recognized. (See *Toxitabellæ Hydrargyri Chloridi Corrosivi.*)

Poisoning.—Because of the ease with which it is obtained corrosive sublimate is one of the most commonly used poisons for suicidal purposes, and the wide-spread employment of tablets of it as antiseptics has led to a number of accidental cases. The symptoms of poisoning by bichloride of mercury generally come on promptly with a metallic taste, burning pain in the gullet and epigastrium, followed by vomiting and purging. The vomitus is first mucous or bilious, but later becomes bloody; the stools also usually contain blood. In many cases there is a profound collapse, as shown by rapid feeble pulse, cold clammy skin, and muscular weakness, even comparatively early in the poisoning. The urine becomes scanty or may be entirely suppressed, albuminous, and sometimes hemorrhagic. If the patient survives for a few days salivation develops and ulcers appear around the mouth and throat. Death may occur within a few hours of the ingestion of the poison, but may be postponed for nearly a fortnight. In postmortem examination the whole alimentary canal is found the seat of a corrosive inflammation, there is violent nephritis and sometimes protoplasmic degenerations in the internal organs. It is not necessary for the poison to be swallowed in order to produce serious or even fatal results; H. C. Wood, Jr. (*American Medicine*, 1902, iv, p. 1006), has found references to more than 150 cases of poisoning from its use as intra-uterine douches of which a large number ended fatally, and Craig (*J. A. M. A.*, 1906, xlvii, p. 1484) has reported death from the application of an alcoholic solution to the back and arm.

Formerly, the prognosis of poisoning by mercuric chloride depended almost entirely upon the dose which had been ingested; there was no treatment known which had any influence upon the progress of the intoxication. Within recent years, however, through the investigations of MacNider (*J. Ex. M.*, 1918, xxvii, xxviii and *J. M. R.*, 1916, xxix, and 1919, xxxix), of Fantus (*J. Lab. and Clin. Med.*, 1916, i, p. 879), of Lambert and Patterson (*A. I. M.*, 1915, p. 65) and others, a very large proportion of cases can be saved even after the ingestion of doses far in excess of those ordinarily fatal.

The modern treatment divides itself into two stages:—efforts to prevent absorption of the poisoning and efforts to lessen the destructive action upon the kidneys after absorption.

There are two methods of preventing the absorption of the poison; one is the mechanical evacuation and the other its chemical precipitation. Both of these are important. The stomach may be evacuated either by the use of an emetic or by the stomach tube, whichever can be obtained most promptly. Vomiting alone, however, should not be relied upon; as soon as possible a stomach tube should be obtained and the stomach washed out repeatedly until the fluid recovered no longer responds to a test with a sulphide.

Formerly, the white of egg was universally recommended as chemical antidote to corrosive sublimate on the theory that it would form an insoluble albuminate of mercury. The albuminate of mercury, however, is not completely insoluble in acid menstruum and sufficient may be dissolved by the gastric juice to exercise a caustic action; moreover, after the albuminate of mercury passes from the stomach to the intestines the mercury is readily absorbed. The experiments of Fantus have demonstrated beyond all cavil that while the administration of egg albumen within two or three minutes after the ingestion of corrosive sublimate may lessen the severity of the gastric lesions it has very little influence upon the final outcome of the poisoning and if not administered immediately does not effect even the gastric lesions. In his experiments he found that the best results were achieved by combinations of sodium phosphite and sodium acetate or of sodium hypophosphite with hydrogen dioxide. Sodium phosphite is not an article commonly found in the pharmacies. Fantus has suggested that tablets containing 0.36 Gm. of sodium phosphite and 0.24 Gm. of sodium acetate might be stocked in pharmacies as mercurial antidote and Linhart (*J. Lab. Clin. Med.*, 1917) has described a process for manufacturing sodium phosphite. The hypophosphite mixture of Fantus contains 1 Gm. of sodium hypophosphite, and 5 cc. of the solution of hydrogen dioxide in 10 cc. of water. This should be given so that there is at least ten times as much of the hypophosphite as of corrosive sublimate. In 1912, Hayward and Allen (*J. A. M. A.*, lx, 1727) in pointing out the inefficiency of egg albumen suggested the use of calcium sulphide (formerly official as Calx Sulphurata) as a chemical antidote. They asserted that 1 Gm. of calcium sulphide is sufficient to completely reduce 2.3 Gm. of mercuric chloride but do not appear to have made any actual tests of its efficacy. Since that time it has been employed by a number of investigators with apparently good results. Wilms (*Lancet Clinic,* 1915, cxiv, 555) goes so far as to assert, on the basis of both experimental and clinical evidence, that even after the absorption of the mercury the intravenous injection of calcium sulphide is capable of preventing its destructive effects on the body tissues but this has been contradicted by Haskell and Courtney (*J. Lab. Clin. Med.*, 1918). Fantus has objected to the use of calcium sulphide because he has found that the antidote itself is toxic to rabbits but the amount that he administered was equivalent to 80 grains (5 Gm.) for an ordinary man, a dose far in excess of that which could conceivably ever be needed. Holm (*Journal of the Michigan State Med. Society,* July, 1917) recommends that one to five grains of calcium sulphide be administered every hour until the odor of hydrogen sulphide is perceptible upon the breath. Whichever antidote is chosen should be repeated every six hours for two days.

The most frequent fatal lesion produced by mercury is nephritis. The experiments of MacNider have shown, first, that there is in mercurial poisoning an acidosis (*i.e.*, a diminished alkalinity of the blood) and secondly, that the more alkaline is the blood the less injurious is mercuric chloride to the kidney. It would seem from these experiments that the most important therapeutic effort, aside from those directed to limit the absorption of the poison, should be to conserve the alkalinity of the blood. The method of treatment which was brought forward by Lambert and Patterson before the publication of MacNider's experiments and which has proven clinically very valuable, although based upon an entirely different theory, probably owes its beneficial effects largely to the alkali which is incidentally introduced. Weiss (*J. A. M. A.*, 1917, lxviii, 1618) recommends, for the purpose of alkalizing the system, the intravenous injection of *Fischer's solution*—which consists of sodium carbonate 10 Gm., sodium chloride 15 Gm., water to 1000 cc.—and in addition the drinking of large quantities of a solution of potassium bitartrate and sodium citrate flavored with lemon or orange juice; the citrates and acetates are oxidized in the system and eventually appear in the blood as carbonates. Whatever the form of alkali employed it is probably a matter of small moment whether it be introduced intravenously, by the mouth or, as suggested by Lambert and Patterson, by colonic irrigation. The important factor is that it should be given in sufficient quantity to render and to keep the urine alkaline. In addition to efforts at alkalizing the body, theory would suggest the introduction of large amounts of fluid, with the idea of diluting the poison in the blood, and there is much clinical evidence in favor of this view. (See Gatewood and Byfield, *A. I. M.*, 1923, xxxii, 456 and Haskell et al., *J. A. M. A.*, 1923, lxxxi, 448.) The use of sweat baths was formerly recommended apparently with the idea that the mercury can be eliminated through the skin. We know of no reason for believing in the usefulness of this measure.

Details of the treatment of corrosive sublimate poisoning as applied in the U. S. Navy may be found in the *A. J. P.*, 1921, xciii, p. 792.

Tests for Corrosive Sublimate.—On account of the extreme virulence of this chloride as a poison, the reagents by which it may be detected form a subject of study of the utmost importance, as connected with medico-legal investigations.

If the mixture suspected of containing corrosive sublimate be wholly inorganic the following tests may be used for its detection: A preliminary test for mercury may be made with copper foil and strong hydrochloric acid. (Reinsch's test.) If the foil be darkened or changed it may be dried, placed in a tube of hard glass and heated when mercury will distil and separate in the cooler portions of the tube where it may be recognized by an examination under the microscope which will reveal the characteristic globules of the element. Tests in an aqueous solution of the substance may also be applied with hydrogen sulphide solution, which precipitates black mercuric sulphide; with potassium iodide solution, which cautiously added in just the proper amount precipitates red mercuric iodide; with an alkaline carbonate or hydroxide, which will precipitate the yellow mercuric oxide; and with stannous chloride solution which will reduce mercuric salts to mercurous and will thus give a white precipitate of calomel. The chlorine may be recognized by the customary silver nitrate test.

If any organic matter be present most or all of the foregoing tests will fail. As the mercury compounds will probably be volatilized if ignition be resorted to, the destruction of the organic matter must be accomplished in the wet way by heating the substance with strong hydrochloric acid, and then cautiously adding powdered potassium chlorate in small portions, continuing the heating until the organic matter is completely destroyed and the dark color which the mixture originally assumed upon heating with the acid, has changed to a clear golden yellow. This solution may then be carefully heated to drive off the free chlorine and the tests as previously described may be applied.

Dose, of corrosive sublimate, from one-fortieth to one-eighth of a grain (0.0015–0.008 Gm.), preferably given after meals, in solution.

Off. Prep.—Liquor Hydrargyri Perchloridi, *Br.;* Toxitabellæ Hydrargyri Chloridi Corrosivi, *U. S.;* Mulla Hydrargyri Chloridi Corrosivi, *N. F.;* Elixir Chloridum *N. F.;* Lotio Flava, *N. F.*

HYDRARGYRI CHLORIDUM MITE.
U. S. (Br.)

MILD MERCUROUS CHLORIDE Hydrarg. Chlor. Mit. [Calomel, Mercurous Chloride, Subchloride of Mercury]

"Mild mercurous chloride contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99.6 per cent. of HgCl." *U. S.* "Mercurous Chloride, HgCl, is obtained as a sublimate by heating a mixture of mercurous sulphate and sodium chloride." *Br.*

Hydrargyri Subchloridum, *Br.;* Mercury Subchloride; Calomelas; Hydrargyri Chloratum; Precipitatum Album; Mercurius Dulce; Chloruretum Hydrargyrosum; Mild Chloride of Mercury; Chlorure Mercureux, Mercure Douce, Precipité Blanc, *Fr.;* Protochlorure de Mercure, *Fr. Cod.;* Hydrargyrum Chleratum, *P. G.;* Quecksilberchlorur, *G.;* Protocloruro di Mercurio, *It.;* Cloruro Mercurioso Sublimado, *Sp.*

Very properly, processes for this compound have been omitted from the Pharmacopœias, as it cannot be made by the pharmacist conveniently. For processes of the U. S. P., 1870, and of the Br. Pharm., 1885, with remarks, see *U. S. Dispensatory,* 19th edition, p. 623.

The original method of making calomel was practised at Apothecaries' Hall, London, by taking advantage of the following reaction:

$$HgSO_4 + 2NaCl + Hg = Na_2SO_4 + 2HgCl$$

To bring the calomel into a state of minute division the method of Joseph Jewell, of London, improved by Ossian Henry, is sometimes employed. It consists in causing the calomel in vapor to come in contact with steam in a large receiver, whereby it is condensed into an impalpable powder, and perfectly washed from corrosive sublimate in the same operation. Calomel made by this process, sometimes called Jewell's or Howard's *hydrosublimate of mercury,* is free from all suspicion of containing corrosive sublimate, and is much finer than when obtained by levigation and elutriation. This kind of calomel is included in the French Codex under a distinct name. (*Mercure* (*Protochlorure de*) *par volatilization.*) For other methods at one time suggested see *U. S. D.*, 20th ed., p. 555.

When in mass, it is generally in the form of a white, fibrous, crystalline cake, the interior of which is often studded with shining transparent crystals, having the shape of quadrangular prisms, and a texture somewhat horny and elastic. When the mass is scratched it yields a yellow streak, which is very characteristic. Its sp. gr. is 7.2. Patch found (*Proc. A. Ph. A.*, 1885, p. 477) the sp. gr. of calomel to vary from 6.94 to 7.93. It is official only in the powdered state. The powder has a light buff or ivory color, if obtained by the levigation of sublimed masses; but if condensed at once in the form of an impalpable powder, it is perfectly white. To protect it from the action of the light, it should be kept in a dark place, or in bottles painted black or covered with black paper. By the action of the fixed alkalies or alkaline earths it immediately becomes black, in consequence of the formation of mercurous oxide, reducible by heat to the metallic state.

The preparation employed under the name of *lotio nigra,* or *black wash,* is used as a local application to syphilitic *ulcers,* etc. (See *Lotio Nigra,* Part III.)

Description and Physical Properties.—" A heavy white, impalpable powder, becoming yellowish-white when triturated with strong pressure, and showing only small, isolated crystals when viewed under a lens having a magnifying power of one hundred diameters. It is odorless, and is stable in the air. Mild Mercurous Chloride is insoluble in water, alcohol, ether, and in cold dilute acids. When heated to about 383° C., Mild Mercurous Chloride is volatilized without fusion or the evolution of brown vapors.

" The salt is blackened by contact with calcium hydroxide T.S., with a solution of an alkali hydroxide, or with ammonia T.S. When heated in a dry glass tube with an equal weight of dried sodium carbonate (free from chloride), Mild Mercurous Chloride yields a sublimate of metallic mercury. When the residue is dissolved in nitric acid and filtered, silver nitrate T.S. produces in the filtrate a white, curdy precipitate, insoluble in nitric acid.

" When volatilized at about 300° C., Mild Mercurous Chloride leaves not more than 0.1 per cent. of residue. Shake 2 Gm. of the salt with 20 cc. of ether for five minutes, filter, and allow the filtrate to evaporate spontaneously: the residue, dissolved in 10 cc. of distilled water and 2 drops of diluted nitric acid, shows no more *chloride* than corresponds to 0.1 cc. of fiftieth-normal hydrochloric acid (*mercuric chloride*). Heat 1 Gm. of the salt with sodium hydroxide T.S.: no ammonia is evolved (*ammoniated mercury*).

" **Assay.**—Dry about 0.7 Gm. of Mild Mercurous Chloride to constant weight over sulphuric acid, weigh accurately, mix well with 10 cc. of distilled water in a glass-stoppered flask, and add 50 cc. of tenth-normal iodine and 5 Gm. of potassium iodide dissolved in 10 cc. of distilled water. Stopper the flask, allow the mixture to stand with occasional agitation until complete solution has taken place, and then titrate the residual iodine with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal iodine corresponds to 0.02361 Gm. of HgCl. Mild Mercurous Chloride, previously dried to constant weight, may also be assayed by the electrolytic method.

" Preserve in well-closed containers, protected from light." *U. S.*

" A heavy dull white powder, sometimes rendered yellowish by prolonged trituration; nearly tasteless. Insoluble in *water,* in *alcohol* (90 per cent.), and in *ether;* soluble in a boiling mixture of *nitric acid* and *hydrochloric acid,* the solution, when diluted with *water,* yielding the *reactions* characteristic of mercuric salts. Volatilises when sufficiently heated, leaving not more than a trace of fixed residue. Warmed with *solution of sodium hydroxide* it becomes black, but does not evolve ammonia (absence of mercuric-ammonium chloride). When 1 gramme is well shaken with 10 millilitres of *water* and filtered, the filtrate is not darkened by *hydrogen sulphide* (absence of mercuric chloride)." *Br.*

Besides being incompatible with the alkalies and alkaline earths, calomel is also decomposed by the alkaline carbonates, soaps, sulphydrates, and, according to some authorities, by iron, lead, and copper. By boiling with the alkaline formates it is decomposed, and metallic mercury liberated. (H. Rose, *Annal. der Physik und Chem.,* cvi, 500.)

Calomel should not be given at the same time with nitrohydrochloric acid, for fear of generating corrosive sublimate; death is reported to have followed such a combination. According to the experiments of Deschamps, calomel is decomposed by bitter almonds and by hydrocyanic acid. In the former case corrosive sublimate, mercuric cyanide, and ammonium chloride are formed; in the latter, corrosive sublimate and mercuric cyanide only; hence this writer considers it very dangerous to associate calomel with bitter almonds or hydrocyanic acid in prescription. This conclusion has been confirmed by Mialhe and Prenleloup, and more recently it has been shown by E. Riegel that cherry-laurel water has the power of converting calomel into corrosive sublimate.

The alkali bromides produce appreciable amounts of mercuric salts when brought into contact with calomel in the presence of water and should never be given in combination.

Uses.—As an alterative calomel may be used for the general properties of the mercurials. (See under *Hydrargyrum.*) It it relatively non-irritant to mucous membranes and may be given in large doses so that it is possible to bring the system under the general influence of the mercury very rapidly. The use of calomel ointment instead of the blue ointment for inunction in *syphilis* has been suggested but Cole and Littman (*J. A. M. A.,* 1919, lxxiii) found the treatment of practically no value.

Aside from its alterative action, mercurous chloride is used as a cathartic, diuretic, and antiseptic. As a laxative it is slow but thorough in its action, affecting both upper and lower bowels. While the former belief that it was a stimulant to hepatic secretion has been shown to be incorrect, it in some way increases the bile in the intestinal tract, perhaps through an action on the bile passages or perhaps through its antiseptic effect preventing the decomposition of the natural bile. It is therefore preferred in cases where there is an absence of this secretion as shown by light-colored stools, and in *biliousness.* It is also a valuable agent to cleanse the intestines in *enteritis* both because of the thoroughness of its effect and of its antiseptic action. When used as a purgative better effects may be obtained with less discomfort by giving it in divided doses; thus a quarter of a grain may be given every half hour until three or four grains have been taken. It is usually advisable to follow it the next day with a saline for the reason that if it should fail to operate sufficient mercury may be absorbed to cause salivation.

The mode of action of calomel as a diuretic is not yet positively determined, but there is abundant evidence that it is one of the most powerful stimulants to the kidney which we possess. According to Fleckseder (*W. K. W.*, 1911, p. 1421), it is especially useful in the severe dropsies of heart disease after the failure of other drugs. An old combination with digitalis and squill, frequently but incorrectly spoken of as *Niemeyer's pill*, is widely employed for this purpose. (See *Pilulæ Digitalis Scillæ et Hydrargyri*, Part III.) To obtain its diuretic effect it is usually necessary to give it in large doses. Ordinarily from a quarter to half a grain may be given every two hours until beginning ptyalism, but in emergencies where an immediate effect is desired it may be well to give five grains (0.32 Gm.) at once, repeating every two hours until fifteen grains (0.9 Gm.) have been taken. Purgative action may be guarded against by the simultaneous exhibition of opium.

Although calomel has long been used both externally and internally for its disinfectant properties, the studies of Schamberg and Kolmer (*J. A. M. A.*, 1914, lxii, p. 1950 and 1915, lxiv, 618) indicate that its germicidal power has been underestimated. According to these investigators, weight for weight it is equal to the corrosive sublimate. Externally it is used for a dusting powder in various infections of the eye, and in *venereal ulcers* and in the form of an ointment in various ulcerated conditions of the nasal or other mucous membranes. Internally it is used for its antiseptic action in various types of *enteritis* or *dysentery*.

Some commercial cosmetic preparations contain calomel in suspension, and it is has always been found difficult or impossible to duplicate these smooth suspensions with commercial calomel, which first forms a curd and then rapidly settles out. F. W. Nitardy (*J. A. Ph. A.*, 1914, p. 965) found it possible to communicate the desired suspending qualities to ordinary calomel by first shaking with a solution containing 5 per cent. by volume of mucilage of acacia, then allowing the calomel to settle out, decanting and discarding the supernatant liquid and replacing it with distilled water. By repeating this operation several times the acacia is all removed but the calomel retains its marked suspending quality.

The *dose* of calomel as an alterative is from one-sixth to one-third of a grain (0.01–0.02 Gm.); as a cathartic, from two to five grains (0.12–0.3 Gm.).

Off. Prep.—Pilulæ Hydrargyri Chloridi Mitis Compositæ, *U. S.;* Pilulæ Hydrargyri Subchloridi Composita, *Br.;* Unguentum Hydrargyri Subchloridi, *Br.;* Pulvis Hydrargyri Chloridi Mitis et Jalapæ, *N. F.;* Tabellæ Santonini Compositi, *N. F.;* Tabellæ Hydrargyri Chloridi Mitis, *N. F.;* Lotio Nigra, *N. F.*

HYDRARGYRI IODIDUM FLAVUM. U. S.

YELLOW MERCUROUS IODIDE Hydrarg. Iod. Flav. [Mercurous Iodide]

"Yellow Mercurous Iodide contains, when dried to constant weight over sulphuric acid, not less than 99 per cent. of HgI." *U. S.*

Hydrargyri Iodidum Viride, *U. S. P.* 1880; Green Iodide of Mercury, Hydrargyri Iodidum, *U. S. P.* 1850; Iodide of Mercury, Yellow Iodide of Mercury; Protiodide of Mercury; Hydrargyrum Iodatum Flavum, Hydrargyri Protoioduretum, Ioduretum Hydrargyrosum; Iodurum Mercuriosum; Protiodure de Mercure, *Fr. Cod.;* Iodure mercureux, *Fr.;* Gelbes Jodquecksilber, *G.*; Protojoduro di mercurio, *It.;* Yoduro mercurioso, Protoyoduro de Mercurio, *Sp.*

The U. S. gives no process for making yellow mercurous iodide. The method of the U. S. P. VIII will be found in the U. S. Dispensatory, 20th ed., p. 558. It was essentially the process recommended by Edward Soetje (*Proc. A. Ph. A.*, 1888, p. 167), being a double decomposition between mercurous nitrate and potassium iodide in solution, *yellow* mercurous iodide and potassium nitrate being formed. From experiments by H. C. Wood, it appears that the *green* iodide is a mixture of yellow iodide and metallic mercury. By continuing the trituration, the powders become more and more yellow, and at length have only a tinge of green. He infers that pure mercurous iodide is yellow, and that the green color is owing to an admixture of the blue of the mercury with the yellow of the mercurous iodide. Flückiger (*Pharmaceutische Chemie,* 2d ed., 1888) agrees with this view, and says that by slow sublimation, at a very gentle heat, the true mercurous iodide can be obtained in small transparent yellow crystals of the quadratic system which are related to the forms of calomel. (See *J. P. C.*, 1894, 67.)

Description and Physical Properties.—"A bright yellow, amorphous powder, without odor or taste. By exposure to light it becomes greenish in proportion as it undergoes decomposition into metallic mercury and mercuric iodide. Yellow Mercurous Iodide is practically insoluble in water, and is insoluble in alcohol and in ether.

"When slowly and moderately heated, Yellow Mercurous Iodide assumes at first an orange and then a red color, becoming yellow again on cooling. When quickly and strongly heated, it is at first partially decomposed into mercury and mercuric iodide, and finally is volatilized. When heated in a dry glass tube with an equal weight of dried sodium carbonate, Yellow Mercurous Iodide yields a sublimate of metallic mercury. When Yellow Mercurous Iodide is heated with surphuric acid and a little manganese dioxide, the vapor of iodine is evolved.

"When volatilized at about 300° C., Yellow Mercurous Iodide leaves not more than 0.2 per cent. of residue. Place 0.5 Gm. of Yellow Mercurous Iodide in a 10 cc. glass-stoppered cylinder, add 10 cc. of alcohol, shake by inverting the cylinder ten times, allow to stand protected from light for two minutes and shake again by inverting the cylinder ten times. Filter at once, refiltering if necessary until the filtrate is clear, and to 5 cc. of the filtrate add an equal volume of hydrogen sulphide T.S. The color produced is not darker than that produced by 5 cc. of hydrogen sulphide T.S. in a mixture of 1 cc. of mercuric chloride solution (made by dissolving 0.5 Gm. of mercuric chloride in 1000 cc. of distilled water) and 4 cc. of alcohol (*mercuric iodide*).

"**Assay.**—Dry about 1 Gm. of Yellow Mercurous Iodide to constant weight over sulphuric acid, weigh accurately, transfer to a glass-stoppered flask, add 50 cc. of tenth-normal iodine and 5 Gm. of potassium iodide dissolved in 10 cc. of distilled water. Stopper the flask, and allow the mixture to stand with occasional agitation until complete solution has taken place, and then filtrate the residual iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal iodine corresponds to 0.03275 Gm. of HgI. Yellow Mercurous Iodide, previously dried to constant weight, may also be assayed by the electrolytic method.

"Preserve in well-closed containers protected from light." *U. S.*

Its sp. gr. is 7.75. If quickly and cautiously heated, it sublimes in red crystals, which afterwards becomes yellow. "Gradually heated in a test-tube, it yields a yellow sublimate, which, upon friction, or after cooling, becomes red, while globules of metallic mercury are left in the bottom of the tube." *Br.* 1867.

Uses.—Mercurous iodide is used in advanced *syphilis.* The dose is one-fifth of a grain (0.012 Gm.), gradually increased to two grains (0.13 Gm.). It should never be given at the same time with potassium iodide, which converts it into mercuric iodide and metallic mercury.

Dose, one-fifth of a grain (0.012 Gm.).

HYDRARGYRI IODIDUM RUBRUM.
U. S., Br.

RED MERCURIC IODIDE Hydrarg. Iod. Rub.
[Mercuric Iodide]

"Red Mercuric Iodide contains, when dried to constant weight over sulphuric acid, not less than 99 per cent. of HgI_2." *U. S.* "Red Mercuric Iodide, HgI_2, is obtained by the interaction of aqueous solutions of mercuric chloride and potassium iodide." *Br.*

Biniodide of Mercury; Red Iodide of Mercury; Mercurous Iodatus Ruber, Deutoioduretum Hydrargyri, Hydrargyrum Iodatum Rubrum, Ioduretum Hydrargyricum; Deutoiodide of Mercury; Iodure mercurique, *Fr.* Deuto-iodure Bi-iodure de Mercure, *Fr. Cod.;* Hydrargyrum Bijodatum, *P. G.* Quecksilberjodid, Rothes Jodquecksilber, *G.;* Bijoduro di mercurio *It.;* Yoduro mercurico, Biyoduro de Mercurio. *Sp.*

No process for preparing this salt is given in the U. S., nor British Pharmacopœias. The U. S. P. VIII process will be found in *U. S. D.,* 19th ed., p. 629.

This process involved a double decomposition between corrosive sublimate and potassium iodide, resulting in the formation of potassium chloride which remains in solution, and mercuric iodide which precipitates. The precipitate is soluble in the reacting salts, and hence a loss of part of it is incurred by an excess of either.

As obtained by this process it is in splendid crimson acicular crystals. When heated the mass becomes yellow at about 150° C., returning to red on cooling. Mercuric iodide is a dimorphous substance, having a different crystalline form in its red and yellow states. According to Schiff, it is only in its yellow form that it is soluble in alcohol; hence it is that, when separated by water from its alcoholic solution, it falls in this condition. (*Ann. Ch. Ph.,* cix, 371.) It forms definite compounds with the iodides of the alkali metals. The compound formed with potassium iodide has been used as a medicine. (See *Mercury and Potassium Iodide,* Part II.)

Description and Physical Properties.—"A scarlet-red amorphous powder without odor. It is stable in the air. *Caution—Red Mercuric Iodide is extremely poisonous.* Red Mercuric Iodide is practically insoluble in water. One Gm. is soluble in 115 cc. of alcohol, 910 cc. of chloroform, and in 120 cc. of ether, at 25° C. One Gm. is soluble in 20 cc. of boiling alcohol. It is dissolved by solutions of the soluble iodides, mercuric chloride, sodium thiosulphate, and by hot solutions of the alkali chlorides. When heated to about 150° C. Red Mercuric Iodide become yellow, but again assumes a red color on cooling. At about 250° C. it fuses to a dark yellow liquid, which, on cooling, forms a yellow, crystalline mass. At about 350° C. it is volatilized.

"Boil about 0.1 Gm. of the salt with 2 cc. of sodium hydroxide T.S., filter, and strongly acidify the filtrate with nitric acid; the liquid becomes yellow from the liberation of iodine, which produces a blue color upon the addition of a few drops of starch T.S. Heat the salt with potassium hydroxide T.S., and add a little lactose; metallic mercury is precipitated.

"When volatilized at about 300° C., Red Mercuric Iodide leaves not more than 0.2 per cent. of residue. Agitate thoroughly about 0.5 Gm. of Red Mercuric Iodide with 10 cc. of distilled water, and filter; the filtrate does not become more than slightly colored upon the addition of hydrogen sulphide T.S. (*soluble mercury salts*). Not more than 0.004 Gm. of insoluble residue remains on dissolving 2 Gm. of Red Mercuric Iodide in 100 cc. of distilled water containing 2 Gm. of potassium iodide.

"**Assay.**—Dry Red Mercuric Iodide over sulphuric acid to constant weight, and assay by the electrolytic method.

"Preserve in well-closed containers, protected from light." *U. S.*

"A crystalline powder of a vermilion color, becoming yellow when heated to about 150° C. Almost insoluble in *water,* sparingly soluble in *alcohol* (90 per cent.), freely and entirely soluble in *ether* (absence of mercurous iodide), and in *solution of potassium iodide.* Yields the *reactions* characteristic of mercuric salts and of iodides. Volatilises at a temperature under redness, leaving not more than a trace of fixed residue. When 0.5 gramme is well shaken with 10 millilitres of *water* and filtered, the filtrate is not colored more than slightly brown by *hydrogen sulphide* (limit of mercuric chloride), and does not become more than opalescent on the addition of *solution of silver nitrate* (limit of chlorides)." *Br.*

Uses.—Mercuric iodide resembles corrosive sublimate in its activities and therapeutic uses. Like the chloride it is an intense local irritant and is capable of giving rise to violent gastroenteritis. It is also an active germicide, probably equal to the bichloride in power, although its sparing solubility has to a large extent prevented its practical employment. The double iodide of potassium and mercury has, however, been recommended as a practical disinfectant; Macfarlan (*A. J. M. S.*, 1920, clix) asserts that it is superior to the bichloride especially because of its lesser irritant and toxic properties. McKenna and Fisher (*Surg. Gyn. and Obstet.*, 1920, xxx, 370) highly recommend a one per cent. solution in acetone for the disinfection of the skin preceding operations. (See also *Mercury and Potassium Iodide,* Part II.) As an internal remedy mercuric iodide is employed especially in old obstinate cases of *syphilis,* and those attended with rheumatoid pains, or *diseases of the bones.*

Cazenave considers mercuric iodide to be the best topical application in *lupus.* He applies it in thin layers, every six or eight days, to small portions of the ulcerated surface at a time, in the form of a caustic ointment, made of equal parts of the iodide, oil, and lard. The application produces severe pain, and gives rise to a sharp inflammation, which soon terminates, leaving the ulcer in an improved condition, with a tendency to cicatrize smoothly and on a level with the surrounding skin. A solution of mercuric iodide in olive oil (1 in 5000), which is to be prescribed as an external application, has been prepared by Delacour. (See *J. P. C.*, 1903, 603; 1904, No. 2.)

Dose, one-twentieth to one-twelfth of a grain (0.003–0.005 Gm.).

Off. Prep.—Liquor Arseni et Hydrargyri Iodidi, *U. S.* (*Br.*); Unguentum Hydrargyri Iodidi Rubri, *Br.*

HYDRARGYRI OXIDUM FLAVUM.
U. S., Br.

YELLOW MERCURIC OXIDE **Hydrarg. Oxid. Flav.**

"Yellow Mercuric Iodide, when dried to constant weight at 150° C., contains not less than 99.5 per cent. of HgO." *U. S.* "Yellow Mercuric Oxide may be obtained by the interaction of aqueous solutions of mercuric chloride and sodium hydroxide. It contains not less than 99.3 per cent. of pure mercuric oxide, HgO." *Br.*

Yellow Oxide of Mercury; Yellow Precipitate; Hydragyr Oxidatum Præcipitatum; Precipitated Oxide of Mercury; Mercuric Oxide; Oxydatum Hydrargyricum Flavum; Oxyde of Mercurique par Precipitation, *Fr.;* Oxide de Mercure Jaune, *Fr. Cod.;* Hydrargyrum oxydatum via humida paratum, *P. G.;* Präcipitirtes (Gelbes) Quecksilberoxyd, *G.;* Ossido mercurico giallo, *It.;* Oxido mercurico amarillo, *Sp.*

No process is given in the U. S. P. X or British Pharm. (1914) for this salt. The U. S. P. VIII process, which may be found in the *U. S. D.*, 20th ed., p. 561, depended on the decomposition of mercuric chloride in solution by sodium hydroxide.

Yellow Mercuric Oxide is a completely amorphous powder, exhibiting no evidence of crystalline particles even under the microscope. It differs from the red oxide only by being amorphous and in a much more minute state of division, the red oxide by trituration acquiring an orange and finally a yellow color. In consequence of its different state of aggregation, it is much more quickly acted on by reagents than is the red oxide. Thus, oxalic acid combines with the yellow oxide at lower temperature, producing the white oxalate, more than it does with the red. The yellow oxide, in contact with chlorine, gives up oxygen to that element, forming hypochlorous acid and corrosive sublimate. The red oxide exercises scarcely any influence on the gas at common temperatures.

Description and Physical Properties.—"A light orange-yellow, odorless, amorphous, heavy, impalpable powder. It is stable in the air, but turns darker on exposure to light. Yellow Mercuric Oxide is practically insoluble in water, and insoluble in alcohol. It is readily dissolved by diluted hydrochloric or nitric acid, forming colorless solutions.

"When moderately heated, Yellow Mercuric Oxide assumes a red color. At about 600° C. it is completely decomposed into oxygen and metallic mercury, and is volatilized.

"When volatilized at about 300° C., Yellow Mercuric Oxide leaves not more than 0.2 per cent. of residue. When moistened with hot, distilled water, Yellow Mercuric Oxide is not alkaline to litmus paper. A solution of 0.5 Gm. of Yellow Mercuric Oxide in 25 cc. of either diluted hydrochloric or diluted nitric acid is not more than slightly turbid. Heat 0.5 Gm. of Yellow Mercuric Oxide for two hours in a test tube, on a water bath, with a solution of 1 Gm. of oxalic acid in 10 cc. of distilled water and 1 cc. of ammonia T.S., replacing from time to time the water lost by evaporation; it is converted into white or yellowish-white mercuric oxalate (*distinction from red mercuric oxide*).

"**Assay.**—Dry about 0.5 Gm. of Yellow Mercuric Oxide to constant weight at 150° C., weigh accurately, and dissolve it in a mixture of 10 cc. of distilled water and 5 cc. of nitric acid, and further dilute the solution with 150 cc. of distilled water. Then add 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate. Each cc. of tenth-normal potassium thiocyanate corresponds to 0.01083 Gm. of HgO. Yellow Mercuric Oxide, previously dried to constant weight, may also be assayed by the electrolytic method.

" Preserve in well-closed containers, protected from light." *U. S.*

"A yellow powder; insoluble in *water;* readily soluble in *hydrochloric acid,* the solution yielding the *reactions* characteristic of mercuric salts. When 1 gramme is shaken with 5 millilitres of *water* for five minutes, the mixture is neutral to *litmus.* When gently heated it assumes a red color. The solution obtained by dissolving 0.5 gramme in 2 millilitres of *nitric acid* and diluting with 20 millilitres of *water* requires not less than 45.8 millilitres of *N/10 solution of ammonium thiocyanate* to produce a permanent pink coloration, *solution of ferric sulphate* being used as indicator. Heated to incipient redness it is resolved into oxygen and the vapor of mercury, leaving not more than 0.5 per cent. of fixed residue." *Br.*

I. Comere explains in a paper in *Répert. de Pharm.,* 1881, 199, the various conditions and modifications in the process necessary to make the oxide vary in color. (*N. R.,* 1882, 149.)

Uses.—The attention which has been paid to the yellow oxide is owing to its peculiar applicability to the local treatment of diseases of the eye, in consequence of its amorphous character. At present the yellow oxide is very largely used by oculists throughout the world in *conjunctivitis, hordeolum,* and other inflammations of the eye. It is generally employed in an ointment of about one-half to one per cent. strength. The red oxide, however carefully it may be triturated, even though in a perfectly impalpable state, still shows under the microscope crystalline particles, which in contact with the conjunctiva cause more or less irritation; it can, therefore, be readily understood that, in the ordinary mode of preparing it for use as an ointment, it may sometimes be productive of serious annoyance. From this objection the yellow oxide is exempt. The yellow oxide is also used largely in various *skin diseases,* notably *eczema* of the external auditory canal.

Off. Prep.—Unguentum Hydrargyri Oxidi Flavi, *U. S., Br.;* Oleatum Hydrargyri, *U. S.*

HYDRARGYRI OXIDUM RUBRUM. N. F., Br.

RED MERCURIC OXIDE Hydrarg. Oxid. Rub. [Red Precipitate]

" Red Mercuric Oxide contains, when dried to constant weight at 150° C., not less than 99.5 per cent. of HgO (216.60)." *N. F.*

" Red Mercuric Oxide may be obtained by heating mercurous nitrate until acid vapors cease to be evolved. Contains not less than 99.3 per cent. of pure mercuric oxide, HgO." *Br.*

Peroxide of Mercury, Red Oxide of Mercury, Red Precipitate; Mercurius Corrosivus Ruber vel Præcipitatus, Oxydum Hydrargyricum; Oxyde de Mercure Rogue, *Fr. Cod.;* Deutoxyde ou Péroxyde de Mercure, Précipité rouge, Poudre de Jean de Vigo, *Fr.;* Hydrargyrum Oxydatum, *P. G.;* Quecksilberoxyd, Rother Praecipitat, Quecksilber Præcipitat, Rothes Quecksilberoxyd, *G.;* Ossido mercurico rosso, *It.;* Oxido mercurico rojo, *Sp.*

This preparation has been dropped from the U. S. P., but is still retained by the N. F. and Br. The present Br. Pharm. gives no process, that of the 1885 edition was as follows:

" Take of Mercury, by weight, *eight ounces* [avoirdupois]; Nitric Acid *four fluidounces and a half* [Imperial measure]; Water *two fluidounces* [Imp. meas.]. Dissolve half the Mercury in the Nitric Acid diluted with the Water, evaporate the solution to dryness, and with the dry salt thus obtained, triturate the remainder of the Mercury until the two are uniformly blended together. Heat the mixture in a porcelain dish, with repeated stirring, until acid vapors cease to be evolved." *Br.* 1885.

For other methods which have been suggested see *U. S. D.,* 20th ed., p. 562.

The preparation is still frequently called by its older name, *red precipitate.* The name of *red mercuric oxide* is appropriate and more definite.

For a process for *Hydrargyrum præcipitatum per se, Precipitate per se,* or *calcined mercury,* all practically identical with red mercuric oxide, see *U. S. D.,* 17th ed., 704.

Description and Physical Properties.—" Red Mercuric Oxide occurs as heavy, orange-red, crystalline scales, or as a crystalline powder, acquiring a yellow color when finely divided; odorless and having a somewhat metallic taste, permanent in the air. Red Mercuric Oxide is almost insoluble in water; insoluble in alcohol; readily dissolved by diluted nitric acid, or by hydrochloric acid.

" When heated to about 400° C., Red Mercuric Oxide becomes dark violet or almost black, but assumes its original color on cooling. A solution of 0.5 Gm. of Red Mercuric Oxide in 25 cc. of either hydrochloric or nitric acid is not more than slightly turbid.

" Heat 0.5 Gm. of Red Mercuric Oxide for two hours, in a test tube on a water-bath, with a solution of 1 Gm. of oxalic acid in 10 cc. of distilled water and 1 cc. of ammonia water, replacing, from time to time, the water lost by evaporation; it will not change color within two hours (distinction from yellow mercuric oxide). At a red heat it is completely decomposed into oxygen and metallic mercury, and is finally volatilized without leaving more than 0.2 per cent. of residue. Mix 1 Gm. of Red Mercuric Oxide with 5 cc. of distilled water, add 2 cc. of sulphuric acid, cool the mixture and carefully pour upon it 2 cc. of ferrous sulphate T.S.; no brown zone develops at the line of contact (*nitrate*).

"**Assay.**—Dissolve about 0.5 Gm. of Red Mercuric Oxide, previously dried to constant weight at 150° C. and accurately weighed, in 10 cc. of distilled water and 5 cc. of nitric acid, and further dilute the solution with 150 cc. of distilled water. Then add 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate to the production of a permanent yellowish red color. Each cc. of tenth-normal potassium thiocyanate used corresponds to 0.01083 Gm. of HgO. Each gram of Red Mercuric Oxide, previously dried to constant weight, corresponds to not less than 91.9 cc. of tenth-normal potassium thiocyanate. Red Mercuric Oxide, previously dried to constant weight, may also be assayed by the electrolytic method (see U. S. P. X).

"Preserve it in well-closed containers, protected from light." *N. F.*

"Orange-red powder, or crystalline scales. Insoluble in *water;* soluble in *hydrochloric acid,* the solution yielding the *reactions* characteristic of mercuric salts. Gently heated it becomes dark violet, but resumes its orange-red color on cooling. Heated in a dry test-tube it does not evolve orange fumes (absence of nitrates). Responds to the quantitative test described under 'Hydrargyri Oxidum Flavum.' Heated to incipient redness it is resolved into oxygen and the vapour of mercury, leaving not more than 0.3 per cent. of fixed residue." *Br.*

Uses.—This preparation is too harsh and irregular in its operation for internal use and for external application is generally inferior to the yellow oxide. It is occasionally employed as a stimulating antiseptic, the powder being sprinkled on the surface of *chancres,* and *indolent, flabby,* or *fungous ulcers.* The powder should be finely levigated.

Hydrargyri Oxidum Nigrum, U. S. 1850. *Black Mercurous Oxide.*—This preparation has been dropped from both Pharmacopœias, and is now very rarely used. For a full account of its preparation, uses, and properties, see *U. S. D.,* 14th ed., 1256.

Off. Prep.—Unguentum Hydrargyri Oxidi Rubri, *N. F., Br.*

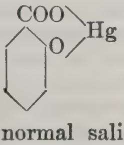
HYDRARGYRI SALICYLAS. U. S.

MERCURIC SALICYLATE Hydrarg Salicyl. [Mercuric Salicylate]

"Mercuric Salicylate is a compound of mercury and salicylic acid containing not less than 54 per cent. nor more than 59.5 per cent. of Hg." *U. S.*

Salicylas Hydrargyri; Salicylated Mercury; Hydrargyrum Salicylicum, *P. G.;* Salicilato Mercurico, *It.*

Mercuric salicylate is a compound of more or less varying chemical composition, having the approximate formula:



It is neither a normal salicylate nor a true subsalicylate as will be seen by the above formula which shows the mercury replacing both the phenolic and carboxylic hydrogen.

It is usually prepared by effecting a combination between freshly precipitated yellow mercuric oxide and salicylic acid in the presence of moisture and with gentle heating.

It is readily dissolved by solutions of alkalies which form double salts with it and from which solutions it is reprecipitated upon the addition of acids. It is decomposed by strong mineral acids.

Description and Physical Properties.—"An odorless, white, slightly yellowish or slightly pinkish powder. Mercuric Salicylate is practically insoluble in water and in alcohol. It is dissolved by solution of the fixed alkalies or their carbonates and by warm solutions of the alkali halides, with the formation of double salts.

"Heat 1 Gm. of Mercuric Salicylate with 10 cc. of hydrochloric acid; a solution is obtained from which salicylic acid separates on cooling. A piece of copper foil added to a portion of the filtered solution, nearly neutralized with ammonia T.S., immediately becomes coated with metallic mercury. To a mixture of 1 Gm. of Mercuric Salicylate with 10 cc. of distilled water add a few drops of ferric chloride T.S.; a violet color is produced.

"When volatilized at about 300° C., Mercuric Salicylate leaves not more than 0.2 per cent. of residue. Mercuric Salicylate does not redden moistened blue litmus paper (*free salicylic acid*). No dark color results at once on shaking about 0.1 Gm. of Mercuric Salicylate with 5 cc. of hydrogen sulphide T.S. (*foreign mercury compounds*). About 0.2 Gm. of Mercuric Salicylate dissolves completely in 4 cc. of normal sodium hydroxide.

"**Assay.**—Digest about 0.5 Gm. of Mercuric Salicylate, accurately weighed, in a mixture of 15 cc. of sulphuric acid and 10 cc. of nitric acid contained in a long neck flask in which a small funnel is inserted. Heat it upon a sand bath until the mixture is nearly colorless, then add another 10 cc. of nitric acid, and heat until the mixture is decolorized. Cool the solution, dilute it with 150 cc. of distilled water, add 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate until a permanent yellowish-red color is produced. Each cc. of tenth-normal potassium thiocyanate corresponds to 0.01003 Gm. of Hg. Mercuric Salicylate may also be assayed by the electrolytic method.

"Preserve in well-closed containers, protected from light." *U. S.*

Uses.—Mercuric Salicylate is used chiefly in the treatment of *syphilis,* especially by intramuscular injection. The advantages claimed for it are that it is locally non-irritant and that it does not salivate. The first of these is due to its insolubility and the second is an evidence of its slow absorption. Nelson and Anderson (*J. A. M. A.,* 1915, lxv, 1905) reach the conclusion that, although there may be a subsidence of the objective manifestations of *syphilis* under the use of mercuric salicylate, the drug does not exercise a real curative effect. Hill (*J. A. M. A.*, 1923, lxxx, 1365), from experimental studies on rabbits, also reached the conclusion that it is of little value in syphilis. Mercuric salicylate is also used locally for its germicidal effect either as a dusting powder in the strengths of ten per cent., or as an injection in *gonorrhea,* one part of the drug being suspended in 300 of mucilage. It is also said to be a useful local application in *alopecia* of syphilitic origin.

For intramuscular injection a ten per cent. suspension in sterile liquid petrolatum may be employed. Of this ten minims (0.6 cc.) may be injected deeply into the muscles of the back or buttocks, under strict asepsis, two or three times a week. It has also been used by mixing with an equal part of potassium carbonate and dissolving in distilled water.

Dose, by mouth, one-twelfth to one-third grain (0.005–0.021 Gm.).

HYDRARGYRUM. U. S., Br.

MERCURY Hydrarg. [Quicksilver]

"Mercury contains not less than 99.5 per cent. of Hg." *U. S.* "Mercury is a liquid metal which may be obtained from native mercuric sulphide." *Br.*

Hydrargyrum Vivum, Mercurius Vivus, Argentum Vivum Hydrargyrum Depuratum, Mercure Purifié, *Fr. Cod.;* Vif Argent, *Fr.;* Hydrargyrum, *P. G.;* Quecksilber, *G.;* Mercurio, *It., Sp.*

Mercury is found pure, forming an amalgam with silver, in the form of chloride (native calomel), but most abundantly as the sulphide or native cinnabar. Mines of this metal are found at Almaden in Spain, at Idria in Carniola, in the former duchy of Deux-Ponts, in Belluno, a province of Venetia, in Corsica, in the Philippine Islands and China, near Huancavelica in Peru, near Azogue in Colombia, at Durango in Mexico, at Yulgilbar, New South Wales, in various localities in Santa Clara County, California, and in Brewster and other counties in Texas. The most ancient mine is that of Almaden in Spain, which was worked before the Christian era. This mine, and the mines of California, are the most productive at the present day, the Spanish mine yielding about three and a quarter millions of pounds, and the California mines about two-thirds of this amount annually. The ore in all the mines mentioned is *cinnabar.* The cinnabar from old Almaden is of a dull-red color in mass, of a dull brick-red color when in fine powder, and of the sp. gr. 3.6. That from New Almaden is of a bright-red color, slightly inclining to purple, not so hard as the Spanish ore, of a brilliant vermilion color in powder, and of the sp. gr. 4.4. The California cinnabar is richer in mercury, because purer, than the Spanish, the former yielding about 70 and the latter about 38 per cent. of mercury, according to the analysis of Adam Bealey. The California mine has been long known to the Indians, but its commercial value was first made known about 1843, by a Mexican, named Castillero, who became its first owner. At present it is in the hands of Americans. Ruschenberger has detected selenium in California cinnabar.

Mercury is obtained from cinnabar by two principal processes. According to one process, the mineral is picked, pounded, and mixed with lime. The mixture is then introduced into cast iron retorts, which are placed in rows, one above the other, in an oblong furnace, and connected with earthenware receivers one-third full of water. Heat being applied, the lime combines with the sulphur, so as to form calcium sulphide and sulphate, while the mercury distils over, and is condensed in the receivers. The other process is practised at Almaden in Spain. Here a square furnace is employed, the floor of which is pierced with many holes, for the passage of the flame from the fireplace beneath. In the upper and lateral part of the furnace, holes are made, communicating with several rows of *aludels,* formed of adapters passing into one another, which terminate in a small chamber that serves both as condenser and receiver. The mineral, having been picked by hand and pulverized, is kneaded with clay, and formed into small masses, which are placed on the floor of the furnace. Heat being applied, the sulphur burns, and the volatilized mercury passes through the aludels to be condensed in the chamber.

Mercury, as found in commerce, is contained in cylindrical wrought iron bottles, called flasks, each containing 75 pounds. The world's production at present is about 9,500,000 pounds. The chief uses of the metal are in mining silver and gold, in preparing vermilion, in making thermometers and barometers, in silvering looking glasses, and in forming various pharmaceutical compounds.

Description and Physical Properties.—"A shining, silver white metal, liquid at ordinary temperatures and easily divisible into spherical globules. When cooled to about –40° C., it forms a ductile, malleable mass. Specific gravity: about 13.5 at 25° C. Mercury is insoluble in the ordinary solvents, in concentrated hydrochloric acid, and at ordinary temperatures, in sulphuric acid, but it dissolves in the latter when boiled with it. It is readily and completely dissolved by nitric acid. Mercury boils at about 358° C.

"When volatilized at about 300° C., Mercury yields not more than 0.02 per cent. of residue. When globules of Mercury are dropped upon white paper, they roll about freely, retaining their globular form and leaving no streaks or traces. Mercury should present a bright surface, even after agitation in contact with air.

"**Assay.**—Dissolve about 0.4 Gm. of Mercury, accurately weighed, in a mixture of 10 cc. of distilled water and 10 cc. of nitric acid, warm the solution gently until red fumes cease to be evolved and the solution is colorless, and add 150 cc. of distilled water. Then add 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate until a permanent reddish color is produced. Each cc. of tenth-normal potassium thiocyanate corresponds to 0.01003 Gm. of Hg. Mercury may also be assayed by the electrolytic method.

"Preserve in strong, well-closed containers." *U. S.*

"A silver-white, heavy liquid with a metallic lustre; easily devisible into globules. Readily volatilises when heated, leaving no appreciable fixed residue (absence of metallic and other impurities)." *Br.*

When perfectly pure it undergoes no alteration by the action of the air or water, but in its ordinary state suffers a slight tarnish. When heated to near the boiling point, it gradually combines with oxygen, and is converted into mercuric oxide; but at the temperature of ebullition it parts with the oxygen with which it had combined, and is reduced again to the metallic state. It boils at 358° C., yielding a colorless vapor, and congeals at –39.4° C., forming a malleable solid of tin-white color. It is a good conductor of heat, and its specific heat is small. It is not attacked by hydrochloric acid, nor by cold sulphuric acid; but boiling sulphuric acid or cold nitric acid dissolves it, producing mercurous sulphate and mercurous nitrate, respectively, with the liberation, in the former case, of sulphurous acid; in the latter, of nitrogen dioxide. Its combinations are numerous, and many of them constitute important medicines. It forms two series of compounds, the *mercurous* compounds containing the atom Hg^{I}, and the *mercuric* compounds containing the atom Hg^{II}.

Mercury, as it occurs in commerce, is in general sufficiently pure for pharmaceutical purposes. Occasionally it contains foreign metals, as lead, tin, zinc, and bismuth. Brande informs us that in examining large quantities of this metal in the London market he found it in only one instance intentionally adulterated. When impure, the metal has a dull appearance, leaves a trace on white paper, is deficient in due fluidity and mobility, as shown by its not forming perfect globules, is not totally dissipated by heat, and when shaken in a glass bottle coats its sides with a pellicle, or if very impure, deposits a black powder. If agitated with strong sulphuric acid, the adulterating metals become oxidized and dissolved, and thus the mercury may to a limited extent be purified. Mercury may be purified by digesting it with a small portion of weak nitric acid, or with a solution of mercuric chloride, whereby the ordinary contaminating metals will be removed. It may also be purified by distillation. For further details regarding the purification of mercury, see *U. S. D.*, 19th edition, p. 635.

Mercury is detected with great delicacy by Smithson's process, which consists in the use of a plate of tin, lined with one of gold, in the form of a spiral. When immersed in a mercurial solution, this galvanic combination causes the precipitation of the mercury on the gold, which consequently contracts a white stain. In order to be sure that the stain is caused by mercury, the metal must be volatilized in a small tube, so as to obtain a characteristic globule. A minute portion of any of the preparations of mercury, either in the solid state or in concentrated solution, being placed on a bright plate of copper, and a drop of a strong solution of potassium iodide added, a silvery characteristic stain will immediately appear on the copper.

For further details regarding the detection of mercury in compounds or preparations containing it, see *Hydrargyri Chloridum Corrosivum.*

It is difficult to accurately weigh small specified quantities of metallic mercury. An ingenious method was suggested by H. Kral, which is as follows: It consists of using a goose quill, into which the necessary quantity of mercury has been weighed. A small hole is then cut immediately above the surface of mercury, and the apparatus is ready for use. By simply immersing it into the bottle containing the mercury, it is filled through the opening, and uniform quantities, sufficiently accurate for practical purposes, are thus easily measured. (*Ph. Centralh.*, 1895, 422, 423.) In pharmaceutical operations a medicine dropper may be used to transfer the mercury.

Uses.—Metallic mercury in bulk is not absorbable, but when in a finely divided condition or in combination as a salt, it is taken up from the alimentary tract. In what form it is absorbed is at present uncertain. There are two widely held views, one that it is converted into an albuminate which is soluble in an excess of protein matter, and the other that it forms in the intestinal tract an oxide which is dissolved by the fatty matters. After its absorption it escapes from the system chiefly through the kidneys, although it has been detected in practically every secretion of the body. The elimination is comparatively slow so that when used over long periods of time it tends to accumulate in the system and may be stored up in the body for long periods. When present in the blood in large amounts it acts as a local irritant to various glandular structures and leads to an increased secretion. The salivary glands are usually the most sensitive so that ptyalism is an early symptom of chronic mercurial poisoning, but both the kidney and bowels are frequently affected.

The effects of small quantities of mercury on the bodily functions are not positively known but it appears to act somewhat like arsenic, restraining destructive metabolism and thereby causing a tendency to increase in weight. A stimulating effect upon the blood making organs is often manifest by an increase in the number of red blood cells, but after toxic doses anemia may result apparently through destruction of the bone marrow. After large doses there is also a diminution in the fibrin content of the blood. Whether this latter change is caused by therapeutic quantities is at present uncertain, but the clinical effects seen in conditions attended with fibrinous exudate would lead one to believe that it does. Sulant (*J. A. M. A.*, 1922, lxxix, 2071) has found that large doses introduced into the blood stream are directly injurious to the heart muscle.

In the form of blue mass (see *Massa Hydrargyri*) and of calomel (see *Hydrargyri Chloridum Mitis*), mercury is used as a cathartic and in the latter form also as a diuretic. All of the soluble salts appear to be more or less actively germicidal, the bichloride being the most widely employed. In this place will be considered the effects of mercury upon the system which are common to all the preparations used internally.

The most marked constitutional effects from mercury are seen in *syphilis.* Its beneficial action in this affection is due to a direct toxic effect upon the spirochetes which are the cause of the disease. Under full mercurialism the obvious lesions of lues may disappear with great rapidity, but some of the germs remain hidden, so to speak, in the internal organs, especially in the central nervous system, and it is usually essential that the administration of mercury be continued for from one to two years. The generally accepted mode of using the metal is to give it in ascending doses until a mild degree of ptyalism is produced, then withdraw the metal for a few days to allow the system to clear itself of the excess and give it in doses just below that which caused salivation. In inflammatory diseases of the serous membranes, as *pleurisy, meningitis,* and *iritis,* especially when there is fibrinous exudate, mercury is often of the utmost value. In similar conditions involving mucous membranes—especially *enteritis*—while it appears to exercise more or less antiphlogistic action, its effects are much less striking.

The first observable signs of mercury inducing *ptyalism* are a coppery taste in the mouth, a slight soreness of the gums, and an unpleasant sensation in the sockets of the teeth when the jaws are firmly closed. Shortly afterwards the gums begin to swell, a line of whitish matter is seen along their edges, and the breath is infected with a peculiar and very disagreeable odor, called the mercurial fetor. The saliva at the same time becomes increased in quantity and more viscid, and, if the affection proceed, the gums, tongue, throat, and face become much swollen; ulcerations attack the lining membrane of the mouth and fauces; the jaws become excessively painful; the tongue is coated with a thick whitish fur, and the saliva flows in streams from the mouth. If the use of the metal be persisted in, as was formerly sometimes the custom, the devitalized tissue affording a favorable place for bacterial growth, extensive necrosis may follow.

In the *treatment* of ptyalism it should be remembered that the inflammation of the salivary glands is the result of an effort at excretion and those drugs, such as potassium iodide, which tend to hasten the elimination of the metal will aggravate the symptoms. The most important element of the treatment is local cleanliness. Antiseptic and astringent mouth washes should be frequently used and ulcerated spots may be touched with solutions of silver nitrate. If the flow of saliva is excessive full doses of atropine may be given. Irvin (*B. M. J.*, Jan. 31, 1921) asserts that the internal use of sulphur is of advantage both as a prophylactic and curative of mercurial ptyalism. Sodium thiosulphate has also been recommended (see under *Sodii Thiosulphas*).

In the foregoing observations we have described the ordinary effects of mercury, but occasionally, in peculiar constitutions, its operation is quite different, being productive of a dangerous disturbance of the vital functions characterized by a small and frequent pulse, anxiety about the præcordia, pale and contracted countenance, great nervous agitation, and alarming debility. Mercury occasionally produces a peculiar eruption of the skin, which is described by writers under the various names of *hydrargyria, eczema mercuriale,* and *lepra mercurialis.* Those who work in mercury, and are, therefore, exposed to its vapor, such as looking-glass silverers, and quicksilver miners, are injured seriously in their health, and not unfrequently affected with shaking palsy, attended with vertigo and other cerebral disorders. The miners are often salivated.

Off. Prep.—Emplastrum Hydrargyri, *Br.;* Hydrargyrum cum Cretæ, *U. S., Br.;* Linimentum Hydrargyri (from Ointment), *Br.;* Massa Hydrargyri, *U. S.* (*Br.*)*;* Unguentum Hydrargyri Mite, *U. S.* (*Br.*)*;* Unguentum Hydrargyri Compositum, *Br.;* Unguentum Hydrargyri Fortius, *U. S.;* Petroxolinum Hydrargyri, *N. F.*

HYDRARGYRUM AMMONIATUM.
U. S., Br.

AMMONIATED MERCURY Hydrarg. Ammon.
[White Precipitate, Mercurammonium Chloride]

"Ammoniated Mercury contains $HgNH_2Cl$, corresponding to not less than 78 per cent. and not more than 80 per cent. of Hg." *U. S.*

Hydrargyri Præcipitatum Album; Hydrargyrum Amidatobichloratum; Hydrargyrum Bichloratum Ammoniatum; Mercurius Præcipitatus Albus; Hydrargyri Ammonio-Chloridum; Ammoniochloride of Mercury, Mercuric Ammonium Chloride; Mercuric amido-chloride; Chloramidure de Mercure, Oxychlorure Ammoniacal de Mercure, Lait Mercuriel, Mercure Précipité Blanc, *Fr.;* Hydrargyrum praecipitatum album, *P. G.;* Weisser Quecksilberpräcipitat, Quecksilber-Chloridamid, *G.;* Cloramiduro di mercurio, *It.*

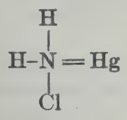
"Mercuric Chloride, 60 *grammes;* Solution of Ammonia, 80 *millilitres;* Distilled Water, *a sufficient quantity.* Dissolve the Mercuric Chloride in *twelve hundred millilitres* of Distilled Water with the aid of heat; pour the liquid into the Solution of Ammonia diluted with *four hundred millilitres* of Distilled Water, constantly stirring; collect the precipitate on a filter; wash it with *two hundred and fifty millilitres* of Distilled Water, and dry at a temperature not exceeding 30° C." *Br.*

No process is recognized by the U. S. P. X; the U. S. P. VIII process, which was essentially similar to the Br., may be found in the *U. S. D.*, 20th ed., p. 568.

The commercial varieties have at times differed somewhat from the present official preparation in composition, the formula being $N_2H_6HgCl_2$ (or *Mercur-diammonium chloride*). (See paper by F. X. Moerk, *A. J. P.*, 1888.)

Of the two possible formulas illustrated by the following:

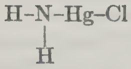
(1)



$\mathrm{H{-}\overset{\displaystyle H}{\underset{\displaystyle Cl}{N}}{=}Hg}$

and

(2)



$\mathrm{H{-}\underset{\displaystyle H}{N}{-}Hg{-}Cl}$

Saha and Choudberry (*Ztschr. Anorg. Chem.*, 1914, 86, 225) concluded that the second formula is the only tenable one, agreeing with certain experiments by which derivatives were formed.

Description and Physical Properties.—"White, pulverulent pieces, or a white, amorphous powder. It is odorless, and is stable in the air. Ammoniated Mercury is insoluble in water and in alcohol. By prolonged washing with water, it is gradually decomposed, assuming a yellow color and becoming converted into a basic salt. It is readily soluble in warm hydrochloric, nitric, and acetic acids and in a cold solution of ammonium carbonate. One Gm. is completely soluble in a cold solution of 5 Gm. of sodium thiosulphate in 5 cc. of water, with the evolution of ammonia. When the latter solution is heated for a short time, red mercuric sulphide is precipitated which upon protracted boiling turns black.

"At a temperature below a red heat Ammoniated Mercury is decomposed without fusion, and at a red heat it is volatilized. When heated with sodium hydroxide T.S., Ammoniated Mercury turns yellow, with the evolution of ammonia. A solution of Ammoniated Mercury in diluted nitric acid yields with potassium iodide T.S. a red precipitate, soluble in an excess of the reagent. The nitric acid solution yields a white precipitate with silver nitrate T.S.

"When volatilized at about 300° C., Ammoniated Mercury leaves not more than 0.2 per cent. of residue. Ammoniated Mercury is completely soluble in warm hydrochloric acid (*mercurous salts*) without effervescence (*carbonates*).

"**Assay.**—Dissolve about 0.5 Gm. of Ammoniated Mercury, accurately weighed, in 2 cc. of hydrochloric acid and 10 cc. of distilled water, warming gently until solution is effected, then dilute with 300 cc. of distilled water, and proceed as directed under *Hydrargyri Chloridum Corrosivum,* page 187, beginning with the word "Pass" in the third line of the Assay. The weight of mercuric sulphide obtained, multiplied by 0.862, indicates its equivalent in mercury (Hg). Each Gm. of Ammoniated Mercury corresponds to not less than 0.9047 Gm. and not more than 0.9279 Gm. of mercuric sulphide. Ammoniated Mercury may also be assayed by the electrolytic method."

"Preserve in well-closed containers, protected from light." *U. S.*

"A white, heavy, tasteless powder; insoluble in *alcohol* (90 per cent.) or *ether;* slowly decomposed by *water.* Digested with *solution of sodium hydroxide* it evolves ammonia, acquiring a pale yellow color, and the liquid, filtered and acidified with *nitric acid,* yields a white precipitate with *solution of silver nitrate.* Boiled with *solution of stannous chloride* it becomes grey, and yields globules of metallic mercury. Volatilises without fusing when sufficiently heated, leaving no appreciable fixed residue. When 0.3 gramme is triturated in a glass mortar with a few drops of *water,* and transferred to a flask with the aid of 40 millilitres of *water,* the mortar being finally rinsed with a solution of 2 grammes of *potassium iodide* in 10 millilitres of *water* and the rinsings added to the contents of the flask, then, the flask being securely closed and rotated frequently until solution is complete, the liquid thus obtained requires for neutralisation not less than 22.5 millilitres of *N/10 solution of hydrochloric acid, solution of methyl orange* being used as indicator (presence of not less than 94.5 per cent. of mercuric-ammonium chloride, NH_2HgCl)." *Br.*

Uses.—Ammoniated mercury is used only as an external application. It is a valuable remedy in parasitic skin diseases, such as *ringworm* or *favus,* and is also employed for destruction of *lice.* Mercur-diammonium chloride is said to produce an ointment more translucent and less white than the genuine, and more apt to become yellow on being kept.

Ammoniated mercury has been swallowed by mistake. It is highly poisonous, producing gastric pain, nausea, and purging. For recovery after taking half a drachm, see *L. L.*, July 4, 1857. The remedies employed were an emetic of zinc sulphate and milk.

Off. Prep.—Unguentum Hydrargyri Ammoniati, *U. S., Br.*

HYDRARGYRUM CUM CRETA.
U. S., Br.

MERCURY WITH CHALK Hydrarg. c. Cret.

"Mercury with chalk contains not less than 37 per cent. nor more than 39 per cent. of Hg." *U. S.*

Gray Powder; Æthiops Cretaceus; Mercure avec la Craie, Poudre de Mercure crayeux, *Fr.;* Quecksilber mit Kreide, *G.*

"Mercury, 38 Gm.; Honey, 10 Gm.; Prepared Chalk, 57 Gm.; Water, a sufficient quantity, to make 100 Gm. Weigh the mercury and honey successively into a strong bottle of the capacity of 100 cc. and add 2 cc. of water. Cork the bottle, and shake it for about half an hour at a time until the aggregate time of shaking reaches ten hours, or until the globules of mercury are no longer visible under a lens magnifying four diameters. The shaking may be more conveniently performed by mechanical means. Rub the prepared chalk with water in a mortar to a thick, creamy paste, and, having added the contents of the bottle, wash out the last portions with a little water, and triturate the whole to a uniform mixture. Finally dry the mixture, first between ample layers of bibulous paper, and afterwards in a dish at the ordinary temperature until it weighs 100 Gm. Then reduce it to a uniform powder without trituration." *U. S.*

"Mercury, 20 *grammes;* Prepared Chalk, 40 *grammes.* Triturate together in a porcelain mortar until the mixture acquires a uniform grey color and metallic globules cease to be visible to the naked eye." *Br.*

Dr. E. R. Squibb suggested the present official method of making mercury with chalk. The process is termed "succussion." When mercury is triturated with certain dry and pulverulent substances, such as chalk or magnesia, it gradually loses its fluidity and metallic luster and becomes a dark-gray powder. A similar change takes place when it is rubbed with viscid or greasy substances, such as honey or lard. The globules disappear, so as in some instances not to be visible even through a good lens, and the mercury is said to be "extinguished." It was formerly thought that the metal was oxidized in the process. At present the change is generally ascribed to the mechanical division of the metal, which in this state is supposed to be capable of acting on the system with greater energy. There is good reason, however, to believe that in this, as in all the analogous preparations of mercury in which the metal is extinguished by trituration, a very small portion is converted into mercurous oxide, while by far the greater part remains in the metallic state.

Robert B. Matter suggests an improved process for its preparation whereby labor and time are saved. It is as follows: "Mix twelve parts of finely powdered gum arabic with twelve parts of prepared chalk, triturate with sufficient water to form a rather thin paste, add thirty-eight parts of mercury, and continue the trituration until the globules of mercury have disappeared. Now add thirty-eight parts of finely powdered prepared chalk and sufficient water to form a thin paste, triturate, and when all the globules of mercury have disappeared, place the mortar in a hot water bath. The mixture distributed around the sides of the mortar will dry rapidly, when it can be easily scraped out, powdered in a clean mortar, passed through bolting cloth, or a fine sieve, and finally rubbed lightly in a clean dry mortar; 8 ounces may be made by this process in an hour." (*A. J. P.,* 1886, 119.)

Many modifications of the earlier processes suggested for the manufacture of this important preparation have appeared from time to time (see *U. S. D.,* 19th ed., p. 639), but the present official process is entirely satisfactory.

Description and Physical Properties.—"A light gray, rather damp powder, free from grittiness. It is odorless, and has a slightly sweet taste. Digest 0.1 Gm. of the powder with 20 cc. of warm acetic acid. The chalk dissolves with effervescence, and a residue of finely divided mercury remains.

"On filtering the mixture obtained in the preceding test, the filtrate becomes not more than slightly opalescent on the addition of a few drops of hydrochloric acid (*mercurous oxide*). Digest 0.1 Gm. of the powder with 20 cc. of warm diluted hydrochloric acid, and filter; the filtrate is not rendered more than slightly brown by hydrogen sulphide T.S. (*mercuric oxide*).

"**Assay.**—Dissolve about 1 Gm. of Mercury with Chalk, accurately weighed, in a mixture of 10 cc. of distilled water and 10 cc. of nitric acid, and heat on a water bath until red fumes cease to be evolved and the liquid becomes colorless. Then add 150 cc. of distilled water and 2 cc. of ferric ammonium sulphate T.S., and titrate the solution with tenth-normal potassium thiocyanate. Each cc. of tenth-normal potassium thiocyanate corresponds to 0.01003 Gm. of Hg. Mercury with Chalk may also be assayed by the electrolytic method.

"Preserve in well-closed containers, protected from light." *U. S.*

"A light-grey powder, free from grittiness; tends to aggregate into minute globules. Insoluble in *water;* partially dissolved by *diluted hydrochloric acid,* the residual mercury being left in a finely divided state; the filtered liquid does not yield any white or grey precipitate on the addition of *solution of stannous chloride* (absence of mercuric compounds)." *Br.*

As found in commerce, mercury with chalk, instead of being the mild preparation intended, sometimes acts very harshly causing vomiting, gastric pains, etc. This has been ascribed to the presence of antimony or arsenic, which, however, must be rare; the ordinary cause of the harshness is no doubt mercuric oxide, produced in minute proportion either during the trituration, or by the spontaneous change which occurs with time, mercurous oxide becoming mercuric oxide by the influence of light. The only sure method to guard against such results is to test the preparation carefully before dispensing it. (See official tests.) Another test for mercuric oxide is to treat a portion of the powder with diluted hydrochloric acid with a moderate heat, and add a solution of stannous chloride, which, if there be any mercuric oxide present, will cause a precipitation of metallic mercury as a black powder.

Uses.—Mercury with chalk is a very mild mercurial, similar in its properties to the blue mass, but much weaker. It is sometimes used as an alterative, particularly in the complaints of children attended with deficient biliary secretion, indicated by white or clay-colored stools. The chalk is antacid, and, though in small quantity, may sometimes be a useful accompaniment of the mercury in *diarrhea.* Eight grains of the U. S. preparation contain about three grains of mercury. It should not be given in pill with substances which become hard on keeping, as the contraction of the mass presses together the particles of mercury, which in time appear in globules in the interior of the pill.

Dose, as an alterative, one-half to one grain (0.03–0.06 Gm.); as a laxative, four to ten grains (0.25–0.65 Gm.).

HYDRASTINÆ HYDROCHLORIDUM. N. F.

[HYDRASTINE HYDROCHLORIDE Hydrastin. Hydrochl. [Hydrastine Chloride]

"The hydrochloride of the alkaloid hydrastine [$C_{21}H_{21}O_6N.HCl$(419.75)]." *N. F.*

This salt, which was formerly recognized by the U. S. IX, is now official in the N. F. For method of isolating the alkaloid hydrastine, as well as for account of its chemical properties see under *Hydrastis.*

Description and Physical Properties.—"Hydrastine Hydrochloride occurs as a white to creamy-white powder, odorless and hygroscopic. It is very soluble in water and in alcohol; slightly soluble in chloroform; very slightly soluble in ether. An aqueous solution of the salt (1 in 20) is neutral or only slightly acid to litmus.

"An aqueous solution of the salt yields with silver nitrate T.S. a white precipitate insoluble in nitric acid, but soluble in ammonia water. Sulphuric acid, when added to Hydrastine Hydrochloride, produces a yellow color which turns to purple of heating. Sulphuric acid containing 0.005 Gm. of molybdic acid in each cc. produces a green color, changing to olive-green, then to brown; nitric acid produces a reddish yellow color; sulphuric acid containing 0.005 Gm. of selenous acid in each cc. gives a light green color changing to brown.

"No weighable ash remains on incinerating 0.1 Gm. of Hydrastine Hydrochloride. A solution of about 0.1 Gm. of Hydrastine Hydrochloride in 10 cc. of diluted sulphuric acid shows no blue fluorescence (*hydrastinine*) but on the gradual addition of potassium permanganate T.S., avoiding excess, a blue fluorescence develops. An aqueous solution of Hydrastine Hydrochloride (1 in 20) is not reddened by chlorine water (*berberine*).

"Preserve it in well-closed containers, protected from light." *N. F.*

Uses.—For account of the physiological action of this salt see under *Hydrastis.* It is used locally in various catarrhs and internally chiefly as a uterine stimulant, especially in hemorrhages of that organ.

Dose, from one-sixth to one-half grain (0.01–0.03 Gm.).

Off. Prep.—Liquor Hydrastinæ Compositus, *N. F.*

HYDRASTIS. U. S. (Br.)

HYDRASTIS [Golden Seal]

"Hydrastis consists of the dried rhizome and roots of *Hydrastis canadensis* Linné (Fam. *Ranunculaceæ*). Hydrastis yields not less than 2.5 per cent. of the ether-soluble alkaloids of Hydrastis and contains not more than 2 per cent. of its stems, or leaves, or more than 2 per cent. of other foreign organic matter, and yields not more than 3 per cent. of acid-insoluble ash." *U. S.* "Hydrastis Rhizome is the dried rhizome and roots of Hydrastis canadensis, *Linn.*" *Br.*

Hydrastis Rhizoma, *Br.;* Hydrastis Rhizome; Rhizoma Hydrastis; Golden Seal, Yellow Root, Yellow Puccoon, Orange Root, Indian Dye, Indian Turmeric, Ohio Turmeric; Indian Paint, Ground Raspberry, Eye Root, Eye balm, Yellow Eye, Jaundice Root; Hydrastis, *Fr. Cod.;* Racine d'Hydrastis du Canada, Sceau d'or, *Fr.;* Canadische Gelbwurzel, Gelbes Blutkraut, *G.;* Idraste, *It.;* Hidrastis del Canada (Rizoma de), *Sp.*

Hydrastis canadensis was known to the Cherokee Indians long before the discovery of America. They employed its underground portion alike for dyeing and as an internal remedy and made the early settlers acquainted with most of its valuable properties. Its rhizomes and roots were first introduced in the Secondary List of the U. S. P. in 1860 and have been recognized in all subsequent editions. It is a small, herbaceous, perennial plant, with a thick, fleshy, yellow rhizome, from which numerous long rootlets arise, and an erect, simple, pubescent stem from six inches to a foot or more in height. There are usually but two leaves, which are unequal, one sessile at the top of the stem, the other attached to the stem a short distance below by a thick roundish footstalk, causing the stem to appear as if bifurcate near the summit. The leaves are pubescent, roundish-cordate, with from three to seven, but generally five, lobes, which are pointed and unequally serrate. A solitary greenish-white flower stands upon a peduncle rising from the base of the upper leaf. It is without corolla, but with a greenish-white calyx, the sepals of which closely resemble petals, and are very caducous, falling very soon after the flower has expanded. The fruit is a globose, compound crimson berry, half an inch or more in diameter, composed of many fleshy carpels, each tipped with a short curved beak, and containing one or rarely two seeds. The plant is native to moist, rich woodlands of eastern North America, and at one time was abundant in the territory bordering the Ohio River from Illinois to Virginia. Most of the wild growing plants are now nearly exterminated, a few good stands persisting in West Virginia, Ohio, Kentucky and Indiana. The fruit bears a close resemblance to the raspberry, but is not edible. The Indians employed it for cuticle staining and dyeing their garments yellow under the name of *yellow puccoon,* and it is said to impart a rich and permanent yellow, and with indigo a fine green, to wool, silk, and cotton. There is but one other species of *Hydrastis* known—viz., *H. jezoensis* Sieb. et Zucc., which is found in northern Japan.

As the natural supplies of Hydrastis are becoming limited many experiments in the cultivation of hydrastis have been made. It can be grown from cuttings of the rhizome and from seed. It furthermore can be grown with the natural shade of the woodlands or by means of artificial shade. The important articles on the cultivation of hydrastis are the following: John Uri Lloyd, *Proc. A. Ph. A.*, 1905, p. 307, and in *A. Ph. A.*, vol. i, p. 5; Walter Van Fleet and G. Fred Klugh, *Circ. No. 6, Bureau of Plant Industry, U. S. Department of Agriculture;* J. C. Baldwin, *A. J. P.*, 1913, p. 147. Most of the commercial supplies are obtained from the Ohio Valley, Indiana contributing the largest quantity. The States producing hydrastis are Oregon, West Virginia, Ohio, Kentucky and Indiana. The chief market is Cincinnati.

Description and Physical Properties.—"*Unground Hydrastis.*—Rhizome subcylindrical, flexuous, from 1 to 5 cm. in length and from 2 to 10 mm. in thickness; more or less annulate and wrinkled longitudinally; yellowish-brown to dark grayish-brown; marked by numerous stem scars or occasional stem- or leaf-bases and numerous roots, frequently broken, leaving circular yellowish scars or short protuberances; fracture short and waxy; internally deep yellow or greenish-yellow; odor distinctive; taste bitter. Roots numerous, filiform, up to 35 cm. in length and 1 mm. in diameter; yellowish; brittle; curved, twisted and matted together or broken into pieces.

"*Structure.*—Rhizome: an epidermis or, more often, a brown, thin-walled, several-rowed cork, a cortex of about 25 rows of thin-walled parenchyma, frequently broken through by root formations; phloem and cambium usually collapsed and indistinct; 12 to 20 radially elongated fibro-vascular bundles separated by medullary rays, the latter up to 30 cells in width; large pith. Root: an epidermis of yellowish-brown, elongated cells with strongly suberized outer lamella and frequently developed into 1-celled root hairs; hypodermis of closely arranged suberized cells; cortex of about 12 rows of thick walled starch-bearing parenchyma; endodermis of slightly lignified cells; central fibro-vascular bundle of 2 to 6 rays, the tracheæ being strongly lignified.

"*Powdered Hydrastis.* — Brownish-yellow; fragments of starch-bearing parenchyma and fibro-vascular bundles; tracheæ small, with simple pores or spiral thickenings; lignified fibers from 0.2 to 0.3 mm. in length with thin walls and simple pores; fragments of reddish-brown, tabular-celled cork; numerous starch-grains from 0.002 to 0.015 mm. in diameter, nearly spherical, mostly single, a few 2- to 6-compound, the larger grains showing a central cleft; calcium oxalate crystals absent.

"Hydrastis moistened with water and mounted directly in sulphuric acid shows the formation of numerous acicular or rod-shaped crystals, some attaining a length of 0.2 mm.

"**Assay.**—Proceed by Type Process A, taking 10 Gm. of Hydrastis, in fine powder, using 100 cc. of ether and decanting an aliquot portion of 50 cc., representing 5 Gm. of Hydrastis. Use ether for the final extraction and determine the alkaloids gravimetrically (Proximate Assays)." *U. S.*

"Rhizome tortuous, simple or branched, from ten to forty millimetres long and from three to ten millimetres thick; yellowish-brown, becoming darker by age. On the upper surface, short ascending branches usually terminated by cup-shaped scars; on the lower surface and sides numerous thin, brittle roots. Fracture clean, resinous; fractured surface brownish-yellow or greenish-yellow. In transverse section, a ring of bright yellow, somewhat distant, wood-bundles. Slight but characteristic odor; taste bitter. Ash not more than 11 per cent." *Br.*

The color of the rhizome, though yellow in the recent root, becomes a dark yellowish-brown by age; that of the rootlets and the interior of the root is yellow, and that of the powder still more so.

Holm gives a valuable illustrated article on the morphology of the hydrastis plant in *Merck's Rep.*, xxii, p. 202. (See also *Chem. Zeit.*, 1894, p. 134.) Rosenthaler has extended his studies of microsublimates to that of hydrastis and finds that the pyroanalytical sublimate of hydrastis gives general alkaloidal reactions and a characteristic reaction with sulphuric acid. (*Ap. Ztg.*, xxviii, p. 991.)

While considerably adulterated in the past, the recent commercial supplies of hydrastis have been generally of good quality. The most common past adulterant has been the rhizome and rootlets of *Jeffersonia diphylla* (L.) Pers., commonly known as *Twinleaf*. This may be distinguished from hydrastis: (1) by its rhizome possessing scattered stone cells both isolated and in groups, broad bundles in young parts, separated by narrow medullary-rays which in older parts become united into a ring, (2) by its longer and thicker rootlets and (3) by the fracture of the dried rhizome which is lighter yellow.

Constituents.—It contains—besides albumen, starch, fatty matter, resin, yellow coloring matter, sugar, lignin, and various salts—three alkaloids, *hydrastine* (discovered by Durand in 1851), *berberine* (discovered by Mahla in 1862) and *canadine* (first isolated by Schmidt in 1888). Berberine is usually the most abundant, being present in proportions of from 3 to 4 per cent.

For a valuable paper by J. U. Lloyd on the preparation of salts of berberine, see *A. J. P.*, 1879, p. 11. Lerre's process based on Lloyd's for preparing hydrastine and berberine will be found in the *U. S. D.*, 19th ed., p. 643.

Wilhelm (*P. J.*, 1888, 325) furnishes a process for obtaining the alkaloids from hydrastis as follows: The extract obtained by treating the coarsely powdered root with water acidified with acetic acid at 37.8° C. is evaporated to a syrup and excess of diluted sulphuric acid added, when berberine sulphate separates. The filtrate neutralized with ammonia water gives a precipitate containing much hydrastine; this is separated, and on adding ammonia water in excess to the filtrate a further precipitate is produced, which contains *canadine.* Both precipitates, boiled with ethyl acetate, give solutions which, on cooling, deposit hydrastine in large crystals, somewhat colored, but rendered pure by recrystallization. The crystals from the second ammonia precipitate are much purer than those from the first; by slow evaporation of the ethyl acetate solution they can be obtained as large as walnuts.

Hydrastine.—This alkaloid was official in the U. S. IX. The hydrochloride is recognized by the N. F. and is described under its own name. The base, $C_{21}H_{21}O_6N$, was described as follows.

"Hydrastine occurs in white to creamy white, glistening prisms or as a white, micro-crystalline powder; permanent in the air. Hydrastine is almost insoluble in water; 1 Gm. is soluble in 170 mils of alcohol, 1.4 mils of chloroform, and in 175 mils of ether at 25° C., also in 22 mils of alcohol at 60° C.; freely soluble in benzene. Its saturated alcoholic solution is alkaline to litmus. It melts at about 131° C. Sulphuric acid produces a yellow color when added to Hydrastine; on heating the mixture, a purple color develops. Sulphuric acid containing 0.005 Gm. of molybdic acid in each mil gives with Hydrastine a green color, changing to olive-green and then to brown; nitric acid yields a reddish-yellow color; sulphuric acid containing 0.005 Gm. of selenous acid in each mil gives a light green color, changing to brown. No weighable ash remains on incinerating 0.1 Gm. of Hydrastine. A solution of about 0.1 Gm. of Hydrastine in 10 mils of diluted sulphuric acid shows no blue fluorescence (*hydrastinine*), but, on the gradual addition of potassium permanganate T.S., avoiding excess, a blue fluorescence develops. An aqueous solution of Hydrastine (1 in 20), made with the aid of a slight excess of diluted hydrochloric acid, is not reddened by chlorine water (*berberine*)." *U. S. IX.*

The name hydrastine must not be confused with the similar name of the eclectic preparation called *hydrastin,* which is an almost inert preparation made by collecting, washing, and drying the precipitate produced by pouring a concentrated alcoholic solution of the drug into a large volume of water.

Hydrastine has been shown to exist in appreciable amounts in the leaves and tops of the plant. Charles S. Herron (*Am. Drug.,* 1918, lxvi, 416) obtained nearly an ounce of this alkaloid from eight pounds of the dried material, which is about three quarters of one per cent.

LaWall (*Proc. Pa. Ph. A.,* 1912, p. 142) made separate assays of the rhizome and rootlets from a 98-pound lot of the drug. There was present 45.5 pounds of rhizome and 48 pounds of rootlets, the balance being dirt and waste. The rhizomes assayed 2.48 per cent. of hydrastine and the rootlets 1.38 per cent. The average of the entire lot was 1.92 per cent.

Berberine occurs in a considerable number of additional plants including Berberis, Xanthoxylum, Calumba, etc. It distinguishes itself from most alkaloids in that its crystals are a bright yellow color and yield yellow solutions with marked staining properties. It is soluble in 300 parts of water. For further description see *Berberis.*

Canadine ($C_{20}H_{21}O_4N$) was extracted by E. Schmidt; it occurs in the form of brilliant, small, white nodules, melting at 134° C. When canadine is dissolved in alcohol and treated with iodine, berberine hydriodide (which is yellow in color) is formed. Canadine was believed to be identical with dihydromethylberberine (*Ph. Post,* 1892, 230), and the formula $C_{21}H_{21}O_4N$ was given to it. E. Schmidt, however (*A. Pharm.,* 1894, 136–154), has found that its true formula is $C_{20}H_{21}O_4N$, and, owing to the fact that iodine forms with it berberine hydriodide, he believes that canadine is a *tetrahydroberberine.* Schmidt also obtained, as an additional product of the iodine reaction, the hydriodide of another base, which he believes is intermediate between berberine and canadine. For a process for isolating canadine, see *Proc. A. Ph. A.,* 1894, 1103. The alkaloid discovered by A. K. Hale, and obtained later by Burt and by Lerchen, and which was named *xanthopuccine,* is now considered to be identical with canadine. For processes for making hydrastine and berberine, see *D. C.,* 1897, 34. It is probable, from the odor of hydrastis, that besides the two alkaloids here mentioned it contains also an active volatile principle, but this has not yet been isolated.

Uses.—Hydrastis owes its virtues almost entirely to hydrastine, the alkaloid berberine, aside from some effect as a bitter, being practically inert. Hydrastine is an active alkaloid which is slowly absorbed and probably eliminated by the kidneys and lower bowel unchanged. When given to the lower animals it primarily stimulates the spinal motor cord, causing tetanic convulsions, with heightened reflexes, followed, if the dose has been large enough, by loss of reflex activity, and motor paralysis, which are probably in part due to depression of the motor centers, and are certainly, at least in part, the outcome of depression of the motor nerves and also of the muscles themselves. Death may occur in a convulsion from cramp-asphyxia, or later from simultaneous paralysis of the respiratory center and of the peripheral apparatus. The arterial pressure is first elevated and secondarily depressed; the first rise of pressure is probably due to the stimulation of the cardiac and arterial muscles; Pilcher and Sollmann (*J. P. Ex. T.,* 1915, vi, 391) have shown that it does not act on the nerves governing the vessels. The fall of pressure is the result of a direct paralytic action exerted upon the muscle fibers in the heart and in the arterioles. Hydrastine notably increases intestinal peristalsis, and, according to Fellner (*Arch. f. Gyn.*, 1906, lxviii), uterine contractions. It would seem to be a universal muscle poison, which acts upon both striated and non-striated muscle fibers in heart, arterioles, intestines, uterus, and generally throughout the body, its first stimulant action being followed by marked depression. Hydrastine has been shown by Fellner and Slavatinski to have a distinct ecbolic action, and premature labor is asserted to have been caused by its hypodermic administration.

Hydrastis has enjoyed a widespread reputation as a local remedy in various forms of *catarrh,* such as *rhinitis, gastritis, vaginitis,* and *urethritis.*

In chronic or subacute *inflammations* of the *colon* and *rectum* injections of hydrastis are often of great service, and it has been used in *hemorrhoids* with asserted excellent results.

The strength of the local application of hydrastis to be used in various diseases of the mucous membrane varies from five to twenty-five per cent. of the fluidextract. In *gonorrhea* from forty to eighty minims (2.5–5.0 cc.) of the fluidextract may be used to the fluidounce (30 cc.). In *hemorrhoids* from two to four drachms to the fluidounce may be used. The glycerite is not so useful a local preparation as the fluidextract diluted with water, a deposit of the insoluble resinous substance upon the mucous membrane and its constant prolonged influence being important.

There is some reason for believing that *berberine* has a special action upon the gastro-intestinal tract. Marfori has, however, found that even in large therapeutic dose it is without perceptible influence upon the circulation or the nervous system. When, therefore, a preparation of hydrastis is to be used for effects other than a local action on the gastro-intestinal or other mucous membrane, a salt of the pure alkaloid hydrastine should be used.

According to the studies of Falck and Guenste, berberine causes in dogs and rabbits restlessness, convulsive tremblings, hurried respiration, and diarrhea, followed, if the dose has been large enough, by decrease of the breathing rate, widespread paralysis, dyspnea, convulsions, and death. In man as yet no serious symptoms have been recorded as produced by it. Buchner is stated to have taken nearly twenty grains without causing anything more serious than a loose stool. Marek (*W. M. W.*, 1911, 2146) has presented evidence that it possesses oxytocic properties, and is useful in *delayed labor.* It has been employed in internal medicine as a simple bitter, in doses of from two to five grains (0.13–0.32 Gm.).

Canadine is said by Marfori to differ from berberine physiologically; it produces in moderate dose an increase in the blood pressure by stimulating the vasomotor center in the medulla. *Opianic, hydrastinic,* and *berberinic acids* are said by the same authority to be almost inert physiologically, except that they are feebly antiseptic. (*T. G.*, 1890.)

For a physiological study of the *methylamine* derivatives of hydrastine (*hydrastine methylamine*), see *V. A. P. A.*, cxlii, 1895.

The alkaloid hydrastine hydrochloride may be used in doses of from one-sixth to one-half grain (0.01–0.03 Gm.).

Dose, of hydrastis, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Extractum Hydrastis, *U. S.;* Fluidextractum Hydrastis, *U. S.* (*Br.*)*;* Tinctura Hydrastis, *U. S., Br.;* Mistura Rhei Alkalina (from Fluidextract), *N. F*

HYOSCYAMINÆ HYDROBROMIDUM. U. S.

HYOSCYAMINE HYDROBROMIDE Hyoscyamin. Hybrobr. [Hyoscyaminæ Hydrobromas, Pharm. 1890, Hyoscyamine Hydrobromate, Hyoscyamine Bromide]

"The hydrobromide [$C_{17}H_{23}O_3N.HBr$], an alkaloid obtained from hyoscyamus and other plants of the *Solanaceæ.*" *U. S.*

Hyoscyaminum Hydrobromicum; Bromhydrate d'Hyoscyamine, *Fr.;* Hyoscyaminhydrobromid, Bromwasserstoffsaures Hyoscyamin, *G.*

Although Brandes announced the existence of an alkaloid in the seeds of *Hyoscyamus niger,* the process which he used to obtain it was not successful in other hands. The credit of first isolating the alkaloid *hyoscyamine* from the plant must be given to Geiger and Hesse, who obtained it in 1833. Höhn and Reichardt's process, in which the seed is used as the source, is as follows. They treat hyoscyamus seed first with ether to separate fatty matter, then with alcohol acidulated with a few drops of sulphuric acid, and afterwards distil the alcoholic solution. The aqueous residue is to be neutralized with sodium hydroxide, and the liquid precipitated by a solution of tannin. The precipitate, having been placed on a porcelain plate to dry, is mixed while yet moist with an excess of lime, and then exhausted by strong alcohol. The alcoholic solution is treated with sulphuric acid, then with sodium hydroxide, and finally with ether, which dissolves the liberated hyoscyamine. By distilling off the ether a colorless oleaginous liquid is left, which at length solidifies.

These investigators originally gave to hyoscyamine the formula $C_{15}H_{23}O_3N$, but Ladenburg (*B. Chem. G.*, 1880, xiii) later showed by a study of its decomposition products that it is isomeric with atropine, $C_{17}H_{23}O_3N$. Hyoscyamine treated with boiling baryta water assimilates a molecule of water and splits up into the same decomposition products as atropine, *tropic acid* and *tropine.* Hyoscyamine is to-day regarded as a stereo-isomer of atropine, from which it differs in certain physical properties, notably in that it is lævorotatory to polarized light, while atropine is optically inert. Hyoscyamine is readily changed into the racemic form, atropine, by melting or by adding alkali to its cold alcoholic solution. For further details concerning its structure see under *Atropina.*

Hyoscyamine crystallizes in colorless, transparent, silky needles, fusing at 108.5° C., is inodorous, of an acrid, disagreeable taste, slightly soluble in water, very soluble in alcohol and ether, and volatilizable with little change if carefully distilled. It is quickly altered by contact with water and an alkali, and when heated with potassium or sodium hydroxide is completely decomposed, with the disengagement of ammonia. It neutralizes the acids, forming crystallizable salts.

Description and Physical Properties.—"White, odorless, deliquescent crystals. *Caution—Hyoscyamine Hydrobromide is extremely poisonous.* Hyoscyamine Hydrobromide is very soluble in water. One Gm. is soluble in 2.5 cc. of alcohol, 1.7 cc. of chloroform, and in 2260 cc. of ether, at 25° C.

"It melts at about 152° C. An aqueous solution of Hyoscyamine Hydrobromide is lævorotatory. Add 5 drops of nitric acid to about 0.01 Gm. of the salt, and evaporate to dryness in a porcelain dish on a water bath: the residue becomes violet upon the addition of alcoholic potassium hydroxide T.S Gold chloride T.S. added to about 1 cc. of an aqueous solution of the salt (1 in 20) produces a precipitate which, when recrystallized from a small quantity of boiling distilled water acidulated with hydrochloric acid, is deposited, on cooling, in minute, lustrous, golden-yellow scales (*difference from atropine and scopolamine*). Silver nitrate T.S. added to an aqueous solution of Hyoscyamine Hydrobromide produces a yellowish-white precipitate which is insoluble in nitric acid. Shake 2 cc. of chloroform with 1 cc. of an aqueous solution of the salt (1 in 10) to which a few drops of chlorine T.S. have been added: the chloroform acquires a brownish color.

"An aqueous solution of Hyoscyamine Hydrobromide (1 in 20) is neutral to litmus paper. The ash from 0.1 Gm. is negligible. Platinic chloride T.S. does not form a precipitate in an aqueous solution of the salt (1 in 20) (*difference from most other alkaloids*). Dissolve about 0.05 Gm. of the salt in 1 cc. of sulphuric acid: the solution is not darker than faint yellow (*readily carbonizable substances*).

"Preserve in well-closed containers, protected from light." *U. S.*

Uses.—The physiological effects of hyoscyamine are qualitatively the same as those of its isomer atropine, although there is some difference quantitatively. Atropine, as pointed out elsewhere, is regarded as a mixture of dextro- and lævorotatory alkaloids. Cushny (*J. P.*, 1903, xxx, p. 177) has shown that the lævorotatory substance (hyoscyamine) is relatively more active in its paralyzing effect on nerve endings and less active in its stimulant action upon the central nervous system. Like atropine hyoscyamine checks secretion by paralyzing the terminals of nerves to the various glands, dilates the pupil by paralyzing the ends of the oculomotor nerve, and increases the pulse rate by paralyzing the pneumogastrics. The rise in blood pressure is comparatively small after hyoscyamine because it exercises but a feeble influence on the vasomotor center; similarly it causes but little increase in the respiration and shows less tendency to cause delirium. The former belief that hyoscyamine possessed narcotic properties was doubtless due to its contamination with scopolamine; there is no convincing evidence that chemically pure hyoscyamine has a depressant action upon the cerebrum. Clinically, hyoscyamine may be substituted for atropine wherever the action on peripheral nerves is desirable, as for instance, to check excessive secretion, to dilate the pupil, or to allay intestinal spasm.

Dose, one two-hundredth to one one-hundredth of a grain (0.0003–0.0006 Gm.).

HYOSCYAMINÆ SULPHAS. Br.

HYOSCYAMINE SULPHATE

"Hyoscyamine Sulphate, $(C_{17}H_{23}O_3N)_2,H_2SO_4,2H_2O$, is the sulphate of an alkaloid, hyoscyamine, obtained from various plants belonging to the natural order Solanaceæ." *Br.*

Sulfate d'Hyoscyamine, *Fr.;* Hyoscyaminum Sulfuricum, Schwefelsaures Hyoscyamin, Hyoscyaminsulfat, *G.;*

Properties.—The British Pharmacopœia describes hyoscyamine sulphate as "a deliquescent crystalline powder. Soluble in 0.5 part of *water.* Melting point from 203° to 204° C. Yields the *reaction* characteristic of sulphates. When treated with *nitric acid* and *alcoholic solution of potassium hydroxide,* as described under 'Atropina,' a violet coloration is produced. 0.05 gramme, dissolved in 5 millilitres of *water* acidified with *hydrochloric acid,* yields with *solution of auric chloride* a yellow precipitate which, recrystallised from *water* acidified with *hydrochloric acid,* forms brilliant golden-yellow scales melting, when dried, at 165° C. Dissolves in *sulphuric acid* without coloration. No appreciable ash." *Br.*

Uses.—The medicinal properties and the dose of this salt of hyoscyamine are precisely those of the hydrobromide.

Dose, one two-hundredth to one one-hundredth of a grain (0.0003–0.0006 Gm.).

HYOSCYAMUS. U. S. (Br.)

HYOSCYAMUS Hyosc. [Henbane, Hyoscyami Folium, P. I.]

"Hyoscyamus is the dried leaf with or without the tops of *Hyoscyamus niger* Linné (Fam. *Solanaceæ*). Hyoscyamus yields not less than 0.065 per cent. of the alkaloids of Hyoscyamus and contains not more than 25 per cent. of its stems none of which is more than 7 mm. in thickness. It yields not more than 12 per cent. of acid-insoluble ash." *U. S.* "Hyoscyamus Leaves are the leaves of Hyoscyamus niger, *Linn.*, collected from the flowering plants, and dried." *Br.*

Hyoscyami Folia, *Br.;* Hyoscyamus Leaves, Henbane Leaves, Black Henbane, Henbell, Stinking Nightshade, Insane Root, Poison Tobacco; Jusquiamus; Jusquiame noire, *Fr. Cod.;* Belene, Chenile, *Fr.;* Herba Hyoscyami, *P. G.;* Bilsenkraut, Bilsenkrautblätter, *G.;* Giusquiamo, *It.;* Beleno, *Sp.*

There are about fifteen species of the genus *Hyoscyamus* known; these are distributed from the Canary Islands over Europe and northern Africa to Asia.

Hyoscyamus niger, or *henbane,* varies in different regions, being either an annual or biennial plant. It possesses a long, tapering, whitish, fleshy, somewhat branching root, not unlike that of parsley, for which it has been eaten by mistake, with poisonous effects. The stem of the biennial variety is erect, branching, from one to four feet high, and thickly furnished with leaves. These are large, oblong-ovate, deeply sinuated with pointed segments, undulated, soft to the touch, and clasping at their base. The upper leaves are generally entire. Both the stem and leaves are hairy, viscid, and of a sea-green color. The flowers form long, one-sided, leafy spikes, which terminate the branches, and hang downward. They are composed of an urn-shaped calyx with five pointed divisions, a funnel-shaped corolla, with five unequal, obtuse segments at the border, five stamens inserted into the tube of the corolla, and a pistil with a blunt, round stigma. The corolla is of an obscure yellow color, beautifully variegated with purple veins. The fruit is a two-celled pyxis, invested with the persistent calyx, and contains numerous small seeds, which are discharged by the horizontal separation of the lid from the top portion of the fruit. The whole plant has a rank, offensive odor.

H. niger is susceptible of considerable diversity of character, causing varieties which have by some been considered as distinct species. Thus, the plant is sometimes annual, the stem simple, smaller, and less downy than in the biennial plant, the leaves shorter and less hairy and viscid, and the flowers often yellow without the purple streaks.

The plant is found in the northern and eastern sections of the United States, occupying waste grounds in the older settlements, particularly cemeteries, old gardens, and the foundations of ruined houses. It is not, however, a native of this country, having been introduced from Europe. In Great Britain, and on the continent of Europe, it grows abundantly along the roads, around villages, amidst rubbish, and in uncultivated places. Both varieties were formerly cultivated in England, but at present the biennial is chiefly or solely grown. The annual plant flowers in July or August, the biennial in May or June. For an account of the cultivation of the biennial variety of Hitchin, England, see *P. J.*, Feb., 1860.

Mitlacher, in connection with other plants, has carried on a series of experiments on the cultivation of Hyoscyamus and reports on the results of his work in *Ph. Post,* 1911, p. 390 and *Zeit. Oest. Apoth. Ver.*, 1912, p. 401. Hyoscyamus has been successfully grown in the testing gardens of the Bureau of Plant Industry. There is usually some difficulty in growing hyoscyamus owing to its destruction by insects, but Newcomb was very successful with his experiments in Minneapolis. (*A. J. P.*, 1914, p. 531.) Schneider also has pointed out that henbane thrives well in California and says that it no doubt will do well in the Coast valleys. (*Pac. Pharm.*, iii, p. 192.) Peckoldt reports that *Hyoscyamus niger* grows wild in portions of Brazil. (*B. P. G.*, xix, p. 33.) Chevalier has shown that by cultivation the alkaloid content of hyoscyamus can be increased to 0.286 per cent. of total alkaloids. (*C. R. A. S.*, 1910, p. 344.) Experiments by Newcomb and Haynes (*A. J. P.*, 1916, lxxxviii, 1) show that *H. niger* cultivated in Minnesota yields very high percentages of total alkaloids, the range being from 0.096 to 0.1561 per cent. The biennial seeds were found to germinate more satisfactorily if first treated with strong sulphuric acid. The seeds are placed in a porcelain dish, the acid poured on them and they are stirred with a glass rod for two and one-half minutes. They are then thrown in a coarse screen and thoroughly washed with water. Seed thus treated gives a fairly uniform germination in from twelve to fifteen days.

H. albus, so named from the whiteness of its flowers, is used in France indiscriminately with the former species, with which it appears to be identical in medicinal properties. *Hyoscyamus muticus* L., of Egypt, is said to grow luxuriantly in the temperate zone and to produce a very much larger proportion of total alkaloids than does the official English plant, although the relative proportions of hyoscine and hyoscyamine are not the same. It appeared in the London market in the form of broken stalks with a few capsular fruits and traces of leaves and may become an important source of the alkaloids to the manufacturers.

Description and Physical Properties.—"*Unground Hyoscyamus.* — Usually much wrinkled, matted and broken, frequently consisting of leaves, stems, and flowering and fruiting tops. Leaves ovate or ovate-lanceolate, inequilateral, with petioles up to one-third the length of the blade, or sessile; apex acute, margin coarsely and angularly 1- to 4-toothed or lobed; hairy, densely so on the lower surface; upper surface dark green, lower surface light gray-green; stems from 2 to 7 mm. in thickness, cylindrical or somewhat compressed, longitudinally wrinkled, hairy, gray-green; flowers nearly sessile, with an urn-shaped, hairy, unequally 5-toothed calyx and a campanulate corolla, yellowish with purplish veins; fruit, a 2-locular pyxis enclosed in the calyx; odor distinctive; taste bitter and acrid.

"*Structure.*—Leaves: One layer of palisade cells with frequent large intercellular spaces;

some of the parenchyma cells with prisms or rosette aggregates of calcium oxalate; in the midrib a girdle or collenchyma about the vascular bundle and the parenchyma occasionally with sphenoidal microcrystals of calcium oxalate. Stems: Cortex thin; wood with numerous tracheæ and lignified fibers; hollow, with a few pith parenchyma cells. Seed: Campylotropous, the coat strongly reticulated, with curved embryo embedded in the endosperm.

"*Powdered Hyoscyamus.*—Grayish-green to dark green. Non-glandular hairs unicellular to 10-celled; glandular hairs with 1- to 4-celled stalk and 6 or more cells in the head; calcium oxalate crystals in single or twin monoclinic prisms or in rosette aggregates from 0.010 to 0.025 mm. in diameter, occasionally in sphenoidal crystals from 0.006 to 0.012 mm. in length; sclerenchyma fibers attaining a length of 1 mm. and a width of 0.030 mm., some with wavy walls and ends variously forked; pollen grains nearly smooth with 3 radiating furrows having a pore in the median part of each furrow, when dry or in alcohol distinctly elliptical and approximately 0.035 by 0.050 mm., but in water spherical and about 0.040 mm. in diameter; epidermal cells of the seed coat with radial and inner walls greatly thickened and incrusted with granular crystals of silicic acid.

"**Assay.**—Proceed by Type Process B, taking 25 Gm. of Hyoscyamus, in fine powder, using ether-chloroform mixture for percolating the drug and chloroform for the final extraction of the alkaloids. Determine the alkaloids volumetrically. Each cc. of tenth-normal acid corresponds to 0.02893 Gm. of the alkaloids of Hyoscyamus (Proximate Assays)." *U. S.*

"Pale green, varying in length but seldom exceeding twenty-five centimetres; mostly sessile; exstipulate, triangular-ovate or ovate-oblong, acute, undulated, irregularly toothed, sinuate or pinnatifid, with conspicuous midrib. On both surfaces, but particularly on the under surface and near the veins, long uniserial hairs terminating in pluricellular glands. In the mesophyll prismatic and cluster-crystals of calcium oxalate." *Br.*

Much of the efficacy of hyoscyamus depends upon the time at which it is gathered. The leaves should be collected soon after the plant has flowered. In the biennial plant, those of the second year are preferred to those of the first. The latter, according to Houlton, are less clammy and fetid, yield less extractive, and are medicinally much less efficient. It is said that the plant is sometimes destroyed by severe winters in England, and that no leaves of the second year's growth are then obtainable. This is, perhaps, one of the causes of the great uncertainty of the medicine as found in commerce. The root also is said to be much more poisonous in the second year than in the first.

The recent leaves have, when bruised, a strong, disagreeable, narcotic odor, somewhat like that of tobacco. Their taste is mucilaginous and very slightly acrid. When dried, they have little odor or taste. Thrown upon the fire, they burn with a crackling noise, as if they contained a nitrate, and at the same time emit a strong odor.

Much of the henbane of commerce is taken from the plant in the first year of its growth. The drug of the market is very variable, frequently containing an excess of sand and the leaves of other species of hyoscyamus. It has recently been admixed with *H. muticus,* a plant growing in Egypt. The latter is readily determined by the presence of characteristic branching non-glandular hairs which are found on both the stems and leaves. (See *A. J. P.,* 1908, p. 361.) The commercial supplies of Hyoscyamus come chiefly from Europe through London.

The seeds are very small, roundish, compressed, somewhat kidney-shaped, a little wrinkled, of a gray or yellowish-gray color, of the odor of the plant, and of an oleaginous, bitterish taste. From experiments made by Hirtz upon the relative medicinal power of extracts from the seeds and from the leaves, he inferred that the former had ten times the strength of the latter. Henbane leaves yield, by destructive distillation, a very poisonous empyreumatic oil.

Geiger and Hesse (1833) were the first to demonstrate the existence of an alkaloid in hyoscyamus. Ladenburg stated in 1880 that there are two alkaloids in the plant,—one crystallizable, *hyoscyamine* $C_{17}H_{23}O_3N$, and the other amorphous, *hyoscine* $C_{17}H_{21}O_4N$ (see *Scopolamina Hydrobromidum* and *Hyoscyaminæ hydrobromidum*). Höhn (*Ann. Ch. Ph.,* clvii, 98) obtained from the seeds a bitter principle which proved to be a glucoside. He calls it *hyoscypicrin,* and gives it the formula $C_{27}H_{52}O_{14}$. The hyoscyamine is the dominant alkaloid. The leaves contain a large proportion of potassium nitrate, F. Mahla having obtained approximately 2 per cent. of that salt. (*A. J. P.,* 1859, p. 402.)

Uses.—The physiological and therapeutic effects of Hyoscyamus are dominated by the alkaloid hyoscyamine and are therefore very similar to those of belladonna. Many physicians believe, however, that the action of the chief alkaloid is modified by the presence of scopolamine and that the plant, therefore, not only has the antispasmodic and drying effects of belladonna but that it has a distinct central narcotic action; the proportion of scopolamine, however, seems too small to exert any important influence. Its most important use is in relief of painful spasmodic affections of the unstriped muscle, as in *lead colic* and *irritable bladder.* It is also employed to allay nervous irritation, as in various forms of *hysteria* or *irritable cough,* but is inferior to scopolamine for these purposes. Externally cataplasms or fomentations of the fresh leaves have been employed to allay pain in *cancerous ulcers* and *hemorrhoids,* but its employment for this purpose is of doubtful advantage.

Hyoscyamus is preferably given in the form of the fluidextract or tincture. The inspissated juice of the fresh leaves (*Extractum hyoscyami viride*, Br.) is exceedingly variable in its operation and is not to be recommended.

Dose, of the leaves, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Extractum Hyoscyami, *U. S., Br.;* Fluidextractum Hyoscyami, *U. S.;* Pilula Colocynthidis et Hyoscyami (from Extract), *Br.;* Tinctura Hyoscyami, *U. S., Br.;* Pilulæ Catharticæ Vegetabiles (from Extract), *N. F.;* Pilulæ Colocynthidis et Hyoscyami (from Extract), *N. F.;* Pilulæ Laxativæ Post Partum (from Extract), *N. F.*

IGNATIA. N. F.

IGNATIA Ignat. [Saint Ignatius' Bean, Ignatia Amara

"Ignatia is the dried ripe seed of *Strychnos Ignatii* Bergius (Fam. *Loganiaceæ*). Ignatia yields not less than 2 per cent. of the alkaloids of Ignatia and not more than 1 per cent. of foreign organic matter." *N. F.*

Semen Ignatiæ, Faba Ignatii, Faba Sancti Ignatii, *Lat.* Fève igasurique, Fève de Saint Ignace, *Fr.;* Ignatiusbohne Bittere Fiebernuss, Ignazbohnen, *G.;* Fava di Santo Ignazio *It.;* Haba de Santo Ignacio, *Sp.*

Strychnos Ignatia Berg. (*Ignatia amara* L. f.) is a large climbing shrub, a native of the Philippine Islands, and introduced into Cochin-China where the seeds were highly esteemed as a medicine, and, having attracted the attention of the Jesuits, were honored with the name of their founder. The fruit is a large ovoid berry being from 5 to 6 inches long and containing from 12 to 24 seeds imbedded in its pulp. The commercial supplies of the seeds come from the Philippine Islands. Flückiger and Arthur Meyer have found that the seed has a close structural analogy to nux vomica. (*P. J.*, 1881, 1.)

Description and Physical Properties.—"*Unground Ignatia.*—Angularly ovate with obtuse angles or irregularly several sided; up to 30 mm. in length and about 15 mm. in breadth and thickness; externally grayish and reddish brown to dark reddish brown or blackish, nearly smooth and with but few hairs; heavy and very hard; fracture granular; translucent in small fragments; a small irregular cavity in the center contains the small embryo. Nearly inodorous and intensely bitter.

"*Structure.*—An epidermal layer of cells with yellowish, granular contents and yellowish walls thickened on the outer side; the remainder of the seed coat made up of about six rows of thin-walled cells; the outer cells of the endosperm tissue, small, the inner large and with thickened walls.

"*Powdered Ignatia.*—Light gray to grayish brown, and exhibits thin brown cells of the epidermis and the subjacent layer of the seed coat; polygonal cells with thickened, pitted walls and granular contents from the endosperm; hairs, few, in spreading clusters, characteristic, thickened at base and having linear markings; embryo tissue of small thin-walled cells.

"**Assay.**—Place 10 Gm. of Ignatia, in fine powder, in a 250 cc. bottle, add 100 cc. of ether-chloroform mixture, and proceed by Type Process A. Decant 50 cc. of the ethereal solution to complete the assay, using chloroform as the immiscible solvent in shaking out the alkaline liquid, and determine the alkaloids volumetrically. Each cc. of tenth-normal acid corresponds to 0.0364 Gm. of the alkaloids of Ignatia." *N. F.*

To Pelletier and Caventou Ignatia beans yielded the same constituents as nux vomica, and, among them, 1.2 per cent. of strychnine and 0.5 per cent. of brucine.

The medicinal uses are the same as those of nux vomica.

Dose, one to two grains (0.06–0.12 Gm.).

Off. Prep.—Extractum Ignatiæ, *N. F.;* Tinctura Ignatiæ, *N. F.*

INFUSA. U. S.

INFUSIONS

Ptisana, Tisanes, Infusions, *Fr.;* Infusa, *P. G.;* Infusionen, Aufgüsse, *G.;* Infusi, *It.;* Infusiones, *Sp.*

These are aqueous solutions obtained by treating drugs with water (without the aid of ebullition). The water employed may be hot or cold according to the objects to be accomplished. Infusions are generally prepared by pouring boiling water upon the vegetable substance and macerating the mixture in a tightly closed vessel until the liquid cools.

The U. S. provides that, when not otherwise specified, infusions shall be of 5 per cent. strength and gives the following general formula for infusions:

"Infusions must be freshly made, and, when their strength is not otherwise directed, they are to be prepared by the following general formula:

"The Drug, coarsely comminuted, 50 Gm.; Water, a sufficient quantity to make 1000 cc. Introduce the drug into a suitable vessel provided with a cover, pour upon it 1000 cc. of boiling water, cover the vessel tightly, and allow it to stand for half an hour. Then strain with pressure, and pass enough water through the strainer to make the Infusion measure 1000 cc. If the activity of the Infusion is affected by heat, cold water only should be used.

"*Caution.—The strength of infusions of energetic or powerful drugs should be specially directed by the physician.*" *U. S.*

Infusions are usually prepared in glazed earthenware or porcelain vessels fitted with covers. Vessels of block-tin are generally well adapted for the purpose.

As infusions do not keep well, especially in warm weather, they should be made extemporaneously and in small quantities. Sterilization of infusions by heating them to the boiling point, then preserving in bottles which have been kept hot to destroy germs, and stoppered with sterilized cotton, is effective, particularly if the bottles have a stopcock near the bottom to draw the infusion when wanted.

Concentrated infusions of the strength of 50 per cent. were introduced into the British Pharmacopœia (1898); they are mostly made by percolation, and were termed "Liquors." This certainly led to confusion in nomenclature, and it is difficult to understand why they were not called concentrated infusions, particularly as their almost universal use is for making ordinary infusions by diluting with water. They were dropped from the British Pharm. 1914.

INFUSUM ALSTONIÆ. Br.

INFUSION OF ALSTONIA

"Alstonia, bruised, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for half an hour; strain while hot." *Br.*

See *Alstonia.*

Dose, one-half to one fluidounce (15–30 cc.).

INFUSUM AURANTII. Br.

INFUSION OF ORANGE PEEL

Tisane d'Ecorce d'Orange, *Fr.;* Pomeranzenschalenaufguss, *G.*

"Dried Bitter-Orange Peel, cut small, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

A grateful stomachic.

Dose, from one-half to one fluidounce (15–30 cc.).

INFUSUM AURANTII COMPOSITUM. Br.

COMPOUND INFUSION OF ORANGE PEEL

Tisane d'Ecorce d'Orange composée, *Fr.;* Pomeranzen und Citronenschalenaufguss, *G.*

"Dried Bitter-Orange Peel, cut small, 25 *grammes;* Lemon Peel, cut small, 10 *grammes;* Cloves, bruised, 5 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

A grateful stomachic in the *dose* of from one-half to one fluidounce (15–30 cc.).

INFUSUM BUCHU. Br.

INFUSION OF BUCHU

Infusum Diosmæ, s. Barosmæ; Tisane de Buchu, *Fr. Cod.;* Buchuaufguss, *G.*

"Buchu Leaves, freshly broken, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

It has the odor, taste, and medicinal virtues of the leaves, and affords a convenient method of administering the medicine.

Dose, from one to two fluidounces (30–60 cc.).

INFUSUM CALUMBÆ. Br.

INFUSION OF CALUMBA

Infusion of Columbo; Tisane de Columbo, *Fr.;* Kolombo-Infusion, Kolomboaufguss, *G.;* Infusion de Colombo, *Sp.*

"Calumba Root, cut small, 50 *grammes;* Distilled Water, cold, 1000 *millilitres.* Infuse in a covered vessel for half an hour; strain." *Br.*

The *infusion of calumba* is likely to spoil very quickly, especially in warm weather. Calumba contains starch and albumen. Cold water extracts the latter without the former; hot water the former with comparatively little of the latter, which is partially coagulated by the heat. Both starch and albumen are liable to spontaneous change, but the former is much the more permanent of the two. Hence it is, according to Greenish, that the hot infusion keeps best. Indeed, he ascribes the change which takes place in the starch of the hot infusion chiefly to the agency of a little albumen which has escaped coagulation. According to these views, the best plan of preparing infusion of calumba is to exhaust the root with cold water, by which the starch is left behind, and then to heat the infusion to the boiling point in order to coagulate the albumen. (*A. J. P.,* xviii, 141; from *P. J.*) Upon comparing specimens of the cold and hot infusion, we have not found the results of Greenish fully confirmed. The cold infusion appeared to keep better than the hot. Nevertheless the plan of preparing the infusion above proposed is probably the best. The infusion of calumba is not colored by salts of iron, and may be conveniently administered in connection with them.

Dose, from one-half to one fluidounce (15–30 cc.).

INFUSUM CARYOPHYLLI. Br.

INFUSION OF CLOVES

Tisane de Girofle, *Fr.;* Gewürznelken-Infusion, Gewürznelkenaufguss, *G.*

"Cloves, bruised, 25 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

The infusion of cloves affords precipitates with lime water, and with the soluble salts of iron, zinc, lead, silver, and antimony. (Phillips.)

Dose, one fluidounce (30 cc.).

INFUSUM CASCARILLÆ. Br.

INFUSION OF CASCARILLA

Tisane de Cascarille, *Fr.;* Kaskarillaufguss, *G.*

"Cascarilla, in No. 10 powder, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

This infusion affords precipitates with lime water, infusion of galls, silver nitrate, lead acetate and subacetate, zinc sulphate, and ferrous sulphate.

Dose, one fluidounce (30 cc.).

INFUSUM CHIRATÆ. Br.

INFUSION OF CHIRETTA

Tisane de Chirette, *Fr.;* Chirettaufguss, *G.*

"Chiretta, cut small, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

Dose, from one-half to one fluidounce (15–30 cc.).

INFUSUM CINCHONÆ ACIDUM. Br.

ACID INFUSION OF CINCHONA

Infusion of Yellow Bark; Infusion of Calisaya Bark; Tisane de Quinquina jaune, *Fr.;* Kalisaya-Rindenaufguss, *G.*

"Red Cinchona Bark, in No. 40 powder, 50.0 *grammes;* Aromatic Sulphuric Acid, 12.5 *millilitres;* Distilled Water, boiling, 1000.0 *millilitres.* Mix the Red Cinchona Bark with the Distilled Water in a covered vessel; add the Aromatic Sulphuric Acid; infuse for one hour; strain while hot." *Br.*

Although the infusion with boiling water is more quickly prepared than the infusion with cold water, and therefore better adapted to cases of emergency, yet the former is a more elegant preparation, not turbid like the latter, and at least equally efficient. We therefore prefer the process of the U. S. Pharmacopœia, 1890, provided it be skilfully conducted. (See *U. S. Dispensatory,* 19th ed., p. 654.)

Dose, one fluidounce (30 cc.).

INFUSUM DIGITALIS. U. S., Br.

INFUSION OF DIGITALIS Inf. Digit.

Infusion of Foxglove; Tisane de Digitale, *Fr.;* Fingerhutaufguss, Digitalisaufguss, *G.;* Infusion de digital, *Sp.*

The U. S. Pharmacopœia has abandoned the antiquated direction to use "bruised" digitalis and now agrees with the Br. in directing that the leaves be in a powdered form, although it differs from the Br. in strength, requiring two and a half times the proportion of drug.

"Digitalis, in fine powder, 15 Gm.; Alcohol, 100 cc.; Cinnamon Water, 150 cc.; Boiling Water, 700 cc.; Cold Water, a sufficient quantity to make 1000 cc. Upon the digitalis, contained in a suitable vessel, pour the boiling water, tightly cover, and allow it to macerate for one hour. Filter, add the alcohol and cinnamon water to the filtrate, and pass enough cold water through the residue on the filter to make the product measure 1000 cc. Mix well." *U. S.*

"Digitalis Leaves, in No. 20 powder, 7 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

It has long been recognized that infusion of digitalis as ordinarily made is an unstable preparation, but according to Hatcher and Eggleston (*J. A. M. A.,* 1915, lxv) this would seem to be due to bacterial action, for they find that if bottled hot and kept stoppered, the infusion will retain its strength for many weeks.

Many clinicians have believed that the infusion of digitalis differed in its action to some extent from that of the tincture; especially that the infusion was more actively diuretic. It has long been surmised that the formerly official method of preparing infusion of digitalis did not entirely extract the potency of the leaf; Bliss (*J. Lab. Clin. Med.,* 1922, vii, 225) found that 10 samples of an infusion prepared at various retail pharmacies showed, on the average, a potency of less than 40 per cent. of the leaf from which they were made. In 1910 Focke (*A. Pharm.,* ccxlix, 323) showed that it was possible to extract 85 per cent. of the activity of digitalis leaf with water. Weiss and Hatcher (*J. A. M. A.,* 1921, lxxvi, 508) suggested a new method of preparing an infusion of digitalis that more completely exhausted the leaf and yielded a uniform product and which they assert maintains its activity unimpaired, if kept hermetically sealed, for years. A method very similar to this was adopted in the present revision of the U. S. Pharmacopœia. As this method more thoroughly extracts the drug the present preparation, despite the fact the proportion of leaf has not been altered, will be found to be somewhat stronger than the former infusion.

Dose, of the U. S. infusion, one-half to three fluidrachms (2–11 cc.).

The British infusion is much weaker and may be given in doses of two to six fluidrachms (7.5–22.5 cc.).

INFUSUM ERGOTÆ. Br.

INFUSION OF ERGOT

Tisane de Seigle ergoté, *Fr.;* Mutterkornaufguss, *G.*

"Ergot, freshly crushed, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

As ergotoxin is not soluble in water this preparation does not fully represent the virtues of ergot.

Dose, two fluidounces (60 cc.).

INFUSUM GENTIANÆ COMPOSITUM. Br.

COMPOUND INFUSION OF GENTIAN

Tisane de Gentiane composée, *Fr.;* Enzianaufguss, *G.*

"Gentian Root, thinly sliced, 12.5 *grammes;* Dried Bitter-Orange Peel, cut small, 12.5 *grammes;* Lemon Peel, cut small, 25.0 *grammes;* Distilled Water, boiling, 1000.0 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

The National Formulary recognizes a compound infusion of gentian which is made with a menstruum containing about 21 per cent. of alcohol and is more than twice the strength of the British. (See Part III.)

The use of the alcohol is to assist in dissolving the bitter principle, and at the same time to contribute towards the preservation of the infusion, which, without this addition, is very prone to spoil. The alcohol has, however, been abandoned by the British Pharmacopœia, and lemon peel substituted.

Dose, from one-half to one fluidounce (15–30 cc.).

INFUSUM KRAMERIÆ. Br.

NFUSION OF KRAMERIA

Infusion of Rhatany; Tisane de Ratanhia, *Fr.;* Ratanhiawurzelaufguss, *G.*

"Krameria Root, bruised, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

The *infusion of rhatany* is undoubtedly most efficient when prepared from the root in a state of moderately coarse powder by the mode of percolation with cold water, as directed in the U. S. process of 1870.

Dose, of the infusion, from one to two fluidounces (30–60 cc.).

INFUSUM QUASSIÆ. Br.

INFUSION OF QUASSIA

Tisane de Quassie, *Fr.;* Quassiaaufguss, *G.;* Infusion de cuasia amarga, *Sp.*

"Quassia Wood, rasped, 10 *grammes;* Distilled Water, cold, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain." *Br.*

Boiling water may be employed when it is desirable to obtain the preparation quickly, but cold water affords a clearer infusion. The fifteen minutes' maceration directed in the British Pharmacopœia, considering that cold water is used, appears to us to be too short for the exhaustion of the wood.

This preparation is used by mouth as a bitter tonic and by enema in the treatment of seat-worms.

Dose, from one-half to one fluidounce (15–30 cc.).

INFUSUM RHEI. Br.

INFUSION OF RHUBARB

Tisane de Rhubarbe, *Fr.;* Rhabarberaufguss, *G.;* Infuso di rabarbaro, *It.;* Infusion de ruibarbo, *Sp.*

"Rhubarb, in thin slices, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

In order that the rhubarb may be exhausted, it should be digested with the water near the source of heat, at a temperature somewhat less than that of boiling water. It is customary to add some aromatic, such as cardamon, fennel seed, or nutmeg, which improves the taste of the infusion and renders it more acceptable to the stomach. One drachm of either of these spices may be digested in connection with the rhubarb.

This infusion may be given as a laxative, and is occasionally used as a vehicle for tonic, antacid, or more active cathartic medicines. The stronger acids and most metallic solutions are incompatible with it.

Dose, one-half to one fluidounce (15–30 cc.).

INFUSUM ROSÆ ACIDUM. Br.

ACID INFUSION OF ROSES

Tisane de Rose composée, *Fr.;* Saurer Rosenaufguss, *G.*

"Red-Rose Petals, dried and broken, 25.0 *grammes;* Diluted Sulphuric Acid, 12.5 *millilitres;* Distilled Water, boiling, 1000.0 *millilitres.* Add the Diluted Sulphuric Acid to the Distilled Water; infuse the Red-Rose Petals in the mixture in a covered vessel for fifteen minutes; strain while hot." *Br.*

The formula of the N. F. for *Infusum Rosæ Compositum* (see Part III) is preferable to that of the Br. Pharm. on account of the presence of sugar.

The red rose serves little other purpose than to impart a fine red color and a slight rose and astringent flavor to the preparation, which owes its medicinal virtues almost exclusively to the sulphuric acid. According to J. B. Barnes, one part of glycerin added to eight or nine parts of infusion of rose increases greatly its brightness and transparency. It is refrigerant and astringent, and affords a useful and not unpleasant drink in *hemorrhages* and *colliquative sweats.* It is much used by British practitioners as a vehicle for saline medicines particularly magnesium sulphate, the taste of which it serves to cover. It is also employed as a gargle in combination with more active drugs.

Dose, one-half to one fluidounce (15–30 cc.).

INFUSUM SCOPARII. Br.

INFUSION OF BROOM

Tisane de Genêt à balais, *Fr.;* Besenginsteraufguss, *G.*

"Broom Tops, dried and bruised, 100 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

This preparation has been introduced in place of the Decoction of Broom of the British Pharmacopœia of 1885. Water thoroughly extracts the virtues of broom, and the large quantity of water in each dose aids the diuretic action.

Dose, from one to two fluidounces (30–60 cc.).

INFUSUM SENEGÆ. Br.

INFUSION OF SENEGA

Tisane de Polygale de Virginie, *Fr.;* Senegaaufguss, *G.*

"Senega Root, in No. 10 powder, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for half an hour; strain while hot." *Br.*

Dose, one fluidounce (30 cc.).

INFUSUM SENNÆ. Br.

INFUSION OF SENNA

Senna Tea; Tisane de Séné, *Fr.;* Sennaaufguss, *G.*

"Senna Leaves, 100 *grammes;* Ginger, sliced, 5 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

We prefer the coriander of the U. S. P. 1870 to the ginger of the British. The infusion deposits, on exposure to the air, a yellowish precipitate, which is said to aggravate its griping tendency; it should, therefore, not be made in large quantities. It is customary to prescribe with it manna and some one of the saline cathartics, which increase its efficacy and render it less painful in its operation. (See *Infusum Sennæ Compositum.*) The cold infusion, especially if made by percolation from the coarsely powdered leaves, while probably not inferior in strength to that prepared with boiling water, is said to be less unpleasant to the taste.

Dose, one to two fluidounces (30–60 cc.).

Off. Prep.—Mistura Sennæ Composita, *Br.*

INFUSUM UVÆ URSI. Br.

INFUSION OF BEARBERRY

Tisane d'Uv Ursi, *Fr.;* Bärentraubenblätteraufguss, *G.*

"Bearberry Leaves, bruised, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

Dose, from one to two fluidounces (30–60 cc.), three or four times a day.

INJECTIO APOMORPHINÆ HYPODERMICA. Br.

HYPODERMIC INJECTION OF APOMORPHINE

Injection hypodermique d'Apomorphine, *Fr.;* Subcutane Apomorphineinspritzung, *G.;* Inyeccion Hipodermica de Cloruro de Apomorfina, *Sp.*

"Apomorphine Hydrochloride, 1 *gramme;* Diluted Hydrochloric Acid, 1 *millilitre;* Distilled Water, recently boiled and cooled, sufficient to produce 100 *millilitres.* Mix the Diluted Hydrochloric Acid with fifty millilitres of the Distilled Water; dissolve the Apomorphine Hydrochloride in the mixture, and add sufficient of the Distilled Water to produce the required volume. This injection should be recently prepared. 100 millilitres contain 1 gramme of Apomorphine Hydrochloride; 110 minims contain 1 grain." *Br.*

Dose, by subcutaneous injection, from two to eight minims (0.12–0.5 cc.).

INJECTIO COCAINÆ HYPODERMICA. Br.

HYPODERMIC INJECTION OF COCAINE

Injection Hypodermique de Cocaine, *Fr.;* Subcutane Cocaineinspritzung, *G.;* Inyeccion Hipodermica de Cloruro de Cocaina, *Sp.*

"Cocaine Hydrochloride, 5.00 *grammes;* Salicylic Acid, 0.15 *gramme;* Distilled Water, 100.0 *millilitres,* or *a sufficient quantity.* Boil the Distilled Water; add the Salicylic Acid; dissolve the Cocaine Hydrochloride in the solution when cool; add, if necessary, sufficient recently boiled and cooled Distilled Water to produce one hundred millilitres of the Injection. This Injection is of one-half the strength of the corresponding preparation of the British Pharmacopœia, 1898. It contains 5 grammes of Cocaine Hydrochloride in 100 millilitres; 110 minims contain 5 grains." *Br.*

Dose, by subcutaneous injection, from two to ten minims (0.12–0.6 cc.).

INJECTIO ERGOTÆ HYPODERMICA. Br.

HYPODERMIC INJECTION OF ERGOT

Hypodermic Injection of Ergotin; Injection hypodermique d'Ergot de Seigle, *Fr.;* Subcutane Mutterkorneinspritzung, *G.;* Inyeccion Hipodermica de Ergotina, *Sp*

"Extract of Ergot, 33 *grammes;* Phenol, 1 *gramme;* Distilled Water, recently boiled and cooled, sufficient to produce 100 *millilitres.* Dissolve. This Injection should be recently prepared. 100 millilitres contain 33 grammes of Extract of Ergot; 110 minims contain 33 grains." *Br.*

This preparation does not fully represent ergot. (See *Ergota.*)

Dose, by subcutaneous injection, from three to ten minims (0.2–0.6 cc.).

INJECTIO MORPHINÆ HYPODERMICA. Br.

HYPODERMIC INJECTION OF MORPHINE

Injection hypodermique de Morphine, *Fr.;* Subcutane Morphineinspritzung, *G.*

"Morphine Tartrate, 2.5 *grammes;* Distilled Water, recently boiled and cooled, sufficient to produce 100.0 *millilitres.* Dissolve. This Injection is of one-half the strength of the corresponding preparation of the British Pharmacopœia, 1898. It contains 2.5 grammes of Morphine Tartrate in 100 millilitres; 110 minims contain 2.5 grains." *Br.*

This solution is made from morphine tartrate in place of the morphine acetate formerly used; this is a great improvement, as the acetate is the most unstable of all morphine salts.

Dose, by subcutaneous injection, from five to ten minims (0.3–0.6 cc.).

INJECTIO STRYCHNINÆ HYPODERMICA. Br.

HYPODERMIC INJECTION OF STRYCHNINE

"Strychnine Hydrochloride, 0.75 *gramme;* Distilled Water, recently boiled and cooled, sufficient to produce 100.0 *millilitres.* Dissolve. This Injection contains 0.75 gramme of Strychnine Hydrochloride in 100 millilitres; 110 minims contain ¾ grain." *Br.*

Dose, by subcutaneous injection, five to ten minims (0.3–0.6 cc.).

INJECTIONES HYPODERMICÆ

HYPODERMIC INJECTIONS

Under this head are classed preparations which are recognized in the British Pharmacopœia for hypodermic application. These preparations are really of very little value, on account of their proneness to undergo decomposition, and the difficulty of maintaining their sterility, and are greatly inferior to the *hypodermic tablets* of various strengths which are now supplied by manufacturing pharmacists. These tablets should be made official, since their convenience, permanence, and accuracy in weight have caused them to come into universal use. The selection of the diluent is an important question; very finely powdered cane sugar has been employed, but is apt to produce local irritation and even abscesses. Sodium chloride has also been recommended, but the best diluent seems to be dried neutral sodium sulphate.

The recent practice of supplying hypodermic solutions and ampules removes some of the objections to this class of preparations (see *Ampullæ,* Part III.)

INULA. N. F.

INULA [Elecampane]

"Inula consists of the dried rhizome and roots of *Inula Helenium* Linné (Fam. *Compositæ*). Inula contains not more than 5 per cent. of its stem bases or more than 2 per cent. other foreign organic matter." *N. F.*

Elecampane, Aunee, Racine d'Aunee, Oeil de Cheval, *Fr;* Alantwurzel, *G;* Enula Campana, *It., Sp.*

Inula Helenium is a stout, perennial herb naturalized from Europe and growing along roadsides and damp pastures from Nova Scotia to North Carolina and westward as far as Missouri. From a large fleshy, fusiform branching rhizome there arises a stout branching stem which attains a height of about 6 feet and a rosette of radical leaves. The stem leaves are alternate, partly clasping, cordate-oblong, woolly on lower surface with unequally serrate margins. The flowers occur during summer in golden-yellow heads, each consisting of a naked receptacle bearing yellow, pistillate, ligulate florets along the margin and a central disk of yellow perfect, tubular florets. The exterior of the receptacle is covered by an imbricated involucre, the outer bracts of which are leaf-like. The fruit is a 4-5 ribbed achene. The rhizome and roots should be collected in August of the second year, cut into slices and carefully dried. Since the dried drug is particularly subject to insect attack, it should be preserved in air-tight containers to which a few drops of carbon tetrachloride may be added from time to time as an insecticide. Most of the drug used in the United States is imported from Europe through Rotterdam and Trieste.

Inula has at times been adulterated with stems and foreign roots. Commercial supplies are occasionally mouldy due to carelessness in drying. Most of the imported drug is consumed by proprietary medicine manufacturers.

Description and Physical Properties.—"*Unground Inula.*—Rhizome usually split into longitudinal or more or less oblique pieces to which may be attached one or more of the roots; up to 8 cm. long and 4 cm. in diameter; externally grayish brown to dark brown, longitudinally wrinkled with occasional buds or stem scars and surmounted at the crown by a portion of the over-ground stem; inner or cut surface somewhat concave, the edges in-curved with the overlapping bark, yellowish brown to grayish brown, longitudinally striate and more or less fibrous near the cambium zone; fracture short and horny; internally light brown and marked by numerous circular or elliptical oleoresin canals; roots cylindrical and tapering, frequently curved or irregularly curled, up to 13 cm. in length and 1.5 cm. in diameter. Odor aromatic; taste acrid, bitter and pungent.

"*Structure.*—A corky layer of from 4 to 7 rows of broad tabular cells; a cortex of numerous parenchyma cells containing inulin in irregular or fan-shaped masses and a number of large, intercellular secretion cavities containing oleoresin, arranged in nearly radial rows and forming interrupted circles; woody portion consisting chiefly of parenchyma, a number of tracheæ with simple pores or reticulate thickenings and associated occasionally with a few, strongly lignified wood fibers, and secretion cavities containing oleoresin similar to those occurring in the bark; parenchyma cells in the pith of the rhizome large, containing less inulin than the cells of the wood and bark and separated by large intercellular spaces.

"*Powdered Inula.*—Light brown; consisting chiefly of fragments of parenchyma containing inulin and small, irregular, separated masses of inulin; tracheæ with simple pores and reticulate thickenings associated occasionally with strongly lignified wood fibers; occasional reddish brown fragments of the walls of the oleoresin canals." *N. F.*

Constituents.—In 1804 Rose found in this root a peculiar carbohydrate which he called *alantin* which is now, however, generally known as *inulin* and which has since been found in many other plants. It differs from starch in that it is not decomposed by boiling water, and gives a yellowish instead of a blue color with iodin. Tanret has also found two related principles that he called *pseudo-inulin* and *inulenin*. According to Dragendorff the amount of inulin in the root gathered in the spring is about 19 per cent. but in the fall approaches 45 per cent. When distilled with water elecampane yields from 1 to 2 per cent. of a crystalline substance mixed with volatile oil. The crystalline portion known as *alant-camphor* appears to be a mixture of *alanto-lactone* (the anhydride of *alantic acid*) $C_{15}H_{20}O_2$, and isoalanto-lactone (*helenin*) C_6H_8O. The oily portion which has a peppermint-like odor is composed chiefly of *alantol,* $C_{10}H_{16}O$ (see Kallen, *B. Chem. G.*, 1873 and 1876).

Korab (*L. L.*, 1885, i, 672) states that helenin is a powerful antiseptic and bactericide, one part in ten thousand being sufficient to kill the ordinary bacteria. He lauds it as antiseptic in surgery and has given it with alleged success internally in *doses* of one-third to one grain (0.021–0.065 Gm.) in tubercular and catarrhal *diarrheas.* It is also stated by J. B. Obiol (*L. L.*, April, 1886) to be an efficient local remedy in the treatment of *diphtheria.* Bockenham (*Th. M.*, 1892, p. 145) asserts that helenin inhibits the growth of tubercle bacilli in the dilution of 1 in 10,000 and it has been employed by various writers in the treatment of *pulmonary tuberculosis* in *doses* of from one-sixth to five grains (0.01–0.32 Gm.).

Elecampane is tonic and gently stimulant, and was employed by the ancients in *amenorrhea* and diseases of women, also in *phthisis,* in various bronchial catarrhs, and in *skin affections,* in all of which diseases it was probably of no service.

Dose, twenty grains to one drachm (1.3–3.9 Gm.).

Off. Prep.—Pilula Antiperiodica, *N. F.;* Pilula Antiperiodica sine Aloe, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.*

IODOFORMUM. U. S., Br.

IODOFORM Iodof.

"Triiodomethane [CHI_3]." *U. S.* "Iodoform, CHI_3, may be obtained in the action of iodine on ethylic alcohol in the presence of solution of potassium carbonate." *Br.*

Triiodomethane, Formyltriiodide; Iodoforme, *Fr. Cod.* Iodure de formyle, *Fr.;* Jodoformium, *P. G.;* Jodoform, Carboneum jodatum, Trijodmethan, *G.;* Jodoformio, Trijodometano, *It.;* Yodoformo, *Sp.*

This compound, discovered by Sérullas about 1828, was later investigated chemically by J. B. Dumas. It was introduced as a remedy, about the year 1837, by R. M. Glover of London, and Bouchardat, of Paris, and was first adopted as official in the U. S. Pharmacopœia of 1870.

Various methods for the manufacture of iodoform by various processes that depend upon the interaction of iodine, alcohol, or acetone in the presence of an alkali or alkaline carbonate have been suggested. (See *U. S. D.,* 19th edition, p. 659.)

Iodoform is now made by electrolysis. An alkaline solution of sodium iodide is electrolyzed in the presence of alcohol; from the iodine which is liberated at the anode, iodoform is obtained by the following reaction:

$$CH_3.CH_2OH + 10I + H_2O = CHI_3 + CO_2 + 7HI$$

The hydriodic acid formed combines with the sodium hydroxide present, to make sodium iodate, which, with the carbon dioxide, forms the side products. The temperature is kept at about 70° C. during the reaction and a diaphragm is used. The yield of iodoform is about 70 per cent. M. Otto produces iodoform industrially, direct from alkaline iodides, as follows: 100 kg. of water, 300 kg. of alcohol, 10 kg. of sodium carbonate and 55 kg. of potassium iodide are heated to 50° C. in a suitable vessel, and a current of ozone is passed through the mixture. Iodoform is deposited and crystallizes in a pure condition on the sides of the vessel and throughout the fluid itself. The alcohol may be replaced by acetaldehyde, acetone, etc. (*Ap. Ztg.,* 1900, 166.)

The fact, noticed by Lieben in 1870, that many other compounds besides ethyl alcohol yield iodoform when treated with iodine and alkali, led Krämer (*B. Chem. G.,* 1880, p. 1000) to propose the iodoform formation as an exact quantitative test for the presence of acetone in methyl alcohol. This "iodoform test" is now used in testing the purity of methyl alcohol for use in the manufacture of aniline dye colors, as well as the purity of acetone itself. It is also used as a confirmatory test for the identification of ethyl alcohol in the absence of acetone or aldehyde. (See *Acetonum.*)

Description and Physical Properties.—"A fine lemon-yellow powder, or lustrous crystals. It has a peculiar, very penetrating, persistent odor. Iodoform is practically insoluble in water to which, however, it imparts its odor and taste. One Gm. of Iodoform is soluble in 60 cc. of alcohol, 80 cc. of glycerin, 10 cc. of chloroform, 7.5 cc. of ether, 2.8 cc. of carbon disulphide, and in 34 cc. of olive oil, at 25° C. One Gm. is soluble in about 16 cc. of boiling alcohol. Iodoform is slightly volatile even at ordinary temperatures, and distils slowly with the vapor of water.

"At about 115° C. it melts to a brown liquid, and at a higher temperature decomposes, emitting vapors of iodine. Its solutions are neutral to litmus paper. Ash: not more than 0.2 per cent. On drying 1 Gm. of Iodoform over sulphuric acid for twenty-four hours, it loses not more than 1 per cent. Shake about 2 Gm. of Iodoform with 5 cc. of distilled water for one minute, and filter: the filtrate is colorless and free from bitter taste (*soluble yellow coloring matter*), and does not affect the color of litmus paper (*acids or alkalies*).

"Preserve in well-closed containers, in a cool place, protected from light." *U. S.*

"Shining, lemon-yellow, small, hexagonal crystals, somewhat unctuous to the touch. Odor and taste persistent and disagreeable. Very slightly soluble in *water;* soluble in 100 parts of *alcohol* (90 per cent.), and in 8 parts of *ether,* the solutions being neutral to *litmus;* soluble also in *chloroform,* in *carbon disulphide,* in volatile oils, and in fixed oils; sparingly soluble in *benzene.* When warmed with *alcoholic solution of potassium hydroxide,* the resulting solution, acidified with *nitric acid,* becomes brown, and, when cold, changes to blue on the addition of *mucilage of starch.* 10 millilitres of *water* with which 1 gramme of Iodoform has been shaken are colorless and not bitter (absence of soluble yellow coloring matters and of picric acid), and yield no *reactions* for iodides. No appreciable ash." *Br.*

Iodoform is a volatile substance, soft to the touch, and totally devoid of corrosive properties. With potassium hydroxide in solution, it is decomposed, yielding potassium formate and iodide. Hence these two principles are incompatible in prescriptions. The specific gravity of iodoform, about which there has been a controversy, was determined by J. Percy Remington to be 4.000; the specific gravity of 2.000, as given in the U. S. P. 1890, was undoubtedly due to the operator taking the specific gravity of iodoform in water, and when this is done it is practically impossible to free the crystals from admixed air; the result was reached by using a saturated solution of iodoform in pure kerosene as the liquid, and by a simple calculation obtaining the equivalent in water. Iodoform is sometimes met with in commerce adulterated with water; Vulpius (*Ph. Cb.*, 1894) on examination detected 13 per cent. in one specimen.

Uses.—When applied to a mucous membrane, iodoform exercises a marked anesthetic action. Although of itself it is almost free of antibacterial properties, when brought in contact with the bodily secretions it gradually liberates some compound—perhaps free iodine—which is actively antiseptic. The experiments of Gosselin of Caen indicate that it is especially inimical to the tubercle bacillus. If taken internally it is gradually absorbed and is partially decomposed, liberating inorganic iodine; a part, however, appears to circulate unchanged. When exhibited in large doses, to the lower animals, it produces narcotic effects, and two stages in its operation have been noticed; the first is marked with more or less prostration, with symptoms of intoxication, the animal tottering, inclining to one side with the head falling, with loss of appetite, but without vomiting. The next day, unless a very large dose has been given complete recovery takes place. A still larger dose induces the second stage, characterized by a remarkably intense excitation, with anxious breathing, strong and short pulse, a true opisthotonos, sometimes very striking, and convulsive movements of the paws, especially the hinder ones. After death fatty degeneration of the heart, liver, and kidneys may be found.

The chief value of iodoform in practical medicine is as an external application. It has long been used in cases of painful *ulcers* and as an antiseptic dressing to *wounds.* The testimony from surgeons is so strong that it is difficult to avoid believing that it is one of the most certain remedies of the class. Its beneficial effects seem to be due partly to absorption of secretions—making an unfavorable soil for bacterial growth—partly to the antiseptic effect of its decomposition products and partly to its local anesthetic effect. Some believe that it exerts some specific influence on cell growth that encourages healing. It is also of much value for its anesthetic powers in *laryngeal tuberculosis* and in *internal hemorrhoids;* in the latter condition it is best applied in the form of a suppository, which may contain from five to ten grains (0.3–0.6 Gm.).

The local application of iodoform in surgical *tuberculosis* has received the highest commendation from numerous surgeons. In the treatment of *tuberculous abscesses,* in tuberculous *empyema,* in *tubercular joints,* in non-suppurating *tuberculous glands,* and even in *tuberculous peritonitis,* numerous cures have been claimed. The manner of application varies with different surgeons. Verneuil, who has had an enormous experience, prefers in the treatment of abscesses and of tuberculous glands, and in most other cases, the injection of a 5 per cent. ether solution. Others prefer glycerin as a vehicle, especially in empyema cases, while others, especially in *peritonitis,* dust the dry powder over the surface which has been laid open.

Internally, iodoform has been used in *syphilis, goiter,* and *phthisis,* originally with the idea that it would act as an iodide. As pointed out above, however, it is only partly broken up in the system and its action therefore is quite different from the inorganic iodides. Whether it is of any real value as internal remedy is at present open to doubt.

Iodoform gauze may be made by saturating surgical gauze with a 5 per cent. solution of iodoform in ether, and allowing it to dry at room temperature.

One of the principal obstacles to its employment is the odor, which, to some patients, is unbearable. Many methods of disguising the odor have been recommended, but in our experience the large quantity required of each deodorizing agent would preclude its employment. Tannin has been recommended, but, as this operates by decomposing the iodoform, it is not to be thought of in this connection. Probably the best class of substances to use are the volatile oils, such as anise, peppermint, fennel, bergamot, almond, coumarin, etc. Balsam of Peru acts by forming a compound, and the aim should be not to destroy the odor, but so to modify it as to remove its objectionable features. Olive oil saturated with camphor is said to dissolve 6 per cent. of iodoform, and is preferred by some surgeons.

Toxicology.—The free use of iodoform as a surgical antiseptic has led to many cases of poisoning. In the most characteristic and severe cases the phenomena of iodoform poisoning resemble somewhat those of meningitis; they are headache, somnolence, deepening into stupor, contracted, motionless pupils, abnormal quiet or restlessness ending in active delirium, with, however, a normal temperature and an exceedingly rapid pulse. Burlureaux affirms that if a piece of silver be placed in the mouth of a person suffering from iodoform poisoning, immediately the taste of garlic will be perceived, and if some of the saliva be mixed with calomel, a canary-yellow precipitate of mercurial iodide will be obtained. The most that such a test can accomplish is to show that the patient is under the influence of some compound of iodine. In cases of this character death almost always follows, although the symptoms may have developed abruptly and the dressing has at once been removed. In other cases the principal symptoms are general malaise and depression, faintness, headache, loss of appetite, and a persistent iodoform taste in the mouth. In some cases there is a slight temporary increase of temperature. Mental depression or excitement is especially noticed. Finally the pulse becomes accelerated, soft, and feeble; in some cases the pulse is very rapid—from 150 to 180—while the temperature remains normal or is only slightly elevated. It is asserted by Samter and Retzlaff (*T. G.*, 1889) that potassium bromide is an antidote in iodoform poisoning, its antidotal powers being due to the fact that it exceeds all other salts in its power of dissolving iodine compounds.

Langenstein has attributed a fatal result to the local application of one drachm of the powder. It is advisable that in ordinary cases not more than thirty grains (2 Gm.) be employed at once as a wound dressing, although in cases of tuberculosis the surgeon is warranted in taking the risk of larger amounts. Verneuil sometimes injects at one sitting 75 grains of the iodoform.

Dose, one to five grains (0.065–0.32 Gm.).

Off. Prep.—Suppositoria Iodoformi, *Br.;* Unguentum Iodoformi, *U. S., Br.;* Glycerogelatinum Iodoformi, *N. F.*

IODUM. U. S., Br.

IODINE

"Iodine contains not less than 99.5 per cent. of I." *U. S.* "Iodine may be obtained from the ashes of seaweeds and from native iodides and iodates. It contains not less than 99 per cent. of pure iodine, I." *Br.*

Iodinium, *U. S.* 1870; Iode sublimé, *Fr. Cod.;* Iode, *Fr.;* Jodum, *P. G.;* Jod, *G.;* Jodo, *It.;* Yodo, *Sp.*

Iodine is a non-metallic element, discovered in 1812 by Courtois, a soda manufacturer of Paris. It exists in certain marine algæ, particularly the kelps and rockweeds, which have long been its most abundant natural source. It has been reported in some fresh water plants, among which are the water cress, brooklime, and fine-leaved water hemlock; also in various terrestrial plants. Traces are present in the water of springs and rivers in many parts of the world. Iodine also occurs in the animal kingdom, as in the sponge, the oyster, crude cod liver oil, and the thyroid gland of mammals. It is found as silver iodide in a rare Mexican mineral, in a zinc ore of Silesia, in native sodium nitrate, and in some kinds of rock salt. It is now obtained commercially from native sodium nitrate, or Chili saltpeter, with which it occurs as sodium iodate. It was first discovered in the United States in the water of the Congress Spring, at Saratoga, by William Usher. It was detected in the Kanawha saline waters by Emmet, and it occurs in the bittern of the salt works of Western Pennsylvania, in the amount of about eight grains to the gallon. In sea weeds the iodine exists probably in the state of sodium iodide.

In different countries sea weeds are burned for the sake of their ashes, the product being a dark-colored fused mass called *kelp-varec* or *barilla* according to the locality where it is produced. This substance, besides sodium carbonate and iodide, contains more or less sodium chloride, potassium chloride, sodium sulphate, etc. The deep sea fuci contain the most iodine, and when these are burned at a low temperature for fuel, as is the case in the island of Guernsey, their ashes furnish more iodine than does ordinary kelp. (Graham.) According to Geo. Kemp, the laminarian species, especially *Laminaria digitata, L. saccharina,* and *L. bulbosa,* which are deep water sea weeds, and contain more potassium than sodium, are particularly rich in iodine.

In Japan the sea weeds most used are species of *Ecklonia* and *Sargassum* which contain about 0.14 per cent. iodine. In France certain species of *Fucus* are employed. These are collected by hand and dried by primitive methods. The dried weeds are burned in covered trenches. The ash sometimes contains over 5 per cent. of iodine but usually runs below 1 per cent. The iodine is recovered by the copper iodide method employed for separating it from Chili saltpeter as described below. On the California coast in America during the World War, sea weeds were largely used for destructive distillation for acetone, acetic acid, etc. The ash was used for the potassium salts and iodine.

All sea weeds do not contain enough iodine to make the industry profitable. Van Itallie has shown that *Zoster Marina* only contains 0.0019 per cent. of total iodine.

Iodine has been reported in waters of certain wells. In Java there is one which contains 120 parts of sodium iodide to the million. This has been recovered by the cuprous iodide method.

In Great Britain, chiefly at Glasgow, the ash of the kelp is lixiviated with water, in which about half dissolves. The solution is concentrated until a pellicle forms and allowed to cool, whereby nearly all the salts, except sodium iodide, are separated, they being less solube than the iodide. The remaining liquor, which is dense and dark-colored, is made very sour by sulphuric acid, which causes the evolution of carbon dioxide, hydrogen sulphide and sulphurous acid, and the deposition of sulphur. The amount of sulphur recovered in this way is more than 100 tons annually. The liquor is then introduced into a leaden still, and distilled with manganese dioxide into a series of glass receivers, inserted into one another, in which the iodine is condensed. In this process the sodium iodide is decomposed, and the iodine evolved according to the reaction:

$$2NaI + 2H_2SO_4 + MnO_2 = MnSO_4 + Na_2SO_4 + 2H_2O + I_2$$

which leaves as residue manganous sulphate and sodium sulphate. In this treatment much care is needed to avoid the liberation of chlorine from chlorides present, which will form volatile iodine trichloride and so occasion loss. This can be avoided by heating the acidified iodide solution with ferric chloride, when iodine is liberated according to the reaction:

$$2NaI + 2FeCl_3 = 2FeCl_2 + 2NaCl + I_2$$

The methods for the separation of the iodine from its combinations in the mother liquors as practised in South America may be divided essentially into three classes. (1) The mother liquors after the crystallization of the saltpeter without further concentration are treated with a solution of sodium sulphite of strength exactly corresponding to the amount of iodine present, for if an excess be used the iodine will be converted into hydriodic acid; the iodine is liberated according to the reaction:

$$2NaIO_3 + 4HNaSO_3 + SO_2 = Na_2SO_4 + 4HNaSO_4 + I_2$$

the iodine thus separated from the sodium iodate is filtered through linen cloth, washed, pressed, and sublimed. (2) The mother liquors are treated with sodium sulphite or bisulphite until the precipitated iodine is converted into HI, and this is precipitated as cuprous iodide by a solution of copper sulphate and sodium sulphite. (3) The concentration of iodine is increased by fractional evaporation and crystallization of the mother liquors, and then, after adding the calculated amount of sodium bisulphite, the iodine is distilled off from the acidified liquor.

The methods formerly practised for obtaining iodine from sea weeds were accompanied with great loss. A notable improvement over the old kelp processes are the "char" and "wet" processes of E. C. C. Stanford (*J. Soc. Chem. Ind.*, 1885, p. 518).

Iodine is purified by sublimation in containers of porcelain, earthenware or glass, taking care to reject any white crystals which may appear in the first portion which comes over, as these consist of cyanogen iodide. Moisture which has sometimes been reported to the extent of 15 or 20 per cent. and which may be suspected if the iodine adheres to the inside of the container in which it is kept, may be readily detected by assaying for the iodine content and also by the fact that such iodine will not make a transparent solution with chloroform.

Description and Physical Properties.—"Heavy, bluish-black, brittle, rhombic plates, having a metallic luster and a distinctive odor. One Gm. of Iodine is soluble in 2950 cc. of water, 12.5 cc. of alcohol, 80 cc. of glycerin, and in 4 cc. of carbon disulphide, at 25° C. It is freely soluble in chloroform, carbon tetrachloride, and in ether, and is dissolved by aqueous solutions of iodides. Its solution in alcohol and in an aqueous solution of potassium iodide has a reddish-brown color. Its solution (1 in 1000) in chloroform, carbon tetrachloride, and in carbon disulphide is of a violet color.

"Specific gravity: about 4.66 at 17° C. Iodine imparts a deep brown, evanescent stain to the skin and slowly destroys vegetable colors. Iodine volatilizes slowly at ordinary temperatures. When heated to about 114° C., it fuses and gradually vaporizes in the form of violet fumes. Add starch T.S. to a saturated aqueous solution of Iodine: a blue color is produced. On boiling the mixture the color vanishes but reappears as it cools, unless it has been subjected to long continued boiling.

"When volatilized, Iodine leaves not more than 0.05 per cent. of residue. Triturate 0.5 Gm. of finely powdered Iodine with 20 cc. of distilled water, and filter the solution. To one-half of the filtrate carefully add tenth-normal sodium thiosulphate until the solution is just decolorized. Then add a few drops of ferrous sulphate T.S. and subsequently a little sodium hydroxide T.S., and heat the mixture gently: the liquid does not become blue upon the addition of a slight excess of hydrochloric acid (*cyanogen*). To the other half of the aqueous filtrate, add, drop by drop, sulphurous acid (free from chloride), previously diluted with several volumes of distilled water, until the iodine color just disappears. Add 5 cc. of ammonia T.S., and follow with 5 cc. of silver nitrate T.S. in small portions. Filter, and acidulate the filtrate with nitric acid: the resulting turbidity is not greater than that produced in a control test made with the same quantities of reagents to which 0.1 cc. of fiftieth-normal hydrochloric acid has been added, but omitting the sulphurous acid (*chloride or bromide*).

"**Assay.**—Place about 0.5 Gm. of powdered Iodine in a tared weighing-bottle, stopper, weigh accurately, and add 1 Gm. of potassium iodide dissolved in 5 cc. of distilled water. Dilute this solution with distilled water to about 50 cc., and titrate with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.01269 Gm. of I.

"Preserve in glass-stoppered bottles, in a cool place." *U. S.*

"In rhombic prisms or octahedrons of the trimetric system, of dark color, and metallic lustre. Characteristic odor. Yields, when gently heated, a violet-colored vapor. Very slightly soluble in *water*, more soluble in *alcohol* (90 per cent.); readily soluble in *solution of potassium iodide*, in *ether*, and in *carbon disulphide*. *Mucilage of starch* colors the aqueous solution deep blue. Sublimes without appreciable residue, the first portion sublimed not including any slender colorless prisms emitting a pungent odor (absence of iodine cyanide). A solution of Iodine in *chloroform* is perfectly clear (absence of moisture). 0.5 gramme, dissolved in 50 millilitres of *water* containing 1 gramme of *potassium iodide*, requires for decolorisation not less than 39 millilitres of *N/10 solution of sodium thiosulphate*." *Br.*

In chemical characters iodine resembles chlorine, but its affinities are weaker. It combines with most of the non-metallic and nearly all the metallic elements, forming a class of compounds called iodides. Some of these are official, as the iron, mercury, lead, potassium and sodium iodides. It forms with oxygen one oxide, *iodic oxide*, I_2O_5, and two acids, *iodic* and *periodic*, and with hydrogen an acid called *hydriodic acid* which is official as the diluted acid and in the syrup.

Tests.—Iodine, in most cases, may be recognized by its characteristic purple vapor; but, where this cannot be made evident it is detected by starch, which produces with it a deep-blue color. Bargu and Starling (*P. J.*, 1914, xcii, 146) have called attention to the fact that other organic compounds besides starch have the property of showing a blue color with iodine, and have published a list of more than sixty such substances.

The detection and estimation of iodine in small amounts in combinations containing organic matter may be accomplished by methods analogous to the one used for the estimation of iodine in thyroid glands, which see.

One of the most delicate reactions yet devised for the qualitative detection of iodine is that discovered by Ciusa and Terni (*Gaz. Ch. It.*, 43, ii, 86) in which a solution composed of 10 grammes of mercuric nitrate, 50 cc. of distilled water, 5 cc. of nitric acid, and 60 cc. of stronger ammonia water, is used. One cc. of the reagent is added to 25 cc. of the solution to be tested, chlorides give a white precipitate and bromides a yellow precipitate, neither of which are distinctive or interfere in any way. If iodides are present even in minute amounts an orange or brownish color or precipitate is produced.

It has been long known that when a mixture of iodine and starch in water is subjected to heat the blue color disappears, and that, if the heat be not too long continued, so as to volatilize the iodine or convert it into hydriodic acid, the color will return on the cooling of the liquid. Various explanations have been given of this curious fact by Personne and others none of which is entirely satisfactory.

Iodine was at one time occasionally adulterated with mineral coal, charcoal, plumbago, and black manganese oxide. These were easily detected by their fixed nature, while pure iodine is wholly volatilized by heat. Such adulterations have long since been discontinued.

Uses.—Iodine was first employed as a medicine in 1819, by Coindet, of Geneva. Iodine, whether taken into the stomach in the form of the element or as one of the salts of hydriodic acid, is absorbed readily and circulates in the blood chiefly in the form of an iodide, although it is probable that a small amount of the iodine is absorbed in the form of a protein compound. Although it can be found in a number of other secretions it is eliminated practically entirely through the kidneys. Herzfeld and Elin (*B. M. J.*, October 5, 1912) state that iodine can be demonstrated in the urine after painting the skin with the tincture, but Wetzel and Sollmann reached the conclusion that appreciable amounts could not be absorbed through the skin either from the tincture or ointment. As iodine circulates as an iodide the effects are the same whether it be given in the elemental state or as a salt of hydriodic acid. Although Macht (*J. H. H. B.*, 1914, xxv) states that the iodine ion is a powerful stimulant when perfused through isolated heart or blood vessels, when introduced into the circulation of the intact mammal it has practically no influence. The common belief that the iodides dilate the arterioles is absolutely without reasonable foundation. (See Capps, *J. A. M. A.*, 1912, lix, 1350.) The only important physiological effect of iodine is its influence upon metabolism. This action is not clearly understood although it is evident that the continued use of this drug increases the rapidity of nitrogenous breakdown; according to Chistoni (*A. I. P. T.*, xxi, p. 339), the elimination of uric acid and other purin bases is increased disproportionately. Grabfield and Prentiss (*J. P. Ex. T.*, 1925, xxv, 411) find that the iodides cause a marked increase of nitrogen in the urine which they interpret to mean an increased katabolism. There were differences in the effects of the various salts. It appears to have some influence upon glands—beyond its action as a salt—not only increasing the quantity but changing the character of their secretions, especially diminishing excessive viscidity. In those morbid states attended with fibrinous exudation, the iodides have a similar effect on the exudate. There is a belief among many practitioners that it will even cause the absorption of organized fibroid tissue; this, however, is not well substantiated. In *syphilis* and *tuberculosis* there is often a very rapid breaking down of the characteristic local lesions. This effect seems to be due to an increased autolysis but whether a specific reaction in certain diseases or merely the manifestations of general effect in the *locum minoris resistentiæ* is uncertain.

In *syphilis* iodine is without a direct curative property, that is, it has no effect upon the growth of the specific micro-organism. Because, however, of its power of causing the breakdown of syphilitic lesions it is a remedy of utmost importance in the tertiary stage, not merely because it lessens the extent of the sequelæ of the luetic affection, but because it drives the spirochetes from their lurking places into the general circulation where they may be reached by direct antisyphilitics. In the early stages iodine is useful because it forms a freely soluble compound with the mercury and thereby tends to prevent the deposit of the metal in internal organs.

Its effect in tuberculosis is analogous to that in *syphilis*, but whether this action in hastening the breakdown of the lesions will be beneficial or otherwise to the tuberculous patient, depends upon the location and character of the infection. Thus in *phthisis* generally the most favorable result is the walling off and ultimate calcification of the local lesion and the iodides by softening the infected area may not only delay the whole process, but may even cause a dissemination of the micro-organisms throughout the lung. On the other hand, in inoperable *lymphadenitis* it will hasten suppuration and may lead to the extrusion of the bacilli. In a somewhat similar way iodine may be useful in *bony tuberculosis.*

In *leprosy* it apparently has a somewhat similar type of action, although less marked. It has also a potent effect in *actinomycosis* and even appears to have a direct curative effect. In inflammations of either the serous or mucous membranes attended with fibrinous exudates or viscid secretions, as *pleurisy, pericarditis,* or *bronchitis,* iodine is often of great value because of its liquefying action. In *bronchitic asthma,* while it has no direct influence upon the paroxysms, by its effect in increasing and liquefying the bronchial secretions it proves itself one of the most frequently serviceable drugs we possess. In chronic inflammatory conditions accompanied with a formation of fibroid connective tissue, as in *interstitial nephritis, arteriosclerosis,* and fibroid degenerations of the nervous centers, it is widely employed, not, however, because it is of proven utility but in a kind of despairing hope that it may produce some amelioration of the condition. In degenerative changes occurring as the result of *syphilis,* however, such as *locomotor ataxia,* it often appears to have some beneficial effect. It is habitually employed in *chronic rheumatism* which it probably influences through its action upon metabolism. It has long been known that iodine is a normal constituent of the thyroid gland. The present evidence is very strong that a supply of iodine is essential for the proper function of this gland. The studies of Marine and Kimball (*J. A. M. A.,* 1920, lxxv, 674) have shown that the exhibition of small amounts of iodides will prevent the occurrence of the simple *goiter* which is endemic in certain districts. The experiments of Reid Hunt (*J. P. Ex. T.,* 1910, ii, 15) suggest that large amounts of iodine excite the functional activity of the thyroid, and various authors have therefore held it to be contra-indicated in the so-called *exophthalmic goiter.* This view was vigorously attacked by Plummer (*J. A. M. A.,* 1923, lxxx, p. 1955) who recommended the use of massive doses of the tincture. Starr (*A. I. M.,* 1924, xxxiv, p. 355) reports that in 80 per cent. of cases of all types of Graves's disease iodine will cause a prompt, although in many instances only temporary, remission of symptoms. Potassium iodide forms in the body a freely soluble compound with either mercury or lead, and is therefore frequently used in the treatment of *lead poisoning* or in *mercurial* cachexia to hasten the elimination of the metal; it must be remembered, however, that by causing the solution of deposits it may cause an exacerbation of symptoms.

Elemental iodine has two important therapeutic properties which its salts do not share. These are as a local irritant and as a germicide. As a counter-irritant it is used especially in various forms of *arthritis,* notably those due to trauma, but is also of service in *bronchitis* or *glandular enlargement.* Its action in these conditions may be aided by absorption through the skin and consequent systemic effects of the drug. It is also employed for its local irritant effect as an injection for the cure of local effusions, as *ovarian dropsy, hydrocele,* and *ganglion.*

ANTISEPTIC USES.—Elemental iodine is a powerful germicide. A one to 1000 solution is sufficient to kill most vegetative forms of bacteria including the staphylococci, tubercle bacillus and the typhoid bacillus (Peck, *P. J.,* 1911, lxxxvii, 450). Maben and White (*C. D.,* 1915, 144) give it a phenol coefficient of 4. There are two qualities which have rendered it of peculiar value as a surgical disinfectant. In the studies of Lambert (*J. Ex. M.,* December, 1916), which were made with human connective tissue cells on artificial culture media, iodine was the only one of the germicides tested that would kill bacteria in strengths that were not injurious to the tissue cells. The second valuable property is its power of penetrating the skin. Turner and Catto (*L. L.,* 1911) found that after the external application of a 3 per cent. solution of iodine the whole thickness of the skin was sterile. Bovee (*Am. J. Obstetrics,* July, 1911) found that the application of 5 per cent. of the U. S. P. tincture of iodine completely sterilized the surface of the skin within 15 minutes but that hairy regions, as the pubes, required 50 per cent. of this tincture (representing 3 per cent. of iodine) for complete sterilization.

In 1908 Grossich (*Cb. Chir.,* 1908, p. 1285) suggested painting of the skin with a 10 per cent. tincture of iodine as a means of sterilizing the site of operation. According to his claims no previous washing was necessary because of the penetrating power of the iodine. The method has been widely followed and with more or less modification is now almost universally employed by surgeons. Probably the most commonly employed routine in this country is to cleanse the skin with liniment of soft soap, thoroughly wash away the soap with alcohol, and then paint with the official tincture of iodine. Among the various solutions which have been suggested instead of the tincture, probably the most widely employed is that in benzin originally suggested by Heussner. This author used a solution containing one part of iodine, 750 of benzin, and 250 of liquid petrolatum. Reich-Brutzkus (*W. K. W.,* 1913) uses a solution containing 3 parts of iodine, 10 parts of alcohol, and 90 of chloroform. From its use in sterilizing the seat of operation iodine has rapidly come into popularity as a surgical disinfectant for a wide variety of purposes. Woodbury (*N. Y. M. J.,* 1912, xcvi, p. 101) recommends it to sterilize the surgeon's hands, instruments, sutures, and dressings. The application of a 3 per cent. solution of iodine to recent wounds is probably the most efficient emergency treatment we have to protect against infection by the pus producing organisms. A number of authors have attributed most brilliant results in *erysipelas* to painting the affected part with tincture of iodine. (See Lammerhirt, *B. K. W.,* 1921, lviii, 1389.) In proper dilutions it is used in various infections of mucous membranes as *conjunctivitis, urethritis, diphtheria, cystitis,* etc. More recently the vapors of nascent iodine have been employed in various local infections. These may be generated by heating iodoform. It is also used locally in various skin diseases both for its antiseptic and alterative effect.

Méhu's method of making *iodized cotton* is as follows: Finely divided iodine (5 to 10 parts) is sprinkled between layers of loose cotton (100 parts) introduced into a tall glass vessel, and the latter placed horizontally on a water or sand bath. As soon as vapors of iodine are seen to rise, and the air has been expelled from the vessel, the latter is tightly stoppered. On continuing to apply a moderate and uniform heat, the iodine vapors penetrate the cotton, and color it yellow. After about two hours, the cotton will have assumed the color of burnt coffee, and the operation is finished. Cotton iodized in other ways, as by immersion in concentrated solutions of iodine in ether or carbon disulphide, retains merely traces of iodine. (*N. R.*, April, 1867.)

Iodine, in the state of vapor, has been employed by inhalation, in the treatment of *phthisis* and *chronic bronchitis,* but has failed to fulfil expectations, and is at present very rarely practised. For details as to methods, the reader is referred to the 14th edition of the *U. S. D.*

Under the names of *iodagol* and *iodéol* suspensions asserted to contain 25 per cent. and 20 per cent., respectively, of *colloidal iodine* have been introduced for local applications.

As an internal remedy one of the salts of hydriodic acid is usually preferred as being less prone to disturb digestion although the compound solution is frequently of service. Although less irritant than iodine the iodides are still very prone to upset the stomach. This fact has led to the official recognition of calioben, and the preparation of a host of compounds many of which are noticed in Part II of this work.

In an overdose elemental iodine acts as an irritant poison. From four to six grains (0.26–0.4 Gm.), in man, cause a sense of constriction in the throat, sickness and pain at the stomach, and at length vomiting and colic. Even in medicinal doses it sometimes causes alarming symptoms such as fever, restlessness, disturbed sleep, palpitations, excessive thirst, acute pain in the stomach, vomiting and purging, violent cramps, frequent pulse, and, finally, progressive emaciation if the medicine be not discontinued. Such violent symptoms are, however, very rare, but where iodine or potassium iodide is given freely a mild *iodism* is not unfrequent. It is usually characterized by pain or heaviness in the region of the frontal sinuses, with or without coryza; in some instances soreness of the mucous membrane of the mouth and throat, or a mild ptyalism, is the prominent symptom, or a papular eruption may be the first manifestation of the constitutional action of the remedy. Various skin lesions of all degrees of severity have followed the internal use of iodides in sensitive persons. Absorption of the mammæ and wasting of the testicles have been reported as caused by the long-continued use of the drug, but such results are extremely rare.

In cases of acute poisoning by iodine, the stomach must be evacuated, and drinks administered containing an amylaceous substance, such as flour, starch, or arrow-root.

Dose, of iodine, one-twelfth to one grain (0.005–0.065 Gm.) well diluted.

Off. Prep.—Liquor Iodi Compositus, *U. S.;* Tinctura Iodi, *U. S.* (*Br.*)*;* Tinctura Iodi Fortis, *Br.;* Tinctura Iodi Mitis, *Br.;* Unguentum Iodi, *U. S., Br.;* Ampullæ Iodi, *N. F.;* Phenol Iodatum, *N. F.;* Dentilinimentum Aconiti et Iodi Compositus, *N. F.;* Liquor Iodi et Zinci Phenolsulphonatis, *N. F.;* Petroxolinum Iodi, *N. F.;* Petroxolinum Iodi Dilutum, *N. F.;* Phenolum Iodatum, *N. F.;* Syrupus Iodotannicus, *N. F.;* Tinctura Iodi Fortior, *N. F.*

IPECACUANHA. U. S. (Br.)

IPECAC Ipecac. [Ipecacuanhæ radix P. I.]

"Ipecac is the dried rhizome and root of *Cephaelis Ipecacuanha* (Brotero) A. Richard, known in commerce as Rio Ipecac (Brazilian Ipecac), or of *Cephaelis acuminata* Karsten, known in commerce as Cartagena or Panama Ipecac (Fam. *Rubiaceæ*).

"Ipecac yields not less than 1.75 per cent. of the ether-soluble alkaloids of Ipecac and contains not more than 5 per cent. of its overground stems, or more than 2 per cent. of other foreign organic matter." *U. S.* "Ipecacuanha Root is the dried root of Psychotria Ipecacuanha, *Stokes.*" *Br.*

Ipecacuanhæ Radix, *Br.;* Ipecacuanha Root; Poaya, *Braz.;* Ipécacuanha annelé, *Fr. Cod.;* Racine brésilienne, *Fr.;* Radix Ipecacuanhæ, *P. G.;* Ruhrwurzel, Brechwurzel, Ipecacuanha, *G.;* Ipecacuana, *It.;* Ipecacuana (Raiz de), *Sp.*

Ipecac has been official in every edition of the U. S. P. since 1820. Martius in his *Flora Brasiliensis* states that the South American aborigines were acquainted with the medicinal properties of the plant and Purchas, in *The Pilgrimes,* published in London in 1625, cites a description of Brazilian ipecac, believed to have been written by M. Tristaon, in which its uses by the Indians are discussed. Piso and Marcgraf, in *Historia Naturalis Braziliæ* (Amsterdam, 1648) give a good account of a brown and a white ipecac, the illustration of the brown variety closely agreeing with the true ipecac, according to Merat (*Dict. Univ. de Mat. Méd.,* Paris, 1846). The root was first introduced as a drug into Europe by Le Gras in 1672, but did not begin to become popular there until toward the close of the eighteenth century.

The term *"ipecacuanha"* had been applied by the aborigines of Brazil to various roots having emetic properties and, as the use of ipecac in Europe began to call for larger importations, many other emetic roots from South America were substituted for it. In this way the characteristics of the plant furnishing the genuine article became almost forgotten and earlier diagnoses by botanists were frequently based upon plant materials other than the genuine ipecac. No less an authority than Linnæus thought the plant now known as *Ionidium Ipecacuanha* St. Hil. to be the source of true ipecac and named it *Viola Ipecacuanha.* In 1781, Linnæus filius, believing the illustration by Piso of the true ipecac plant to be identical with a Peruvian emetic plant sent him with a description by Mutis, named it *Psychotria emetica.* Dr. Gomez collected some authentic plants in Brazil in 1800, corrected this error in his memoir published in Lisbon the following year and re-established the nearly forgotten characteristics of the true botanical source. He gave some of his specimens to Brotero who describes the species under the name of *Callicocca Ipecacuanha* in the *Transactions of the Linnean Society,* 1802. In 1813, Tussac renamed the same species which Brotero described, *Cephaelis Ipecacuanha* and distinguished it from *Psychotria emetica* Mutis. Achille Richard, in his *Natural and Medical History of Different Ipecac Species of Commerce* (Paris, 1820), again mentioned the differences between these two species. While Tussac preceded Richard in placing the authentic plant in the genus *Cephaelis,* his work did not become as well known as that of Richard and so some systematists give the credit of authorship to Richard.

There exists considerable difference of opinion as to which of the generic terms should be definitely adopted as the standardized generic name of the true ipecac species. Chief among those listed in the literature as synonyms are the following: *Uragoga,* L. 1731, *Psychotria,* L. 1759, *Evea,* Aublet 1775, *Tapogomea,* Aublet 1775, *Cephaelis,* Swartz 1788, and *Callicocca,* Schreber 1789. According to the rule of priority in starting nomenclature with 1753, *Uragoga* would be correct as the proper designation of the Ipecac genus and *Uragoga Ipecacuanha* Baillon (*Nat. Hist. Pl.,* London, 1881) the proper designation of the species; but *Cephaelis* of Swartz is alone listed in the *Nomina Conservanda* of the last International Congress of Botanists, evidently because it had received the greatest publicity and use and is, accordingly, recognized in the U. S. P.

Cephaelis Ipecacuanha is a low, straggling shrub indigenous to Brazil but also found growing in Colombia where it flourishes in deep, moist humous soils of forests. Its underground portion consists of a somewhat branched root system, the root being annulated and wiry, and a submerged portion of the stem which has generally been gathered with the roots as the drug of commerce. The latter arches upward, becoming green and angular above ground and attaining a length of a foot or less. It bears a few opposite, petiolate, stipulate, obovate and entire leaves and heads of small, white flowers, the corollas of which are funnel-shaped. The fruits occur as clusters of dark purple berries, each containing two plano-convex seeds.

The U. S. P. recognizes two sorts of ipecac which it ascribes to different botanical species although Humboldt regarded the differences between the plants as merely geographic variations. The *Rio, or Brazilian, Ipecac* is from the *Cephælis Ipecacuanha.* It grows in moist, dense and shady woods in Brazil and Bolivia. It is said to be most abundant within the limits of the eighth and twenty-second degrees of south latitude. *Cartagena Ipecac* (also called *Savanilla* and *Panama Ipecac*) is from the *C. acuminata.* It grows in the moist forests of United States of Colombia. The roots are gathered from January to late March by the natives who seize all the stems of a clump, loosen them from the soil and then, by thrusting a pointed stick under the roots, tear up the whole mass. The roots are then freed from adhering soil and packed in bags or bales of hide in which they are stored until purchased by traders; Rio Ipecac comes chiefly from the interior provinces of Matto-Grosso and Minas Geraes and is shipped to the U. S. A. mainly from Rio de Janeiro, Bahia and Pernambuco. Cartagena Ipecac is exported to this country from Cartagena and Savanilla, Colombia. It differs from the Rio variety in being thicker, grayish-brown or gray, and in showing less pronounced annulations.

Attempts have been made by the British in 1866 and 1872 to cultivate ipecac in India from root cuttings sent from Brazil but without commercial success. In 1886, it was found that ipecac flourished in the Straits Settlements. The *Johore,* or *Indian, Ipecac* is obtained there. Some success has recently been attained in growing the plant in the State of Selangor, near Singapore, from which considerable roots have been shipped to England.

Substitutes and Adulterants.—The chief adulterant of ipecac is the aerial stem of the same plant. The submerged portion of the stem from which roots emanate and which might be called the rhizome has been asserted by Viehoever and Ewing (*J. A. Ph. A.,* 1921, p. 766) to contain the ether-soluble alkaloids of ipecac in substantial amounts. The rhizome, which is now recognized in the official description must not be confused with an aerial continuation of it, the overground stems, which is comparatively inferior in alkaloidal content. The latter may be distinguished from the rhizome by its thinner bark, numerous chloroplasts, and by opposite leaf scars in its terminal portion.

Undulated Ipecac.—This is the root of *Richardsonia scabra* St. Hilaire (Fam. *Rubiaceæ*), indigenous to Brazil. It occurs in somewhat tortuous pieces which differ from ipecac in being less completely and regularly annulated and in possessing a porous wood and a bark that is often violet-colored within.

Greater Striated Ipecac.—The root of *Psychotria emetica* L. (Fam. *Rubiaceæ*) closely resembles the Cartagena Ipecac from which it can be distinguished by its violet-colored bark and total absence of starch, as viewed in transverse sections under a microscope.

Trinidad Ipecac.—The rhizomes and roots of *Asclepias curassavica* L. (Fam. *Asclepiadaceæ*) have been offered as a substitute in Europe. This spurious article is entirely devoid of ipecac alkaloids, has a yellowish-brown external color, a white interior and a bitter taste.

Lesser Striated Ipecac (Planchon). *Ipecac des Côtes d'Or* (Pelletier), *Black Ipecac. Black Striated Ipecac. Striated Brittle Ipecac* (Attfield). *False Ipecac* (Holmes).—This appears to be obtained from a species of *Richardsonia.* It occurs in very short fragments, 2 or 3 cm. long, and 2 or 3 mm. in thickness; some nearly cylindrical, others narrowly fusiform; others again formed of roundish or pyriform segments, somewhat thicker than the preceding, placed end to end. The color is generally of a gray-brown, darker than that of Greater Striated Ipecac. The longitudinal striæ are fine, and regular on the transverse section. The cortical portion starchy and often dark violet in color, and its consistence firmer than in the larger kind; the wood is yellowish, and porous.

White Ipecac is obtained from *Ionidium Ipecacuanha* St. Hil. (Fam. *Violaceæ*), indigenous to Brazil. The root is much branched, free from annulations and of a grayish-white or light brownish-yellow color. The bark is very thin and the wood is light-yellow and porous. It is distinguished by the presence of stone cells and freedom from starch. It contains inulin and no emetine. According to Pelletier, it has however, emetic properties.

In addition to the above the following adulterants have occasionally been found as admixtures of the drug: (1) The roots of *Heteropteris pauciflora* (Fam. *Malphigiaceæ*) which are devoid of starch and possess rosette aggregates of calcium oxalate and stone cells; (2) numerous other foreign roots. Kraemer (*Proc. A. Ph. A.*, 1900, p. 214) has published a note on a so-called ipecac which proved to be derived from *Polygala angulata* DC. The best work on the differentiation of ipecac is that of Hartwich. (*A. Pharm.*, 1904, p. 677; 1905, p. 647.) Tunmann (*Gehe and Co., Handelsbericht,* 1912, p. 165) has submitted this drug to pyroanalysis and obtained characteristic sublimate crystals. For elaborately illustrated articles upon the microscopy of ipecac and its adulterations, see Henry G. Greenish, *P. J.*, 1895, 685, and Albert Schneider, *Am. Drug.*, 1897. According to Greenish, the distinctive characteristics of the powder of either Brazilian or Cartagena ipecac are: (a) the form and size of the starch grains; (b) the absence of vessels, presence of perforated trachoides; (c) the acicular raphides; to these may be added (d) the emetine reaction with chlorine. The stem may in either case be distinguished from the root (in powder) by the presence (a) of sclerenchymatous cells; (b) of lignified cells of the pith; (c) of spiral vessels.

The root of a species of *Ionidium* growing in Quito has attracted some attention as a remedy in *elephantiasis,* under the South American name of *cuichunchulli.* The plant received from Bancroft the name of *I. Marcucci;* but Hooker found the specimen received from Bancroft to be the *I. parviflorum* of Ventenat. Lindley thinks a specimen he received under the same name from Quito to be the *I. microphyllum* of Humboldt. If useful in elephantiasis, it is so probably by its emeto-purgative action. (See *A. J. P.*, vii, 186.)

Description and Physical Properties.—"*Unground Rio Ipecac.*—Roots in cylindrical pieces, mostly curved and sharply flexuous, occasionally branched, from 3 to 15 cm. in lenth, from 1 to 4 mm. in thickness, reddish-brown to dark brown, either smooth or closely annulated, with thickened, incomplete rings and usually exhibiting transverse fissures with vertical sides; bark of smooth root thin, approximately one-ninth of the diameter of the root, that of the annulated root approximately two-thirds of the entire diameter; fracture of bark short, easily separable from the tough, fibrous wood; odor distinctive, the dust sternutatory; taste bitter, nauseous and acrid. Rhizomes cylindrical, attaining a length of 10 cm. and a thickness of 2 mm., finely longitudinally wrinkled, with a few elliptical scars and a distinct pith approximately one-sixth of the entire diameter.

"*Structure of Rio Ipecac.*—Outer layer dark brown, consisting of several layers of cork cells, some showing distinct granular masses covering the tangential walls; cortex grayish-white, consisting chiefly of parenchyma cells filled with starch grains, a few containing raphides of calcium oxalate; wood, light yellow, consisting of tracheids with bordered or slit-like pores, modified medullary rays of prosenchymatic cells containing starch grains, the latter up to 0.01 mm. in diameter and a few lignified fibers with oblique slit-like pores and more or less attenuated ends.

"*Unground Cartagena Ipecac.*—As compared with Rio Ipecac, from 4 to 6.5 mm. in thickness; externally grayish-brown, annulations less numerous; single starch grains, in the average, larger in the medullary rays of the wood.

"*Powdered Ipecac.*—Light brown. Elements of identification: the cork cells; the starch grains single and up to 5- to 7-compound, the single grains up to 0.015 mm. in diameter (Rio Ipecac) and up to 0.020 mm. in diameter (Cartagena Ipecac); raphides of calcium oxalate up to 0.050 mm. in length and fragments of the porous tracheids." *U. S.*

"In somewhat tortuous pieces seldom more than fifteen centimetres long or six millimetres thick; from dark brick-red to very dark brown;

closely annulated externally, the annulations not taking the form of narrow ridges partially encircling the root (distinction from Cartagena ipecacuanha). Fracture short, the fractured surface exhibiting a thick greyish bark and small dense wood. Bark consisting of thin-walled parenchymatous cells, some containing slender raphides, but most filled with simple or compound starch grains, the simple seldom exceeding fifteen microns in length; wood consisting chiefly of tracheids and containing no vessels or typical medullary rays. In the powdered Root, thin-walled parenchymatous tissue, abundant simple or compound starch grains, the single grains seldom exceeding 15 microns in diameter, acicular calcium oxalate crystals, fragments of brown cork, lignified tracheids and wood-parenchyma; but not more than a very occasional vessel or strongly thickened sclerenchymatous cell. Slight odor; taste bitter. Ash not more than 5 per cent. Yields not less than 2 per cent. of alkaloids when tested by the following process." *Br.*

Cartagena ipecac is usually to be distinguished from the Brazilian by its lighter color and the fact that many of its roots are scarcely at all annulated, and some are even smooth. On the other hand, in most specimens of Cartagena ipecac which we have examined, some of the roots could not be distinguished from those of the Brazilian variety. The cultivation of ipecac, which was introduced into India by the British Government, has especially succeeded in the neighborhood of Johore (Straits Settlement). On account of the great local demands in India, only a small amount of this ipecac comes into general commerce, and very little of it reaches the United States. *Johore* or *Indian Ipecac* is especially characterized by the excellent appearance, regularity and large size of the roots, which are deeply annulated, somewhat light in color, and having to a marked degree the general physical and microscopical characteristics of the Brazilian root. Beilee asserts that the Indian Ipecac is usually inferior to the Brazilian, yielding only 0.54 per cent. of emetine (*Bull. Soc. de Pharm. de Bordeaux,* xlvi, p. 171), but according to Ransom, Paul and Cownley, and to Umney and Swinton, it is very rich in alkaloids, and, like the Brazilian root, has for its dominant alkaloid, emetine. Many years ago there was imported from Carácas into the United States a large gray ipecac with badly marked rings. This variety disappeared for a time but is probably the *Colombian* or *Cartagena Ipecac* of modern commerce. It is quite common to find in commerce mixtures of Rio and Cartagena Ipecac. These are usually distinguished from each other by the larger size of the starch grains in the medullary-rays of the wood of the Cartagena variety. (See Schneider, *Jour. of Pharmacology* (*N. Y. C. P.*), 1897, p. 1; and Collin, *J. P. C.,* xx, p. 293.) Hartwich (*Ap. Ztg.,* xxvi, p. 57), however, points out that the size of the starch grains is not sufficient to differentiate these varieties and states that there is a greater difference in the cells of the woody portion of the root.

"**Assay.**—Proceed by Type Process A, taking 10 Gm. of Ipecac, using 100 cc. of ether and decanting an aliquot portion of 50 cc., representing 5 Gm. of Ipecac. Use ether for the final extraction and determine the alkaloids volumetrically. Each cc. of tenth-normal acid corresponds to 0.024 Gm. of the ether-soluble alkaloids of Ipecac (Proximate Assays)." *U. S.*

" Shake 7 grammes of the Root, in No. 60 powder, frequently during 5 minutes with 70 millilitres of a mixture of 1 volume of *chloroform* and 3 volumes of *ether;* add 5 millilitres of *solution of ammonia* and shake frequently during one hour; then add 5 millilitres of *water* or sufficient to make the powder agglomerate on violently shaking. Separate 50 millilitres of the clear liquid, and shake first with 10 millilitres of *N/10 solution of hydrochloric acid,* and then with three successive portions, each of 3 millilitres, of *water.* Mix the several aqueous solutions, make alkaline with *solution of ammonia,* and shake out first with 10 millilitres and then with three successive portions, each of 5 millilitres, of a mixture of 6 volumes of *ether* and 1 volume of *chloroform.* Mix the several ethereal solutions, evaporate, dry the residue at 80° C. and weigh. It weighs not less than 0.100 gramme. Powdered Ipecacuanha Root, when used for official purposes other than the production of standardised preparations, must be adjusted, if necessary, by the addition of powdered Milk Sugar to contain in 100 grammes when tested by the foregoing process 2 grammes of the alkaloids of Ipecacuanha Root. *Limit of error* 0.1 gramme in excess or defect." *Br.*

According to the researches of A. R. L. Dohme (*A. J. P.,* 1895), the stems adhering to the ipecac roots contain from fifteen to twenty per cent. less of the alkaloids than do the roots themselves. Moreover, it appears to be established that the portions of the stem distinct from the root contain much less of the alkaloids than does the base of the stem, so that the Pharmacopœia very properly directs that not more than 7 cm. of the stems shall be allowed. The bark of ipecac root should make eighty per cent. of the whole. When the bark in either variety of ipecac is opaque, with a dull amylaceous aspect, the root is less active. As the woody part is nearly inert, and much more difficult of pulverization than the cortical it often happens that, when the root is powdered, the portion last remaining in the mortar possesses scarcely any emetic power, and care should be taken to provide against any defect from this cause. The German Pharmacopœia provides for the rejection of the last fourth of the powder.

Constituents.—The alkaloid emetine found in ipecac by Pelletier, in 1817, was shown by Paul and Cownley (*A. J. P.,* 1895, p. 256, and 1901, p. 87) to consist of three alkaloids, *emetine, cephaeline,* and *psychotrine.* J. U. Lloyd reports the presence of another alkaloid which he called *kryptonine* but subsequently changed to *emetoidine*. More recently, Hesse (*P. J.*, 1914, xciii, p. 425) reported two new bases, *ipecamine* and *hydroipecamine*. These are of minor importance only as shown by the researches of Pyman, quoted later. Willigk discovered *ipecacuanhic acid*, which was shown by Reich (*A. Pharm.* (2), cxiii, p. 208) to be a glucoside and to have the formula $C_{14}H_{18}O_7$. Finnemore and Braithwaite (*Trans. Br. Ph. Con.*, 1912, p. 496) confirmed the glucosidal nature of this body and suggested the name *ipecacuanhin*.

There has been considerable dispute as to the composition of the ipecac alkaloids, especially of emetine. The United States Pharmacopœia gives $C_{30}H_{44}O_4N_2$, which is the formula of Paul and Cownley. Kunz-Krause later suggested $C_{30}H_{44}O_5N_2$. Still later Hesse proposed the formula $C_{30}H_{42}O_4N_2$, but subsequently he accepted the Kunz-Krause formula. Carr and Pyman (*Proc. Chem. Soc.*, 1913, xxix, 226), however, believe that the proper formula for emetine is $C_{29}H_{40}O_4N_2$. Carr and Pyman give for the formula of cephaeline, $C_{28}H_{38}O_4N_2$. According to Carr and Pyman, psychotrine has the formula $C_{28}H_{36}O_4N_2$. In 1917 Pyman isolated *o-methylpsychotrine*, $C_{29}H_{38}O_4N_2$, from the non-phenolic group of ipecac alkaloids (the emetine group), and also *emetamine*, $C_{29}H_{36}O_4N_2$. This latter alkaloid differs from *emetine* in containing two unsaturated linkages.

There is evidently a close inter-relationship between the various ipecac alkaloids. Pyman (*Tr. Chem. Soc.*, 1917, cxi, 438) has shown that psychotrine can be converted either into o-methylpsychotrine or into cephaeline, which in turn, upon methylation, yields emetine. A stereo-isomeride of emetine called *isoemetine* has been produced by Pyman from *methylpsychotrine* by reduction.

Browne (*J. A. Ph. A.*, 1917, vi, 1043) has made some further investigation of Lloyd's *kryptonine* (emetoidine). It is a colloidal base of a red color and very bitter. It is an emetic by local action and when injected intravenously it lowers the blood pressure similarly to emetine. It is less toxic to paramecia and to rabbits, than emetine.

Huerre (*J. P. C.*, 1920, xxi, 425) believes that the tannin-like body *ipecacuanhic acid* also plays a rôle in ipecac therapy. This acid which exists in the root to the extent of 3 or 4 per cent. is of a glucosidal character. According to Paul and Cownley, the melting point of emetine is 60° C., of cephaeline 102° C., and of psychotrine 138° C. Psychotrine and its salts are rapidly decomposed on exposure to light, in this respect differing from emetine and cephaeline, neither of which are affected by light. It crystallizes from ether, in prisms of lemon-yellow color.

The medicinal virtues of ipecac reside chiefly, if not solely, in the alkaloids emetine and cephaeline. Different samples of ipecac root vary not only in the total percentage of alkaloidal contents, but also in the proportion of the alkaloids, and the question whether Rio and Cartagena ipecac ought to be considered as interchangeable remedies has become one of importance. Paul and Cownley (*A. J. P.*, 1901, lxxiii, 57), as the result of an exhaustive study, found that the two ipecacs do not differ materially in the total amount of alkaloid contained, but that whereas in the Brazilian root emetine is the dominant alkaloid, in the Colombian root cephaeline predominates, and that therefore the two roots cannot be considered as therapeutically identical. This work of Paul and Cownley has been confirmed by Carl Lowin (*A. I. P. T.*, 1902), so that it would appear to be settled that in general terms Rio ipecac contains 1.5 per cent. of emetine and 0.5 of cephaeline; Cartagena contains 0.9 of emetine and 1.2 of cephaeline. The practical accuracy of these researches, however, has been challenged by the large dealers in the products of ipecac. In 1903, as the result of twenty assays of different lots of each drug, Cæser and Loretz, of Halle, report the results given in the following table:

	Total Alkaloids.	Emetine.	Cephaeline.	Ash.
Rio (Matto Grosso Root)	2.73	1.98	0.50	3.34
Rio (Bahia Root)	2.19	1.36	0.63	3.21
Indian from Johore	2.45	1.46	0.62	2.93
Cartagena	2.75	1.47	1.39	6.02

Formerly Brazilian ipecac commanded in the American market a higher price than did the Cartagena variety. At times the Cartagena ipecac has been from ten to fifteen cents a pound higher than the Brazilian, indicating that in some way it especially recommends itself to the manufacturing pharmacists.

W. G. Whiffen patented in Germany in 1898 a process for making emetine, basing it on the separation of emetine hydrobromide from extract of ipecac; cephaeline hydrobromide crystallizes with great difficulty, while emetine hydrobromide is easily crystallized and separated. (*C. D.*, 1898, 694.)

According to the researches of Tokuye Kimura (*A. J. P.*, 1903, 1), ipecacuanhic acid occurs as a brown, hygroscopic, amorphous mass, freely soluble in warm water and alcohol but very slightly soluble in cold water or ether, insoluble in chloroform, having the formula $C_{17}H_{26}O_{10}$ or a multiple of the same. As a glucoside it is allied to the saponin acids but has no hemolytic action and does not form soapy solutions. Its most characteristic reaction is that its solution strikes with ferric chloride a green alizarin tint, which, by the addition of ammonia or saturated baryta water, changes to violet or blackish, with the final separation of a blackish-brown precipitate. On the addition to the discolored solution of diluted hydrochloric acid the green color returns. According to the experiments of Kimura, ipecacuanhic acid is readily absorbed but is possessed of feeble physiological activity and is not germicidal, so that the value of ipecac in dysentery can scarcely depend upon its presence.

The double salts of bismuth iodide and ipecac alkaloids which are sparingly soluble in acids but hydrolyzed by weak alkalies, and which therefore pass through the stomach with little or no dissociation have been recommended for the therapeutic applications of this drug. For methods of preparing this compound, see *Ph. Wb.*, 1919, lvi, 786 and *Proc. A. Ph. A.*, 1919, 521.

Uses.—Ipecac was employed as an emetic by the natives of Brazil when that country was first settled by the Portuguese, but, though described in the work of Piso, it was not known in Europe until 1672, and did not come into use until some years afterwards. John Helvetius, grandfather of the famous author of that name, having been associated with a merchant who had imported a large quantity of ipecac into Paris, employed it as a secret remedy, and with so much success in dysentery and other bowel affections that general attention was drawn to it, and the fortunate physician received from Louis XIV a large sum of money and public honors on the condition that he should make it public.

Ipecac is in large doses emetic, in smaller doses, diaphoretic and expectorant, and in still smaller, stimulant to the stomach, exciting appetite and facilitating digestion. In quantities not quite sufficient to cause vomiting, it produces nausea, and frequently acts on the bowels. As an emetic it is mild, but tolerably certain, and free from corrosive or narcotic properties.

The researches of Waters and Koch (*J. P. Ex. T.*, 1917, x, 73) have shown that psychotrine is practically non-toxic and probably plays no part in the action of ipecac. Cephaeline and emetine are similar in their effects although differing in degree. Emetine is a more active amebicide but less irritant and emetic, and also less toxic, than cephaeline. Eggleston and Hatcher (*J. P. Ex. T.*, 1915, vii, 225, and 1923, xxi, p. 1) have found that both of these alkaloids have a direct stimulant action upon the vomiting center in the medulla. They believe, however, that the emetic effect is due not only to this action but in part to their local irritant effect upon the gastric mucosa. Because of the promptness with which the emesis occurs it is scarcely possible for enough of the active principles to be absorbed from the stomach to produce direct systemic effects. When injected subcutaneously or intravenously in large dose, however, the alkaloids act as depressants to the motor side of the spinal cord and probably also to the respiratory center. It would seem that they have some special predilection for the lungs for after toxic doses alternating areas of pallor and intense hyperemia have been found in the pulmonary tissue.

Originally introduced into Europe as a remedy for *dysentery,* ipecac for centuries was alternately lauded as a specific and condemned as useless in this disease. In 1911 Vedder (*Bull. Manila Med. Soc.*, March, 1911; also *J. A. M. A.*, 1914, lxii, p. 501) showed that an infusion of ipecac representing one part of the drug in ten thousand destroyed the viability of the *Entamebæ,* and that the alkaloid emetine in a one to one-hundred thousand solution had the same effect. He also showed that the drug was possessed of no bactericidal virtues. Since this research, reasons for the diversions of opinion as to the usefulness of ipecac are apparent. There are two types of dysentery, one due to a specific ameba and the other caused by a bacillus. In the latter form of the disease the drug is useless but is probably the most efficacious remedy we possess in the amebic type of dysentery. The great difficulty in its employment has always been to obviate the emetic effect which sometimes made it almost impossible to get enough of the drug into the intestinal tract to have an effect. In 1912 Rodgers (*B. M. J.*, 1912, i, p. 1424, and ii, p. 405) introduced the hypodermic administration of the alkaloid emetine which has since then become the standard treatment of *amebic dysentery.* (See *Emetinæ Hydrochloridum.*) Simon (*J. A. M. A.*, 1918, lxxi, 2042) maintains that the whole drug administered by mouth gives better results than the subcutaneous injection of the alkaloid, especially in the chronic cases where the ameba has become encysted. Ipecac is also of value in the various sequelæ of dysentery, such as *abscess of the liver,* although it does not always produce complete cure. Following the announcement of Smith and Barrett (*J. A. M. A.*, 1914, lxiii, 1746) that *pyorrhea alveolaris* was due to a specific ameba, emetine was employed to a considerable extent in tooth pastes and mouth washes in this condition. The present evidence, however, indicates that the ameba found in the mouth in this disease is not the causative agent, and there is no convincing evidence of the curative value of emetine.

As an emetic ipecac is rarely used merely for the purpose of evacuating the stomach, but when an action upon the portal circulation is desirable, as in the so-called *biliousness* or *acute alcoholism,* it is often of service. Many clinicians believe that it has a direct influence upon hepatic secretion, but it is more probable that its effects upon the liver are due simply to its emetic action. By virtue of their nauseating effect small doses of ipecac tend to increase various secretions of the body, thus it is widely used as a diaphoretic, especially in combination with opium (see *Pulvis Ipecacuanhæ et Opii*) in the early stages of *acute coryza* and other mild infections. In the same way it acts as an expectorant, and in the early stages of *acute bronchitis* it is one of the most valuable remedies we possess. Many years ago Trousseau affirmed that ipecac possessed valuable hemostatic powers, especially useful in *hemoptysis,* but this use of it failed to receive general recognition. The treatment has been revived by Flandin (*Press. Med.,* 1913) and other French clinicians.

As an emetic ipecac may be given in substance in the dose of twenty to thirty grains (1.3–2.0 Gm.), repeated in fifteen to twenty minutes if necessary. As an expectorant the syrup is generally preferred. If ipecac itself is used in dysentery it should be given in doses of five grains every hour combined with opium to prevent vomiting. To obviate the nauseating effect of emetine when given by the mouth, Bass and Johns have used a combination with Lloyd's reagent.

Under the name of *riopan,* a preparation asserted to contain 50 per cent. of combined cephaeline and emetine has been introduced. This is marketed in the form of tablets each containing one-thirtieth of a grain (0.002 Gm.), which is stated to be equivalent to about a grain and a half of ipecac (0.096 Gm.).

Dose, emetic, twenty to thirty grains (1.3–2.0 Gm.); nauseating, two grains (0.13 Gm.); diaphoretic, one grain (0.065 Gm.); stomachic, one-fourth to one-half grain (0.016–0.032 Gm.).

Off. Prep.—Fluidextractum Ipecacuanhæ, *U. S.* (*Br.*)*;* Pilula Ipecacuanhæ cum Scilla, *Br.;* Pulvis Ipecacuanhæ et Opii, *U. S.* (*Br.*)*;* Syrupus Ipecacuanhæ, *U. S.;* Trochiscus Ipecacuanhæ, *Br.;* Trochiscus Morphinæ et Ipecacuanhæ, *Br.;* Vinum Ipecacuanhæ (from Fluidextract), *Br.;* Mistura Rhei Composita (from Fluidextract), *N. F.;* Pilulæ ad Prandium (Chapman's), *N. F.;* Pilulæ Laxativæ Compositæ, *N. F.;* Syrupus Asari Compositus (from Fluidextract), *N. F.;* Syrupus Ipecacuanhæ et Opii (from Tincture), *N. F.;* Tinctura Ipecacuanhæ et Opii (from Fluidextract), *N. F.*

IPOMŒA. U. S. (Br.)

IPOMEA Ipom. [Orizaba Jalap Root, Mexican Scammony Root]

"Ipomea is the dried root of *Ipomœa orizabensis* Ledenois (Fam. *Convolvulaceæ*). Ipomea yields not less than 15 per cent. of the total resins of Ipomea, and not more than 3 per cent. of acid-insoluble ash." *U. S.*

"Orizaba Jalap Root is the dried root of Ipomœa orizabensis, *Ledanois.*" *Br.*

Ipomœæ Radix, *Br.;* Orizaba Root, Male Jalap, Light, Woody, or Fusiform Jalap; Jalap stalks; Purgo Macho (*Mexican*).

The genus *Ipomœa* (Fam. *Convolvulaceæ*) comprises about 300 species of herbs and shrubs, some being erect, others prostrate, but very many climbing. They are remarkable for their showy flowers, as in *I. purpurea,* the common morning glory of the garden. Many of the species produce large tuberous roots which contain a drastic purgative resin and several of them have been used in medicine. Because of the growing scarcity of scammony, the B. P. 1914 permitted the employment of the resin of Orizaba jalap root to be used in formulas calling for scammony resin, and the U. S. P. X omitted scammony altogether, substituting the Orizaba jalap.

Ipomœa orizabensis is a climbing vine indigenous to Mexico. It produces a large, fusiform, more or less branching root attaining a length of 5 dm., yellow on its outer surface, milky-white within. The stem is cylindrical, slightly villous and climbing. The leaves are large, petiolate, cordate, acuminate and villous on the veins. The corolla is campanulate and reddish-purple. The capsule is 2-locular and one-seeded. The roots are gathered around Orizaba in the Mexican Andes, cut into transverse disks and rapidly dried in the sun. It is exported from Mexico City to the United States.

Power and Rogerson (*A. J. P.,* 1908, p. 255) have shown that the root of the *I. purpurea* or common morning glory, contains a purgative resin. Shimoyama has found in the *I. triloba* (*Pharbitis triloba*) of Japan a similar resin and according to Hyrano the seeds of this plant have long been used in Japan under the name of "kengashi." *Turpeth,* the root of the East Indian *I. Turpethum,* was at one time recognized by the French Codex under the name of *Turbith Végétal.*

Ipomea root becomes official in the U. S. P. X not because of any therapeutic superiority to Levant scammony root, but as the nearest available substitute for a valuable drug which has not been commercially obtainable for a number of years. Besides being yielded by a species of a different genus, it shows marked structural differences. Whereas Levant scammony root occurred in cylindrical, grayish- to reddish-brown, usually twisted segments, from 10 to 25 cm. in length, ipomea occurs in nearly flat, light- or dark-brown, transverse slices or in pieces of irregular shape, made by vertical or oblique sectioning of these slices, and whereas scammony was mottled internally by the apparently scattered appearance of its bundles in the parenchyma, that of ipomea is not mottled and shows a regular concentric arrangement of its bundles. Moreover, Levant scammony root contained calcium oxalate crystals only in monoclinic prisms and possessed a variety of stone cells, while Ipomœa contains calcium oxalate crystals chiefly of the rosette aggregate type, only an occasional rhombohedral crystal being found, and stone cells are absent.

Description and Physical Properties.—"*Unground Ipomea.*—Nearly flat transverse slices, from 2 to 12 cm. in diameter, and from 1 to 5.5 cm. in thickness; externally light to dark brown, very deeply wrinkled; fracture tough, fibrous, cut surface light brown, showing concentric rings from which coarse fibers protrude; odor distinct, somewhat aromatic; taste slightly sweet, becoming somewhat acrid.

"*Structure.*—A corky layer consisting of several rows of brownish, thin-walled, narrow tabular cells; outer cortex of several layers of colorless, thin-walled cells; a broad cortical layer made up of thick-walled, tangentially elongated cells, containing either starch grains or crystals of calcium oxalate and numerous large cells containing brown resinous latex; alternate rings or zones of collateral fibrovascular bundles separated by broad medullary rays; sieve in semicylindrical strands outside of the wood wedges; resin cells numerous and distributed throughout the parenchyma and medullary rays; the parenchyma cells both in and surrounding the bundles more or less collapsed and containing either starch or calcium oxalate crystals.

"*Powdered Ipomea.*—Light grayish-brown; starch grains from 0.003 to 0.035 mm. in diameter, mostly single, also 2- to 4-compound and usually with a central cleft; calcium oxalate crystals numerous, mostly in rosette aggregates, occasionally in the form of rhombohedra, from 0.010 to 0.045 mm. in length; fragments of yellowish-brown resin cells; tracheæ mostly with bordered pores and associated with numerous thick walled wood fibers with simple pores.

"**Assay.**—Proceed as directed under *Jalapa.*" *U. S.*

It is described in the Br. as follows: "In irregular, tough, or fibrous pieces of varying size and shape, but often in portions, three to five centimetres wide and two to four centimetres thick, of transverse slices of large roots. Externally greyish-black and wrinkled, internally greyish or brownish. From the transverse surface coarse fibres protrude in irregular concentric circles. Slight odor; taste faintly acrid. Yields to *alcohol* (90 per cent.) a resin which has the properties enumerated under 'Scammoniæ Resina.'" *Br.*

Constituents.—The purgative power of ipomea undoubtedly resides in its resin. Dean determined the amount of resin in a specimen and, in a separate paper, gives the method employed and the results, as follows: The drug was powdered, exhausted by percolation with alcohol (90 per cent.), the greater part of the alcohol distilled off, and the resulting strong tincture poured into three times its volume of water. The resin separated as a mass of honey-like consistence. It was well washed with boiling water until the washings were free from sugar and from color, and then dried on a water bath until the weight was constant. The yield of resin amounted to 18.5 Gm. from 100 Gm. of the powdered drug; this is the highest percentage yet recorded from this source. The dried resin was pale brown, and almost entirely soluble in ether, the insoluble portion from 18.5 Gm. weighing less than 0.25 Gm. It has the general characteristics of scammony resin. The powdered drug, dried at 100° C., yielded 9.89 per cent. of ash. (*P. J.*, March 5, 1904.) Power and Rogerson (*Tr. Chem. Soc.*, 1912, ci, 398) obtained approximately 15 per cent. of resin of which from 70 to 75 per cent. was soluble in ether. Taylor (*A. J. P.*, 1909, lxxxi, 105), however reported that from 96 to 99 per cent. of the resin of Mexican scammony was ether-soluble.

Speaking in a general manner ipomea resin has a higher specific rotatory power than the scammony resin and a lower ester and saponification value. These differences, however, are not great enough to make a trustworthy distinction (see *Resina Ipomœæ*).

Uses.—Although ipomea has been admitted as a substitute for scammony, the therapeutic identity of the resins from the two is open to serious question. According to Bourdier (*J. P. C.*, 1912, 252), the ipomea resin is more irritant and likely to provoke nausea than true scammony. It is stated (*J. P. C.*, xxiv, 166) that thirty to sixty grains (2–3.9 Gm.) of ipomea root is actively purgative. It is, however, rarely employed and is official only as a source of scammony resin.

Off. Prep.—Resina Ipomea, *U. S.*

ISPAGHULA. Br.

ISPAGHULA

"Ispaghula consists of the dried seeds of Plantago ovata, *Forsk.*" *Br.*

Ispaghue, Spogel Seeds.

Plantago ovata Forskal (*P. Ispaghula* Roxb.) is a herbaceous plant (Fam. *Plantaginaceæ*) growing in India and Persia and extending westward to Spain and the Canary Islands. It is either erect or decumbent and varies in height from 2.5 cm. to 1 dm. The leaves are ovate and either glabrous or shaggy hairy. The flower spikes are either cylindrical or reduced to a globular head. The seeds closely resemble those of other species of *Plantago.*

They are described as follows: "Seeds boat-shaped, somewhat acute at one end, from two to three millimetres long and from one to one and a half millimetres wide; pale greyish-brown, with a darker elongated spot on the convex side; on the concave side the hilum covered with the remains of a thin white membrane. In *water* the testa swells, producing a viscous mucilage. No odor or taste." *Br.*

The seeds of the *Plantago amplexicaulis* Cav. are also sold in the Indian bazaars as Ispaghula. They resemble the official seeds, but are of a darker color.

The seeds of *Plantago Psyllium* L., commonly known as flea seeds, are smaller than the official seeds; they are described in Part II.

Ispaghula seeds yield to water a viscid mucilage. They are used in India as a demulcent in *dysentery* and various intestinal irritations, and are also slightly laxative. On roasting they are said to become astringent, and as such are used for *diarrheas,* especially of children. By European practitioners they have been chiefly employed in *chronic diarrhea.* In India they are also used for their demulcent effect in catarrhal conditions, especially of the genito-urinary tract.

Dose, from one to two and a half drachms 3.9–9.8 Gm.).

Off. Prep.—Decoctum Ispaghulæ, *Br.*

IRIS. N. F.

ORRIS [Orris Root]

"Orris is the rhizome of *Iris florentina* Linné, *Iris germanica* Linné, or *Iris pallida* Lamarck (Fam. *Iridaceæ*), freed from the roots, peeled and dried. Orris contains not more than 1 per cent. of foreign organic matter." *N. F.*

Iridis Rhizoma; Rhizoma Iridis, *P. G.;* Radix Iridis Florentinæ, Radix Ireos, Iris de Florence, *Fr.;* Florentinische Violenwurzel, Veilchenwurzel, *G.;* Ireos, *It.;* Lirio de Florencia (Rizoma de), *Sp.*

In all the species belonging to this genus, so far examined, the roots are more or less acrid, and possessed of cathartic and emetic properties. In Europe, *Iris fœtidissima* L., *I. pseudacorus* L., and *I. tuberosa* L. have at various times been admitted into use, in addition to those here described.

The three species recognized, under the title "Iris," by the N. F. are valued rather for their pleasant odor than for their cathartic properties. The *Iris versicolor* is described in the succeeding article.

Iris Germanica, commonly known as *Fleur-de-Lys,* is a perennial herb with dark blue or purplish flowers, native to central and southern Europe, but extensively cultivated as an ornamental plant in the United States and has become sparingly naturalized in Virginia. It is cultivated on a commercial scale in Italy, especially in the neighborhood of Verona, and also in Morocco. *I. pallida,* Lam. which is a native of the eastern Mediterranean countries, has pale bluish flowers. The rhizomes of these two species constitute what is known as *Verona Orris.* The *Florentine orris* is from the *I. Florentina* L. It has large white flowers and is of about the same distribution as the *I. pallida.* Its rhizome is generally the most fragrant although it is less widely cultivated than the other two species.

The rhizomes of these three species resemble one another so closely that it is often impossible to distinguish between them. They are gathered usually in the late summer from plants two or three years old and dried in the sun. The fresh rhizomes are without odor and have an acrid taste, but during the process of drying they lose much of their acridity and develop the characteristic fragrance. The Florentine variety is usually lighter in color and more pronounced in odor than the Veronese and also more carefully peeled. The commercial supplies of orris root come to the U. S. A. from Leghorn, Italy, and to a lesser extent from Mogador, Morocco.

Description and Physical Properties.—"*Unground Orris.*—In pieces of various forms and sizes, usually jointed and branched, from 5 to 10 cm. long and from 1.5 to 3 cm. wide, rounded or flattened, with knotty enlargements; under surface with numerous root scars, the upper with leaf scars; externally yellowish white; internally light yellow; fracture hard, rough and at times mealy, showing a narrow cortex, a distinct endodermis and a large stele with numerous vascular bundles, especially near the endodermis. Odor fragrant, resembling that of violet flowers; taste slightly aromatic, bitterish, somewhat irritating.

"*Structure.*—Cortex composed mostly of starch-bearing parenchyma, the cells with thickened, porous walls and intercellular spaces within which occur large prisms of calcium oxalate which are also found in certain parenchyma cells with suberized walls; a distinct endodermis of collenchyma-like cells containing starch; a large central cylinder composed of starch-containing parenchyma with concentric vascular bundles irregularly placed throughout, the latter being most numerous near the endodermis.

"*Powdered Orris.*—Light yellow. Parenchyma cells of the cortex and central cylinder filled with characteristic starch grains, the latter oval, rounded at one end and flattened at the other, some curved or with irregular protuberances, mostly single, from 0.020 to 0.050 mm. in length and with an X-shaped cleft in the large rounded end of the grain, two of the fissures extending in the form of a horseshoe toward the small end of the grain; elements of vascular bundles, with tracheæ showing spiral, annular, scalariform or reticulate markings, the tracheæ from 0.010 to 0.025 mm. in width; calcium oxalate in prisms up to 0.500 mm. in length and 0.030 mm. in width." *N. F.*

Orris root contains much starch, a bitter and acrid fixed oil or soft resin and a crystallizable volatile oil. According to Landerer (*A. Pharm.,* lxv, p. 302), the acrid principle is volatile and separates in the form of a steareopten from water distilled from the root. By distillation with steam the root yields about 0.1 or 0.2 per cent. of a semi-solid aromatic substance known as *oil of orris* or powder of orris. Flückiger (*A. J. P.,* 1876, 411; 1885, p. 133) has shown that this consists chiefly of myristic acid containing a small amount of the true odorous principle. The myristic acid, however, seems not to pre-exist in the orris root, but is probably liberated from a fat by the influence of the steam. The fragrance of the root has been shown by Tiemann to be due to *irone* ($C_{13}H_{20}O$) which is a methyl ketone isomeric with ionone. In attempting its synthesis, Tiemann prepared an isomeric compound *pseudoionone* which however did not possess a pleasant odor but could be changed into *ionone* which has the violet-like odor. This complex ketone is now manufactured synthetically for use in perfumery. Ionone, of commerce, is a mixture of *alpha* and *beta* isomers which have been successfully separated. *Alpha ionone* has a sweet penetrating odor resembling orris while *beta ionone* is said to more closely resemble the violet odor.

Uses.—In large doses, orris root is cathartic and emetic and was formerly employed as a medicine. At present it is valued chiefly for its agreeable odor. It is occasionally chewed to conceal an offensive breath and enters into the composition of tooth powders.

Off. Prep.—Species Pectorales, *N. F.*

IRIS VERSICOLOR. N. F.

BLUE FLAG [Iris Vers.]

"Blue Flag is the dried rhizome of *Iris versicolor* Linné, or of *Iris caroliniana* Watson (Fam. *Iridaceæ*). Blue Flag contains not more than 5 per cent. of its roots and leaf bases or other foreign organic matter." *N. F.*

Blue Flag, Larger Blue Flag; Amerikanische Schwertel, *G.;* Iris Varié, *Fr.*

Iris versicolor L., or blue flag, is found in all parts of the United States, flourishing in low wet places in meadows.

The somewhat leafy stem is taller than the equitant basal leaves and often branched; the flowers are a violet blue variegated with green, yellow or white and purple-veined. They afford a blue infusion which has been used as a test for acids and alkalies. The fresh rhizome is almost odorless and has a nauseous, acrid taste; the acrimony and apparently also the medicinal activity is impaired by age. According to Andrews, however, if cut, when fresh, into slices, dried at the temperature of about 37.8° C., then powdered and kept in bottles excluded from the air, the root retains its virtues unimpaired for a considerable time. Commercial supplies of this drug have been recently obtained from Florida, Missouri, New Jersey, New York, Michigan and North Carolina.

Description and Physical Properties.—"*Unground Blue Flag.*—Rhizome frequently branched, up to 20 cm. in length and 3 cm. in thickness at the nodes, usually cut into longitudinal pieces; outer surface grayish brown to purplish brown, somewhat annulate, the upper surface with markings of leaf bases, the lower with numerous root scars and root remnants; fracture short, the broken surface yellowish white, pink or pale to dark purplish brown and exhibiting a central stele with whitish fibrovascular bundles distributed throughout, a distinct endodermis, and cortex. Odor slight, not distinctive; taste acrid, nauseous.

"*Structure.*—A more or less exfoliating epidermal layer of cells with brownish walls; a hypodermis of about two rows of cells with uniformly thickened, strongly lignified walls, some of which contain a reddish-brown amorphous substance; a narrow cortex of characteristic structure with ovoid or spheroidal parenchyma cells with large intercellular spaces, some of the parenchyma containing starch, others a reddish-brown amorphous substance; an endodermis of a single layer of cells with walls lignified and thickened on the inner and radial surfaces; a central cylinder made up of numerous nearly spherical parenchyma, between which are intercellular spaces not as large as those in the cortex; concentric vascular bundles occasional in the cortex, more numerous in the parenchyma of the central cylinder.

"*Powdered Blue Flag.*—Reddish-brown; numerous resin cells filled with a reddish-brown amorphous substance; starch grains few, or in some specimens abundant, simple or 2- to 4-compound, the simple grains being spherical or elliptical, up to 0.022 mm. in diameter; calcium oxalate in prisms up to 0.350 mm. in length; tracheæ with spiral or reticulate markings or bordered pores; fibers few, lignified and with oblique pores." *N. F.*

The active principle of blue flag is unknown. The name *iridin* is applied to the oleoresin obtained by precipitating the tincture of the root with water. *Irisin* is a somewhat similar preparation in which the oleoresin is stiffened by the addition of the powdered root. For chemical examination of the resin see Power and Salway (*A. J. P.*, 1911, lxxxiii, p. 14).

Uses.—Blue flag root is a cathartic and emetic said to have been used by the Indians of the Southern United States. By some it is supposed to have a special effect upon the liver and is used as a cathartic in *biliousness.* The eclectic physicians attribute to it also alterative powers and employ it in various *skin diseases, chronic rheumatism* and similar complaints.

Dose, ten to thirty grains (0.6–2 Gm.).

Off. Prep.—Fluidextractum Iridis Versicoloris, *N. F.;* Elixir Corydalis Compositum, *N. F.;* Fluidextractum Stillingiæ Compositum, *N. F.;* Syrupus Stillingiæ Compositus, *N. F.*

JALAPA. U. S., Br.

JALAP Jalap.

"Jalap is the dried tuberous root of *Exogonium Jalapa* (Nuttall et Coxe) Baillon (Fam. *Convolvulaceæ*). Jalap yields not less than 7 per cent. of the total resins of Jalap." *U. S.* "Jalap consists of the dried tubercules of Ipomœa Purga, *Hayne.*" *Br.*

Radix Jalapæ, Jalapæ Radicis Tubera; Jalap Tubéreux, *Fr. Cod.;* Tuber Jalapæ, *P. G.;* Jalape, Jalapenknollen, Jalapenwurzel, *G.;* Gialappa, Sciarappa, *It.;* Jalapa (Raiz de), *Sp.*

The botanical origin of jalap has long been a subject of much controversy among botanists. Linnæus, at first, is said to have placed the plant in the genus *Mirabilis.* In 1827, J. R. Coxe of Philadelphia grew jalap plants from tuberous roots he received from Mexico. These plants were studied by Nuttall who, in 1830, published a description of the species, naming it *Ipomœa Jalapa,* Nutt. and Coxe. During the same year

Scheide and Wenderoth published separate descriptions of the plant, the former naming it *Convolvulus jalapa* Scheide and the latter *Convolvulus Purga* Wenderorth. But Scheide and Wenderoth, apparently working with dried material, overlooked the true character of the stigma of the jalap flower which is simple and capitate, a character which distinguishes *Ipomœa* from *Convolvulus,* the latter genus having two linear or ovate stigmas. In 1833, Hayne published a monograph on the species, reinstated it in the genus *Ipomœa* and named it *Ipomœa Purga* (Wenderoth) Hayne (*Arzneigew.,* 1833), a name which has persisted in the British Pharmacopœia. Choisy, in 1833, divided the Ipomœas and placed those bracteate forms having exserted stamens and salverform corolla in his genus *Exogonium.* This group is recognized as a genus by Peter and Hallier but merely as a section of Ipomœa by Griesebach and Meissner. In 1840, Bentham described the species (*Pl. Hartw.,* 1840) first placing it in the genus *Exogonium* and naming it *Exogonium Purga* (Wenderoth) Bentham, a name which was later adopted by Engler in his *Syllabus der Pflanzenfamilien* and by the U. S. IX. In 1884, Baillon, recognizing the priority of the specific name *Jalapa* which had been established by Nuttall and Scheide, again revised the nomenclature and assigned to it the name of *Exogonium Jalapa* (Wenderoth) Baillon (*Bot. Med.,* 1884, xi, 1263). This name has been adopted in the U. S. X.

The root of *Exogonium Jalapa* (*Ipomœa Purga* Hayne) is a roundish, somewhat pear-shaped tuber, externally blackish, internally white, with long fibers proceeding from its lower part, as well as from the upper root-stalks. The stem is round, smooth, much disposed to twist, and rises to a considerable height upon neighboring objects, about which it twines. The leaves are petiolate, heart-shaped, entire, smooth, pointed, deeply sinuated at the base and prominently veined on their under surface. The lower leaves are nearly hastate or with diverging angular points. The flowers, which are large and of a lilac-purple color, stand upon peduncles about as long as the petioles. Each peduncle supports two or, more rarely, three flowers. The calyx is without bracts, five-leaved, obtuse, with two of the divisions external. The corolla is funnel-form. The stamens are five in number, with oblong, white, somewhat exserted anthers. The stigma is simple and capitate.

The jalap plant is a native of Mexico, where it is dug during the whole year, and usually dried over the hearths of the Indian huts. Because of this method of drying over fires, the drug usually possesses a smoky odor and taste. It derives its name from the city of Jalapa, in the state of Vera Cruz, in the neighborhood of which it grows, at the height of about 6000 feet above the ocean. The drug is brought from Vera Cruz and Mexico City in bags containing usually between 100 and 200 pounds. It has also been cultivated in India, Jamaica, South America and Ceylon. For an account of the cultivation of jalap in Madras, see *Am. Drug.,* 1896, 127.

Description and Physical Properties.—"*Unground Jalap.*—Fusiform, irregularly ovoid or pyriform, the larger roots often incised or cut into pieces; from 4 to 15 cm. in length and from 1 to 10 cm. in diameter; externally dark brown, longitudinally wrinkled or furrowed and with numerous lenticels; hard, compact, not fibrous, internally light grayish-brown to dark brown, with a distinct brown cambium line; odor slight but distinctive and smoky; taste somewhat sweet and acrid.

"*Structure.*—Cork of several or many rows of small, thin-walled brownish cells; cortex narrow; fibro-vascular bundles small, numerous, arranged in several concentric zones, bicollateral, each bundle with several tracheæ, several small groups of sieve tissue and inconspicuous cambium except in the outermost zone where the cambium is conspicuous, with 6 to 10 rows of cells and forming a complete circle; parenchyma abundant, starch-bearing, with numerous large secretory cells scattered through it.

"*Powdered Jalap.*—Light brown; starch grains numerous, single or 2- to 3-compound, more or less swollen, ellipsoidal or ovoid with concentric or excentric lamellæ and radiating clefts, from 0.003 to 0.035 mm. in diameter; calcium oxalate in rosette aggregates from 0.010 to 0.035 mm. in diameter; tracheæ short, wide, with simple or bordered pores; secretory cells with yellowish brown, resinous contents." *U. S.*

Jalap is apt to be attacked by insect larvæ, which are said to devour the amylaceous or softer parts, and to leave the resin, so that the worm-eaten drug is more powerfully purgative than that which is sound. Hence, worm-eaten jalap should be employed for obtaining the resin, but should not be pulverized, as it would afford a powder of more than the proper strength. The drug is also liable to various adulterations, or fraudulent substitutions, which, however, can usually be detected without difficulty by means of the microscope.

According to Herlant, even in powder it is easy to detect the presence of the root of *Mirabilis Jalapa,* which is sometimes used as an adulterant to jalap, by the presence of raphides of calcium oxalate.

Since about 1915 the root of *Piptostegia Pisonis* Mart. (Fam. *Convolvulaceæ*), commonly known as *Piptostegia Root* or *Brazilian Jalap,* has appeared in the American and European markets. It occurs in transverse, oval or circular sections up to .8 cm. in thickness. Its cut surface is pale yellowish-brown and shows many resin dots and several concentric rings. For structural details of this substitute see Farwell (*J. A. Ph. A.,* 1918, p. 854).

Jalap is usually kept by pharmacists in the state of powder, which is of a yellowish-gray color, and when inhaled irritates the nostrils and

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throat, and provokes sneezing and coughing. Jalap yields its active properties partly to water, and completely to diluted alcohol.

"**Assay.**—Place 10 Gm. of Jalap in fine powder in a dry flask, add 50 cc. of alcohol and stopper the flask with a perforated cork holding a reflux condenser. (An open glass tube of not less than 0.6 M. in length will suffice.) Place the flask on a water bath, and digest for three hours with occasional shaking. Then transfer to a small percolator, allow to drain, and percolate with alcohol until the percolate measures 100 cc. Allow to cool to room temperature, and add alcohol to make exactly 100 cc. Mix well. Transfer 20 cc. of this tincture accurately measured, representing 2 Gm. of Jalap, to a separator, and add 10 cc. of chloroform and 20 cc. of a saturated solution of potassium citrate (20 Gm. of potassium citrate dissolved in 12 cc. of distilled water). Shake well during two minutes, then set aside for not less than ten hours or overnight. Draw off and discard the lower aqueous liquid, and filter the alcohol-chloroform solution through a small filter, wetted with alcohol-chloroform, into a tared flask or beaker. Rinse the separator with a mixture of 10 cc. of alcohol and 5 cc. of chloroform, and pass the rinsing through the filter. Mix the chloroformic liquids, evaporate on a water bath, dry at 100° C., and weigh." *U. S.*

Constituents.—The purgative powers of jalap undoubtedly reside in its resin. G. A. Kayser separated jalap resin into two parts, the first hard and insoluble in ether, the other soft and soluble in that menstruum. The ether insoluble portion he called *rhodeoretin* and showed it to be identical with the substance previously described by Buchner and Herberger under the name of *jalapin.* Mayer confirmed these observations. He gave the name of *convolvulin* to Kayser's rhodeoretin and by treating with alkalies obtained what he believed to be two glucosidal substances which he named *purgic* and *convolvulic acids.* Power and Rogerson (*J. Am. C. S.*, 1910, xxxii, p. 80) have found, however, that these substances are not chemical individuals. By successive extraction with various solvents they showed that the jalap resin was an extremely complex mixture. Approximately 10 per cent. of the total resin is soluble in ether. They found that the various fractions separated by successive treatment with ether chloroform and ethyl acetate were all about equally active as purgatives.

The terms *jalapin* and *scammonin* (or *convolvulin*) can no longer be regarded as names of definite substances. They are, however, often used to indicate different fractions of the Convolvulus resins, the term jalapin being applied to the ether soluble portion and convolvulin to the insoluble fraction.

The average percentage of resin in jalap has of late years distinctly lessened; indeed this fact has received official recognition. The U. S. P., 1890, required 12 per cent., and the French Codex, 1884, 16 to 18 per cent. The poor quality of commercial jalap appears to be due, not, as believed by Flückiger, to the extraction of the resin from the roots in Mexico, but to the fact that the wild tubers are collected indiscriminately from November to March; the cultivators of India are also very careless in their methods. The lowness of the U. S. P. standard (7 per cent.) is to be regretted, especially as the Br. Ph. requires 11 per cent., but it is probably necessary, practically, to meet the commercial conditions. From a compilation by M. I. Wilbert (*J. A. Ph. A.*, 1914, 1286) the range of 173 reported analyses of jalap was from 3.67 per cent. to 21.76 per cent. (For various analyses of commercial jalap, see *U. S. D.*, 18th ed., also *J. P.*, lxxii, p. 152.)

A comparison of various methods of assay was made by Dr. P. Seidler (*Ph. Ztg.*, 1912, No. 2, 15), who recommends the process of the P. G. V., which he says can be still further improved.

Tampico Jalap (*Purga de Sierra Gorda,* Mexican).—This drug closely resembles in appearance, odor, and taste the true jalap, but the tubers are somewhat smaller, more elongated and shrivelled. According to Ambrose Andouard, it is the *jalap digité majeur* of Guibourt. It grows along the Sierra Gorda, near San Luis de la Paz. In this place it is purchased from the Indians, and conveyed by mules to Tampico, where it enters into commerce. The plant differs from *Exogonium Jalapa* by its bell-shaped corolla and pendulous flower-buds. To it Hanbury gave the name *I. simulans.* (*A. J. P.*, July, 1870.) H. Spirgatis, of Königsberg, obtained a resin to which he gave the name of *tampicin.* Its physical properties are similar to those of the jalap resin. It is brittle, tasteless, inodorous, insoluble in water, soluble in ether and alcohol, and in solution has a feeble acid reaction. (See *N. R.*, 1871, p. 50.) The melting point of tampicin is 130° C.; its formula is $C_{34}H_{54}O_{14}$. The percentage of it yielded by the drug varies from a minimum of 10 per cent. (Hanbury) to a maximum of 15 per cent. (Umney). Andouard states that it is purgative.

Jalap should be rejected when it is light, of a whitish color internally, of a dull fracture, spongy, or friable. Powders of calomel and jalap, taken on long voyages to southern climates, are said, when brought back, to have become consolidated, and so far chemically altered as plainly to exhibit globules of mercury. This change is ascribed by Schacht and Wackenroder to a fungous growth. (*A. Pharm.*, xxxix, 239.)

Uses.—Jalap is an active cathartic, operating briskly and sometimes painfully upon the bowels, and producing copious watery stools. The aqueous extract purges moderately, without much griping, and is said to increase the flow of urine. The portion not taken up by water gripes severely. The aqueous extract obtained from jalap, previously exhausted by rectified spirit, is said to have no cathartic effect. Jalap was introduced into Europe in the latter part of the sixteenth or the beginning of the seventeenth century, and at one time ranked among the purgative medicines most extensively employed. It is applicable to most cases in which an active cathartic is required, and from its hydragogue powers is especially adapted to the treatment of *dropsy.* It is generally given in connection with other medicines, which assist or qualify its operation. In dropsical complaints it is usually combined with potassium bitartrate.

The combination of jalap with calomel has long been popular, in the United States, in *bilious fever* and other complaints attended with *congestion of the liver* or portal circle.

In overdoses jalap may produce dangerous hypercatharsis. It is said to purge when applied to a wound. Jalapin when taken internally is probably absorbed, but as yet its presence has never been detected in the urine, and it remains uncertain whether it is eliminated or destroyed. Müller (*In. Dis.,* Dorpat, 1885) found traces of it in the blood, and even in the heart, lungs, and spleen of cats poisoned with it.

The *dose* of jalap, in powder, is from ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Pulvis Jalapæ Compositus, *U. S., Br.;* Pulvis Scammonii Compositus, *Br.;* Resina Jalapæ, *U. S.* (*Br.*)*;* Tinctura Jalapæ, *Br., N. F.;* Tinctura Jalapæ Composita, *Br., N. F.;* Fluidextractum Jalapæ, *N. F.;* Pilulæ Catharticæ Vegetabiles (from Resin), *N. F.;* Pulvis Hydrargyri Chloridi Mitis et Jalapæ, *N. F.;* Syrupus Sennæ Aromaticus, *N. F.*

JUGLANS. N. F.

JUGLANS [Butternut Bark]

"Juglans is the dried inner bark of the root of *Jugulans cinerea* Linné (Fam. *Juglandaceæ*) Juglans contains not more than 2 per cent. of adhering wood or other foreign organic matter." *N. F.*

Oil Nut; White Walnut; Ecorce de Noyer gris, *Fr.;* Graue Wallnussrinde, *G.*

J. cinerea is a tree extending in rich woods from New Brunswick to the mountains of Georgia and west to the Dakotas, East Kansas and Arkansas. It possesses rough gray bark and alternate imparipinnate leaves with 7 to 17 ovate-lanceolate leaflets having serrate margins and pubescent beneath. The fruit is an elongated ovate drupe containing a sweet edible oily kernel. The immature fruit is sometimes pickled for food purposes, and, when ripe, affords in its kernel a grateful article of food. The bark is used for dyeing wool a dark-brown color, though inferior for this purpose to that of the black walnut. It is said to be rubefacient when applied to the skin. The inner bark is the medicinal portion, that of the root being considered most efficient. It should be collected in autumn. The crude drug comes chiefly from North Carolina, Virginia and Michigan.

On the living tree, the inner bark, when first uncovered, is of a pure white, which immediately on exposure becomes a fine lemon color, and ultimately changes to deep brown. It has a fibrous texture.

Description and Physical Properties.—"*Unground Juglans.*—In quills, curved strips, or in chips, from 3 to 10 mm. in thickness; of a deep brown color on both surfaces and throughout, except for the faint, intersecting, whitish, radial, and tangential lines shown in the transverse section; outer surface smooth, somewhat warty; inner surface smooth and striate, bearing fragments of thin stringy fibers; fracture short, rather weak, somewhat fibrous. Odor faintly aromatic; taste bitter, astringent, somewhat acrid.

"*Structure.*—Outer bark, if present, exhibiting several layers of well developed cork cells containing starch or tannin or rosette crystals of calcium oxalate, and groups of stone cells; inner bark with numerous interrupted zones of bast fibers, a few crystal fibers and sieve tissue, alternating with layers of parenchyma cells containing starch or calcium oxalate or tannin, and traversed by somewhat wavy medullary rays, the latter mostly 1–4 cells wide.

"*Powdered Juglans.*—Dark brown; numerous rosette crystals of calcium oxalate, up to 0.055 mm. in diameter; simple rounded or occasionally 2- to 4-compound starch grains, the individual grains up to 0.015 mm. in diameter, sometimes with a cleft through the center; stone cells, some with thick walls, with simple or branching pores, up to 0.125 mm. long and 0.070 mm. wide, sometimes with reddish contents; long thick-walled fibers up to 0.032 mm. in width, occasionally associated with crystal fibers, the latter containing prisms of calcium oxalate from 0.010 to 0.050 mm. in length; parenchyma cells containing starch, calcium oxalate, tannin or oily drops; fragments of tissue composed of polygonal cells having yellowish brown walls, some with reddish-brown contents." *N. F.*

E. D. Truman (*A. J. P.,* 1893, 426) made proximate analyses of the root bark and the trunk bark for comparison. In the trunk bark, instead of the crystallizable juglandic acid, he found an uncrystallizable acid and a crystalline resin. Tanret and Villers isolated from the leaves a carbohydrate, *nucite,* which has since been shown to be identical with *inosite.* Tanret (*Jahresb. f. Pharm.,* 1876, 198) believed he had obtained an alkaloid from walnut leaves, which he proposed to call *juglandine.*

Extractum Juglandis. U. S. 1890. *Extract of Juglans.* "Juglans, in No. 30 powder, *one thousand grammes;* Diluted Alcohol, *a sufficient quantity.* Moisten the powder with *four hundred cc.* of Diluted Alcohol, and pack it firmly in a cylindrical percolator; then add enough Diluted Alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding Diluted Alcohol, until *three thousand cc.* of tincture are obtained, or the Juglans is exhausted. Distil off the Alcohol from the tincture by means of a water-bath, and evaporate the residue, on a water-bath, to a pilular consistence." *U. S.*, 1890.

Several products of *Juglans regia* L., or common European *walnut,* are used medicinally in Europe. The hull of the fruit has been employed as a vermifuge from the times of Hippocrates, and has been recommended in *syphilis* and for old *ulcers.* The expressed oil of the fruit has been deemed efficacious against the *tapeworm,* and is also used as a laxative injection. The leaves, long occasionally employed for various purposes in both regular and domestic practice, are astringent and bitter. For an exhaustive chemical examination of black walnut leaves by Miss L. J. Martin, see *A. J. P.,* 1886, p. 468. The leaves of *J. nigra* L. (*black walnut*), and those of *J. cinerea,* probably possess the same properties.

In 1872 Thiebaud found in the bark of the walnut tree a volatilizable acid—which he called *juglandic acid*—forming bright orange yellow crystals and apparently related to chrysophanic acid. According to Maisch this is identical with *nucin* (or *juglon*) which is found in pericarp of the European walnut (*A. J. P.,* 1874, p. 167).

It is generally believed that nucin of Vogel and *regianin* of Phipson are identical with juglon. *Juglon,* $C_{10}H_6O_3$, the characteristic constituent of the bark of *Juglans regia,* has been prepared synthetically by Bernthsen and Semper, and is now recognized as *a-oxynaphthoquinone,* $C_{10}H_5(OH)O_2$, as it can be made from dioxynaphthalene by the action of chromic acid mixture. It is in brownish-red, crystalline needles having a faint odor of walnut hulls, and is sternutatory. (*B. Chem. G.,* 1887, 934.)

Uses.—Juglans is a mild cathartic resembling rhubarb in its action, but less certain. It was much used during our Revolutionary war as an habitual laxative, and was especially esteemed by Rush in the treatment of *dysentery* and *hepatic congestions.*

Dose, from thirty to sixty grains (2–4 Gm.).

Off. Prep.—Fluidextractum Juglandis, *N. F.;* Elixir Cascaræ Sagradæ Compositum, *N. F.*

JUNIPERUS. N. F.

JUNIPER BERRY Junip.

"Juniper Berry is the carefully dried ripe fruit of *Juniperus communis* Linné (Fam. *Pinaceæ*). Juniper Berry contains not more than 10 per cent. of immature or discolored berries and not more than 3 per cent. of foreign organic matter." *N. F.*

Juniperi Fructus, *P. G.;* Baccæ Juniperi; Genevrier, *Fr. Cod.;* Genièvre, Baies de Genièvre, *Fr.;* Gemeiner Wachholder, Wachholderbeeren, *G.;* Ginepro, *It.;* Enebro, Bayas de Enebro, *Sp.*

Juniperus communis L. is an evergreen shrub, usually small, but sometimes twelve to fifteen feet high, with numerous very close branches, and thin, acerose leaves—occurring in 3's—from 12 to 21 mm. long and grayish on lower surface. The fruit is a subglobular galbulus containing three bony seeds.

The common juniper is a native of Europe and the northern regions of Asia and North America. *J. communis* var. *depressa* Pursh, the variety which thrives northward, is a trailing shrub, seldom more than 2 to 4 dm. high, spreading in all directions, throwing out roots from its branches, and forming beds which are often many rods in circumference. Its leaves are up to 13 mm. long, green above, sharp-pointed, with a white stripe on their under surface. The common juniper flowers in May, but does not ripen its fruit until late in the following year. All parts of the plant contain a volatile oil, which imparts to them a peculiar flavor. The wood has a slight aromatic odor, and was formerly used for fumigation. A terebinthinate juice exudes from the tree and hardens on the bark. This has been erroneously considered as identical with the gum known commercially as *sandarach.*

The berries, as the fruit is commonly called, were formerly occasionally brought to the Philadelphia market from New Jersey. But, though equal to the European in appearance, they are inferior in strength, and are not much used. The best come from the south of Europe, particularly from Leghorn, Italy.

Description and Physical Properties.—"*Unground Juniper Berry.*—Nearly globular, about 8 mm. in diameter; externally smooth, shining black-brown to purplish black with a blue-gray bloom, at the apex a three-rayed furrow marks the cohesion of the three fleshy bracts forming the outer tissue; internally loosely fleshy, greenish brown, containing numerous large schizogenous cavities; seeds usually three, triangular ovate, hard, brown, with large uneven oil glands on the surface. Odor aromatic; taste sweet, pleasant, terebinthinate, slightly bitter.

"*Structure.*—Pericarp consisting of an epidermis of a row of rounded polygonal cells which contain a brownish granular substance and which become at the sutures of the bracts, blunt papillæ; a hypodermis of two or three rows of brownish red, collenchymatous cells; a fleshy portion composed of irregular loose parenchyma with large oval canals and traversed by fibro-vascular bundles with areolated fibers; inner layer of the pericarp of small thick walled cells many containing crystals of calcium oxalate; seed coat with a ring of stone cells of 2 to 10 rows, with very thick pitted walls, many enclosing prismatic crystals of calcium oxalate;

endosperm and embryo of the seed rich in fixed oil and aleurone grains.

"*Powdered Juniper Berry.*—Dark brown; fragments composed of stone cells, the latter up to 0.145 mm. in length; monoclinic prisms of calcium oxalate occurring either singly or within parenchyma or stone cells, from 0.005 to 0.030 mm. in length occasionally larger; numerous fragments made up of polygonal cells of the epicarp; endosperm tissue of cells containing aleurone grains and oil globules; fragments of oil glands and resin masses." *N. F.*

Juniper berries owe their medicinal virtues to a volatile oil. (See *Oleum Juniperi.*) The proportion of volatile oil is most abundant in those which have attained their full growth and are still green, or in those which are on the point of ripening. In the latter Trommsdorff found 1 per cent. of the oil. In those perfectly ripe it has been partly changed into resin, and in those quite black, completely so. They are very largely consumed in the preparation of gin.

The tops of juniper were formerly directed by the Edinburgh and Dublin Colleges. Their odor is balsamic, their taste resinous and bitterish, and they possess similar virtues with the berries.

Uses.—The therapeutic properties of juniper berries are those of the volatile oil (see *Oleum Juniperi*). They are chiefly used as an adjuvant to the so-called alterative diuretics in the treatment of *cystitis* and similar complaints. For most purposes the oil is to be preferred. An infusion made by macerating an ounce of the bruised berries in a pint of boiling water is sometimes employed.

Dose, one drachm (4 Gm.).

Off. Prep.—Fluidextractum Juniperi, *N. F.;* Fluidextractum Buchu Compositum, *N. F.;* Elixir Buchu Compositum, *N. F.;* Elixir Buchu, Juniperi et Potassii Acetatis, *N. F.*

KALADANA. Br.

KALADANA [Semen Pharbitidis, Pharbitis Seeds]

"Kaladana consists of the dried seeds of Ipomœa hederacea, *Jacq.*" *Br.*

Closely allied to *Ipomœa hederacea* is *I. muricata,* the seeds of which are largely imported into Bombay, from Persia, under the name of *tukm-i-nil.* The juice of this plant is employed to destroy bedbugs, and the seeds are said to be identical in their medicinal properties with those of the official plant.

Ipomœa hederacea Jacq. (*I. cœrulea* Kon.; *Pharbitis Nil,* Choisy) is a twining annual plant belonging to the *Convolvulaceæ.* It has large blue flowers whence the specific name *Nil* which signifies, in Hindustani, blue. The leaves are three-lobed and the plant, while common throughout India, is found throughout the tropical regions of both hemispheres. Flückiger found it to contain 8.2 per cent. of resin which corresponded in its various properties to the resin of jalap.

Kaladana seeds are in the form of the segment of a sphere, black, somewhat hairy, weighing from one-half drachm to nearly one drachm. They are described by the British Pharm., 1914, as follows: "Seeds in the form of a segment of a sphere; usually about five millimetres long, but sometimes much smaller; nearly black. In transverse section, minute dark resin-cells in the plaited cotyledons. Slight odor; taste acrid." *Br.*

According to Kassner (*In. Dis.,* London, 1924) the term "Kaladana" signifies black seed in Hindustani and is applied in India to a number of unrelated seeds including, besides that official, those of the *Peganum Harmala* L. (*Rutaceæ*), the *Ocimum Basilicum* L. (see Part II) as well as other species of *Ipomœa.*

He has made an elaborate study of the histology of the seeds of *Ipomœa hederacea* and of the *I. muricata* Jacq. which are often substituted for the official. The most important diagnostic feature is the epidermis; the official seeds may be distinguished from all the others by the characteristic shape of the wavy walls and the dimensions of the epidermal cells in surface section and by the presence of sparsely scattered diagnostic trichomes of a restricted size.

Kassner found these seeds to contain about 15.7 per cent. of crude resin and about 12.4 per cent. of fixed oil. He found also indications of a saponin and of glucosidal matter. The true resin of kaladana he believes is non-glucosidal. He found that in doses of four grains (0.25 Gm.) this resin produced copious purgation, but that the glucosidal material even in double this dose had no effect. The resin as prepared by the official process is a mixture of the active and inert resinous material. What he calls the true resin was obtained by extracting with alcohol seeds which had been previously exhausted with acetone. The material so obtained he states is not convolvulin.

For literature on the subject of kaladana see Kassner's paper.

Uses.—Kaladana seeds were used by the Arabian physicians, under the name of *Habbun-nil,* and have been recommended as a safe and active cathartic by various English physicians resident in India. Their action is probably similar to that of jalap.

Dose, thirty to forty-five grains (2–3 Gm.).

Off. Prep.—Kaladanæ Resina, *Br.;* Pulvis Kaladanæ Compositus, *Br.;* Tinctura Kaladanæ, *Br.*

KALADANÆ RESINA. Br.

KALADANA RESIN [Pharbitisin]

"Kaladana Resin is a mixture of resins obtained from Kaladana." *Br.*

The resin is prepared from Kaladana by a process similar to that employed in isolating the resin from jalap. It is as follows: "Exhaust coarsely powdered Kaladana with Alcohol (90 per cent.). Recover most of the alcohol by distillation; pour the concentrated solution thus obtained into eight times its volume of Distilled Water; allow the resin that separates to subside, wash with Distilled Water, and dry at a gentle heat." *Br.*

It is officially described as "in brownish, opaque fragments, translucent at the edges; brittle, breaking with a resinous fracture; readily reduced to a grey powder. Somewhat disagreeable odor, especially when warmed; taste sweetish, acrid. Readily soluble in *alcohol* (90 per cent.); almost insoluble in *benzene, ether, chloroform,* or *carbon disulphide.* When 1 gramme of the powdered Resin is triturated with 20 millilitres of *water* and filtered, the filtrate is almost colorless. A solution of 0.1 gramme in 10 millilitres of *solution of sodium hydroxide,* boiled for a few moments and cooled, when acidified with *hydrochloric acid,* may become opalescent but not immediately turbid (absence of certain other resins)." *Br.*

For further information about this resin see under *Kaladana.* It is used as cathartic.

Dose, two to eight grains (0.12–0.5 Gm.).

KAOLINUM. N. F., Br.

KAOLIN

"A native hydrated aluminum silicate, powdered, and freed from gritty particles by elutriation." *N. F.*

"Kaolin is a native aluminium silicate, powdered, and freed from gritty particles by elutriation." *Br.*

Terra porcellanea; Porcelain Clay, Bolus Alba; Terre à porcelaine, *Fr.;* Porcellanerde, Porcellanthon, *G.*

The term "clay" is applied rather loosely to various forms of earth which with water form more or less tenacious and plastic masses. The clays, which appear to owe their origin to the decomposition of rocks, are to be sharply distinguished from diatomaceous earth which is composed of the mineral constituents of microscopic algæ (see *Terra Silicea Purificata*); they differ not only in their physical properties, but also in their chemical composition. The clays proper have for their basis aluminum silicate and contain various quantities of sand, alkaline earths and other ingredients. Various forms of clay have been used in the arts and in medicine and are denominated by adjectives derived from the purpose for which they are employed. Kaolin or *china clay* is a hydrated aluminous silicate; *pipeclay* is a very white substance containing a somewhat larger percentage of silica; brick clay contains sand and some ferruginous material to which it owes its color. *Fuller's earth* is a non-plastic form of clay, so-called because of its use in fulling cloth. *Shale* is a clay rock which tends to split into thin lamina; *marl* is a clay which contains a large amount of calcareous matter with some potassium and phosphate. *Terra Sigillata* was a form of clay from Asia Minor once so highly esteemed that its production was only permitted under governmental authority and it was sent to the market in masses each bearing the imprint of the seal of the authorities; hence the name.

Nearly all of the clays will absorb a considerable amount of water, but some of them in addition have the power of *ad*sorbing solid constituents; that is they will remove dissolved substances from solution. By virtue of this adsorbtive power they may act as decolorizing agents and will also remove many alkaloids and apparently even bacterial toxins from aqueous solutions. To what this adsorbing power is due is, at present, somewhat obscure although it appears to be in part dependent upon the colloidal nature of the earth. *Lloyd's reagent* is a form of clay which has an extraordinarily high adsorptive property. On account of this adsorptive power for active principles and vegetable colors, clays should never be used as filtering or clarifying mediums without some preliminary experiments to determine the effect upon the finished preparation which is likely to be rendered inert.

Because of its property of absorbing large amounts of liquid, fuller's earth is used for many pharmaceutical purposes, especially in the preparation of pills. Fantus (*J. A. M. A.,* 1915, lxiv, p. 1838) has shown that there is considerable difference in the adsorbing power of various substances sold under the name of fuller's earth. (See also Jensen, *P. J.,* 1920, cv, 97.)

Kaolin, $Al_2(SiO_3)_3 + Al_2O(OH)_4$, occurs in abundant deposits as a decomposition product of felspar; the latter is a double silicate of aluminium and alkali, and in its weathering, the alkali is gradually eliminated. A pure kaolin contains approximately 47 per cent. of silica, 40 per cent. of alumina, and 13 per cent. of water.

Thomas J. Keenan, in an interesting article in the *Am. Drug.,* 1914, p. 55, gives a history of kaolin and its uses and points out the uncertainty of the product, due to the loose application of the name and proposes that the name be restricted to a compound having the composition $H_2Al_2Si_2O_8 + H_2O$.

Pure kaolin is almost infusible, but the presence of impurities, notably undecomposed felspar, increases its fusibility greatly. On the other hand, fire clays which are infusible are kaolins containing a considerable amount of free silica.

Large deposits of kaolin have been recently opened in Florida. It is now used extensively for clarifying oils, such as lard and cotton seed oils and mineral lubricating oils.

Description and Physical Properties.—"Kaolin occurs as a soft, white or yellowish white powder, or in lumps, insoluble in water, and in cold dilute acids and solutions of the alkali hydroxides. It has an earthy or clay-like taste. When moistened with water, Kaolin assumes a darker color and develops a marked clay-like odor.

"Mix 1 Gm. of Kaolin with 10 cc. of distilled water and 5 cc. of sulphuric acid in a porcelain dish; no effervescence occurs. Evaporate the mixture until the excess of water is removed, and further heat the residue until dense white fumes of sulphuric anhydride appear, then add 20 cc. of distilled water, boil for a few minutes and filter; there remains on the filter a gray residue of impure silica. To one-half of the filtrate just obtained add ammonia water; a gelatinous precipitate of aluminum hydroxide is obtained which is insoluble in an excess of the reagent. To a remaining half of the filtrate add sodium hydroxide T.S.; a gelatinous precipitate is produced which is completely or almost completely soluble in an excess of the reagent. Rub 2 Gm. of Kaolin in a mortar with 10 cc. of distilled water; the mixture does not acquire more than a slight reddish tint on the addition of 0.5 Gm. of sodium salicylate (*iron*). Ignite Kaolin at a red heat; not less than 85 per cent. of a non-volatile residue remains." *N. F.*

The British Pharmacopœia describes it as "a soft whitish powder, insoluble in *water,* or in diluted acids. When the product of its fusion with alkalies is digested with *water,* the filtered solution acidified with *hydrochloric acid,* evaporated to dryness, and the residue digested with *diluted hydrochloric acid,* a deposit of silica is obtained, and the supernatant acid solution yields the *reactions* characteristic of aluminium." *Br.*

Uses.—Various forms of clay have been used in medicine from time immemorial either as external or internal remedies. The value of these appears to reside in their absorbing properties, although there are some who attribute to them direct antiseptic action. There is no convincing proof of this assertion and the almost complete insolubility of clay renders it highly improbable. It is of service in various local infections, but its value in these conditions is generally explicable on mechanical grounds. It has been used with apparently good results in *suppurating wounds, tuberculous ulcers, weeping eczema, ozena, leucorrhea,* and similar conditions where its absorbent powers make it valuable. The claim is made that in many of these conditions because of its very fine pulverization it penetrates into the infected area and carries with it various antiseptics which may have been added. Rappaport (*J. A. M. A.,* 1916, lxvi, 943) reports that the application of thoroughly dried and finely powdered kaolin is useful for the removal of *diphtheria* bacilli and other bacteria from the throat and nose. It has been used internally in *Asiatic cholera* (see Walker, *L. L.,* Aug. 6, 1921), *gastro-enteritis,* and *dysentery.* Its effects in the latter conditions are probably those of a protective to the mucous membrane. Its virtues in these conditions appear to be due in part to the adsorption of the irritant secretions, and in part to its protective influence upon the mucous membrane. According to Hess (*J. A. M. A.,* 1916, lxvi, p. 106), fuller's earth surpasses either bismuth or chalk in lessening diarrhea. Probably by the formation of colloidal compounds it delays the absorption of toxic alkaloids from the alimentary tract, and Fantus has shown that it is an effective chemical antidote in the treatment of *strychnine poisoning.* While the adsorption of some alkaloids is delayed more than others, it probably has a wide field of usefulness in poisoning. (See also Clowes and Walters, *J. A. M. A.,* 1920, lxxv, 655.)

Kaolin is also widely used in the form of the cataplasm (see *Cataplasma Kaolini*) as a carrier of heat and moisture in various local inflammations instead of poultices. It is also recommended because of its mechanical properties as an aid in cleansing the hands of the surgeon. Kaolin is not easily affected by most chemical reagents, and it forms a good diluent or excipient for silver nitrate, potassium permanganate, or other salts which are decomposed by organic substances.

Dose, one-half to two ounces (15.5–60 Gm.) several times a day.

Off. Prep.—Cataplasma Kaolini, *N. F.*

KAVA. N. F. (Br.)

KAVA [Methysticum, Kava Kava]

"Kava consists of the dried rhizome and roots of *Piper methysticum* Forster (Fam. *Piperaceæ*). Kava contains not more than 1 per cent. of foreign organic matter." *N. F.*

"Kava Rhizome is the peeled, dried, and divided rhizome of Piper methysticum, *Forst. fil.*" *Br.*

Kavæ Rhizoma, *Br.;* Kava Rhizome.

The genus *Piper* includes a large number of sub-tropical plants, which are mostly shrubs, and rarely herbs or trees. A number of the species are of great economic importance. *Piper methysticum* is a shrub, several feet high, indigenous to many of the South Sea Islands. The plant has cordate, acuminate leaves and very short axillary spikes of flowers. The natives prepare a fermented liquor from the upper portion of the rhizome and the base of the stems.

Description and Physical Properties.—"*Unground Kava.*—Consisting of a large, irregular knotty crown, often 12 cm. or more in diameter, from which proceed numerous, long, cylindrical, tough, nearly simple roots, which tend to fray out into bare, separated fibrovascular bundles; sometimes cut into irregular angular pieces; the crown soft, light, spongy, and granular and very starchy; externally dark brown or blackish, the crown frequently partly scraped and light brown to light gray; internally white. Odor faint but characteristic; taste aromatic and pungent, slightly bitter, more or less local anæsthesia resulting.

"*Powdered Kava.*—Whitish; exhibits numerous, simple, or 2- to 3-compound starch grains, the individual grains being up to 0.045 mm. in diameter, many with radial clefts or triangular fissures at the center; yellow resin and oil cells; narrow sclerenchymatous fibers with thin, strongly lignified walls; tracheæ with scalariform or reticulate markings, up to 0.150 mm. in width;

few nearly isodiametric wood parenchyma cells from the remains of the stem." *N. F.*

The Br. describes it as "in whitish or light brownish-grey irregularly cuboid or roughly wedge-shaped fragments from which the periderm has been sliced off; from one to five centimetres thick. In transverse section, usually exhibiting a central dense pith, surrounded by a distinct ring of narrow, radiating, vascular bundles separated by relatively broad, paler, medullary rays. Fracture starchy. Slight agreeable odor; taste pungent and bitter." *Br.*

The pharmacognosy of this drug has been written up by Semenow in *Ap. Ztg.*, 1890. Hoffstadt has made an extensive study of the stem anatomy of *Piper methysticum.* She finds that it contains peripheral and pith bundle systems, the latter in two rows, differing from *P. umbellata,* a Mexican species which possesses but one row of pith bundles and mucilage canals extending through the center of the stem (*A. J. P.*, 1916, p. 485). Powdered Kava consists of numerous starch grains which are either single or 2- to 3-compound, the individual grains having central radial clefts with triangular fissures varying from 0.006 to 0.035 mm. in diameter. The sclerenchymatous fibers have thin walls which are strongly lignified. The tracheæ have scalariform or reticulate markings. The oil cells frequently contain a yellowish resin. The drug should not yield more than 8 per cent. of ash. (See also True, *Ph. Rev.*, xiv.)

Constituents.—Gobley isolated from kava root a crystalline principle, *methysticin,* or *kavahin,* $C_{15}H_{14}O_5$, which is without odor and taste, and is probably inert. It is the methyl ester of p-piperonyl acetic acid, and when purified forms silky, lustrous needles melting at 138° to 139° C. Kavahin differs from piperin and cubebin in being colored red by hydrochloric acid, the red color fading on exposure to air into a bright yellow, and in being colored by strong sulphuric acid a purplish violet, which passes into green. In 1844 Morson discovered a greenish-yellow, strongly aromatic and acrid resin which he called *kawine.* Lewin (*A. J. P.*, 1886) separated it into two resins, of which the β-resin is greasy and of a reddish-brown color, appearing in mass almost black. This is less active than the α-resin, which is yellowish-brown, has the characteristic odor of the drug, is freely soluble in alcohol, and placed upon the tongue produces a burning sensation followed by local anesthesia. Borsche and Gerhardt (*Riedels Archives,* 1914, 50) report the presence of a glucoside, *yangonin.* Lavialle (*L'Union Pharm.*, Jan., 1889) claims to have obtained an alkaloid, *kavaine.* (See also *Proc. A. Ph. A.*, 1897, 564.)

Murayama and Mayeda have taken up the investigation of *kava acid* previously reported by Murakami, and find it to contain a methoxyl group and to have the formula $C_{15}H_{16}O_2$. Upon hydrolysis with alcoholic solution of potassium hydroxide it yields benzaldehyde and a substance having the composition $C_{14}H_{16}O_3$. From the mother liquor of *kava acid* they obtained a crystalline compound, $C_{14}H_{18}O_4$, melting at 102°, which they termed *beta kava acid.* Borsche and Roth (*B. Chem. G.*, 1921, liv, 2229) report kava acid as having the composition $C_{13}H_{12}O_3$, melting at 164° C. and believe it to be an isomer of *cinnamylodeneaceto-acetic acid.*

Uses.—Under the names of *Ava* or *Kava* the natives of the Sandwich Islands have used as an intoxicant a beverage prepared from kava rhizome. The intoxication is wholly unlike that caused by alcohol, being of a silent and drowsy character, accompanied by incoherent dreams, with great loss of muscular power, which is probably due to the action of kava resin upon the spinal cord.

The physiological action of kava and its resin has been investigated by L. Lewin (*Piper Methysticum,* Berlin, 1886), and David Cerna (*T. G.*, 1891). The phenomena which follow the hypodermic injection of the fluidextract of kava or of a solution of its resin are, anesthesia at the point of injection, followed, after absorption, by general paralysis, due to a direct action on the motor side of the spinal cord; the motor nerves and the muscles remain intact. The local anesthesia is due to a paralysis of the sensory nerve filaments and when the resin is brought in contact with the mucous membranes there is a burning pain, followed in time by a complete loss of sensibility, which is remarkably permanent, since Lewin found that from six to seven minims of a solution of kava injected beneath the skin produced a complete loss of sensibility in the surrounding area, which did not pass away for eight days. (*D. M. Ztg.*, Feb., 1886.) The action of the drug upon the circulation is subordinate to its nervous influence, but according to the experiments of Cerna it does stimulate the heart, although it decreases the number of pulsations by stimulating the inhibitory nerve centers. The same investigator found that at first it stimulates, afterwards depresses, and finally paralyzes the respiratory center. The insolubility and irritant action of kava resin has lessened its use as a practical local anesthetic.

As long ago as 1857 kava root was employed in the treatment of *gonorrhea,* and there is much testimony to its value both in the acute and the chronic form of the disease, as well as in *cystitis, vaginitis, leucorrhea, nocturnal incontinence,* and similar conditions of the genito-urinary tract. It is rather too stimulating to be suitable for acute conditions.

Under the name of *gonosan* a twenty per cent. solution of kava resin in oil of sandalwood is used internally in the treatment of *gonorrhea.* The preparation is marketed in capsules containing 0.3 Gm. of which two to four may be given several times a day. (For the methods of determining kava resins in this and similar preparations, see *Ph. Ztg.*, 1914, 284.)

Dose, of kava rhizome, from fifteen to forty-five grains (1–3 Gm.).

Off. Prep.—Extractum Kavæ Liquidum, *Br.;* Fluidextractum Kavæ, *N. F.*

KINO. U. S., Br.

KINO

"Kino is the dried juice obtained from the trunk of *Pterocarpus Marsupium* Roxburgh (Fam. *Leguminosæ*). Kino yields not less than 45 per cent. of alcohol-soluble extractive and not less than 80 per cent. of water-soluble extractive." *U. S.* "Kino is the juice obtained from incisions in the trunk of Pterocarpus Marsupium, *Roxb.*, heated to boiling and evaporated to dryness. Known in commerce as East Indian, Malabar, Madras, or Cochin kino." *Br.*

Gummi (s. Resina) Kino; Indian Kino, Malabar Kino; Kino de l'Inde, *Fr. Cod.;* Kino, *G.;* Goma quino, *Sp.*

The term kino or "kano" was originally applied to a vegetable extract or inspissated juice taken to London from the western coast of Africa, and introduced to the notice of the profession by Fothergill. Vegetable products obtained from various other parts of the world, resembling kino in appearance and properties, afterwards received the same name, and some confusion and uncertainty still exist, in relation to the botanical and commercial history of the drug. We shall first consider the general properties of official kino, then the several varieties.

The official variety is that known commercially as *East India, Malabar, Madras,* or *Cochin* kino. It is the product of *Pterocarpus Marsupium,* a lofty tree growing upon the mountains of the Malabar coast of Hindostan and in Ceylon. It possesses alternate, imparipinnate leaves with 5- to 7-notched leaflets, pale yellow flowers and orbicular legumes, each containing one seed. The red juice of the kino tree occurs in rows of short cells, axially arranged in the inner bark. Vertical incisions with oblique ones running into them are made in the bark and the juice, upon flowing out, is collected in cups or other receptacles. It is evaporated in the sun to the consistency of a hard dark mass and broken into small fragments, in which condition it is packed in wooden boxes for exportation. The drug comes to the United States either direct from Bombay or through London.

From a communication by F. Mason, it appears that kino is also collected in the Tenasserim provinces, in Farther India, and has been exported from Maulmain to Europe. It is produced by a tree called *Pa-douck,* which Christison recognized from a description furnished to him by Begbie, of Maulmain, as *Pterocarpus Marsupium,* so that this kino has the same origin as that from Malabar. *Pterocarpus indicus,* of the Mauritius Islands, where it is known as *sang-dragon,* also yields a red kino to commerce.

Description and Physical Properties.—"*Unground Kino.*—Small, brittle, angular fragments, usually less than 10 mm. in diameter, varying in color from dark reddish-brown to reddish-black; inodorous; taste very astringent; upon mastication coloring the saliva pink.

"*Powdered Kino.*—Dark red; in angular fragments, with a glass-like, conchoidal surface, the thinner pieces translucent, yellowish-red or brownish-red; upon mounting in water, the fragments become rounded and gradually disintegrate, leaving colorless, granular particles among which are rod-shaped bacteria and a very few cellular fragments; in an alcohol mount, the red color of the fragments deepens, the translucency increases, and the sharp angular outlines are preserved while solution takes place. An aqueous solution of Kino has a faint acid reaction, gives a dark green precipitate with ferric chloride T.S. and a reddish-violet color with an aqueous solution of an alkali.

"**Assay.**—Proceed as directed under alcohol-soluble extractive, and water-soluble extractive." *U. S.*

"In small, angular, glistening, opaque, reddish-black, brittle fragments; transparent and ruby-red in thin laminæ. Inodorous; taste very astringent. Almost entirely soluble in *alcohol* (90 per cent.), slowly and incompletely soluble in cold *water,* not less than 75 per cent. soluble in boiling *water,* the solutions being deep red in color. Almost entirely insoluble in *ether.* An aqueous solution (1 in 20) yields a voluminous reddish precipitate with dilute mineral acids, and, when largely diluted with *water,* a greenish-black precipitate with *T. Sol. of ferric chloride.* Ash not more than 2.5 per cent. In India and the Eastern Divisions of the Empire, Butea Gum (Buteæ Gummi) may be employed in making the official preparations for which Kino (distinguished in commerce as East Indian, Malabar, Madras, or Cochin kino) is directed to be used." *Br.*

If in large masses, it may be reduced without difficulty into minute fragments. It is without odor, and has a bitter, highly astringent taste, with a somewhat sweetish after-taste. It burns with little flame, and does not soften with heat. It imparts its virtues and a deep red color to water and alcohol, but is nearly insoluble in ether. Cold water forms with it a clear infusion. Boiling water dissolves it more largely, and the saturated decoction becomes turbid on cooling, and deposits a reddish sediment. The tincture is not disturbed by water. When long kept, it often gelatinizes, and loses its astringency. (See *Tinctura Kino.*) Edmund White made an investigation into the cause of the gelatinization of tincture of kino (*P. J.,* May, 1903), from which it appears that this phenomenon was due to the presence in the kino of an enzyme belonging to the oxydases, and that this enzyme may be destroyed by boiling, a belief which seems to be shared by the editors of the Br. P. which provides that the juice shall be heated to the boiling temperature before evaporation.

Constituents.—The therapeutic value of kino is due to the presence of *kino-tannic acid,* a non-glucosidal tannin that gives a green coloration with ferric salts. The proportion of this principle in a good quality of drug is between 70 and 85 per cent., although much lower figures have been reported.

Kino-red is a phlobaphene which results from the oxidation of kino-tannic acid. Apparently there is a ferment present in kino which produces this change, so that kino loses its astringent properties when kept, both its aqueous and alcoholic solutions becoming gelatinous and non-astringent. It is stated that if these solutions are previously heated to the boiling point, which would destroy any enzyme present, this change will not take place. There is present also a small amount of a colorless non-astringent principle called *kinoin* discovered by Etti, with the formula $C_{28}H_{24}O_{12}$. The subtraction of H_2O from this formula gives $C_{28}H_{22}O_{11}$ which is the kino-red and subtraction of another H_2O gives $C_{28}H_{20}O_{10}$, which is known as *dianhydride.* All of these substances are found in small quantities in the natural juice. (See Allen's *Commercial Organic Analysis;* also White, *P. J.,* 1903; and Gathercoal, *J. A. Ph. A.,* 1924, xiii, 103.) Small amounts of pyrocatechin and of protocatechuic acid have also been found in kino.

It is said that catechu, broken into small fragments, has sometimes been sold as kino. Genuine kino is sometimes substituted by the extract of krameria. The latter is more brittle and dissolves more quickly in water.

Unofficial Kinos.—A number of astringent extracts, some from sources not related to the official kino, have from time to time been used in medicine. The more important of these are noted below.

African Kino.—The original kino employed by Fothergill is now known to be the product of a tree growing in Senegal, the *Pterocarpus erinaceus* of Lamarck and Poiret. A particular account of *P. erinaceus* and its concrete juice, with a figure, by W. F. Daniell, is contained in the *P. J.,* 1854. The importation of African kino has long ceased. In 1896, however, a consignment of African kino reached London. It was examined by E. M. Holmes (*C. D.,* 1896, 226). It is said to be still used by the Portuguese of Angola, under the name of *Sangue de Drago.* As described by Fothergill, the African kino, for which he proposed the name of *gummi rubrum astringens Gambinense,* was in lumps of about the size of those of gum Senegal or dragon's blood, and so similar in appearance to the latter that a good judge might easily be deceived. These lumps were hard, brittle, opaque, and almost black, but minute fragments were reddish and transparent like garnet. The drug was inodorous, of a strongly astringent and sweetish taste, and soluble in water to the extent of about five or six parts out of seven, forming a deep red astringent infusion.

West India or *Jamaica Kino.*—This is believed to be the product of the *Coccoloba uvifera* L. (Fam. *Polygonaceæ*), or *sea-side grape.* It grows in the West Indies and neighboring parts of the continent. The kino is said to be obtained by evaporating a decoction of the wood and bark, which are very astringent.

Although it has been many years since any large quantity appeared in our markets, it may occasionally be met. It is contained in large gourds, into which it was evidently poured while in a liquid or semi-liquid state, and then allowed to harden. When taken from the gourd it breaks into fragments of various sizes, upon an average about as large as a hazelnut, and having some tendency to the rectangular form. The consistence of these fragments is uniform, their surface smooth and shining, and their color a dark reddish-brown approaching to black. They are, however, neither so glistening nor so black as the East India kino. In mass they are quite opaque, but in thin splinters are translucent and of a ruby redness. They are readily broken by the fingers into smaller fragments, are easily pulverized, and yield a dull-reddish powder, considerably lighter colored than that of the East Indian variety. The West India kino is without odor, and has a very astringent, bitterish taste, with a scarcely observable sweetish after-taste. It adheres to the teeth when chewed, although rather less than the East Indian variety, and colors the saliva red. According to Kremel (*A. J. P.,* 1883) it contains pyrocatechuic acid but no kinoin. Robert Bridges found that cold water dissolved 89 per cent., and alcohol 94 per cent. The portion dissolved by alcohol and not by water was probably of a resinous nature, as it appeared to be viscid, and very much impeded the filtration of the aqueous solution. Considering the nature of this substance, the form of kino in which it was found is probably, like that from the East Indies, an inspissated juice.

South American or *Caraccas kino,* in appearance, taste, odor and other sensible properties closely resembles the West India variety. It is probable that they are derived from the same plant, as the *Coccoloba uvifera* grows as well upon the continent as in the islands. South American kino was found by Bridges to yield 93.5 per cent. to cold water, and 93 per cent. to alcohol; the want of a minute proportion of resinous matter in the South American kino is the only apparent difference between the two drugs.

Macaranga kino is obtained from *Macaranga Roxburghii* Wright, of the Deccan peninsula. It occurs in the form of odorless, tasteless tears or irregular masses. The tears have fibrous fractures and when immersed in water yield unravelling fibers giving the appearance of a sea anemone. According to Hopper, this kino yields from 6 to 15 per cent. of a peculiar tannin and is closely allied to Butea kino, from which it is distinguished by fibrous tears and the fact that it contains so much gum which swells without dissolving in water. (*P. J.*, lxvi, 616.)

Myristica Kino.—There has been produced in Southern India a kino consisting of smaller or larger angular pieces, of deep garnet color, in thin fragments, and having the general characteristics of Malabar kino; according to E. Schaer, it is a product of *Myristica malabarica,* of *M. fragrans,* and probably of other species of the genus. In all important respects these kinos are said to correspond with Malabar kino, but to be distinguishable by containing crystals of calcium tartrate. Myristica Kino is probably a distinctive product from the so-called *Syndai varnish,* a rich red fluid obtained from the *Myristica gibbosa* Hook. f., and employed in Assam as a varnish. This varnish is highly astringent and after exposure becomes perfectly impervious, the changes being due to the presence of a ferment or enzyme. As has been shown by D. Hooper (*P. J.,* June 20, 1903), Syndai varnish, if kept in corked bottles, gelatinizes in a few weeks.

Botany or *Blue Mountain kino* is obtained from *Angophora lanceolata* Cav. (Fam. *Myrtaceæ*) of Australia. *Colombo kino* is obtained from a number of species of *Angophora.* Hooper (*P. J.,* 1908, xxvii, 161) reports the occurrence of three new astringent plant juices or kinos. They are derived from *Jatropha Curcas,* from South Salem; *Xylia dolabriformis,* from Burma; and *Parkia insignis* ("*Myauk-tanyet*"), also from Burma.

Incompatibilities.—The aqueous solution is precipitated by gelatin, the soluble salts of iron, silver, lead, and antimony, mercuric chloride, and sulphuric, nitric, and hydrochloric acids. The precipitate with iron is of an olive or greenish-black color. The alkalies favor the solubility of kino in water, but essentially change its nature and destroy its astringency.

Uses.—Kino is powerfully astringent. In this country it is used chiefly in the treatment of *diarrhea,* not attended with febrile excitement or inflammation. It is often an excellent adjunct to opium and the absorbent medicines, and is a favorite addition to chalk mixture. It is occasionally employed as a local application in *leucorrhea* and in *passive hemorrhages.* The infusion may be made by pouring eight fluidounces of boiling water on two drachms of the extract, and straining when cool; aromatics may be added, if deemed advisable. The dose of this infusion is a fluidounce (30 cc.). The proportion of alcohol in the tincture renders it frequently an unsuitable preparation.

Dose, eight to thirty grains (0.5–2.0 Gm.).

Off. Prep.—Pulvis Catechu Compositus, *Br.;* Pulvis Kino Compositus, *Br.;* Tinctura Kino, *U. S., Br.*

KOLA. N. F.

KOLA [Cola]

"Kola is the dried Cotyledon of *Cola nitida* (Ventenat) Schott and Endlicher, or of other species of *Cola* (Fam. *Sterculiaceæ*). Kola yields not less than 1 per cent. of caffeine, and contains not more than 1 per cent. of foreign organic matter." *N. F.*

Kola Nuts; Semen (Nuces) Colæ; Cola, *Fr. Cod.;* Noix de Gourou, Café du Soudan, *Fr.;* Kolanuss, *G.;* Gooroo Nuts; Bichy Nuts; Bissy Nuts.

The *Cola acuminata* Schott and Endlicher (*Sterculia acuminata* Beauv.) is a large tree, indigenous to Guinea in western tropical Africa. It is largely cultivated in the West Indies and South America for the sake of its seeds, the present commercial supply of these coming chiefly from the Western Hemisphere. The fruit consists of 5 woody follicles, each of which contain 1 to 3 large white or crimson seeds, the kernels of which deprived of their seed-coats have long been used by the natives of Africa as a caffeinic stimulant under the name of *guru nuts.* It is stated that the negroes of Brazil use the seeds of the *Sterculia chica* A. St. Hil. and of the *S. striata* A. St. Hil. for similar purposes. Considerable of the kola nut of commerce is obtained from *Sterculia nitida* Vent., a West Indian tree.

Other species which are employed by the natives of Africa include the *Cola astrophora* Warburg whose seeds are red, the *C. alba,* whose seeds are whitish, and the *C. vera* Schumann, which is perhaps a hybrid of the two latter, its seeds being sometimes red and sometimes white.

Three varieties of *kola nuts* are said to be the product of *Cola acuminata.* The most valuable, the kola of Sakhala, is the largest, and is of a white color. The kola of Kassi, of Siarra, and of Touté, is of medium size, red or white. The kola of Maninian is small and red. Of the white kola there are two varieties, one whitish, resembling the kola of Sakhala but smaller; the other more or less rose-colored and larger.

Description and Physical Properties.—"*Unground Kola.*—Irregularly plano-convex, broadly oval, or approaching circular in outline, from 2.5 to 5 cm. in length, heavy, hard and tough; brown with the outer surfaces slightly wrinkled, the inner surfaces lighter and smoother; edges slightly incurved and sharp. Odorless; taste slightly astringent.

"*Powdered Kola.*—Reddish brown; numerous starch grains, some of which show alteration, the normal grains up to 0.045 mm. in diameter, the smaller ellipsoidal or spherical, the larger ellipsoidal or irregularly oblong and occasionally with a protuberance on one side; many of the larger grains show lamellæ and a circular hilum or a fissure through the center; parenchyma cells numerous, about 0.065 mm. in diameter, with reddish brown walls.

"**Assay.**—Place 6 Gm. of Kola, in fine powder, in a suitable flask or bottle, add 120 cc. of chloroform and shake. Allow to stand five minutes, then add 6 cc. of ammonia water and shake the mixture continuously during one hour, or intermittently (see Proximate Assays, Type Process A) during two hours. Allow the mixture to stand over night, again shake intermittently during one-half hour, then allow the drug to settle. Decant, or filter off through a pledget of purified cotton, 100 cc. of the chloroformic liquid, representing 5 Gm. of Kola and evaporate it to dryness. Treat the residue with 10 cc. of weak (about 1 per cent.) sulphuric acid with the aid of a gentle heat, allow to cool, filter through a small filter into a separator, and wash the dish and filter with successive small portions of distilled water until no test for alkaloid is obtained by acidulating a few drops of the filtrate strongly with sulphuric acid and adding iodine T.S. Now add ammonia water until the liquid is distinctly alkaline to litmus, and completely extract the caffeine with successive portions of chloroform, as shown by testing with iodine T.S. Evaporate the combined chloroform solutions, and dry the residue at 80° C. to constant weight. The weight is the amount of caffeine from 5 Gm. of Kola." *N. F.*

The so-called *male kola* is essentially distinct from kola, being said to be the fruit of a small tree, *Garcinia Kola* (Fam. *Guttiferæ* Heck.), and containing no caffeine. The fruit is oblong, about one and a half to three inches long and from three-quarters to one inch broad; it is trigonal in section with a readily removable thin testa of a reddish-yellow to dark brown color, covered by markings which resemble those on the seed coat of the nutmeg. It is bitter and astringent. In the section the microscope reveals a number of resinous masses surrounded by cells rich in starch.

The seeds of *Lucuma mammosa* Griesebach (Fam. *Sapotaceæ*), sometimes mixed with kola nuts, are recognized at once by their strong odor of prussic acid. Heckel and Schlagdenhauffen have observed the seeds of *Heritiera litoralis* Dryand (Fam. *Sterculiaceæ*) mixed with kola nuts. These *false kola nuts* contain no caffeine, and are nearly orbicular and flattened in shape, one of the fleshy, purplish-brown cotyledons being only half the size of the other. (*A. J. P.*, 1887, 446.)

Constituents.—The composition of kola has been frequently and thoroughly investigated, and conflicting reports have appeared in the literature concerning the principles which are present. The investigation by Heckel and Schlagdenhauffen (*P. J.*, 1883, xiv) reported caffeine 2.34 per cent., theobromine traces, protein 6.76 per cent., cellulose 29.83 per cent., ash 3.32 per cent., and undetermined amounts of fat, tannin, kola dextrose, gum, and coloring matter. These results were practically confirmed about ten years later by Uffelmann and Bomer, but in 1897 Knox and Prescott (*J. Am. C. S.*, xix, p. 63) made an investigation in which they showed that the caffeine existed partly in the free state and partly in combination as a tannate. The free caffeine they found to be present to the extent of 1.85 per cent. and the combined caffeine 1.78 per cent., and the total caffeine therefore was 3.64 per cent. They claimed that *kolanin* was a mixture of the tannates of caffeine and theobromine. Other authorities, working on the subject more recently, have suggested that *kolanin* is a mixture of *kola-red* and caffeine, and Tschirch states that kola-red is produced by a ferment existing in the fresh seeds and that this ferment is destroyed by heating to 80° C. for thirty minutes. Goris and Chevalier (*P. J.*, 1908, xxvi, p. 31) isolated a phenolic principle from fresh kola, which they named *kolatin*, C_8H_8O. This is present to the extent of less than 1 per cent. and yields kola-red on oxidation. Knebel (*A. J. P.*, 1892) finds kolatin to be a glucoside, which upon hydrolysis splits up into caffeine, glucose, and kola-red. It seems probable that the enzyme reported by Tschirch accomplishes this hydrolysis. Goris (*P. J.*, 1906, lxxvi) further asserts that the kolatin is physiologically active and that it disappears from the nuts on drying, which would explain the difference in the effects of kola upon the natives as reported by travellers and the results of European investigators.

Uses.—The effects of kola nuts as they appear in European commerce, is indistinguishable from that of the other caffeinic drugs. The experiments of Mosso (*A. I. B.*, xix) seem to demonstrate conclusively the inertness of kola-red.

Kola is about equivalent to guarana, tea, coffee, etc., and may be substituted for them. In *dose* of one hundred and fifty grains (9.8 Gm.) a day, A. Hudson (*T. G.*, ii) has found the nuts to act decisively in cardiac weakness.

Dose, one drachm (4 Gm.).

Off. Prep.—Fluidextractum Kolæ, *N. F.*

KRAMERIÆ. U. S. (Br.)

KRAMERIA [Rhatany]

"Krameria is the dried root of *Krameria triandra* Ruiz et Pavon, known in commerce as Peruvian Rhatany, or of *Krameria argentea* Martius, known in commerce as Para or Brazilian Rhatany (Fam. *Leguminosæ*)." *U. S.*

"Krameria Root is the dried root of Krameria triandra, *Ruiz and Pav.* (Peruvian Rhatany), and also of another species of Krameria, probably Krameria argentea, *Mart.* (Pará Rhatany)." *Br.*

Krameria Radix, *Br.*; Rhatany Root, Radix Ratanhæ; Krameria Triandra, *Fr. Cod.*; Radix Ratanhiæ, *P. G.*; Ratanhiawurzel, *G.*; Ratania, *It.*, *Sp.*

This drug, dismissed from the U. S. at the ninth revision, has been re-admitted at the tenth.

The genus *Krameria* was named in honor of J. G. H. Kramer, a physician and botanist of Temesvar, Hungary. The name *rhatany* is said to express in the tongue of the Peruvian Indians the creeping character of the plant yielding the root.

Krameria triandra is a shrub, having a long, much-branched, spreading root, of a blackish-red color; with a round, procumbent, very dark colored stem, divided into numerous branches of which the younger are leafy and thickly covered with soft hairs, giving them a white, silky appearance. The leaves are few, sessile, oblong-ovate, pointed, entire, presenting on both surfaces the same silky whiteness of the young branches. The flowers are bright scarlet, and stand singly on short peduncles at the axils of the upper leaves. The stamens are three. The nectary is of four leaflets, the two upper spatulate, the lower roundish and shorter. The fruit is globular, of the size of a pea, surrounded by stiff reddish-brown prickles, and having one or two seeds. It is a native of the Peruvian Andes, growing in dry argillaceous and sandy places. It flowers at all seasons, but is at the height of its bloom in October and November. The root is dug up after the rains, and, according to Tschudi, it is especially obtained in the southern provinces of Peru. Closely allied to it is *K. Ixina* L., which yields *Savanilla Rhatany.* It is, however, distinguished by having four stamens, and occurs in Guiana and northern Brazil. This variety was formerly recognized but was omitted from the U. S. X because it is not commercially obtainable.

Para or *Brazilian Rhatany* was described by Berg in 1865, and is believed to be the root of the *K. argentea* Martius. It closely resembles the Savanilla variety. Two forms of rhatany which Cotton has described as *Black* and *Brown Antilles rhatany*—because produced in these islands—have been pronounced by Flückiger (*P. J.,* July, 1870) to be identical with the Para Rhatany. According to the studies of Dunwoody (*A. J. P.,* 1890), this rhatany contains the same active principles as the root of *K. triandra,* but in slightly less quantity.

Peruvian Krameria is shipped to the U. S. A. from Peru; Brazilian or Para Krameria from Para and Rio de Janeiro, Brazil. During 1924, 1500 pounds of Krameria were imported into this country from Hamburg, Germany.

Description and Physical Properties.—"*Unground Peruvian Rhatany.*—Crown knotty, several- to many-headed, with numerous branching roots; the latter up to 50 cm. in length and usually less than 1 cm. in thickness, cylindrical or somewhat tapering, flexuous or wavy, externally light reddish-brown or brownish-red, more or less marked with darker scaly cork especially in the upper portion, somewhat longitudinally wrinkled but devoid of transverse fissures; fracture of bark slightly fibrous, of wood tough and splintery; the bark pinkish-brown internally and less than one-third of the radius, the wood yellowish or pinkish-white and finely radiate; inodorous; bark astringent, wood nearly tasteless.

"*Unground Para Rhatany.*—Roots usually separate from the crown, less flexuous, tapering, tough and internally darker in color than those of Peruvian Rhatany, and usually not exceeding 12 mm. in thickness; externally purplish-brown or chocolate-brown and marked with numerous fissures; the bark about two-fifths or more of the radius.

"*Powdered Krameria.*—Reddish-brown; starch grains single or 2- to 4-compound, the individual grains spherical, ellipsoidal, or plano-convex, sometimes with a central, radial, or star-like cleft, and from 0.003 to 0.035 mm. in diameter; bast-fibers more or less wavy in outline with very much attenuated ends and with non-lignified walls; tracheæ with simple or bordered pores associated with numerous wood-fibers which are narrow, spindle-shaped and with thick, porous, slightly lignified walls; numerous cellular fragments with yellowish- or reddish-brown walls; calcium oxalate in monoclinic prisms, from 0.010 to 0.100 mm. in length, and occasionally in spherical microcrystals." *U. S.*

The British Pharmacopœia recognizes two varieties of rhatany, which are described as follows: "Peruvian Rhatany is nearly cylindrical, slightly flexuous, reddish-brown; length variable; thickness not exceeding fifteen millimetres. Cork scaly; fracture splintery; wood yellow. In transverse section, bark bright reddish-brown and occupying about one-third of the radius of the section. Pará Rhatany is cylindrical, nearly straight, dark purplish-brown or almost black, and marked with deep transverse cracks. Fracture short; wood pale reddish-brown. In transverse section, bark dark reddish-brown and occupying about one-half of the radius of the section. Both varieties inodorous; taste of the bark astringent, of the wood scarcely perceptible. Ash not more than 4 per cent." *Br.*

Spurious rhatanys of unknown botanical origin have been reported by Holmes (*P. J.,* 1903, lxxvi, 878) and by P. H. Marsden, *P. J.,* 1901, 618.

According to an analysis made in the University of Wisconsin, the *Krameria lanceolata* Torrey, of North America, yields 34.5 per cent. of extract and 17 per cent. of tannin, and is therefore richer than the official drug. When treated with iron it strikes a deep-purple color, and is thus easily distinguished from Para rhatany, which gives a dirty brown color, and from Savanilla rhatany, which gives a violet color.

Payta krameria, which comes from Chile, is said to be the product of *K. cistoides.*

Constituents.—Krameria contains tannic acid, lignin, and minute quantities of gum, starch, saccharine matter, and an acid named *krameric* (or *rhatanic*) *acid.* The tannic acid of rhatany (*kramerio-tannic* or *ratanhia-tannic acid*), of which the root contains about 8 or 9 per cent., gives a dark-green precipitate with ferric chloride, a flesh-colored one with gelatin, and none with tartar emetic. In the presence of potassium hydroxide, it is transformed into protocatechuic acid and phloroglucin, and with diluted acids gives glucose and a red phlobaphene called *rhatany-red,* $C_{26}H_{22}O_{11}$.

In examining a specimen of extract of rhatany from America, Wittstein discovered an alkaloid *rhatanine* which he thought to be identical with tyrosine. Goldschmidt has shown (*D.

C., 1914, 17) that it is *N-methyltyrosine*, $C_{10}H_{13}O_3N$, and is identical with *angeline, geoffrayine* and *andirine* which have been described in various plants. He obtained it in crystalline needles, melting at 280° C.

Cold water extracts all the astringency of rhatany, forming a clear deep red infusion, which upon careful evaporation yields an almost perfectly soluble extract. The root yields its virtues also to boiling water by maceration, but the resulting infusion becomes turbid upon cooling, in consequence of the deposition of apotheme taken up by the water when heated. By boiling with water a still larger proportion of the apotheme is dissolved, and a considerable quantity of the pure tannin becomes insoluble in cold water, and medicinally inert, either by combining with the starch which is also dissolved, or by conversion into apotheme through the agency of the atmosphere. The decoction is, therefore, an ineligible preparation, and the extract resulting from its evaporation, though greater in weight than that from the cold infusion, contains much less soluble and active matter. Alcohol dissolves a larger proportion of the root than water, but this is owing to the solution of apotheme, and the alcoholic extract contains little if any more of the astringent principle than that prepared by cold water, while it is encumbered with much inert matter. (See *Extractum Krameriæ.*)

A very delicate test for the presence of rhatany is given by Glücksmann (*Ph. Post,* 1912, 65), who states that if an extract containing it be diluted with water until almost colorless, the addition of 0.5 Gm. of sodium bicarbonate to 10 cc. of the liquid will produce a rose red color.

Uses.—Rhatany is an active astringent, and may be advantageously given in *chronic diarrhea.* It has long been used in Peru as a remedy in bowel complaints, as a corroborant in cases of enfeebled stomach, and as a local application to spongy gums. Ruiz, one of the authors of the *Peruvian Flora,* first made it known in Europe. In the form of infusion, tincture, or extract, rhatany has been used locally in *fissure of the anus, prolapsus ani,* and *leucorrhea.*

Dose, of the powder, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Extractum Krameriæ, *Br., N. F.;* Infusum Krameriæ, *Br.;* Pulvis Catechu Compositus, *Br.;* Tinctura Krameriæ, *Br., U. S.;* Trochiscus Krameriæ (from Extract), *Br.;* Trochiscus Krameriæ et Cocainæ (from Extract), *Br.;* Fluidextractum Krameriæ, *N. F.;* Fluidglyceratum Krameriæ, *N. F.*

LACTOSUM. U. S.

LACTOSE Lactos. [Saccharum Lactis, U. S. P. IX, Milk Sugar]

"A sugar [$C_{12}H_{22}O_{11}.H_2O$] obtained from cow's milk." *U. S.*

"Milk Sugar is a crystallized sugar, $C_{12}H_{22}O_{11},H_2O$, obtained from the whey of milk." *Br.*

Saccharum Lactis, *Br.;* Sugar of Milk; Lactin; Sucre de Lait, *Fr.;* Milchzucker, *G.;* Lattioso, Zucchero di latte, *It.:* Azucar de leche, Lactosa, *Sp.*

Preparation.—Sugar of milk is found in milk of which it forms about 5 per cent. (Boussingault). It is manufactured largely in Switzerland and the Bavarian Alps, especially from the whey left over in cheese making. Within recent years the numerous "creameries" in the United States have produced milk sugar in such large quantities as a by-product that its importation from Switzerland has almost ceased. The American method of manufacturing sugar of milk is described by LaWall (*Alumni Report Philadelphia Coll. Pharmacy,* April, 1902): The whey left after the first curding of the milk (by the separator system) is run into vats, and treated with about 1 per cent. of hydrochloric acid to remove coagulable protein, the liquid being heated to the boiling point, and exactly neutralized with calcium hydroxide. The whey is then generally filtered through a filter press and evaporated *in vacuo* to a thick syrup, run into pans, and allowed to stand for two days, when granular crusts form. These are then centrifuged and washed with cold water to remove calcium chloride and soluble impurities, and the washings are reserved for future operations. The crude milk sugar is of a very light yellow color, and has little taste or odor. It is redissolved in water and the solution filtered through bone black. The colorless syrupy percolate is concentrated *in vacuo* to a pasty mass, which is washed with cold water in a centrifugal machine. The mass is then dried on strainers in a drying chamber at 60° C., powdered in a ball mill, and bolted. The casein obtained by acidulation of the skim milk, and subsidence, is washed and heated with water containing a small amount of sulphuric acid, to remove impurities. The moist pulpy mass left after the removal of the water is then shredded by means of cutting knives run by a high-speed engine, the flakes being transferred to wire gauze frames and rapidly dried with a current of air at 140° F. It is then powdered with high-speed disintegrators. The soluble albumin, not coagulated by the acid treatment but subsequently coagulated by heat, has thus far not found any market although it could be produced in large amount if there were any demand for it, as its collection and purification would be a comparatively simple matter. See paper by England on American Milk Product Industry (*Proc. A. Ph. A.,* 1902, 354).

Description and Physical Properties.—"White, hard, crystalline masses, or a white powder, producing a gritty sensation on the tongue. It is odorless, and has a faintly sweet taste. It is stable in the air, but readily absorbs odors. One Gm. of Lactose is soluble in 4.9 cc. of water at 25° C., also in 2.6 cc. of boiling water. It is very slightly soluble in alcohol; insoluble in chloroform and in ether.

"The specific rotation $[\alpha]_D$ of Lactose determined at 25° C. in an aqueous solution containing in each 100 cc. 10 Gm. of Lactose, previously dried to constant weight at 80° C., and using a 200 mm. tube, is not less than +52.2° and not more than +52.5°, page 447. The solution must be allowed to stand overnight before observing the rotation. Add an equal volume of sodium hydroxide T.S. to 5 cc. of a hot, saturated, aqueous solution of Lactose, and gently warm the mixture: the liquid turns yellow and finally brownish-red. On the subsequent addition of a few drops of cupric sulphate T.S., a precipitate of cuprous oxide forms.

"An aqueous solution of Lactose (1 in 20) is neutral to litmus paper. Ash: not more than 0.1 per cent. A solution of 3 Gm. of Lactose in 10 cc. of boiling distilled water is clear, colorless, and odorless. Add 20 cc. of 70 per cent. (by volume) alcohol to 2 Gm. of finely powdered Lactose, shake the mixture frequently during half an hour at 15° C., and filter; a 10 cc. portion of the filtrate remains clear after mixing with an equal volume of dehydrated alcohol (*dextrin*), and this liquid upon evaporation on a water bath leaves not more than 0.03 Gm. of residue (*sucrose or glucose*). An aqueous solution of Lactose (1 in 20) meets the requirements of the test for *heavy metals.* Boil 1 Gm. of powdered Lactose with 50 cc. of distilled water, cool, and add a drop of iodine T.S.; no blue color is produced (*starch*).

"Preserve in tightly-closed containers." *U. S.*

"A white powder, or in crystalline masses; no odor, taste slightly sweet. Soluble in 7 parts of cold *water* and in about 1 part of boiling *water.* 5 grammes dissolved in *water* require for neutralisation not more than 1.5 millilitres of *N/10 solution of sodium hydroxide* (limit of acidity). When 5 grammes are well shaken with 20 millilitres of *alcohol* (90 per cent.) and filtered, the filtrate leaves no appreciable residue on evaporation (absence of sucrose). Ash not more than 0.25 per cent." *Br.*

In commerce sugar of milk frequently occurs in cylindrical masses, the axis of which is a wooden stick, around which the crystals have been deposited. Experiments have shown that much of the milk sugar of commerce contains micro-organisms which have resulted from the decomposition of animal constituents in milk, and the tests of the Pharmacopœias do not exclude such impurities. (*D. C.*, 1893, 250; *Bull. Pharm.*, 1893, v, 5; *P. J.*, 1894, 853.) Its specific gravity is 1.54. It is not susceptible of the vinous fermentation by the direct influence of yeast; but after hydrolysis by dilute acids, it is capable of furnishing a spirituous liquor by subsequent fermentation. It is well known that both mares' and cows' milk, after becoming sour, are capable of forming an intoxicating drink, by fermentation. By the action of nitric acid, lactose is converted into mucic acid. When anhydrous it consists of $C_{12}H_{22}O_{11}$; when crystallized, of $C_{12}H_{22}O_{11} + H_2O$. (Staedeler and Krause.) It is, therefore, isomeric with sucrose. Lactose, when treated with weak sulphuric acid, is inverted or changed into a mixture of *galactose,* and dextrose, both of the formula $C_6H_{12}O_6$. The galactose crystallizes in fine needles, fusing at 163° C.

J. W. England (*Proc. Penna. Pharm. Assn.*, 1915, p. 240) reported upon 17 lots of milk sugar, aggregating one-half million pounds, which showed a minimum purity of 99.73 per cent. by the polariscope with negligible traces of nitrogen, ash, and fat.

It is sometimes difficult to obtain lactose free from mechanical impurities introduced during handling. The special test for complete solubility is intended to guard against such impurities.

Uses.—Sugar of milk differs physically from cane sugar in the fact that it is less sweet. Because of its relative tastelessness it is sometimes preferred as an article of diet, especially in the feeding of infants, especially also, because it does not readily undergo the alcoholic fermentation. Its relation to metabolism is precisely the same as that of cane sugar except that the inversion into galactose takes place after its absorption and is probably accomplished by the epithelial cells of the intestines. Like other crystalloids when ingested in large quantities by modifying the osmotic relations of the blood it acts as a diuretic and has been practically used for this purpose by Germain Sée and others with advantage in the treatment of *cardiac dropsies.* If the kidneys be sound the lactose is said not to appear in the urine. It is used in doses of from 6 drachms to 6 ounces (23.5–186 grammes). It is used as a diluent in various official preparations.

LAC VACCINUM. N. F.

COWS' MILK

"The fresh, unpasteurized milk of the domestic cow, *Bos taurus* Linné (Fam. *Bovidæ*), without modification, and complying with the legal standards of the State or community in which it is sold." *N. F.*

Milk; Lait, *Fr.;* Milch, *G.;* Latte, *It.*

Milk, which is the secretion of the mammary gland of the mammalia provided for the nourishment of the young, is a natural emulsion containing proper proportions of nutritive constituents adapted for the particular species secreting it. Cows' milk is that most commonly used as food by man in civilized countries and is what is legally understood when the word "milk" is used unqualifiedly, but the milk of other animals is sometimes used. Among these may be mentioned the goat, sheep, llama, mare and reindeer.

The preference for cows' milk is a matter of custom determined largely by the fact that the hides and flesh of these animals are necessary to man, and by the naturally large volume of milk yielded which has been further augmented by selective breeding and scientific feeding.

Milk consists principally of water, casein and other proteins, fat, milk sugar, and mineral salts. Minute amounts of lecithin and nuclein, of enzymes and vitamines are also present and probably are of great value as nutritional factors. The proportion of the various ingredients in milk varies considerably, not only with the species of animal, but also, to a considerable extent, at different periods of lactation. Speaking in general terms, cows' milk contains a larger percentage of solid matters than human milk, although the latter is relatively richer in carbohydrate. The following table compiled from various authorities gives the approximate composition of human and bovine milk. One hundred parts contain:

	Water	Protein	Fat	Sugar	Ash
Human........	87-90	1.7-3.7	3.0-5.0	4.5-6.2	0.2-0.3
Cow........	84-87	3.7-4.5	3.5-6.0	4.3-5.0	0.6-0.7

Milk contains several proteins. *Casein,* the principal member of this group, is a phosphoprotein; albumin and a globulin-like protein are also present to a lesser extent and recently the presence of an alcohol-soluble protein has been announced. These four proteins have been shown to be immunologically distinct.

Tryptophane has also been shown to be present both in cows' milk and human milk.

The vitamines present in milk are the fat-soluble A and the antiscorbutic vitamine C. The latter is destroyed by heating and dried milk is deficient in this factor although not impaired in its growth-promoting vitamine.

The physical properties and composition of cows' milk are subject to a certain amount of variation due to the species of cattle, character and amount of food, time of milking, etc. The reaction of cows' milk, when fresh, is amphoteric, that is, alkaline to red litmus paper and acid to blue litmus paper. The specific gravity averages about 1.0315, but varies with the percentage of butter fat which, being a more concentrated emulsion, rises to the surface of the milk as cream, leaving below it a liquid containing very little fat but almost all of the casein, sugar and salts, and known as skim milk. Gravity cream, or cream which separates on standing, has been largely replaced by separator cream in which centrifugal force is applied to a stream of milk entering the device known as a separator, which continuously separates it into cream and skim milk, the relative richness of the cream and freedom of the skim milk from butter fat being regulated by the speed of the centrifugal motion. During recent years there has come into use an apparatus known as a homogenizer, in which the milk is subjected to the influence of great pressure and is at the same time forced through diaphragms containing minute perforations. The normal size of the fat globules, which is from 0.0025–0.0035 millilitres, is much reduced and the physical properties of the cream or milk are modified to such an extent that the subsequent separation of cream takes place much more slowly and the supernatant cream layer is bulkier and less rich in butter fat. The milk therefore appears richer to the eye judging from the apparent amount of cream which separates. The use of the homogenizer gives to cream which is to be used for ice cream manufacturing, properties which make for smoothness and higher quality of the resulting product. The homogenizer can also be used to combine butter with skim milk to make products simulating either cream or milk, depending upon the proportions of the ingredients. Fats normally foreign to milk, such as vegetable or animal oils, may be incorporated with skim milk by the use of this apparatus, and the resulting product used as a substitute for cream or milk. Such products are on the market usually under coined names, as they are frequently offered and sold in place of evaporated or condensed milk; their sale has been prohibited in some states, unless the label contains specific and plainly printed warnings that it is not to be used in infant feeding.

The normal decomposition of milk upon standing is accompanied by the development of lactic acid (the acid of sour milk) which is formed by bacterial action from the lactose (see *Lactic Acid*). Under some circumstances milk undergoes the butyric fermentation with the development of butyric acid from the fats of the milk. The alcoholic fermentation of milk is discussed under *Kefir* (which see).

Condensed or *evaporated* milk is milk which has had part of its water removed by evaporation in a vacuum apparatus. The concentration is usually two-fold, but in some instances is higher. Sweetened condensed milk is milk which has been concentrated by evaporation and to which has been added either cane sugar or invert sugar. So-called *"evaporated cream"* is frequently evaporated milk which has been concentrated to a higher degree than usual. There is a real evaporated cream on the market which contains nearly 70 per cent. butter fat. Milk may also be evaporated to the condition of a dry powder by the use of special forms of apparatus in which the effect of a vacuum is supplemented by distributing the milk in a very thin layer on a large metal cylinder or allowing it to escape into a very high vacuum or hot chamber in a very fine jet. *Powdered milk* may either be whole milk or skim milk. Both of these articles are now produced upon a very large scale for use in manufacturing confectionery, such as milk chocolate, and for combining in concentrated food products. Separated *milk fat,* free from the salt, curd and moisture which are present in butter, is also a commercial article, offered for special food manufacturing purposes.

Malted milk "is the product made by combining whole milk with the liquid separated from a mash of ground barley malt and wheat flour, with or without the addition of sodium chloride, sodium bicarbonate and potassium bicarbonate in such a manner as to secure the full enzymic action of the malt extract and by removing water. The resulting product contains not less than 7.5 per cent. of butter fat and not more than 3.5 per cent. of moisture."

Malted milk not only contains a higher percentage of carbohydrate, derived from the grain, but according to Ballard (*J. A. Ph. A.*, 1918, vii, 326), chemical change has taken place both in the carbohydrates and proteins through the action of the enzymes of the malt.

The U. S. minimum standards for these various forms of milk are as follows: Milk, 3.5 per cent. fat, 8.5 per cent. solids not fat; Cream, 18 per cent. fat; Evaporated milk, 34.3 per cent. milk solids and 7.8 per cent. fat (sweetened or unsweetened); Skim milk, 9.25 per cent. milk solids.

Some of the individual States have slightly different standards from the above U. S. standards, which apply only to milk shipped into interstate commerce.

The watering of milk is usually detected by the chemical analysis, a proportion of non-fatty solids less than 8.5 per cent., rendering the sample open to suspicion in this respect. The presence of added water is usually confirmed by taking the specific gravity of the milk serum or whey or by observing its refractive index by the use of an immersion refractometer. The freezing of the whey is another important factor in recognizing watered milk.

The use of preservatives in milk is universally prohibited and instances of such adulteration are now rarely met with. Among the preservatives, which were in more or less widespread use at one time, were formaldehyde, borax, salicylic or benzoic acid, fluorides and hydrogen dioxide. The latter preservative disappears within 48 hours by reduction to H_2O. Its use may be inferred, however, by the disappearance of the characteristic enzymes of milk, which may be readily determined by appropriate tests. It is the presence of these enzymes together with the vitamines, which are undoubtedly responsible for much of the value of milk as a food, apart from the fat, protein and carbohydrates present. It is of interest to note that in modern methods of milk concentration these enzymes are usually unaffected and remain in the finished product. Artificial coloring, such as annatto or coal tar colors are sometimes used in milk to give a false appearance of richness. They are prohibited by law and are easily detected by appropriate tests. Such crude methods of milk adulteration as the addition of starch or chalk or similar thickeners, have entirely disappeared. One method of increasing the viscosity or apparent richness of milk, the homogenizer or viscolizer as the machine is sometimes called, has already been referred to. Another method is by the addition of calcium sucrate which may readily be detected by specific reactions for sugar and excess of calcium in the ash.

Modern methods of milk control are concerned with the production of clean milk as well as pure milk. The bacterial count therefore plays an important part in judging of its quality. Standards vary in different localities, but the following is an example. In Chicago the milk, as it arrives in the city, it is limited to 1,000,000 bacteria per cc. from May 1 to September 1, and 500,000 per cc. during the remainder of the year. Municipal requirements for pasteurization usually reduce this figure to 50,000 per cc. when delivered to the consumer. *Certified milk* is required to be free from *B. tuberculosis* and to contain less than 10,000 bacteria per cc. (Class A), and 100,000 bacteria per cc. (Class B), without pasteurization.

As boiling milk is generally believed to lessen its digestibility as well as destroy its enzymes, the process known as *pasteurization* is employed to produce partial sterilization. For this purpose the milk is heated to a temperature of about 68° C. for from twenty to thirty minutes. This will destroy practically all the pathogenic bacteria likely to occur in milk without causing serious changes in its chemical composition.

Uses.—Any discussion of the value of milk as a food would trespass into fields foreign to the purpose of this work. Milk is of importance for more strictly medicinal purposes in two ways; as a vehicle it lessens the irritating effect of such drugs as iodides or salicylates upon the stomach. Recently it has been used hypodermically as a means of provoking the so-called protein reaction (see *Protein Therapy*, Part II). It is recognized in the National Formulary for the preparation of fermented milk. (See Part III; also *Kephir*, Part II.)

Off. Prep.—Lac Fermentatum, *N. F.*

LAMELLÆ.

DISCS

Gelatina Medicata in Lamellis; Medicated Gelatin Disks; Disques de Gélatine, *Fr.;* Gelatinlamellen, Gelatinplättchen, *G.*

Under this head are included in the British Pharmacopœia minute *gelatin discs* which contain traces of alkaloids, and which are designed to be inserted by oculists under the eyelid, in order to produce, through solution in the tears such effects as desired. A hot solution of gelatin containing the alkaloid in proper proportion is poured on a slightly greased or waxed glass or porcelain plate, cooled and dried, and then cut into discs, which, by previous calculation, will be found to contain the requisite quantity of medicament. A little glycerin is added to keep them from getting too hard and dry.

In Appendix X, British Pharmacopœia, a general formula is inserted as follows:

"*Process for Preparation of Discs* (*Lamellæ*), *Br.*—Discs are prepared by the following process:—Gelatin, 18 *grammes;* Glycerin, 2 *grammes;* Distilled Water, 88 *grammes.* Mix the Glycerin with the Distilled Water, allow the Gelatin to soak in the mixture till soft, and then dissolve by a gentle heat; cool the basis so produced. Take the prescribed quantity of the above basis, melt it by a gentle heat, add the prescribed quantity of medicament, dissolve and mix. Pour the melted and medicated basis upon a sheet of plate glass 10 centimetres square, previously thinly coated with White Beeswax, in such a manner that the solution is evenly distributed. Dry at a temperature not exceeding 36° C., and from the film thus obtained cut discs 3 millimetres (nearly ⅛ inch) in diameter."

LAMELLÆ ATROPINÆ. Br.

DISCS OF ATROPINE

Disques d'Atropine, *Fr.;* Atropinplättchen, *G.*

"Discs of Atropine are discs of Gelatin with Glycerin, each weighing about 1.3 milligrams (1/50 grain) and containing 0.013 milligram (1/5000 grain) of Atropine Sulphate. Prepare as directed in Appendix X, employing 0.016 gramme of Atropine Sulphate and 8.8 grammes of *basis.*" *Br.*

LAMELLÆ COCAINÆ. Br.

DISCS OF COCAINE

Disques de Cocaine, *Fr.;* Cocainplättchen, *G.*

"Discs of Cocaine are discs of Gelatin with Glycerin, each weighing about 3.5 milligrams (1/20 grain) and containing 1.3 milligrams (1/50 grain) of Cocaine Hydrochloride. Prepare as directed in Appendix X, employing 1.65 grammes of Cocaine Hydrochloride and 15 grammes of *basis.*" *Br.*

LAMELLÆ HOMATROPINÆ. Br.

DISCS OF HOMATROPINE

Disques d'Homatropine, *Fr.;* Homatropinplättchen, *G.*

"Discs of Homatropine are discs of Gelatin with Glycerin, each weighing about 2.1 milligrams (1/32 grain) and containing 0.65 milligram (1/100 grain) of Homatropine Hydrobromide. Prepare as directed in Appendix X, employing 0.82 gramme of Homatropine Hydrobromide and 10.1 grammes of *basis.*" *Br.*

Lucas (*C. D.*, 1899, 959) furnishes an improved formula for these discs; it is as follows: Gelatin, 30 gr.; Glycerin, 3 gr.; Distilled Water, 150 gr.; Homatropine hydrobromide, 10 gr. Dissolve and pour on to a waxed plate, so as to produce a film exactly 4 inches square. When dry, but still supple, punch out discs 1-7 inch diameter.

The product is about 784 discs, the remainder of the film being wasted. Each disc will weigh rather less than 1-20 gr. No inconvenience has been found in using discs weighing 1-15 gr., as, owing to their extreme tenuity, they soften as soon as they are inserted beneath the eyelid.

LAMELLÆ PHYSOSTIGMINÆ. Br.

DISCS OF PHYSOSTIGMINE [Discs of Eserine]

Disques d'Esérine, *Fr.;* Physostigminplättchen, *G.*

"Discs of Physostigmine are discs of Gelatin with Glycerin, each weighing about 1.3 milligrams (1/50 grain) and containing 0.065 milligram (1/1000 grain) of Physostigmine Sulphate. Prepare as directed in Appendix X, employing 0.082 gramme of Physostigmine Sulphate and 8.45 grammes of *basis.*" *Br.*

LAPPA. N. F.

LAPPA Lap. [Burdock Root]

"Lappa is the dried first year root of *Arctium Lappa* Linné, or of *Arctium minus* Bernhardi (Fam. *Compositæ*). Lappa contains not more than 5 per cent. of its leaf bases or more than 2 per cent. of other foreign organic matter." *N. F.*

Burdock Root; Radix Bardanæ; Bazzies; Beggars' Buttons; Cuckoo Button; Harebur; Bardane, Glouteron, *Fr.;* Klettenwurzel, *G.;* Bardana, *It.*

Although a native of Europe, burdock is abundant in the United States, where it grows on the roadsides, among rubbish, and in cultivated grounds. There are three recognized species of *Arctium* in North America—viz., *A. tomentosum* (Lam.) Schk. (*Woolly* or *Cottony Burdock*); *A. Lappa* L. (*Burdock* or *Great Bur*); and *A. minus* Schk. (*Common Burdock*).

The stem of the burdock is succulent, pubescent, branching, and three or four feet in height, bearing very large, cordate, denticulate leaves, which are green on their upper surface, whitish and downy on the under, and stand on long petioles. The flowers are purple, with heads globose, and in terminal panicles. The involucre consists of imbricated scales, with hooked extremities, by which they adhere to the clothing of man and the coats of animals. The achenes are oblong, somewhat compressed and three-angled, ribbed, truncate.

Burnier (*Presse. Med.*, 1918) says that the drug must be gathered in the spring, that collected in the fall being inert.

Description and Physical Properties.—"*Unground Lappa.*—Nearly simple, fusiform, of variable length, from 5 to 20 mm. in diameter near the crown; frequently split or in broken pieces; externally grayish brown, longitudinally wrinkled, the crown somewhat annulate, sometimes surmounted by a wooly tuft of leaf remains; fracture somewhat horny; a dark cambium separating the thick brownish bark from the yellowish porous and radiate wood, centrally hollow or containing a white, pith-like tissue. Odor slight, becoming pyroligneous on milling; taste mucilaginous, sweetish, and slightly bitter.

"*Powdered Lappa.*—Light brown; exhibits parenchyma cells of the cortex, medullary ray cells and wood parenchyma containing amorphous masses or sphero-crystals of inulin; yellow resin cells from the cortical parenchyma of young roots; wood fibers few; starch and calcium oxalate absent." *N. F.*

The commercial supplies of Burdock root are obtained chiefly from Belgium and France. They are shipped in bags containing either the whole or cut root from Brussels, Antwerp and Marseilles to the United States.

Henderschott (*Proceedings of Mich. Pharm. Assoc.*, 1887) and also Trimble (*Ph. Era*, 1888, p. 133) have reported in the root a bitter, crystalline glucoside. Thos. Donaldson (*A. J. P.*, 1890, p. 123) found 8.6 per cent. of yellow fixed oil and about 1 per cent. of white waxy matter. A small quantity of volatile oil (0.065 per cent.) has been found in burdock root according to *Haensel's Report*, Oct., 1902. It also contains considerable amounts of inulin.

An interesting account of burdock and its use as an edible vegetable in Japan, by Inazo Nitobe, may be found in *A. J. P.*, 1897, 416.

Uses.—Burdock root has been employed as a diuretic and diaphoretic alterative, especially in the *gouty, scorbutic,* and *syphilitic* and *scrofulous diatheses;* also in various chronic skin diseases, especially in *psoriasis, prurigo* and *acne.* The fresh leaves have been employed both externally and internally in cutaneous eruptions and ulcerations. There is no sufficient reason, however, to believe it has any medicinal virtue.

Dose, thirty to ninety grains (2.0–5.8 Gm.).

Off. Prep.—Fluidextractum Lappæ, *N. F.*

LAUROCERASI FOLIA. Br.

CHERRY-LAUREL LEAVES

"Cherry-Laurel Leaves are the fresh leaves of Prunus Laurocerasus, *Linn.*" *Br.*

English Laurel, Cherry Bay; Laurier-cerise, *Fr.;* Kirschlorbeer, *G.;* Lauroceraso, *It.;* Laurel-cerezo (Hoja de), *Sp.*

Prunus Laurocerasus (Fam. *Rosaceæ*) is a small evergreen bush or tree indigenous to Southeastern Europe and Southwestern Asia but cultivated in temperate regions. It attains a height of 10 feet. It possesses long, spreading branches, which, with the trunk, are covered with a smooth, blackish bark. The leaves are oval-oblong, lanceolate, or oblanceolate, petiolate, from five to seven inches in length, acute, finely toothed, firm, coriaceous, smooth, beautifully green and shining, with two to four yellowish glands at the base. The flowers are small, white, strongly odorous, and disposed in simple, axillary or terminal racemes. The fruit is an oval drupe, very similar in shape and structure to a small black cherry.

The leaves are packed in bales and shipped to the United States from Leghorn, Italy and Marseilles, France.

In their recent and entire state cherry-laurel leaves are devoid of odor; but, when bruised, they emit the characteristic odor of hydrocyanic acid and bitter almond oil. Their taste is somewhat astringent and strongly bitter, with the flavor of the peach kernel. They are officially described as "thick, coriaceous, on short, strong petioles, oblong or somewhat obovate, from twelve to eighteen centimetres long, tapering towards each end, recurved at the apex, distantly but sharply serrate and slightly revolute at the margins; dark green, smooth and shining above, much paler beneath; midrib prominent, with one or two glandular depressions on the under surface near its base. Inodorous, but emitting when bruised an odor resembling that of prussic acid." *Br.*

Cherry-laurel leaves are sometimes substituted by the leaves of other species of *Prunus.* These are readily distinguished in that they do not possess the characteristic glandular hairs which occur on the basal portion of the leaves and petioles of *P. Laurocerasus.* (*B. P. G.,* 1907, p. 325.)

Cherry-laurel leaves contain a glucoside formerly called *laurocerasin* but now known as *prulaurasin* which is isomeric with mandelonitrile glucoside, found in wild cherry bark, and related to amygdalin. They contain also a ferment, known as *prunase,* similar to, if not identical with, emulsin, which causes the decomposition of the glucoside and the formation of hydrocyanic acid and benzaldehyde. As the emulsin is stored in the veins and the prulaurasin found in the parenchyma of the leaf, the production of hydrocyanic acid takes place only after the leaves are broken. One pound, avoirdupois, of the fresh leaves yields 40.5 grains of a volatile oil which resembles that of bitter almonds.

Uses.—Cherry-laurel leaves are used chiefly as a flavoring agent similar to bitter almond especially in the form of the water. As Broker (*B. F. M. R.,* 1868) found that the proportion of hydrocyanic acid from the leaves varies with the season, age of the plant and the character of the soil and weather, they are inferior for this purpose to the oil of bitter almond. Several cases of prussic acid poisoning have been reported from their use. It is not, therefore, to be regretted that the want of the plant in this country has prevented the general introduction of so variable a remedy as the distilled water. (See *Aqua Laurocerasi.*)

Off. Prep.—Aqua Laurocerasi, *Br.*

LEPTANDRA. N. F.

LEPTANDRA Leptand. [Culver's Root]

"Leptandra consists of the dried rhizome and roots of *Veronica virginica* Linné (Fam. *Scrophulariaceæ*). Leptandra contains not more than 5 per cent. of its stem bases or other foreign organic matter and yields not more than 6 per cent. of acid-insoluble ash." *N. F.*

Culver's Root; Culver's Physic; Bowman's Root; Tall Speedwell; Tall Veronica; Black Root; Racine de Leptandra, ou de Véronique de Virginie, *Fr.;* Leptandra-Wurzel, *G.*

Veronica virginica is an herbaceous perennial, with a simple, erect stem, three or four feet high, smooth or downy, furnished with leaves in whorls, and terminating in a long spike of white flowers. The leaves, of which there are from four to seven in each whorl, are short-petiolate, lanceolate, pointed, and minutely serrate. A variety was seen by Pursh with purple flowers, which was described and figured as a distinct species by Rafinesque, under the name of *L. purpurea.* The plant flowers in July and August. It grows throughout the United States east of the Mississippi, affecting mountain meadows in the South and rich woods in the North, and is not unfrequently cultivated.

The rhizomes and roots are collected from plants of the second year's growth. The commercial supplies are largely obtained from North Carolina and southern Virginia.

Description and Physical Properties.—"*Unground Leptandra.*—Rhizome usually of horizontal growth, nearly cylindrical, somewhat branched; branches readily separable from the main rhizome, from 4 to 10 cm. in length and from 4 to 13 mm. in diameter; externally grayish-brown to dark reddish-brown; annulate from circular scars of bud-scales, upper surface with short stem remnants, occasionally with buds, and numerous circular stem-scars; from the under and lateral portions arise numerous coarse roots; fracture very tough and woody; internally, bark rather thin, dark brown and resinous, wood about the same thickness as the bark, light brown and porous, pith large, more or less hollow, the color being similar to that of the bark. Roots from 1 to 10 cm. in length and from 0.5 to 2 mm. in diameter; externally dark brown to purplish brown, smooth and faintly longitudinally wrinkled; fracture short; internally with a thick brownish black cortex and small light brown central cylinder. Odor characteristic; taste very bitter and acrid.

"*Powdered Leptandra.*—Brown to yellowish brown; consisting of numerous irregular fragments, many of them being colored pink or violet upon the addition of hydrated chloral T.S.; starch grains numerous, mostly in the parenchyma cells, the individual grains nearly spherical or more or less polygonal, up to 0.009 mm. in diameter; tracheæ with spiral thickenings or with simple or bordered pores; wood fibers with thick lignified walls, with simple pores or with bordered pores resembling tracheids; fragments of parenchyma containing a light brown or brownish-black resin, the latter frequently closely coherent with the starch grains in the cells thus preventing the separation of the individual starch grains; mounted in chloral hydrate T.S., occasional elongated cells with a lemon-yellow oily substance are observed." *N. F.*

For a microscopical description of leptandra, by A. P. Breithaupt, see *A. J. P.*, 1897, 235.

The active principle of leptandra is unknown. In 1856 E. S. Wayne reported the presence of a crystalline bitter substance which F. F. Mayer (*A. J. P.*, 1863) classed as a glucoside. Steinmann (*A. J. P.*, 1887) obtained a bitter principle which was neither glucosidal nor alkaloidal. On the other hand Power and Rogerson (*Tr. Chem. Soc.*, 1910, xcvii, p. 1944) were unable to obtain any substance corresponding to the earlier reports. They found in the plant about 6 per cent. of a brown resin from which they obtained a peculiar phytosterol, for which they proposed the name *verosterol;* dimethoxycinnamic and p-methoxycinnamic acids, and a brown amorphous substance, with an intensely bitter taste, amounting to about 1.6 per cent. of the drug. They believe that the crystals reported by Steinmann were probably dimethoxycinnamic acid contaminated with some of the bitter amorphous substance.

The substance sold under the name of "leptandrin" is an indefinite mixture made by adding water to a strong alcoholic tincture.

Uses.—Leptandra is a cathartic, in the fresh state acting rather violently, but when dried much milder. It is by some believed to have a special effect upon the liver and is used either as a substitute for or in conjunction with the mercurials.

Dose, fifteen to sixty grains (1–3.9 Gm.); of the impure resin, two to four grains (0.13–0.26 Gm.).

Off. Prep.—Extractum Leptandræ, *N. F.;* Fluidextractum Leptandræ, *N. F.;* Pilulæ Catharticæ Vegetabiles, *N. F.*

LIMONIS CORTEX. U. S., Br.

LEMON PEEL Limon Cort.

"The outer yellow rind of the fresh ripe fruit of *Citrus medica* var. *Limonum* (Risso) Hooker filius (Fam. *Rutaceæ*)." *U. S.* "Lemon Peel is the fresh outer part of the pericarp of the fruit of Citrus medica, *Linn.*, var. β Limonum, *Hook f.*" *Br.*

[*] Limonis Pericarpium; Ecorce (Zeste) de Citron, de Limon, *Fr. Cod.;* Cortex Citri Fructus, *P. G.;* Citronenschale, Limonenschale *G.;* Scorza di Limone, *It.*

For general remarks on the genus *Citrus,* see *Aurantii Cortex.*

Citrus medica, or lemon tree, closely resembles *Citrus Aurantium,* before described. Like the orange-tree it is a native of Asia. It is now known to grow wild in northern India, and was introduced into Europe from Persia or Media. It was first cultivated in Greece, afterwards in Italy, as early as the second century, and has now spread over the whole civilized world, being raised by artificial heat where the climate is too cold to admit of its exposure during winter to the open air. The leaves, however, are larger, slightly indented at the edges, and their petioles are destitute of the winged appendages that characterize the other species. The flowers, moreover, have a purplish tinge on their outer surface, and the fruit is different in appearance from the orange. There are several varieties of *Citrus medica,* which some botanists consider as distinct species, but which scarcely differ except in the character of their fruits. Those particularly deserving of notice are the citron, lemon, and lime. 1. In the *citron, C. medica genuina,* the fruit is very large, sometimes six inches in length, ovoid, with a double rind, of which the outer layer is yellowish, thin, unequal, rugged, with innumerable vesicles filled with essential oil; the inner is white, very thick and spongy. It is divided in the interior into nine or ten loculi, filled with small oblong vesicles, which contain an acid juice precisely like that of the lemon, and used for the same purposes. The rind is applied to the preparation of conserves to which it is adapted by its thickness. The fruit is called *cédrat* by the French. 2. The *lemon, C. medica* var. *Limonum* (*Citrus Limonum* of Risso), is smaller than the preceding, with a smoother and thinner rind, a pointed nipple-shaped summit, and a very juicy, acid pulp. In other respects it closely resembles the citron, to which, however, it is usually preferred in consequence of the greater abundance of its juice. (See *Succus Limonis.*) 3. The *lime* is still smaller than the lemon, with a smoother and thinner rind, oval, rounded at the extremities, of a pale-yellow or greenish-yellow color, and abounding in a very acid juice. It is the product of *C. medica acida.*

Description and Physical Properties.—"The outer lemon-yellow or dark-yellow layer, recently separated by grating or paring; consisting of the epidermis and numerous parenchyma cells containing yellow chromoplastids and large oil reservoirs with globules of the volatile oil; odor fragrant, distinctive; taste aromatic." *U. S.*

"Outer surface pale yellow and more or less rough; with only a small amount of the white spongy part of the pericarp on the inner surface; in transverse section numerous large oil-glands below the epidermis. Strong, characteristic and fragrant odor; taste aromatic and bitter." *Br.*

It contains a bitter principle, and yields, by expression or distillation, an essential oil, which is much used for its flavor. Both this and the rind itself are recognized in the Pharmacopœias. (See *Oleum Limonis.*) When the white, spongy portion of the rind is boiled in water, and the decoction evaporated, crystals are deposited of a substance called *hesperidin.* This is a glucoside, and has the formula $C_{50}H_{60}O_{27}$, and is decomposed by diluted acids into *hesperetin,* $C_{16}H_{14}O_6$, and rhamnose. It turns dingy black when gently warmed with alcoholic solution of ferric chloride. It is bitter, but as it is found most largely in the spongy and comparatively tasteless part of the rind, it may be doubted whether it is entitled to be considered as the active bitter principle. E. G. Clayton has called attention to the distinction between lemon peel and orange peel when moistened by strong hydrochloric acid. Orange peel under these circumstances changes in color from a yellow to a rich dark green color, while lemon peel retains its hue or assumes a dingy yellowish-brown tint.

Uses.—The rind of the lemon is used to qualify the taste and increase the power of stomachic infusions and tinctures.

Off. Prep.—Tinctura Limonis, *U. S.* (*Br.*); Infusum Aurantii Compositum, *Br.;* Syrupus Limonis, *Br.*

LINIMENTA

LINIMENTS

Embrocations; Liniments, Embrocations, *Fr.;* Linimenta, Linimente, Einreibungen, *G.*

These are preparations intended for external use, of such a consistence as to render them conveniently applicable to the skin by gentle friction with the hand.

LINIMENTUM ACONITI. Br.

LINIMENT OF ACONITE

"Liniment of Aconite contains in 100 millilitres 0.2 gramme of the ether-soluble alkaloids of Aconite Root." *Br.*

Liniment d'Aconit, *Fr.;* Akonitliniment, *G.*

"Aconite Root, in No. 40 powder, 500 *grammes;* Camphor, Alcohol (90 per cent.), of each, *a sufficient quantity.* Moisten the Aconite Root with part of the Alcohol, pack in a percolator, and percolate with more of the Alcohol until the Root is exhausted. Reserve the first seven hundred and fifty *millilitres* of the percolate; evaporate the remainder to a syrup and add it to the reserved portion. Determine the weight of ether-soluble alkaloids in fifteen *millilitres* of the tincture thus obtained by the process described under 'Aconiti Radix.' Add to the remainder of the tincture sufficient of the Camphor and of the Alcohol to produce a Liniment of Aconite containing in 100 millilitres 0.2 gramme of the ether-soluble alkaloids of Aconite Root and 3 grammes of Camphor. Examined by the foregoing process Liniment of Aconite is found to contain in 100 *millilitres* 0.2 gramme of the ether-soluble alkaloids of Aconite Root. *Limit of error* 0.01 gramme in excess or defect." *Br.*

This preparation of the British Pharm., 1914, is now made of a definite strength through the introduction of an assay process. It is a very strong tincture of aconite root with camphor; that of the U. S. P., 1870, was almost equivalent to a fluidextract of aconite.

Uses.—Aconite liniment is counter-irritant and locally anesthetic. It may be applied alone by means of a camel's-hair pencil, or in connection with two parts or more of soap liniment or chloroform liniment, by rubbing it on the part affected. It must be used with caution lest sufficient aconite be absorbed through the skin to cause poisoning.

LINIMENTUM AMMONIÆ. Br.

AMMONIA LINIMENT Lin. Ammon.
[Volatile Liniment, Hartshorn Liniment]

Liniment of Ammonia, Linimentum volatile, Linimentum ammoniacale, *Fr. Cod.;* Savon ammoniacal, *Fr.;* Linimentum Ammoniatum, *P. G.;* Flüchtiges Liniment, Flüchtige Salbe, *G.;* Linimento ammoniacale, *It.;* Linimento amoniacal, *Sp.*

"Solution of Ammonia, 250 *millilitres;* Almond Oil, 250 *millilitres;* Olive Oil, 500 *millilitres.* Shake together." *Br.*

This useful liniment has been—unfortunately, according to our opinion—omitted from the U. S. X. It is recognized by the N. F. (see Part III).

The Br. preparation is made with almond oil and olive oil with the proviso that "In India, and in the Eastern, African, Australasian, and North American Divisions of the Empire, Arachis Oil or Sesame Oil, but no other oil or fat, may be employed in making the official Liniments, Plasters, Ointments, and Soaps for which Olive Oil is directed to be used." *Br.*

In this process, the ammonia reacts with the oil to form a soap, which is partly dissolved, partly suspended in the water, producing a white, opaque emulsion. The liniment is an excellent rubefacient, with the added advantage of being relatively inexpensive, in *inflammatory joint affections* and in *rheumatic pains* and the like. It is applied by rubbing it, or placing a piece of flannel saturated with it, over the affected part. Should it occasion too much inflammation, it must be diluted with oil.

LINIMENTUM BELLADONNÆ. Br.

BELLADONNA LINIMENT Lin. Bellad.

Liniment of Belladonna; Liniment de Belladone, *Fr.;* Belladonnaliniment, *G.*

"Liquid Extract of Belladonna, 500 *millilitres;* Camphor, 50 *grammes;* Distilled Water, 100 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Dissolve the Camphor in three hundred *millilitres* of the Alcohol; add the Liquid Extract of Belladonna, the Distilled Water, and sufficient of the Alcohol to produce the required volume. Set aside for twenty-four hours; filter." *Br.*

Belladonna liniment is an irrational preparation. It is highly improbable that applied in the manner of a liniment the belladonna penetrates the skin in sufficient quantities to have any effect, and it is difficult to understand what beneficial action could result if it did penetrate the skin. A solution of camphor and alcohol would be therapeutically equivalent to this liniment.

LINIMENTUM CALCIS. U. S., Br.

LIME LINIMENT Lin. Calc. [Carron Oil]

Liniment of Lime; Liniment calcaire, Savon calcaire, *Fr.;* Kalkliniment, *G.;* Linimento de calce, *It.;* Linimento Oleo-calcareo, *Sp.*

"Solution of Calcium Hydroxide, 500 cc.; Linseed Oil, 500 cc.; to make 1000 cc. Mix them by agitation." *U. S.*

"Solution of Lime, 500 *millilitres;* Olive Oil, 500 *millilitres.* Shake together." *Br.*

The lime forms a soap with part of the oil, the remainder of the oil then being easily emulsified by shaking, so that a thick creamy mixture results. Olive oil, as directed by the British Pharmacopœia, is often substituted for that of flaxseed, which was originally used, but it possesses no other advantage than that of having a less unpleasant odor and of being somewhat less expensive.

This is an emulsion of the water in oil type, in which a calcium soap is the emulsifying agent.

The name of Carron oil was given to this emulsion from the fact that it was first employed at the Carron Iron Works in Scotland. For many years it has enjoyed a great popularity as an application in *burns* and *scalds.* The values claimed for it are that it relieves pain by excluding the air and tends to restore alkalinity to the burnt area. Many modern surgeons, however, object to this method of treatment on the ground that it makes it almost impossible to keep the injured area sterile.

LINIMENTUM CAMPHORÆ. U. S., Br.

CAMPHOR LINIMENT Lin. Camph. [Camphorated Oil]

"Camphor Liniment yields not less than 19 per cent. and not more than 21 per cent. of camphor. *Caution—This preparation is not intended for hypodermic use.*" *U. S.*

Liniment of Camphor, Linimentum Camphoratum; Huile camphrée, Liniment camphré, *Fr.;* Kampherliniment, Kampheröl, *G.;* Oleum Camphoratum, *P. G.*

"Camphor, in coarse powder, 200 Gm.; Cottonseed Oil, 800 Gm; to make 1000 Gm. Pour the cottonseed oil into a suitable dry flask or bottle, heat it on a water bath, introduce the camphor, and stopper the container securely. Dissolve the camphor by agitation without the further application of heat." *U. S.*

"Camphor, in flowers, 200 *grammes;* Olive Oil, 800 *grammes.* Dissolve the Camphor in the Olive Oil in a closed vessel." *Br.*

"**Assay.**—Place 5 cc. of Camphor Liniment in a tared, porcelain dish, having a diameter of about 75 mm., weigh accurately, heat at about 110° C. for ninety minutes, or until the odor of camphor is no longer discernible, cool, and weigh; the loss in weight is not less than 19 per cent. and not more than 21 per cent." *U. S.*

S. D. Wetterstroem prefers cold solution to the official method, thus avoiding any loss of camphor. (*West. Drug.,* 1897, 68.) For methods of assaying camphor liniment, see *C. D.,* 1900, 338; *P. J.,* 1898, 545; *P. J.,* 1902, 106; *Am. Drug.,* 1905, 345.

Uses.—This liniment is a very popular counter-irritant embrocation in *sprains, bruises, rheumatism, acute bronchitis,* and various other inflammatory states. Camphor liniment should not be confounded with camphorated oil of the German Pharmacopœia which is much weaker (1 in 10).

For fatal case of poisoning from swallowing this liniment, see Barker, *B. M. J.,* 1910, ii, p. 921. (See also under *Camphora.*)

The term "camphorated oil" is sometimes applied to a solution of camphor in olive oil intended for hypodermic use; the liniment of camphor must not be used for this purpose.

Off. Prep.—Linimentum Chloroformi, *Br.;* Linimentum Hydrargyri, *Br.;* Linimentum Terebinthinæ Aceticum, *Br.;* Ceratum Camphoræ, *N. F.*

LINIMENTUM CAMPHORÆ AMMONIATUM. Br.

AMMONIATED LINIMENT OF CAMPHOR

Compound Liniment of Camphor, *Br.;* Liniment ammoniacal camphré, *Fr.;* Linimentum Ammoniacale Camphoratum, *Fr. Cod.;* Linimentum ammoniato-camphoratum, *P. G.;* Flüchtiges Kampherliniment, Ammoniak- und Kampher-Liniment, *G.;* Linimento ammoniacale canforato, *It.;* Linimento amoniacal alcanforado, *Sp.*

"Camphor, 125 *grammes;* Oil of Lavender, 5 *millilitres;* Strong Solution of Ammonia, 250 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Dissolve the Camphor and Oil of Lavender in six hundred *millilitres* of the Alcohol; add the Strong Solution of Ammonia gradually, shaking frequently; finally add sufficient of the Alcohol to produce the required volume." *Br.*

This is inferior to the camphor liniment because the absence of a lubricant makes rubbing difficult.

LINIMENTUM CHLOROFORMI. U. S., Br.

CHLOROFORM LINIMENT Lin. Chlorof.

Liniment of Chloroform; Liniment au Chloroforme, *Fr. Cod.;* Chloroformliniment, *G.*

"Chloroform, 300 cc.; Soap Liniment, 700 cc.; to make 1000 cc. Mix them by agitation." *U. S.*

"Chloroform, 500 *millilitres;* Liniment of Camphor, 500 *millilitres.* Mix." *Br.*

A very great improvement was made in this preparation by the Committee of Revision of 1880, in the substitution of soap liniment for the olive oil. This change had been proposed in a previous edition of the Dispensatory, and it was desirable on account of the greasy residue which was left on the skin by the old preparation. The British Pharmacopœia has retained the oily vehicle. An accurate and expeditious method of assaying this liniment for its chloroform content is suggested by Jos. L. Mayer (*Proc. N. Y. S. P. Assn.*, 1912, p. 295), which consists in distilling the chloroform and collecting it in a graduated cylinder containing distilled water. The chloroform is measured when it ceases to come over and the calculation readily made. This is an excellent local application in painful affections. As the chloroform rapidly evaporates, it is desirable, in order to obtain its full counter-irritant effect, to guard against this by using waxed paper, or some other impermeable covering.

LINIMENTUM CROTONIS. Br.

LINIMENT OF CROTON OIL

Linimentum Tiglii, *N. F. IV;* Liniment crotoné, *Fr.;* Krotonölliniment, *G.*

"Croton Oil, 120 *millilitres;* Oil of Cajuput, 440 *millilitres;* Alcohol (90 per cent.), 440 *millilitres.* Mix." *Br.*

This is a pustulating preparation, the irritant influence of which has been increased by the substitution of the oil of cajuput and alcohol for the olive oil of the original formula. From ten to thirty minims (0.6–1.8 cc.) may be rubbed upon a limited surface, and repeated twice a day or oftener until an eruption is produced.

LINIMENTUM HYDRARGYRI. Br.

LINIMENT OF MERCURY

Linimentum Mercuriale; Liniment mercuriel, *Fr.;* Quecksilberliniment, *G.*

"Ointment of Mercury, 50 *grammes;* Solution of Ammonia, 40 *millilitres;* Liniment of Camphor, 80 *millilitres.* Shake the Solution of Ammonia with the Liniment of Camphor, and triturate the Ointment of Mercury with the mixture. This Liniment contains approximately three-fifths of the proportion of Mercury contained in the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

This is a stimulating liniment, employed for both its local and constitutional effects in *syphilitic pains,* in *glandular enlargements, swellings of the joints,* and to promote the absorption of fluid. It is said to be more likely to salivate than is mercurial ointment. One fluidrachm (3.75 cc.) may be rubbed upon the affected part night and morning. It should be thoroughly agitated before being applied.

LINIMENTUM OPII. Br.

LINIMENT OF OPIUM

Anodyne Liniment; Liniment opiacé, *Fr.;* Opiumliniment, *G.*

"Tincture of Opium, 500 *millilitres;* Liniment of Soap, 500 *millilitres.* Mix; set aside for a few days; filter." *Br.*

The use of this class of preparations is founded on error, as opium is not efficient as a local remedy.

LINIMENTUM POTASSII IODIDI CUM SAPONE. Br.

LINIMENT OF POTASSIUM IODIDE WITH SOAP

Liniment savonneux ioduré, *Fr.;* Jodkalium-Seifenliniment, *G.*

"Curd Soap, recently prepared and in shavings, 40 *grammes;* Potassium Iodide, 30 *grammes;* Glycerin, 20 *millilitres;* Oil of Lemon, 2 *millilitres;* Distilled Water, 200 *millilitres.* Mix the Curd Soap with the Distilled Water and Glycerin in a tared porcelain dish on a water-bath; when the Soap is dissolved make up to the original weight with Distilled Water; pour the liquid into a mortar containing the Potassium Iodide, previously powdered; mix briskly by trituration; continue the trituration until the mixture is cold, set aside for an hour; then add the Oil of Lemon, and again triturate the gelatinous product." *Br.*

This preparation is apparently intended, by application to the surface, which may be attended with a gentle friction, to produce the absorption of the iodide, an occurrence which in light of our present knowledge seems very improbable. The soap and glycerin act as demulcents, and thus obviate in some measure the local irritation of the salt.

LINIMENTUM SAPONIS. U. S., Br.

SOAP LINIMENT Lin. Sapon.

Tinctura Saponis Camphorata, *U. S.* 1850; Spiritus Nervinus Camphoratus; Camphorated Tincture of Soap; Liquid Opodeldoc; Liniment savonneux camphré, *Fr.;* Linimentum saponato camphoratum, *P. G.;* Flüssiger Opodeldok, *G.;* Linimento di sapone con canfora, *It.*

"Soap, dried and granulated, or powdered, 60 Gm.; Camphor, in small pieces, 45 Gm.; Oil of Rosemary, 10 cc.; Alcohol, 700 cc.; Water, a sufficient quantity; to make 1000 cc. Dissolve the camphor and the oil of rosemary in the alcohol, add the soap, and then sufficient water to make the product measure 1000 cc. Agitate the mixture until the soap is dissolved, set it aside in a cool place for twenty-four hours, and filter." *U. S.*

"Soft Soap, 80 *grammes;* Camphor, 40 *grammes;* Oil of Rosemary, 15 *millilitres;* Distilled Water, 170 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Dissolve the Soap, Camphor, and Oil of Rosemary in six hundred *millilitres* of the Alcohol; add the Distilled Water and sufficient of the Alcohol to produce the required volume; set aside for a week; filter." *Br.*

This process is intended to furnish a saturated solution of Castile soap. The improvement was made in the eighth revision of the U. S. P. of making a gelatinous mass of the soap by adding it to sufficient boiling water and heating it until dissolved; the soft mass easily dissolves in the alcoholic solution of the oils, but in the U. S. P. X retains the process of the ninth revision in which process the granulated or powdered soap is added to the alcohol and when the water is introduced solution occurs almost at once. The liquid should be cold before filtration to avoid precipitation in cold weather. The British preparation is now made with soft (potash) soap; this method was recommended by J. T. Hornblower. (*C. D.,* 1894, 571.) The liniment is said to be made more quickly and precipitation is avoided. Various other soaps have been recommended. (See *U. S. D.,* 20th ed., p. 621.)

Any pharmaceutical difficulty encountered in making a satisfactory preparation by the official formula can usually be attributed to the use of soap which is not in compliance with the official requirements.

The N. F. recognizes under the title *Linimentum Saponis Camphoratum* a semi-solid preparation which had a wide popularity under the name *opodeldoc.* (See Part III.)

Soap liniment is much used as a gently rubefacient embrocation, in *sprains, bruises,* and *rheumatic* or *gouty pains,* but is too feeble to exercise any pronounced effect. It is largely used as a vehicle for more active counter-irritants.

Off. Prep.—Linimentum Chloroformi, *U. S.;* Linimentum Opii, *Br.;* Linimentum Aconiti et Chloroformi, *N. F.*

LINIMENTUM SAPONIS MOLLIS. U. S.

LINIMENT OF SOFT SOAP Lin. Sapon. Moll.
[Tincture of Green Soap]

Tinctura Saponis Virdis, *U. S. P.* 1880; Spiritus Saponis Kalini Hebra; Teinture de Savon vert, *Fr.;* Hebra's Seifenspiritus, *G.*

"Soft Soap, 650 Gm.; Oil of Lavender, 20 cc.; Alcohol, a sufficient quantity, to make 1000 cc. Mix the oil of lavender with 300 cc. of alcohol, dissolve in this the soft soap by stirring or by agitation, and set the solution aside for twenty-four hours. Then filter it through paper, adding sufficient alcohol to make the product measure 1000 cc." *U. S.*

C. E. Smith suggested the preparation of this liniment from the fixed oil directly, which has the advantage of convenience as well as of greater uniformity of strength. (See *U. S. D.,* 19th ed., p. 698.) If a green color is desirable in this preparation, it may be obtained by using hemp seed oil or Malaga olive oil. (See *Proc. A. Ph. A.,* 1903, 420.)

LINIMENTUM SINAPIS. Br.

LINIMENT OF MUSTARD

Linimentum Sinapis Compositus, *N. F.;* Liniment Sinapisé composé, *Fr.;* Zusammengesetztes Senfliniment, Senfliniment, *G.*

"Volatile Oil of Mustard, 35 *millilitres;* Camphor, 55 *grammes;* Castor Oil, 125 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Dissolve the Camphor and the Oils in the Alcohol." *Br.*

The N. F. preparation differs from the Br. in containing fluidextract of mezereum in addition to the mustard oil and camphor (see Part III). It affords a convenient method of applying the volatile oil of mustard, and may often be appropriately used as a substitute for sinapisms. The castor oil seems to be added in order to increase somewhat the consistence of the liniment, and was probably chosen from among oleaginous substances in consequence of its solubility in alcohol. The effect is increased if the liniment be applied on flannel, and volatilization guarded against by covering it with oiled silk.

LINIMENTUM TEREBINTHINÆ. Br.

TURPENTINE LINIMENT

Linimentum Terebinthinatum; Liniment of Turpentine; Liniment térébenthiné, *Fr.;* Terpentinliniment, *G.*

"Soft Soap, 75 *grammes;* Camphor, 50 *grammes;* Rectified Oil of Turpentine, 650 *millilitres;* Distilled Water sufficient to produce 1000 *millilitres.* Mix the Soft Soap with one hundred *millilitres* of the Distilled Water; dissolve the Camphor in the Oil of Turpentine; gradually add the latter solution to the former, triturating until the mixture becomes a thick creamy emulsion; add sufficient Distilled Water to produce the required volume." *Br.*

More than a century ago a Doctor Kentish proposed for the treatment of *burns* a mixture of resin cerate and oil of turpentine; this was long known as *Kentish's ointment.* This was official in the first edition of the U. S. P. and remained practically unchanged through the ninth revision but was dropped from the tenth. The original formula, for some inexplicable reason, was changed in the 1867 revision of the Br. by the substitution of soft soap for the cerate and an increase in the proportion of the oil of turpentine. This change produced a preparation of entirely different therapeutic properties, more fitted for a counter-irritant liniment than for the treatment of inflammatory conditions of the skin. The present British preparation, so far as regards its rubefacient operation, may be looked upon as almost undiluted oil of turpentine, the soft soap having little other effect than to give consistence to the liniment, and the camphor acting as an anodyne, and both being too small in bulk to dilute the oil materially.

LINIMENTUM TEREBINTHINÆ ACETICUM. Br.

LINIMENT OF TURPENTINE AND ACETIC ACID

Linimentum Album; Acetic Turpentine Liniment, Stokes' Liniment; Liniment térébenthiné acétique, *Fr.;* Terpentin- und Essig-liniment, *G.*

"Glacial Acetic Acid, 110 *millilitres;* Liniment of Camphor, 445 *millilitres;* Rectified Oil of Turpentine sufficient to produce 1000 *millilitres.* Mix." *Br.*

Under this name the National Formulary (see Part III) contains a formula for *St. John Long's Liniment,* which unfortunately is not identical with the process of the British Pharm., 1914.

This is a powerful rubefacient liniment, combining the irritant properties of the oil of turpentine and acetic acid, though somewhat diluted by the camphor liniment. Glacial acetic acid was substituted for acetic acid in the 1885 revision in equivalent proportion; the change is an improvement pharmaceutically, as it now affords a clear solution.

LINUM. U. S. (Br.)

LINSEED [Flaxseed]

"Linseed is the dried ripe seed of *Linum usitatissimum* Linné (Fam. *Linaceæ*). Linseed contains not more than 2 per cent. of other seeds or foreign organic matter, and yields not less than 30 per cent. of non-volatile ether-soluble extractive, at least 98 per cent. of which is saponifiable." *U. S.* "Linseed consists of the dried ripe seeds of Linum usitatissimum, *Linn.*" *Br.*

Lini Semina, *Br.;* Semence de Lin, *Fr. Cod.;* Grains de Lin, *Fr.;* Semen Lini, *P. G.;* Leinsamen, Flachssamen, *G.;* Lino, Semi di Lino, *It.;* Lino (Semilla de), Linaza, *Sp.*

Off. Prep.—Lini Semina Contusa, *Br.;* Species Emollientes, *N. F.*

LINI SEMINA CONTUSA. Br.

CRUSHED LINSEED

"Crushed Linseed is Linseed reduced to a coarse powder. It should be recently prepared." *Br.*

Linum Contusum, *Br.* 1898; Crushed Flaxseed.

Common *flax* is an annual plant, with an erect, slender, smooth stem, about two feet in height, branching at top, and bearing alternate, linear-lanceolate, sessile leaves. The flowers are terminal, and of a delicate-blue color. The fruit is a globular capsule, about the size of a small pea, having the persistent calyx at the base, crowned with a sharp spine, and containing ten seeds in distinct cells. This highly valuable plant, now almost everywhere cultivated, is said by some to have been originally derived from Egypt, by others from the great elevated plain of Central Asia. Its original home is unknown. It flowers in June and July, and ripens its seeds in August.

The flax plant was cultivated for its fiber by the American colonists soon after the landing of Columbus. Soon thereafter it was grown for its seed and already in 1792 the United States exported nearly 300,000 bushels of flaxseed. Very early the linseed oil industry was developed in the United States and in 1810 there were nearly 300 linseed oil mills in the 14 states, more than half of them being in Pennsylvania. It is estimated that at the present time 12,000,000 bushels of seed are crushed annually for the oil. The annual crop of flaxseed in the United States exceeds 30,000,000 bushels of which nearly one-half is produced in North Dakota. A large quantity of seed is annually exported as well as oil-cake, the latter being extensively used as a cattle food.

Description and Physical Properties.—"*Unground Linseed.*—Ovate or oblong-lanceolate, flattened, obliquely pointed at one end, from 4 to 6 mm. in length; externally brown, smooth and shiny; raphe a distinct yellow ridge along one edge, the hilum and micropyle in a slight depression just below the pointed end; internally light yellow or brownish, oily; odor slight; taste mucilaginous and oily.

"*Structure.*—Epidermis with a mucilaginous outer wall covered by a very thin, more or less broken sheath of cutin; two layers of parenchyma overlying a continuous layer of stone cells; a pigment layer, the cells having reddish-brown contents; endosperm of from 6 to 10 rows of cells, surrounding two large, plano-convex cotyledons, cells of cotyledons and endosperm containing a fixed oil and aleurone grains.

"*Powdered Linseed.*—Yellowish-brown; consisting chiefly of large, oil globules and irregular fragments of endosperm and seed-coat; seed-coat characterized by tabular pigment cells filled with reddish-brown insoluble contents and by the somewhat radially elongated stone cells with yellowish, porous walls and rather large lumina;

aleurone grains from 0.003 to 0.020 mm. in diameter.

"*Linseed Meal.*—Yellow with numerous brown fragments; the fragments of both seed-coat and kernel mostly very coarse and with the same cellular tissues as those of the powder.

"Boil 1 Gm. of fat-free Linseed Powder or Meal with 50 cc. of water, cool, and filter: the filtrate shows, upon the addition of iodine T.S., not more than a faint blue color (*starch or starch-bearing seeds*).

"**Assay.**—Proceed as directed under non-volatile, ether-soluble extractive, page 466, using 4 Gm. of ground or powdered Linseed. Treat the anhydrous extractive as directed under saponification value." *U. S.*

"Seeds small, brown, glossy, nearly flat; from about four to six millimetres long; ovate, somewhat obliquely pointed; surface glabrous and minutely pitted. Internally yellowish-white, with a narrow oily endosperm and two large oily cotyledons. Epidermal cells filled with mucilage which swells and dissolves in *water*. No odor; taste mucilaginous, oily." *Br.*

The linseeds in commerce have been divided by E. M. Holmes into two groups. The first group, characterized by the seeds being of sufficient size for six or seven to weigh a grain, contains Bombay, Bold Calcutta, Sicilian, and Ionian seed; in the group of small seeds (10 to 12 to the grain) are English, Dutch, Russian, and ordinary Calcutta varieties. An important practical point noticed by Holmes is that much of the drug of commerce is adulterated with weed seeds, which are nearly always smaller than the linseeds, and can therefore be separated by the sieve. When linseed meal is to be made for medicinal use, this separation should always be insisted upon, as many of the weed seeds are from Cruciferæ, and are irritating. For detailed information as to varieties of linseed, weed seeds, etc., the reader is referred to Holmes's paper. (*P. J.*, July, 1881; also *N. R.*, 1881.)

The ground seeds are found in commerce under the name of *flaxseed meal*. This is of a brownish gray color, highly oleaginous, and when mixed with hot water forms a soft adhesive mass, much employed for luting by practical chemists.

Crushed flaxseed is "a coarse, brownish-yellow powder, with readily visible fragments of the brown seed-coats. Bland, not pungent or rancid, odor when mixed with warm *water*. Yields not less than 30 per cent. of oil when exhausted by *carbon disulphide;* the oil thus obtained responds to the tests described under 'Oleum Lini'; the residual powder exhibits no starch grains when examined under the microscope. Ash not more than 5 per cent." *Br.*

Much of the linseed meal of commerce is simply cake meal, which was, indeed, official in the former Br. Ph., but such meal is unfit for medicinal use, not only because it contains very little oil, but also because the oil which is in it has, through rupture of the cells and partial expression, been so exposed to the air as to become rancid. The residue after expression of the oil is used as a cattle-food. Linseed meal is sometimes adulterated with corn meal, or other meals containing starch, whose presence is at once revealed by the iodine test. It has been found in the market adulterated with petroleum or other mineral oil, doubtless made by powerfully pressing the pure linseed meal and substituting for the linseed oil the less expensive product, petroleum. (*A. J. P.*, 1902, 31.)

The absolute value of a sample of crushed linseed can be determined by analysis. It should contain from 25 to 35 per cent. of oil, not more than 8 or 8.5 per cent. of husk, and less than 8 per cent. of ash. The following *test* is said to be sufficient for practical purposes: "Put half an ounce of the meal into a glass vessel, pour six ounces of boiling water over it, stir well, and allow it to stand for twelve hours. If first-class, it should absorb all the water, and show a thin scum of white glutinous liquid on the top, which will adhere closely to a glass rod or a wooden pencil dipped into it. If the meal does not absorb nearly all the water, it is of inferior quality. The amount of inferiority must be judged by the amount of water not absorbed, and by the character of the fluid on the top of the solution. If it is thin and nonglutinous, the meal is of inferior quality."

Linseed contains from 30 to 40 per cent. of a characteristic fixed oil (see *Oleum Lini*) besides wax, resin, tannin, gum and protein. For some years there has been a discussion as to the presence of starch. Certain tissues of the seed coat beneath the mucilaginous epidermis may give a starch reaction and it is stated that even the cells may contain starch (*Proc. A. Ph. A.*, 1907, lv, p. 326). The present indications are that starch grains are not usually present in the ripe seed although they may occur in appreciable quantities in the immature seeds (*Ph. Ztg.*, li, p. 658). The investing coat of the seed abounds in a peculiar gummy matter or mucilage amounting to about 6 per cent. of the seeds. This is readily soluble in hot water forming a thick viscid mucilage which deposits white flakes upon the addition of alcohol and affords a copious dense precipitate with lead subacetate. Albuminous matter is present to the extent of about 20 per cent. and sugars to the extent of about 18 per cent.

The ash of flaxseed amounts to from 2 to 6 per cent. of the weight of the seed.

The gum of linseed contains in the dry state more than 10 per cent. of mineral substances; when freed from these and dried at 110° C., it has, like althæa mucilage, the formula $C_{12}H_{20}O_{10}$. The seeds by exhaustion with cold or warm water afford about 15 per cent. of this mucilage. By boiling with nitric acid, it yields crystals of mucic acid; by diluted mineral acids, it is broken up into dextrogyrate gum, sugar, and cellulose. (Kirchner and Tollens, *Ann. Ch.*

Ph., clxxv, 215.) For further information on the histology and pharmacognosy of the flaxseed, see Winton and Moeller, "The Microscopy of Vegetable Foods;" Kate B. Winton, *Bot. Gaz.*, lviii, p. 2445; Collin, *J. P. C.*, 1909, xxix, p. 369.

Jorissen and Hairs (*Drogues Simples*, t. ii, 685) obtained from the young plant a glucoside, to which they gave the name of *linamarin*, which crystallizes in colorless needles, melting at 134° C., without odor, but possesses a fresh and bitter taste. It differs from amygdalin in not being decomposed by emulsin, but diluted acids decompose it into sugar, hydrocyanic acid, and a third product which is volatile and possesses certain of the characters of the acetones. No benzaldehyde is formed.

Uses.—Because of the mucilage and oil it contains, flaxseed is both demulcent and emollient. The meal mixed with hot water forms an excellent emollient poultice which is of much value in the treatment of local inflammations such as *furunculosis*. Its peculiar usefulness is due partially to the oil which softens the skin and partially to the fact that the flaxseed poultice retains heat much better than most substitutes. There is a popular notion that the mucilaginous substances can be absorbed and exercise an internal demulcent action, and an infusion made by treating the whole seeds with boiling water is widely employed in catarrhs of the respiratory or urinary tracts. But as the gums, like other carbohydrates, are affected by digestive juices, much benefit is not to be expected from such a use of the drug. The whole seed is occasionally given in tablespoonful doses as a laxative.

LIQUOR ACIDI ARSENOSI. U. S. (Br.)

SOLUTION OF ARSENOUS ACID Liq. Acid. Arsen. [Hydrochloric Solution of Arsenic, Solution of Arsenic Chloride]

"Solution of Arsenous Acid contains, in each 100 cc., the equivalent of not less than 0.975 Gm. and not more than 1.025 Gm. of As_2O_3." *U. S.*

Liquor Arsenici Hydrochloricus, *Br.;* Liquor Arsenici Chloridi, *U. S. P.* 1870; Liqueur de Boudin, Liqueur arsénicale hydrochlorique, *Fr.;* Chlorarsenik-Lösung, *G.*

"Arsenic Trioxide, 10 Gm.; Diluted Hydrochloric Acid, 50 cc.; Distilled Water, a sufficient quantity to make 1000 cc. Mix the diluted hydrochloric acid with 250 cc. of distilled water in a flask, add the arsenic trioxide, and boil the liquid until the arsenic trioxide is completely dissolved. Allow the solution to cool, transfer it to a 1000 cc. graduated flask or cylinder, rinse the vessel in which the solution was boiled, with several portions of distilled water, and add the rinsings and enough distilled water to make the product measure 1000 cc. Filter if necessary." *U. S.*

"Arsenious Anhydride, in powder, 10 *grammes;* Hydrochloric Acid, 12 *millilitres;* Distilled Water sufficient to produce 1000 *millilitres*. Dissolve the Arsenious Anhydride and the Hydrochloric Acid in five hundred *millilitres* of Distilled Water by the aid of heat; cool; add sufficient Distilled Water to produce the required volume." *Br.*

This solution is stronger than the *Liquor Arsenici Chloridi* of the U. S. P., 1870. The name has also been changed, as the former title was a misnomer. The hydrochloric acid does not enter into combination with the arsenic trioxide; it merely aids in its solution. True arsenic chloride, As_2Cl_6, cannot exist in aqueous solution but is immediately hydrolized into arsenous and hydrochloric acids. The British title is, in our opinion, to be preferred, because the U. S. name does not indicate the presence of the hydrochloric acid.

Description and Physical Properties.—"A clear, colorless liquid without odor. Solution of Arsenous Acid is acid to litmus paper. Hydrogen sulphide T.S. added to Solution of Arsenous Acid produces a lemon-yellow precipitate of arsenic trisulphide, which is completely soluble in ammonium carbonate T.S.

"**Assay.**—Measure exactly 20 cc. of Solution of Arsenous Acid and dilute with about 50 cc. of distilled water, dissolve enough sodium bicarbonate in this solution to make it distinctly alkaline (usually about 2 Gm.), and titrate with tenth-normal iodine, using starch T.S. as indicator. Each cc. of tenth-normal iodine corresponds to 0.004948 Gm. of As_2O_3." *U. S.*

According to the British Pharmacopœia, it is "a colorless liquid; acid to *litmus*. 25 millilitres diluted with *water* discharge the color of 50.4 millilitres of *N/10 solution of iodine*, the presence of a slight excess of *sodium bicarbonate* being maintained throughout the operation. This Solution contains 1 gramme of Arsenious Anhydride in 100 millilitres; 110 minims contain 1 grain." *Br.*

Uses.—The medicinal properties of this solution are the same as those of Fowler's solution, with which it corresponds in strength.

Dose, from two to eight minims (0.12–0.5 cc.).

Off. Prep.—Elixir Chloridorum, *N. F.*

LIQUOR ACIDI CHROMICI. Br.

SOLUTION OF CHROMIC ACID

Soluté d'Acide Chromique, *Fr. Cod.;* Chromsaurelösung, *G.*

"Chromic Anhydride, 25 *grammes;* Distilled Water sufficient to produce 100 *millilitres*. Dissolve." *Br.*

This was officially described in the British Pharm., 1898, as "an orange-red, inodorous, caustic, strongly acid liquid. Specific gravity, 1.185. It should respond to the tests described under 'Acidum Chromicum.'"

It is simply a definite solution of chromic anhydride (25 per cent.), which unites with the water to form chromic acid, H_2CrO_4, and will probably be found convenient as a caustic application. (See *Chromii Trioxidum.*) It is not used internally.

LIQUOR AMMONII ACETATIS.
U. S., Br.

SOLUTION OF AMMONIUM ACETATE Liq. Ammon. Acet. [Spirit of Mindererus]

“Solution of Ammonium Acetate contains, in each 100 cc., not less than 6.5 Gm. and not more than 7.5 Gm. of $NH_4C_2H_3O_2$, with small amounts of acetic and carbonic acids. *Caution—Only a recently prepared Solution of Ammonium Acetate should be dispensed.*” *U. S.*

Spiritus Mindereri; Liquor Ammoniæ Acetatis; Acétate d'Ammoniaque liquide, Esprit de Mindérérus, *Fr.;* Liquor Ammonii Acetici, *P. G.;* Ammoniumacetatlösung, Essigsaure Ammoniumlösung, *G.*

“Ammonium Carbonate, in hard, translucent pieces, 5 Gm.; Diluted Acetic Acid, 100 cc. Dissolve the ammonium carbonate in the diluted acetic acid without strong agitation.

“Solution of Ammonium Acetate may also be prepared as follows: *Solution No. 1.* Ammonium Carbonate, in hard, translucent pieces, 50 Gm.; Distilled Water, a sufficient quantity to make 500 cc. *Solution No. 2.* Acetic Acid, 160 cc.; Distilled Water, a sufficient quantity to make 500 cc. Cautiously mix the two solutions in equal volumes in a capacious vessel, in quantities sufficient to produce the amount of Solution of Ammonium Acetate needed.” *U. S.*

“Acetic Acid, 162.5 *millilitres;* Ammonium Carbonate, 50.0 *grammes,* or a sufficient quantity; Distilled Water sufficient to produce 1000.0 *millilitres.* Mix the Acetic Acid with five hundred *millilitres* of the Distilled Water; neutralise with Ammonium Carbonate; add sufficient Distilled Water to produce the required volume.” *Br.*

This preparation is an aqueous solution of ammonium acetate. The process by which it is formed involves the decomposition of ammonium carbonate by diluted acetic acid. In order to prepare this solution of official quality and the proper reaction the ammonium carbonate must be in translucent pieces as directed, and must not be effloresced.

Description and Physical Properties.—“A clear, colorless liquid, free from empyreumatic odor. It has a mildly saline, acidulous taste, and an acid reaction. Solution of Ammonium Acetate responds to the reactions for ammonium, and for acetates. Not more than 0.003 Gm. of ash remains on evaporating 20 cc. of the Solution and igniting the residue.

“**Assay.**—Transfer 25 cc. of Solution of Ammonium Acetate to a distilling flask, dilute with 100 cc. of distilled water, add 25 cc. of 10 per cent. sodium hydroxide solution, and distil the liquid until all of the ammonia has been driven over (about 100 cc. of distillate), receiving the distillate under the surface of 50 cc. of normal sulphuric acid contained in a flask. Titrate the excess of acid with normal sodium hydroxide, using methyl orange T.S. as indicator. Each cc. of normal sulphuric acid corresponds to 0.07707 Gm. of $NH_4C_2H_3O_2$.” *U. S.*

“Specific gravity 1.016. Mixed with an equal volume of a saturated aqueous solution of *hydrogen sulphide* not more than the slightest darkening in color results (limit of heavy metals). Solution of Ammonium Acetate should be preserved in a vessel free from lead.” *Br.*

Uses.—Solution of ammonium acetate is used as a saline diaphoretic and diuretic, especially in febrile conditions.

Dose, from half a fluidounce to a fluidounce and a half (15–45 cc.) every three or four hours, mixed with water and sweetened with sugar.

Off. Prep.—Liquor Ferri et Ammonii Acetatis, *U. S.*

LIQUOR AMMONII CITRATIS. Br.

SOLUTION OF AMMONIUM CITRATE

Citrate d'Ammoniaque liquide, *Fr.;* Ammoniumcitratlösung, Citronensaure Ammoniak-Flüssigkeit, *G.*

“Citric Acid, 125.0 *grammes;* Ammonium Carbonate, 87.5 *grammes,* or a sufficient quantity; Distilled Water sufficient to produce 1000.0 *millilitres.* Dissolve the Citric Acid in five times its weight of Distilled Water; neutralise with Ammonium Carbonate; add sufficient Distilled Water to produce the required volume. Specific gravity, 1.057. Mixed with an equal volume of a saturated aqueous solution of *hydrogen sulphide* not more than the slightest darkening in color results (limit of heavy metals). Solution of Ammonium Citrate should be preserved in a vessel free from lead.” *Br.*

This solution is also official in the N. F. (See Part III.)

This solution may be used for the same purposes as *Solution of Ammonium Acetate.*

Dose, from two to six fluidrachms (7.5–22.5 cc.).

LIQUOR ARSENI ET HYDRARGYRI IODIDI.
U. S. (Br.)

SOLUTION OF ARSENOUS AND MERCURIC IODIDES Liq. Arsen. et Hydrarg. Iod. [Donovan's Solution]

“Solution of Arsenous and Mercuric Iodide is an aqueous solution containing, in each 100 cc., not less than 0.95 Gm. and not more than 1.05 Gm. of AsI_3, and not less than 0.95 Gm. and not more than 1.05 Gm. of HgI_2.” *U. S.*

Liquor Arsenii et Hydrargyri Iodidi, *Br.;* Solution of Arsenious and Mercuric Iodides; Liquor Arsenici et Hydrargyri Iodidi, *Br.* 1867, *U. S.* 1870; Solution of Hydriodate of Arsenic and Mercury; Solutio Donovani; Soluté d'Iodo-arsénite de Mercure, Liqueur de Donovan, *Fr.;* Jodquecksilber Arseniklösung, Donovansche Tropfen, *G.*

“Arsenous Iodide, 10 Gm.; Red Mercuric Iodide, 10 Gm.; Distilled Water, a sufficient quantity to make 1000 cc. Triturate the arsenous iodide and red mercuric iodide in a mortar, add 150 cc. of distilled water, and continue the trituration until solution is effected. Filter the solution, and pass sufficient distilled water through the filter to make the product measure 1000 cc. Mix thoroughly. It must not be dispensed if darker than pale yellow.” *U. S.*

“Arsenious Iodide, 10 *grammes;* Red Mercuric Iodide, 10 *grammes;* Distilled Water sufficient to produce 1000 *millilitres.* Triturate the Arsenious Iodide and Red Mercuric Iodide with two hundred and fifty *millilitres* of the Distilled Water until dissolved; filter; pass through the filter sufficient Distilled Water to produce the required volume. This Solution contains the equivalent of 1 gramme of Arsenious Iodide and 1 gramme of Red Mercuric Iodide in 100 millilitres; 110 minims contain the equivalent of 1 grain of each salt." *Br.*

This solution was introduced to the notice of the medical profession in 1839 by Donovan, of Dublin, as a therapeutic agent combining the medicinal virtues of its three ingredients, and was adopted as an official preparation in the U. S. and Dublin Pharmacopœias of 1850. The formula is the simplified one of Procter, which consists essentially in dissolving equal weights of arsenic triiodide and mercuric iodide (red iodide) in a measured quantity of distilled water.

Description and Physical Properties.—"A clear, colorless or pale yellowish liquid. Lead acetate T.S. produces in Solution of Arsenous and Mercuric Iodide, diluted with 10 volumes of distilled water, a bright yellow precipitate. Add 5 drops of Solution of Arsenous and Mercuric Iodide to a mixture of about 0.5 Gm. of zinc and 5 cc. of diluted hydrochloric acid in a test tube, and cover the mouth of the test tube with mercuric bromide test paper: a yellow stain appears upon the inner surface of the test paper within one minute. Solution of Arsenous and Mercuric Iodide responds to the tests for mercury, page 443.

"**Assay for Arsenous Iodide.**—Measure accurately 25 cc. of Solution of Arsenous and Mercuric Iodide into a flask, dilute with 25 cc. of distilled water, then dissolve 2 Gm. of sodium bicarbonate in this solution, and titrate with tenth-normal iodine, using starch T.S. as indicator. Each cc. of tenth-normal iodine corresponds to 0.02279 Gm. of AsI_3.

"**Assay for Mercuric Iodide.**—Measure accurately 25 cc. of Solution of Arsenous and Mercuric Iodide into a flask, add 5 cc. of potassium hydroxide T.S. and 5 cc. of formaldehyde T.S., and warm the mixture on a water bath until the mercuric salt has been completely reduced to metallic mercury. Carefully decant the clear, supernatant liquid from the residue of metallic mercury, and wash the mercury carefully by decantation with two successive portions of 25 cc. each of distilled water. Dissolve the residue of metallic mercury in 5 cc. of nitric acid by the application of gentle heat, dilute the solution with 50 cc. of distilled water, add 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate. Each cc. of tenth-normal potassium thiocyanate corresponds to 0.02272 Gm. of HgI_2.

"Preserve in well-filled, amber-colored bottles." *U. S.*

Uses.—This preparation has been found decidedly useful as an alterative in various chronic diseases of the skin, such as in the later stages of *syphilis,* especially with "night pains;" in certain cases of *lymphadenitis* and in some forms of chronic joint disease.

Dose, from one to five minims (0.06–0.3 cc.), three times a day, given preferably in distilled water.

LIQUOR ATROPINÆ SULPHATIS. Br.

SOLUTION OF ATROPINE SULPHATE

Soluté de Sulfate d'Atropine, *Fr.;* Schwefelsaure Atropinlösung, *G.*

"Atropine Sulphate, 1 *gramme;* Distilled Water, recently boiled and cooled, sufficient to produce 100 *millilitres.* Dissolve. This Solution should be freshly prepared. It contains 1 gramme of Atropine Sulphate in 100 millilitres; 110 minims contain 1 grain." *Br.*

This solution contains 1 per cent. of atropine sulphate. Camphor water was substituted for distilled water on account of its antiseptic properties at the 1885 revision. Salicylic acid and distilled water were used (1898) with the same object in view, but the British Pharm., 1914, discarded preservatives. The solution readily develops a mould and loses strength. Therefore it should be freshly prepared as ordered.

Dose, one-half to one minim (0.03–0.06 cc.).

LIQUOR BISMUTHI ET AMMONII CITRATIS. Br.

SOLUTION OF BISMUTH AND AMMONIUM CITRATE

Liquor Bismuthi; Solution of Bismuth, Liquid Bismuth; Soluté de Citrate de Bismuth ammoniacal, *Fr.;* Citronensaure Wismuth-Ammoniak-Lösung, Wismuth-Ammoniakcitratlösung, *G.*

"Bismuth Oxynitrate, 70 *grammes;* Citric Acid, 52 *grammes;* Solution of Ammonia, Distilled Water, of each, *a sufficient quantity.* Powder the Citric Acid and mix it in a mortar with the Bismuth Oxynitrate and twenty *millilitres of Distilled Water.* Allow the mixture to stand, with occasional stirring, for half an hour, or until a small portion is completely soluble in Solution of Ammonia. Transfer to a beaker, using four hundred *millilitres* of Distilled Water to rinse the mortar. Allow the precipitate to settle, remove the clear liquid by decantation, and wash the precipitate with three successive quantities, each of four hundred *millilitres,* of Distilled Water. Add to the washed precipitate, while moist, just sufficient Solution of Ammonia to dissolve it, and then add sufficient Distilled Water to produce one thousand *millilitres* of the Solution." *Br.*

Various formulas for a similar solution have been suggested (see *U. S. D.,* 17th ed., 794, and 19th ed., 706), but that official is probably as good as any.

The British Pharmacopœia describes this preparation as "a colorless liquid, freely miscible with *water;* taste somewhat metallic; slightly alkaline to *litmus.* Evolves ammonia when heated with *solution of sodium hydroxide.* 10 millilitres, evaporated to dryness and the residue ignited, yield not less than 0.5 gramme of bismuth oxide." *Br.*

Uses.—See under *Bismuthi et Ammonii Citratis.*

Dose, from one-half to one fluidrachm (1.8–3.75 cc.).

LIQUOR CALCII HYDROXIDI. U. S. (Br.)

SOLUTION OF CALCIUM HYDROXIDE Liq. Calc. Hydrox. [Liquor Calcis, U. S. P. IX, Lime Water]

"Solution of Calcium Hydroxide is an aqueous solution containing, in each 100 cc., not less than 0.14 Gm. of $Ca(OH)_2$ at 25° C. The strength in calcium hydroxide varies with the temperature at which the solution is stored, being about 0.17 Gm. per 100 cc. at 15° C. and diminishing as the temperature rises." *U. S.*

Liquor Calcis, *Br.;* Aqua Calcariæ Ustæ, Calcaria Soluta, Solutum Calcis; Solution of Calcium Hydrate, Solution of Lime; Eau (Soluté) de Chaux, *Fr.;* Aqua Calcis, *Fr. Cod.;* Aqua Calcariæ, *P. G.;* Kalkwasser, *G.;* Acqua di calce, *It.;* Agua de cal, *Sp.*

"Lime, 25 Gm.; Water, a sufficient quantity. Slake the Lime by the addition of about 50 cc. of warm water. Transfer the mixture to a bottle having a capacity of about 4000 cc., and add 950 cc. of water. Agitate the mixture occasionally during half an hour, allow it to settle, and then decant and reject the clear liquid. To the residue add sufficient water to make about 4000 cc., agitate thoroughly, stopper the bottle and set it aside in a cool place. Decant and dispense the clear liquid. The undissolved portion should not be used for making additional quantities of Solution of Calcium Hydroxide unless the solution so prepared, is found to be of full strength when assayed." *U. S.*

"Calcium Hydroxide, 50 *grammes;* Distilled Water, *a sufficient quantity.* Wash the Calcium Hydroxide with Distilled Water until free from chlorides; then shake it with five thousand *millilitres* of Distilled Water in a stoppered green glass bottle for two or three minutes; set aside until clear. The clear Solution may be drawn off with a siphon as required for use, and should then be transferred to a green glass bottle." *Br.*

A solution of calcium hydroxide, $Ca(OH)_2$, in water is the result of these processes. By the slaking of the lime it is reduced to powder, and rendered more easily diffusible through the water. According to both Pharmacopœias, the solution is to be kept in bottles with a portion of undissolved hydroxide, which causes it always to be saturated whatever may be the temperature. If care be taken to have a considerable quantity of the solution in the bottle, and to avoid unnecessary agitation, the upper portion will always remain sufficiently clear for use. Water dissolves but a minute proportion of lime, and, contrary to the general law, less when hot than when cold. Hence the propriety of employing cold water in the process. For Green's automatic device for dispensing lime water in excellent condition, see *Proc. A. Ph. A.,* 1893, 474; see also 1904, 66.

The practice of using the undissolved lime indefinitely by refilling the bottle with water, is reprehensible, as notwithstanding the excess, its tendency to become carbonated and insoluble is great, and lime water is often dispensed deficient in strength; it is much safer to use the lime but once or twice than to run the risk of dispensing a liquid of insufficient strength.

The small tubes or vials of purified calcium hydroxide which are now available for the quick and convenient preparation of lime water are satisfactory only when properly preserved and when used exactly according to directions. Lime water cannot be instantly prepared extemporaneously as is sometimes attempted. The preparation when made too quickly is usually deficient in strength. Exposed to the air it attracts carbon dioxide, and becomes covered with a pellicle of insoluble calcium carbonate, which, subsiding after a time, is replaced by another, and so on successively until the whole of the lime is precipitated. Hence the necessity of keeping lime water either in closely corked bottles which should be full, or, what is more convenient, in bottles with an excess of lime.

Description and Physical Properties.—"A clear, colorless, odorless liquid with an alkaline taste. Specific gravity: about 1.00 at 25° C. Solution of Calcium Hydroxide is strongly alkaline to litmus paper. It absorbs carbon dioxide from the air, a film of calcium carbonate forming on the surface of the liquid. On being heated it becomes turbid, due to the separation of calcium hydroxide which redissolves when the liquid is cooled. The alkaline reaction of the Solution entirely disappears after it has been saturated with carbon dioxide and subsequently boiled (*alkalies and their carbonates*).

"**Assay.**—Titrate exactly 50 cc. of Solution of Calcium Hydroxide, at 25° C., with tenth-normal sulphuric acid, using phenolphthalein T.S. as indicator. Each cc. of tenth-normal sulphuric acid corresponds to not less than 0.003705 Gm. of $Ca(OH)_2$.

"Preserve in well-filled, tightly-stoppered bottles." *U. S.*

"Twenty-four millilitres require for neutralisation 10 millilitres of *N/10 solution of sulphuric acid.* Yields no characteristic *reactions* for lead or chlorides. This Solution contains the equivalent of rather more than 0.1 gramme of Lime, CaO, in 100 millilitres; 110 minims contain the equivalent of 1/10 grain." *Br.*

Uses.—Lime water is mildly antacid and astringent, often useful in *dyspepsia* with acidity of stomach or *diarrhea.* Mixed with from one to three measures of milk, which completely covers its offensive taste, it is of service in *nausea* and *vomiting* dependent on irritability of stomach. It is often added to milk to prevent the formation of hard curds, and thus increase its digestibility. In severe repeated vomiting with loss of digestive power a diet exclusively of lime water and milk (one to six) is often very effectual. It was formerly employed as a local remedy in *pseudo-membranous croup* by directing lime water spray, produced by the atomizer, so that it shall be inhaled by the patient. When employed to allay *nausea,* it is usually given in the dose of a tablespoonful mixed with the same quantity of milk, and repeated at intervals of half an hour, an hour, or two hours.

Dose, one to four fluidounces (30–120 cc.).

Off. Prep.—Linimentum Calcis, *U. S., Br.*

LIQUOR CALCIS CHLORINATÆ. Br.

SOLUTION OF CHLORINATED LIME

Soluté d'Hypochlorite de Chaux, *Fr. Cod.;* Chlorure de Chaux liquide, *Fr.;* Chlorkalklösung, Chlorkalk-Flüssigkeit, *G.*

"Chlorinated Lime, 100 *grammes;* Distilled Water, 1000 *millilitres.* Mix; transfer the mixture to a stoppered bottle; set aside for three hours, shaking occasionally; filter through calico. Preserve the filtrate in a stoppered bottle in a cool dark place." *Br.*

For the properties and uses of this preparation, see *Calx Chlorinata.* The British Pharmacopœia gives the following tests: "If 2 *millilitres* are added to a solution of 1 gramme of *potassium iodide* in 25 *millilitres* of *water,* acidified with 2 *millilitres* of *hydrochloric acid,* a brownish-red solution is obtained which requires for decolorisation not less than 11.7 *millilitres* of *N/10 solution of sodium thiosulphate* (presence of not less than 2 per cent. of available chlorine). When freshly prepared, this Solution yields about 3 per cent. of available chlorine." *Br.*

This solution loses strength rapidly and should therefore be prepared as needed. It is one of the best antidotes against poisoning by hydrogen sulphide, ammonium sulphydrate, potassium sulphide, and hydrocyanic acid. For external application the solution may be diluted with twice its bulk of water, or may be used of the full strength in some cutaneous affections.

Dose, for internal use, from ten to thirty minims (0.6–1.9 cc.).

LIQUOR CALCIS SACCHARATUS. Br.

SACCHARATED SOLUTION OF LIME

Syrupus Calcis (*U. S. VIII*); Syrup of Lime; Syrup of Calcium Hydroxide; Syrupus Calcariæ; Syrup of Calcium Hydroxide; Sirop de Chaux, *Fr.;* Kalksyrup, *G.*

"Calcium Hydroxide, 50 *grammes;* Refined Sugar, in powder, 100 *grammes;* Distilled Water, 1000 *millilitres.* Mix the Calcium Hydroxide with a solution of the Refined Sugar in the Distilled Water. Set aside in a stoppered green glass bottle for a few hours, shaking occasionally; separate the clear Solution by means of a siphon, avoiding unnecessary exposure to air. Specific gravity, 1.055. Twenty millilitres require for neutralisation 13.2 millilitres of *N/1 solution of sulphuric acid.* Yields no characteristic *reactions for lead.* This Solution contains the equivalent of nearly 2 grammes of Lime, CaO, in 100 millilitres; 110 minims contain nearly 2 grains." *Br.*

Sugar forms with lime certain definite compounds which may be looked upon as sucrates. According to M. S. Benedikt (*J. P. C.,* 4e sér., xix, 96), there are at least four of these combinations. Some, if not all, of them are much more soluble than the lime itself, so that in this way a much stronger solution of lime can be obtained than by the instrumentality of water alone. The syrup remains perfectly transparent, and is in no degree disturbed by dilution with water. It has a decidedly alkaline and even caustic taste, and should always be largely diluted when administered. It is sometimes employed as a milk thickener and when added to cream increases the viscosity so it may be easily "whipped."

Uses.—Syrup of lime is an active antacid and astringent, which may be used as a substitute for lime water in all cases in which that preparation is suitable. Twenty minims of it (1.3 cc.) are equal to a fluidounce of lime water.

Dose, fifteen to sixty minims (0.9–3.75 cc.).

LIQUOR CRESOLIS COMPOSITUS. U. S. (Br.)

COMPOUND SOLUTION OF CRESOL Liq. Cresol. Co.

Liquor Cresol Saponatus, *Br.;* Solution of Cresol with Soap; Soluté de Crésol composé, *Fr.;* Liquor Cresoli saponatus, *P. G.;* Kresolseifenlösung, *G.*

"Cresol, 500 cc.; Linseed Oil, 350 cc.; Dekanormal Solution of Potassium Hydroxide, 22 cc.; Dekanormal Solution of Sodium Hydroxide, 88 cc.; Water, a sufficient quantity to make 1000 cc. Mix the cresol and linseed oil, add the dekanormal solutions (see pages 501 and 504) and mix well. Heat the mixture to about 70° C. until a portion gives a clear solution when mixed with nine volumes of cold water, cool, and add sufficient water to make the product measure 1000 cc.

"NOTE.—The 22 cc. of dekanormal solution of potassium hydroxide directed above may be replaced by 14.52 Gm. of 85 per cent. potassium hydroxide and the 88 cc. of dekanormal solution of sodium hydroxide may be replaced by 39.11 Gm. of 90 per cent. sodium hydroxide, dissolving the hydroxides in 50 cc. of water. If upon assay the potassium and the sodium hydroxides are found to be of any other strength, a proportionately larger or smaller quantity should be taken." *U. S.*

For description of the dekanormal solutions, see Part III.

"Cresol, 500 *grammes;* Castor Oil, 350 *grammes;* Potassium Hydroxide, 80 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Mix the Cresol with the Castor Oil and heat to 80° C. Dissolve the Potassium Hydroxide in seventy *millilitres* of the Distilled Water. Mix the two solutions and heat the mixture until one volume of it forms a clear liquid with ten volumes of Distilled Water. Cool, and add sufficient Distilled Water to produce the required volume." *Br.*

The formula of the U. S. X differs from that of the previous edition in that it contains both potassium and sodium hydroxide.

A number of suggested improvements have appeared in the literature for making this solution. F. M. Jordan (*Ph. Era,* 1919, lii, p. 175) uses the official ingredients but modifies the directions somewhat. S. L. Hilton (*J. A. Ph. A.*, 1919, viii, p. 759) employs oleic acid and sodium hydroxide in making the soap and claims that a fine preparation can be made in fifteen minutes, costing but 60 cents a litre.

Assay.—" Mix in a 500 cc. distilling flask 50 cc. of Compound Solution of Cresol, accurately measured at 25° C., with 150 cc. of purified kerosene. Add 3 Gm. of sodium bicarbonate and distil through an upright condenser, at the rate of not more than 2 drops per second, until the distillate comes over strongly yellow, receiving the distillate in a 250 cc. to 300 cc. separatory funnel. Run off the lower aqueous layer, shake the kerosene layer with 10 cc. of sulphuric acid (49 to 51 per cent.), allow to stand for two hours, then draw off the acid layer completely, and discard it. Add to the kerosene layer 40 cc. of an aqueous sodium hydroxide solution (15 per cent.), accurately measured at 25° C., shake well for five minutes, then allow to stand until complete separation has taken place, and draw off the sodium hydroxide layer into a graduated cylinder. Shake the kerosene layer again with a fresh portion of 20 cc. of the 15 per cent. sodium hydroxide solution, accurately measured at 25° C., allow the two layers to separate completely, and draw off the sodium hydroxide layer into the graduated cylinder. Adjust the sodium hydroxide solution in the graduated cylinder to a temperature of 25° C. and note the volume. The difference between the volume noted and the total volume of sodium hydroxide solution used represents the volume of cresol present in 50 cc. of Compound Solution of Cresol. This difference is not less than 23 cc. and not more than 26 cc. Transfer the sodium hydroxide solution of the cresol obtained in the assay to a separatory funnel and add sufficient hydrochloric acid to render the solution distinctly acid. Allow the precipitated cresol to separate completely and draw off the lower aqueous layer. Wash the cresol with several successive portions of 20 cc. each of a saturated aqueous solution of sodium chloride until the washings are neutral or only slightly acid. Then add to the washed cresol about 5 Gm. of freshly ignited potassium carbonate, shake gently at frequent intervals during three hours, and allow to stand overnight. The cresol decanted from the potassium carbonate meets the distillation requirements for *Cresol,* when determined by Method II." *U. S.*

Uses.—This solution is intended as a substitute for the many commercial preparations of cresol on the market. Although it forms a clear solution with distilled water, with tap water it becomes cloudy, owing to precipitation of lime soaps. This change, however, does not appear to interfere with its therapeutic properties. It is a powerful germicidal mixture, at least twice as strong as phenol as a destroyer of micro-organisms. It is also less caustic than phenol, but the statement that it is much less poisonous has been shown to be untrue. A large number of deaths are reported annually from solutions of this type. It is especially useful for sterilizing instruments and the skin, its soapy nature making it peculiarly valuable for the latter purpose. It may be diluted with from 30 to 90 times its bulk of water (3 per cent. to 1 per cent. solution). It has been used to a small extent internally as an antiseptic in *fermentative gastritis.*

Numerous methods have been suggested for assaying this preparation. None of them are simple and satisfactory enough for adoption as an official method. See the following references for methods of assay. Verda (*Schweiz. Apoth. Ztg.,* 1920, lviii, p. 238); Van Os (*Ph. Wb.,* 1920, lvii, p. 692); Jordan (*C. D.,* 1921, xciv, p. 843); Bohrisch (*Pharm. Zentralh.,* 1921, lxii, 297).

Dose, one to two minims (0.06–0.12 cc.).

LIQUOR EPINEPHRINÆ HYDROCHLORIDI. U. S. (Br.)

SOLUTION OF EPINEPHRINE HYDROCHLORIDE
Liq. Epineph. Hydrochlor.

" Solution of Epinephrine Chloride is a solution of epinephrine in water and hydrochloric acid, containing in each 100 cc. not less than 0.095 Gm. and not more than 0.105 Gm. of $C_9H_{13}O_3N$. Solution of Epinephrine Hydrochloride, diluted with physiological solution of sodium chloride in the proportion of one part of the Solution of Epinephrine Hydrochloride to 99 parts of the salt solution, and injected intravenously into dogs by the method described below, produces a rise in the systolic blood-pressure of the dog corresponding to that produced by an equal amount of the standard solution of epinephrine hydrochloride prepared as directed below." *U. S.*

Liquor Adrenalini Hydrochloricus, *Br.;* Hydrochloric Solution of Adrenalin; Solution of Adrenalin Hydrochloride.

" Adrenalin, 1 *gramme;* Chloroform, 5 *millilitres;* Sodium Chloride, 9 *grammes;* Diluted Hydrochloric Acid, 3 *millilitres;* Distilled Water, recently boiled and cooled, sufficient to produce 1000 *millilitres.* Dissolve the Chloroform and the Sodium Chloride in nine hundred *millilitres* of the Distilled Water, add the Diluted Hydrochloric Acid, dissolve the Adrenalin in the mixture, and add sufficient Distilled Water to produce the required volume. Preserve the Solution in amber glass bottles." *Br.*

Epinephrine was originally placed upon the market in the form of a proprietary solution containing one part of the hydrochloride in 1000 and is still chiefly used in this form. The Br.

gives a formula for the preparation of this solution, but the U. S. omits any formula because the revisers considered that the preparation of a satisfactory solution of this salt required such technical skill that it was not practicable for retail pharmacists. This solution contains free acid and sodium chloride with a little chloroform to act as a preservative. Care should be used to avoid the presence of iron in compounding prescriptions as it is incompatible. Steel spatulas must not be brought in contact with adrenalin solutions. In fact, it is desirable to prescribe the solution without admixture, and in original containers.

The reason for this is found in the fact that not only is epinephrine very unstable in solution except under certain carefully regulated conditions, but that if improperly prepared it will prove either irritating or inert. The stability is best attained in the presence of small amounts of acid. If, however, the acid is present to the extent of more than a few hundredths per cent. the solution becomes very irritating especially when used in conditions where inflammation is present. If the acidity is too low, the reaction is likely to become alkaline from the natural alkalinity of the glass and the preparation becomes discolored and inert. In the case of ampules, which must be sterilized it is necessary to use special glass, free from alkalinity even when treated with water at high temperatures. The solutions on the market are frequently protected from oxidation also by replacing the air in the container with carbon dioxide.

Description and Physical Properties.—"A nearly colorless, slightly acid liquid, gradually turning dark on exposure to air and light. When the solution has become brown in color or contains a precipitate, it must be rejected.

"The addition of 1 drop of ferric chloride T.S. to 10 cc. of the solution produces an emerald-green color which soon turns to a cherry-red and finally to brown. Other oxidizing agents produce red to pink or violet colors which change on standing. Fixed alkali hydroxides darken it, but do not precipitate the epinephrine.

"Preserve in small, well-filled, amber-colored bottles." *U. S.*

Assay.—It has been suggested to standardize epinephrine solution by the change of color which is caused by oxidizing agents; indeed this principle was official for suprarenal glands in the U. S. IX, which employed manganese dioxide as the oxidizant. A process similar in principle but using potassium iodate has been proposed by White (*P. J.*, 1917, xcviii, 159). None of these methods, however, have proven entirely satisfactory and the present U. S. P. makes use of a biological assay process which is as follows:

"Prepare a standard solution of epinephrine hydrochloride from the standard epinephrine by dissolving 0.050 Gm. of epinephrine in 5 cc. of tenth-normal hydrochloric acid, and dilute this to 50 cc. by the addition of distilled water, thus making a 1 in 1000 solution. For the assay, add 1 cc. of this 1 in 1000 solution to 99 cc. of physiological solution of sodium chloride. This dilute solution (1 in 100,000) must be freshly prepared when needed. On account of the possibility of deterioration, the 1 in 1000 solution must have been recently prepared. It will keep for a short time if preserved in amber-colored bottles in a refrigerator, but it must be discarded if any signs of deterioration, such as discoloration, are observed. Add 1 cc. of the Solution of Epinephrine Hydrochloride to be tested to 99 cc. of physiological solution of sodium chloride, and thoroughly mix. For the purpose of the assay, the dog to be used should be of medium size and be anesthetized with a suitable anesthetic. It is prepared for blood-pressure estimations by inserting a cannula into the carotid artery and connecting the same with a mercury manometer. The trachea may also be exposed and a cannula inserted so that the animal may receive artificial respiration during the course of the experiment if necessary. The injections are made into the exposed femoral vein. Before the test is made, in case any muscular movement such as twitching is present, the dog should receive by intravenous injection a sufficient dose of curare (page 475), but if the animal is deeply anesthetized, this is not necessary. The dog should also receive a sufficient dose of atropine sulphate (from 0.001 Gm. to 0.002 Gm.) to paralyze the vagi, this paralysis being proved by electrical stimulation. The blood-pressure tracing is recorded on a kymograph. Injections must be made at regular intervals of approximately five minutes. Determine the amount of standard solution necessary to cause a rise in blood-pressure of from 30 to 60 mm. by injecting intravenously varying doses of the solution and after a satisfactory dose has been ascertained, the uniformity of reaction should be tested by the injection of two or more doses of equal size. If these injections produce approximately equal increases in blood-pressure, alternate injections of the solution to be tested and of the standard are made, varying the amount of the unknown until two or more successive injections raise the blood-pressure to the same height, indicating that the amount of active agent is the same in the doses used. From the results thus obtained, the strength of the unknown solution may be determined and adjusted." *U. S.*

Beckwith (*J. A. Ph. A.*, 1914, iii, 293) found that the commercial solution of adrenalin chloride, if protected against light and heat in the original container, will retain its activity for a long period of time. If the stopper is removed, however, the air will exercise a destructive oxidation upon the adrenalin. This is evidenced by change of color as to pink, then red and finally brown. Solutions having more than a slight pinkish tint should not be dispensed. Beckwith found that the non-oxidizing mineral acids—such as hydrochloric or sulphuric—had a protective rather than destructive effect. Among the more important incompatibilities he mentions iron, iodine and mercuric chloride.

For other incompatibilities and for medical uses of this solution see *Epinephrina.*

Dose, five to fifteen minims (0.3–1. cc.).

LIQUOR EPISPASTICUS. Br.

BLISTERING LIQUID

Linimentum Cantharidis; Liqueur Vésicant, Huile de Cantharides térébenthinée, *Fr.;* Spanischfliegenliniment, Blasenziehende Flüssigkeit, *G.*

"Cantharidin, 4 *grammes;* Castor Oil, 25 *millilitres;* Resin, 12 *grammes.* Acetone sufficient to produce 1000 *millilitres.* Dissolve. This Blistering Liquid contains approximately the same proportion of Cantharidin as the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

This liquid is used in making the Blistering Collodion. (See *Collodium Vesicans.*) Greenish and Wilson propose that the official blistering liquid be prepared by the following formula. Cantharidin, 1 part; castor oil, 6 parts; rosin, 3 parts; acetic ether, enough to make 300 fluid parts. The castor oil and rosin are added to replace the natural fat of the cantharides, and are necessary to aid the absorption of the cantharides by the skin. (*P. J.*, 1898, 259.)

Off. Prep.—Collodium Vesicans, *Br.*

LIQUOR ETHYL NITRITIS. Br.

SOLUTION OF ETHYL NITRITE

"Solution of Ethyl Nitrite contains not less than 2.5 or more than 3 per cent. by weight of ethyl nitrite in a mixture of ninety-five parts by volume of Absolute Alcohol with five parts by volume of Glycerin. The ethyl nitrite may be obtained by the interaction of alcohol (90 per cent.), sodium nitrite, and diluted sulphuric acid, at a low temperature. Solution of Ethyl Nitrite should be stored in small bottles." *Br.*

Soluté de Nitrite d'Ethyle, *Fr.;* Aethylnitritlösung, *G.*

This was a new official preparation in the Br. Ph., 1898; it might be called improved spirit of nitrous ether; it is difficult to explain the reason for its introduction without the dismissal of spirit of nitrous ether; the strength is very slightly greater than that of the British spirit (less than the U. S. spirit of nitrous ether), and a choice should be made between them. The addition of glycerin as a preservative and the substitution of absolute alcohol for rectified spirit, are relied upon to make a permanent solution. This method was proposed by Dunstan and Dymond (*P. J.*, 1888, 861), who believe that ethyl nitrite is the sole valuable constituent in spirit of nitrous ether; glycerin prevents loss of the very volatile ethyl nitrite, while the absence of water is secured by the use of absolute alcohol, water in the alcohol being shown to be the principal cause of decomposition and loss of ethyl nitrite. Solution of ethyl nitrite was strongly recommended by Leech, and the advantage claimed for it is that it is free from aldehyde. The increased cost, due to the use of absolute alcohol, will be apt to prevent the extensive use of the solution.

It is described as "a nearly colorless transparent liquid, of characteristic apple-like odor and taste. Specific gravity 0.823 to 0.826. When poured on an acidified strong solution of *ferrous sulphate* contained in a test-tube, a deep olive-brown coloration is produced at the surface of contact of the two liquids. Does not effervesce when shaken with *sodium bicarbonate* (absence of acid). 10 millilitres, mixed with 5 millilitres of *N/1 solution of sodium hydroxide* and 5 millilitres of *water,* do not assume a yellow color (absence of acetaldehyde). 1 volume, shaken briskly at intervals during five minutes in a brine-charged nitrometer with 1 volume of *solution of potassium iodide* and 1 volume of *diluted sulphuric acid,* yields at 15.5° C., and normal pressure, not less than 6.5 or more than 7.8 volumes of nitric oxide gas." *Br.*

This preparation affords a means of giving ethyl nitrite internally.

Dose, from twenty to sixty minims (1.3–3.75 cc.). (See *Spiritus Ætheris Nitrosi.*)

LIQUOR FERRI CHLORIDI. U. S. (Br.)

SOLUTION OF FERRIC CHLORIDE Liq. Ferr. Chlor. [Solution of Iron Perchloride]

"Solution of ferric chloride contains ferric chloride [$FeCl_3$], corresponding to not less than 10 per cent. nor more than 11 per cent. of Fe." *U. S.*

"This Solution contains 20 grammes of Iron in 100 millilitres; 110 minims contain 20 grains." *Br.*

Liquor Ferri Perchloridi Fortis, *Br.;* Liquor Ferri Muriatici Oxydati, Strong Solution of Ferric Chloride, Solution of Chloride of Iron; Chlorure Ferrique dissous, Soluté de Perchlorure de Fer, Chlorure Ferrique liquide, *Fr.;* Liquo-Ferri Sesquichlorati, *P. G.;* Flüssiges Eisenchlorid, Eisenchloridlösung, *G.*, Solucion de Cloruro Ferrico, *Sp.*

The U. S. X does not give any formula for preparing this solution; that of the Br. is as follows:

"Iron, 70 *grammes;* Hydrochloric Acid, 410 *millilitres;* Nitric Acid, 30 *millilitres;* Distilled Water, *a sufficient quantity.* Place the Iron in a flask; add a mixture of two hundred and fifty millilitres of Hydrochloric Acid and one hundred and forty millilitres of Distilled Water; expose to a moderate temperature until effervescence ceases; then boil; filter from undissolved Iron; rinse the flask and contents with a little Distilled Water; pour the rinsings over the filter; add to the filtrate one hundred and forty millilitres of Hydrochloric Acid; mix; pour the solution in a slow continuous stream into the Nitric Acid, chemical action being promoted if necessary by gently warming; evaporate the product until a precipitate begins to form; add twenty millilitres of Hydrochloric Acid, and sufficient Distilled Water to produce three hundred and fifty millilitres, or to make the resulting Solution respond to the following tests." *Br.* (See below.)

The U. S. P. strength is from 10 to 11 per cent. The British preparation contains 20 per cent. of iron. By the reaction between the hydrochloric acid and the iron, ferrous chloride is produced, which by the subsequent agency of the hydrochloric and nitric acids is converted into ferric chloride, or, as it is denominated in the British Pharmacopœia, perchloride of iron, this being retained in solution by the water with the excess of acid. This excess of acid is limited by a special test in the U. S. P., because too great excess would complicate other formulas in which the tincture is used, such as the tincture of ferric citro-chloride.

When iron is treated with hydrochloric acid there is a copious evolution of hydrogen, and an emerald-green solution of ferrous chloride ($FeCl_2$) results. Green crystals having the composition $FeCl_2,4H_2O$ separate if the solution is permitted to rest. Formerly the nitric acid was added to the solution; now the order is reversed, to prevent frothing. The reaction between the acids and the solution may be thus expressed:

$$\underset{\text{Ferrous chloride.}}{6FeCl_2} + \underset{\text{Nitric acid.}}{2HNO_3} + \underset{\text{Hydrochloric acid.}}{6HCl} =$$

$$\underset{\text{Ferric chloride.}}{6FeCl_3} + \underset{\text{Nitrogen dioxide.}}{N_2O_2} + \underset{\text{Water.}}{4H_2O}$$

If the solution should have a dark color, and not a clear ruby-red, it is due to the presence of a nitro-compound composed of a portion of ferrous chloride and nitrogen dioxide, $FeCl_2 + N_2O_2$. As this compound is easily decomposed, all that is necessary is to heat the liquid and add a few drops of nitric acid, when the dark color soon disappears, nitrogen dioxide is liberated, and a ruby-red solution remains. Any excess of nitric acid is to be evaporated. The final addition of hydrochloric acid is to compensate for any loss which may have been suffered by heating the solution, and to secure an excess of the acid in the finished preparation; otherwise a reddish-brown deposit of oxychloride would gradually form, and precipitation would result upon dilution with alcohol in making the official tincture.

The use of chlorine instead of nitric acid for converting the ferrous chloride to the ferric condition is advocated by C. W. Weiss (*N. R.*, 1883, p. 247), and J. W. England devised a process, based upon such substitutions. (See *U. S. D.*, 19th ed., p. 714.)

Description and Physical Properties.—"A yellowish-brown liquid, having a faint odor of hydrochloric acid and an acid reaction. It is miscible in all proportions with alcohol. Specific gravity: from 1.29 to 1.32 at 25° C. An aqueous dilution of the Solution (1 in 10) responds to the reactions for ferric iron, and for chlorides.

"Weigh about 4 cc. of the Solution, dilute to 100 cc. with distilled water, and precipitate the iron completely by adding an excess of ammonia T.S., and filter: the filtrate is colorless. One-half of the filtrate does not yield a precipitate with hydrogen sulphide T.S. (*zinc, lead, or copper*). The residue obtained upon evaporation and ignition of the remaining half of the filtrate does not exceed 0.1 per cent. (*salts of the fixed alkalies*). Mix 1 cc. of the solution with 10 cc. of ferrous sulphate T.S., and superimpose the mixture upon 5 cc. of sulphuric acid contained in a test tube: the line of contact does not assume a brown or reddish-brown color (*nitrate*). Add a few drops of freshly prepared potassium ferricyanide T.S. to an aqueous dilution of the Solution (about 1 in 20): a brown color is produced which does not at once turn green or greenish-blue (*ferrous salts*). Add 10 cc. of distilled water and 50 cc. of tenth-normal silver nitrate to about 0.5 Gm. of Solution of Ferric Chloride, accurately weighed, shake vigorously then add 2 cc. of nitric acid and sufficient distilled water to measure exactly 100 cc., and mix well. Pass the mixture through a filter not previously moistened (rejecting the first 10 cc. portion), and determine the excess of silver nitrate in 50 cc. of the filtrate by titration with tenth-normal potassium thiocyanate. The percentage of chlorine found is not less than 3 per cent. and not more than 5 per cent. in excess of that required to combine as ferric chloride with the iron present. The percentage of iron (see Assay below) multiplied by 1.9 gives the percentage of chlorine combined at ferric chloride (*free hydrochloric acid*). Each cc. of tenth-normal silver nitrate corresponds to 0.003546 Gm. of Cl.

"**Assay.**—Transfer about 2 Gm. of Solution of Ferric Chloride to a tared flask, stopper, weigh accurately, add 5 cc. of hydrochloric acid, 25 cc. of distilled water and about 3 Gm. of potassium iodide. Securely stopper the flask, and allow the mixture to stand for thirty minutes as a temperature of 40° C. Cool the liquid, dilute it with 100 cc. of distilled water, and then titrate the liberated iodine with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of Fe.

"Preserve in glass-stoppered bottles, protected from light." *U. S.*

"An orange-brown solution with a strong styptic taste. Miscible with *water* and with *alcohol* (90 per cent.) in all proportions. Specific gravity about 1.49. Yields the *reactions* characteristic of ferric salts and of chlorides. Yields no characteristic *reactions* for lead, copper, zinc, calcium, sodium, potassium, ammonium, or ferrous salts. On adding a clear crystal of *ferrous sulphate* to a cooled mixture of equal volumes of *sulphuric acid* and of the Strong Solution diluted with nine times its volume of *water* the crystal does not become brown, nor does a brownish-black color develop around it (limit of nitrates). *Arsenic limit* 10 parts per million. 5 millilitres diluted with 80 millilitres of water yield, upon the addition of an excess of *solution of ammonia,* a reddish-brown precipitate, which, when well washed and incinerated, weighs 1.42 grammes. This Solution contains 20 grammes of Iron in 100 millilitres; 110 minims contain 20 grains." *Br.*

Water and alcohol unite with it in all proportions. The British preparation (*Liquor Ferri Perchloridi Fortis*) is stronger than the U. S., the sp. gr. of the former being about 1.49 at 15.5° C., of the latter from 1.29 to 1.32 at 25° C. It should be remembered, however, that there is in the British Pharmacopœia, another solution of ferric chloride which is weaker; it has the sp. gr. 1.110 and is termed *Liquor Ferri Perchloridi.*

Uses.—This preparation is interesting as having led Pravaz to the invention of a syringe—which was the forerunner of the modern hypodermic—for the purpose of injecting solution of ferric chloride in the destruction of *nevi* and other vascular tumors through the precipitation of the blood. This treatment, however, has largely passed out of vogue because of the danger of emboli being carried to other parts. The drug is, however, a very powerful astringent and styptic and is useful for arresting *hemorrhages* from cut surfaces or wounded vessels which it does by causing the formation of a hard coagulum by precipitation of proteins.

It is, in itself, rarely employed as an internal remedy but is the basis for the very popular tincture of ferric chloride. Garrett (*B. M. J.,* 1913, i) recommends the stronger solution of iron chloride Br. as a local application in *ringworm* of the scalp; he states that it must be applied full strength to get good results. Zeissl has used it as a local remedy in *acne rosacea.* Bourget has employed a gelatinized solution of ferric chloride in the treatment of *gastric ulcer.* (*Th. M.,* 1909, p. 353.) His solution consists of 100 grammes each of gelatin, glycerin, and water, and 50 grammes of the *liquor ferri perchloridi,* P. G.

Dose of the U. S. preparation, one to five minims (0.06–0.3 cc.).

Off. Prep.—Liquor Ferri Perchloridi, *Br.;* Tinctura Ferri Chloridi, *U. S.* (*Br.*)*;* Gossypium Stypticum, *N. F.;* Tinctura Ferri Chloridi Ætherea, *N. F.;* Tinctura Ferri Citro-chloridi, *N. F.*

LIQUOR FERRI ET AMMONII ACETATIS. U. S.

SOLUTION OF IRON AND AMMONIUM ACETATE

Liq. Ferr. et Ammon. Acet. [Basham's Mixture]

"Solution of Iron and Ammonium Acetate contains, in each 100 cc., ammonium acetate corresponding to not less than 0.6 Gm. and not more than 0.8 Gm. of NH_3, and not less than 0.16 Gm. and not more than 0.20 Gm. of Fe." *U. S.*

Mistura Ferri et Ammonii Acetatis, *U. S. P.* 1880; Mistura Bashami.

"Tincture of Ferric Chloride, 40 cc.; Diluted Acetic Acid, 60 cc.; Solution of Ammonium Acetate, 500 cc.; Aromatic Elixir, 120 cc.; Glycerin, 120 cc.; Distilled Water, a sufficient quantity to make 1000 cc. To the solution of ammonium acetate (which must be slightly acid) add, successively, the diluted acetic acid, the tincture of ferric chloride, the aromatic elixir, and the glycerin, and lastly enough distilled water to make the product measure 1000 cc." *U. S.*

It should be borne in mind that this was never intended to be a permanent solution, and in time precipitation and decomposition surely set in although somewhat retarded by the presence of glycerin. Some pharmacists adopt the plan of keeping all the ingredients, except the tincture of ferric chloride and water, mixed together in advance, and when called upon to dispense the solution, to add the proper quantity of tincture and water; this saves time and enables them to dispense a clear solution.

Description and Physical Properties.—"A clear, reddish-brown liquid, having an aromatic odor. Specific gravity: about 1.039 at 25° C. The solution is acid to litmus paper. The Solution yields a blue precipitate with potassium ferrocyanide T.S. No precipitate is produced upon the addition of ammonia T. S. When Solution of Iron and Ammonium Acetate is heated with sodium hydroxide T.S., ammonia is evolved. Add 1 cc. each of sulphuric acid and alcohol to 5 cc. of the Solution, and boil the mixture: ethyl acetate is formed, recognizable by its odor.

"**Assay for Ammonia.**—Transfer to a distilling flask with the aid of distilled water exactly 25 cc. of Solution of Iron and Ammonium Acetate, and add sufficient distilled water to make about 200 cc. Add 20 cc. of 20 per cent. sodium hydroxide solution, and distil about 150 cc., receiving the distillate in 40 cc. of half-normal sulphuric acid. Titrate the excess of acid with half-normal sodium hydroxide, using methyl orange T.S. as indicator. Each cc. of half-normal sulphuric acid corresponds to 0.008520 Gm. of NH_3.

"**Assay for Iron.**—Transfer to a dish with the aid of a little distilled water exactly 25 cc. of Solution of Iron and Ammonium Acetate. Evaporate to dryness and gently ignite. Heat the residue with 10 cc. of hydrochloric acid, and when all of the iron has dissolved, add 10 cc. of solution of hydrogen dioxide, and evaporate to dryness on a water bath. Add 5 cc. of hydrochloric acid, warm until all is dissolved, and transfer the solution to a glass-stoppered flask with the aid of about 30 cc. of distilled water. Add about 2 Gm. of potassium iodide, allow to stand for thirty minutes at about 40° C., cool, and titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of Fe." *U. S.*

When freshly made, it is a transparent,

bright red liquid. When cloudy, the absence of sufficient free acid is indicated. The iron is in the form of an acetate, while there is formed, as one of the products of decomposition, a small quantity of ammonium chloride, the larger proportion of ammonium acetate remaining undecomposed.

Basham's mixture is actively chalybeate, and also astringent, and is very largely used in *chronic Bright's disease.* There has arisen a popular superstition that it exercises a curative effect in nephritis, but its value is probably simply that of a hematinic and not superior to other forms of iron.

Dose, from one-fourth to one-half fluidounce (7.5–15 cc.).

LIQUOR FERRI PERCHLORIDI. Br.

SOLUTION OF FERRIC CHLORIDE

Solution of Perchloride of Iron.

"Strong Solution of Ferric Chloride, 250 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Mix." Br.

This is one-fourth the strength of the *Liquor Ferri Perchloridi* of the Br. Pharmacopœia of 1864, which is the *Liquor Ferri Perchloridi Fortis* of the present edition. (See p 631.) It is of the same ferruginous strength as the British Tincture of Ferric Chloride. The specific gravity of this solution is 1.110, and it may be substituted for the tincture of ferric chloride when alcohol is objectionable, as it has the same strength; it is very astringent.

Dose, from five to fifteen minims (0.3–1.0 cc.), well diluted.

LIQUOR FERRI TERSULPHATIS. U. S. (Br.)

SOLUTION OF FERRIC SULPHATE Liq. Ferr. Tersulph. [Solution of Iron Tersulphate]

"An aqueous solution containing normal ferric sulphate [$Fe_2(SO_4)_3$], corresponding to not less than 9.5 per cent. nor more than 10.5 per cent. of Fe." *U. S.*

Liquor Ferri Persulphatis, *Br.;* Solution of Normal Ferric Sulphate, Solution of Tersulphate of Iron; Solution of Persulphate of Iron; Persulfate de Fer liquide, *Fr.;* Ferrisulfatlösung, Schwefelsaure Eisenoxydlösung, Flüssiges Schwefelsaures Eisenoxyd, *G.*

"Ferrous Sulphate, 500 Gm.; Sulphuric Acid, 96 Gm.; Nitric Acid, Distilled Water, each, a sufficient quantity to make 1000 Gm. Add the sulphuric acid to about 250 cc. of distilled water in a tared, capacious porcelain dish, heat the mixture to nearly 100° C., then add 56 Gm. of nitric acid, and mix well. Divide the ferrous sulphate, coarsely powdered, into four approximately equal portions, and add these portions one at a time to the hot liquid, stirring after each addition until effervescence ceases. When all of the ferrous sulphate is dissolved, if the solution has acquired a black color, add nitric acid, a few drops at a time, heating and stirring until red fumes cease to be evolved, and the solution assumes a clear reddish-brown color; then boil the liquid until it is free from nitric acid, as indicated by the test given below. During the heating add distilled water from time to time to maintain about the original volume. Lastly, add enough distilled water to make the product weigh 1000 Gm. Filter, if necessary." *U. S.*

"Ferrous Sulphate, 400.0 *grammes;* Sulphuric Acid, 37.5 *millilitres;* Nitric Acid, 37.5 *millilitres;* Distilled Water, *a sufficient quantity.* Add the Sulphuric Acid to five hundred *millilitres* of the Distilled Water; dissolve the Ferrous Sulphate in the mixture with the aid of heat; mix the Nitric Acid with one hundred *millilitres* of the Distilled Water; add to this diluted acid, warmed, the solution of Ferrous Sulphate; concentrate by boiling, until, on the sudden disengagement of ruddy vapors, the liquid ceases to be black and acquires a red color. If any ferrous salt remain in the solution, add a few drops of Nitric Acid, and boil again. When the solution is cold add, if necessary, sufficient Distilled Water to produce five hundred and fifty *millilitres.*" *Br.*

The ferrous sulphate is preferably in clear crystals, meaning by this "not effloresced," because when the crystals are coated with a whitish powder they have lost water of crystallization, and the proportion of iron present is variable. The nitric acid in the process gives up enough of its oxygen to convert it entirely into ferric sulphate, and the effervescence is owing to the escape of nitrogen dioxide; this becomes red nitrogen tetroxide by contact with the air. The conversion of the ferrous salt into ferric salt is incomplete until the effervescence ceases, and the color, instead of black, as it was at first, has become reddish-brown. Indeed, in order to convert the whole into ferric sulphate it is necessary to continue the heat until nitrous odor ceases to be evolved and thus the entire absence of nitric or nitrous acid from the solution is insured. In consequence of the higher oxidation of the iron the sulphuric acid of the sulphate is insufficient to saturate it. Enough sulphuric acid, therefore, is added to meet this demand. The process is completed by adding enough water to make a definite weight. The U. S. and British formulas are the same in principle.

Description and Physical Properties.—"A reddish-brown liquid, almost odorless, having an acid, strongly styptic taste, and an acid reaction. Solution of Ferric Sulphate is miscible with water and alcohol. Specific gravity: about 1.432 at 25° C. Solution of Ferric Sulphate responds to the reactions for ferric iron, and for sulphates.

"Mix 1 cc. of the Solution with 10 cc. of ferrous sulphate T.S. and superimpose it upon 5 cc. of sulphuric acid contained in a test tube; the line of contact does not assume a brown or brownish-black color (*nitrate*). Add a few drops of freshly prepared potassium ferricyanide T.S. to 2 cc. of an aqueous dilution of the Solution (1 in 20); a brown color is produced without a tinge of green or greenish-blue (*ferrous salt*).

"**Assay.**—Transfer about 1.5 Gm. of Solution of Ferric Sulphate to a tared flask, stopper and weigh accurately, then add 5 cc. of hydrochloric acid, 25 cc. of distilled water, and 2 Gm. of potassium iodide, securely stopper the flask, and allow the mixture to stand for thirty minutes at a temperature of 40° C. Cool the liquid, dilute it with 50 cc. of distilled water, and titrate the liberated iodine with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of Fe." *U. S.*

"A dark-red solution. Inodorous; very astringent. Miscible in all proportions with *alcohol* (90 per cent.) and *water*. Specific gravity about 1.441. Yields the *reactions* characteristic of ferric salts and of sulphates. Yields no characteristic *reactions* for ferrous salts. *Arsenic limit* 5 parts per million. 5 millilitres diluted with 80 millilitres of *water* yield, upon the addition of excess of *solution of ammonia*, a precipitate which, when well washed and incinerated, weighs 1.04 grammes." *Br.*

Uses.—This solution, though powerfully astringent, is too irritant for general use. The chief employment of it is in making other ferruginous preparations in which the ferric hydroxide is wanted, and it should always be kept on hand for the quick preparation of the antidote to arsenic.

LIQUOR FORMALDEHYDI. U. S., Br.

SOLUTION OF FORMALDEHYDE Liq. Formaldehyd.

"An aqueous solution containing not less than 37 per cent. by weight of CH_2O or $H.CHO$ (30.02), with variable amounts of ethyl or methyl alcohol to prevent polymerization." *U. S.* "Solution of Formaldehyde is an aqueous solution containing in 100 millilitres not less than 36 and not more than 38 grammes of formaldehyde, CH_2O. Formaldehyde may be obtained by the limited oxidation of methyl alcohol." *Br.*

Formol, Formalin; Soluté d'Aldehyde Formique, *Fr.;* Formaldehydum solutum, *P. G.;* Formaldehydlösung, *G.;* Formol, *Sp.*

Preparation.—*Formaldehyde* was first prepared in 1868 by Hofmann by passing a mixture of air and methyl alcohol vapor over heated platinum, and it is still practically obtained only from the oxidation of methyl alcohol.

Formaldehyde is now manufactured by the process of Orloff in which rectifying columns are used. The igniters, or activators, are masses of platinized asbestos, or asbestos impregnated with silver. The yield by this method is almost equal to the theoretical; the copper method yielding less than half this amount. The conversion temperature is 450° C. The process is automatically regulated so as to deliver a product containing about 40 per cent. of formaldehyde, 14 per cent. of methyl alcohol and the balance water. Formaldehyde has never been prepared directly from methane, although various attempts have been made in this direction. After a certain process of purification, enough water is added to the formaldehyde so obtained to form a 40 per cent. solution; but this solution is not, strictly speaking, a solution of formaldehyde, as the pure formaldehyde polymerizes the moment the temperature rises above 20° C., and it is this property which renders the addition of water or alcohol necessary. Hence the aqueous solution of formaldehyde probably contains some paraformaldehyde and some unconverted methyl alcohol is always present which is allowed to remain because of the preservative effect it has in preventing polymerization. This change which sometimes occurs in commercial solutions of formaldehyde during the winter months is accompanied by the deposition of a white precipitate sometimes occupying a bulk equal to one-half of the original liquid and when it has occurred the only method of restoration is to acidify with sulphuric acid and redistil the liquid. The commercial products are always aqueous solutions, the common strength being the 37 per cent. solution; a 50 per cent. solution is not permanent.

Recently formaldehyde has been successfully made by reduction of formic acid. Anhydrous formic acid vapors are conducted over asbestos which has been mixed with zinc oxide and powdered zinc. A zinc salt is first produced which then resolves itself into methyl formate and zinc oxide. The methyl formate is subsequently decomposed into methyl alcohol and formaldehyde. (*Ph. Wb.*, 1919, lvi, 406.)

Description and Physical Properties.—"A clear, colorless or nearly colorless liquid, having a pungent odor. Its vapor irritates the mucous membrane of the throat and nose. On long standing, especially in the cold, Solution of Formaldehyde sometimes becomes cloudy, due to the separation of paraformaldehyde. It is miscible with water and alcohol.

"Dilute 2 cc. of Solution of Formaldehyde with 10 cc. of distilled water in a test tube, and add 1 cc. of silver ammonium nitrate T.S.; metallic silver is produced either in the form of a finely divided gray precipitate, or as a bright metallic mirror on the sides of the test tube. Add 2 drops of Solution of Formaldehyde to 5 cc. of sulphuric acid in which about 0.02 Gm. of salicylic acid has been dissolved, and warm the liquid very gently; a permanent, deep red color appears. Not more than 1 cc. of normal sodium hydroxide is required to neutralize 20 cc. of Solution of Formaldehyde, using 2 drops of phenolphthalein T.S. as indicator (*free acid*).

"**Assay.**—Transfer 3 cc. of Solution of Formaldehyde to a tared flask containing 10 cc. of distilled water, tightly stopper, and weigh accurately. Add 50 cc. of normal sodium hydroxide, and follow this immediately but slowly through a small funnel with 50 cc. of hydrogen dioxide T.S. which has previously been rendered neutral to litmus T.S. with sodium hydroxide T.S. Heat the mixture cautiously on a water bath for five minutes, shaking it occasionally. Allow the mixture to cool, rinse the funnel and sides of the flask with distilled water, and, after allowing it to stand thirty minutes, titrate with normal sulphuric acid, using litmus T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.03002 Gm. of H.CHO.

"Preserve in a moderately warm place, protected from light." *U. S.*

"A colorless liquid with a characteristic, pungent odor. Neutral or slightly acid to *litmus*. Miscible with *water* and with *alcohol* (90 per cent.) in all proportions. Caustic when applied to the skin. Specific gravity 1.079 to 1.081. Yields, when evaporated to dryness, a whitish, amorphous residue which leaves no appreciable ash on incineration. Yields with *solution of silver ammonio-nitrate* a precipitate of metallic silver. On the addition of 2 drops of the Solution to 5 millilitres of *sulphuric acid*, in which a little *salicylic acid* has been previously dissolved, a deep red coloration is produced. When 1 millilitre is mixed with 10 millilitres of *N/10 solution of iodine*, the mixture nearly decolorised with *solution of sodium hydroxide* and warmed, no yellow, crystalline precipitate is produced (absence of acetone). Diluted with four times its volume of *water* it yields no characteristic *reactions* for iron, copper, lead, calcium, chlorides, or sulphates. Contains in 100 millilitres not less than 36 and not more than 38 grammes of formaldehyde, CH_2O, as determined by the following process:—To 50 millilitres of *N/1 solution of sodium hydroxide* add 3 millilitres of Solution of Formaldehyde and 50 millilitres of *solution of hydrogen peroxide* and warm on a water-bath; similarly mix 50 millilitres of *N/1 solution of sodium hydroxide* with 50 millilitres of *solution of hydrogen peroxide* and warm on a water-bath. When the reactions are complete and all effervescence has ceased, add a few drops of *solution of phenolphthalein* to each mixture and titrate with *N/1 solution of sulphuric acid*. The difference between the two titrations is not less than 36 and not more than 38 millilitres." *Br.*

Formaldehyde may be determined in aqueous solutions by treatment with excess of standard ammonia, which converts it into hexamethylenamine. The excess of ammonia may then be titrated with standard acid. The mixture of the formaldehyde solution and ammonia should stand for at least twelve hours. This method, however, has not been found in practice to be as accurate as the hydrogen dioxide method, which was therefore chosen by the Revision Committee as the basis of the official assay process. In this method standard sodium hydroxide is used in connection with hydrogen dioxide, the reaction being as follows: $2CH_2O + 2NaOH + H_2O_2 = H_2 + H_2O + 2HCO.ONa$.

Because of the use of formaldehyde as a preservative of milk and food products the detection of small amounts of it is a matter of great importance. Several of the tests proposed are primarily applicable to milk only, being based on reactions which take place in the presence of milk proteids, so that if these tests are to be applied in testing other liquids for the presence of formaldehyde, the material must be mixed with an equal quantity of milk which has been shown previously to be free from formaldehyde. The principal tests may be divided into two groups, those in which a colored zone is obtained at the junction of two liquids, one of which has been superimposed upon the other, and those in which a color reaction is obtained in the body of the liquid tested. The first group includes the resorcinol-sulphuric acid test, the phenol-sulphuric acid test, and the sulphuric acid test of Hehner (carried out in the presence of milk). The method of application of the two tests first mentioned is as follows: To 5 cc. of the liquid to be tested, one or two drops of a one per cent. aqueous solution of phenol or resorcinol are added, and this liquid is then allowed to bow gently down the inside of the test tube containing 2 or 3 cc. of the sulphuric acid so as to form a layer above the acid without mixing. In the presence of formaldehyde a rose-colored zone is produced in extreme dilution, or in more concentrated solutions an opaque pinkish zone above the rose-colored one. In the Hehner test, the liquid to be tested is mixed with an equal volume of formaldehyde-free milk, and this mixture is allowed to flow down the inside of the test tube upon 2 or 3 cc. of commercial sulphuric acid containing a trace of ferric chloride. A violet zone is formed in the presence of formaldehyde. The general color tests constituting the second group of tests are the phenylhydrazine test with its modifications, the phloroglucinol test, the resorcinol-soda test, and the hydrochloric acid test. (A full discussion and comparison of these tests by C. H. LaWall will be found in *Am. Drug.*, 1905, vol. xlvii, p. 33.)

The foregoing tests are all group tests for aldehydes and positive results will be obtained in the presence of furfurol, vanillin, and many other aldehydic bodies. The best specific test given by formaldehyde only is that of Rimini, and is carried out as follows: To 10 cc. of the clear liquid or distillate is added 0.05 gramme phenylhydrazine hydrochloride followed by 3 drops of a 5 per cent. aqueous solution of sodium nitroprusside, and, finally, by 1 cc. (or an excess) of a 10 per cent. sodium hydroxide solution. In the presence of formaldehyde a blue or greenish-blue color is immediately produced which, however, quickly changes to yellow and finally to red.

The test is so sensitive as to detect the substance in a solution containing but one drop of commercial formaldehyde solution in five gallons of water.

A. B. Lyons (*Proc. A. Ph. A.*, 1905, 326) proposes the use of *beef peptone* in place of milk (except when milk is under investigation) in Hehner's test (see above). He also suggests the use of morphine and sulphuric acid as a test for formaldehyde. (*Proc. A. Ph. A.*, 1905, 329.)

Uses.—Formaldehyde was introduced as a disinfectant by Trillat in 1888. It is remarkable among germicidal agents for the fact that its action in solution is less powerful than as a vapor. Its solutions are about equivalent in germicidal activity to those containing the same percentages of phenol. Burgess (*L. L.*, 1900, i, p. 1797) found that a 2 per cent. solution would kill the *B. coli communis* in five minutes and Slater and Rideal found that it required 50 minutes for a one per cent. solution to destroy various non-sporulating micro-organisms. Its action as an antiseptic, however, far exceeds that of phenol. In Slater and Rideal's experiments one part in five thousand absolutely inhibited and one in twenty thousand greatly restrained the growth of bacteria. As regards the effects of formaldehyde vapor, it has been shown that as little as one part in three thousand parts of air will destroy many bacteria, and, according to Kenwood, one or two per cent. will rapidly disinfect all surfaces. It should be remarked in this connection that the penetrating power of formaldehyde has been usually over-estimated and that bundles of clothing or similar material are not effectually disinfected by such strengths of the gas.

Formaldehyde is an intense local irritant both to mucous membranes or if in sufficient concentration, to the skin. In strong solution it precipitates albumen or gelatin, but very minute quantities are asserted to prevent the coagulation of albumen by heat. When injected into the circulation in such dilutions as not to precipitate the proteins of the blood, or after its absorption through the gastro-intestinal mucosa, it exercises relatively slight effects on the vital functions. According to McGuigan (*J. A. M. A.*, 1914, lxii, p. 984), large quantities lower the blood pressure by a direct action upon the heart and vessel walls. Fleig states that it causes contraction of the renal vessels. It is rapidly oxidized in the system and appears in the urine as formic acid, so that after the administration of even relatively large doses no formaldehyde can be found in the excretions.

Formaldehyde is used in medicine chiefly for its disinfectant properties. Because of its local irritant influence it is rarely of service as a surgical application to the living body. It is occasionally used for the disinfection of surgical instruments and apparatus. For this purpose the vapor is more efficient than the solution. The most important use of formaldehyde is for the disinfection of rooms and various objects like books which might be injured by steam. Although it has a powerful effect on some forms of organic matter, things which are likely to come in contact with patients suffering from infectious diseases, such as clothing and the decorations in the sick room, are not injured by disinfectant strengths. Because of its affinity for ammonia and for hydrogen sulphide it has strong deodorizing properties. Various methods for the vaporization of formaldehyde are used in room disinfection; these include (1) direct generation by oxidizing methyl alcohol; (2) spontaneous evaporation of a solution sprinkled around the room; (3) evaporation of the official solution by means of heat; (4) vaporization of the official solution by oxidizing agents; and (5) decomposition of its polymer known as paraform. The first of these has been largely abandoned because of its cumbersomeness and the uncertainty of amount, the second because of its inefficiency and injurious effect upon the operators. The decomposition of paraform by heat is a convenient method for disinfecting small spaces, such as boxes containing surgical appliances, or closets, but is too expensive for general use; moreover, the presence of considerable amounts of aqueous vapor in the air is essential for best results with formaldehyde, and in most of the apparatuses using paraform insufficient provision is made for this. The method of evaporating aqueous solutions of formaldehyde with heat is the basis of a number of efficient apparatuses, but it is doubtful whether these have any real advantage over the cheap and handy method of volatilizing by means of oxidizing agents. The substances which have been used for the latter service include potassium permanganate, quick lime, barium peroxide, and sodium dichromate. The method recommended by the Pennsylvania State Board of Health (Dixon, *A. J. P.*, July, 1912) is as follows: For a thousand cubic feet of air space, one pint of the official solution of formaldehyde and eight ounces of potassium permanganate. Place the potassium permanganate in a bucket with at least ten times the capacity of the amount of disinfectant. Pour the formaldehyde on the permanganate. Eighty per cent. of the formaldehyde is liberated in the first five minutes. Doerr recommends the proportion of one part each of potassium permanganate, formaldehyde solution, and water. Hall and Roberts assert that seven parts of potassium permanganate to ten of formaldehyde solution is the most economical; this gives a liberation of 63 per cent. of the total formaldehyde. If water is added the percentage of liberation is lower, but the water is advantageous in aiding the disinfectant properties. It should be remembered that with careless use there is a possibility of setting fire to the room. In 1914, owing to the scarcity of potassium permanganate caused by the European war, a method was devised by LaWall (*J. A. M. A.*, 1914, lxiii, 1025) in which sodium dichromate takes the place of potassium permanganate. Notwithstanding some criticism of this process, as destroying a larger amount of the formaldehyde than the potassium permanganate method, tests made by the Pennsylvania Health Department bacteriologist, working under conditions such as are actually encountered in practical disinfection work, show all bacteria to be killed when the directions are carefully followed.

Inhalations of formaldehyde vapors have been tried in the treatment of pulmonary disorders, notably *phthisis,* with the idea of direct destructive action upon the bacteria, but they are so irritant to mucous membranes that the treatment has done more harm than good. Formaldehyde is also of service for the purpose of hardening the skin and of stopping excessive sweating in various forms of *hyperidrosis.* For this use the official solution should be diluted with from one to three parts of water. Hammond (*Am. Med.,* 1912, xviii, p. 391) has used formaldehyde with asserted success as a caustic in removal of *warts, corns, moles,* etc; he applies the full strength official solution four or five times a day for two or three days, being careful not to get it on the healthy skin. It is used in pharmacy for hardening gelatin capsules. (See under *Gelatinum.*)

Although its physiological action is comparatively slight, yet when swallowed it is a dangerous poison on account of its local irritant effects. The symptoms of formaldehyde poisoning are immediate severe abdominal pains with blood-stained vomiting, general collapse often with loss of consciousness, and albuminous, bloody or suppressed urine. Out of ten cases collated by McLoughlin (*Cleveland Med. Journ.,* 1909) three ended fatally. The smallest fatal dose of which we have any knowledge is the case reported by Eli (*J. A. M. A.,* liv) in which "a few drops of a 40 per cent. solution of formaldehyde" killed a three-year-old child with symptoms of edema of the larynx. The ordinarily fatal dose for an adult is about three fluidounces of the official solution. The diagnosis is usually easy from the odor of formaldehyde in the vomitus. The treatment requires an immediate evacuation of the stomach, the use of dilute ammonia water as an antidote, subsequently demulcents and symptomatic remedies as they may be indicated.

Festiform is a solution of formaldehyde solidified by the addition of soap. *Autan* is a mixture of paraform and barium peroxide which in the presence of water liberates formaldehyde gas. *Formysol* is a formalized soft soap as is also *veroform. Lysoform* is another saponaceous mixture containing formaldehyde.

Off. Prep.—Liquor Formaldehydi Saponatus, *Br.*

LIQUOR FORMALDEHYDI SAPONATUS. Br.

SOLUTION OF FORMALDEHYDE WITH SOAP

"Soft soap, 400 *grammes;* Alcohol (90 per cent.), 300 *millilitres;* Solution of Formaldehyde, 200 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Dissolve the Soft Soap in the Alcohol; add the Solution of Formaldehyde and sufficient Distilled Water to produce the required volume." *Br.*

LIQUOR HAMAMELIDIS. Br.

SOLUTION OF HAMAMELIS

Aqua Hamamelidis, *N. F.;* Witch Hazel Water; Distilled Extract of Witch Hazel; Witchhazel extract; Eau distillée de hamamelis, *Fr.;* Hamameliswasser, *G.*

"Fresh Hamamelis Leaves, 1000 *grammes;* Distilled Water, 2000 *millilitres;* Alcohol (90 per cent.), 160 *millilitres.* Macerate for twenty-four hours; then distil one thousand *millilitres.*" *Br.*

This preparation is no longer recognized by the U. S. but a similar one is official in the N. F. (see *Aqua Hamamelidis,* Part III).

Uses.—This water was introduced on account of the large demand for it which has grown out of the wide advertisements of a certain proprietary medicine, and the universally recognized need in American families for an embrocation which appeals to the psychic influence of faith. As the tannic acid of hamamelis bark does not come over into the distillate the water is therapeutically a mixture of water and alcohol, the volatile oil being found in too minute a proportion to possess any therapeutic value.

LIQUOR HYDRARGYRI NITRATIS ACIDUS. Br.

ACID SOLUTION OF MERCURIC NITRATE

Liquor Hydrargyri Nitratis, *N. F.;* Solution of Mercuric Nitrate; Solution of Nitrate of Mercury; Solution of Pernitrate of Mercury; Liquor Hydrargyri Nitrici Oxydati; Azotate Mercurique liquide, *Fr. Cod.;* Deutazotate (Pernitrate) de Mercure liquide, *Fr.;* Mercurnitratlösung, Quecksilberoxydnitratlösung, Flüssiges Salpetersaures Quecksilberoxyd, *G.*

"Mercury, 120 *grammes;* Nitric Acid, 150 *millilitres;* Distilled Water, 45 *millilitres.* Mix the Nitric Acid with the Distilled Water in a tared flask; dissolve the Mercury in the mixture without the application of heat; then boil gently until the Solution weighs three hundred and sixty *grammes.* Preserve it in a stoppered bottle not exposed to the light." *Br.*

The N. F. recognizes a very similar solution (see Part III).

In the British process, mercury is dissolved, with the assistance of heat, in an excess of nitric acid, and there is formed an acid mercuric nitrate, which is brought to a determinate bulk by evaporation. The proportion of nitric acid is sufficient not only to form mercuric nitrate, but also to furnish a large excess of acid.

Properties.—Solution of mercuric nitrate is a clear, nearly colorless, heavy liquid, having a faint odor of nitric acid, and a strongly acid reaction. "Specific gravity about 2.0. Yields no characteristic *reaction* for mercurous salts." *Br.*

Mercuric nitrate, the salt present in this preparation, can be obtained in large crystals of the composition $Hg(NO_3)_2 + 4H_2O$, when its solution is allowed to evaporate slowly over sulphuric acid. The same salt, which is very deliquescent, is obtained as a crystalline magma by adding strong nitric acid to the concentrated solution.

Uses.—This preparation is used as a caustic application to *cancers, lupus, ulcerations* of the *cervix, chancres,* etc. When a very free use is desired, it may be applied to the diseased surface by a camel's-hair brush, or cotton applicator. In *acne* and *boils* a drop, proportioned in size to the pustule, applied to the apex is sometimes of service. The parts touched immediately become white, the surrounding parts inflame, and in a few days a yellow scab is formed, which gradually falls off. Sometimes the application produces salivation. When it is desirable to avoid this result, the cauterized part should be washed with water immediately after the application of the caustic. It is not used internally.

LIQUOR HYDRARGYRI PERCHLORIDI. Br.

SOLUTION OF MERCURIC CHLORIDE

Liquor Hydrargyri Bichloridi; Solution of Bichloride of Mercury; Solution of Corrosive Sublimate; Sublimatlösung, *G.*

"Mercuric Chloride, 1 *gramme;* Distilled Water, sufficient to produce 1000 *millilitres.* Dissolve. This Solution should be kept protected from light. 100 *millilitres* contain 0.1 gramme of Mercuric Chloride; 110 minims contain 1/10 grain." *Br.*

This solution may be used as affording a convenient method of exhibiting corrosive sublimate. The ammonium chloride formerly used (Br.Ph., 1885) to aid in dissolving the mercuric chloride has been omitted in the process of the Br. Ph., 1914.

Dose, from one-half to one fluidrachm (1.8–3.75 cc.).

LIQUOR HYDROGENII DIOXIDI. U. S. (Br.)

SOLUTION OF HYDROGEN DIOXIDE Liq. Hydrog. Diox. [Solution of Hydrogen Peroxide]

"Solution of Hydrogen Dioxide is an aqueous solution containing not less than 3 per cent. by weight of H_2O_2." *U. S.*

"Solution of Hydrogen Dioxide is an aqueous solution containing not less than 3 per cent. by weight of H_2O_2, corresponding to not less than 10 volumes of available oxygen." *U. S.* "Solution of Hydrogen Peroxide is an aqueous solution of hydrogen peroxide, H_2O_2, prepared by the interaction of water, barium peroxide, and a dilute mineral acid, at a temperature below 10° C." *Br.*

Liquor Hydrogenii Peroxidi, *Br.;* Solution of Hydrogen Peroxide; Aqua Hydrogenii Dioxidi, Oxygenized Water, Oxygen Hydrate; Péroxide d'Hydrogene; Solutio Hydrogenii Peroxydati, *Fr. Cod.;* Wasserstoffhyperoxyd, Wasserstoffhyperoxidlösung, *G.;* Hydrogenium Peroxydatum Solutum, *P. G.;* Acqua ossigenata, *It.;* Agua oxigenada, *Sp.*

The U. S. P., 1890, process (see *U. S. D.,* 18th edition, p. 214) consisted in the decomposition of barium dioxide by phosphoric acid, barium phosphate being thrown down as a precipitate, hydrogen dioxide being found dissolved in the supernatant aqueous liquid; the barium phosphate is filtered out, and any trace of barium salt is finally removed by the cautious addition of sulphuric acid, which precipitates it as insoluble barium sulphate; the very fine precipitate which usually passes through the pores of filter paper is caught and held on the filter by the starch, and the clear solution may be adjusted to contain 3 per cent., *by weight,* of absolute hydrogen dioxide by assay.

Commercially it is usually made by a process essentially the same as that given above, the phosphoric acid being regenerated from the precipitate of barium phosphate by the addition of sulphuric acid which converts it into insoluble barium sulphate with the liberation of almost the original amount of phosphoric acid used. Another method is also used in which hydrofluoric acid is employed. This yields the comparatively insoluble barium fluoride as a by-product and the hydrofluoric acid may be regenerated from this also by the use of sulphuric acid. On the large scale it is necessary to reduce the temperature of the reaction by refrigeration of some kind in order to get anywhere near the full theoretical yield from the barium dioxide used. One of the important points is the preliminary hydration of the barium dioxide which is accomplished by allowing the dioxide to stand in contact with an excess of water until it attains a creamy consistence. It may also be prepared by the action of carbon dioxide upon hydrated barium peroxide, under pressure.

It has also been prepared from sodium peroxide as well as from perborates and persulphates. By the latter method concentrations up to 30 per cent. strength have been obtained by simple distillation of persulphuric acid, hydrogen peroxide distils over and leaves the sulphuric acid behind and the latter may again be converted into persulphuric acid by electrical energy.

Pure crystallized 100 per cent. H_2O_2 has been obtained by fractional extraction with ether and removal of the latter under reduced pressure in connection with the use of liquid carbon dioxide for reducing the temperature. Pure H_2O_2 melts at –2° C. It explodes with great violence when brought into contact with certain catalyzers and sets fire to fabrics with which it is brought into contact.

Hydrogen dioxide may be evaporated *in vacuo* at a gradually increasing temperature, a nearly pure hydrogen dioxide coming over at about 84° C. Wolffenstein states that he has prepared, after repeated fractioning, hydrogen peroxide (99.1 per cent.). (See *B. Chem. G.,* 1894, 3307. See also Schiloff's process, *Chem. News,* 1896, 38.) Crystallized hydrogen dioxide has been made by W. Staedel by applying a freezing mixture to a very strong solution of the dioxide, and collecting the separated columnar crystals; it is a very active body, being decomposed with explosive violence on coming in contact with manganese dioxide. (*Ph. Centralh.,* 1902, 546.)

A solidified compound of urea, 1 molecule, and hydrogen peroxide, 1 molecule, stabilized with citric acid is known under the trade names *hyperol* and *perhydrite.* It contains over 30 per cent. H_2O_2. The official solution is strong enough for most practical uses, for, although it can readily be made stronger, the difficulties of preserving it largely increase with its increased strength, and hence the Committee of Revision wisely fixed the standard at *ten volumes of available oxygen.* The British Pharmacopœia requires that the Solution shall indicate a yield of from *nine to eleven volumes* of oxygen when tested by the nitrometer test.

Solution of hydrogen dioxide is a powerful oxidizer and the simple contact with various substances, as platinum, gold and silver, causes it to be resolved into oxygen and water. On the contrary, certain other substances, even though ordinarily evincing a strong affinity for oxygen, as phosphorus, for example, are unaffected by it, and there are a number of bodies which have the property not only of being unaffected by it, but of restraining its oxidizing influence on other bodies, while some salts, like silver oxide, are actually reduced by it. Traces of impurities modify the stability of hydrogen dioxide; acids increase, alkalies decrease, its stability. Some manufacturers add a certain proportion of oxalic acid to the solution of hydrogen dioxide to raise the apparent value of the product, as shown by the permanganate assay; for a method of detecting this fraud, see a paper by G. Arth (*D. C.,* 1902, p. 141).

Description and Physical Properties.—"A colorless liquid, odorless, or having an odor suggesting ozone. It is slightly acid to the taste and produces a peculiar sensation and froth in the mouth. It is prone to deteriorate upon keeping or upon protracted agitation, and rapidly decomposes by contact with many oxidizing as well as reducing substances. When exposed to the air at the ordinary temperature or when heated on a water bath at a temperature not exceeding 60° C., the Solution loses chiefly water. When rapidly heated, it frequently decomposes suddenly. Solution of Hydrogen Dioxide is acid to litmus paper.

"Shake 1 cc. of Solution of Hydrogen Dioxide with 10 cc. of distilled water containing 1 drop of diluted sulphuric acid, and add 2 cc. of ether; the subsequent addition of a drop of potassium dichromate T.S. produces a blue color in the aqueous layer. Upon agitation and standing, this blue color passes into the ether layer.

"Not more than 0.03 Gm. of residue remains on evaporating 20 cc. of the Solution to dryness on a water bath (*non-volatile matter*). It requires not more than 2 cc. of tenth-normal sodium hydroxide, phenolphthalein T.S. being used as indicator, to neutralize 25 cc. of Solution of Hydrogen Dioxide (*free acid*). Add 1 cc. of ammonia T.S. to 1 cc. of the Solution, and evaporate the liquid to dryness on a water bath: the residue meets the requirements of the test for *arsenic.* Evaporate 1 cc. of the Solution to dryness on a water bath, and dissolve the residue in 10 cc. of distilled water containing 1 cc. of diluted hydrochloric acid: the liquid meets the requirements of the test for *heavy metals.* To 50 cc. of the Solution add sodium hydroxide T.S. until it is alkaline, then evaporate it on a water bath, and transfer the dry residue to a platinum crucible. Moisten the residue with sulphuric acid, and cover the crucible with a watch glass, the convex side of which is coated with a thin layer of bees wax which is scratched so as to expose the glass. Cool the watch glass by placing water in the concave side and standing in this a small beaker which must be kept filled with cold water. Now heat the crucible and contents on a water bath for one hour; the surface of the watch glass after the removal of the wax shows no sign of corrosion (*hydrofluoric acid*). The addition of 2 drops of diluted sulphuric acid to 10 cc. of the Solution produces no turbidity or precipitate within ten minutes (*barium*). Add 4 drops of sodium acetate T.S. to 10 cc. of the Solution, and follow with 4 drops of calcium chloride T.S.; no turbidity or precipitate is produced within ten minutes (*oxalic acid*). Shake out 100 cc. of Solution of Hydrogen Dioxide in a separator with a mixture of 3 volumes of chloroform and 2 volumes of ether, using 50 cc., 25 cc., and 25 cc., respectively, and evaporate the combined solutions to dryness at room temperature in a tared glass dish; the residue, if any, weighs not more than 0.04 Gm. (*limit of preservative*).

"Preserve in a cool place protected from light and dust. If the stopper of the bottle is coated with paraffin or replaced by a pledget of purified cotton, deterioration is retarded," *U. S.*

"**Assay.**—Dilute about 2 cc. of Solution of Hydrogen Dioxide, accurately weighed, with 20 cc. of distilled water, add 20 cc. of diluted sulphuric acid, and titrate with ten-normal potassium permanganate. Each cc. of tenth-normal potassium permanganate corresponds to 0.001701 Gm. of H_2O_2." *U. S.*

"A colorless and odorless liquid. Taste slightly acid. Decomposed by heat into water and oxygen. On adding a few drops to 10 millilitres of *water* mixed with a drop of *solution of potassium chromate,* 10 drops of *diluted sulphuric acid,* and 2 millilitres of *ether,* a blue layer appears between the ethereal and the aqueous liquid, and, after shaking, the *ether* also becomes blue. 2 millilitres vigorously shaken in a brine-charged nitrometer with 4 millilitres of *solution of copper ammonio-sulphate* liberate, at 15.5° C., and normal pressure, not less than 18 and not more than 22 millilitres of oxygen, corresponding to about 10 volumes of available oxygen in 1 volume of the Solution. 25 millilitres require for neutralisation not more than 2.5 millilitres of *N/10 solution of sodium hydroxide, solution of methyl orange* being used as indicator (limit of acidity). Yields no characteristic *reactions* for barium. Evaporated to dryness on a water-bath, not more than 1 per cent. of solid residue remains." *Br.*

F. X. Moerk has proposed a rapid and effective method of assaying this solution (see *A. J. P.*, 1893, 65). Kolthoff (*Ph. Wb.*, 1919, lvi, 949) also reviews the assay methods and suggests one in which ammonium molybdate is used as a catalyzer to liberate iodine from potassium iodide, the titration being made with sodium thiosulphate solution.

Another assay method has been proposed by Von Bertalan (*D. C.*, 1920, lxiv, 340), based on the oxidation of stannous chloride and the reduction of methylene blue to the leuco base.

Solution of hydrogen dioxide should be kept in a cool place, and not too tightly stoppered. (A plug of absorbent cotton is often used.) Neglect of these precautions, particularly in hot weather, will be likely to result in an explosion and fracture of the bottle containing it, due to a brisk evolution of oxygen in a confined space, on account of the increased temperature.

Hydrogen dioxide solution is usually preserved at the present time by the use of acetanilid or some other equally efficacious agent for retarding its decomposition. The presence of acetanilid was first called attention to in pharmaceutical literature by LaWall (*A. J. P.*, 1906, p. 582). Boroglycerin, caffeine, and other substances have also been used for the purpose. When acetanilid is used the solution upon standing for some time occasionally acquires a disagreeable odor due to the formation of nitrobenzene and other decomposition derivatives of the acetanilid. The amount of acetanilid used as a preservative is very small, being about 0.05 per cent. A study of the effect of various preservatives was reported by A. M. Glover (*A. J. P.*, 1913, p. 538), who found acetanilid to be the best of all that were tried. Kolthoff (*loc. cit.*) suggests either phenol, benzoic, or salicylic, acid in the proportion of 100 milligrammes per liter.

It has been claimed that its deterioration is often due to the alkalinity of the glass bottles in which it is stored, and that if alkali-free glass containers be used it will keep for extended periods without a preservative. (*Pharm. Era*, liv, 1921, p. 385.) Jordan (*J. A. Ph. A.*, 1913, ii, p. 344) finds that solutions of hydrogen dioxide kept in bottles stoppered with cotton, instead of a cork, retain their activity very much better, he believes, on account of the evaporation of the water. He also found that bottles protected from the light retained their activity better than those exposed to the light. Most of the samples examined were below pharmacopœial strength. One contained as little as 0.24 per cent. of H_2O_2, but the majority of them ranged from 2.5 to 3 per cent.

Uses.—Hydrogen peroxide in solution undergoes a slow process of reduction liberating a portion of its oxygen. Certain organic matters, however, among which may be mentioned pus and blood, exercise a powerful catalyzing action so that the oxygen is given off very rapidly. Evidently this nascent oxygen must have a powerful oxidizing effect and thereby destroy many forms of organic matter. It should be noted that in the presence of these reducing agents the antibacterial powers of the drug are greatly reduced. As long as there is effervescence caused by the application of hydrogen dioxide to a wound there is no great destruction of bacteria. Upon the system generally hydrogen peroxide does not, and cannot, exert any physiological action, because it cannot exist in the blood.

The most important use for this agent is as an antibacterial agent. The germicidal activity of hydrogen peroxide is generally greatly overestimated. Although in relatively dilute solution it will eventually destroy many of the pathogenic micro-organisms, its action is extremely slow, unless the solution be fairly concentrated. Gifford (*N. Y. M. R.*, 1888) found that a neutral solution containing 15 per cent. by volume of H_2O_2 (therefore stronger than the official solution) would destroy anthrax spores after five minutes' exposure, and pus cocci in one minute, but that the same solution when diluted with four parts of water did not kill the pus cocci after thirty minutes. Traugott found that 1 per cent. by weight killed typhoid bacilli in five minutes and staphylococci in fifteen to thirty minutes. On the other hand, if allowed sufficient time relatively small quantities are highly efficient. Heinemann (*J. A. M. A.*, 1913, lx, p. 1603) reaches the conclusion from his experiments that three teaspoonfuls of the official solution after six hours' exposure will destroy 99 per cent. of the bacteria present in a liter of drinking water; this quantity makes about a one to one thousand solution of hydrogen peroxide. In the presence of organic matter this compound is so rapidly broken down that it is even less efficient; as pointed out by Gifford, its germicidal action does not depend upon the liberated oxygen, but upon the hydrogen peroxide molecule.

The addition of hydrogen dioxide solution has at times been recommended as an emergency method for the preservation of milk. It effects a partial or complete sterilization on the milk and quickly disappears, being dissociated into H_2O and O. A paper dealing with the length of time during which the H_2O_2 persists in the milk has been published in the *Analyst*, 1915, p. 482, by M. E. Hines. The use in milk and cream is common in Great Britain. As it was first suggested by Budd, products so preserved are sometimes called "buddized."

The solution of hydrogen dioxide is used in medicine as a means of cleansing infected *wounds*, freely suppurating *ulcers*, and the like. Its value in these conditions is probably more due to removing organic detritus which forms a breeding place for the micro-organisms than to its antibacterial action. Its styptic effect—probably due to the activation of the fibrin ferment of the blood and consequent more rapid coagulation—as well as its harmless nature make it a very popular antiseptic for household use. It is sometimes injected into deep cavities for the purpose of determining the presence of pus, which will be signalized by effervescence; the method, however, must be used with caution, because if there be not a free vent for the gas sufficient pressure may be generated within the cavity to cause serious results. Because of its lack of toxicity it is a favorite disinfectant for application to various mucous membranes, especially those of the nose and throat. In *diphtheria* or *tonsillitis* the official solution may be applied pure, either by means of an atomizer or cotton applicator. Diluted with equal parts of water it is often employed as a gargle in *pharyngitis,* or as a mouth wash in *stomatitis,* but it appears frequently to exercise an injurious effect upon the epithelium of the buccal mucous membrane. In slow *hemorrhages* it often exercises a styptic effect, perhaps through activating the specific ferments of the blood which lead to clot formation. Internally the solution of hydrogen dioxide has been used with success by Goodman (*Penna. M. J.,* 1910) and others, in the treatment of *hyperchlorhydria.* It is asserted that it diminishes the acidity of the gastric juice, increases the secretion of mucous and exercises an antiseptic action in the stomach.

One great disadvantage of the solution of hydrogen dioxide is the rapidity with which it deteriorates. The New Hampshire State Board of Health reported in 1912 that more than half of the samples examined were below the Pharmacopœial standard.

Solution of hydrogen dioxide is used in 10 or 15 per cent. aqueous solutions, for various commercial purposes, such as cleaning and bleaching old and stained engravings or oil paintings, or as an auricome for bleaching dark colored hair. It is employed, moreover, in increasing degree in the textile industries for bleaching. Lunge has proposed its use in the ready valuation of chlorinated lime or bleaching powder, which is decomposed by it with the simultaneous liberation of oxygen from both substances in equal amount.

Under the name of *perhydrol* a solution asserted to represent 100 volume per cent. (30 per cent. by weight) of hydrogen dioxide is upon the market.

Dose, one fluidrachm (3.75 cc.).

LIQUOR IODI COMPOSITUS. U. S.

COMPOUND SOLUTION OF IODINE Liq. Iodi. Co.
[Lugol's Solution]

"Compound Solution of Iodine is an aqueous solution containing, in each 100 cc., not less than 4.8 Gm. and not more than 5.2 Gm. of I and not less than 9.8 Gm. and not more than 10.2 Gm. of KI." *U. S.*

Liquor Iodinii Compositus, *U. S.* 1870; Soluté ioduré de Lugol, *Fr.;* Lugolsche Jodlösung, *G.*

"Iodine, 5 Gm.; Potassium Iodide, 10 Gm.; Distilled Water, a sufficient quantity, to make 100 cc. Dissolve the iodine and potassium iodide in a sufficient quantity of distilled water to make the product measure 100 cc." *U. S.*

In this solution iodine is dissolved in water with the assistance of potassium iodide. Iodine dissolves sparingly in water, but freely in a solution of this salt. In using potassium iodide to render iodine more soluble in water, the iodide is generally taken in a quantity twice the weight of the iodine, and this is the proportion adopted in the U. S. formula.

In the Br. Pharmacopœia a solution is directed having much more iodine and less potassium iodide than the U. S. solution under the name *Tinctura Iodi Fortis.*

Description and Physical Properties.—"A transparent liquid having a deep brown color, and an odor of iodine. A drop of Compound Solution of Iodine added to 1 cc. of starch T.S., diluted with 10 cc. of water, produces a deep blue color.

"**Assay for Potassium Iodide.**—Measure exactly 5 cc. of Compound Solution of Iodine, evaporate in a tared dish or watch-glass on a water bath, and add several small successive portions of distilled water, drop by drop, until all of the iodine has volatilized and a white residue remains; the residue should weigh not less than 0.490 Gm. and not more than 0.510 Gm. and should respond to the identity tests under *Potassii Iodidum.*

"**Assay for Iodine.**—Dilute exactly 5 cc. of Compound Solution of Iodine with 25 cc. of distilled water, and titrate with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.01269 Gm. of I.

"Preserve the solution in glass-stoppered bottles, protected from light." *U. S.*

Uses.—Doctor Lugol, to whose investigations carried on about 1830 is due chiefly the introduction of iodine as a drug, used solutions of varying strength according to the purpose for which they were employed. His *iodine lotion,* used as a wash in scrofulous *ophthalmia,* in *ozena,* etc., contained two grains of iodine and four of potassium iodide in a pint of water. His *rubefacient iodine solution* is formed by dissolving half an ounce of iodine and an ounce of potassium iodide in six fluidounces of water. *Lugol's caustic iodine solution* containing iodine and potassium iodide, each, an ounce, dissolved in two fluidounces of water, was used to destroy soft and fungous granulations, and in *lupus.* To-day the aqueous solution is comparatively rarely employed externally. The official solution is used chiefly internally as a means of obtaining the therapeutic effects of iodine. It is also an efficient chemical antidote to most of the alkaloidal poisons.

Dose, of the U. S. P. solution, from two to five minims (0.12–0.3 cc.), three times a day, given in at least four tablespoonfuls of water or of milk, so as to avoid irritation of the stomach.

Off. Prep.—Liquor Iodi Phenolatus, *N. F.*

LIQUOR MAGNESII BICARBONATIS. Br.

SOLUTION OF MAGNESIUM BICARBONATE [Fluid Magnesia]

Liquor Magnesii Carbonatis, *Br.* 1898; Eau magnésienne, Magnésie liquide, *Fr.;* Kohlensaure Magnesialösung, Magnesiawasser, *G.*

"Magnesium Sulphate, 40 *grammes;* Sodium Carbonate, 50 *grammes;* Distilled Water, *a sufficient quantity.* Dissolve the two salts separately, each in two hundred *millilitres* of the Distilled Water; heat the solution of Magnesium Sulphate to the boiling point; add to it the solution of Sodium Carbonate; boil until carbon dioxide ceases to be evolved; collect the precipitate on a calico filter; wash it with Distilled Water until the filtrate is free from sulphates. Mix the washed precipitate with four hundred *millilitres* of Distilled Water; place the mixture in a suitable apparatus; force into it pure washed carbon dioxide; let the mixture remain in contact with excess of carbon dioxide, retained under a pressure of about three atmospheres, for twenty-four hours or longer; decant the resulting solution, and again pass carbon dioxide into it. Keep the Solution in securely closed bottles." *Br.*

The title of this solution was changed in the British Pharm., 1914, to "Solution of Magnesium *Bicarbonate.*" It was formerly solution of Magnesium *Carbonate;* the word bicarbonate more accurately describes the magnesium salt in the finished preparation.

The object of this process is to obtain a solution of magnesium bicarbonate by means of carbon dioxide, the carbonate being insoluble in pure water. The first step is to prepare a freshly precipitated hydrated magnesium carbonate, which is more readily dissolved than is a carbonate which has been kept for some time. As the magnesium carbonate of the Br. Pharmacopœia consists of three molecules of the neutral carbonate and one of magnesium hydroxide with four molecules of water, it follows that, in its preparation from the two salts used in the process, a portion of carbon dioxide escapes, and the boiling is directed to be continued until the escape of the gas ceases, so that the normal composition may be insured, and a longer heat, which might affect the constitution of the carbonate so as to diminish its solubility, avoided. The precipitate is thoroughly washed, in order to remove every trace of sodium sulphate, which may be indicated by the non-action of the test of barium chloride. The next step is to dissolve the precipitated carbonate in water impregnated with carbon dioxide, and, as the solution even thus favored is slowly effected, the carbonate is directed to remain exposed to the action of carbon dioxide, under pressure, for twenty-four hours, and still the whole of the carbonate is not dissolved, and filtration is necessary. According to the Br. Pharm., the solution "effervesces slightly, or not at all, when the containing vessel is first opened. Yields no characteristic *reactions* for sulphates. *Lead limit* 0.5 part per million. *Arsenic limit* 0.2 part per million. 20 millilitres evaporated to dryness yield a white residue, which after calcination weighs not less than 0.16 and not more than 0.19 gramme. This residue is insoluble in *water,* and when dissolved in a dilute acid yields the *reactions* characteristic of magnesium. This Solution contains the equivalent of about 2 grammes of the official Magnesium Carbonate in 100 millilitres; 1 fluid ounce contains the equivalent of about 10 grains." *Br.*

On exposure to the air, some of the carbon dioxide escapes, and a portion of the salt is deposited. According to Muncy, the preparation as it occurs in commerce is usually much below the standard strength.

This solution is but slightly effervescent, is clear, and should be free from bitterness. Nevertheless, its taste is more disagreeable than is that of the undissolved carbonate or hydroxide, over which it has no advantage. (See *Magma Magnesiæ.*)

Dose, as an antacid laxative, from one to two fluidounces (30–60 cc.).

LIQUOR MAGNESII CITRATIS. U. S.

SOLUTION OF MAGNESIUM CITRATE Liq. Mag. Cit.

"Solution of Magnesium Citrate contains, in each 100 cc., magnesium citrate corresponding to not less than 1.5 Gm. of MgO." *U. S.*

Liquor Magnesii Citrici; Solution of Citrate of Magnesium; Limonada Magnesii Citrici; Potio Magnesii Citrici; Limonade purgative au Citrate de Magnésie, *Fr.;* Flüssige Citronensaure Magnesia, Magnesiumcitratlösung, Magnesiumlimonade, *G.;* Limonata magnesiaca, *It.;* Limonada purgante de citrato magnesico, *Sp.*

"Magnesium Carbonate, 15.0 Gm.; Citric Acid, 35.0 Gm.; Syrup, 60.0 cc.; Purified Talc, 5.0 Gm.; Oil of Lemon, 0.1 cc.; Potassium Bicarbonate, 2.5 Gm.; Distilled Water, a sufficient quantity, to make 350 cc. Dissolve the citric acid in 150 cc. of hot distilled water in a suitable dish, and, having added the magnesium carbonate previously mixed with 100 cc. of distilled water, stir until it is dissolved. Then add the syrup, heat the mixed liquids to the boiling point, immediately introduce the oil of lemon, previously triturated with the purified talc, and filter the mixture, while hot, into a strong bottle (previously rinsed with boiling water) of suitable capacity. Add enough boiled distilled water to make the product measure 350 cc. Stopper the bottle with purified cotton, allow to cool, drop in the potassium bicarbonate, and immediately stopper the bottle securely. Lastly, shake the solution occasionally until the potassium bicarbonate is dissolved. Keep the bottle on its side in a cool place, preferably in a refrigerator. NOTE.—In this process the 2.5 Gm. of potassium bicarbonate may be replaced by 2.1 Gm. of sodium bicarbonate, preferably in tablet form." *U. S.*

This formula first appeared in the second edition of the U. S. Pharmacopœia of 1850. The original formula was soon found to have defects. The chief objection to the formula as originally framed was that the magnesium citrate, when the solution was kept for some days, crystallized out in the form of a white granular precipitate, which rendered the solution unfit for medicinal use. This precipitate was found by Procter to be $Mg_3(C_6H_5O_7)_2 + 14H_2O$. This still occurs to some extent, although more slowly, and probably cannot be avoided except by a very great reduction in the amount of magnesia. The U. S. P. (8th Rev.) process improved the formula by increasing the quantity of citric acid, using 33 Gm. instead of 30 Gm. formerly used. The use of potassium bicarbonate introduces potassium citrate, but in too small a proportion to be of any consequence.

Special bottles which have a "patent stopper" attached are very convenient, but they have been practically superseded by the crown stopper in many localities. Solid magnesium citrate is best used in the form of the effervescent magnesium citrate of the U. S. P., 1890. (See *U. S. D.*, 19th edition, p. 726.)

The formula of the U. S. evidently intends a partial sterilization by such recommendations as: boiling the mixed liquids, rinsing the bottle with boiling water, using boiled water for diluting the mixed liquids, and stoppering the bottle with purified cotton. These measures are helpful in destroying bacteria, but after all has been done the potassium bicarbonate or sodium bicarbonate added at the last may introduce germs which may develop growths. The oil of lemon should be fresh and without terebinthinate odor. The tincture made from fresh lemon peel would probably prove more satisfactory as a flavor.

Description and Physical Properties.—"A slightly yellow, clear, effervescent liquid, having a sweet, acidulous taste and a lemon flavor.

"Add 1 cc. of glacial acetic acid and 3 cc. of an aqueous solution of potassium acetate (1 in 2) to 10 cc. of Solution of Magnesium Citrate, shake the mixture vigorously, then gently rub the sides of the test tube with a glass rod for a few minutes, and allow to stand for one hour; no white crystalline precipitate soluble in ammonia T.S. is produced (*tartaric acid*). Dilute 2 cc. of the Solution with 8 cc. of distilled water, and add 5 drops of hydrochloric acid and 1 cc. of barium chloride T.S.; no turbidity is produced within one minute (*sulphate*). Dilute 2 cc. of the Solution with distilled water to 45 cc., add 5 cc. of ammonium oxalate T.S., and mix well; the resulting turbidity, if any, is not greater than the turbidity in a control test made with 1 cc. of a solution prepared as follows: Dissolve 1 Gm. of calcium carbonate, previously dried to constant weight at 200° C., in 1 cc. of acetic acid and 5 cc. of distilled water. Boil for about one minute, and dilute with distilled water to 100 cc. (*calcium*). Boil down exactly 10 cc. of the Solution to about 5 cc. to expel carbon dioxide, dilute with 15 cc. of distilled water, and titrate with half-normal sodium hydroxide, using phenolphthalein T.S. as indicator; it requires not less than 9.5 cc. of the alkali for neutralization (*minimum of acidity*). Concentrate the liquid, and transfer it completely with the aid of a little distilled water to a platinum or porcelain crucible, evaporate to dryness, and proceed as directed under the assay for alkali salts of organic acids, page 431; not less than 28 cc. of half-normal sulphuric acid should be consumed (*minimum of total citric acid*).

"**Assay for Magnesium Oxide.**—Measure exactly 10 cc. of Solution of Magnesium Citrate, transfer to a platinum or porcelain dish, evaporate to dryness, and ignite until most of the carbonaceous matter has burned off. Add to the residue 20 cc. of diluted hydrochloric acid, heat on a water bath for fifteen minutes, filter if necessary, and wash the residue thoroughly with hot distilled water. To the combined filtrate and washings, which should measure about 100 cc., add an excess of sodium phosphate T.S. (about 20 cc.), then gradually add ammonia T.S. with constant stirring until slightly alkaline. After ten minutes add 30 cc. of ammonia T.S., and allow the mixture to stand for twelve hours. Then filter, and wash the precipitate with a mixture of 1 volume of ammonia T.S. and 19 volumes of distilled water until free from chloride. Dry, and ignite to constant weight. The weight of the magnesium pyrophosphate ($Mg_2P_2O_7$) so obtained is not less than 0.414 Gm., indicating an equivalent of not less than 1.5 Gm. of MgO in 100 cc. of the Solution." *U. S.*

Overlooking the excess of acid which it contains, the salt present is the tribasic citrate, in which the six atoms of hydrogen from two molecules of citric acid are replaced by three atoms of magnesium. Accordingly, it consists of two molecules of citric acid and three atoms of magnesium. It is advisable in preparing the solution to introduce the magnesia in small portions, for if too hastily added it is liable to cause the formation of the neutral citrate, which cannot afterwards be readily dissolved. Dorvault made a solid magnesium citrate which is perfectly and readily soluble, by melting on a sand bath 100 parts of crystallized citric acid in its water of crystallization, and thoroughly incorporating with it 29 parts of calcined magnesia. A pasty mixture is formed, which soon hardens, and may be pulverized for use. Magnesium citrate, thus prepared, is soluble in twice its weight of water. When in saturated solution it soon precipitates as a nearly insoluble hydroxide, but with eight or ten times its weight of water it forms a permanent solution. Simonin found that an insoluble magnesium citrate may be restored to solubility in boiling water by being thoroughly rubbed up with water so as to form a paste. The necessary trituration will be abridged if a little citric acid be added. For other modifications, suggestions, etc., see Kondratowisch, *N. R.*, 1883, p. 246; Neynaber, *A. J. P.*, 1884, p. 472 (the proposed substitution of acetic acid by the latter is not desirable, because of the impossibility of avoiding an empyreumatic taste); also A. B. Stevens, *Proc. Mich. State Pharm. Assoc.*, 1885; and F. W. Sennewald, *Nat. Drug.*, 1887.

Magnesium metatartrate has been proposed, in the place of the citrate, by Léger, who, however, states that as a purgative it is more powerful than the citrate, resembling the sulphate. On account of its pleasant taste it might, perhaps, be substituted for Epsom salt.

Uses.—This solution is a cooling cathartic, and operates mildly. It has come into extensive use in the United States, on account of the facility with which it may be taken and its acceptability to the stomach.

Dose, as a purge, the whole quantity directed in the formula, or twelve fluidounces (360 cc.); as a laxative, half that quantity.

LIQUOR MORPHINÆ ACETATIS. Br.

SOLUTION OF MORPHINE ACETATE

Soluté d'Acétate de Morphine, *Fr.;* Essigsaure Morphinlösung, *G.*

"Morphine Acetate, 1 *gramme;* Diluted Acetic Acid, 2 *millilitres;* Alcohol (90 per cent.), 25 *millilitres;* Distilled Water, sufficient to produce 100 *millilitres.* Mix the Alcohol with an equal volume of Distilled Water, adding the Diluted Acetic Acid; dissolve the Morphine Acetate in the mixture, and add sufficient Distilled Water to produce the required volume. This Solution contains 1 gramme of Morphine Acetate in 100 millilitres; 110 minims contain 1 grain." *Br.*

Morphine acetate often contains a little uncombined morphine, in consequence of the escape of a portion of the acid during its evaporation, and especially when this is pushed to dryness. It is on this account apt to be unreliable. Hence the addition of the diluted acetic acid, which at the same time neutralizes the alkaloid in excess and enables the solution to be completely effected. The alcohol is added as a preservative. The present solution contains about 1 per cent. of morphine acetate and is, therefore, about equivalent in strength to tincture of opium.

Dose, from ten to thirty minims (0.6–1.8 cc.).

LIQUOR MORPHINÆ HYDROCHLORIDI. Br.

SOLUTION OF MORPHINE HYDROCHLORIDE

Solution of Hydrochlorate of Morphine, *Br.* 1885; Liquor Morphinæ Muriatis, *Dub.;* Solution of Muriate of Morphia; Soluté de Hydrochlorate de Morphine, *Fr.;* Salzsaure Morphinlösung, *G.*

"Morphine Hydrochloride, 1 *gramme;* Diluted Hydrochloric Acid, 2 *millilitres;* Alcohol (90 per cent.), 25 *millilitres;* Distilled Water, sufficient to produce 100 *millilitres.* Mix the Alcohol with an equal volume of Distilled Water, adding the Diluted Hydrochloric Acid; dissolve the Morphine Hydrochloride in the mixture, and add sufficient Distilled Water to produce the required volume. This Solution contains 1 gramme of Morphine Hydrochloride in 100 millilitres; 110 minims contain 1 grain." *Br.*

The use of the alcohol is to prevent spontaneous decomposition, that of the acid probably to assist in the solution of the salt. The solution contains about 1 per cent. of morphine hydrochloride.

Dose, from ten to thirty minims (0.6–1.8 cc.).

LIQUOR MORPHINÆ TARTRATIS. Br.

SOLUTION OF MORPHINE TARTRATE

Soluté de Tartrate de Morphine, *Fr.;* Weinsteinsaure Morphinlösung, *G.*

"Morphine Tartrate, 1 *gramme;* Alcohol (90 per cent.), 25 *millilitres;* Distilled Water, sufficient to produce 100 *millilitres.* Mix the Alcohol with an equal volume of Distilled Water; Dissolve the Morphine Tartrate in the mixture; add sufficient Distilled Water to produce the required volume. This Solution contains 1 gramme of Morphine Tartrate in 100 millilitres; 110 minims contain 1 grain." *Br.*

This solution was introduced into the Br. Ph., 1898, because of the superior solubility and stability of the morphine tartrate, alcohol being used to preserve the liquid. It is of the same strength as the other solutions of morphine, about 1 per cent. It is not intended for hypodermic use and should not be confounded with the *Injectio Morphinæ Hypodermatica. Magendie's Solution of Morphine* was of the strength of 16 grains to the fluidounce.

Dose, from ten to thirty minims (0.6–1.8 cc.).

LIQUOR PANCREATIS. Br.

PANCREATIC SOLUTION

"Pancreatic Solution contains the digestive principles of the fresh pancreas of the pig." *Br.*

Liquor Pancreatius; Soluté de Pancreátine, *Fr.;* Pancreatinlösung, Pankreasessenz, *G.*

"Mix two hundred and fifty *millilitres* of Alcohol (90 per cent.) with two hundred *millilitres* of Glycerin and sufficient Distilled Water to produce one thousand *millilitres.* In this mixture macerate for seven days two hundred and fifty *grammes* of the pancreas, freed from fat and external membrane, and finely divided by trituration with washed sand or powdered pumice stone; filter." *Br.*

This official preparation of the Br. Ph., 1898, has been introduced to supply the demand for a liquid digestive solution made from the pancreas; it closely resembles the preparation recommended by Benger. (*Proc. Roy. Soc.*, xxxii, 145; see also *Pancreatinum.*) "When 3 *millilitres* of the Solution together with 0.2

gramme of *sodium bicarbonate* and 20 *millilitres* of *water* are added to 80 *millilitres* of milk and the mixture kept at 45° C. for one hour, on placing 5 millilitres of this liquid with 5 *millilitres* of *ether* and 5 drops of *nitric acid* in a stoppered tube and gently inverting the tube three times, no curdy precipitate appears in the lower layer." *Br.*

The solution digests albuminoids, converts starch into sugar in an alkaline solution, albumin and fibrin into peptones, and peptonizes milk. As it acts normally in alkaline solutions, while the gastric juices are strongly acid, its practical value as an internal medicament is doubtful. Its chief value is for the predigestion of foods.

Dose, from one to two fluidrachms (3.75–7.5 cc.).

LIQUOR PICIS CARBONIS. Br.

SOLUTION OF COAL TAR

Soluté de Goudron de Houille, *Fr.;* Kohlenteerlösung, *G.*

"Prepared Coal Tar, 200 *grammes;* Quillaia Bark, in No. 20 powder, 100 *grammes;* Alcohol (90 per cent.), 1000 *millilitres.* Exhaust the powdered Quillaia Bark with the Alcohol by the *percolation process.* To the resulting tincture add the Prepared Coal Tar, and digest the mixture at 50° C. for two days, stirring occasionally. Cool and decant, or filter." *Br.*

This solution of the Br. Ph., 1898, is practically identical with *Liquor Carbonis Detergens, Coal Tar Saponin,* and the *Liquor Picis Carbonis* of the N. F. (see Part III), and similar well-known preparations which have been largely used by dermatologists. The process for solution of coal tar is modelled after that for *compound tincture of coal tar,* proposed by L. A. Duhring. It owes its virtues largely to phenol and other derivatives of coal tar. (See *Pix Carbonis Præparata.*)

Solution of coal tar is stimulating, and is prescribed, diluted with from ten to fifty parts of water, as a wash in *eczema, psoriasis, pruritus,* and other skin diseases.

LIQUOR PITUITARII. U. S.

SOLUTION OF PITUITARY Liq. Pituitar.

[Liquor Hypophysis, U. S. P. IX, Pituitary Extract]

"Solution of Pituitary contains the water-soluble principle or principles from the fresh posterior lobe of the pituitary body of cattle, 1 cc. having an activity upon the isolated uterus of the virgin guinea-pig, corresponding to not less than 80 per cent. and not more than 120 per cent. of that produced by 0.005 Gm. of the Standard Powdered Pituitary, prepared as directed below. The solution should be sterile." *U. S.*

This solution was introduced into the U. S. P. IX because of the great difference in the potency of the commercial preparations on the market. The hope that an official standard would lead to a unification in the output of various manufacturers has, however, not been realized, perhaps because the official solution was much weaker than most of those put out by various manufacturing houses under trade names. The present Pharmacopœia has continued the solution modifying, however, the standard of strength.

Because of the impracticability for the ordinary retail pharmacists to manufacture solutions of the pituitary body, the Pharmacopœia does not give any process.

"**Description and Physical Properties.**—A transparent liquid, colorless, or nearly so, having a faint, characteristic odor." *U. S.*

Assay.—In our complete ignorance of the active principle of the pituitary, the only possible means of standardizing this preparation is by a physiological test. Although several methods for the bio-assay have been suggested the only one which has found any general favor is that based on the increase in the contractions of the isolated uterus caused by the drug as compared to the action of a substance of known activity. Formerly the U. S. P. recognized as the standard for comparison beta-iminazolylethylamine, but experience having shown that it is practicably impossible to obtain this of uniform quality the present revision employs a standard preparation of pituitary which is made as follows:

Standard Powdered Pituitary.—"Select a number, not less than 25, of fresh posterior lobes of the pituitary body of cattle, removed within thirty minutes of the death of the animal and carefully free them from all extraneous tissue, immediately after their removal. As soon as they are so prepared, drop them into a flask containing a quantity of acetone corresponding to not less than 4 cc. of acetone for each pituitary body. Allow them to remain in the acetone for three hours, and then remove them and immediately cut them into small pieces with scissors and place the material in fresh acetone equal in quantity to that first employed. Leave the material in the acetone over night, and then remove it and dry it in a vacuum desiccator over calcium chloride, at a temperature not above 50° C., for five hours. At the end of this time remove the material and grind it in a mortar until it will pass through a No. 40 sieve. Dry this powder for at least twelve hours in a vacuum desiccator over calcium chloride at a temperature not over 50° C. Extract this dried powder in a small Soxhlet continuous extraction apparatus with acetone for three hours and again dry it in a desiccator over calcium chloride for twelve hours. This dried powder should be preserved in a cool, dark place, in sealed ampuls *in vacuo,* or in vacuum desiccators over calcium chloride until used for the preparation of the standard solution." *U. S.*

"Prepare a solution as follows: Carefully weigh a suitable amount of the dried Standard Powdered Pituitary, place this weighed powder in a small agate mortar and moisten with a few drops of distilled water containing 0.25 per cent. of acetic acid. Triturate the moistened powder thoroughly until the whole is of an impalpable frothy consistence. Add a few cc. of the 0.25 per cent. acetic acid solution and stir the mixture thoroughly. Transfer to a hard glass test tube or beaker; rinse the small agate mortar with the acetic acid solution and add the rinsings to the pituitary mixture; then add enough 0.25 per cent. acetic acid to make the final volume of the mixture of the same number of cc. as the number of milligrams of dried pituitary powder originally taken. Heat this mixture to the boiling point for not more than one minute and filter. The filtrate contains in each cc. the active principle of 0.001 Gm. of the dried standard powder. Place this solution in hard glass ampuls and sterilize by fractional sterilization for twenty minutes on three successive days at a temperature not exceeding 100° C. Preserve in a cool place (from 5° to 20° C.). This standard solution should not be kept more than six months.

"The apparatus used for making the test may be any modification of the general type for studying the activity of the isolated smooth muscle of mammals. It must be provided with an accurate temperature-regulating device. The chamber in which the uterus is suspended should have a capacity of not less than 100 cc. Use healthy guinea pigs weighing between 175 Gm. and 350 Gm. They should not have been pregnant and should not be in heat. It is recommended that young female pigs be segregated at the time of weaning and kept thereafter out of sight and smell of the males.

"Kill a guinea pig by a blow on the head, or by decapitation and immediately remove the entire uterus from the body. Suspend a part or all of one horn of the uterus in a chamber containing oxygenated Locke-Ringer solution (page 489), one end of the uterus being attached to a muscle lever which is weighted as necessary. The temperature of the bath should be between 37° and 38° C. but should not vary more than one-tenth of a degree throughout the whole assay. When the uterus is completely relaxed, which is generally in from fifteen to thirty minutes, it is ready to begin the test. This is done by adding alternately varying doses of the standard extract and of the solution to be tested to the bath in the muscle chamber until quantities of the two solutions are found which give equal, sub-maximal contractions in at least two successive pairs of contractions. The strengths of the two solutions are in inverse ratio to the quantities necessary to produce these equal contractions." *U. S.*

The uterine assay method requires such complex apparatus and presents so many technical difficulties that the results are reliable only when carried out in especially equipped laboratories by thoroughly experienced observers. A brief description of the general principles of the method may, however, not be out of place. The test is performed by adding a carefully measured quantity of the solution to a bath containing the uterus suspended in a warm physiological solution (see *Locke-Ringer Solution,* Part III), one end of the uterus being attached to a fixed point and the other end to a light lever which records the movements of the muscle upon a smoked surface. The usual feeble, spontaneous, contractions of the uterus can be overcome by weighting the lever so as to put a certain amount of tension on the muscle. In carrying out the test a carefully measured quantity of the standard solution is injected into the bath (the amount of which will vary with the amount of fluid in the bath as well as the susceptibility of the individual muscle) and records made of the resultant contraction. After these have reached their maximum the fluid is withdrawn from the bath and the bath filled with fresh, previously warmed Locke solution in order to wash out any traces of the drug. This is in turn again withdrawn and the bath filled with fresh solution into which is injected a quantity of the solution to be tested and the contractions recorded as before. This process, of repeated injections of the pituitary into the bath and its withdrawal, is continued with varying doses alternately of the standard preparation and of the one being tested until contractions of equal size are produced by the two solutions.

The following are some of the more obvious technical details which must be observed: The temperature of the bath in which the uterus is suspended must be constantly the same throughout the whole course of the experiment. This is usually accomplished by inserting the container in a large tank of warm physiological salt solution whose temperature is kept constant by means of some heating mechanism either electrical or a Bunsen burner.

The fresh Locke solution which is added between each test must be of the same temperature as the bath in which the uterus is suspended. This can be most conveniently accomplished by keeping the containers of the Locke solution in the same large tank in which the uterine bath is kept.

Arrangements must be made for constant fresh supply of oxygen in the uterine bath. This is generally done by having a tube, connected with an oxygen tank, pass into the bath and a small quantity of oxygen allowed to bubble up continuously through the fluid.

The weight upon the lever must be sufficient to completely relax the uterus but not too heavy for the muscle to lift.

The delicacy of the reactions and the necessity for absolute similarity of conditions may be suggested by noting some of the sources of error which have been reported: variations in the quality of sodium chloride, even when using the purest salt obtainable (see Pittenger and Quici, *J. A. Ph. A.*, 1923, xii, 14); changes in the hydrogen ion concentration of the Locke solution due either to original impurities in the glucose or to alterations occurring on standing; changes in the quality of oxygen bubbling up through the bathing solutions.

Hamilton (*J. A. Ph. A.*, 1919, viii, 58) prefers a blood-pressure test. The technique for this is the same as for that described under *Liquor Epinephrinæ*, except that the intervals between injections must be longer; the comparison of activity may be made with a standard pituitary solution prepared according to the official method.

Smith and McClosky (*U. S. Hygienic Lab.*, 1924, Bull. 138) find that pituitary solutions carefully prepared and sterilized do not depreciate in activity at least for one year if kept in a low temperature. In warm places deterioration takes place more or less rapidly in proportion to the degree of warmth; at a temperature of 37° C. the solutions retain their activity practically unimpaired for two months, but at 60° C. there is almost complete destruction of the active principles within three months. Similar conclusions were reached by Tate (*P. J.*, 1921, cvi, 268).

Uses.—The solution of the posterior lobe of the pituitary body possesses the physiological action and therapeutic properties of this organ, but has the great advantage of being in a convenient form for administration, especially for hypodermic use. While it is probable that even when given by the mouth the pituitary exerts an effect upon the functions of the body, it is certainly more active when administered hypodermically and is to-day rarely exhibited orally. As it is impracticable for the retail pharmacist to prepare sterile solutions of the hypophysis of definite activity, the apothecary will ordinarily stock one of the commercial solutions. These preparations—which are sold under various trade names as *pituitrin, pituitol, pituglandol, hypophysin, pituitary extract*, etc.—vary, however, greatly in their activity. According to Pittenger (*J. A. Ph. A.*, 1917, vi), the commercial solutions of hypophysis are from two to five times as strong as the standard given in the U. S. P.; a fact which it is important that both the physician and the druggist realize, as overdoses of this remedy are capable of much harm. It is to be hoped that with the present practicable standards manufacturers will make their products to conform to the official requirements. The most frequent use of this drug is as a uterine stimulant, especially in *labor*, although it is sometimes used as a circulatory stimulant in surgical *shock*. (See under *Pituitarium.*) It is also used as an intestinal stimulant, especially in post-operative tympanitis.

Dose, of the U. S. P. preparation, ten to twenty minims (0.6–1.2 cc.).

LIQUOR PLUMBI SUBACETATIS.
U. S. (Br.)
SOLUTION OF LEAD SUBACETATE Liq. Plumb. Subacet [Goulard's Extract]

"An aqueous solution containing lead subacetate, approximately $Pb_2O(CH_3.COO)_2$, corresponding to not less than 18 per cent. of Pb." *U. S.*

Liquor Plumbi Subacetatis Fortis, *Br.;* Strong Solution of Lead Subacetate; Acetum Plumbi, Acetum Saturni, Plumbum Hydrico-Aceticum Solutum; Acétate (sous-) de Plombliquide, Extrait de Goulard, Vinaigre de Plomb (de Saturne), *Fr.;* Liquor Plumbi Subacetici, *P. G.;* Bleiessig, *G.*

"Lead Acetate, 220 Gm.; Lead Monoxide, 140 Gm.; Distilled Water, a sufficient quantity to make 1000 cc. Triturate the lead monoxide to a smooth paste with 100 cc. of distilled water, and transfer the mixture to a bottle of about 1000 cc. capacity, using an additional 100 cc. of distilled water for rinsing. Dissolve the lead acetate in 700 cc. of distilled water, and add the solution to the lead oxide mixture. Shake vigorously for five minutes, then set it aside for seven days, shaking frequently during this time. Finally filter, protecting the solution from undue contact with the air, and pass enough distilled water through the filter to make the product measure 1000 cc. This solution may also be prepared as follows: Boil the mixture of lead acetate, lead monoxide, and water for half an hour in a suitable flask, adding small portions of distilled water as necessary to maintain the volume. Then cool, and filter. The funnel during filtration should be covered to protect the solution from the action of air, and enough boiled distilled water passed through the filter to make the product measure 1000 cc." *U. S.*

"Lead Acetate, 250 *grammes;* Lead Oxide, in powder, 175 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres*. Dissolve the Lead Acetate in seven hundred and fifty *millilitres* of the Distilled Water, add the Lead Oxide, set aside for forty-eight hours, shaking occasionally; filter, and pass through the filter sufficient Distilled Water to produce the required volume." *Br.*

The Br. Pharm., 1914, adopted a "cold process" for making this solution and inserts an assay process as a test. This is necessary to secure uniformity and establish a standard.

The U. S. P. X process does not differ essentially from that formerly official. Several methods have been proposed for making this by a process which will eliminate the necessity of boiling. For Haussmann's method by agitating the lead salts with hot water and subsequently adding the lead oxide and occasionally agitating until cold, see *A. J. P.*, 1897, 559; *M. R.*, 1896, 329; *Ph. Rev.*, 1896, 250.

In many pharmaceutical manufacturing laboratories when this preparation is made on the large scale, the cold process is always used as it seems to work very well with large quantities, and the final adjustment is then made to the standard strength after assaying the preparation.

Description and Physical Properties.—"A clear, colorless, odorless liquid, having a very sweet, astringent taste. It is alkaline to litmus paper but not to phenolphthalein T.S. On exposure to the air it absorbs carbon dioxide, which causes the formation of a white precipitate.

" Specific gravity: about 1.25 at 25° C. When 1 cc. of Solution of Lead Subacetate is added to 5 cc. of mucilage of acacia (1 in 10), it produces a dense white precipitate (*distinction from normal lead acetate*). Solution of Lead Subacetate responds to the reactions for lead, and for acetates. Solution of Lead Subacetate yields with potassium ferrocyanide T.S. a white precipitate, tinged with neither red nor blue (*copper or iron*).

"**Assay.**—Place about 1 cc. of Solution of Lead Subacetate, accurately weighed, in a 200 cc. volumetric flask, dilute with 50 cc. of recently boiled distilled water, and add 50 cc. of tenth-normal oxalic acid. Agitate the mixture thoroughly for five minutes, fill to the mark with distilled water, shake, and filter, rejecting the first 20 cc. of the filtrate. Add 5 cc. of sulphuric acid to 100 cc. of the filtrate, warm to about 70° C., and titrate the residual oxalic acid with tenth-normal potassium permanganate. Each cc. of tenth-normal oxalic acid corresponds to 0.01036 Gm. of Pb.

" Preserve in well-stoppered bottles." *U. S.*

"A clear colorless liquid, with a sweet astringent taste; alkaline to *litmus.* Becomes turbid by exposure to the air. Forms an opaque white jelly with *mucilage of gum acacia.* Yields the *reactions* characteristic of lead and of acetates. Specific gravity 1.275. When 1 gramme is diluted with 20 millilitres of *water* and mixed with excess of *N/1 solution of oxalic acid,* the precipitate collected, washed, transferred to a flask and decomposed with excess of *diluted sulphuric acid,* the mixture thus obtained heated to 60° C., decolorises not less than 17 millilitres of *N/10 solution of potassium permanganate." Br.*

When concentrated by evaporation, it deposits on cooling crystalline plates, which, according to Barker, are flat, rhomboidal prisms, with dihedral summits. Jeannel prepares *crystallized lead subacetate* in accordance with the following formula: Triturate six parts of neutral lead acetate with two parts of pure litharge, and add one part of water. Heat in a porcelain dish, stirring with a glass rod, until fusion and finally ebullition occur. After two or three minutes of boiling, filter through paper in a funnel heated by a sand bath. Allow to cool and crystallize. (*J. P. C.*, 4e sér., xi, 54.)

Incompatibilities.—One of its most striking properties is the extreme facility with which it is decomposed. Carbon dioxide throws down a white precipitate of lead carbonate; and this happens by mere exposure to the air, or by mixture even with distilled water, if this has not been recently boiled. Solutions of gum, tannin, most vegetable coloring principles, and many animal substances, particularly albumin, produce with it precipitates consisting of the substance added and lead oxide. It should be kept in well-stoppered bottles. It is distinguished from the solution of lead acetate by being precipitated by gum arabic.

Owing to the liability to serious results due to the frequent confounding of the name lime water and lead water, it is safer to dispense lead water in a slightly opalescent condition, while lime water should be perfectly transparent.

Uses.—This solution is astringent and sedative but is employed only as an external application. It is widely used, especially mixed with an equal part of tincture of opium—a mixture commonly known as *lead water and laudanum*—in inflammation arising from *sprains, bruises, burns, blisters,* etc., to which it is applied by means of linen cloths, which should be removed as fast as they become dry. It always, however, requires to be diluted. Blackburn (*J. A. M. A.*, 1906, xlvi, p. 954) reports erythema following the local application of lead water and laudanum, and we have seen blistering apparently resulting from this popular embrocation. From four fluidrachms to a fluidounce (15–30 cc.), added to a pint (480 cc.) of distilled water, forms a solution sufficiently strong in ordinary cases of external inflammation. When applied to the skin denuded of the cuticle, the solution should be still weaker, as constitutional effects might result from the absorption of the lead. Paralysis is said to have been produced by its local action; and poisoning by its injection for *gonorrhea* has been reported. (*Dublin Journ. Med. Sci.*, 1874.) The common name of Goulard's extract is derived from a surgeon of Montpellier by whom it was introduced into general notice, though previously employed.

Off. Prep.—Liquor Plumbi Subacetatis Dilutus, *N. F., Br.;* Ceratum Plumbi Subacetatis, *N. F.;* Glycerinum Plumbi Subacetatis, *Br.;* Unguentum Plumbi Subacetatis, *Br.*

LIQUOR PLUMBI SUBACETATIS DILUTUS. Br.

DILUTED SOLUTION OF LEAD SUBACETATE

Aqua Saturnina; Goulard's Lotion, Goulard's Water, Lead Water; Diluted Solution of Subacetate of Lead; Lotion à l'Acétate de Plomb, Eau de Saturne, Eau de Goulard, Eau blanche, *Fr.;* Aqua Plumbi, *P. G.;* Bleiwasser, Kuhlwasser, *G.*

" Strong Solution of Lead Subacetate, 12.5 *millilitres;* Distilled Water, recently boiled and cooled, sufficient to produce 1000.0 *millilitres.* Mix." *Br.*

The direction to dilute the strong solution with distilled water *previously boiled and cooled* is an improvement, as even the small amount of carbon dioxide dissolved in distilled water usually made the lead water cloudy.

This preparation is too weak to be of any real value. A similar solution is recognized by the N. F.

LIQUOR POTASSII ARSENITIS.
U. S. (Br.)

SOLUTION OF POTASSIUM ARSENITE Liq. Pot. Arsen. [Fowler's Solution Liquor arsenicalis Fowleri P I.]

" Solution of Potassium Arsenite contains, in each 100 cc., potassium arsenite ($KAsO_2$), equivalent to not less than 0.975 Gm. and not more than 1.025 Gm. of As_2O_3." *U. S.*

Liquor Arsenicalis, *Br.;* Arsenical Solution; Solutio Arsenicalis Fowleri, Kali Arsenicosum Solutum; Liquor Fowleri; Aqua Arsenitis Potassici; Solutio Kalii Arsenicosi, *Fr. Cod.;* Soluté d'Arsenite de Potasse, Liqueur de Fowler, Liqueur arsénicale de Fowler, *Fr.;* Liquor Kalii arsenicosi, *P. G.;* Fowlersche Lösung, *G.;* Soluzione alcalina di arsenito de potassio, Liquore del Fowler, *It.;* Solucion de arsenito potasico, Licor arsenical de Fowler, *Sp.*

"Arsenic Trioxide, 10 Gm.; Potassium Bicarbonate, 20 Gm.; Compound Tincture of Lavender, 30 cc.; Distilled Water, a sufficient quantity to make 1000 cc. Boil the potassium bicarbonate and arsenic trioxide in a flask with 100 cc. of distilled water until solution is effected. Cool the solution, and transfer it to a 1000 cc. graduated container, rinsing the flask in which the liquid was boiled with several portions of distilled water to make a solution measuring 970 cc. Add the compound tincture of lavender, mix thoroughly, and filter if necessary." *U. S.*

"Arsenious Anhydride, in powder, 10 *grammes;* Potassium Carbonate, 10 *grammes;* Compound Tincture of Lavender, 30 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Dissolve the Arsenious Anhydride and the Potassium Carbonate in five hundred *millilitres* of Distilled Water by the aid of heat; cool; add the Compound Tincture of Lavender and sufficient Distilled Water to produce the required volume." *Br.*

This preparation originated with Fowler, of Stafford, England, and was intended as a substitute for the celebrated remedy known under the name of "the *tasteless ague drop.*" It now contains potassium arsenite corresponding in amount to 1 per cent. of arsenic trioxide, corresponding with the International Protocol. It is a potassium arsenite dissolved in water, and is formed by the combination of the arsenic trioxide with the potassium of the bicarbonate or carbonate, carbon dioxide being evolved. In the present U. S. process the bicarbonate has been preferred to the carbonate and in order to expedite the process the quantity has been doubled. As the bicarbonate is decomposed to carbonate by boiling water, there is present in the finished solution some potassium carbonate. According to M. H. Buignet, ebullition disengages the carbon dioxide slowly, so that after four hours' boiling the solution still retains about one-sixth of this gas. The name by which the preparation is designated in the U. S. Pharmacopœia is the more correct. The contact of arsenic trioxide with potassium bicarbonate in the presence of a small quantity of boiling water gives rise to effervescence with decomposition of bicarbonate. The compound tincture of lavender is added to give it taste and prevent its being mistaken for water. For Oldberg's process, see *Proc. A. Ph. A.*, 1893, 430; see also *A. J. P.*, 1895, 403.

Vanderkleed and E'we (*Proc. P. Ph. A.*, 1916, p. 283) point out that there are substances of widely differing composition offered in the market under the name of potassium arsenite. One of these consists of pure $KAsO_2$, while the other is $KAsO_2.H_3AsO_3$.

Description and Physical Properties.—"A clear or faintly opalescent liquid, having a pink color and a slight odor of lavender. It is alkaline to litmus paper.

"Add to 10 cc. of the Solution an excess of hydrochloric acid and an equal volume of hydrogen sulphide T.S.: a yellow precipitate is produced which is soluble in ammonium carbonate T.S.

"Acidulate 4 cc. of Solution of Potassium Arsenite with diluted nitric acid, add 1 cc. of silver nitrate T.S., and superimpose a layer of ammonia T.S. upon this liquid: no red or reddish-brown color is observed at the line of contact (*arsenate*).

"**Assay.**—Measure exactly 20 cc. of Solution of Potassium Arsenite, dilute with 75 cc. of distilled water, acidify the mixture very slightly with diluted hydrochloric acid, then dissolve in the solution 2 Gm. of sodium bicarbonate, and titrate the resulting liquid with tenth-normal iodine, starch T.S. being used as indicator. Each cc. of tenth-normal iodine corresponds to 0.004948 Gm. of As_2O_3." *U. S.*

"A reddish liquid, alkaline to *litmus,* and having the odor of lavender, 25 millilitres, neutralised with *hydrochloric acid,* discharge the color of 50.4 millilitres of *N/10 solution of iodine,* the presence of a slight excess of *sodium bicarbonate* being maintained throughout the operation. This Solution contains 1 gramme of Arsenious Anhydride in 100 millilitres; 110 minims contain 1 grain." *Br.*

According to R. Fresenius, solutions of alkaline arsenites slowly absorb oxygen from the air, and are in part converted into arsenates. Hence the propriety of keeping this solution in small bottles well filled. Mohr states that the alkaline reaction of the official solution delays the change, and experience has confirmed this statement. The slight precipitate found in this solution after keeping proved to be silicic acid, caused by the action of the alkaline solution on the glass container.

Uses.—This solution has the general action of the arsenical preparations on the animal economy, already described under the head of *Arseni Trioxidum.* Its liquid form makes it convenient for exhibition and gradual increase, and it is the preparation generally resorted to when arsenic is given internally. It has been much employed in *intermittent fever, skin diseases,* and the other affections for which arsenic is employed. In *chorea* it is almost a specific, and in *nervous diseases* of debility it is often very useful. In *malarial affections* and *chorea* it should be administered in ascending doses until the puffiness about the eyes or disturbance of the bowels betrays the arsenical impression. For the peculiar effects upon the human organisms, see *Arseni Trioxidum.*

Dose, three to five minims (0.2–0.3 cc.), which may be gradually increased.

LIQUOR POTASSII CITRATIS. U. S.

SOLUTION OF POTASSIUM CITRATE Liq. Pot. Cit. [Neutral Mixture]

"Solution of Potassium Citrate contains, in each 100 cc., not less than 8 Gm. of $K_3C_6H_5O_7$, with small amounts of citric and carbonic acids. *Caution—This preparation must not be dispensed unless it has been recently prepared.*" *U. S.*

Mistura Potassii Citratis; Liquor Kalii Citrici; Citrate de Potasse liquide, *Fr.;* Flüssiges Citronensaures Kali, Kaliumcitratlösung, *G.*

"Potassium Bicarbonate, 8 Gm.; Citric Acid, 6 Gm.; Distilled Water, a sufficient quantity to make 100 cc. Dissolve the potassium bicarbonate and the citric acid, each, in 40 cc. of distilled water. Filter the solutions separately, and wash the filters with enough distilled water to obtain in each case 50 cc. Mix the two solutions, and when effervescence has ceased, transfer to a bottle and stopper tightly." *U. S.*

The official solution is stronger than the so-called mixture of citrate of potassium (or *neutral mixture*), which it superseded some years ago. The latter preparation was directed to be prepared from fresh lemon juice, and, while more palatable, was very irregular in its strength which was entirely dependent upon the citric acid content of the lemon juice. An improvement has been made in the present official solution in directing the acid and the alkaline salt to be dissolved separately, and the direction to dispense the preparation in a fresh condition will undoubtedly lead to the keeping of the filtered solutions, by the pharmacist, in separate bottles, and mixing in equal measures or weights when prescribed. The solutions keep well for a considerable length of time, and there is thus greater convenience and a saving of time and labor.

Description and Physical Properties.—"A clear, colorless, odorless liquid, slightly acid to litmus paper. It meets the requirements of the tests for identity and purity of an aqueous solution of potassium citrate under *Potassii Citras* when suitably concentrated.

"**Assay.**—Measure exactly 15 cc. of Solution of Potassium Citrate, evaporate to dryness, and proceed as directed under the Assay for alkali salts of organic acids. Each cc. of half-normal sulphuric acid corresponds to 0.05106 Gm. of $K_3C_6H_5O_7$." *U. S.*

Uses.—The solution of potassium citrate has long been used under the name of *neutral mixture, saline mixture,* or *effervescing draught.* It formerly was much used as a refrigerant diaphoretic, in cases of *fever* with dry skin, but has been largely superseded by the more potent antipyretics. It has the therapeutic virtues of potassium citrate and the presence of the carbonic acid often makes it more acceptable to the stomach.

Dose, of official solution, four fluidrachms (15 cc.).

LIQUOR POTASSII HYDROXIDI. U. S. (Br.)

SOLUTION OF POTASSIUM HYDROXIDE Liq. Pot. Hydrox. [Liquor Potassæ Pharm. 1890, Solution of Potassa]

"Solution of Potassium Hydroxide contains, in each 100 cc., not less than 4.5 Gm. and not more than 5.5 Gm. of KOH." *U. S.* "Solution of Potash is an aqueous solution containing in 100 millilitres 5 grammes of pure potassium hydroxide, KOH. It should be preserved in a green glass bottle furnished with an air-tight stopper." *Br.*

Liquor Potassæ, *Br.;* Kali Hydricum Solutum, Lixivium Causticum; Solution of Potash; Potasse caustique liquide, Lessive caustique, *Fr.;* Liquor Kali Caustici, *P. G.;* Aetzkalilauge, Kalilauge, *G.*

"Dekanormal Solution of Potassium Hydroxide, 90 cc.; Distilled Water, a sufficient quantity to make 1000 cc. Mix the dekanormal solution, with sufficient distilled water to make 1000 cc. NOTE.—The 90 cc. of dekanormal solution of potassium hydroxide may be replaced by 60 Gm. of potassium hydroxide, containing 85 per cent. of KOH." *U. S.*

For description of dekanormal solution of potassium hydroxide, see Part III.

The British Pharmacopœia, 1914, does not give a detailed process, merely specifying that one hundred millilitres shall contain five grammes of potassium hydroxide.

Description and Physical Properties.—"A clear, colorless, odorless liquid, strongly alkaline and caustic, readily absorbing carbon dioxide from the air. Specific gravity: about 1.046 at 25° C. It meets the requirements of the tests for identity and purity for an aqueous solution of potassium hydroxide under *Potassii Hydroxidum* when suitably concentrated. Measure exactly 20 cc. of Solution of Potassium Hydroxide into a suitable flask and titrate directly with normal hydrochloric acid, using methyl orange T.S. as indicator: it shows, in each 100 cc., not more than 5.5 Gm. of alkali, calculated as KOH (*carbonate*).

"**Assay.**—Measure exactly 50 cc. of Solution of Potassium Hydroxide into a 250 cc. measuring flask, add 20 cc. of barium chloride T.S., and fill the flask to the mark with recently boiled distilled water. Thoroughly agitate the liquid, filter it through a filter not previously moistened, reject the first 20 cc., and titrate 100 cc. of the filtrate, representing 20 cc. of the Solution, with normal hydrochloric acid, using phenolphthalein T.S. as indicator. Each cc. of normal hydrochloric acid corresponds to 0.05611 Gm. of KOH.

"Preserve in bottles made of hard glass, and provided with rubber stoppers or with glass stoppers coated with petrolatum." *U. S.*

"A colorless, strongly alkaline liquid. Yields no characteristic *reactions* for lead, copper, arsenic, iron, aluminium, calcium, magnesium, sodium, or ammonium, and not more than the slightest *reactions* for carbonates, chlorides, or sulphates. Specific gravity 1.045. 20 millilitres require for neutralisation 17.8 millilitres of *N/1 solution of sulphuric acid.* This Solution contains 5 grammes of Potassium Hydroxide, KOH, in 100 millilitres; 110 minims contain 5 grains." *Br.*

It acts rapidly on animal and vegetable substances, and when rubbed between the fingers produces a soapy feeling, in consequence of a partial solution of the cuticle. It dissolves gum, resins, and extractive matter, and forms soap with oily and fatty bodies. It is incompatible with acids, acidulous salts, and all metallic and earthy salts held in solution by an acid; also with all ammonia salts, and with calomel and corrosive sublimate. The two official solutions of potassium hydroxide are now nearly identical in strength, the U. S. solution having the sp. gr. 1.046 at 25° C., and the Br. 1.045 at 15.5° C. On account of its strong attraction for carbon dioxide, solution of potassium hydroxide should be carefully preserved from contact with the air.

Uses.—Solution of potassium hydroxide is powerfully antacid, and mildly diuretic, and was formerly much used, but, on account of its irritant properties, has been superseded by the carbonated alkalies as an internal remedy.

Dose, ten to thirty minims (0.6–1.8 cc.).

LIQUOR POTASSII PERMANGANATIS. Br.

SOLUTION OF POTASSIUM PERMANGANATE

Soluté de Permanganate de Potasse, *Fr.;* Kaliumpermanganatlösung, *G.;*

" Potassium Permanganate, 10 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Dissolve. This Solution contains 1 gramme of Potassium Permanganate in 100 millilitres; 110 minims contain 1 grain." *Br.*

This is an unstable 1 per cent. solution of potassium permanganate which decomposes upon exposure and deposits manganese oxides.

Dose, officially given in the Br., is from two to four fluidrachms (7.5–15 cc.), equivalent to from 1.1 to 2.2 grains of the salt, but very few stomachs will bear more than one grain (0.065 Gm.) of the permanganate.

LIQUOR SODÆ CHLORINATÆ.
U. S., Br.

SOLUTION OF CHLORINATED SODA Liq. Sod. Chlorinat. [Labarraque's Solution]

" An aqueous solution of chlorine compounds of sodium, containing not less than 2.5 per cent. of NaOCl, equivalent to not less than 2.5 per cent. of available chlorine." *U. S.*

Liquor Sodæ Chlorati, *U. S.* 1890; Liquor Natri Chlorati; Liquor Natri Hypochlorosi· Bleaching Solution; Chlorure de Soude liquide, *Fr. Cod.;* Liqueur de Labarraque, *Fr.;* Chlornatronlösung, Bleichflüssigkeit, *G.;* Solucion de hipoclorito sodico, Licor de Labarraque, *Sp.*

" Monohydrated Sodium Carbonate, 70 Gm.; Chlorinated Lime, 100 Gm.; Water, a sufficient quantity to make 1000 Gm. Triturate the chlorinated lime with 500 cc. of water gradually added until a uniform mixture results. Dissolve the monohydrated sodium carbonate in 500 cc. of warm water, and add this solution to the chlorinated lime mixture contained in a suitable vessel. Stir or shake the mixture thoroughly, and if it becomes gelatinous warm the vessel very gently until its contents again liquefy. Then transfer the mixture to a wetted muslin strainer, and return the first portion until the liquid passes through clear. Add a few drops of sodium carbonate T.S. to 10 cc. of this clear filtrate. If it remains clear on the addition of the reagent, continue the operation without further treatment. If the filtrate becomes cloudy, return the mixture to the vessel, add sufficient monohydrated sodium carbonate to precipitate the excess of lime and again filter, returning the first portions until the liquid passes through clear. When no more liquid drains from the filter, wash the precipitate with enough water to make the product weigh 1000 Gm." *U. S.*

" Chlorinated Lime, 100 *grammes;* Sodium Carbonate, 150 *grammes;* Distilled Water, 1000 *millilitres.* Dissolve the Sodium Carbonate in two hundred and fifty *millilitres* of the Distilled Water; thoroughly triturate the Chlorinated Lime with the remainder of the Distilled Water; mix the two liquids; shake occasionally during three or four hours; filter. This Solution should be freshly prepared." *Br.*

This solution was first brought into notice as a disinfecting agent by Labarraque, an apothecary of Paris. It must not be confused with Dakin's solution (see *Liquor Sodæ Chlorinatis Surgicalis*). The U. S. process is practically that of Payen, adopted in the French Codex of 1837. It consists in decomposing a solution of monohydrated sodium carbonate by one of chlorinated lime. Calcium carbonate is precipitated and the chlorinated soda remains in solution. The proportion employed gives an excess of sodium carbonate, the presence of which renders the solution more permanent.

Description and Physical Properties.—"A clear, pale greenish liquid, having a faint odor suggesting chlorine, and a disagreeable, alkaline taste. The Solution at first colors red litmus paper blue and then bleaches it. The addition of hydrochloric acid to the Solution causes an evolution of chlorine and carbon dioxide.

"**Assay.**—Mix in a flask about 7 cc. of Solution of Chlorinated Soda, accurately weighed, with 50 cc. of distilled water, add 1 Gm. of potassium iodide and 5 cc. of acetic acid, and titrate the liberated iodine with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.003546 Gm. of Cl.

" Preserve in well-stoppered bottles, in a cool place, protected from light." *U. S.*

" A colorless alkaline liquid with a faint odor of chlorine and astringent taste. Decomposed by *hydrochloric acid,* evolving chlorine. Yields not more than slight *reactions* for calcium or carbonates. Specific gravity 1.054. If 5 millilitres are added to a solution of 1 gramme of *potassium iodide* in 100 millilitres of *water* acidified with 5 millilitres of *hydrochloric acid,* a brownish-red solution is obtained, which requires for decolorisation not less than 37.6 millilitres of *N/10 solution of sodium thiosulphate* (presence of not less than 2.5 per cent. by weight of available chlorine)." *Br.*

The two official assays are essentially similar.

Assuming the chlorinated lime to be essentially calcium hypochlorite with calcium chloride, the solutions, after decantation from the precipitated calcium carbonate, will contain *sodium hypochlorite* with sodium chloride:

$$Ca(OCl)_2 + CaCl_2 + 2Na_2CO_3 = 2CaCO_3 + 2NaOCl + 2NaCl$$

Besides these there will be present more or less sodium carbonate, according as there happens to be in the chlorinated lime less or more chlorine to decompose it. In all cases, however, there will be an excess of sodium carbonate, as the best chlorinated lime does not contain sufficient chlorine to effect its entire decomposition, in the proportion in which it is taken in the formula.

Arny and Dawson (*Proc. A. Ph. A.,* 1908, p. 841) criticized the process for making this solution and recommended the reduction of the U. S. P. standard for chlorinated lime from 30 per cent. of available chlorine to 25 per cent. largely because it is difficult for pharmacists to procure the drug commercially of this strength.

Uses.—The solution of chlorinated soda possesses the germicidal value of its available chlorine. For the disinfection of large masses of organic matter it is inferior to chlorinated lime, not merely because of its greater cost, but also because of its lower content of chlorine. It is, however, an excellent agent for the disinfection of various utensils which are not injured by its bleaching action, such as clinical thermometers and glass or china ware which have been used by patients with contagious disease.

Under the name of *antiformin* an alkaline solution of sodium hypochlorite is largely used in the bacteriological laboratory. This solution contains about 7.5 per cent. of sodium hydroxide and 5.2 per cent. of chlorine. Its especial value lies in its property of liquefying various organic matters and of dissolving most varieties of bacteria. It is especially employed for the purpose of recognizing tubercle bacilli in the sputum; it liquefies the sputum, so that centrifugation is possible, and dissolves other bacteria.

LIQUOR SODÆ CHLORINATÆ CHIRURGICALIS. U. S.

SURGICAL SOLUTION OF CHLORINATED SODA

Liq. Sod. Chlorinat. Chir. [Modified Dakin's Solution]

"An aqueous solution of chlorine compounds of sodium, containing not less than 0.45 per cent. and not more than 0.50 per cent. of NaOCl equivalent to from 0.43 to 0.48 per cent. of available Cl." *U. S.*

Dakin's Solution, Carrel-Dakin's Solution, Solution of Sodium Hypochlorite.

"Chlorinated Lime, Exsiccated Sodium Phosphate, Water, each, a sufficient quantity to make 1000 cc. Assay the chlorinated lime (see *Calx Chlorinata*) and, having determined its percentage of available chlorine, prepare the solution as directed below, using the quantities of chlorinated lime and exsiccated sodium phosphate indicated in the following table:

Per cent of available chlorine in the chlorinated lime used	Gm. of chlorinated lime for each 1000 cc. of solution	Gm. of exsiccated sodium phosphate for each 1000 cc. of solution
20	29	38
21	28	36
22	27	34
23	26	32
24	25	30
25	24	28
26	23	26
27	22	24
28	21	22
29	20.5	21
30	20	20
31	19.5	20
32	19	20
33	18	20
34	17.5	20
35	17	20

"Triturate the necessary amount of chlorinated lime, as indicated by the table, with 400 cc. of water gradually added, until a uniform mixture results. Dissolve the required amount of exsiccated sodium phosphate, which has been recently dried, in 400 cc. of water, heated to 50° C., and add this solution to the chlorinated lime mixture. Shake thoroughly and allow it to stand for fifteen minutes. Transfer the mixture to a filter, returning the first portions of filtrate until it runs through clear, and when no more liquid drains from the filter, wash the precipitate with sufficient water to make the product measure 900 cc. Assay a portion as directed below, and dilute the remainder with sufficient water to make the finished Solution contain 0.48 per cent. of NaOCl." *U. S.*

In 1915 as a result of experiences in the treatment of gun shot wounds in the great European War, Doctor Dakin called attention to the value of a solution of chlorinated soda neutralized with boric acid (*B. M. J.,* 1915, ii, p. 318). His original formula was soon afterwards modified by Doctor Carrel. Subsequently a considerable number of modifications of these solutions have been suggested, but they are all known generically as *Carrel-Dakin solutions* and they all depend for their activity upon the presence of definite proportions of sodium hypochlorite.

It is important that this solution be clearly distinguished from the old Labarraque's solution. It differs in the first place in being much weaker, secondly in containing definite proportions of available chlorine by assay, and thirdly in being free from caustic alkali. It is important to note that in some cases the strength of the solution is expressed in parts per cent. of sodium hypochlorite. This has caused considerable confusion in statements concerning advisable concentrations. Sodium hypochlorite represents 47.65 per cent. of chlorine, all of which is capable of being liberated in oxidation reactions. In such reactions each chlorine atom is equivalent to one oxygen atom, so "available chlorine" is simply a trade expression in which the figure representing the replaceable chlorine is multiplied by 2. This makes the available chlorine content of sodium hypochlorite at about 95 per cent., so in this case there is little difference between the strengths as expressed in terms of sodium hypochlorite, or as available chlorine.

The formula as originally given by Dakin (*B. M. J.*, 1915, ii, p. 318) is as follows: 140 Gm. of dry sodium carbonate (or 400 Gm. of the crystalline) are dissolved in 10 liters of tap water. Add 200 Gm. of chlorinated lime and shake well. Half an hour later siphon off the clear fluid and filter through cotton. Add 40 Gm. of boric acid, which should yield a solution only faintly alkaline. This solution represents, according to Dakin, between 0.5 to 0.6 per cent. of sodium hypochlorite. Later Dr. A. Carrel submitted a formula for what is called "*Carrel-Dakin Solution*" (Daufresne's technic), which largely replaced the original. Numerous other formulas have been suggested, the most widely used directing the use of sodium bicarbonate as the neutralizing and stabilizing ingredient. In the official process this has been replaced by exsiccated sodium phosphate, the process being based on one that has been used for some years with satisfaction at the Johns Hopkins Hospital in Baltimore.

Description and Physical Properties.—"A colorless or faintly yellow liquid having a slight odor suggesting chlorine. Add about 0.02 Gm. of powdered phenolphthalein to 20 cc. of Surgical Solution of Chlorinated Soda: no red color is produced on agitation (*maximum alkalinity*). Add about 0.5 cc. of phenolphthalein T.S. to 5 cc. of the Solution contained in a test tube: a momentary red flash is produced (*minimum alkalinity*).

"**Assay.**—Dilute 25 cc. of the Solution, accurately weighed, with 50 cc. of distilled water, add 1 Gm. of potassium iodide and 5 cc. of acetic acid, and titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.003723 Gm. of NaOCl.

"Preserve in well-stoppered bottles, preferably for not more than seven days, in a cool place, protected from light." *U. S.*

Cullen and Taylor (*J. A. M. A.*, June 15, 1918) point out that the end point indicated by phenolphthalein is not neutrality but a distinct alkalinity; as too great alkalinity makes the solution irritant they recommend the use of some other indicator such as o-cresolphthalein (see under *Indicators*).

Some of the commercial solutions of sodium hypochlorite, which are intended for the extemporaneous preparation of solutions similar in character to Dakin's solution, are of a remarkably high degree of stability. Whether this be due to the presence of some preservative or to some unusual method of manufacture or to an extraordinary purity, can not be stated at this time.

Sherman (*J. A. M. A.*, 1917, lxix, 187) tested stability of Dakin's solution: Exposed to sunlight there was a notable loss of strength within a week, the solution dropping from 0.52 per cent. of NaOCl to 0.49 per cent.; the same original solution, kept in the dark, at the end of 40 days showed 0.50 per cent. of NaOCl. Becker also (*J. A. Ph. A.*, 1925, xiv, 129) reached the conclusion that daylight had a marked deteriorating effect on this solution but that heating did not affect its potency. According to Chevrier (*D. C.*, 1918, lxii, 263) contact with rubber tubing causes rapid deterioration; from 43 to 39 in 12 hours. Daufresne adds a trace of potassium permanganate, 5 milligrammes per liter, to stabilize Dakin's solution (*C. D.*, 1918, xc, 184).

Under the name of *Eusol*, an aqueous solution of hypochlorous acid has been used in the same manner as the sodium hypochlorite.

Hyclorite (*N. N. R.*, 1924) is a commercial solution which is stated to contain 4.05 per cent. of sodium hypochlorite, .025 per cent. of calcium hydroxide and to represent not less than 3.85 per cent. of available chlorine. It is, therefore, approximately seven or eight times as strong as the official solution. *Zonite* is another commercial solution of sodium hypochlorite, which is claimed by the manufacturers to contain 0.9 per cent. of available chlorine and therefore to be twice as strong as the official solution. These solutions are, like Dakin's solution, disinfectant. They do not, however, possess all of the characteristic properties and must never be used as substitutes for the official preparation where this is ordered.

The peculiar therapeutic virtues of Dakin's solution depend on a special combination of certain chemical properties, namely (1) a definite concentration of sodium hypochlorite; either too much or too little destroys its value and (2) the complete absence of caustic alkali, with, however, a feebly alkaline reaction. These qualities can be produced only by the most rigid adherence to the details of the formula. The practice, at one time not uncommon, of dispensing solutions of chloramine in the place of Dakin's solution is a sordid type of dishonesty fraught with the possibility of most serious danger to the patient. (See Smyth, *A. J. P.*, 1923, p. 232.)

Uses.—Dakin's solution is used solely for its antibacterial properties especially in the treatment of surgical *wounds*. Tilley (*J. Agricult. Research*, 1920, xx, p. 85) has shown that sodium hypochlorite in germicidal power ranks with bichloride of mercury. In the absence of organic material one part in 25,000 kills most non-sporulating bacteria, and one part in 200 killed the highly resistant anthrax spores after two hours. In the presence of blood serum, however, the germicidal action is very much weaker, a one to 400 solution requiring two hours to kill the ordinary vegetative forms; this latter strength is approximately equivalent to 50 per cent. of the official surgical solution. The peculiar value of this solution in surgery depends, however, not merely on its antibacterial action, but to a large extent upon its power of dissolving necrotic tissue, and hence aid in getting rid of undesirable detritus. This solvent power, however, may become very dangerous in some conditions. Chevrier (*D. C.*, 1918, lxii, p. 212) points out the danger of secondary hemorrhage from dissolving of ligature material, and Sheldon (*P. J.*, 1918, ci, p. 150) has demonstrated a solvent action upon catgut, silkworm gut, silk thread and horse hair; he found linen thread much more resistant. Frequently the solution is applied by a method of continuous irrigation, in which case care must be observed to protect the skin surrounding the wounded area. It is sometimes used for irrigation of internal cavities like the bladder. It is employed in concentrations ranging from full strength down to one in four according to the condition for which it is applied.

LIQUOR SODII ARSENATIS. Br.

SOLUTION OF SODIUM ARSENATE Liq. Sod. Arsen.

Liquor Sodii Arseniatis, *Br.* 1885; Solution of Arseniate of Sodium; Natrium Arsenicicum Solutum; Solutio Arsenatis Natrii; Soluté d'Arseniate de Soude, *Fr.*; Arsensaure Natronlösung, *G.*

"Anhydrous Sodium Arsenate, 1 *gramme;* Distilled Water, sufficient to produce 100 *millilitres.* Dissolve. This Solution contains the equivalent of 1 gramme of Anhydrous Sodium Arsenate in 100 millilitres; 110 minims contain the equivalent of 1 grain." *Br.*

The salt is directed to be dried, in order that the solution may be of a uniform strength, as, from the mode in which the sodium arsenate is ordered to be prepared, it is scarcely possible that it should always contain precisely the same quantity of water of crystallization. It is important in drying it to limit the heat to 150° C., lest a portion of the arsenic should be volatilized.

Dose, from three to five minims (0.2–0.3 cc.), to be cautiously increased, if necessary.

LIQUOR SODII CHLORIDI PHYSIOLOGICUS. U. S.

PHYSIOLOGICAL SOLUTION OF SODIUM CHLORIDE Liq. Sod. Chlor. Physio. [Physiological Salt Solution Normal Saline Solution]

"Sodium Chloride, 8.5 Gm.; Distilled Water, a sufficient quantity to make 1000 cc. Dissolve the sodium chloride in sufficient freshly distilled water, neutral to litmus paper, to measure 1000 cc., and filter, returning the filtrate until free from foreign particles. Transfer the solution to a sterile flask of insoluble glass, having a capacity of about 1000 cc., and stopper with a plug of purified absorbent cotton, wrapped in gauze. Fasten stout, non-absorbent paper or tinfoil over the top of the plug and the lip of the container, and sterilize in an autoclave under steam pressure maintaining a temperature of 115° C., for thirty minutes. This solution should be used within twenty-four hours if it is to be employed for intravenous injection. For other uses it is preferable that the solution be resterilized after each opening, and that it be used within a month after its preparation." *U. S.*

The Pharmacopœia directs that salt solution be sterilized in an autoclave; the previous recommendation was to boil it for one hour. If this be done a considerable amount of the water may be evaporated and the concentration of the solution materially altered. It is advisable to sterilize the container separately by dry heat as it is possible some spores might resist the autoclave temperature.

Uses.—When pure water is brought in contact with the blood it causes alteration in the red blood corpuscles, allowing the escape of hemoglobin from them into the plasma; this is known as "laking" of the blood. The addition of inorganic salts to the water, in quantities sufficient to make a solution of the same osmotic tension as the blood serum, prevents this action on the corpuscles. When a solution contains just the amount of salt necessary to prevent laking it is said to be isotonic with the blood. Because of its non-toxicity sodium chloride is the salt usually employed for the purpose of preparing an isotonic solution. The amount of salt necessary for this purpose varies in different animals; in the human being it requires an 0.85 per cent. solution of sodium chloride, but an 0.6 per cent. is isotonic with ox blood. This isotonic solution is sometimes spoken of as *normal salt solution,* an unfortunate term, as it is likely to be confused with the normal volumetric solution of sodium chloride used by chemists, which is nearly seven times stronger. A much better term is the official name, *physiological salt solution.* In 1882 Ringer showed that after all the blood has been washed out of the heart with an isotonic sodium chloride solution, the addition of small amounts of calcium and potassium would cause that organ again to begin to contract, and that it would continue beating for some time if supplied with these salts. He therefore suggested that calcium and potassium be added to the sodium chloride solution in preparing a physiologically indifferent fluid. Although Ringer originally recommended the addition of calcium phosphate to saturation for the purpose of supplying the needed lime, as at present used in physiological laboratories *Ringer's solution* has the following composition: sodium chloride, 0.7 per cent.; potassium chloride, 0.03 per cent.; calcium chloride, 0.025 per cent. Subsequently it was shown that if this solution was rendered slightly alkaline it offered a still more favorable medium for the heart. In 1895 Locke suggested the addition of dextrose in order to furnish a food stuff to the heart. *Locke's solution* (see also *Locke-Ringer's solution,* Part III), which is widely used in physiological laboratories, contains: sodium chloride, 0.9 Gm.; calcium chloride, 0.024 Gm.; potassium chloride, 0.042 Gm.; sodium bicarbonate, 0.02 Gm.; dextrose, 0.1 Gm.; water, 100 cc. A still more recent modification known as *Tyrode's solution* has the following combination: sodium chloride, 0.8 per cent.; potassium chloride, 0.02; calcium chloride, 0.02; magnesium chloride, 0.01; sodium phosphate, 0.005; sodium bicarbonate, 0.1 per cent. Although theoretically these solutions are preferable to that of simple sodium chloride, because more nearly approximating the composition of the bodily fluids, yet practically the reserve supply of calcium and potassium in the human body is so large that it is extremely doubtful whether they are ordinarily superior for medical purposes. Mellon and his co-workers (*J. A. M. A.*, 1922, lxxviii, p. 1026) believe that many of the unpleasant reactions which have followed the intravenous injection of large amounts of physiological salt solutions have been due to abnormal hydrogen-ion concentration—that is, incomplete neutrality. This is due in part to the acidity which is developed in distilled water by boiling and in part to the fact that sodium chloride of the market is generally not absolutely neutral. They suggest, to guard against these effects, the use of a mixture of monobasic and dibasic sodium phosphates as buffer salts; these must be added after sterilization as they are likely to be precipitated by boiling.

Physiological salt solution is used for the purpose of introducing large quantities of water into the system more rapidly than could be done through the alimentary tract. In cases of low blood pressure due either to severe *hemorrhage*—in which the volume of blood is so greatly reduced as to be unable to properly fill the blood vessels—or due to vasomotor paresis, such as *surgical shock*—when the vessels are so dilated that the normal quantity of blood is unable to fill them—the introduction of large amounts of blood into the circulation, as by intravenous injection of physiological salt solution, by filling the vascular system restores a normal resistance and thereby tends to bring the blood pressure back to the normal. While this venoclysis has temporarily a very beneficial effect, it has been found that the fluid escapes from the vessels so rapidly that its practical value is open to question. Various substances such as acacia, gelatin or glucose have been added with the idea that an increase of viscosity would lessen the escape of the water. A discussion of the details of these solutions and of the related blood transfusions is, however, somewhat foreign to the field of this work, and the reader is referred to books on surgical technic.

In cases of severe dehydration of the body—as in the violent purgation of *Asiatic cholera* or *arsenic poisoning*—the administration of salt solution by increasing the volume of blood is often of much benefit. As is well known, the volume of the urine and of the sweat depends in large measure upon the volume of the blood and the introduction of large quantities of fluid, as by the injection of physiological salt solution, tends to increase these secretions. It is probable that the increased output of water under these circumstances will carry with it certain toxic substances, and the method of treatment is widely used in certain cases of systemic poisoning, such as *uremia,* with the idea of increasing the elimination of the toxic material. It is more likely, however, that the benefit from the injection of fluids in cases of extraneous poisonings, such as *corrosive sublimate* or *lead poisoning,* is due more to the dilution of the blood than to the actual increase in elimination.

Physiological salt solution may be administered either intravenously, subcutaneously (*hypodermoclysis*), or through the colon (*enteroclysis*). Absorption through the last channel is relatively slow and enteroclysis is employed chiefly in those conditions where it is desirable to avoid the administration of water by the mouth. In either hypodermic or intravenous injection it is essential that the salt solution be absolutely sterile. For this reason it is necessary not only that the solution be made with freshly distilled water, but that it should be resterilized after the addition of the sodium chloride. It is, of course, equally essential that the vessels used for the injection, and also the skin of the patient, should also be properly sterilized. From one pint to two quarts (500–1900 cc.) of the physiological salt solution may be injected at one dose and repeated again if necessary in a few hours.

LIQUOR SODII HYDROXIDI. U. S.

SOLUTION OF SODIUM HYDROXIDE Liq. Sod. Hydrox. [Liquor Sodæ, U. S. 1890, Solution of Soda]

"Solution of Sodium Hydroxide contains, in each 100 cc., not less than 4.5 Gm. and not more than 5.5 Gm. of NaOH." *U. S.*

Liquor Sodæ, *U. S.* 1890; Solution of Soda; Solution of Caustic Soda; Natrium Hydricum Solutum; Soude caustique liquide, Lessive des Savonniers, *Fr.;* Liquor Natri Caustici, *P. G.;* Aetznatronlauge, Natronlauge, *G.;* Solucion de sosa caustica, *Sp.*

"Dekanormal Solution of Sodium Hydroxide, 125 cc.; Distilled Water, a sufficient quantity to make 1000 cc. Mix the dekanormal solution (page 1573) with sufficient distilled water to make 1000 cc. NOTE.—The 125 cc. of dekanormal solution of sodium hydroxide may be replaced by 56 Gm. of sodium hydroxide, containing 90 per cent. of NaOH." *U. S.*

Description and Physical Properties.—"A clear, colorless, odorless liquid, strongly alkaline and caustic. It readily absorbs carbon dioxide from the air. Specific gravity: about 1.056 at 25° C. It meets the requirements of the tests for identity and purity for an aqueous solution of sodium hydroxide under *Sodii Hydroxidum,* when suitably concentrated. Measure exactly 20 cc. of Solution of Sodium Hydroxide into a suitable flask and titrate directly with normal hydrochloric acid, using methyl orange T.S. as indicator: it shows, in each 100 cc., not more than 5.5 Gm. of alkali, calculated as NaOH (*carbonate*).

"**Assay.**—Measure exactly 50 cc. of Solution of Sodium Hydroxide into a 250 cc. measuring flask, add 20 cc. of barium chloride T.S., and fill the flask to the mark with recently boiled distilled water. Thoroughly agitate the liquid, filter it through a filter not previously moistened, reject the first 20 cc., and titrate 100 cc. of the filtrate, representing 20 cc. of the Solution, with normal hydrochloric acid, using phenolphthalein T.S. as indicator. Each cc. of normal hydrochloric acid corresponds to 0.04001 Gm. of NaOH.

"Preserve in bottles made of hard glass and provided with rubber stoppers or with glass stoppers coated with petrolatum." *U. S.*

Its properties and tests are the same as those of solution of potassium hydroxide, with the exception that no precipitate is produced by platinic chloride or tartaric acid.

Uses.—The solution of sodium hydroxide is mildly caustic and actively antacid. For most of the local uses for which caustic soda is employed it is generally too feeble, while for internal administration it is too irritant to the stomach and is rarely employed as a medicine.

Dose, ten to thirty minims (0.6–1.8 cc.).

LIQUOR STRYCHNINÆ HYDROCHLORIDI. Br.

SOLUTION OF STRYCHNINE HYDROCHLORIDE
[Solution of Hydrochlorate of Strychnine, Brit. Pharm. 1885]

Liquor Strychniæ; Soluté de Chlorhydrate de Strychnine, *Fr.;* Salzsaure Strychninlösung, *G.*

"Strychnine Hydrochloride, 1 *gramme;* Alcohol (90 per cent.), 25 *millilitres;* Distilled Water, sufficient to produce 100 *millilitres.* Mix the Alcohol with an equal volume of Distilled Water; dissolve the Strychnine Hydrochloride in the mixture, and add sufficient Distilled Water to produce the required volume. This Solution contains 1 gramme of Strychnine Hydrochloride in 100 millilitres; 110 minims contain 1 grain." *Br.*

This is the solution of hydrochloride of strychnine of the British Pharmacopœia which was formerly official as *Liquor Strychniæ;* the name has been made definite, and the strength slightly increased, so as to make it conform with the other active solutions; it contains about 1 per cent. of strychnine. The spirit is added for its preservation.

Dose, from three to six minims (0.2–0.4 cc.), equal respectively to about one-thirtieth and one-eighteenth of a grain (0.002–0.004 Gm.) of the alkaloid.

LIQUOR ZINCI CHLORIDI. U. S., Br.

SOLUTION OF ZINC CHLORIDE Liq. Zinc. Chlor.

"Solution of Zinc Chloride is an aqueous solution containing not less than 48.5 per cent. nor more than 52 per cent. of $ZnCl_2$." *U. S.*

Chlorure de Zinc liquide, Soluté de Burnett, *Fr.;* Flüssiges Chlorzink, Chlorzinklösung, *G.*

No process is given in the U. S.; that of the Br. is as follows:

"Granulated Zinc, 400 *grammes;* Hydrochloric Acid, 1100 *millilitres;* Distilled Water, *a sufficient quantity.* Mix the Hydrochloric Acid with five hundred *millilitres* of Distilled Water in a porcelain dish; add the Zinc; apply gentle heat until gas is no longer evolved; boil for half an hour, supply the water lost by evaporation; allow the product to cool. Test a few drops of the resulting liquid for iron and lead. If either be present, filter the remainder of the cooled product into a bottle, and add *solution of chlorine* by degrees, with frequent shaking, until the liquid acquires a permanent odor of chlorine; add Zinc Carbonate in small quantities at a time, with renewed shaking until the whole of the iron or lead is precipitated; filter the liquid and evaporate to one thousand millilitres. If no iron or lead be present, filter the remainder of the cooled product, and evaporate it to one thousand millilitres." *Br.*

The zinc chloride is made in the usual way, by dissolving zinc in hydrochloric acid. The commercial zinc is often contaminated with iron. In the Br. process the iron, if present, is converted into ferric chloride by the addition of chlorine solution and then precipitated by alkalizing with zinc carbonate. In the former process of the U. S. IX nitric acid was added which, by its oxidizing effect, assured the conversion of the iron into ferric chloride. Hydrogen dioxide has been used instead of nitric acid as an oxidizing agent by Besthorn and others. The preparation is completed by bringing it to a certain weight by the addition of distilled water, and by filtration to separate the precipitated iron and any excess of the carbonate. On account of the difficulty of freeing zinc from iron contamination, Francis Hemm proposes the simpler process of making this solution from iron-free zinc oxide; he dissolves 300 Gm. of such zinc oxide in 840 Gm. of hydrochloric acid in a porcelain dish, with the aid of heat, cools, filters, and evaporates the filtrate to 1000 Gm. (*Am. Drug.,* 1900, 199.)

Description and Physical Properties.—"A clear, colorless or slightly yellow, odorless, caustic liquid. It is strongly acid to litmus paper. Specific gravity: about 1.548 at 25° C. Solution of Zinc Chloride responds to the reactions for zinc, and for chlorides, and meets the requirements of the tests for purity for an aqueous solution of the salt under *Zinci Chloridum,* when taken in proportionate amount.

"**Assay.**—Place in a tared flask about 0.5 cc. of Solution of Zinc Chloride, weigh accurately, and proceed as directed under the Assay for chlorides. Each cc. of tenth-normal silver nitrate corresponds to 0.006815 Gm. of $ZnCl_2$." *U. S.*

"A colorless liquid; taste astringent and sweetish. Specific gravity 1.530. Yields no characteristic *reactions* for lead, copper, cadmium, arsenic, iron, aluminium, calcium, magnesium, or sulphates." *Br.*

Uses.—The solution of zinc chloride is actively caustic and a powerful germicide, possessed of deodorant properties. In dilute solution it acts as a stimulating astringent with some antiseptic powers. It has been employed, either in full strength or with equal parts of water, for the destruction of *cancerous ulcers,* especially when there is fetid discharge. It has, however, the disadvantages that it destroys healthy as well as diseased tissue and that its action is accompanied with a considerable amount of pain. In dilute solution it is used for its astringent and antiseptic influence in *gleet, vaginitis* and, occasionally, in inflammations of the other mucous membranes; for these purposes it may be employed in strengths of from 1 to 5 per cent. Formerly the solution of zinc chloride was largely used as a general disinfectant both for surgical and sanitary purposes but has been largely replaced by other agents. It is also commonly used for the preservation of bodies for dissection. *Burnett's Disinfecting Fluid* was an aqueous solution of zinc chloride very similar to the present official solution; as originally recommended it was made by dissolving one pound of zinc chloride in five gallons of water, but was commercially often prepared by the natural deliquescence of the crystals.

LIQUORES.

SOLUTIONS

Solutés, *Fr.;* Liquores, *P. G.;* Lösungen, *G.;* Soluzione, *It.;* Solucion, *Sp.*

The U. S. Pharmacopœia includes in this class of preparations all aqueous solutions without sugar in which the substance acted on is wholly soluble in water, excluding those in which the dissolved matter is gaseous or very volatile, as in the Aquæ, or Waters. The British Pharmacopœia does not make this distinction and includes several alcoholic solutions of volatile principles among the liquors.

The Br. Pharm., 1898, introduced ten concentrated infusions, with the object of affording an easy method of making, through dilution, ordinary infusions. The titles were very inappropriate, and the British Pharmacopœia, 1914, dismissed *concentrated infusions.*

LITHII BENZOAS. N. F.

LITHIUM BENZOATE Lith. Benz.

"Lithium Benzoate contains, when dried for 24 hours over sulphuric acid, not less than 98.5 per cent. of $LiC_7H_5O_2$ (128.01)." *N. F.*

Benzoas Lithicus; Benzoate de Lithium, *Fr.;* Lithium Benzoicum, *Fr. Cod.;* Bromsäure Lithium, *G.*

This salt may be made by the action of benzoic acid upon lithium. It was at one time recognized by the Pharmacopœia but was dropped at the ninth revision. It has been made official in the N. F.

Description and Physical Properties.—"A white powder or small crystalline scales. It is odorless, and is stable in the air. One Gm. of Lithium Benzoate dissolves in about 3 cc. of water and in about 16 cc. of alcohol at 25° C. It is slightly more soluble in these solvents when hot.

"When heated the salt at first fuses, then at higher temperatures it chars, emitting inflammable vapors having a benzoin-like odor and finally leaves a residue of lithium carbonate and carbon. This residue is alkaline to litmus paper, effervesces with acids and colors a non-luminous flame crimson. The addition of mineral acids to an aqueous solution of Lithium Benzoate (1 in 20) produces a voluminous white precipitate of benzoic acid. Ferric chloride added to the aqueous solution produces a flesh colored precipitate of ferric benzoate.

"Dissolve 0.6 Gm. of Lithium Benzoate in 25 cc. of water, add 5 cc. of diluted hydrochloric acid, filter and wash the precipitate with about 25 cc. of distilled water. Evaporate the combined filtrate and washings on a water bath to a small volume in a beaker or dish, then transfer completely with the aid of a little water into a flat-bottomed flask of about 50 cc. capacity and evaporate almost to dryness on a water bath. Add 10 cc. of amyl alcohol and cautiously heat the mixture until all the water has evaporated. The removal of the water from the amyl alcohol mixture may be facilitated by passing a current of air through the hot solution. Then add 3 drops of hydrochloric acid and boil the solution for 3 minutes. If any insoluble residue remains, collect it on a filter, wash it with amyl alcohol and dry at 110° C. to constant weight. The weight of the residue should not exceed 0.004 Gm. (other *alkalies*). Dissolve about 1 Gm. of Lithium Benzoate in 20 cc. of water in a separatory funnel, add 10 cc. of diluted sulphuric acid, extract the precipitate of benzoic acid by shaking with 2 portions of 20 cc. each of ether, and evaporate the ether solution to dryness at a low temperature. One half Gm. of the residue of benzoic acid thus obtained complies with the test for *chlorine* described in the U. S. P. under *Acidum Benzoicum.* The aqueous layer from the above test, warmed to expel ether and diluted to 50 cc. does not respond to the test for *heavy metals.*

"**Assay.**—Weigh accurately about 0.5 Gm. of

Lithium Benzoate, which has previously been dried for 24 hours over sulphuric acid, mix it with 1 Gm. of dried and powdered ammonium sulphate and cautiously ignite in a porcelain crucible to constant weight. The weight of the residue of lithium sulphate thus obtained, multiplied by 2.328, represents its equivalent of Lithium Benzoate." *N. F.*

According to Curtman, lithium benzoate is often contaminated with sodium benzoate which increases its solubility.

Uses.—Lithium benzoate possesses the therapeutic virtues of the other benzoates (see *Sodii Benzoas*), but it is not apparent that it possesses any advantage over the sodium salt.

Dose, from ten to twenty grains (0.6–1.2 Gm.).

Off. Prep.—Elixir Hydrangeæ et Lithii, *N. F.*

LITHII BROMIDUM. N. F.

LITHIUM BROMIDE Lith. Brom.

"Lithium Bromide contains, when dried for twenty-four hours over sulphuric acid, not less than 85 per cent. of LiBr (86.86)." *N. F.*

Lithium Bromatum; Bromure de Lithium, *Fr.;* Bromlithium, Lithiumbromid, *G.*

Yvon prepares *lithium bromide* by mixing 37 parts of lithium carbonate, 200 parts of distilled water, and 80 parts of bromine, and passing a current of hydrogen sulphide through the mixture until the color of bromine has disappeared. A slight heat is then applied, to drive off excess of hydrogen sulphide and to agglutinate the sulphur. After filtration the liquor is concentrated and finally crystallized by desiccating it under a bell glass, over sulphuric acid. It may also be obtained by double decomposition between lithiun sulphate and potassium bromide in the presence of water and a little alcohol.

Description and Physical Properties.—"Lithium Bromide is a white, granular salt, odorless and having a sharp, slightly bitter taste; very deliquescent. One Gm. of Lithium Bromide dissolves in 0.6 cc. of water at 25° C.; also in 0.4 cc. of boiling water; freely soluble in alcohol and soluble in ether.

"An aqueous solution of the salt (1 in 20) is neutral or slightly alkaline to litmus. At a low red heat the salt fuses, and at a higher heat it is slowly volatilized. It imparts a crimson color to a non-luminous flame. Add to 10 cc. of a solution of Lithium Bromide (1 in 20) a slight excess of chlorine T.S., then add 5 cc. of chloroform and shake the mixture, the chloroform separates with a red or reddish brown color.

"Add a few drops of ferric chloride T.S. and 1 cc. of chloroform to 10 cc. of an aqueous solution of the salt (1 in 20) and shake the mixture. The chloroform does not acquire a violet tint (*iodide*). Drop 1 cc. of diluted sulphuric acid on about 1 Gm. of the powdered salt; no yellow color appears at once (*bromate*). Dissolve about 0.1 Gm. of Lithium Bromide in 5 cc. of distilled water, add an excess of silver nitrate T.S. and a few drops of nitric acid; filter and wash the precipitate with distilled water, then digest it for ten minutes with 5 cc. of ammonium carbonate T.S. and filter. Dilute the filtrate to 40 cc. and supersaturate with nitric acid, not more than a slight turbidity is produced at once (*chloride*). Five cc. of an aqueous solution of the salt (1 in 100) acidulated with 4 drops of hydrochloric acid shows no immediate turbidity with 1 cc. of barium chloride T.S. (*sulphate*). Add 5 cc. of hydrochloric acid and 5 cc. of chlorine T.S. to 0.4 Gm. of Lithium Bromide contained in a flat-bottomed flask of 50 cc. capacity, evaporate the mixture almost to dryness on a water-bath, add 10 cc. of amyl alcohol and cautiously heat the mixture until the lower aqueous layer has evaporated. Then add 3 drops of hydrochloric acid and boil the solution for three minutes; the resulting insoluble residue, if any, when collected on a filter, washed with amyl alcohol and dried at 110° C., weighs not more than 0.002 Gm. (*other alkalies*). The removal of water from the amyl alcohol mixture is facilitated by passing a current of air through the hot solution. An aqueous solution of the salt does not respond to the Test for heavy metals.

"**Assay.**—Introduce into a tared weighing-bottle about 0.35 Gm. of Lithium Bromide, previously dried for twenty-four hours over sulphuric acid, stopper, weigh accurately, and proceed as directed under the Assay for bromides. Each cc. of tenth-normal silver nitrate corresponds to 0.008686 Gm. of LiBr. Each Gm. of Lithium Bromide corresponds to not less than 97.9 cc. of tenth-normal silver nitrate.

"Preserve it in air-tight containers." *N. F.*

Uses.—Lithium bromide was first brought into notice as a remedy by S. Weir Mitchell, who asserts that its action differs from that of the other bromides only in being more hypnotic. Although careful physiological studies of it are wanting, there is little reason for believing that it differs essentially from other bromides in its influence upon the human organism. It should be administered in dilute aqueous solution. Each drachm of it contains fifty-five grains of bromine, and it therefore exceeds potassium bromine in bromine strength.

Dose, ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Elixir Bromidorum Quinque, *N. F.;* Syrupus Bromidorum, *N. F.*

LITHII CARBONAS. N. F., Br.

LITHIUM CARBONATE Lith. Carb.

"Lithium Carbonate contains, when dried to constant weight at 100° C., not less than 98.5 per cent. of Li_2CO_3(73.89)." *N. F.*

"Lithium Carbonate may be obtained from native silicates of lithium. It contains not less than 98.5 per cent. of pure lithium carbonate, Li_2CO_3." *Br.*

Carbonas Lithicus; Carbonate of Lithia; Carbonate de Lithine, Carbonate lithique, *Fr.;* Lithium Carbonicum, *P. G.;* Lithiumcarbonat, Kohlensaures Lithium, *G.;* Carbonato di litio, *It.;* Carbonato de litina o litico, *Sp.*

Lithium was discovered by Arfvedson in 1817, in certain minerals from the iron mines of Utö, as *petalite, triphane,* and a variety of *tourmaline.* (Berzelius.) It has since been found in other minerals, as *lepidolite, spodumene, amblygonite,* etc., and in numerous mineral waters, as those of Carlsbad, Salsomaggiore, Pyrmont, Kissingen, Kreuzmach, Aix-la-Chapelle, Vichy, etc., in Europe, and the Gettysburg spring in the United States, in which it exists generally as a carbonate or a bicarbonate. By spectrum analysis it has been detected in the waters of the Atlantic Ocean and of the Thames, the Delaware, the Potomac and many other rivers; in the ashes of plants grown on a granite soil, and even in milk and human blood. In the mother waters of tartaric acid, in the factories, it has been found in a proportion to justify extraction. It was at one time largely obtained from a *phosphatic triphyline* found in Bavaria, in which it existed as a phosphate, but this source is said to have been exhausted. There are several methods of extracting lithia from the minerals containing it, an account of which may be seen in *Roscoe and Schorlemmer,* vol. ii, Part I, page 158. Lithium carbonate is prepared from lepidolite in the following manner. Ten parts of finely powdered lepidolite, 10 parts of barium carbonate, 5 parts of barium sulphate, and 3 parts of potassium sulphate are fused at a very high temperature in a wind furnace. The heavy barium silicate and sulphate sink to the bottom, and a layer of potassium and lithium sulphates is found at the top of the fused mass. These can be extracted by simple lixiviation, and then the carbonate prepared by double decomposition with ammonium carbonate.

In another process the lepidolite is digested with hot sulphuric acid which produces the sulphates of aluminum and lithium principally, and these are separated by crystallization or precipitation operations.

The element which was first separated and purified by Bunsen and Matthiessen, in 1855, is silver-white, brilliant, softer than lead, ductile, capable of welding, and the lightest known metallic element. Its sp. gr. is 0.594, melting point 180° C., atomic weight 6.94, and symbol Li. For a method of making lithium for scientific demonstration on the small scale by electrolysis, see *Ph. Rev.,* 1899, 264.

Lithium carbonate may be prepared from lithium sulphate or chloride in concentrated solution by adding ammonium carbonate. The precipitated salt should be washed with alcohol and dried.

Description and Physical Properties.—"Lithium Carbonate is a light, white powder, odorless, and having an alkaline taste; permanent in the air. One Gm. of Lithium Carbonate dissolves in 78 cc. of water at 25° C.; also in 140 cc. of boiling water; almost insoluble in alcohol; dissolved by diluted acids with effervescence.

"At a low red heat the salt fuses; at a higher temperature it loses some of its carbon dioxide, and is partially converted into lithium oxide. It imparts a crimson color to a non-luminous flame. A saturated aqueous solution of the salt is alkaline to litmus and effervesces when acid is added.

"Lithium Carbonate when dissolved in 40 parts of diluted acetic acid, leaves not more than 0.15 per cent. of insoluble residue. Mix 1 part of Lithium Carbonate with 20 parts of distilled water and add hydrochloric acid, drop by drop, with agitation until solution takes place. The resulting solution, after boiling and cooling, responds to the following tests when applied to separate portions: The addition of ammonia water to 5 cc. of this solution until it has an alkaline reaction produces neither turbidity nor precipitation either before or after boiling (*iron, aluminum*). Dilute another portion of 4 cc. of this solution with 6 cc. of distilled water; it does not respond to the test for heavy metals. Add a slight excess of diluted hydrochloric acid to 0.2 Gm. of Lithium Carbonate contained in a flat-bottomed flask of 50 cc. capacity, evaporate the mixture almost to dryness on a water bath, add 10 cc. of amyl alcohol and cautiously heat the mixture until the lower aqueous layer has evaporated. Then add 3 drops of hydrochloric acid and boil the solution for three minutes. The resulting insoluble residue, if any, when collected on a filter, washed with amyl alcohol and dried at 110° C., weighs not more than 0.002 Gm. (*other alkalies*). The removal of the water from the amyl alcohol mixture is facilitated by passing a current of air through the hot solution." *N. F.*

"White powder, or minute crystalline grains. Taste slightly alkaline. Soluble in 80 parts of *water;* insoluble in *alcohol* (90 per cent.). Aqueous solution alkaline to *litmus.* Soluble with effervescence in *hydrochloric acid;* the solution evaporated to dryness leaves a residue which communicates a crimson color to flame, and, redissolved in *water,* yields a precipitate with *solution of sodium phosphate.* 1 gramme, diffused in about 50 millilitres of *water,* requires for neutralisation not less than 26.6 or more than 27.1 millilitres of *N/1 solution of sulphuric acid, solution of methyl orange* being used as indicator. Yields no characteristic *reactions* for copper, iron, aluminium, zinc, magnesium, or chlorides, and not more than the slightest *reactions* for calcium or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

"**Assay.**—Dissolve about 1.5 Gm. of Lithium Carbonate, previously dried to constant weight at 100° C. and accurately weighed, in 50 cc. of normal sulphuric acid and titrate the solution with normal potassium hydroxide, methyl orange T.S. being used as indicator. Each cc. of normal sulphuric acid corresponds to 0.03694 Gm. of Li_2CO_3. Each Gm. of Lithium Carbonate, previously dried, corresponds to not less than 26.7 cc. of normal sulphuric acid." *N. F.*

F. A. Flückiger states that lithium carbonate is less soluble in warm water than in cold water.

He recommends as a test of purity that it should require for solution 70 parts or a little more of water at 15° C. and states further that its solution saturated at 90° C. has the sp. gr. 1.009 at 15° C.; this latter solution contains 1 part of the salt in 111.3 parts of water. (*A. Pharm.*, 1887, p. 509.)

Effervescing Lithium Carbonate may be made as follows: Take of citric acid, 40 parts, sodium bicarbonate, 50 parts, and lithium carbonate, 10 parts. Powder and mix well, then introduce into a wide flat-bottomed dish, and heat to about 100° C., stirring constantly until the powder becomes granular. Separate the granules of uniform size by means of appropriate sieves, and preserve them in well-stoppered bottles. (See *Lithii Citras Effervescens.*)

Uses.—In 1843 Alexander Uré called attention to the fact that uric acid was comparatively freely soluble in solutions of lithium carbonate. This observation was confirmed by Garrod in 1857 who recommended the use of the metal in both acute and chronic forms of gout. This recommendation has been blindly followed by a large proportion of the medical profession for more than fifty years without questioning the validity of the scientific basis and without any close analysis of the clinical results. Garrod's experiment, however, as pointed out by H. C. Wood, Jr. (*J. A. M. A.*, 1916, lxvi, p. 1069), involved conditions which are absolutely inapplicable to human medicine; as a matter of fact it has been shown that the addition of lithium carbonate even in fatally large doses does not affect the solubility of sodium urate in the blood. Moreover there is no convincing clinical evidence of the usefulness of lithia in *gout*.

The clinical results which have been achieved with the "Lithia Waters" have been due to the water in them and not to the lithium. Of a large number of natural "Lithia Waters" examined by the Bureau of Chemistry of the U. S. Department of Agriculture, none contained more than one twentieth grain per gallon, while most of them contain only spectroscopic traces.

In sufficient quantities lithium acts upon the system very much like potassium, being depressant to the nerve centers and to the circulation. The non-toxic salts of lithium, like those of potassium, have a diuretic effect, and if given in sufficient dose may aid in the elimination of various substances from the blood, and incidentally the poisons of *gout*, but are probably not superior to the potash salts. Lithium carbonate has the properties of the other earthy carbonates but, being less soluble than the sodium and potassium salts, is perhaps somewhat less prone to irritate the stomach.

Dose, five to fifteen grains (0.32–1.0 Gm.).

Off. Prep.—Sal Potassii Bromidi Effervescens Compositum, *N. F.*

LITHII CITRAS. N. F., Br.

LITHIUM CITRATE Lith. Cit.

"Lithium Citrate contains not less than 98.5 per cent. of $Li_3C_6H_5O_7.4H_2O$ (281.95)." *N. F.*

"Lithium Citrate may be obtained by the interaction of citric acid and lithium carbonate. It contains not less than 98.5 per cent. of pure lithium citrate, $Li_3C_6H_5O_7,4H_2O$." *Br.*

Lithiæ Citras, Lithium Citricum; Citrate of Lithium, Citrate of Lithia; Citrate de Lithine, *Fr.;* Citronensaures Lithium, Lithiumcitrat, *G.;*

Description and Physical Properties.—"Lithium Citrate occurs as a white powder, or in the granular form; odorless and having a cooling, faintly alkaline taste. It is deliquescent on exposure to moist air and loses its water of crystallization when heated to 150° C. One Gm. of Lithium Citrate dissolves in 1.4 cc. of water at 25° C.; very slightly soluble in alcohol.

"An aqueous solution of the salt (1 in 20) is faintly alkaline to litmus but is not reddened by one drop of phenolphthalein T.S. At a red heat the salt chars, emits inflammable vapors having a pungent odor, and finally leaves a black residue of lithium carbonate mixed with carbon. It imparts a crimson color to a non-luminous flame. Boil an aqueous solution of Lithium Citrate (1 in 20) with an equal volume of calcium chloride T.S.; a white precipitate forms.

"Treat the residue obtained by igniting 0.4 Gm. of the salt at a red heat with a slight excess of diluted hydrochloric acid, filter, wash the residue with distilled water, evaporate the filtrate and washings almost to dryness on a water bath, in a flat-bottomed flask of 50 cc. capacity, add 10 cc. of amyl alcohol and cautiously heat the mixture until the lower aqueous layer has evaporated. Then add 3 drops of hydrochloric acid and boil the solution for three minutes. The resulting insoluble residue, if any, when collected on a filter, washed with amyl alcohol and dried at 110° C., weighs not more than 0.004 Gm. (*other alkalies*). The removal of the water from the amyl alcohol mixture is facilitated by passing a current of air through the hot solution. An aqueous solution of the salt does not respond to the Test for heavy metals.

"**Assay.**—Proceed as directed under the Assay for alkali salts of organic acids. Each cc. of half-normal sulphuric acid corresponds to 0.04699 Gm. of $Li_3C_6H_5O_7.4H_2O$. Each Gm. of Lithium Citrate corresponds to not less than 21 cc. of half-normal sulphuric acid.

"Preserve it in air-tight containers." *N. F.*

Lithium citrate is described by the Br. as: "Small white crystals. Taste saline, cooling. Soluble in 2 parts of *water*. Yields the *reactions* characteristic of citrates. Heated to redness it blackens, evolving inflammable gases; and the residue, neutralised with *hydrochloric acid*, yields with *alcohol* (90 per cent.) a solution which burns with a crimson flame. 1

gramme, heated to redness till gases cease to be evolved, leaves an alkaline residue which, when treated with *water,* filtered, and well washed, yields a clear solution requiring for neutralisation not less than 10.5 millilitres of *N/1 solution of sulphuric acid. Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million. Free from the impurities indicated under 'Lithii Carbonas.'" *Br.*

It is somewhat deliquescent in moist, and efflorescent in dry, air. It usually shows a feebly alkaline reaction with litmus.

Uses.—Lithium citrate, like the corresponding salts of sodium and potassium, is oxidized in the system and appears in the urine as a carbonate. It may be used for precisely the same purposes as the other citrates, but has no real advantage. It is the compound which is employed in making the widely used so-called "lithia tablets."

Dose, from ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Lithii Citras Effervescens, *Br.;* Sal Lithii Citras Effervescens, *N. F.*

LITHII CITRAS EFFERVESCENS. Br.

EFFERVESCENT LITHIUM CITRATE

Limonade sèche au Citrate de Lithine, *Fr.;* Brauselithiumcitrat, *G.*

"Sodium Bicarbonate, in Powder, 580 *grammes;* Tartaric Acid, in powder, 310 *grammes;* Citric Acid, in powder, 210 *grammes;* Lithium Citrate, in powder, 50 *grammes.* Mix the Lithium Citrate with the Citric Acid, then add the Tartaric Acid, and, lastly, the Sodium Bicarbonate, triturating thoroughly. Place the mixture in a dish or pan of suitable form heated to between 90° and 105° C. When the mixture, by the aid of careful manipulation, has assumed a granular character, separate it, by means of suitable sieves, into granules of uniform and convenient size. Dry the granules at a temperature not exceeding 55° C. The product weighs about one thousand *grammes.*" *Br.*

A similar preparation is in the N. F. (see *Sal Lithii Citratis Effervescens,* Part III).

Uses.—This effervescent salt forms an agreeable method of administering lithia; its medicinal properties are those of lithium citrate.

Dose, two drachms (7.7 Gm.), given in solution.

LITHII SALICYLAS. N. F.

LITHIUM SALICYLATE Lith. Salicyl.

"Lithium Salicylate contains, when dried to constant weight at 120° C., not less than 98.5 per cent. of $LiC_7H_5O_3$ (144.02)." *N. F.*

Salicylate de Lithine, *Fr.;* Lithium Salicylicum, *P. G.;* Lithiumsalicylat, *G.;* Salicilato de Litina, *Sp.*

No process is given in the N. F. for making this official salt. It may be prepared by adding to a mixture of eleven parts of salicylic acid and three parts of lithium carbonate, twenty-five parts of water, and heating until effercescence ceases, filtering and evaporating. It may be obtained in crystals but is usually seen in the form of a granular powder.

Description and Physical Properties.—"Lithium Salicylate occurs as a white or grayish white powder; deliquescent in a moist atmosphere; odorless, taste sweetish. It is very soluble in water and in alcohol.

"When heated, the salt is decomposed, emitting the odor of phenol, and finally leaving a residue of lithium carbonate and carbon. It imparts a crimson color to a non-luminous flame. An aqueous solution of the salt (1 in 20) is neutral or slightly acid to litmus, and when freshly made is colorless (*iron and organic coloring matter*); it does not effervesce upon the addition of diluted acids (*carbonate*). Copper sulphate T.S. added to an aqueous solution of the salt (1 in 20) produces a bright green color. Add a few drops of ferric chloride T.S. to an excess of an aqueous solution of the salt (1 in 4); a deep red color is produced. In a dilute solution of the salt (1 in 100) ferric chloride T.S. produces a deep violet-blue color. Hydrochloric acid added to an aqueous solution of the salt (1 in 20) produces a voluminous white precipitate of salicylic acid. Dissolve 0.7 Gm. of the salt in 10 cc. of distilled water, add an excess of hydrochloric acid and filter. Evaporate the filtrate almost to dryness on a water bath, in a 50 cc. Erlenmeyer flask, and then add 10 cc. of amyl alcohol and cautiously heat until the lower aqueous layer is evaporated; then add three drops of hydrochloric acid and boil the liquid for three minutes; the insoluble residue weighs not more than 0.005 Gm. (*other alkalies*). The removal of the water from the amyl alcohol mixture is facilitated by passing a current of air through the hot solution. Dissolve 1 Gm. of the salt in 50 cc. of distilled water, precipitate the salicylic acid by the addition of a slight excess of hydrochloric acid and filter; the filtrate does not respond to the Test for heavy metals.

"**Assay.**—Weigh accurately 1 Gm. of Lithium Salicylate which has been previously dried for 24 hours over sulphuric acid, mix it with 2 Gm. of powdered ammonium sulphate in a porcelain crucible and cautiously ignite it. The weight of the residue of lithium sulphate multiplied by 2.629 represents it equivalent in Lithium Salicylate.

"Preserve it in well-closed containers, protected from heat." *N. F.*

The proportion of lithium in this salt is too small to sensibly modify the action of the salicylic acid. It may be used for the same purposes as the other salicylates.

Dose, ten to twenty grains (0.6–1.3 Gm.).

Off. Prep.—Elixir Hydrangeæ et Lithii, *N. F.;* Elixir Manacæ Compositum, *N. F.*

LOBELIA. U. S., Br.

LOBELIA Lobel.

"Lobelia consists of the dried leaves and tops of *Lobelia inflata* Linné (Fam. *Lobeliaceæ*). Lobelia contains not more than 10 per cent. of stems or more than 2 per cent. of other foreign organic matter, and yields not more than 5 per cent. of acid-insoluble ash." *U. S.* "Lobelia is the dried flowering herb of Lobelia inflata, *Linn.*" *Br.*

[1] Indian or Wild Tobacco, Asthma-weed, Puke-weed, Gag-root, Vomitwort, Bladder Pod, Eyebright; Lobélie enflée, *Fr.;* Herba Lobeliæ, *P. G.;* Lobelienkraut, *G.;* Lobelia, *It.*

Lobelia inflata is an annual or biennial plant common in roadsides and neglected fields throughout the Eastern United States and Canada, usually a foot or more in height, with a fibrous root, and a solitary erect, angular, very hairy stem, much branched about midway, but rising considerably above the summits of the highest branches. The leaves are scattered, or alternate, petiolate, the upper sessile, ovate, or oblong, about two inches (5 cm.) long, irregularly toothed, pubescent, pale green. The flowers are numerous, small, disposed in leafy terminal, axillary racemes. The calyx is five-toothed and much inflated in fruit. The corolla, which is of a delicate blue, has a labiate border, with the upper lip divided into two, the lower into three segments. The united anthers are curved, and enclose the stigma. The fruit is an oval, striated, inflated capsule, crowned with the persistent calyx, and containing, in two cells, numerous very small, oblong, reticulated brown seeds. Most of the commercial supplies of the drug come from Massachusetts, Michigan and New York.

All parts of it are medicinal, but, according to Eberle, the root and inflated capsules are most powerful. The plant should be collected in August or September, when the capsules are numerous, and should be carefully dried. The German Pharmacopœia directs that Lobelia should be gathered at the end of the flowering period. A number of the foreign Pharmacopœias do not permit the inclusion of the fruit. The drug of commerce ofttimes is collected late in the season after most of the leaves have fallen and the plant has gone to seed. At times the commercial drug consists of the entire herb, and again may consist chiefly of the thick and inert stems. It may be kept whole or in powder. As found in commerce, it is often in oblong compressed cakes, prepared by the Shakers or the herb dealers. It has been suggested that in cultivating *Lobelia inflata* the seeds should be planted in the autumn. (*Ann. Rep. U. S. Dept. Agric.*, 1905, p. 147.)

Dried lobelia has a slightly irritating color, and when chewed, though at first without much taste, soon produces a burning acrid impression upon the posterior parts of the tongue and palate, very closely resembling that occasioned by tobacco, and attended in like manner with a flow of saliva and a nauseating effect.

Description and Physical Properties.—"*Unground Lobelia.*—Leaves alternate, sessile or narrowing into a short petiole, usually more or less broken; when entire, blades ovate or oblong from 2 to 9 cm. in length, obtusely toothed or irregularly serrate-denticulate, each tooth with a yellow-brown, gland-like apex; pale green and with scattered bristly hairs; stem cylindrical, coarsely and irregularly furrowed, yellowish-green, occasionally purplish and with numerous spreading hairs; flowers pale blue, in a long, loose raceme with short pedicels, calyx tubes ovoid, with 5 subulate teeth, corollas tubular, from 3 to 4 mm. in length, 5-parted, the upper 2-lobed portion cleft nearly to the base; stamens with anthers united above into a curved tube enclosing the bifid stigma; capsule ovoid or ellipsoidal, from 5 to 8 mm. in length, light brown, wholly inferior and enclosing numerous brownish, oblong and coarsely reticulate seeds; odor slight and irritating; taste strongly acrid.

"*Powdered Lobelia.*—Dark green; fragments of seed-coat composed of more or less polygonal cells with thick, yellowish walls; occasional non-glandular hairs, elongated-conical, from 0.30 to 1.11 mm. in length; fragments of stem with tracheæ showing annular or spiral thickenings or simple pores associated with narrow wood-fibers, the walls of the latter being rather thin, more or less lignified and porous; fragments of epidermis of leaf with elliptical stomata, up to 0.035 mm. in length, and usually with 3 or 4 neighboring cells; pollen grains nearly spherical, from 0.020 to 0.030 mm. in diameter." *U. S.*

"Stems angular, channelled, and furnished with narrow wings; often of a purplish tint; bearing one-celled hairs and the scars of alternate leaves. Leaves irregularly toothed and hairy. Capsules inflated, two-celled, containing when ripe, minute, oblong, reticulated, brown seeds. In transverse section of the stem, laticiferous vessels in the bast. Somewhat irritating odor; taste at first not marked, but subsequently burning and acrid. Ash not more than 12 per cent." *Br.*

The morphology of *Lobelia inflata* is described and illustrated by Holm in *Merck's Rep.*, xvi, p. 341.

Constituents.—The activity of lobelia depends on the presence of a liquid alkaloid first isolated by Procter in 1838 and by him named *lobeline.*

Ordinarily lobeline is a yellowish liquid, lighter than water, of a somewhat aromatic odor, and a very persistent, acrid taste, but when absolutely pure is odorless and colorless. It is sparingly soluble in water, but much more copiously in alcohol and ether, and the latter fluid readily removes it from its aqueous solution. It has an alkaline reaction, and forms soluble and crystallizable salts with sulphuric, nitric, and hydrochloric acids, and a very soluble, but not crystallizable salt, with acetic acid. It forms an insoluble compound with tannic acid, which instantly precipitates it from its solution. By a boiling heat it is entirely evaporated, but the salts it forms with acids are not volatile. Siebert (*In. Dis.*, Marburg, 1891) from a study of the crystallized hydrochloride and chloroplatinate, derived the formula $C_{18}H_{23}O_2N$ for the free alkaloid. Wieland (*B. Chem. G.*, 1921, liv, 1784) has found a second alkaloid *lobelidine*. This is crystalline and has the formula $C_{20}H_{25}O_2N$. He also reported the presence of a third alkaloid, to which, however, he gave no definite name. A British patent granted to Böhringer describes three alkaloids: *alpha-lobeline,* $C_{21}H_{23}O_2N$, crystalline; *beta-lobeline,* amorphous and *gamma-lobeline,* also amorphous (see *D. C.*, 1921, lxv, 102).

Pereira found a peculiar acid which he named *lobelic acid;* besides gum, resin, chlorophyl, fixed oil, lignin, salts of lime and potassium, with ferric oxide. Enders' *lobelacrin,* according to Lewis (*P. J.*, 1878, viii), is a mixture of lobeline lobelate, with lobelic acid. Lloyd has isolated a crystalline neutral principle (*Ph. Rund.*, 1887, 32) which melts at 225° C., to which he gave the name *inflatin.* It does not appear to have any therapeutic value. According to Procter the seeds contain a much higher percentage of lobeline than the rest of the plant; from the whole plant he obtained a yield of one-fifth of one per cent. The alkaloid appears to be a rather unstable body, being decomposed by boiling temperature as well as by the caustic alkalies.

Vanderkleed and E'we (*Proc. P. P. A.*, 1916, p. 276) propose a method for assaying this drug and its preparations.

Uses.—Lobelia is said to have been used as a medicine by the aborigines of America, but was first brought into general professional notice by Cutler, of Massachusetts. The leaves or capsules, chewed for a short time, occasion giddiness, headache, general tremors, and ultimately nausea and vomiting. When swallowed in the full dose, the medicine produces speedy and severe vomiting, attended with continued and distressing nausea, copious sweating, and great general relaxation. When toxic doses are taken, these symptoms are very severe, and have added to them burning pain in the fauces or esophagus, progressive failure of voluntary motion, rapid, feeble pulse, fall of temperature, and finally collapse with stupor or coma; in some cases convulsions precede death. Death has often resulted from its empirical use. Its poisonous effects are most likely to occur when, as sometimes happens, it is not rejected by vomiting.

In large quantities lobelia has a paralyzant effect on the peripheral motor nerves like that of curare, but this action plays little rôle in its therapeutic usefulness. Edmunds (*A. J. Phys.*, 1904, xi, p. 80) finds that the chief effect is upon the sympathetic ganglia like nicotine, first stimulating and secondarily depressing. During the primary stage of stimulation there is increased flow of saliva, dilation of the pupil, constriction of the blood vessels, slowing of the pulse, and other evidences of sympathetic excitation. The slowing of the pulse at first more than counterbalances the vascular constriction, and the blood pressure is usually lowered; later, however, the pulse becomes very rapid and the blood pressure high. The vomiting appears to be due to an action upon the emetic center. In the secondary stage of poisoning the pupil is contracted, salivary secretion checked, respirations slow, and the blood pressure falls. Wieland and Mayer (*A. E. P. P.*, 1922, xcii, 195) state that pure lobeline does not excite either the emetic center nor the sympathetic ganglia, nor does it have any marked action on the vagus; they find its chief action is as a respiratory stimulant. These results are, in a measure, confirmed by the work of Behrens and Pulewka (*B. K. W.*, 1924, iii, 1677) who report a beneficial action on the respiration in poisoning by carbon monoxide. According to Muto and Iwakawa (*A. E. P. P.*, 1910, lxii), lobeline is a primary stimulant to the respiratory center, the failure in respiration which occurs after toxic doses being due to its paralytic effect on the phrenic nerve. According to Dixon and Brodie (*J. P.*, 1903, xxix), it causes a relaxation of the bronchial muscles which may, however, be preceded by a short stage of constriction.

As an emetic lobelia should never be employed. Its most important use in medicine is as a nauseating expectorant in *bronchitis,* especially when associated with bronchial spasm. Large doses will sometimes cause complete cessation of the *asthmatic* paroxysms, but it is more commonly employed between the paroxysms for its combined expectorant and antispasmodic influence.

By the eclectics lobelia is used in a host of convulsive and inflammatory disorders, including *epilepsy, tetanus, diphtheria,* and *tonsillitis.*

The tincture affords the most eligible mode of administration; in asthmatic cases it may be given in doses of fifteen minims (0.9 cc.) every hour until an effect is produced. Numes (*T. G.*, 1889) asserts that he has used lobeline in a number of cases of *asthma* with most excellent results in doses of from three-fourths of a grain to six grains a day; but it can scarcely be doubted that he had a very impure alkaloid, and that such doses of a pure sample would be highly dangerous. There is on the market a preparation stated to be alpha-lobeline which is recommended as a respiratory stimulant in doses of one-twentieth to one-sixth of a grain (0.003–0.01 Gm.).

Dose, of lobelia, one to five grains (0.06–0.3 Gm.).

Off. Prep.—Tinctura Lobeliæ, *U. S.;* Tinctura Lobeliæ Ætherea, *Br.;* Fluidextractum Lobeliæ, *N. F.*

LOTIO HYDRARGYRI FLAVA. Br.

YELLOW MERCURIAL LOTION

Aqua Phagedænica Flava; Yellow Wash, Yellow Lotion; Eau phagédénique, Eau divine de Fernel, Phagédénique, *Fr.;* Phagedänisches Wasser, Altschadenwasser, *G.*

"Mercuric Chloride, 4.6 *grammes;* Solution of Lime, 1000.0 *millilitres.* Mix." *Br.*

This lotion is about 11 per cent. stronger than that official in the Br. Ph., 1885. A similar preparation, but differing in strength, is official in the N. F. (See *Lotio Flava,* Part III.)

The reaction between the mercuric chloride and the calcium hydroxide in this preparation results in the precipitation of the yellow mercuric oxide in a hydrated form and in a very finely divided condition. It is used as a soothing and antiseptic application in *scrofulous* or *syphilitic ulcers;* it has been especially recommended in scrofulous *conjunctivitis.*

LOTIO HYDRARGYRI NIGRA. Br.

BLACK MERCURIAL LOTION

Aqua Phagedænica Nigra; Aqua Nigra, Aqua Mercurialis Nigra; Black Wash, Black Lotion; Eau Phagédénique noire, *Fr.;* Schwarzes Wasser, *G.*

"Mercurous Chloride, 6.85 *grammes;* Glycerin, 50.00 *millilitres;* Solution of Lime, sufficient to produce 1000.00 *millilitres.* Triturate the Mercurous Chloride with the Glycerin and gradually add sufficient Solution of Lime to produce the required volume." *Br.*

The addition of glycerin improves this lotion by aiding in the suspension of the insoluble powder. By the reaction between the calomel and calcium is formed the black mercurous oxide. This lotion has medical properties very similar to those of the yellow wash. It has also been recommended by Shoemaker in *ivy poisoning.* A similar preparation is official in the N. F. IV. (See *Lotio Nigra,* Part III.)

LOTIONES.

LOTIONS

Washes; Lotions, *Fr.;* Waschungen, *G.*

This class has been introduced into the British Pharmacopœia in order to give official recognition to two preparations, the *black wash* or *lotio nigra,* and the *yellow wash,* or *lotio flava,* which have long been in use, and which will be found above.

LUPULINUM. N. F.

LUPULIN

"Lupulin consists of the glandular trichomes separated from the strobiles of *Humulus Lupulus* Linné (Fam. *Moraceæ*). Lupulin yields not less than 60 per cent. of ether-soluble extractive and not more than 10 per cent. of acid-insoluble ash." *N. F.*

Lupulinic Glands; Lupulin, *Fr. Cod.;* Lupulite, *Fr.;* Glandulæ Lupuli, Hopfenmehl, Lupulin, *G.;* Luppolino, *It.;* Lupulino, *Sp.*

The collective fruit of the hop known as "strobile" (see *Humulus*) consists of leafy stipules and bracts at the base of which are the minute fruits. Scattered over the fruit and the neighboring portions of the bract are numerous yellowish brown glands. These may be separated by agitation of the strobiles. These separated granules are the glandular trichomes recognized under the name of *lupulin.* To a considerable extent they are shaken free in the ordinary handling of hops and much of the commercial lupulin is obtained by sifting the sweepings from the floor of hop kilns, and therefore contains much extraneous matter like sand and dirt of various kinds.

Description and Physical Properties.—"A bright yellowish-brown, granular powder, having the characteristic odor and taste of hops. Glandular trichomes somewhat globular or ellipsoidal, from 0.1 to 0.3 mm. in diameter, consisting of a single layer of secreting cells assuming the form of a shallow cup, from the inner surface of which the cuticle has been separated by the secreted yellowish brown oleo-resin.

"Preserve Lupulin in tightly closed containers, protected from the light. Lupulin which has become a dark reddish color and developed a disagreeable and valerian-like odor due to aging must not be used.

"**Assay.**—Proceed as directed under ether-soluble extractive." *N. F.*

It is inflammable, and when moderately heated becomes somewhat adhesive.

Lupulin consists of an ether-soluble portion of considerably over half the weight of the lupulin, the predominating constituent in this portion being *beta resin* and a *beta acid,* similar to those referred to under hops. An alpha resin and an alpha acid are also present, and a gamma resin and a fatty oil. The ether-soluble portion contains the inorganic constituents: albuminoids, pentosans, crude fiber, tannin, etc. Lecithin has been reported in some samples of lupulin and also minute traces of an alkaloid. The odor of lupulinic grains resides in the essential oil. This is obtained to the extent of 0.9 per cent. by distilling hops with water. When distilled from the fresh strobiles the oil has a greenish color, but a reddish-brown when old hops have been employed. It is devoid of rotatory power, neutral to litmus paper, and gives no remarkable coloration with concentrated sulphuric acid. According to Chapman (*J. Chem. S.,* 1895, liv, 780), the essential oil consists of two terpenes. one $C_{10}H_{16}$, and the other $C_{10}H_{18}$, boiling between 160° and 171° C. and a sesquiterpene called *humulene,* boiling at 263° to 266° C. This latter makes up almost two-thirds of the oil. There is also a small amount of an oxygenated constituent, probably $C_{10}H_{18}O$.

Lupulin is supposed to possess the therapeutic properties of hops. (See *Humulus.*)

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Fluidextractum Lupulini, *N. F.*

LYCOPODIUM. U. S.

LYCOPODIUM Lycopod.

"Lycopodium consists of the spores of *Lycopodium clavatum* Linné (Fam. *Lycopodiaceæ*)." *U. S.*

Club Moss, Stag's horn, Semen Lycopodii, Pulvis Lycopodii, Sulphur Vegetabile; Vegetable Sulphur; Lycopode, *Fr. Cod.;* Soufre végétal, *Fr.;* Lycopodium, *P. G.;* Bärlappsamen, Streupulver, Hexenmehl, Blitzpulver, *G.;* Licopodio, *It.*, *Sp.*

Lycopodium clavatum, commonly called *club moss,* has a trailing, branching stem, several feet long, and thickly beset with linear-awl-shaped, flat, ribless, smooth leaves, tipped with a fine bristle, curved upward, and of a light green color. The fructification is in terminal spikes, single or in pairs, with crowded ovate, entire, pointed scales, bearing in the axil a transversely oval sporangium which splits nearly to the base and contains the narrow reticulate spores. The plant is a native of Europe, Asia, and America, being especially common in the dry woods northward. The spores are collected in the Ukraine, Poland, Switzerland and Germany. Most of the drug of commerce is now gathered in Poland and the Ukraine. It is shipped to this country in bags and cases from Danzig, Hamburg and London.

Description and Physical Properties.—"A light, yellow, very mobile powder, odorless and tasteless; the spores shaped as a three-sided pyramid with convex base, from 0.025 to 0.040 mm. in diamter; the outer surface reticulate, the reticulations being polygonal and formed by straight-sided delicate ridges, which form a delicate fringe at the edge of the spore; when viewed with the rounded surface of the spore on the under side, a distinct triangular marking is seen, formed by the edges of the flat surfaces of the spore.

"Lycopodium is not wetted by water but floats upon it; when boiled with water, it sinks. When Lycopodium is thrown into a flame, it burns with a quick flash. Lycopodium shows very few, if any, pollen grains from 0.040 to 0.070 mm. in diameter, and consisting of a central, convex, generative cell separating two spherical cells or wings containing air (*pine pollen*). Lycopodium boiled with water and cooled does not give a bluish or reddish color with iodine T.S. (*starch or dextrin*)." *U. S.*

Lycopodium is composed of nearly 50 per cent. of fatty oil, from 3 to 6 per cent. of nitrogen, as albuminous principles, and considerable carbohydrate material. The ash, which ranges from 3 to 5 per cent., is about half P_2O_5. The fatty oil is mainly olein although there is present small amounts of phytosterin, and traces of the glycerides of arachitic, palmitic and stearic acids. A distinctive acid, lycopodic acid, has been reported to the extent of about 2 per cent. in the oil. The *lycopodic acid* crystallizes in silky needles, it is doubly refracting like quartz, and appears to be isomeric with dioxystearic acid. (*D. C.*, 1891, 155; see also *A. Pharm.*, 1908, 246.) Stenhouse found volatile bases to be present in very small amount. Lycopodium is frequently adulterated with such substances as slightly roasted and colored starch, dextrine, powdered colophony, talc, various pollens and a number of other substances. All of these may be readily detected by the microscope. The pollen of coniferous trees has been sold in Austria under the name of *Lycopodium Hungaricum.*

Folleto recommends two reactions to detect pollen: one by adding to a syrupy solution of zinc chloride, potassium iodide and iodine to saturation; the pollen is colored yellow by this reagent, lycopodium is not colored; the other reagent is methyl-green, which colors pollen green, but does not color lycopodium. (*Ph. Centralh.*, 1896, 527.)

Uses.—Lycopodium was formerly used as an absorbent application to *excoriated surfaces,* but has been largely replaced by other dusting powders. Its chief employment is in pharmacy for the purpose of facilitating the rolling of the pilular mass, and of preventing the adhesion of the pills when formed. The club moss itself (under the titles of *Herba Lycopodii* or *Herba Musci Clavati*) has been esteemed diuretic and antispasmodic; its decoction has been employed in *rheumatism, diseases of the lungs and kidneys,* but it has fallen into complete desuetude. One of the ingenious uses for lycopodium in microscopy is to mix a little of it with an unknown powder or on a slide on which a mount is made. The spores are easily recognizable and distinguishable from other elements and give an excellent idea of the approximate size of the elements which are being observed, as the spores are almost uniformly 40 microns in size.

MAGMA MAGNESIÆ. U. S.

MAGNESIA MAGMA Magma. Mag. [Milk of Magnesia]

"Magnesia Magma yields not less than 6.5 per cent. nor more than 7 per cent. of $Mg(OH)_2$." *U. S.*

"Magnesium Sulphate, 300 Gm.; Sodium Hydroxide, 100 Gm.; Distilled Water, a sufficient quantity to make about 1000 cc.

"Dissolve the magnesium sulphate in sufficient distilled water to make 650 cc., place this in a vessel of about 5000 cc. capacity, and heat to boiling. Dissolve the sodium hydroxide in sufficient distilled water to make 1000 cc., add this slowly to the boiling solution of magnesium sulphate, and continue the boiling for thirty minutes. Transfer the mixture to a cylindrical container of not less than 5000 cc. capacity, and fill with hot distilled water. Allow to stand until separation has occurred, and remove the supernatant liquid. Wash repeatedly with hot distilled water until sulphates have practically been eliminated, as shown by testing the supernatant liquid with barium chloride T.S. Concentrate the mixture by evaporation until it contains not less than 7 per cent. of magnesium hydroxide. Note—one-half cc. of oil of peppermint, or a sufficient quantity of oil of anise or other suitable flavoring may be added if desired." *U. S.*

Many suggested improvements for the preparation of milk of magnesia have appeared in the pharmaceutical literature during recent years. Bertha Mueller (*A. J. P.*, 1920, xcii, 162) makes the preparation by hydrating light magnesium oxide under specified conditions. R. W. Terry (*J. A. Ph. A.*, 1919, viii; 1920, ix, 148) in a most exhaustive research upon the subject makes a number of specific recommendations based upon analysis of numerous market samples and many experiments in preparing the product.

The present official formula differs from that of the U. S. IX, which was based on a reaction between magnesium carbonate and sodium hydroxide suggested by McNeary (*J. A. Ph. A.*, 1916, p. 611). For other formulas see *U. S. D.*, 20th ed., p. 671.

Description and Physical Properties.—"A viscous, opaque, white mixture, from which more or less water usually separates on standing; free from mustiness.

"It is alkaline to litmus paper and to phenolphthalein T.S.

"A solution of 2 cc. of diluted hydrochloric acid and 1 cc. of Magnesia Magma responds to the reactions for magnesium.

"The addition of 2 cc. of diluted hydrochloric acid to 1 cc. of Magnesia Magma causes not more than a slight effervescence (*carbonate*), and the resulting solution is not more than slightly turbid. Dilute 20 cc. of Magnesia Magma with distilled water to make 200 cc., and allow it to stand until the precipitate has settled. Remove 50 cc. of the clear liquid, and evaporate it to dryness on a water bath. The residue, when dried to constant weight at 150° C., does not exceed 0.005 Gm. To another 50 cc. portion of the supernatant liquid, add 1 drop of methyl orange T.S., and titrate with tenth-normal sulphuric acid: not more than 0.4 cc. is required to produce a red color (*soluble alkalies*).

"Preserve in wide-mouthed bottles, tightly stoppered with corks which have been dipped in melting paraffin.

"**Assay.**—Place about 5 Gm. of Magnesia Magma in a tared flask, stopper, and weigh accurately, add 25 cc. of normal sulphuric acid, and after solution is complete titrate the excess of acid with normal sodium hydroxide, using methyl orange T.S. as indicator. Each cc. of normal sulphuric acid corresponds to 0.02917 Gm. of $Mg(OH)_2$." *U. S.*

The incompatibilities of milk of magnesia are, in general, those of magnesium oxide. It should be remembered that this suspension is due to the colloidal condition of the magnesium hydroxide which is likely to be disturbed by various salts.

Magma magnesia, popularly known as *milk of magnesia*, is an excellent and convenient alkali, useful as an antacid and mild laxative in *hyperacidity of the stomach*, whether due to *hypochlorhydria* or *fermentative dyspepsia*, and is useful for the other purposes for which magnesium oxide is used. One drachm is equivalent to approximately four grains of magnesium oxide. Milk of magnesia is also widely employed as a mouth-wash, and especially for the correction of acid conditions of the mouth. For this purpose the addition of a trace of some aromatic oil, such as peppermint or anise, is a great advantage.

Dose, one to four fluidrachms (3.75–15 cc.).

MAGNESII CARBONAS. U. S. (Br.)

MAGNESIUM CARBONATE Mag. Carb.

"Magnesium Carbonate is a mixture of hydrated magnesium carbonate and magnesium hydroxide, corresponding to not less than 39.2 per cent. of MgO." *U. S.*

Magnesii Carbonas Levis, Light Magnesium Carbonate, *Br.;* **Magnesii Carbonas Ponderosus**, Heavy Magnesium Carbonate, *Br.;* Magnesia Hydrico-carbonica, Carbonas Magnesicus, Magnesia Alba, Magnesiæ Carbonas, Carbonate of Magnesia; Magnesii Hydrocarbonicum, *Fr. Cod.;* Magnésie blanche, *Fr.;* Magnesium carbonicum, *P. G.;* Magnesiumcarbonat, Kohlensaure Magnesia, Weisse Magnesia, *G.;* Idrocarbonato di Magnesio, Carbonato di Magnesia, *It.;* Carbonato Magnesico, Magnesia blanca, *Sp.*

This corresponds nearly with "Magnesii Carbonas Levis" of the British Pharmacopœia. A Heavy Magnesium Carbonate is also official in the British Pharmacopœia.

Magnesium is a white, very brilliant metal, of sp. gr. 1.75, resembling silver, malleable, fusible at a low temperature, and convertible into magnesium oxide by the combined action of air and moisture. It burns with great facility, and affords by its combustion a light which is intensely white and very rich in actinic, or chemically active, rays, so that it finds wide application in signal lights and for photography. Many of the so-called "flash powders" contain metallic magnesium in a finely divided state as their basis. With nitric and hydrochloric acids magnesium forms salts which are soluble in either water or alcohol and very deliquescent. It is precipitated from its saline solutions by the pure alkalies in the state of a hydroxide, and by potassium and sodium carbonates as a carbonate, but it is not precipitated by the alkaline bicarbonates, nor by ammonium carbonate.

Magnesium carbonate sometimes occurs as a native mineral known as *magnesite*, the best deposits of which are those of the Grecian Archipelago, though a common variety is found in Chester Co., Pa., and a large deposit has been discovered in Clark Co., Nevada. That which is sold in commerce is prepared on a large scale by the manufacturer. In the British Pharmacopœia directions are given for preparing it in two forms. The following are the directions:

1. MAGNESII CARBONAS LEVIS. *Light Magnesium Carbonate*, Br.—"Light Magnesium Carbonate is a hydrated magnesium oxycarbonate obtained by the following process:—Magnesium

Sulphate, 125 *grammes;* Sodium Carbonate, 150 *grammes;* Distilled Water, *a sufficient quantity.* Dissolve the Magnesium Sulphate and the Sodium Carbonate separately, each in one thousand *millilitres* of cold Distilled Water; mix the solutions; boil the mixture for fifteen minutes; transfer the precipitate to a calico filter; wash it with boiling Distilled Water until the washings are free from sulphates, and dry at a temperature not exceeding 100° C." *Br.*

The resulting carbonate is characterized in the British Pharmacopœia as "a very light, white powder, which, when examined under the microscope, is found to consist of amorphous particles with numerous slender prisms intermixed. It otherwise possesses the general characters and responds to the tests described under 'Magnesii Carbonas Ponderosus.'" *Br.*

2. MAGNESII CARBONAS PONDEROSUS. *Heavy Magnesium Carbonate,* Br.—"Heavy Magnesium Carbonate is a hydrated magnesium oxycarbonate obtained by the following process: —Magnesium Sulphate, 125 *grammes;* Sodium Carbonate, 150 *grammes;* Distilled Water, boiling, *a sufficient quantity.* Dissolve the Magnesium Sulphate and the Sodium Carbonate separately, each in two hundred and fifty *millilitres* of the Distilled Water; mix the solutions, and evaporate to dryness; digest the residue for half an hour with five hundred *millilitres* of the Distilled Water; collect the insoluble matter on a calico filter, wash with the Distilled Water until the washings are freed from sulphates, and dry at a temperature not exceeding 100° C." *Br.*

This is essentially the old process of the Dublin College, and yields a product which is characterized in the British Pharmacopœia as "a white granular powder. Readily soluble with effervescence, in the diluted mineral acids, the solutions yielding the *reactions* characteristic of magnesium. Loses from 56 to 58 per cent. of its weight when heated to redness. Yields no characteristic *reactions* for aluminium, copper, or calcium, and not more than the slightest *reactions* for iron, chlorides, or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million." *Br.*

The following method is said to be pursued by some of the best manufacturers. To a saturated solution of 100 parts of magnesium sulphate, a solution of 125 parts of crystallized sodium carbonate is gradually added, the solutions being constantly stirred. The mixture is heated to ebullition, to complete the precipitation of the magnesia, which is then washed with tepid and finally with cold water, until the washings no longer give a precipitate with barium salts. When sufficiently washed, the carbonate is allowed to drain for one or two days on large linen filters, and is then placed in wooden moulds with a porous bottom of brick or gypsum, and subjected to pressure in order to give it a square and compact form. Pattinson's process is the one chiefly used by the larger manufacturers. It depends upon the fact that, on treating calcined dolomite, in the presence of water, with carbon dioxide under pressure, the magnesia dissolves as bicarbonate before any of the accompanying lime enters in solution. The calcined and finely powdered mineral is introduced, together with water, into a cylinder with a horizontal axis, and, while it is being kept in constant motion by a stirring apparatus, carbon dioxide, under a pressure of five to six atmospheres, is forced into it. The resulting solution of magnesium bicarbonate, which is perfectly free from lime, if the process has been properly managed, is then transferred to a vertical cylinder, where it is heated with steam, whereby magnesium carbonate is separated, which is collected, formed into prismatic pieces, and dried. The carbon dioxide required issues from the earth immediately outside of the factory, and the dolomite is furnished by the quarries of May and Urban, near Dietz and Steelen on the Lahn. (*A. Pharm.*, Aug., 1880; *N. R.*, Sept., 1881.) When made from bittern, magnesium carbonate is contaminated with calcium carbonate, salts of lime being contained in sea water, and when it is prepared from magnesite, or from magnesian schist, iron is almost always present. The only way in which these impurities can be avoided is to prepare pure magnesium sulphate by repeated crystallization, and to use a pure sodium carbonate. It is also necessary that the water with which the precipitate is washed should be free from earthy salts, which would be decomposed and contaminate the magnesia. Kippenberger prepares crystallized magnesium carbonate by shaking *freshly* precipitated magnesium carbonate with a solution of potassium bicarbonate at the ordinary temperature; much of the magnesium carbonate dissolves and crystallizes out of the filtered solution upon standing for a day. Sodium bicarbonate may be used instead of the potassium salt, but the crystals are smaller. (*Zeit. Anorg. Chem.*, 1894, 177.) J. G. Ferrier criticized the processes for making the carbonates by the British Pharmacopœia; he stated that there was a conspicuous want of uniformity in the results obtained. (*P. J.*, 1904, 586.)

The density of magnesium carbonate is said to depend upon the strength of the solutions from which it is first precipitated, and its fineness and softness to the touch upon the use of sodium carbonate in its preparation. Much of the magnesium carbonate formerly used in this country was imported from England and Ireland, but that now consumed in the United States is chiefly a home product. The composition of magnesium carbonate and its physical condition are exhaustively discussed by Broeksmit (*Ph. Wb.*, 1921, lviii, 210) who points out that a crystalline $MgCO_3.3H_2O$ occurs on standing.

The formula given by the British Pharmacopœia of 1898 is $3MgCO_3 + Mg(OH)_2 + 4H_2O$; in other words, a combination of three molecules of magnesium carbonate, one of magnesium hydroxide, and four of water. While the U. S. Pharmacopœia gives no formula in the text it is written in the molecular weight tables as follows: "Basic (approximately) $(MgCO_3)_4Mg(OH)_2 + 5H_2O$." The composition of this salt varies with the mode of preparation.

Description and Physical Properties.—"Light, white, friable masses, or a bulky, white powder. It is odorless, and is stable in the air. Magnesium Carbonate is practically insoluble in water, to which, however, it imparts a slightly alkaline reaction. It is insoluble in alcohol, but is dissolved by dilute acids with effervescence. When strongly heated, it loses water and carbon dioxide, and is converted into magnesium oxide.

"When Magnesium Carbonate is treated with diluted hydrochloric acid, it dissolves with effervescence and the resulting solution responds to the reactions for magnesium.

"Mix 1 Gm. of Magnesium Carbonate with 50 cc. of distilled water, heat the mixture to the boiling point, and cool. Then filter, and evaporate the filtrate to dryness on a water bath. The weight of the residue does not exceed 0.01 Gm. (*soluble salts*). Dissolve 2.5 Gm. of Magnesium Carbonate in 50 cc. of diluted hydrochloric acid and 200 cc. of distilled water: the solution is colorless. Transfer 50 cc. of this solution to a 50 cc. graduated cylinder and add 0.2 cc. of potassium ferrocyanide T.S. After mixing well, the color produced in the solution, if any, when viewed downward against a white surface is not greater than the color of a control solution prepared as follows: Dilute 0.2 cc. of ferric chloride T.S. with sufficient distilled water to make 1000 cc. Transfer 25 cc. of this solution to another 50 cc. graduated cylinder, and add 10 cc. of diluted hydrochloric acid and sufficient distilled water to make 50 cc. Then add 0.2 cc. of potassium ferrocyanide T.S. The two cylinders used in this test must be matched, be of practically colorless glass and have the same internal diameter (*iron*). Dissolve 0.5 Gm. of Magnesium Carbonate in a slight excess of diluted hydrochloric acid (about 5 cc.), and dilute with distilled water to 25 cc.: a 10 cc. portion of this solution meets the requirements of the test for *heavy metals*. Dissolve 4 Gm. of Magnesium Carbonate in 50 cc. of diluted hydrochloric acid in a beaker of about 900 cc. capacity. Dilute this solution to about 400 cc. with distilled water, add 5 Gm. of ammonium chloride, heat to boiling, and add 50 cc. of ammonium oxalate T.S., followed by 5 drops of methyl orange T.S., and afterwards by ammonia T.S. (previously diluted with two volumes of distilled water), added slowly in small portions, stirring constantly until the liquid has assumed a yellow color. This operation normally requires about twenty minutes. Allow the liquid to stand for four hours or over night, collect the precipitate on a filter, wash it with hot, distilled water containing 1 per cent. of ammonium oxalate solution, until the washings, after strongly acidifying with nitric acid, cease to react with silver nitrate T.S. Dissolve the precipitate by pouring 50 cc. of warm diluted hydrochloric acid in small portions over the filter, wash the filter with about 100 cc. of distilled water, collect the solution of the precipitate and washings in the same beaker, then dilute to 400 cc. with distilled water, and reprecipitate as before (omitting the addition of 5 Gm. of ammonium chloride). Allow the new precipitate to stand four hours or over night, filter, and wash as before, then dry the precipitate within the filter paper and after cautious ignition in a platinum crucible, heat the residue until of constant weight. The heat should be applied gently at first, the temperature should then be gradually increased, and finally the heat of a blast lamp should be applied for fifteen minutes or longer if necessary. Cool the crucible and contents in a desiccator before weighing. The weight of CaO so obtained does not exceed 0.032 Gm., corresponding to not more than 0.8 per cent (*limit of calcium oxide*).

"**Assay.**—Dissolve about 1 Gm. of Magnesium Carbonate, accurately weighed, in 30 cc. of normal sulphuric acid, and determine the residual acid by titrating with normal sodium hydroxide, using methyl orange T.S. as indicator. From the volume of the normal sulphuric acid consumed, deduct the volume of normal sulphuric acid corresponding to the per cent of calcium oxide found. The difference represents the normal sulphuric acid equivalent to the magnesium oxide present. Each cc. of normal sulphuric acid corresponds to 0.02016 Gm. of MgO or to 0.02804 Gm. of CaO." *U. S.*

A solution in carbonic acid water, prepared by passing carbon dioxide into a reservoir containing magnesium carbonate suspended in water, has been introduced into use as a cathartic and antacid. *Dinneford's Magnesia* is a solution of this nature and contains the dissolved magnesia in the form of bicarbonate into which the carbonate is converted by the carbon dioxide under pressure. According to Christison, it contains only nine grains of carbonate in the fluidounce, though alleged to contain twice that quantity. Its taste is more disagreeable than that of the undissolved carbonate. A formula for this preparation has been introduced into the British Pharmacopœia, with the name of *Liquor Magnesii Bicarbonatis.*

An investigation of the properties of magnesium carbonate as a clarifying and filtering agent was made by one of the Fellows of the Mellon Institute of Industrial Research (*Am. Drug.*, 1921, lxix, p. 24). The clarifying value was stated to be due to the great absorbent powers of this compound. General recommendations for its use in this connection were made without any warning of the injury that would result to preparations affected by alkalies.

It has long been recognized in pharmacy that magnesium carbonate has very limited uses in this connection because of the neutralizing power upon acids, the precipitating effect upon alkaloids, and the fact that aqueous solutions become slightly alkaline. For this reason it was abandoned many years ago as a filtering medium in the preparation of the official aromatic waters.

Uses.—Magnesium carbonate is antacid, and, by combining with acid in the stomach, usually acts as a cathartic. When it undergoes no change in the alimentary canal it produces no purgative effect. Under these circumstances it may usually be made to operate by following it with draughts of lemonade. It is useful in all cases which require a laxative antacid, and, though prone to produce flatulence in consequence of the liberation of its carbon dioxide in the stomach and bowels, and therefore, in ordinary cases, inferior to calcined magnesia, it sometimes operates favorably, in consequence of this very property, in *sick stomach* attended with acidity. As an antacid, it has the advantages over sodium carbonate of being less irritating and of neutralizing a larger proportion of acid. It is best administered in water or milk. In order that it may be uniformly diffused through water, it should be previously rubbed up with syrup or ginger syrup.

Dose, as an antacid, five to twenty grains (0.32–1.3 Gm.); as a laxative, one-half to two drachms (2–7.7 Gm.).

Off. Prep.—Trochiscus Bismuthi Compositus, *Br.;* Mistura Carminativa, *N. F.;* Liquor Aromaticus Alkalinus, *N. F.;* Mistura Magnesiæ Asafœtidæ et Opii, *N. F.*

MAGNESII CHLORIDUM. N. F.

MAGNESIUM CHLORIDE Magnes. Chlorid.

"Magnesium Chloride contains, when dried for twenty-four hours over sulphuric acid, not less than 95 per cent. of $MgCl_2.6H_2O$ (203.34)." *N. F.*

Description and Physical Properties.—"Magnesium Chloride occurs as colorless, transparent crystals, or as white, translucent pieces; deliquescent in moist air. One Gm. dissolves in about 0.6 cc. of water; it is readily soluble in alcohol. The aqueous solution of the salt (1 in 20) is neutral to litmus paper.

"An aqueous solution of the salt, acidulated with nitric acid yields a white precipitate upon the addition of silver nitrate T.S. A mixture of 10 cc. of an aqueous solution of the salt (1 in 20) with 10 cc. of ammonium chloride T.S., rendered slightly alkaline with ammonia water, yields a white precipitate on the addition of sodium phosphate T.S.

"One Gm. of the salt dissolves in 10 cc. of alcohol, leaving not more than 1 per cent. of insoluble residue (*substances insoluble in alcohol*). Add 3 cc. of potassium sulphate T.S. to 10 cc. of an aqueous solution of the salt (1 in 20), slightly acidulated with hydrochloric acid; no turbidity results (*barium*). Ten cc. of an aqueous solution of the salt (1 in 200), acidulated with hydrochloric acid, is not reddened by potassium thiocyanate T.S. (*iron*). Warm 5 cc. of an aqueous solution of the salt (1 in 10) with 10 cc. of sodium hydroxide T.S.; the odor of ammonia is not evolved. A mixture of 10 cc. of an aqueous solution of the salt (1 in 20), 10 cc. of ammonium chloride T.S. and 5 cc. of ammonia water, is not rendered more than slightly turbid upon the addition of ammonium oxalate T.S. (*calcium*). An aqueous solution of the salt does not respond to the Test for heavy metals. An aqueous solution of the salt meets the requirements of the Test for arsenic.

"**Assay.**—Dissolve about 0.5 Gm. of Magnesium Chloride previously dried to constant weight over sulphuric acid and accurately weighed, in 50 cc. of distilled water in a 200 cc. measuring flask; add 3 cc. of nitric acid, then add 50 cc. of tenth-normal silver nitrate and sufficient distilled water to make the mixture measure 200 cc. Mix thoroughly, filter through a dry filter, reject the first 20 cc. of filtrate, then collect 100 cc. of filtrate, add 2 cc. of ferric ammonium sulphate T.S. and titrate the excess of silver nitrate with tenth-normal potassium thiocyanate. Each cc. of tenth-normal silver nitrate used, corresponds to 0.010167 Gm. of $MgCl_2.6H_2O$. Each Gm. of Magnesium Chloride corresponds to not less than 93.4 cc. of tenth-normal silver nitrate." *N. F.*

Chilbret (*R. P.*, 1910, p. 646) has revived the use of this salt as a laxative, and believes it superior to either the sulphate or citrate, but its advantage seems very questionable. Being deliquescent, it is necessary to give it in solution.

Dose, from one to four drachms (3.75–15 Gm.).

Off. Prep.—Liquor Hydrastinæ Compositus, *N. F.*

MAGNESII OXIDUM. U. S. (Br.)

MAGNESIUM OXIDE Mag. Oxid. [Magnesia, Light Magnesia]

"Magnesium Oxide contains, after ignition, not less than 96 per cent. of MgO. Upon ignition it loses not more than 10 per cent." *U. S.* "Light Magnesia, MgO, is prepared by exposing Light Magnesium Carbonate to a dull red heat." *Br.*

Magnesia Levis, *Br.;* Calcined Magnesia; Oxydum Magnesii, Oxide of Magnesia, Magnesia Calcinata; Magnésie calcinée, Magnésie, *Fr.;* Magnesii Oxydatum, *Fr. Cod.;* Magnesia Usta, *P. G.;* Gebrannte Magnesia, *G.;* Ossido di magnesio, *It.;* Oxido magnesico, *Sp.*

In the British Pharmacopœia, 1885, directions were given for preparing two forms of magnesia, one called *Magnesia Levis,* or *Light Magnesia,* from the light carbonate, and the other *Magnesia Ponderosa,* from the heavy carbonate. It is the former which corresponds with our ordinary magnesia. Neither Pharmacopœia gives a detailed process. "Take of Light Carbonate of Magnesium, *four ounces.* Put it into a Cornish or Hessian crucible closed loosely by a lid, and expose it to a low red heat until a small quantity, taken from the center of the crucible, cooled, moistened with water, and dropped into warm diluted sulphuric acid, causes no effervescence." *Br.*, 1885.

By exposure to a red heat, the water and carbon dioxide of the magnesium carbonate are expelled, and the oxide remains. Taking the accepted formula for the carbonate as the starting point, the reaction is as follows:

$$(MgCO_3)_4 + Mg(OH)_2 + 5H_2O = 5MgO + 6H_2O + 4CO_2$$

About the close of the process the earth exhibits a luminous or phosphorescent appearance, which is said to be a good criterion of its freedom from carbon dioxide. (Duncan.) A more certain indication, however, is the absence of effervescence when hydrochloric acid is added to a little of the magnesia, previously mixed with water. It is an error to suppose that a very intense heat is requisite in the calcination. The temperature of ignition is sufficient for the expulsion of the water and carbon dioxide, and any increase serves only to render the magnesia harder, denser, less readily soluble in acids, and consequently less useful as a medicine.

Many processes have been proposed for manufacturing *light calcined magnesia* as it was formerly called. These will be found in *U. S. D.*, 20th ed., p. 674.

The sp. gr. of magnesium oxide is commonly stated at 2.3. It was deemed infusible until melted by means of the oxyhydrogen blowpipe of Hare. When sufficiently heated, it conducts electricity and shines with an intense light, which fact is utilized in the Nernst lamp. Water sprinkled upon it is absorbed to the extent of about 18 per cent., but with scarcely any increase of temperature, producing thereby the hydroxide $Mg(OH)_2$. It is almost insoluble, requiring, according to Fyfe, 5142 parts of water at 15.5° C., and 36,000 parts of boiling water, for solution.

Description and Physical Properties.—"A white, very bulky, odorless powder. On exposure to air, it absorbs moisture and carbon dioxide.

"Magnesium Oxide is practically insoluble in water and is insoluble in alcohol. It is dissolved by dilute acids.

"A solution of Magnesium Oxide in diluted hydrochloric acid responds to the reactions for magnesium.

"Boil 1 Gm. of Magnesium Oxide with 50 cc. of distilled water, cool, and filter: the filtrate is not more than faintly alkaline to litmus paper, and when evaporated to dryness leaves not more than 0.02 Gm. of residue (*soluble salts*). Boil a mixture of 0.1 Gm. of Magnesium Oxide with 5 cc. of distilled water, and after cooling pour it into 5 cc. of acetic acid: solution takes place without the evolution of more than a few isolated gas bubbles (*carbonate*). It meets the requirements of the test for *iron* under *Magnesii Carbonas*, using 1 Gm. of Magnesium Oxide. Dissolve 0.5 Gm. of Magnesium Oxide in a slight excess of diluted hydrochloric acid, and dilute with distilled water to 25 cc.: a 10 cc. portion of this solution meets the requirements of the test for *heavy metals*. Transfer to a porcelain crucible about 1 Gm. of Magnesium Oxide, weigh accurately, and expose to a low red heat (about 600° C.), it loses not more than 10 per cent. of its weight (*water and other volatile substances*). When determined by the method described under *Magnesii Carbonas*, using about 1.5 Gm. of freshly ignited Magnesium Oxide, accurately weighed, it shows not more than 2 per cent. of calcium oxide.

"Preserve in well-closed containers." *U. S.*

"A white powder differing only from 'Magnesia Ponderosa' in its bulk, the volumes corresponding to the same weight having the ratio of three and a half to one." *Br.*

"**Assay.**—Ignite about 0.5 Gm. of Magnesium Oxide to constant weight at a low red heat, weigh the residue accurately, dissolve it in 30 cc. of normal sulphuric acid, and determine the residual acid by titrating with normal sodium hydroxide, using methyl orange T.S. as indicator. From the volume of the normal sulphuric acid consumed, deduct the volume of normal sulphuric acid corresponding to the per cent. of calcium oxide found. The difference represents the normal sulphuric acid equivalent to the magnesium oxide present. Each cc. of normal sulphuric acid corresponds to 0.02016 Gm. of MgO or to 0.02804 Gm. of CaO." *U. S.*

Magnesia is liable to contain, as impurities, magnesium carbonate, lime, alumina, silica, and small quantities of the soluble salts employed or produced in the preparation of the carbonate from which it is procured. Lime is a very frequent impurity, and imparts to the magnesia a more strongly alkaline and more disagreeable taste. According to Wittstein, calcium oxalate is soluble in the neutral salts of magnesium, requiring 50 parts of magnesium chloride, and 90 of magnesium sulphate, and consequently there might be no precipitate, or one redissolved by the liquid, should the proportion of lime be very small. (*J. P. C.*, 4e sér., iii, 216.) On this account a special method of determining small amounts of calcium salts has been introduced into the texts of magnesium oxide and magnesium carbonate of the U. S. P.

Uses.—Magnesium oxide is used in medicine chiefly for its antacid properties. In cases of *gastric hyperacidity*, whether due to overactivity of the acid-secreting glands of the stomach or to fermentative changes in the foodstuff, it is one of the best correctives that we have. It has the advantages over bicarbonate of soda that it is less irritating to the mucous membrane, that it does not evolve any gas, and that the dose required is smaller. One grain of magnesium oxide has about the same neutralizing power as four grains of sodium bicarbonate. When given in large enough dose it exercises a laxative effect. This aperient action is due to the union of the magnesium with the acids of the primæ viæ. When it meets with no acid, it is apt to linger in the stomach or bowels, and should in that case be followed by lemonade. It may be administered in water or milk, and thoroughly triturated so as to render the mixture uniform. If mixed with less than 14 or 15 times its weight of water, and allowed to stand for a day or two, magnesia is apt to form a more or less concrete mass, owing to the production of a hydroxide. This change does not take place, or at least takes place much less readily, when magnesia already saturated with moisture is employed instead of that freshly calcined. In this connection Duncan recommends boiling the magnesia for a few moments with half the quantity of water prescribed to prevent subsequent caking. It has been conjectured that anhydrous magnesia might prove injurious to the stomach by solidifying its liquid contents, and the oxide which has become saturated with moisture by exposure to a damp air is preferably recommended. Freshly precipitated magnesium hydroxide will serve as an antidote to arsenic trioxide, though less efficient than ferric hydroxide. The experiments of Carles have shown that the soluble *magnesium saccharate* is not superior as an antidote for arsenic to simple magnesia. Ohleyer (*L. L.*, July, 1873) employs magnesia as a dressing in *ulcers* and *abrasions,* while Vergley recommends for *burns* calcined magnesia triturated with milk so as to form a paste, which should be applied thickly several times a day.

Dose, as an antacid, five to twenty grains (0.32–1.3 Gm.); as a laxative, one-half to one drachm (2–3.9 Gm.).

Off. Prep.—Ferri Hydroxidum cum Magnesii Oxido, *U. S.;* Pulvis Rhei Compositus, *Br.*

MAGNESII OXIDUM PONDEROSUM. U. S. (Br.)

HEAVY MAGNESIUM OXIDE Mag. Oxid. Pond. [Heavy Magnesia]

"Heavy Magnesium Oxide contains, after ignition, not less than 96 per cent. of MgO. Upon ignition it loses not more than 10 per cent." *U. S.* "Heavy Magnesia, MgO, is prepared by exposing Heavy Magnesium Carbonate to a dull red heat." *Br.*

Magnesia Ponderosa, *Br.;* Heavy Calcined Magnesia; Oxide of Magnesium; Magnésie Calcinée pesante, *Fr.;* Schwere Gebrannte Magnesia, *G.*

This was directed, in the British Pharmacopœia, 1885, to be prepared precisely in the same manner as light magnesia, using, however, the heavy carbonate (Heavy Magnesium Carbonate, *Br.*).

Description and Physical Properties.—"A white, dense, odorless and very fine powder, which meets the requirements of the tests for identity, purity, and the Assay under *Magnesii Oxidum.* Preserve in well-closed containers." *U. S.* It is described by the Br. Ph., as "a white powder, insoluble in *water,* but readily dissolved by acids, the solution yielding the *reactions* characteristic of magnesium. Yields no characteristic *reactions* for aluminium and copper, and not more than the slightest *reactions* for iron, calcium, carbonates, and sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million. Loses not more than 1 per cent. of its weight when heated to dull redness." *Br.*

The two varieties of light and heavy magnesia differ only in their weight in the same bulk, the volumes corresponding to the same weight being to each other in the ratio of three and one-half to one. (See *Magnesii Oxidum.*)

Dose, five to sixty grains (0.32–3.9 Gm.).

Off. Prep.—Pulvis Rhei et Magnesiæ Anisatus, *N. F.*

MAGNESII SULPHAS. U. S., Br.

MAGNESIUM SULPHATE Mag. Sulph. [Epsom Salt]

"Magnesium Sulphate contains not less than 48.60 per cent. and not more than 53.45 per cent. of $MgSO_4$, corresponding to not less than 99.5 per cent. of the crystallized salt [$MgSO_4.7H_2O$]." *U. S.* "Magnesium Sulphate may be obtained by the interaction of the native magnesium carbonates and diluted sulphuric acid; or by purifying the native sulphate. It contains not less than 97.4 per cent. of pure magnesium sulphate, $MgSO_4,7H_2O$." *Br.*

Sal Amarum, Sal Epsomense, Sal Anglicum, Sal Sedlicense, Sulphas Magnesicus; Sulphate of Magnesia; Sulfate de Magnésie, *Fr. Cod.;* Sel d'Epsom, Sel de Sedlitz, Sel. amer, *Fr.;* Magnesium Sulfuricum, *P. G.;* Magnesiumsulfat, Schwefelsaures Magnesia, Bittersalz, *G.;* Solfato di magnesio, Sulfato magnesico, *Sp.*

Magnesium Sulphate is a constituent of sea water, and of some saline springs. It also occurs native, either crystallized in slender, prismatic, adhering crystals, or as an efflorescence on certain rocks and soils which contain magnesia and a sulphate or sulphide. In the United States it is found in the great caves so numerous to the west of the Allegheny Mountains. In one of these caves, near Corydon in Indiana, it formed a stratum on the bottom several inches deep, or appeared in masses sometimes weighing ten pounds, or disseminated in the earth of the cavern, one bushel of which yielded from four to twenty-five pounds of the sulphate. It also appeared on the walls of the cavern, and, if it was removed, acicular crystals again appeared in a few weeks. (Cleveland.) An enormous deposit has been reported at Basque, British Columbia.

Under the name of *kieserite,* a mineral is obtained from the saline deposits at Stassfurt, in Germany, which consists chiefly of impure magnesium sulphate. It is used as a source for preparing magnesium sulphate, and is exported from Germany; for a historical paper on Epsom salt by M. I. Wilbert, see *Proc. A. Ph. A.,* 1904, 351.

Magnesium sulphate was originally procured by evaporating the waters of saline springs at Epsom, in England. Grew prepared it in this manner in 1675. It was afterwards discovered that the brine remaining after the crystallization of common salt from sea water furnished by careful evaporation precisely the same salt, and, as this was a much cheaper product, it superseded the former for a time. At present, in the neighborhood of Genoa and Nice, magnesium sulphate is prepared in large quantities from a schistose rock containing magnesia and iron sulphide. The mineral is roasted, and exposed in heaps for some months to the action of air and water. It is then lixiviated, the ferrous sulphate decomposed by lime water, and the salt obtained pure by repeated solution and crystallization. It is also extensively manufactured in Baltimore and Philadelphia from a silicious magnesium hydroxide. This mineral occurs in veins in the serpentine and other magnesian rocks which abound in the neighborhood of Baltimore and in the southern counties of Pennsylvania. The mineral is reduced to a fine powder and saturated with sulphuric acid. The mass is then dried and calcined at a red heat, in order to convert any ferrous sulphate which may be present into ferric oxide. It is then dissolved in water, and calcium sulphide added to separate any remaining portion of iron. The salt is crystallized and dissolved a third time, in order to purify it. The sulphate prepared by this process is generally very pure and clean, although it sometimes contains a trace of ferrous sulphate. A very pure magnesium sulphate free from chloride is obtained as a by-product in the manufacture of carbon dioxide from magnesite when sulphuric acid is used to decompose the carbonate. This industry at one time assumed large proportions because of the demand for liquefied carbon dioxide in the manufacture of aerated and effervescing mineral waters. In the modern method of making carbon dioxide, however, acid is not used, the CO_2 being evolved by simply heating the magnesite (magnesium carbonate) to a little over 300° C. Magnesium sulphate is also obtained from *kieserite* and *kainite* from the Stassfurt mines, Germany. There are deposits of native magnesium sulphate, *epsomite,* in Wyoming, Utah, Washington and California. *Dolomite* (a native magnesio-calcium carbonate) is also used for the manufacture of magnesium sulphate, calcium sulphate being obtained as a by-product.

Description and Physical Properties.—"Small, colorless, prismatic needles or rhombic prisms, without odor, and having a cooling, saline, and bitter taste. One Gm. of Magnesium Sulphate is soluble in 1.3 cc. of water and in about 1.1 cc. of glycerin, at 25° C. One Gm. is soluble in about 0.2 cc. of boiling water. It is sparingly soluble in alcohol at 25° C. When exposed to warm air, the salt loses some of its water of crystallization and is converted into a white powder. Further heating removes more water, and at a temperature somewhat above 200° C. it is rendered anhydrous.

"An aqueous solution of the salt (1 in 20) responds to the reactions for magnesium and for sulphates. An aqueous solution of the salt (1 in 20) is neutral to litmus paper.

"One Gm. of the salt shows no more *chloride* than corresponds to 0.2 cc. of fiftieth-normal hydrochloric acid. An aqueous solution of the salt meets the requirements of the test for *heavy metals.* An aqueous solution of the salt meets the requirements of the test for *arsenic.*

"Preserve in well-closed containers." *U. S.*

"In small, colorless, transparent, rhombic prisms. Taste bitter. Soluble in 1 part of *water.* Yields the *reactions* characteristic of magnesium and of sulphates. When 0.5 gramme is dissolved in 50 millilitres of *water,* and to the solution 20 millilitres of *solution of ammonium chloride,* 20 millilitres of *strong solution of ammonia,* and excess of *solution of sodium phosphate* are added in succession, the mixture, after well stirring and setting aside for twelve hours, yields a precipitate which, when collected, washed with *strong solution of ammonia* diluted with three times its volume of *water,* dried and heated to redness, weighs not less than 0.220 and not more than 0.226 gramme. Yields no characteristic *reactions* for zinc, and not more than the slightest *reactions* for chlorides. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million. 10 grammes dissolved in 20 millilitres of *water,* and heated on a water-bath for one hour in a closed flask, yield a clear, colorless solution (absence of insoluble impurities and of more than traces of iron)." *Br.*

Assay.—"Dissolve about 1 Gm. of Magnesium Sulphate, accurately weighed in 100 cc. of distilled water, gradually add to the solution, with constant stirring, an excess of sodium phosphate T.S. (about 20 cc.), allow the mixture to stand for ten minutes, then add 30 cc. of ammonia T.S., and let stand for four hours. Collect the precipitate on a filter, wash it with dilute ammonia T.S. (1 volume of ammonia T.S. to 19 volumes of distilled water) until the washings are free from sulphates. Dry, and ignite to constant weight. The weight of magnesium pyrophosphate ($Mg_2P_2O_7$) when multiplied by 1.081 indicates its equivalent in $MgSO_4$. Each Gm. of Magnesium Sulphate corresponds to not less than 0.4495 Gm. and not more than 0.4944 Gm. of magnesium pyrophosphate ($Mg_2P_2O_7$)." *U. S.*

It usually occurs in small acicular crystals, which are produced by agitating the solution while crystallizing. It slowly effloresces in the air. Exsiccated magnesium sulphate is employed in some localities under the title *Magnesium Sulphuricum Siccum.* It is a fine white powder of which about 65 parts represents 100 parts of the crystallized salt.

Magnesium sulphate is completely decomposed by potassium and sodium hydroxides and their carbonates, by lime, barium and strontium oxides, and their soluble salts. Ammonia partially decomposes it, and forms with the remainder a double sulphate. Potassium and sodium bicarbonates do not decompose it, except by the aid of heat. An economic use which has been recommended of magnesium sulphate is the addition of a strong solution to ordinary white-wash, whereby a beautiful whiteness may be given to walls and ceilings. A little of it, moreover, added to starch considerably increases its stiffening properties, and at the same time in some degree resists the action of fire.

Uses.—Magnesium sulphate is an active cathartic operating with but little pain or nausea, and producing watery stools. Its cathartic action is due in part to its attraction for water, but it seems also to exercise a direct stimulant effect upon the glands of the intestinal tract. It has but little direct effect upon peristalsis, the increased movements of the intestinal muscles being due chiefly to the over distention with the fluid. It may be used whenever it is desired to clean out the alimentary canal, especially when a prompt action is desired, as in cases of *poisoning* or certain types of *acute enteritis.* It is a valuable remedy when it is desired to encourage the elimination of metabolic poisons through the bowel, as in *gout* or *uremia.* It is also highly esteemed for the evacuation of *dropsical effusions.* As an habitual laxative, although widely used, it is generally inferior to the vegetable cathartics.

When injected into the circulation magnesium sulphate acts as a violent poison, lessening respiration and depressing the circulation by a direct action upon the heart. It also paralyzes the peripheral ends of the motor nerves and, according to Meltzer and Auer (*A. J. Phys.,* 1905, xiv, p. 366, and xvii, p. 313), also the sensory nerves. Guthrie and Ryan (*A. J. Phys.,* 1910, xxiv, p. 329) dispute the conclusions of Meltzer and Auer that it has a true anesthetic action, believing that the apparent anesthesia is due to the motor paralysis, but the experiments of Wiki (*A. I. P. T.,* 1911, xxi, p. 415) seem to demonstrate that when applied locally it is a paralyzant to the sensory nerves. As an internal remedy it has been employed by intraspinal injection as an anesthetic and in the treatment of *tetanus.* Its action in tetanus appears to be solely that of an anticonvulsant, not a true curative, and whether it has any superiority over other methods of controlling the convulsions is at present uncertain. As an antitetanic fifteen to thirty grains (1–2 Gm.) may be injected daily into the subarachnoid space in 10 per cent. solution. For intraspinal anesthesia, although it has been used with apparent success in a few cases, it appears to have no advantage over the cocaine series and has shown itself distinctly irritant to the kidney.

As a local remedy magnesium sulphate has proven useful in a large number of inflammatory conditions, its value probably to be attributed to its osmotic influence. Because of the fact that it does not diffuse readily, it attracts more water to itself than other salts. Not only is it widely employed as a local dressing in *sprains* and *bruises,* but Tucker (*T. G.,* 1907) and a number of subsequent investigators as Freese (*N. Y. M. J.,* Feb. 14, 1914) have reported favorable results in *erysipelas, cellulitis, epididymitis, lymphangitis* and similar external inflammations. Meltzer (*J. P. Ex. T.,* 1918, xii), from experiments upon rabbits as well as in observations on human beings, found a 25 per cent. solution to be of great value in the treatment of *burns* of both first and second degree. Morrison and Tulloch (*Brit. Journ. Surgery,* Oct., 1915, p. 276) have even recommended the local use of a sterilized solution of magnesium sulphate in septic wounds.

Following the suggestion of Meltzer that the intraduodenal application of magnesium sulphate produced a relaxation of the sphincter of the common bile duct, Lyon (*J. A. M. A.,* 1919, lxxii, p. 980) applied the drug by means of a duodenal tube in the diagnosis and treatment of *cholecystitis.* While the method has been more or less favorably commented on by several writers, Frazer (*J. A. M. A.,* 1922, lxxix, p. 1594) in experiments upon dogs was unable to note any constant action upon the flow of bile either from the liver or gall bladder.

As Christison reported the case of a boy ten years old who was said to have been killed by two ounces of the salt without the induction of purgation, it is possible that, under some circumstances, when very large amounts of magnesium sulphate are given by the mouth, sufficient may be absorbed to produce poisonous effects.

Dose, one to eight drachms (3.9–31 Gm.).

Off. Prep.—Infusum Sennæ Compositum, *U. S.;* Magnesii Sulphas Effervescens, *N. F., Br.;* Mistura Sennæ Composita, *Br.;* Liquor Magnesii Sulphatis Effervescens, *N. F.;* Sal Kissingense Factitium Effervescens, *N. F.;* Sal Vichyanum Factitium, *N. F.;* Sal Vichyanum Factitium Effervescens, *N. F.*

MAGNESII SULPHAS EFFERVESCENS. Br.

EFFERVESCENT MAGNESIUM SULPHATE

Magnesium Sulphuricum Effervescens; Magnesiæ Sulphas Effervescens; Effervescent Sulphate of Magnesia; Effervescent Epsom Salt; Brausendes Magnesiumsulfat, *G.;* Sulfato magnesico effervescente, *Sp.*

"Magnesium Sulphate, in crystals, 500 *grammes;* Sodium Bicarbonate, in powder, 360 *grammes;* Tartaric Acid, in powder, 190 *grammes;* Citric Acid, in powder, 125 *grammes;* Refined Sugar, in powder, 105 *grammes.* Dry the Magnesium Sulphate at about 55° C. until it has lost twenty-three per cent. of its weight; powder the dried product; mix it with the Refined Sugar and then with the other ingredients. Place the mixture in a dish or pan of suitable form heated to between 90° and 105° C. When the mixture, by the aid of careful manipulation, has assumed a granular character, separate it into granules of uniform and convenient size by means of suitable sieves. Dry the granules at a temperature not exceeding 55° C. The product weighs about one thousand *grammes.*" *Br.*

This effervescent salt is intended to furnish a less disagreeable form of administering Epsom salt. Although it represents only 50 per cent. of magnesium sulphate, it is almost equally active, both the sodium tartrate and citrate which are formed being laxative. A similar preparation is recognized by the N. F. (see Part III).

Dose, from two drachms to one ounce (7.7–31 Gm.).

MALTUM. U. S.

MALT

"Malt is the grain of one or more varieties of *Hordeum sativum* Jessen (Fam. *Gramineæ*), partially germinated artificially, and containing amylolytic enzymes." *U. S.*

Maltum Hordei; Barley Malt; Malt d'Orge, *Fr.;* Gerstenmalz, Malz, *G.*

Preparation.—Malt is prepared on an enormous scale for brewing purposes in many parts of the world where the climate is suited to the growth of barley. The object of the process for making malt, commonly known as malting, is to allow germination of grain to go just far enough to develop the maximum amount of diastase, the ferment by which the starch is converted into sugar, which may afterwards undergo the alcoholic fermentation during the process of brewing. In order to achieve this, the barley is first "steeped"—*i.e.,* allowed to remain one or two days in cold water, of which it absorbs from 10 to 50 per cent.; second, "couched"—*i.e.,* thrown into heaps upon a floor and allowed to develop heat and germinate; third, when the acrospire or shoot is one-third the length of the grain, the latter is "floored"—*i.e.,* spread upon wide floors to dry; fourth, kiln-dried—*i.e.,* exposed to such a temperature as thoroughly to dry it and kill the young plant. If the temperature be raised high enough to scorch the grain, it becomes *Amber Malt,* or *Black Malt,* according to the extent of the caramelizing; only the light colored varieties of malt are suitable for pharmaceutical purposes, the black varieties being practically devoid of diastatic value and being used for coloring mainly. Besides the diastase, a second soluble ferment is formed during the malting process, the so-called *peptase,* which in the after-mash process changes the proteids of the malt into peptones and para-peptones which give nutritive value to the beer. Malt contains the alkaloid *hordenine.* (See under *Hordeum,* Part II.)

Malt is now frequently germinated by what is called the pneumatic system in which the operation is carried out in large perforated iron drums which are caused to revolve very slowly, and in which the temperature is carefully regulated by ventilating fans. Another mechanical system of malting which is extensively used in some countries, especially in France, is based upon the principle of the ordinary conveyer, a separate section being used for each day that the germination lasts.

The commercial value of a sample of malt is determined by its diastatic power and also by its content of aqueous extract estimated under specified conditions. Between one-half and three-fourths of malt is soluble in cold water.

It is composed of germinated grains with the radicles and acrospires adhering.

Description and Physical Properties.—"Yellowish or amber-colored grains. Malt is crisp when broken, the interior surface being nearly white. It has an agreeable, characteristic odor and a sweet taste, due to the conversion of the starch of the seed into maltose through the action of the diastase. Malt floats on cold water. For the subsequent tests prepare an infusion as follows: Mix 10 Gm. of Malt, in coarse powder, with 100 cc. of distilled water, and maintain the mixture at a temperature of from 50° to 55° C. for one hour, occasionally stirring. Place it upon a filter, and, when the liquid has passed through, wash the contents of the filter with distilled water, in small portions, until the combined infusion and washings measure 200 cc.

"The weight of the solid soluble constituents of Malt, obtained by evaporating to dryness on a water bath an aliquot portion of the freshly prepared, aqueous infusion and drying the residue for one hour at 100° C., is not less than 70 per cent. of the Malt taken. The acidity of Malt, determined by titrating an aliquot portion of the freshly prepared infusion with tenth-normal sodium hydroxide, using phenolphthalein T.S. as indicator does not exceed 0.3 per cent. calculated as lactic acid.

"Preserve protected from heat and moisture." *U. S.*

Uses.—Malt is not itself used directly in medicine, but is official as the basis of Extract of Malt. From it are also prepared the so-called *Malt Liquors* by making an infusion (*wort*) of the bruised malt, adding hops and various other substances, and fermenting. *Ale, brown stout,* and *porter* are made by rapid fermentation at a comparatively high temperature 23.8 C., while *lager beer* is prepared by a very slow, prolonged fermentation at a low temperature.

Off. Prep.—Extractum Malti, *U. S.*

MALVÆ FOLIA. N. F.

MALLOW LEAVES Malv. Fol.

"Mallow Leaves consist of the dried leaves of *Malva sylvestris* Linné and of *Malva rotundifolia* Linné (Fam. *Malvaceæ*). Mallow Leaves contain not more than 10 per cent. of other parts of plants yielding the drug and not more than 5 per cent. of foreign organic matter." *N. F.*

Malva sylvestris; Mallow; Folia Malvæ, *P. G.;* High Mallow; Cheese-Cake Flower, Pancake Plant; Pick-Cheese, Maul, Round Dock.

M. rotundifolia: Low Mallow, Running Mallow, Dutch Cheese, Doll Cheese, Pellas.

The National Formulary recognizes two species of mallow. The *Malva sylvestris,* or high mallow, is an erect biennial herb with more or less sharply five- to seven-lobed leaves and reddish-purple flowers. The *M. rotundifolia,* common mallow, has an annual or biennial procumbent stem, and orbicular obscurely lobed leaves and pale blue flowers. The common term of "cheeses" is applied to these plants because of the peculiar shape of the fruit. These are circular, flattish, berry-like capsules consisting of numerous carpels united in a ring around a central axis from which they separate after ripening. Both of these species are natives of Europe and Western Asia, but have been more or less naturalized in the United States. The high mallow, however, is not very common in this country. The leaves often show brownish spots due to a fungous growth; when so infected they should not be used.

The commercial supplies of this drug are imported from Hamburg, Leghorn, Budapest and London. The drug is shipped in bales.

Description and Physical Properties.—"*Unground Mallow Leaves.*—Leaves of *Malva sylvestris,* petiolate with petioles up to 10 cm. in length, orbicular or reniform, slightly truncate or cordate at the base, from 10 to 11 cm. in length, and from 15 to 20 cm. in width, with 3 to 7 shallow, angular or rounded lobes, venation palmate, margins crenate-dentate, pubescent on both sides. Leaves of *Malva rotundifolia,* with petioles up to 20 cm. in length, orbicular, up to 8 cm. in width, base deeply cordate, 5 to 7 shallow lobes, venation palmate, margins with rounded blunt teeth, pubescence more scant than in *M. sylvestris.* Intermixed with the leaves are frequently found dark purple flowers and glabrous reticulated carpels (*M. sylvestris*) or pale bluish flowers and pubescent rounded carpels (*M. rotundifolia*). Inodorous; on chewing it becomes very mucilaginous, taste bland.

"*Structure.*—Epidermis containing mucilage cells; numerous stomata on both surfaces, each with 3 or 4 neighboring cells; trichomes of 3 distinct types, small short-stalked glandular hairs, single, large, one-celled curved hairs with thick walls and compound or stellate hairs in groups of 2 to 6 cells (the latter especially numerous in *M. sylvestris*); palisade tissue of 1 to 2 rows of cells, the spongy parenchyma of 3 or 4 rows; the parenchyma containing calcium oxalate in rosette crystals and numerous mucilage cells which are distributed in the tissue of the veins; veins with collateral bundles.

"*Powdered Mallow Leaves.*—Light green; exhibits the characteristic hairs, the single non-glandular hairs up to 1 mm. in length, occasionally longer, fragments of epidermal tissue with stomata, the latter up to 0.038 mm. in length; fragments of pith parenchyma, fibers and tracheæ from the stems; mucilage cells, fragments of spongy parenchyma and palisade, containing many branching vascular bundles, the tracheæ with spiral annular or reticulate markings; rosette crystals of calcium oxalate up to 0.025 mm. in diameter." *N. F.*

The herb and flowers have a weak, herbaceous, mucilaginous taste, without odor. They abound in mucilage, which they readily impart to water, and the solution is precipitated by lead acetate. The infusion and tincture of the flowers are blue, and have been used as indicators, being reddened by the acids and rendered green by alkalies. The roots and seeds also are mucilaginous. Common mallow is emollient and demulcent.

The infusion and decoction are sometimes employed in *catarrh, dysentery,* and *nephritis complaints,* and are applicable to all other cases which call for the use of mucilaginous liquids.

Off. Prep.—Species Emollientes, *N. F.*

MANACA. N. F.

MANACA Manac.

"Manaca is the dried root of *Brunfelsia Hopeana* Benth (*Franciscea uniflora* Pohl.) (Fam. *Solanaceæ*)." *N. F.*

Manacan, Vegetable Mercury, Geratacáca, Camgániba, Mercurio vegetal.

Brunfelsia Hopeana Benth. (*Franciscea Hopeana* Hook.; *F. uniflora* Pohl) is a slender shrub indigenous to Brazil and the West Indies. It possesses lanceolate-oblong, dark green leaves and small, pale violet-blue flowers, turning white with age and occurring solitary or in pairs along the leafy branches, and berry fruits.

Manaca occurs in pieces that are frequently longitudinally cut, of variable length and from 1 to 3 cm. thick. Externally the root is dark reddish-brown, longitudinally wrinkled; bark thin, scaly or flaky and adhering to reddish-yellow wood; fracture tough-fibrous; inner surface of bark reddish-brown and of wood, yellowish and radiate as viewed with hand lens; odor disagreeable; taste of bark sweet followed by a sharp bitter sensation; taste of wood slightly bitter.

Description and Physical Properties.—"*Unground Manaca.*—Nearly cylindrical or more or less tortuous, of variable length and up to about 3 cm. in diameter; externally dark brown, wrinkled and with scaly yellowish cork patches, the latter being easily removed from the thin cortex which adheres closely to the wood; inner surface, bark thin, wood light yellowish, hard and finely radiate; fracture short and very tough; taste bitter; odor slight.

"*Powdered Manaca.*—Pale yellow; consisting chiefly of fragments composed of thick-walled lignified fibers associated with rectangular medullary ray cells with thick lignified porous walls and with tracheæ having bordered pores, occasional fragments composed of cork cells with lignified walls or of cortical parenchyma containing a brownish amorphous content or spheroidal starch grains the latter up to about 0.015 mm. in diameter; thick-walled stone cells and occasional rosettes of calcium oxalate." *N. F.*

Miller described a substitute root which he found in samples formerly on the market in amounts ranging from 75 to 100 per cent. It was 7 to 25 mm. thick, yellowish-gray externally with bark twice as thick as that of manaca, neither scaly nor flaky and readily separable from the wood. The wood was softer than manaca, tasteless, of a pale yellow color, with medullary rays plainly visible, without magnification, and pores distinctly visible under a hand-lens. (See *Lilly Scientific Bull.*, 1913, ser. 1, no. 3, p. 115.)

Probably because of confusion among the various substances which are natively known as manaca, there has been some uncertainty as to its composition. Although some authorities have denied the presence of any alkaloid, Lenardson (*In. Dis.*, Dorpat, 1884) found in it a weakly basic substance, *manacine,* besides a fluorescent substance probably identical with gelsemic acid. Manacine is an amorphous bitter principle soluble in water and not precipitated by the alkaloidal reagents. In solution it easily decomposes into *manaceine* and a fluorescent substance probably identical with esculotin (dioxycoumarin).

Uses.—It is not very obvious what evidence of therapeutic value led to the recognition of this drug. Although it has been before the profession for many years, it never has achieved any widespread use. E. P. Bruer (*T. G.*, 1882), as the result of experiments made upon the lower animals, arrived at the conclusion that manaca acts upon the spinal cord, first stimulating, and then abolishing, the activity of the motor centers, the action being shared in by the respiratory centers. All the glands, especially the kidneys, were stimulated by it. In large doses he found it to produce in man lassitude, perspiration, and loose, greenish alvine discharges. Manaca has been used chiefly in the treatment of chronic or subacute *rheumatism* and *syphilis.*

Dose, of the fluidextract, from ten to thirty minims (0.6–1.8 cc.) three times a day.

Off. Prep.—Fluidextractum Manacæ, *N. F.;* Elixir Manacæ Compositum, *N. F.*

MANGANI CITRAS SOLUBILIS. N. F.

SOLUBLE MANGANESE CITRATE

Mangan. Cit. Sol. [Manganese and Sodium Citrate]

"Manganous citrate rendered soluble by the presence of sodium citrate. It contains, when dried to constant weight at 120° C., to not less than 48 per cent. and not more than 52 per cent. of $Mn_3(C_6H_5O_7)_2$ (542.93)." *N. F.*

For account of the sources and general properties of the metal manganese see Part II.

Description and Physical Properties.—"Soluble Manganese Citrate occurs as a yellowish or pinkish white powder, or as translucent scales; odorless, and having a slightly bitter and astringent taste. It is permanent in the air. One Gm. dissolves slowly in about 4 cc. of water; slightly more soluble in boiling water, nearly insoluble in alcohol.

"When strongly heated, it chars and finally leaves a residue which effervesces with acids and imparts an intensely yellow color to a non-luminous flame. An aqueous solution of Soluble Maganese Citrate (1 in 20) rendered alkaline with ammonia water, yields a salmon-colored precipitate on warming with ammonium sulphide T.S. Ten cc. of an aqueous solution of Soluble Manganese Citrate (1 in 20), slightly acidulated with acetic acid and mixed with 2 cc. of calcium chloride T.S., remains clear while cold, but yields a white crystalline precipitate when heated to boiling.

"Separate portions of 10 cc. each of an aqueous solution of Soluble Manganese Citrate (1 in 100), when acidulated with hydrochloric acid, are not more than slightly reddened by potassium thiocyanate T.S. (*iron*); nor rendered turbid at once by barium chloride T.S. (*sulphate*); nor show more than an opalescence with silver nitrate T.S. when acidulated with nitric acid (*chloride*). An aqueous solution of Soluble Manganese Citrate (1 in 20) is slightly acid or slightly alkaline to litmus, but does not redden phenol-phthalein T.S. Mix about 0.5 Gm. of Soluble Manganese Citrate with 5 cc. of sulphuric acid in a porcelain dish previously rinsed with sulphuric acid, protect the mixture from dust, and heat it for fifteen minutes on a water bath; no color darker than yellow develops (*tartrates or other readily carbonizable substances*). An aqueous solution of Soluble Manganese Citrate does not respond to the Test for heavy metals.

"**Assay.**—Dissolve about 0.5 Gm. of Soluble Manganese Citrate, previously dried to constant weight at 120° C. and accurately weighed, in 100 cc. of distilled water, add 50 cc. of solution of hydrogen dioxide, and 10 cc. of ammonia water, and boil the mixture for several minutes. Collect the precipitate on a filter, wash it thoroughly with hot distilled water, dry and ignite to constant weight. The weight of the manganous-manganic oxide (Mn_3O_4) so obtained is not less than 20.23 per cent. or more than 21.92 per cent. of the weight of the salt taken, corresponding to not less than 48 per cent. nor more than 52 per cent. of $Mn_3(C_6H_5O_7)_2$. Each Gm. of manganous-manganic oxide is equivalent to 2.3728 Gm. of $Mn_3(C_6H_5O_7)_2$." *N. F.*

Uses.—Because of the erroneous belief that manganese is a normal constituent of the blood certain French physicians many years ago were led to suggest its use as in *anemia.* Chemists of to-day, however, are agreed that when this element occurs in the blood it is only as an accidental—foreign—substance. The uselessness of the metal clinically was demonstrated by Garrod as far back as 1863. Its continued use is due chiefly to the vigorous advertising of certain proprietary nostrums.

Dose, two to five grains (0.12–0.3 Gm.).

Off. Prep.—Liquor Ferri Peptonati et Mangani, *N. F.*

MANGANI GLYCEROPHOSPHAS SOLUBILIS. N. F.

SOLUBLE MANGANESE GLYCEROPHOSPHATE

Mangan. Glycerophos. Sol. [Soluble Manganous Glycerinophosphate]

"Manganous Glycerophosphate rendered soluble by the aid of citric acid. It contains not less than 70 per cent. nor more than 75 per cent. of $MnC_3H_7PO_6$ (225.04)." *N. F.*

Description and Physical Properties.—"Soluble Manganese Glycerophosphate occurs as a yellowish or pinkish white powder, odorless, and having an acid taste. One Gm. dissolves in 4 cc. of water at 25° C. The aqueous solution is strongly acid to litmus and becomes turbid on heating. Alcohol dissolves the citric acid, leaving a residue which is nearly insoluble in water.

"Add an excess of ammonium sulphide T.S. to an aqueous solution of Soluble Manganese Glycerophosphate; on standing, it yields a salmon-colored precipitate soluble in acetic acid. No yellow turbidity is produced immediately on mixing 5 cc. of an aqueous solution (1 in 20) with 10 cc. of ammonium molybdate T.S. (*phosphate*), but on prolonged standing, or on heating, a yellow precipitate is formed. Heat a powdered mixture of about 0.1 Gm. of Soluble Manganese Glycerophosphate and about 0.5 Gm. of potassium bisulphate; pungent vapors of acrolein are evolved.

"Separate portions of 10 cc. each of an aqueous solution of Soluble Manganese Glycerophosphate (1 in 20) are not rendered more than slightly turbid by barium chloride T.S. when mixed with a few drops of hydrochloric acid (*sulphate*); nor by silver nitrate T.S. after acidulation with nitric acid (*chloride*). Add a few drops of hydrochloric acid and 1 cc. of chlorine T.S. to 10 cc. of an aqueous solution of Soluble Manganese Glycerophosphate (1 in 200) and boil; no reddish color is produced in the liquid by potassium thiocyanate T.S. after cooling (*iron*). An aqueous solution of Soluble Manganese Glycerophosphate does not respond to the Test for heavy metals.

"**Assay.**—Dissolve about 0.5 Gm. of Soluble Manganese Glycerophosphate, accurately weighed, in 100 cc. of distilled water, add 10 cc. of ammonia water and 5 cc. of ammonium sulphide T.S., and boil the mixture until the precipitate formed has become greenish. Allow the precipitate to settle, then transfer it to a filter, wash with hot distilled water containing a few drops of ammonium sulphide T.S., dry the filter and contents and incinerate them in an open crucible, first at a low temperature and then at strong red heat, until the weight is constant. The residue of manganous-manganic oxide (Mn_3O_4) so obtained is not less than 23.7 per cent. nor more than 25.4 per cent. of the weight taken, corresponding to not less than 70 per cent. nor more than 75 per cent. of $MnC_3H_7PO_6$. Each Gm. of manganous-manganic oxide is equivalent to 2.95 Gm. of $MnC_3H_7PO_6$.

Uses.—Whatever therapeutic virtue it may possess is due to its glycerophosphoric radicle. It is used in the treatment of *phosphaturia, deficient nerve nutrition, neurasthenia,* etc. It is rarely prescribed by itself but is an ingredient of the Compound Elixir of Glycerophosphates.

Dose, three to five grains (0.12–0.32 Gm.) several times daily.

Off. Prep.—Elixir Glycerophosphatis Compositum, *N. F.*

MANGANI HYPOPHOSPHIS. N. F.

MANGANESE HYPOPHOSPHITE [Mangan. Hypophos.]

"Manganese Hypophosphite contains not less than 97 per cent. of $Mn(PH_2O_2)_2.H_2O$ (203.06)." *N. F.*

Manganum Hypophosphorosum; Manganous Hypophosphite; Hypophosphis Manganosis; Hypophosphite de Manganèse, Hypophosphite Manganeux, *Fr.;* Unterphosphorigsaures Manganoxydul, *G.*

Manganese hypophosphite may be prepared by the interaction of manganese sulphate and calcium hypophosphite, by mixing a solution containing 1.31 parts of the former with a solution containing 1 part of the latter, filtering out the precipitated calcium sulphate, evaporating and crystallizing.

Description and Physical Properties.—"Manganese Hypophosphite is a pink, granular or crystalline powder; odorless and nearly tasteless; permanent in the air. It is freely soluble in water; insoluble in alcohol.

"An aqueous solution of the salt (1 in 20) is neutral or acid to litmus, and yields with ammonium sulphide T.S. a salmon-colored precipitate of manganese sulphide, soluble in acetic acid. When strongly heated in a dry test tube, the salt evolves spontaneously inflammable hydrogen phosphide and finally leaves a residue of manganous pyrophosphate. When an aqueous solution of the salt (1 in 20) acidulated with hydrochloric acid, is added, drop by drop with agitation, to an excess of mercuric chloride T.S. a white precipitate of mercurous chloride is formed, and, upon the further addition of the solution of Manganese Hypophosphite, the precipitate becomes gray from reduction to metallic mercury.

"Add about 0.5 Gm. of the salt to 5 cc. of acetic acid; no effervescence is produced (*carbonate*). Boil 0.25 Gm. of the salt with 10 cc. of sodium hydroxide T.S.; a white precipitate is formed which gradually acquires a brown color on exposure to the air. The filtrate from this mixture, after being slightly acidulated with hydrochloric acid, boiled for a minute, and then rendered alkaline with ammonia water, yields no precipitate upon the addition of magnesia mixture T.S. (*phosphate*). Dissolve 1 Gm. of the salt in 20 cc. of diluted hydrochloric acid with the aid of heat, and then add 1 cc. of barium chloride T.S.; not more than a slight turbidity is produced (*sulphate*). Dissolve 0.5 Gm. of Manganese Hypophosphite in 10 cc. of hot distilled water, add 10 cc. of solution of hydrogen dioxide and 10 cc. of sodium hydroxide T.S., boil for one minute, then render slightly acid with acetic acid and again warm. Now cool, filter, and add 1 cc. of ammonium oxalate T.S. to 10 cc. of the filtrate; no turbidity is produced within one minute (*calcium*). Pour 5 cc. of an aqueous solution of the salt (1 in 30) into an evaporating dish containing 3 cc. of nitric acid diluted with about 10 cc. of distilled water, and evaporate to dryness on a water bath; the residue meets the requirements of the Test for arsenic.

"**Assay.**—Dissolve about 1 Gm. of Manganese Hypophosphite, accurately weighed, in 30 cc. of boiling distilled water in a 250 cc. measuring flask. Add 25 cc. of solution of hydrogen dioxide and 15 cc. of sodium hydroxide T.S. and heat for ten minutes on a water bath with frequent agitation. Cool, add distilled water to make the volume exactly 250 cc., mix well and filter through a dry filter. Evaporate 25 cc. of the clear filtrate to dryness with 10 cc. of nitric acid, dissolve the residue in 10 cc. of nitric acid and again evaporate to dryness; then dissolve the residue in 10 cc. of distilled water, transfer it to a 100 cc. flask with the aid of a few cc. of distilled water, add a drop of phenolphthalein T.S. and sufficient sodium hydroxide T.S. (free from chloride) to produce a pink color, then add 50 cc. of tenth-normal silver nitrate and agitate the mixture well. Now gradually add zinc oxide (free from chloride) in small portions, agitating vigorously after each addition until the liquid is neutral to litmus. Then add distilled water to make 100 cc., agitate the mixture thoroughly, filter through a dry filter, collect 50 cc. of the filtrate, add 2 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate to the production of a permanent red color. Each cc. of tenth-normal silver nitrate used corresponds to 0.003384 Gm. of $Mn(PH_2O_2)_2.H_2O$. Each Gm. of Manganese Hypophosphite corresponds to not less than 286.6 cc. of tenth-normal silver nitrate.

"Preserve it in well-closed containers." *N. F.*

This salt probably possesses no medicinal virtues.

Dose, three to five grains (0.2–0.32 Gm.).

Off. Prep.—Liquor Hypophosphitum Compositus, *N. F.;* Syrupus Hypophosphitum Compositus, *N. F.*

MANNA. U. S.

MANNA

"Manna is the dried exudation of *Fraxinus Ornus* Linné (Fam. *Oleaceæ*). Manna yields not less than 75 per cent. of anhydrous alcohol-soluble extractive, using 90 per cent. alcohol." *U. S.*

Manne, *Fr. Cod.;* Manna, *P. G., It.;* Mana, *Sp.*

The term "manna" is applied to saccharine exudates from various trees. The official variety occurs on the manna ash, *Fraxinus Ornus.* The term "manna" has also been applied to certain substances which have no relation to true manna, notably to the lichen, *Lecanora esculenta,* which at times has suddenly fallen like rain over immense tracts of country, from Persia to the African Sahara. It occurs in the form of small roundish lumps, from the size of a pin's head to that of a pea, yellowish or grayish externally and whitish within, hard, inodorous, and insipid. It has been affirmed that this lichen does not contain starch, but it is really used as an article of food, and good bread is said to have been made out of it. (*Nature,* Jan., 1891.) It is probable that it is the manna of Scripture. In the *Chemist & Druggist,* xcii, p. 750, E. M. Holmes interestingly discusses the source of Biblical manna and expresses the belief that it was a fungus similar to that found in Central Africa in the district of Tanganyika.

Fraxinus Ornus, or the *European flowering ash,* is a tree of moderate height, usually from twenty to twenty-five feet, with opposite, petiolate, pinnate leaves, composed of three or four pairs of leaflets, and an odd one at the end. The leaflets are oval, acuminate, obtusely serrate, about an inch and a half in length, smooth, and of a bright green color. The flowers are white, and usually expand with the leaves. They grow in close panicles at the extremities of the young branches, and have a very short calyx with four teeth, and four linear-lanceolate petals.

The manna ash is a native of Southern Europe and is largely cultivated in Italy and Sicily. It yields manna after the eighth year, and continues to yield it for ten or twelve years, when it is usually cut down and young sprouts are allowed to grow up from the root. (Stettner, *A. Pharm.,* liii, 194.) During the hot months the juice exudes spontaneously from the bark, and concretes upon its surface, but, as the exudation is slow, it is customary to facilitate the process by making deep longitudinal incisions on one side of the trunk. In the following season these are repeated on the other side, and thus alternately for the whole period during which the tree yields manna. Straw or chips are frequently placed so as to receive the juice, which concretes upon them. The manna varies in its character according to the mode of collection, the nature of the season, and the period of the year at which the exudation takes place. For information on manna collection in Sicily, see notes by J. S. Ward. (*P. J.,* 1893, 381.)

Ebert (*Zeit. Oest. Apoth. Ver.,* xlvi, p. 427) has contributed a very able paper, containing citations of all the literature up to 1908, regarding the origin and pharmacognosy of the different varieties of manna. Probably the most comprehensive monograph on the ash manna is that of Tschirch in his large work entitled *"Handbuch der Pharmakognosie,"* Band II, p. 103.

In commerce the following varieties are distinguishable:

1. FLAKE MANNA, or *Manna canulata* (*cannellata*), is the purest variety, and is chiefly obtained from Palermo. It exudes spontaneously, or from incisions, during the hottest and dryest weather in July and August. According to Stettner, it is furnished by the upper incisions upon the trunk, while the lower incisions yield the inferior varieties. It is in irregular, elongated, flattened, 3-sided pieces, often several inches long, resembling stalactites, rough, light, porous, brittle, whitish or yellowish-white, and frequently concave on the surface by which they were attached to the trunk, and which is often soiled by impurities, sometimes by adherent fragments of the bark. The entire pieces vary from 10 to 25 cm. in length and constitute the *"long flake manna"* of commerce. When broken, these pieces exhibit a crystalline or granular structure. This variety is sometimes in small pieces, generally less than an inch in length, when it is called *"small flake manna."*

2. MANNA IN SORTS, *Manna communis,* is next in quality, and is collected in Italy and Sicily in September and the beginning of October, when the heat of the weather has begun to moderate. The juice does not now concrete so readily, and a portion, falling on the ground at the root of the tree, becomes more or less mixed with impurities, and forms imperfectly solid masses, which require to be further dried in the sun. Manna in sorts consists of whitish or yellowish fragments, similar to the pieces of flake manna, but much smaller, mixed with a soft, viscid, uncrystallized brownish matter.

Most of the world's supply of manna is yielded by five Italian provinces. Flake manna is produced in Capaci, Geraci and Frassino, these yielding in order 62.15 per cent., 62 per cent., and 47 per cent. of mannite. Manna in sorts is produced in Capaci, Geraci and Castelbuono, yielding respectively 37 to 55 per cent., 37 per cent., and 28 to 30 per cent. of mannite.

Manna is shipped to the United States in cases from Palermo, Italy, only the large and small flake varieties being imported at present. The chief past adulterants for manna have been glucose, sucrose and bread crumbs.

Fictitious Manna.—Attempts have been made to counterfeit manna, but the facility of detection renders such frauds unprofitable, and they are not often practised. R. P. Thomas described (*A. J. P.*, xxiv) a sophisticated manna which differed from the genuine drug both in sensible and in chemical properties, not even containing mannite. Baumé describes a method in which common manna is purified so as to resemble flake manna. It consists in dissolving common manna in a little water, allowing the liquid to settle, decanting it in order to separate the impurities, then inspissating it so that it will congeal on cooling, and immersing threads in the inspissated liquid, several times successively, in the manner practised by candle makers. It may be still further purified by the use of animal charcoal. Thus prepared, it contains less mannite than flake manna, and less of the nauseous principle, but is said not to operate less effectively as a laxative.

Description and Physical Properties.—"In irregular, more or less elongated, flattened, 3-sided pieces; externally yellowish-white; friable; internally nearly white, porous and crystalline in appearance; odor slight; but characteristic; taste sweet, slightly bitter and faintly acrid. Also in irregular masses, consisting in part of brittle or soft fragments from yellowish-white to yellowish-gray in color. The quantity of these yellowish-white fragments must not be less than 40 per cent. of the whole.

"**Assay.**—Proceed as directed under alcohol-soluble extractive, using boiling 90 per cent. alcohol, by volume, and filter rapidly through purified cotton while hot, washing the cotton with boiling alcohol." *U. S.*

Manna has a slight, peculiar odor, and a sweet taste, which in the impure kinds is also very nauseous, but in the finest flake manna scarcely so much so as to be disagreeable. Its sp. gr. is 0.834. It melts with heat, and takes fire, burning with a blue flame. When pure it is soluble in three parts of cold and in its own weight of boiling water. From a boiling saturated aqueous solution it separates in partially crystalline masses on cooling. Alcohol also dissolves it. Boiling alcohol will dissolve 15 parts of manna, and upon cooling deposit beautiful crystals of mannite.

Constituents.—Manna is variable in its constituents. The principal constituent, mannite, ranges from 30 to 90 per cent., the lower percentage being in the poorer varieties and the higher percentage in the better varieties of this drug. Sucrose and invert sugar ranges in amounts from 2 per cent. to 30 per cent., the higher amounts being in the lower grades of manna. There is also present gum, dextrin and traces of citric acid, and *fraxin.* Tanret, after an exhaustive investigation of manna, reported the following carbohydrates as having been identified by him: Mannite, dextrose, levulose, *mannotetrose,* and *mannotriose.* The manna which occurs in tears and distinct fragments is much higher in mannitol than other grades.

The greenish color of certain pieces of manna is produced by *fraxin,* $C_{16}H_{18}O_{10}$, a glucoside closely resembling æsculin. Fraxin crystallizes in colorless prisms, easily soluble in hot water and in alcohol, and has a faintly astringent and bitter taste. By diluted acids it is resolved into *fraxetin,* $C_{10}H_8O_5$, and glucose, $C_6H_{12}O_6$. Even its diluted solutions are fluorescent.

Mannite (*mannitol* or *hexanhexol*) is white, inodorous, crystallizable in semi-transparent needles, of a sweetish taste, soluble in five parts of cold water, scarcely soluble in cold alcohol, but readily dissolved by that liquid when hot, and deposited when it cools. Its composition is $C_6H_{14}O_6$, and it is considered as belonging to the class of hexatomic alcohols. It was discovered by Proust in manna in 1806. With lime, barium and strontium oxides, it forms definite compounds, soluble in water, and precipitable from their aqueous solutions by alcohol. It does not reduce an alkaline solution of copper oxide; and a test of its purity is thus presented. Emil Fisher has shown that there are three mannites obtainable; the ordinary mannite is the dextrorotatory variety, and is always obtained in the reduction of *a-mannose* with sodium amalgam; a lævorotatory variety is obtained by the reduction of *l-mannose;* and an inactive mannite is obtained from the inactive mannose. These three physical isomers differ slightly in their fusing points and crystalline form. The native variety may be obtained by boiling manna in alcohol, allowing the solution to cool, and redissolving the crystalline precipitate; pure mannite is now deposited. Another method is to dissolve flake manna in water, precipitate by solution of lead subacetate, filter, throw down the excess of lead by sulphuric acid, evaporate the solution, and mix with alcohol. On cooling, the mannite is deposited. (Bonsall, *A. Pharm.*, cxxxiv, 70.) Mannitol occurs in the larch, celery and sugar cane in small amounts. *Agaricus integer* contains 20 per cent. of mannitol. When heated mannitol yields two anhydrides, *mannitan*, $C_6H_{12}O_5$, and *mannide*, $C_6H_{10}O_4$. There are four stereo-isomerides known. They are *dulcitol, sorbitol, talitol* and *iditol.* Dulcitol occurs in a number of plants naturally, the others are synthetic products. Mannitol hexanitrate is described under *Nitrated Alcohols*, Part II. It is said to be gently laxative in the dose of from one to two ounces (31–62 Gm.).

Manna, when long kept, acquires a deeper color, softens, and ultimately deliquesces into a liquid, which on the addition of yeast undergoes the vinous fermentation. This is probably owing to its conversion into sugar by the absorption of enough oxygen to cause it to pass over into some variety of glucose or fermentable sugar. That which is driest resists this change the longest. It is said that manna recently gathered is less purgative than it afterwards becomes.

A number of exudates from other sorts of trees have from time to time appeared in the markets under the name of manna; these *false mannas* are to-day of no commercial importance but the following are those which in the past have had more or less prominence; for further information concerning these see *U. S. D.*, 20th ed., p. 685.

European False Manna, or *Briançon Manna,* an exudation from the common European larch (*Larix europæa*, or *Pinus Larix*), differs chemically from ordinary manna in containing no mannite. Berthelot (1859) found in it a sugar, *melezitose.*

California Manna, or *Father Picolo's Manna.*—Proust (1806) alluded to a manna mentioned by Father Picolo as being deposited on a species of grass in California. J. U. Lloyd (*A. J. P.*, 1897, 337) believes Picolo's manna to be a saccharine deposit, caused by aphides on *Phragmites communis.* It is apparently still collected by the Indians.

Turkish Manna is a sweet product obtained from *Echinops persica* Fisch., and is obtained by treating the cocoons of a coleopterous insect (*Larinus maculatus*) with hot water, filtering and crystallizing the sugar. From it Berthelot (1857) obtained sugar, trehalose. *Pinus Cedrus,* of Mount Lebanon, yields a similar product, which has some repute in Syria as a remedy in *phthisis.* (*P. J.*, xiii, 411.) In the neighborhood of Diarbekir, in Asiatic Turkey, a saccharine substance, known as *Diarbekir Manna,* is found on the leaves of dwarf oaks, from which it appears to be exuded. *Quercus Valonea* Kotschy, and *Q. persica* Jaub. et Spach, yield "*oak manna,*" through insect agency.

Persian Manna.—Several manna-like exudates are, or were, produced in Persia. Of these, *Gez* has been identified (*C. D.*, 1894) as being derived from the *Astragalus anisicanthus* (Fam. *Leguminosæ*). *Chirkhest* appears to come from the *Salix fragilis* L. and perhaps other species of willow.

Taranjabin, or *Alhagi Manna,* is yielded by the camelthorn, *Alhagi Camelorum* Fisch., in Persia and Afghanistan, and probably by *Alhagi Maurorum* Tournefort, a leguminous thorny shrub abundant in India—if indeed the two species be distinct. According to A. Villiers, it is nearly pure melezitose. (*P. J.*, 1876.) *Gazanjabin,* or *Tamarisk Manna,* is yielded by *Tamarix gallica* var. *mannifera* Ehrenberg (Fam. *Tamariscinæ*).

Several sweet exudates have been sold in the Indian bazaars. Of these the most important is the *Shirkoit,* or *Oriental Manna.* By Haussknecht it is referred to *Atraphaxis spinosa;* but J. E. T. Atchison states that it is yielded by the *Cotoneaster nummularia* Fisch. et Mey., a tall, stout shrub, whose smaller branches in July become covered with an exudation. *Bamboo Manna,* or *tabashir,* is obtained from the surface of the stems of the *Bambusa stricta* Roxb. (Fam. *Graminæ*).

Australian Mannas.—A manna-like exudation on the *Eucalyptus viminalis* Labill., growing in New South Wales, contains melitose. (See *A. J. P.*, xxviii, 157.) *Lerp* is produced upon the leaves of *Eucalyptus dumosa,* when very small, and sometimes appears spread over large extents of country like a kind of snow. *Myoporum platycarpum* R. Brown, the *sandalwood-* or *dogwood-tree* of Australia, exudes an exceedingly sweet and pleasant manna, which is much used as an article of food, the product containing nearly 90 per cent. of mannite. F. W. Passmore obtained from *Eucalyptus Gunnii* Hook., a sugar termed *melitriose.* (*P. J.*, 1891, 718.) *Blue Grass Manna* is, according to R. T. Baker (*Journ. and Proc. Roy. Soc. New South Wales*, xxx, 1897), produced in the form of nodules at the nodes of the stems of the blue grass *Andropogon annulatus.* It contains numerous crystals of mannite, amounting, according to the analysis of H. G. Smith, to 50 per cent.

Uses.—Manna is a gentle laxative, usually operating mildly, but in some cases producing flatulence and pain. It is usually prescribed with other purgatives, particularly senna, rhubarb, magnesia, and the neutral salts, the taste of which it conceals, while it adds to the purgative effect. It is usually given dissolved in water or some aromatic infusion; but the best flake manna may be administered in substance. Manna forms a combination with iron, which it preserves against oxidation. (See *P. J.*, March, 1873.) Under the name of *dulcinol* a mixture of mannite and common salt has been recommended by Sternberg (*D. M. W.*, 1906, p. 1707) as a sweetening agent in *diabetes.*

Dose, half to one ounce (15.5–31 Gm.).

Off. Prep.—Infusum Sennæ Compositum, *N. F.;* Syrupus Mannæ, *N. F.*

MASSA FERRI CARBONATIS. U. S.

MASS OF FERROUS CARBONATE Mass. Ferr. Carb. [Vallet's Mass.]

"Mass of Ferrous Carbonate contains not less than 35 per cent. of $FeCO_3$." *U. S.*

Pilula Ferri Carbonatis, *Br.* 1885, also *U. S.* 1870; Pilulæ Ferri Carbonici, Pilulæ Ferratæ Valleti; Pill of Carbonate of Iron, Vallet's Ferruginous Pills, Vallet's Pill Mass; Pilules de Carbonate ferreux, *Fr. Cod.;* Pilules ferrugineuses, Masse Pilulaire de Vallet, *Fr.;* Valletsche Pillen, *G.;* Pillole di Vallet, *It.*

"Ferrous Sulphate, 100 Gm.; Monohydrated Sodium Carbonate, 46 Gm.; Honey, 38 Gm.; Sucrose, in coarse powder, 25 Gm.; Syrup, Distilled Water, each, a sufficient quantity to make 100 Gm. Dissolve the ferrous sulphate and monohydrated sodium carbonate, each, separately, in 200 cc. of boiling distilled water, and, having added 20 cc. of syrup to the solution of the iron salt, filter both solutions, and cool. Place the solution of sodium carbonate in a bottle having a capacity of about 500 cc. and gradually add the solution of the iron salt, rotating the bottle frequently, until carbon dioxide no longer escapes. Add sufficient distilled water to fill the bottle, stopper tightly and set it aside so that the ferrous carbonate may subside. Pour off the supernatant liquid, and, having mixed syrup and distilled water in the proportion of 1 volume of syrup to 19 volumes of distilled water, wash the precipitate with the mixture by decantation until the washings no longer have a saline taste. Drain the precipitate on a muslin strainer, and express as much of the water as possible. Then mix the precipitate at once with the honey and sucrose in a tared dish, and by means of a water bath evaporate the mixture with constant stirring until it is reduced to 100 Gm." *U. S.*

"**Assay.**—Dissolve about 1 Gm. of Mass of Ferrous Carbonate, accurately weighed, in 15 cc. of diluted sulphuric acid, dilute the solution with distilled water to about 100 cc., and immediately titrate with tenth-normal potassium dichromate, potassium ferricyanide T.S. being used as indicator. Each cc. of tenth-normal potassium dichromate corresponds to 0.01159 Gm. of $FeCO_3$." *U. S.*

The effect of saccharine matter in protecting iron from oxidation has been explained under the heads of *Ferri Carbonas Saccharatus* and *Syrupus Ferri Iodidi.* The U. S. mass of ferrous carbonate is another example of a ferruginous preparation in which the iron is protected from further oxidation by the same means. The process of the U. S. X is nearly the same as that of the previous pharmacopœia. The salts employed are the same as those used for obtaining the formerly official ferric subcarbonate; this was misnamed, as in forming that preparation the carbonate, which is at first precipitated, absorbs oxygen and loses nearly all its carbon dioxide in the processes of washing and drying. When, however, as in the U. S. formula above given, the reacting salts are dissolved in weak syrup instead of water, and the washing is performed with weak syrup also, the absorption of oxygen and loss of carbon dioxide during the separation of the precipitate are almost completely prevented. It only remains, therefore, to preserve it unaltered, and to bring it to the pilular consistence, and this is effected by admixture with honey and sugar, and evaporation by means of a water bath. It is essential to the success of this process that the ferrous sulphate should be pure, otherwise some ferric oxide will be present in the product. The process is that of Vallet, of Paris, after whom the preparation is popularly called.

The British Pharmacopœia, 1898, omitted Vallet's mass. (See *Ferri Carbonas Saccharatus.*) Gonnermann prepares *powdered Vallet's mass* by mixing intimately ten parts of milk sugar and five parts of powdered licorice root with sufficient freshly precipitated ferrous carbonate to make, when dried, thirty-five parts, and adding enough powdered licorice root to make the whole weigh forty parts. (*Ph. Post,* 1893, 238.)

Properties.—The U. S. preparation is in the form of a soft pilular mass, of a dark greenish-gray color, becoming black on exposure, and with a strong ferruginous taste. When carefully prepared, it is wholly and readily soluble in acids. It contains nearly half its weight of ferrous carbonate. The corresponding pill, obtained from the saccharine carbonate, may be supposed to contain one-third of ferruginous matter.

Uses.—The U. S. mass of ferrous carbonate, or Vallet's ferruginous mass, is an excellent preparation for use in simple *anemia* and *chlorosis.* Its chief merits are its unchangeableness, its freedom from astringency, and its ready solubility in acids.

Dose, in pills, from three to five grains (0.20–0.32 Gm.), after meals.

MASSA HYDRARGYRI. U. S. (Br.)

MASS OF MERCURY Mass. Hydrarg. [Blue Mass Blue Pill]

"Mass of Mercury contains not less than 32 per cent. nor more than 34 per cent. of Hg." *U. S.*

Pilula Hydrargyri, *Br.;* Mercury Pill; Pilulæ Hydrargyri, *U. S.* 1870; Pilulæ Cœruleæ, Massa Cœrulea; Pills of Mercury; Mercurial Pill; Pilules mercurielles simples, *Fr. Cod.;* Pilule de Mercure, Pilules bleues, *Fr.;* Mercurialpillenmasse, *G.*

"Mercury, 33 Gm.; Oleate of Mercury, 1 Gm.; Glycyrrhiza, in very fine powder, 10 Gm.; Althea, in very fine powder, 15 Gm.; Glycerin, 9 Gm.; Honey of Rose, 32 Gm.; to make 100 Gm. Triturate the oleate of mercury in a warm mortar, gradually add the mercury, then introduce a small amount of honey of rose, and triturate the mixture until globules of mercury are no longer visible under a lens magnifying ten diameters. Incorporate the remainder of the honey of rose and the glycerin, gradually add the glycyrrhiza and althea, and continue the trituration until the mass is homogeneous." *U. S.*

"Mercury, 40 *grammes;* Confection of Roses, 60 *grammes;* Liquorice Root, in powder, 20 *grammes.* Triturate the Mercury with the Confection of Roses until metallic globules are no longer visible; add the Liquorice Root; mix to form a mass." *Br.*

"**Assay.**—Place about 0.5 Gm. of Mass of Mercury, accurately weighed and rolled into one or two pills, in a Kjeldahl flask of about 300 cc. capacity. Add 10 cc. of sulphuric acid, and heat on a water bath during ten minutes, gently agitating at frequent intervals to disintegrate the mass. Insert a small funnel in the neck of the flask, and slowly add 10 cc. of nitric acid. Heat the mixture with a Bunsen burner, at first gently, gradually increasing the heat until the solution is colorless or only slightly yellow, adding more nitric acid if necessary, and keep the funnel in the neck of the flask during heating. Allow the solution to cool sufficiently, and add carefully through the funnel about 30 cc. of distilled water, rinsing the stem of the funnel with a few cc. of distilled water and allowing the rinsings to run into the flask. Then add to the warm solution, potassium permanganate T.S. until a slight pink color persists. Cool the solution, discharge its color by the addition of just sufficient oxalic acid T.S., add 3 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate to a permanent reddish color. Each cc. of tenth-normal potassium thiocyanate corresponds to 0.01003 Gm. of Hg." *U. S.*

The precise condition of the mercury in this preparation is somewhat uncertain. By far the greater proportion is in a state of minute mechanical division, and not chemically altered. Some maintain that the whole of the metal is in this state, others, that a small portion is converted during the trituration into mercurous oxide, and that this is the ingredient upon which the activity of the pill depends. Harold Senier (*P. J.,* 1876) analyzed a number of samples of blue mass, with the view of determining the amount of metallic mercury and of mercurous and mercuric oxides. The results showed that the latter gradually increased in quantity with the age of the blue mass, which, 18 hours after preparation, contained but a trace of mercurous oxide; after three months, 0.24 per cent. of mercuric and 0.62 per cent. of mercurous oxides were obtained, and in another sample, 0.44 and 1.60 per cent., respectively. After two years, 1.80 per cent. of mercuric and 4.22 per cent. of mercurous oxides were present. It is obvious that the effects of the preparation are not due to the oxide. The U. S. VIII provided a test which limited the quantity of mercurous oxide and proved the absence of mercuric oxide; it will be difficult for the ordinary "blue mass" of commerce to withstand these requirements: "If a portion of the Mass be triturated in a mortar, with warm acetic acid, the filtrate should not become more than slightly opalescent on the addition of a few drops of hydrochloric acid (limit of *mercurous oxide*). If another portion of the Mass be digested with warm, diluted hydrochloric acid and a little purified animal charcoal, the filtrate should not be affected by hydrogen sulphide T.S., or by stannous chloride T.S. (absence of *mercuric oxide*)." *U. S. VIII.*

All agree that the efficacy of the preparation is proportionate to the extinguishment of the mercury; in other words, to the smallness of the metallic globules. This may be effected by trituration with various substances, and manna, syrup, honey, licorice, mucilage, soap guaiac, and extract of taraxacum have been recommended, among others, for this purpose; but the oleate of mercury has been adopted by the U. S. P. as less open to objection than any other. The mercury is known to be completely extinguished when, upon rubbing a portion of the mass with the end of the finger upon a piece of paper, no globules appear, or the extinguishment may be more accurately judged by the official microscopic test. Powdered licorice root and powdered marshmallow root are added in order to give due consistence to the mass. It is possible for the apothecary to make moderate quantities extemporaneously with no other appliances than the mortar and pestle. As the trituration requires to be long continued, which renders the process very laborious, when conducted on the large scale it is customary to prepare the mass by machinery. A machine for preparing blue mass, capable of being worked by hand or steam power, invented by J. W. W. Gordon, of Baltimore, was at one time in extensive use. (*A. J. P.*, xxi, 6.) A more modern method is to extinguish the mercury in the original iron cylinder, or "flask" in which mercury is shipped, by mechanical agitation with the oleate of mercury and honey of rose, and then incorporate the other ingredients in a mixing machine. The preparation slowly changes color upon being kept, assuming an olive and sometimes even a reddish tint, in consequence, probably, of the further oxidation of the mercury.

The blue pill is sometimes wanted in the state of powder, but, from its peculiar constitution, it is not eligible for reduction to this form, as the mercury is disposed to aggregate during pulverization, and, from the honey it contains, it is likely, when pulverized, to attract moisture from the air. Chas. Bullock recommended the following method of preparing a powder which, as nearly as possible, represents the blue pill, in reference to its therapeutic effects:

Powdered Blue Mass.—Take of finely powdered Elm bark, finely powdered Sugar, and Mercury, equal parts, and of Alcohol a sufficiency. Rub the mercury with the powdered bark, adding from time to time enough alcohol to maintain a pasty consistence, until the mercury is completely extinguished; then spread the mass on paper to dry. When dry, powder it, add the sugar, and rub the mixture thoroughly until the powder will pass through a sieve of fine bolting cloth.

Uses.—Blue mass has the therapeutic properties of the mercurials (see *Hydrargyrum*), but is to-day chiefly employed for its cathartic action. It seems to be somewhat less irritant than calomel and the purgation caused is less frequently accompanied with griping. When used as a cathartic it is sometimes necessary to follow it after some hours with a saline.

Dose, as an alterative, one to three grains (0.065–0.2 Gm.), as a laxative, from five to fifteen grains (0.32–1.0 Gm.).

Off. Prep.—Pilulæ Aloes, Hydrargyri et Podophylli, *N. F.;* Pilulæ Digitalis, Scillæ et Hydrargyri, *N. F.*

MASTICHE. N. F.

MASTIC

"Mastic is a concrete resinous exudation from *Pistacia Lentiscus* Linné (Fam. *Anacardiaceæ*). Mastic contains not more than 1 per cent. of foreign organic matter." *N. F.*

Mastich; Mastix; Mastic, *Fr.;* Resina Mastiche, *G.;* Almaciga, Mastic, *Sp.;* Sakes, *Turk.;* Arah, *Arab.*

The mastic tree, which is also called *lentisk* or *lentiscus,* is a shrub or small tree, seldom more than twelve feet in height, much branched towards the top, and furnished with petiolate, abruptly pinnate leaves. The flowers are diœcious, and very small. The tree is a native of the countries bordering upon the Mediterranean. The fruit yields by expression a fixed oil, of a deep green color, and liquid at about 32.3° C., which the Arabs use both as an article of diet and for light. A resinous exudation from the stem and branches is the official part, but it does not appear to be collected in all places where the tree flourishes. Under the names of *Bombay mastic* and *East Indian mastic,* there occur in India masses of oleoresin said to be derived from the *Pistacia Khinjuk* Stokes and probably other species of *Pistacia,* having the general appearance of true mastic with a darker color, but lacking fragrance, and dissolving in hot alcohol.

The mastic imported into the United States and Great Britain is obtained only from the island of Scio, or Chios, in the Grecian Archipelago, where the tree is cultivated for this product. Incisions are made in the trunk and principal branches, from which the juice slowly exudes, and either hardens in tears upon the bark, or drops on the ground, where it is received upon cloths or the bare earth, and concretes in irregular masses. The tears are most esteemed, and are the only form recognized by the N. F. They are of various sizes, oval or roundish, often compressed, smooth, semi-transparent, of a pale-yellow color, of a shining fracture, friable, and usually covered with a whitish powder, occasioned by their friction against each other. They are brittle, but unlike Sandarach become plastic when chewed. The masses consist of yellowish agglutinated tears, with others of a darker color and less translucent, and often fragments of wood, bark, or earthy matter intermingled.

According to J. Léon Subeiran, the valuable tears are produced by spontaneous exudation from the branches. But the greater part of the resin comes from longitudinal incisions in the stem, made with a knife, close together and extending from the root to the branches. In fifteen or twenty days the resin has concreted, and is collected in little panniers of white paper or cotton cloth. (*Proc. A. Ph. A.,* 1897, 563.)

Chian turpentine, which is also collected in the island of Chios, as well as in Cypress, is from the *Pistacia Terebinthus.* It is a thick tenacious liquid varying from yellow to green in color, with an odor similar to but more pleasant than, that of turpentine. On exposure to air it thickens into a translucent yellowish mass.

For description of the mode of production, etc., see *Proc. A. Ph. A.,* 1897, p. 563. It was recommended by Clay, of England in 1880 as a local application for *uterine cancers.*

Description and Physical Properties.—"In sub-globular, lenticular, elongated or pear-shaped tears, about 3 mm. in diameter, pale yellow or greenish yellow, transparent, having a glass-like luster, the surface sometimes very slightly dusty; brittle, becoming plastic when chewed. Odor slight, balsamic; taste mild, terebinthinate.

"Not less than 97 per cent. of Mastic is soluble in ether and not less than 80 per cent. is soluble in alcohol. The acid number is not less than 50." *N. F.*

Mastic is nearly inodorous, unless rubbed or heated, when it becomes fragrant. Its taste is weak, but agreeably terebinthinate, and, after long chewing, very slightly acrid. It is at first friable under the teeth, but soon becomes soft and ductile, and acquires a white, opaque appearance. Its sp. gr. is 1.074. It is fusible and inflammable by heat.

Alcohol dissolves about 90 per cent. of it. The insoluble residue is a viscid substance which becomes brittle when dried, and for which the name of *masticin* or *betaresin of mastiche* has been proposed. This substance, though not dissolved by alcohol, softens and swells up in it, as gluten does in water. Hlasiwetz gives $C_{20}H_{31}O$ as the formula of the resin. The portion dissolved by the alcohol is called by Johnston *alpha resin of mastiche* or *mastichic acid* because of its acid properties, and has the formula $C_{20}H_{32}O_2$. (*Handwörterbuch der Chemie,* iv, p. 280.) Schimmel & Co. (*Schim. Rep.,* April, 1897) state that mastic resin yields from 0.9 to 2.5 per cent. of a powerful balsamic essential oil of the same odor as the raw material, a sp. gr. of from 0.855 to 0.87 at 15° C., and an optical rotation (100-mm. tube) of from $+22°$ to $+27°$. Tschirch and Reutter (*A. Pharm.,* 1904, 104) examined mastic carefully; they found approximately 42 per cent. of free resin acids. These are: the isomeric α- and β-masticinic acids, $C_{23}H_{36}O_4$, *masticolic acid,* $C_{23}H_{36}O_4$ (slight amount), amorphous α-masticonic acid, $C_{32}H_{48}O_4$ (20 per cent.), and β-masticonic acid, $C_{32}H_{48}O_4$ (18 per cent.). Besides this, mastic contains 30 per cent. α-masticoresin, $C_{35}H_{36}O_4$, soluble in alcohol; 20 per cent. of β-masticoresin (masticin), insoluble in alcohol, and 2 per cent. of an ethereal oil, possessing a pale yellow color and a somewhat camphoraceous odor. Finally, there is also a bitter principle, which could not be isolated in pure form. For a chemical investigation of Egyptian mastic by Reutter, see *S. W. P.,* 1913, 537.

Mastic is occasionally adulterated with olibanum, sandarach, and other resinous bodies, and, in seasons of scarcity, with sea salt.

Uses.—Mastic was formerly thought to possess properties analogous to those of the turpentines, and was used in *debility of the stomach, hemoptysis* from ulcerations, *leucorrhea, chronic diarrhea,* etc.; but its virtues were overrated, and it is at present scarcely ever given internally except in certain cathartic pills. In the East, however, an aqueous infusion is said to be still used in *cholera infantum.* Dissolved in alcohol or oil of turpentine, it forms a brilliant varnish. A solution made by macerating half an ounce of mastic and fifteen grains of caoutchouc in two fluidounces of chloroform, and filtering in closed vessels, forms a valuable *varnish* for microscopic work. The following mode of applying it to carious teeth has been recommended. Dissolve four parts of mastic in one of ether, in a bottle well stoppered. With the solution thus formed, which is yellow and of an oily consistence, saturate a small piece of cotton of the size of the carious cavity, and, having well cleansed and dried the cavity, introduce the cotton, without painful pressure, so as to fill it exactly. The resin attaches itself to the diseased surface of the tooth, which it protects from the air, and from the food taken into the mouth. It has been highly recommended by various surgeons as a dressing for wounds. Its use is chiefly for the purpose of preventing bacteria upon the surrounding skin getting into the wound. Voos (*M. M. W.,* 1911) paints the skin up to the edges of the wound without previous washing, with a solution of mastic in benzol and then cleanses the wound in the ordinary manner and applies an aseptic dressing. A *mastic varnish,* made with chloroform, is official in the N. F. Another preparation of a similar nature is upon the market under the name of *mastisol.*

Dose, thirty grains (2 Gm.).

Off. Prep.—Pilula Aloes et Mastiches, *N. F.;* Solutio Mastiches Chloroformica, *N. F.*

MATICO. N. F.

MATICO Matic.

"Matico is the dried leaf of *Piper angustifolium* Ruiz et Pavon (Fam. *Piperaceæ*). Matico contains not more than 5 per cent. of stems, flower spikes or other foreign organic matter, and yields not more than 6 per cent. of acid-soluble ash." *N. F.*

Feuilles de matico, *Fr. Cod.;* Maticoblätter, *G*

Piper angustifolium is a shrub with a jointed stem and 4-angled branches about twelve feet in height. The leaves are short-petioled, alternate and lanceolate with finely scalloped margins, acute apex, subcordate base and tessellated upper surface. The flowers are small, yellow in color and borne in slender axillary spikes. The fruit is a small, reddish-brown drupe containing a single seed. The plant is a native of Peru, where the fruit, under the name of *thohothoho,* is employed in the same manner as cubeb. This species is also found in other parts of South America. The commercial drug matico is furnished, according to G. Dethan and R. Bertault (*J. P. C.,* 1897, 537), by two varieties of *Piper angustifolium*—viz., *α-cordulatum* (*Artanthe elongata* Miq.), and *β-ossanum,* which differ somewhat in the shape of the leaves. The former has the leaves larger, shorter, and broader, with an oblique cordate base. The midrib of *α-cordulatum* is much less convex below than in the other variety. The leaves of other species of *Piper* have occasionally been found admixed with commercial lots of matico.

Description and Physical Properties.—"*Unground Matico.*—Usually in compressed, matted masses with leaves more or less broken;

leaves short petiolate, lanceolate, about 4 times as long as broad, from 10 to 20 cm. in length and from 2 to 5 cm. in breadth; apex tapering and acute; base slightly unequal, cordate, margin finely crenulate; upper surface dark green, distinctly tessellated; lower surface pale green, reticulate with prominent, yellowish brown midrib and veins forming small quadrangular meshes clothed with matted pubescence. Odor distinct, aromatic; taste pungent, pepper-like.

"*Structure.*—Epidermis of the upper side composed of regular polygonal cells and of the lower side of somewhat irregular and undulate cells, especially where covering the veins; numerous stomata, with large neighboring cells, on the lower side; the hypodermis of one or more rows of cells and palisade cells in 2 or 3 rows; loose spongy tissue; outer layer of mid-rib of thick-walled cork cells; secretion cells filled with yellow oil; upper surface with papillæ and few bristly hairs; hairs of the lower surface of two kinds, the one, 6 to 10 cells in length, pointed, bent and matted, having thick walls and a striate cuticle; the other, bristle hairs of one stem cell and a head cell; calcium oxalate crystals few in parenchyma tissue of the venation, in the form of raphides or monoclinic prisms.

"*Powdered Matico.*—Greenish yellow; exhibits the characteristic multicellular non-glandular hairs having enlarged joints, up to 0.9 mm. in length; polygonal epidermal cells; fragments of irregular epidermal cells with stomata, the latter up to 0.030 mm. in length, and secretion cells of the leaf." *N. F.*

In 1864 Bentley (*P. J.*, Jan., 1864) described a *false matico* from Central America believed to be yielded by the *Piper aduncum* L. It is distinguished by the want of the reticulations on the upper, and the down on the under, surface which characterize true matico. (See also Thoms, *Arbeiten a. d. Pharm. Institut d. Universität, Berlin,* 1910, p. 70.) The most recent adulterant and substitute is the leaves of *Eupatorium glutinosum* Lam. (Fam. *Compositæ*). These differ from matico in being opposite, with serrate margin, cordate base, coarsely bullate upper surface and numerous glandular hairs (*S. R. A.*, xxiii, 1918, p. 97).

The medicinal properties of matico probably reside in the volatile oil of which it yields from 1 to 3.5 per cent. Both Flückiger and Kugler (*A. J. P.*, 1884, 477) reported that when the oil of matico was allowed to stand in a cold place it deposited a crystalline substance, which has been known as *matico camphor.* Apparently, however, the oils of today do not contain this camphor but some of them yield the solid *asarone.* Thoms (*A. J. P.*, 1904, p. 584) found apiol in an oil known to be from the *P. angustifolium,* but neither matico camphor nor asarone. Marcotte in 1864 reported the presence of a crystallizable acid which he called "artanthic" acid, but its existence has not been confirmed by other investigators. There are a variety of "oils of matico" on the market.

Uses.—A South American tradition attributes the name of this herb to a Spanish soldier named Matico, of the eighteenth century, who applied the leaves to a wound with an arrest of hemorrhage. The term "soldier's tree" as well as "matico" has been applied to other plants, notably the *Eupatorium glutinosum,* about which similar tales are current. It was introduced into European medicine by Jefferys in the early part of the nineteenth century. As a local application matico has been used as a stimulating astringent in *ulcers* and *chronic catarrhs,* especially leucorrhea, or to arrest *hemorrhages.* Internally it has been given in the treatment of *diarrheas,* and also in catarrhs of the genito-urinary organs. The powder is sometimes used, but the fluidextract (see Part III), is preferable for internal administration.

Dose, forty-five to seventy-five grains (3–5 Gm.).

Off. Prep.—Fluidextractum Matico, *N. F.*

MATRICARIA. N. F.

MATRICARIA Matricar. [German Chamomile]

"Matricaria is the dried flower-head of *Matricaria Chamomilla* Linné (Fam. *Compositæ*). Matricaria contains not more than 5 per cent. of stems or other foreign organic matter, and yields not more than 4 per cent. of acid-insoluble ash." *N. F.*

Flores Chamomillæ; Horse Gowan, Dog's Camovyne; Camomille commune (d'Allemagne), *Fr.;* Flos Chamomillæ, *P. G.;* Kamillen, Kamillenblumen, *G.;* Camomilla commune, *It.;* Manzanilla (Flor de), *Sp.*

Matricaria Chamomilla is an annual plant, with a branching stem a foot or two in height, bearing alternate leaves, the lower being tripinnate, the upper bipinnate or simply pinnate, and all of them very green, and nearly or quite smooth. The leaflets are linear and very small. The flower-heads appear singly at the ends of the stem and branches. The bracts of the involucre are obtuse, green in the middle, and whitish, membranous, and translucent at the margin. The ray-florets are pistillate, white, at first spreading, and ultimately reflected. The disk is of a deep yellow color, at first flat, but in the end convex, and in some cases somewhat conical. The plant is a native of Europe and Western Asia, and is occasionally cultivated in our gardens. It is also naturalized in North America, Central America and Australia. Mitlacher gives the results of methods of cultivating matricaria in *Zeit. Oest. Apoth. Ver.*, l, p. 410. Meyer has suggested (*Pharm. Zeit.*, lviii, p. 790) the practicability of scientifically collecting matricaria from the wild grown plants. All parts of it are active, but the flower heads only are official. These are gathered from May to August and shrink in drying, so that they are scarcely half as large as in their recent state. Matricaria is shipped to the United States in cases chiefly from Budapest, Szeged, Hamburg and Trieste.

The 1924 supply of this drug was of exceptionally good quality. Siftings consisting of ray and disk florets are imported into this country in bags.

Description and Physical Properties.—"*Unground Matricaria.*—Flower-heads composed of a few white ray-florets and numerous yellow disk-florets on conical, hollow receptacles, the latter being from 3 to 10 mm. in breadth; disk-florets tubular, perfect, and without a pappus; ray-florets from 10 to 20, pistillate, corolla white, 3-toothed and 4-veined, usually reflexed; involucre hemispherical, composed of from 20 to 30 imbricated, oblanceolate, and pubescent scales; peduncles light green to brownish green, longitudinally furrowed, more or less twisted and attaining a length of 2.5 cm.; achenes somewhat obovoid and faintly 3- to 5-ribbed; pappus none, or only a slight membranous crown. Odor pleasant, aromatic; taste aromatic and bitter.

"*Powdered Matricaria.*—Yellowish brown; exhibits numerous spinose, spherical or triangulate pollen grains with 3 pores, and up to 0.025 mm. in diameter; fragments of corolla from ray-florets with papillate epidermal cells; few short glandular hairs; fragments of achene tissue with epidermal cells having scalariform markings or wavy longitudinal walls and parenchyma containing rosette aggregates of calcium oxalate, the latter up to 0.010 mm. in diameter; fragments of characteristic tissue of anthers composed of elongated cells with scalariform walls; fragments of stigmas, the upper end bearing characteristic papillæ; vascular bundles with tracheæ having spiral, annular, or reticulate markings; fragments of the involucral scales bearing porous fibers, tracheæ and elliptical stomata, the latter up to 0.030 mm. in length.

"Preserve Matricaria in tightly closed containers." *N. F.*

"The similar flower-heads of *Anthemis arvensis* L., and *Maruta Cotula* De Candolle (Fam. *Compositæ*), have conical, solid, and chaffy receptacles." *U. S. VIII.*

In addition to the above it is sometimes admixed with the flower-heads of other European species of *Anthemis.* The flowerheads of the common daisy (*Chrysanthemum Leucanthemum* L.) as well as other species of *Chrysanthemum* have been present in the drug of commerce. G. Edman states the adulterant most commonly employed to be the flowers of one or more species of *Artemisia.* He has made careful microscopic examination of the flowers from six *Artemisia* species and describes his findings in detail (*Svensk. Farm. Tidskr.,* xxvi, 1922, p. 229).

The dried flowers of matricaria are considerably smaller than those of dog fennel, and exhibit a larger proportion of the disk-florets compared with those of the ray.

Matricaria contains a volatile oil and a bitter substance. The oil, which is obtained by distillation with water, is thick, somewhat tenacious, of a fine deep blue color becoming green and brown by age, and almost opaque in mass. Though supposed by Gerhardt to be identical with the oil of chamomile (*Anthemis nobilis*), it has been shown to be distinct. It congeals at – 20° C., has the sp. gr. 0.920 to 0.955, and contains a terpene, $C_{10}H_{16}$, *chamomillol,* $C_{10}H_{16}O$ and *trichamomillol,* $C_{30}H_{48}O_3$, the latter being the portion of the oil which possesses the blue color. *Schimmel & Co.'s. Report* for April, 1897, states that the German chamomile oil contains a paraffin hydrocarbon, which was obtained as a snowy white solid melting at 53° to 54° C. The blue color has also been stated to be due to a volatile principle called *azulene* by Piesse, and *cærulein* by Gladstone and others; also found in oil of absinthe, yarrow and some other blue volatile oils. This, when distilled with potassium, yields a terpene, $(C_{10}H_{16})_3$, and with phosphoric oxide a hydrocarbon, $C_{10}H_{14}$. (Kachler, *Ber. d. Chem. Ges.,* iv, 36.)

Uses.—Matricaria is a mild tonic, very similar to chamomile in medicinal properties, and, like it, in very large doses an emetic. It is considered also in Europe to be antispasmodic and anthelmintic. It is much employed in Germany, but in this country scarcely at all, unless by German practitioners. It may be given for the same purposes and in the same manner as chamomile.

Dose, half an ounce (15.5 Gm.).

Off. Prep.—Species Emollientes, *N. F.*

MEL. U. S.

HONEY

[Mel Depuratum, U. S. IX, Clarified Honey]

"A saccharine substance, gathered mostly from the nectar of flowers, and deposited in the honeycomb by the bee, *Apis mellifera* Linné (Fam. *Apidæ*). It must be free from foreign substances such as parts of insects, leaves, etc." *U. S.* "Purified Honey is honey of commerce melted and strained, the specific gravity, if necessary, being adjusted to 1.36 by the addition of Distilled Water." *Br.*

Mel Depuratum, *Br.;* Purified Honey; Mel Despuruatum; Miel, *Fr. Cod.;* Mel, *P. G.;* Honig, *G.;* Miele, *It.;* Miel, *Sp.*

The U. S. IX recognized two forms of honey; the commercial substance and one purified by dissolving in water, adding shredded paper pulp and filtering and evaporating the water, and adding glycerin to prevent crystallization. The improvement in the commercial article has made unnecessary the process of purification and the present revision agrees with the Br. in describing only one although under a different title.

From the nectaries of various flowers the bee and other insects extract a thin, aqueous fluid, nearly without flavor and insipidly sweet, usually known as *nectar.* As honey is made out of this substance it is very much affected by the character of the nectar, so that the nature of the plants which predominate in the vicinity of the hive is a matter of great importance to the bee culturist, not only in regard to the flavor of the honey which is yielded, but even to its freedom from poisonous qualities, cases having been reported from time to time of poisoning produced by the eating of honey which had not been tampered with after extraction from the hive. In the United States honey made by the bee from the flowers of the Mountain Laurel (*Kalmia*) is especially poisonous. See *N. J. M. R.*, 1852, 46; "*Poisonous Honey*," by L. F. Kebler, *Proc. A. Ph. A.*, 1896, 167; H. Bley, *Ph. Ztg.*, Nov., 1885. The latter states that *Datura Stramonium* and *Gelsemium* are for honey making especially dangerous plants. The nectar when taken in by the bee is chemically changed by secretions from glands in the head and thorax; levulose, dextrose, and, rarely, sucrose being formed. The finest honey is that which is allowed to drain from the comb. As beeswax is a valuable product in itself, modern centrifugal extractors are now employed by apiculturists to separate the honey from the comb, after cleanly slicing off the ends of the cells with a sharp knife. Centrifuged honey is much cleaner than that produced by other methods. If obtained from hives that have never swarmed, it is called *virgin honey*. An inferior kind is procured by submitting the comb to pressure, and if heat be employed previous to expression, the product is still more impure. The honey which is most highly esteemed is that made from the nectar of the white clover blossom. Equally valuable is the honey derived from raspberry blossoms and bass-wood flowers. The honey made late in the summer from the flowers of the buckwheat is darker in color. The largest producer of honey in the United States is California. The United States is said to be the greatest honey producing region on the globe, the annual production being between 60,000,000 and 75,000,000 pounds. Nearly 2,000,000 pounds of wax are also produced in this country.

The former method for clarifying honey was as follows:

"Honey, *a convenient quantity*, Distilled Water, Glycerin, each, *a sufficient quantity*. Weigh the honey in a tared dish, mix it intimately with *two per cent.* of paper pulp, which has been previously reduced to shreds, thoroughly washed and soaked in water, and then strongly expressed and again shredded. Then heat on a water bath at a temperature not exceeding 70° C., and carefully remove the scum which rises to the surface. Add enough distilled water to make up the loss incurred by evaporation, strain, and mix the strained liquid with *five per cent.* of its weight of glycerin." *U. S.*

For other methods of clarification, see *U. S. D.*, 20th ed., p. 691.

In the recent state honey is fluid, but on being kept it is apt to form a crystalline deposit, and to be ultimately converted into a soft granular mass. In commerce it is found of every consistence, from that of a viscid liquid, like thin syrup or oil, to that of lard or soft suet. Its color is sometimes white, but usually yellowish, and occasionally of a brownish or reddish tinge. It has a peculiar agreeable odor, varying somewhat with the flowers from which it was collected, and a very sweet, feebly aromatic taste, which is followed by a slight prickling or sense of acridity in the fauces. Cold water dissolves it readily, alcohol with less facility.

Description and Physical Properties.—"A thick, syrupy liquid of a light yellowish or yellowish-brown color. It is translucent when fresh, but frequently becomes opaque and granular from crystallization of dextrose. It has a characteristic odor and a sweet, faintly acrid taste.

"Honey is lævorotatory at 20° C., and is slightly acid to litmus paper. Diluted with twice its weight of water, Honey is only moderately turbid, is not stringy, and has a specific gravity of not less than 1.099 at 25° C. Incinerate about 2 Gm. of Honey, accurately weighed, at a low temperature in a platinum crucible, in small portions at a time: not more than 0.3 per cent. of ash remains. A solution of 10 Gm. of Honey in 50 cc. of distilled water requires not more than 0.5 cc. of normal sodium hydroxide for neutralization, phenolphthalein T.S. being used as indicator. Ten cc. portions of a filtered aqueous solution of Honey (1 in 10) show no more *chloride* than corresponds to 0.2 cc. of fiftieth-normal hydrochloric acid and no more *sulphate* than corresponds to 0.2 cc. of fiftieth-normal sulphuric acid, page 462. Boil about 2 Gm. of Honey with 20 cc. of water, cool, and add 2 drops of iodine T.S.: no blue, green, or reddish color is produced (*starch or dextrins*). The color of an aqueous solution of Honey (1 in 2) is not immediately changed when mixed with an equal volume of ammonia T.S. (*foreign coloring matter*), and a 5 cc. portion does not at once acquire a red or rose color on the addition of a few drops of hydrochloric acid (*azo dyes*). Triturate about 1 Gm. of Honey with 20 cc. of ether in a mortar, filter into a porcelain dish or crucible, allow the ether to evaporate, and add to the residue one drop of resorcinol T.S. At most only a pink color is produced, which disappears in half a minute, but not an orange, cherry, or brown-red color (*artificial honey or added invert sugar*)." *U. S.*

The British Pharm. describes it as "a syrupy, translucent, pale yellowish liquid. Aromatic odor; taste at first sweet, afterwards faintly acrid. Specific gravity 1.36. *Optical rotation* at 15.5° C. of a solution in *water*, containing 25 grammes in 100 millilitres, decolorised by filtration with *animal charcoal*, in a tube 200 millimetres long, between 0° and –5° C.; 5 millilitres of the same solution when fixed with 15 millilitres of *absolute alcohol* do not become more than faintly opalescent (absence of starch sugar). When 2 grammes are dissolved in 20 millilitres of boiling *water* and cooled, the solution does not become blue on the addition of one drop of *N/10 solution of iodine* (absence of starch). Ash not more than 0.25 per cent.; solution of the ash in *water* is not alkaline to *litmus,* and when acidified with *nitric acid* yields not more than a very faint opalescence with *solution of barium chloride,* or with *solution of silver nitrate* (limit of sulphates and of chlorides)." *Br.*

Genuine honey varies somewhat in its composition. The principal constituents are a mixture of dextrose and levulose in the same proportions as present in artificial invert sugar and in an amount ranging from 65 per cent. to nearly 80 per cent. Sucrose is present in from ½ per cent. to 8 per cent. The ash of honey varies from 0.3 per cent. to 0.50 per cent. and the water from 12 per cent. to 33 per cent. In a standard honey the sucrose should not be over 8 per cent., the water not over 25 per cent. nor the ash over 0.25 per cent. Honeys obtained by bees feeding upon the saccharine exudations of coniferous trees have been found to contain dextrose as the preponderating sugar and to have a dextrorotatory optical rotation instead of lævorotatory, as in the ordinary varieties. Such honeys usually come from foreign countries, although several specimens have been reported from the western part of the United States, and one specimen containing melezitose was reported from Pennsylvania, this rare carbohydrate having originated as an exudation on the twigs of *Pinus virginiana.*

According to Wm. A. Selser, who separated wax from honey on a large scale, the proportion of wax in the honey comb averages 1 per cent.; from 1500 pounds he obtained 14¼ pounds of wax by actual experiment. (*A. J. P.,* 1904, 267.)

A large number of samples of genuine honey analyzed in 1897 for the Department of Inland Revenue, Canada (Bull. 47), showed the following variations:

Direct polarization, –2.4 to –19.
Invert polarization, –10.2 to –28.
Sucrose (by Clerget), 0.5 to 7.64 per cent.
Invert sugar, 60.37 to 78.8 per cent.
Water, 12 to 33 per cent.
Ash, 0.03 to 0.50 per cent.

Neufeld in *Der Nahrungsmittelchemiker als Sachsverständiger,* Berlin, 1907, p. 275, gives the following limits for pure honey of European origin:

Water	8.30 to 33.59 per cent.
Protein	0.03 to 2.67 per cent.
Invert sugar	49.59 to 93.96 per cent.
Sucrose	0.10 to 10.12 per cent.
Dextrin	0.99 to 9.70 per cent.
Formic acid	0.03 to 0.21 per cent.
Ash	0.02 to 0.68 per cent.

Browne has published a comprehensive article on American honey (*U. S. Dept. Agric., Bur. of Chem., Bull.* 110, 1908) of which the tabular analyses are given in Leach, "*Food Inspection and Analysis,*" 3d ed., p. 635.

Künnmann and Hilger (*A. J. P.,* 1896, 570) state that dextrin is present in all honey, whether dextrorotatory or lævorotatory, and claim to have identified it as achroö-dextrin. Müllenhoff believes that the honey is preserved in the sealed cells of the comb by the secretion with it of a minute quantity of formic acid, and has found by experiment that the addition of one part of 25 per cent. formic acid is sufficient to keep permanently 250 parts of honey, but in this connection it should be remembered that the absence of contact with the air would account for the preservation of honey in the comb.

Honey is sometimes adulterated with artificial glucose. This cannot be detected by the official tests with certainty, but the safest method is to employ the polariscope. (See Leach, "*Food Adulteration and Analysis.*")

According to Oscar Haenle, glucose can also be detected by first dialyzing thoroughly and then polarizing, under which circumstance, if glucose be present, rotation to the right occurs; if the honey be pure the light is not affected. Undialyzed honey ordinarily polarizes to the left, but unadulterated conifer honeys are dextrogyrate. (*P. J.,* xxi.)

Honey has been frequently adulterated with artificial invert sugar. This is best detected by the official method given above.

Uses.—Honey is a valuable foodstuff; not only on account of its characteristic flavor but chiefly because it consists largely of invert sugar, and is therefore more rapidly absorbed, it is often more acceptable to the stomach than cane sugar. In medicine it is sometimes used as a flavoring agent especially for gargles. Its recognition by the Pharmacopœia, however, is because of its employment in certain pharmaceutical processes, especially in the preparation of blue mass.

Dose, one to four fluidrachms (3.75–15 cc.).

Off. Prep.—Confectio Piperis, *Br.;* Mel Boracis, *Br.;* Mel Rosæ, *U. S.;* Oxymel, *Br.;* Confectio Rosæ, *N. F.;* Mel Sodii Boratis, *N. F.*

MEL BORACIS. Br.

BORAX HONEY

Mel Sodii Boratis, *U. S.* 1870; Honey of Borax, Honey of Borate of Sodium; Miel boraté, Mellite de Borax, *Fr.;* Boraxhonig, *G.*

"Purified Borax, in powder, 10 *grammes;* Glycerin, 5 *grammes;* Purified Honey, 85 *grammes.* Mix." *Br.*

This preparation was very properly dropped from the U. S. Pharmacopœia at the 1880 revision, but is recognized by the N. F. V, the formula being identical with the British process given above. Borax honey is used in the *thrush* of infants and in *aphthous ulcerations* of the mouth.

MEL ROSÆ. U. S.

HONEY OF ROSE

Mellitum Rosatum; Mellite de Rose rouge, *Fr. Cod.;* Miel Rosat, *Fr.;* Mel Rosatum, *P. G.;* Rosenhonig, *G.;* Miele rosatol *It.;* Miel de rosas, *Sp.*

"Fluidextract of Rose, 120 cc.; Honey, a sufficient quantity, to make 1000 Gm. Mix the fluidextract of rose in a tared vessel with enough honey to make the product weigh 1000 Gm." *U. S.*

Though one of the official preparations in the London and Edinburgh Pharmacopœias, the Honey of Rose has been dropped in the British. As is well known, honey of rose deposits honey sugar upon standing even but a short time. Touflet (*Ph. Centralh.*, xxxvi, 307) obviates this precipitation in the following manner: Take of Powdered Rose Leaves, 25 parts; Alcohol, sp. gr. 0.875, 75 parts; Honey, 80 parts; Sugar, 34 parts. Percolate the rose leaves with the alcohol, filter and distil off the filtrate to 40 parts. To this add the honey and sugar, and bring to the boiling point.

Honey of rose forms a pleasant addition to the gargles employed in *inflammation* and *ulceration* of the *mouth* and *throat*. It is official because of its use in blue mass.

Dose, one fluidrachm (3.75 cc.).

Off. Prep.—Mel Rosæ et Sodii Boratis, *N. F.*

MELILOTUS. N. F.

MELILOT Melilot. [Yellow Melilot, Yellow Sweet Clover]

"Melilot consists of the dried leaf and flowering top of *Melilotus officinalis* (Linné) Lamarck (Fam. *Leguminosæ*). Melilot contains not more than 3 per cent. of its stems over 3 mm. in diameter, or other foreign organic matter." *N. F.*

An annual or biennial plant indigenous to Europe but naturalized in the United States, where it frequently abounds on waste ground and in fields. It bears alternate, trifoliate leaves with obovate to oblong leaflets whose apex is either rounded, truncate or slightly notched and margin closely serrate The flowers are small and yellow, occurring in spicate racemes. The fruit is an obovate, one-seeded legume. The plant, when in flower, has a peculiar sweet odor, which, by drying, becomes stronger and more agreeable, somewhat like that of the tonka bean.

Description and Physical Properties.—"*Unground Melilot.*—Stems mostly less than 3 dm. in length, slender, straight, mostly simple, often leafy below, terminating in long slender racemes, the younger portions very finely pubescent; leaves glabrous or nearly so; petiolate, trifoliate, stipulate, the stipules subulate, entire, the leaflets, from 1 to 3 cm. in length, varying from narrowly oblong to oval or occasionally broader above the middle, rounded, truncate, or slightly notched at the summit, sharply serrate; racemes 1 dm. or less in length, many flowered, the flowers yellow, from 5 to 6 mm. in length; calyx bell-shaped, the five, nearly equal lobes shorter than the tube, corolla papilionaceous, the keel shorter than the other petals, which are about equal; legumes reflexed, from 2.5 to 3.5 mm. in length, obovate, wrinkled, one-seeded. Odor aromatic, tonka-like; taste sweetish, slightly pungent and bitter.

"*Powdered Melilot.*—Light green; numerous uniseriate, 3-celled non-glandular hairs from 0.130 to 0.385 mm. in length, the two lower cells usually small and thin-walled, the upper cell much elongated, pointed and with thick, roughly spinose walls; fragments of leaf tissue composed of epidermal cells with broadly elliptical stomata the latter from 0.020 to 0.035 mm. in length; fragments composed of chlorenchyma and fibro-vascular tissue associated with crystal fibers containing prisms of calcium oxalate, the latter from 0.010 to 0.020 mm. in length; portions of stem tissue composed of wood and pith parenchyma, fibers and tracheæ with spiral markings or simple pores; pollen grains ellipsoidal, from 0.022 to 0.032 mm. in diameter; occasional glandular hairs consisting of 2- to 3-celled stalks and multicellular heads." *N. F.*

The pleasant odor of melilotus is due to the presence of coumarin (see *Coumarinum*). It is present in melilot, combined with *melilotic* (*hydrocoumaric*) *acid*, $C_9H_{10}O_3$ and *coumaric acid*, $C_9H_8O_3$, of which latter acid *coumarin* is the anhydride.

Uses.—Melilotus has been attributed with analgesic properties and consequently employed in *neuralgias*. The evidence of any therapeutic virtue, however, is far from convincing.

Off. Prep.—Species Emollientes, *N. F.*

MENTHA PIPERITA. U. S.

PEPPERMINT Menth. Pip.

"Peppermint consists of the dried leaves and tops of *Mentha piperita* Linné (Fam. *Labiatæ*). Peppermint contains not more than 2 per cent. of stems over 3 mm. in diameter, or other foreign organic matter." *U. S.*

American Mint, Brandy Mint; Menthe poivrée, *Fr.*; Folia Menthæ Piperitæ, *P. G.*; Pfefferminzblätter, *G.*; Menta piperita, *It.*, *Sp.*; Herba Menthæ.

The genus *Mentha* comprises at least fifteen species, of which there are also a great many varieties. Some of the mints have been in use for culinary and medicinal purposes since antiquity, but no well-defined distinction is made as to just what plants were employed. It is stated that *M. piperita* L., the most important member of this genus, was long ago cultivated by the Egyptians. It is mentioned in the Icelandic Pharmacopœia of the thirteenth century. Peppermint is now grown in considerable amounts in Europe, North America, and Eastern Asia and is also found growing wild in other parts of the world, as South America and Australia. The oldest existing peppermint district is in the neighborhood of Mitcham (Surrey), England. The chief peppermint plantations of the United States are in Michigan, the western part of New York, Ohio and Indiana. The best peppermint comes from Michigan, Northern Indiana and Germany. Inferior peppermint, containing from 30 to 50 per cent. of spearmint, has recently been received from Virginia and North and South Carolina. (See Russell, *Spatula*, 1921, xxvii, 481.) On the continent of Europe other species of *Mentha* (particularly *M. arvensis*) grow with *M. piperita,* deteriorating the product. In America other plants (as *Erigeron canadensis* and *Erechthites hieracifolia*) cause the same trouble. Besides *M. piperita* other species are cultivated, as some Asiatic varieties of *M. arvensis, M. spicata, M. longifolia* (var. *undulata*), *M. gentilis, M. dalmatica,* and *M. Pulegium.* Miss Henkel reviews the situation regarding the cultivation of peppermint in the United States and describes the three kinds of mint grown for the production of peppermint oil: *Mentha piperita* L.; *Mentha piperita vulgaris* Sole, and *Mentha piperita officinalis* Sole. (*Bul. Bur. Plant Ind., U. S. Dept. Agric.,* No. 90, 1906.) A comprehensive article on the cultivation of peppermint in Japan by Inouyé is in *Schim. Rep.,* November, 1908, p. 199. Peppermint has recently been successfully grown in Wisconsin. (*Paint, Oil and Drug Rev.,* xliv, p. 18.) The cultivation of peppermint is a growing industry on the reclaimed lands of Louisiana. (*Spatula,* xvii, p. 18.) (For accounts of the cultivation of peppermint in Germany, see Thoms in *B. P. G.,* xx, p. 244; in Austria, see Mitlacher, *Ph. Post,* xliv, p. 215; *Zeit. Oest. Apoth. Ver.,* l, p. 422; and in Russia, see *Proc. A. Ph. A.,* 1902, 831.) It has been repeatedly pointed out that the essential oil-bearing plants of the *Labiatæ* are very capricious and constantly changing character with change of soil and climate.

Peppermint is a perennial herb native to low wet soils of Europe. It produces prolific creeping stolons from which arise numerous quadrangular, purplish erect stems which branch toward the top. The leaves are opposite, petiolate, ovate, sharply serrate, pointed, smoother on the upper than on the under surface, and of a dark green color above, paler beneath. Its small purple flowers occur both in terminal, obtuse spikes, and in paired axillary cymes, the latter only in the upper leaf axils. The calyx is tubular, often purplish, furrowed, glabrous below, and five-toothed, the teeth being hirsute. The corolla is purplish, tubular, with its border divided into four segments, of which the uppermost is broadest, and notched at its summit. The four short stamens are concealed within the tube of the corolla; the style projects beyond it, and terminates in a bifid stigma. The fruit consists of four ellipsoidal nutlets. The plant should be cut for medicinal use during the dry periods of summer, while in flower. Two varieties of peppermint occur under cultivation in the United States and Europe, viz., *white mint* and *black mint.* White mint or *M. piperita* var. *officinalis* Sole is slender, one to two feet in height with light colored stems and leaves. Black mint or *M. piperita* var. *vulgaris* Sole is stout, two to three feet in height with usually purple-colored stems and dark green foliage. John C. Umney points out differences between white and black peppermint in *P. J.,* 1896, 123.

Description and Physical Properties.—"*Unground Peppermint.*—Leaves more or less crumpled and frequently detached from the stem; ovate-oblong to oblong-lanceolate, petiole from 4 to 15 mm. in length, slightly pubescent, blade from 1 to 9 cm. in length, acute and sharply serrate, light green to purplish-brown; upper surface nearly glabrous, lower surface glandular-hairy, especially on the veins; stem quadrangular, from 1 to 3 mm. in diameter, glabrous except for a few scattered deflexed hairs; flower-whorls usually in a compact, oblong or oval spike, from 1 to 1.5 cm. in breadth, rounded at the summit, and in fruit attaining a length of from 3 to 7 cm.; bracts oblong-lanceolate, from 4 to 7 mm. in length; calyx tubular, equally 5-toothed, pubescent and glandular-punctate, often dark purple in color; corolla tubular-campanulate, 4-cleft, about 3 mm. in length and often light purple; stamens 4, short and equal; nutlets ellipsoidal, about 0.5 mm. in diameter, blackish-brown; odor aromatic, characteristic; taste aromatic, pungent, followed by a cooling sensation in the mouth.

"*Powdered Peppermint.*—Green fragments of leaf epidermis with wavy vertical walls and, if from the lower surface of the leaf, with numerous stomata and glandular and non-glandular hairs, especially along the veins; glandular hairs with a 1- to 2-celled stalk and 1- to 8-celled head, usually set in a depression in the leaf and containing volatile oil and frequently yellowish or brownish crystals which refract polarized light; non-glandular hairs with thin, papillose walls, 1 to 8 cells long, the terminal cell pointed or sometimes globular; fragments of chlorenchyma with vascular tissue, the tracheæ spiral or with simple pores and but slightly lignified; fragments of collenchyma and of thin-walled, non-lignified fibers associated with parenchyma; pollen grains spheroidal and smooth." *U. S.*

For a paper on the histology of powdered peppermint by Smith Ely Jelliffe, see *D. C.,* 1899, 252. The morphology of *Mentha piperita* and other species of *Mentha* are discussed by Eriksson in *B. P. G.,* xviii, p. 244. The herb, both in the recent and in the dried state, has a peculiar, penetrating, grateful odor. Peppermint is quite frequently contaminated with spearmint and in one instance the leaves of belladonna were found. The latter, while no doubt accidental, shows the necessity for the examination of crude drugs generally. (*Pharm. Prax.,* iv, p. 38.) There is sometimes difficulty in distinguishing between the leaves of peppermint and those of spearmint. The outstanding physical differences between these are the following: The petioles of peppermint are 4 to 12 mm. in length whereas those of spearmint are less than 5 mm. in length. The blades of peppermint are of a darker shade of green than those of spearmint. Moreover, upon masticating the leaves of peppermint and drawing in the breath, a cooling sensation is experienced, no such sensation being evidenced with spearmint leaves. According to Joseph Schrenk, crystals can always be found in the glandular hairs of the peppermint, but are absent in those of the spearmint. The crystals are doubly refractive, and so transparent that sometimes a polariscope is necessary for their easy detection. These crystals have been thought to be menthol, but they seem not to dissolve in alcohol, and are probably hesperidin.

The medicinal properties depend on a volatile oil, of which from 1 to 1.25 per cent. can be obtained from the herb. The leaves are said to contain a little tannic acid.

Uses.—Peppermint is an aromatic stimulant, much used to allay *nausea,* relieve *spasmodic pains of the stomach and bowels,* expel *flatus,* or cover the taste or qualify the nauseating or griping effects of other medicines. (See *Oleum Menthæ Piperitæ.*)

Dose, one drachm (3.9 Gm.).

Off. Prep.—Spiritus Menthæ Piperitæ, *U. S.*

MENTHA VIRIDIS. U. S.

SPEARMINT Menth. Vir.

"Spearmint consists of the dried leaves and tops of *Mentha spicata* Linné (Fam. *Labiatæ*). Spearmint contains not more than 2 per cent. of stems over 3 mm. in diameter, or other foreign organic matter." *U. S.*

Herba Menthæ Acutæ (vel Romanæ); Brown, Lamb, Garden, or Mackerel Mint; Menthe verte, *Fr. Cod.;* Menthe romaine, Baume vert, Menthe à épi, *Fr.;* Grüne Münze, Römische Minze, *G*

Spearmint, sometimes called simply *mint,* differs from *M. piperita* chiefly in having nearly sessile, oblong or ovate-lanceolate, unequally serrate leaves of a lighter green color; elongated, interrupted, narrow spikes; setaceous bracts; and stamens longer than the tube of the corolla. It is a native of Europe and Asia, and naturalized in moist waste places from Nova Scotia as far south as Florida and westward to Minnesota and Kansas. It is also cultivated for domestic use and for the sake of its oil. Its flowering season is August. The drug is harvested in late summer and dried like hay. The commercial supplies are obtained chiefly from Michigan, the Carolinas and Virginia. Northern grown spearmint is the more highly esteemed.

Description and Physical Properties.—"*Unground Spearmint.*—Leaves more or less crumpled, ovate-lanceolate, unequally serrate, nearly sessile or with a petiole less than 5 mm. in length, of a bright green color and somewhat glandular-hairy on the under surface; stem, occasionally with characteristic opposite branches, distinctly quadrangular, from 1 to 3 mm. in diameter, nearly glabrous and light brown or purplish-colored; flowers arranged in opposite clusters and in more or less interrupted or crowded lanceolate, nearly acute spikes; bracts linear-lanceolate, subulate, from 7 to 10 mm. in length, subtending the flower clusters; calyx tubular, 5-toothed, glandular-punctate and somewhat pubescent near the teeth; corolla nearly white or light brown; stamens extending beyond the corolla tube; odor slightly pungent characteristic; taste aromatic, characteristic but not followed by a cooling sensation in the mouth.

"*Powdered Spearmint.*—Green; closely resembling the powder of Peppermint, except in the absence of crystals from the globular heads of the glandular hairs." *U. S.*

Spearmint was cultivated in the Convent gardens of the ninth century. It is largely used as a domestic and popular flavor in foods, chewing gum, and confectionery and is used in culinary practice for mint sauce and for flavoring green vegetables, as peas, etc. It is also the mint of mint julep fame. The plant is widely cultivated, and Schimmel and Co. present a review of its cultivation in Michigan, Indiana and New York in *Schim. Rep.,* October, 1910, p. 131. Experiments have also been conducted in Louisiana, and Phenis states the resulting oil to be of the highest grade. (*Paint, Oil, and Drug Review,* xlvi, p. 27.) Successful experiments have also been conducted in Wisconsin. (*Ibid.,* xliv, p. 18.) Mitlacher has reported that *Mentha crispa* L. can be successfully grown in Austria. (*Ph. Post,* xliv, p. 215.)

Spearmint is frequently admixed with peppermint. This is particularly noticeable in the supplies of this drug coming from Virginia and North and South Carolina which have contained from 30 to 50 per cent. of peppermint. This is probably due to carelessness. The taste and odor of spearmint are retained for some time by the dried plant. They depend on a volatile oil. (See *Oleum Menthæ Viridis.*)

Dose, one drachm (3.9 Gm.).

Off. Prep.—Spiritus Menthæ Viridis, *U. S.*

MENTHOL. U. S., Br.

MENTHOL

"An alcohol [$C_{10}H_{19}OH$] obtained from oil of peppermint or other mint oils." *U. S.* "Menthol, $C_{10}H_{20}O$, is a crystalline substance obtained by cooling the oil distilled from the fresh herb of Mentha arvensis, *DC., vars.* piperascens et glabrata, *Holmes;* and probably other species of Mentha." *Br.*

Peppermint Camphor; Camphora Menthæ; Camphre de Menthe, Mentholum, *Fr.;* Mentholum, *P. G.;* Menthol, Pfefferminzkampher, Mentha-Kampher, Pipmenthol, *G.;* Mentolo, *It.;* Mentol, *Sp.*

Menthol, or *peppermint camphor,* may be obtained from either *American, Chinese* or *Japanese oil of peppermint,* by cooling the oil to a very low temperature, when the menthol crystallizes out, often in a dense mass; the adhering oil may be separated by expression. Menthol may also be obtained by fractional distillation, and there is reason to believe that the oil of peppermint of commerce is often contaminated with the dementholized oil. American oil of peppermint is obtained from *Mentha piperita,* the Chinese oil from *M. arvensis* var. *glabrata,* and the Japanese oil from *M. arvensis* var. *piperascens.* A larger yield of menthol is obtained from Japanese or Chinese oils, and for this reason Japanese menthol is largely found in commerce. It is practically identical with American menthol, differing, however, in the character of its crystals, which occur in small prisms instead of in long needles.

Description and Physical Properties.—"Colorless, acicular crystals, having a strong, peppermint-like odor. Menthol is slightly soluble in water; very soluble in alcohol, chloroform, ether, and in petroleum benzin. It is freely soluble in glacial acetic acid, liquid petrolatum, and in fixed or volatile oils. When Menthol is triturated with about an equal weight of camphor, chloral hydrate, phenol, or thymol, the mixture liquefies.

"Menthol melts between 42° and 44° C. Its alcoholic solution is lævorotatory. Heat 2 Gm. of Menthol in an open dish on a water bath: it gradually volatilizes without leaving more than 0.05 per cent. of residue (*wax, paraffin,* or *inorganic substances*). Dissolve about 0.1 Gm. of Menthol in 1 cc. of glacial acetic acid, and add 3 drops of sulphuric acid and 1 drop of nitric acid: no green color is produced (*thymol*).

"Preserve in well-closed containers, in a cool place." *U. S.*

"Colorless acicular crystals or crystalline masses. Melting point 42° to 43° C. Odor and taste recalling peppermint; produces a sensation of warmth on the tongue and, if air is inhaled, a sensation of cold. Entirely volatilized by the heat of a water-bath. Very slightly soluble in *water,* but readily soluble in *alcohol* (90 per cent.), the solutions being neutral to *litmus.* Boiled with *sulphuric acid* diluted with half its volume of *water,* Menthol acquires an indigo-blue or ultramarine color, the acid becoming brown." *Br.*

Menthol is a stearopten. Its formula may be written $C_{10}H_{19}OH$, as it is recognized as being a saturated secondary alcohol. Chromium trioxide oxidizes menthol to *dextro-* and *lævomenthone,* $C_{10}H_{18}O$, which is the ketone corresponding. The *menthones* are liquids, with an odor resembling that of peppermint. They boil at 207° C. Distillation with zinc chloride or phosphoric anhydride changes menthol into liquid *menthene,* $C_{10}H_{18}$, boiling at 167° C. (See papers by Kremers, Urban, and Richtmann on the menthol group, *Proc. A. Ph. A.,* 1893, 185; also 1896, 200.) Menthol has been grossly adulterated with spermaceti, paraffin, etc., and, after being compressed into pencils or cones, sold as a local panacea for headache and neuralgia.

Menthol may be made synthetically by the reduction of *menthone* or of *pulegone.* There are a number of homologues of menthol which have been prepared artificially. There have been a number of isomeric menthols produced also, none of which are of medicinal importance.

For assay of preparations containing menthol when no interfering substances are present it is simply necessary to salt out with sodium chloride or shake out with petroleum ether and evaporate the latter in a desiccator. (See papers by Schaefer, *Pract. Drug.,* Aug., 1919, p. 28 and Mayer, *J. A. Ph. A.,* 1919, viii, 572.)

Uses.—According to Schwenkenbecher (*M. M. W.,* 1908, lv, p. 1495), menthol in large doses is a narcotic, paralyzing eventually both the sensory and motor systems. It cannot, however, be regarded as highly toxic, for he, himself, took 8 Gm. within a period of two hours without suffering serious symptoms. When locally applied it stimulates the nerves for the perception of cold, but depresses those for pain. It is actively antibacterial; according to McDonald, it is about twice as powerful as phenol. Menthol is used for its local anesthetic influence in various *skin diseases,* accompanied with *itching,* such as *urticaria.* Probably by virtue of the same property it is also frequently of service in *nausea* and *gastrodynia.* In *headache* and other forms of *neuralgia* the external application of menthol will frequently produce considerable degree of relief; the action in these cases is probably that of a counter-irritant rather than anesthetic. A solution containing one or two per cent. of menthol in liquid petrolatum is very widely employed for its antiseptic and anesthetic influence in inflammations of the upper respiratory tract, such as *acute coryza, pharyngitis,* or *laryngitis.* It is also occasionally employed as a gastro-intestinal antiseptic. According to S. A. Russel an ethereal solution of from 10 to 50 per cent. applied 2 or 3 times a day has a remarkable power of controlling superficial inflammations, such as *boils* or *carbuncles.* Berliner (*B. K. W.,* 1910, p. 967) and others have injected, hypodermically, its oily solution with asserted benefit in various forms of *tuberculosis.* A number of cases of dangerous asphyxiation, at least one of which ended fatally, have followed the local application of menthol in infants for the relief of *coryza.* (See Lublinski, *B. K. W.,* 1912, xlix.)

Dose, one to two grains (0.065–0.13 Gm.).

Off. Prep.—Emplastrum Menthol, *Br.;* Inunctum Mentholis, *N. F.;* Inunctum Mentholis Compositum, *N. F.;* Liquor Antisepticus, *N. F.;* Liquor Pepsini Antisepticus, *N. F.;* Menthol Camphoratum, *N. F.;* Nebula Aromatica, *N. F.;* Nebula Mentholis, *N. F.;* Nebula Mentholis Composita, *N. F.;* Petroxolinum Mentholis, *N. F.;* Pulvis Antisepticus, *N. F.;* Dentilinimentum Aconiti Compositum, *N. F.;* Dentilinimentum Aconiti et Iodi Compositum, *N. F.*

METHENAMINA. U. S. (Br.)

METHENAMINE Methenam. [Hexamethylenamina, U. S. P. IX, Hexamethylenetetramine]

"Methenamine contains not less than 99 per cent. of $(CH_2)_6N_4$." *U. S.* "Hexamine may be obtained by the interaction of ammonia with formic aldehyde. It contains not less than 98 per cent. of pure hexamethylenetetramine, $C_6H_{12}N_4$." *Br.*

Hexamina, *Br.;* Urotropine, Urotropin, Cystogen, Formin, Aminoform, Cystamine, Uritone.

The full name of this compound is hexamethylenetetramine, which was originally used by Nicolaier.

It may be made by the gradual addition of 70 parts of stronger ammonia water to 100 parts of a forty per cent. solution of formaldehyde which must be kept well cooled. The ammonia water must be added carefully in small quantities until in slight excess, which is indicated by its odor remaining after the liquid has stood several hours; then ten parts of ammonia water are added and the solution allowed to stand until crystallization is completed. The hexamethylenetetramine is purified by treatment with animal charcoal and recrystallization. The reaction is as follows:

$$6HCHO + 4NH_4OH \qquad (CH_2)_6N_4 + 10H_2O$$

Description and Physical Properties.—"Colorless, lustrous crystals, or a white, crystalline powder. It is odorless. One Gm. of Methenamine is soluble in 1.5 cc. of water, 12.5 cc. of alcohol, and in about 10 cc. of chloroform, at 25° C. At about 263° C. it sublimes without melting, partly decomposing and evolving a disagreeable odor. When brought into contact with fire, it readily ignites, burning with a smokeless flame.

"An aqueous solution of Methenamine is alkaline to litmus paper. Heat an aqueous solution of Methenamine (1 in 10) with diluted sulphuric acid: it decomposes with the liberation of formaldehyde recognized by its odor or by its darkening paper moistened with silver ammonium nitrate T.S. On the subsequent addition of an excess of solution of sodium hydroxide, ammonia is liberated.

"Ash: not more than 0.05 per cent. Add 1 cc. of alkaline mercuric potassium iodide T.S. to 10 cc. of an aqueous solution of Methenamine (1 in 20): no darker color is produced than results from the addition of the same amount of the reagent to 10 cc. of distilled water (*ammonium salts*). An aqueous solution of Methenamine (1 in 50) does not become colored or turbid when mixed with an equal volume of hydrogen sulphide T.S. (*heavy metals*). The addition of 5 drops of barium chloride T.S. to 10 cc. of an aqueous solution of Methenamine (1 in 50), acidulated with 5 drops of hydrochloric acid, produces no turbidity within one minute (*sulphate*). One Gm. of Methenamine shows no more *chloride* than corresponds to 0.2 cc. of fiftieth-normal hydrochloric acid.

"Preserve in well-closed containers.

"**Assay.**—Place about 1 Gm. of Methenamine, accurately weighed, in a beaker, add 40 cc. of normal sulphuric acid, and evaporate on a water bath (or boil gently, adding a little distilled water from time to time, if necessary) until the odor of formaldehyde is no longer perceptible. Cool, add 20 cc. of distilled water, and titrate the excess of acid with normal sodium hydroxide, using methyl orange T.S. as indicator. Each cc. of normal sulphuric acid corresponds to 0.03504 Gm. of $(CH_2)_6N_4$." *U. S.*

"Colorless crystals or crystalline powder. Inodorous; taste at first sweetish, afterwards bitter. Soluble in 1.5 parts of *water*, and in 8 parts of *alcohol* (90 per cent.). The aqueous solution is alkaline to *litmus*. When heated to 263° C., it sublimes without fusing, and partially decomposes. When heated with *diluted sulphuric acid* formic aldehyde is evolved, and when the solution is cooled and made alkaline with *solution of sodium hydroxide* ammonia is liberated. 0.1 gramme warmed with 5 millilitres of *sulphuric acid* and 0.1 gramme of *salicylic acid* develops a carmine color. A solution of 1 gramme in *water*, mixed with 35 millilitres of *N/1 solution of sulphuric acid*, evaporated on a water-bath until the odor of formaldehyde has disappeared, requires for neutralisation not more than 7 millilitres of *N/1 solution of sodium hydroxide, solution of methyl orange* being used as indicator. No appreciable ash." *Br.*

Methenamine is slightly hydrolyzed, even by water, with the liberation of ammonia by the following reaction:

$$(CH_2)_6N_4 + 6H_2O = 4NH_3 + 6CH_2O.$$

This decomposition is prevented or diminished by the presence of alkalies and is increased by the presence of acids. Being a feeble base methenamine combines with acids to form salts. It also has the effect of decomposing salts of alkalies weaker than itself and thus liberates NH_3 from ammonium salts.

It frequently becomes necessary to test for the presence of hexamethylenetetramine in differentiation from formaldehyde. The best test for this purpose is bromine water which gives an orange precipitate when added to aqueous solutions containing even minute traces of hexamethylamine. No precipitate or reaction is produced under these conditions with formaldehyde. This test is applicable directly to urine, but not to body fluids, because of the interfering effect of the proteins therein contained.

If the bromine water test is not directly applicable the fluid is tested for formaldehyde before and after distillation with sulphuric acid. The best test for formaldehyde under such conditions is that of Rimini (*Ann. di Farm.*, 1891, xvii, 97) and is applied as follows: To 10 cc. of the fluid to be tested are added in rapid succession, agitating after each addition, the following reagents in the prescribed amounts: 3 drops of a 0.5 per cent. aqueous solution of phenylhydrazine hydrochloride, 2 drops of a 0.5 per cent. aqueous solution of sodium nitroprusside and 3 drops (or a slight excess) of a 15 per cent. aqueous solution of sodium hydroxide. In the presence of formaldehyde even in amounts as small as 1 in 1,000,000, a fugitive green or blue color is produced which quickly changes to yellow and finally to yellowish-red. In the absence of formaldehyde no shade of green or blue is observed when the sodium hydroxide is added.

Methenamine is physically incompatible with lithium benzoate and similar salts, liquefaction occurring. With acetylsalicylic acid and with antipyrine chemical decomposition results. It should not be dispensed in capsule form because of the possible liberation of formaldehyde which would render the capsules insoluble and impervious to the digestive fluids.

Uses.—Locally methenamine is mildly irritant and feebly antiseptic. It is absorbed rapidly from the alimentary tract and circulates in the blood unchanged. Although the greater part is eliminated through the kidneys it has been detected in practically every secretion of the body. After it has passed through the kidney if the urine be, as it normally is, acid in reaction, the methenamine is slowly broken up with the liberation of formaldehyde. The rapidity of its decomposition appears to be in direct proportion to the degree of acidity and there is strong evidence that when the urine is alkaline the drug remains unchanged in the bladder.

Methenamine was originally introduced into medicine as a solvent for uric acid but Haskins (*A. I. M.*, December, 1915) has shown that although the solubility of uric acid in water is greatly increased by the presence of methenamine, the administration of 2 Gm. (30 grains) by mouth does not appreciably augment the solvent power of the urine and that even when given in very large dose it does not increase the solvent action of the urine as greatly as alkalization. The drug has consequently passed largely out of vogue as a uric acid solvent and is to-day used almost exclusively for its antiseptic action, especially in the urinary tract, as in *cystitis* and *pyelitis*. As its antiseptic effect is due chiefly to the decomposition of the salt and liberation of formaldehyde and as this decomposition does not take place in the urine except in the presence of an acid reaction, it is manifest that in those types of cystitis where the urine is alkaline it will be of little service unless this excretion can be rendered acid. On the other hand, in those cases of bladder infection by organisms which do not lead to ammoniacal fermentation of the urine, it is one of the most efficient antiseptics we possess. It has also been used to kill typhoid bacilli in the urine in cases of *typhoid fever*, especially during the convalescent stage. It has been recommended for the purpose of preventing infection of the kidney in *scarlet fever* and other infectious diseases but its mode of action in these conditions is not evident.

In 1908 Crowe (*A. I. P. T.*, 1908, xviii, p. 315) demonstrated the appearance of methenamine in the bile and reported three cases of *cholecystitis* in which the bile became practically sterile after its administration. Although Hanzlik (*J. A. M. A.*, 1914, lxii, p. 295) disputes these conclusions and asserts that on account of the alkalinity of the bile the drug cannot act as an antiseptic in the gall bladder, there is considerable evidence as to its value as a preventative against *gall-stones* and curative of various infections of the bile passages. Miller, in 1911, used it with good results in the treatment of *acute coryza*, and Eisenberg (*J. A. M. A.*, 1912, June 29), in *acute bronchitis*. Despite the theoretical objections which have been urged against this treatment the clinical evidence of its value in those various respiratory infections commonly called *colds*, is too strong to be denied. In our experience, if used within twenty-four hours after the onset of symptoms, in a considerable proportion of cases the infection can be completely aborted. It has also been suggested for its influence in preventing the growth of germs in the cerebro-spinal fluid, as in *meningitis* and *poliomyelitis*, but its usefulness in these conditions has not been established.

If, as seems at present probable, the value of methenamine depends upon the liberation of formaldehyde, it is evident that it must be used in sufficiently large doses to form an antiseptic quantity of this reagent. Hinman (*J. A. M. A.*, 1913, lxi, p. 1601), as the result of experimental studies, reaches the conclusion that on account of the fact that some of the drug escapes decomposition, at least forty-five grains (3 Gm.) a day are required in *cystitis*.

When given in very large doses it often causes violent inflammation of the urinary tract evidenced by albuminuria, hematuria and tenesmus. Generally the inflammatory condition is limited to the bladder but Abt (*Med. Clinic of Chicago*, 1917, ii, 904) has seen fatal nephritis due to its over-use. As these irritations are due to an excess of formaldehyde liberated the treatment consists in the administration of sufficient doses of bicarbonate or citrate of soda to keep the urine alkaline and of large amounts of water to dilute it.

Not only are there a large number of compounds of methenamine upon the market, but the official drug is sold under an almost innumerable number of trade names. The compounds of hexamethylenetetramine are considered in Part II.

An interesting and novel use of hexamethylenamine is afforded by its ready inflammability, and the fact that it burns with a smokeless flame. In the absence of a Bunsen burner or an alcohol lamp, a five grain tablet of methenamine placed upon a metal or other non-inflammable surface and ignited will develop enough heat to boil a test tube full of liquid, to sterilize a hypodermic needle or to make a test for albumen in urine.

Dose, five to twenty grains (0.32–1.3 Gm.).

METHYLIS SALICYLAS. U. S. (Br.)

METHYL SALICYLATE Methyl. Salicyl.
Oil of Gaultheria, Oil of Wintergreen, Oil of Betula
Oil of Sweet Birch, Oil of Teaberry]

"Methyl Salicylate is produced synthetically or is obtained by distillation from the leaves of *Gaultheria procumbens* Linné (Fam. *Ericaceæ*) or from the bark of *Betula lenta* Linné (Fam. *Betulaceæ*). The label must indicate whether the Methyl Salicylate has been made synthetically or distilled from either of the above mentioned plants. It contains not less than 98 per cent. of $C_6H_4(OH)CO_2CH_3$." *U. S.* "Methyl Salicylate is the methyl ester of salicylic acid. It may be obtained by the interaction of methyl alcohol and salicylic acid. It contains not less than 98 per cent. of pure methyl salicylate, $CH_3C_7H_5O_3$." *Br.*

Methyl Salicylas, *Br.;* Synthetic Oil of Wintergreen; Salicylate de Méthyle, *Fr.;* Methylsalicylat, Künstliches Wintergrünol, *G.*

Methyl Salicylate occurs in a number of volatile oils (see *Oleum Gaultheriæ*). It is also manufactured on a large scale from synthetic salicylic acid. Although there was, at one time, a widespread belief that synthetic methyl salicylate was more toxic than the natural oil, it is without scientific support (see *J. A. M. A.*, 1913, lxi, 979). Because of the established identity in action and because of the impossibility in distinguishing between the synthetic and natural oil, the U. S. Pharmacopœia at the ninth revision dismissed the title of "Oil of Wintergreen." Many investigators have attempted to devise tests for differentiating the oils of wintergreen and birch and methyl salicylate, but as soon as a reaction is proposed and described, its unreliability is quickly proved by other investigators. Vanillin and alcohol, heliotropin and sulphuric acid, chloral hydrate and sulphuric acid are among the reagents which have been proposed, none of which seem to be infallible with mixtures, although they do show decided differences with the pure oils. References to some of the articles on this subject are as follows: *Schim. Rep.*, 1914, Apr., p. 99; *J. A. Ph. A.*, 1914, p. 1658; Hurley (*Pract. Drug.*, 1921, xxxix, 121) and LaWall (*A. J. P.*, 1920, xcii, 891).

Methyl salicylate may be made by distilling salicylic acid or a salicylate, with methyl alcohol and strong sulphuric acid. The reaction is as follows:

$$C_6H_4OHCOOH + CH_3OH = C_6H_4OHCOOCH_3 + H_2O.$$

The sulphuric acid plays no part in the reaction except to serve as a dehydrating agent. The following process was devised by G. M. Beringer (*A. J. P.*, 1887, p. 8). Dissolve half an ounce of salicylic acid in two fluidounces of absolute methyl alcohol, then gradually add one fluidounce of sulphuric acid; warm gently for twenty-four hours, then distil from a retort into which a current of steam is introduced. The distillate is to be well washed, and separated by decantation. The odor improves with age. Methyl salicylate has been found in a great number of plants. (See *A. J. P.*, 1898, 412; *Ph. Rev.*, 1898, 130; *Schim. Rep.*, 1898, 45; 1899, 46.)

Description and Physical Properties.—"A colorless, yellowish, or reddish liquid, having the characteristic odor and taste of gaultheria. Methyl Salicylate is slightly soluble in water, but is miscible with alcohol and with glacial acetic acid. It is soluble in about 7 volumes of 70 per cent. alcohol at 25° C. with not more than a slight cloudiness.

"Specific gravity at 25° C.; synthetic, 1.180 to 1.185; from gaultheria or betula, 1.176 to 1.182. It boils between 219° and 224° C. Synthetic Methyl Salicylate, or that from betula, is optically inactive. Methyl Salicylate from gaultheria is slightly lævorotatory, not exceeding $-1.5°$ in a 100 mm. tube at 25° C. A deep violet color is produced by shaking a drop of Methyl Salicylate with about 5 cc. of distilled water and adding a drop of ferric chloride T.S.

"An alcoholic solution of Methyl Salicylate is neutral or slightly acid to moistened litmus paper. Add 10 cc. of potassium hydroxide T.S. to 1 cc. of Methyl Salicylate contained in a capacious test tube, and agitate the mixture: a clear, or slightly cloudy, and colorless or faintly yellowish solution results without the separation of any oily drops either on the surface or at the bottom of the liquid (*other volatile oils or petroleum products*). Methyl Salicylate meets the requirements of the test for *heavy metals in volatile oils.*

"Preserve in amber colored bottles, well stoppered in a cool place." *U. S.*

"A colorless liquid. Characteristic, aromatic odor; taste sweetish, warm, aromatic. Slightly soluble in *water;* readily soluble in *alcohol* (90 per cent.), in *glacial acetic acid,* and in *carbon disulphide.* Specific gravity 1.185 to 1.192. Boiling point from 219° to 221° C. Optically inactive. The solution in *alcohol* (90 per cent.) is neutral or faintly acid to *litmus.* The aqueous solution is colored violet by the addition of a drop of *T. Sol. of ferric chloride.* Contains not less than 98 per cent. of the *ester* methyl salicylate, $CH_3C_7H_5O_3$." *Br.*

"**Assay.**—Place about 2 cc. of Methyl Salicylate, accurately weighed, in a tared flask, add 50 cc. of half-normal alcoholic potassium hydroxide, connect the flask with a reflux condenser, and heat the mixture on a water bath for two hours. Add a few drops of phenolphthalein T.S., and titrate the excess of alkali with half-normal hydrochloric acid. Each cc. of half-normal alcoholic potassium hydroxide corresponds to 0.07605 Gm. of $C_6H_4(OH)CO_2CH_3$.

"Preserve in well-stoppered, amber-colored bottles, in a cool place." *U. S.*

Uses.—Methyl salicylate is used chiefly in the treatment of various forms of *rheumatism* in which other preparations of salicylic acid are of service. It has the advantage over the inorganic salicylates of being less unpleasant to the taste, but in our experience is somewhat more prone to cause digestive disturbances and according to Hanzlik and Wetzel (*J. P. Ex. T.*, 1919, xiv, p. 43) is less perfectly absorbed. Because of its volatility it is capable of being absorbed through the skin and is frequently applied externally for its systemic effect. For this purpose it may be mixed with equal parts of lard and a drachm of the mixture spread over a surface as big as the palm of the hand and covered with an impermeable dressing to prevent evaporation. It is also employed for its counter-irritant action in various liniments. As a flavoring agent two minims may be used for each fluidounce.

Internally it is best administered in emulsion, although sometimes taken by dropping into a teaspoonful of sugar. The custom of giving it in capsules is to be deprecated as it is much more likely to irritate the stomach under these circumstances.

For cases of methyl salicylate poisoning see Rosenbloom and Johnston, *J. A. M. A.*, 1919, lxxii, 22.

Dose, from five to twenty minims (0.3–1.2 cc.).

Off. Prep.—Inunctum Mentholis Compositum, *N. F.;* Liquor Antisepticus, *N. F.;* Liquor Antisepticus Alkalinus, *N. F.;* Liquor Ferri Salicylatis, *N. F.;* Liquor Pepsini Antisepticus, *N. F.;* Nebula Aromatica, *N. F.;* Nebula Mentholis Composita, *N. F.;* Petroxolinum Methylis Salicylatis, *N. F.;* Odontalgicum, *N. F.*

METHYLTHIONINÆ CHLORIDUM. U. S.

METHYLTHIONINE CHLORIDE Methylthionin. Chlor. [Methylene Blue]

"Tetramethylthionine chloride [$C_{16}H_{18}N_3ClS.3H_2O$]." *U. S.*

Methylthionine Hydrochloride; Medicinal Methylene Blue; Methylenium Ceruleum, *Fr. Cod.;* Chlorhydrate de Tetraméthylthionine, *Fr.;* Tetramethylthioninchlorid, Methylen Blau, *G.*

This synthetic dye color belongs to the class of *thiazines* or dyestuffs in which two benzene nuclei are united by a nitrogen atom and a sulphur atom. *Methylene blue* was discovered by Caro in 1876, and was made by the oxidation of *p*-amido-dimethyl aniline with ferric chloride in the presence of hydrogen sulphide. Both the hydrochloride of the base and the zinc chloride double salt of the same are known by the name of methylene blue. It is only the former that is used in medicine and constitutes the official salt. Methylene Blue must not be confounded with *methyl blue,* a dark blue powder which is used as an antiseptic; the latter is sodium triphenyl-pararosaniline-sulphonate.

The dye known as methylene blue differs in composition from the medicine being the chloride of zinc and methylthionine; it is much more poisonous.

Description and Physical Properties.—"Dark green crystals or a crystalline powder, having a bronze-like luster. It is odorless, and is stable in the air. Methylthionine Chloride is freely soluble in water and in alcohol; soluble in chloroform, the solutions having a deep blue color.

"The addition of hydrochloric acid to its aqueous solution changes the color to a lighter shade of blue. The addition of sodium hydroxide T.S. changes the color to a purplish shade, and, if added in excess, produces, on standing, a precipitate having a dull violet color. A solution of Methylthionine Chloride in diluted sulphuric acid is gradually decolorized upon the addition of zinc dust.

"Methylthionine Chloride, dried to constant weight at 110° C., loses not more than 16 per cent. (*moisture*). Ash: not more than 1 per cent. Intimately mix 0.2 Gm. of Methylthionine Chloride with about 0.5 Gm. each of powdered potassium nitrate and anhydrous sodium carbonate, and heat the mixture in a crucible until the organic matter is completely oxidized. Dissolve the cooled residue in 15 cc. of diluted sulphuric acid, and evaporate the solution over a flame until the vapors of sulphuric acid begin to evolve: the residue so obtained meets the requirements of the test for *arsenic.* Heat 0.5 Gm. of Methylthionine Chloride at a temperature below a red heat until it is completely carbonized, boil the powdered residue with 10 cc. of diluted hydrochloric acid for five minutes, filter, and wash the residue with 10 cc. of distilled water. Boil the combined filtrate and washings with 1 cc. of nitric acid, supersaturate with ammonia T.S., and filter if necessary: the liquid remains clear upon the addition of an equal volume of hydrogen sulphide T.S. (*zinc.*) Dissolve 1 Gm. of Methylthionine Chloride in 50 cc. of boiling alcohol, filter through counterbalanced filters, wash the residue on the filter with boiling alcohol until the washings cease to be colored blue, and dry it at 100° C.: the weight corresponds to not more than 1 per cent. (*dextrin*)." *U. S.*

Uses.—When taken internally methylene blue is absorbed and eliminated chiefly from the kidneys, coloring the urine blue or greenish. In therapeutic doses it produces no symptoms except occasionally some irritation of the bladder, and we know of no serious cases of poisoning with the pure article. It is a feeble antiseptic and has been used to a considerable extent in *gonorrhea, cystitis* and *pyelitis,* but its value is certainly not great. As an analgesic, it has been employed in *neuralgia, locomotor ataxia,* etc., but is inferior to other aniline derivatives. In 1891, Ehrlich and Guttmann (*B. K. W.,* xxviii), led by its power as a staining agent over the plasmodium malariæ, suggested its practical use as an antiperiodic, and its value as such is well established. In 425 cases collected by H. C. Wood, Jr. (*Trans. Phila. County Med. Soc.,* 1904), there were 85 per cent. of cures. It does not produce disturbances of the special senses or of the gastro-intestinal tract, and therefore may be preferable to quinine in aural or gastro-intestinal affections. Further, on account of its lack of action upon the kidney, it is especially valuable in those forms of *malaria* accompanied with *hematuria,* the so-called "*black water fever.*" If the statement of Iwanoff, that it especially acts upon the adult forms of plasmodium be correct, it should be especially valuable in *chronic malaria,* and experience may prove that the best treatment of this condition is the administration of full doses of quinine at intervals of seven days, with the continuous use of the methylene blue. Slack (*Atlanta Journal and Record of Medicine,* 1907) recommends the internal use of methylthionine in *carcinoma;* it seems not only to relieve the pain but also to delay the growth of the tumor. Binger (*J. Inf. D.,* 1919, xxv, 277) from a study of its effect on the meningococcus has suggested its use in *meningitis.*

Methylene blue is preferably administered in capsule. In malaria from ten to twenty grains (0.65–1.3 Gm.) may be given in the course of a day for ten days, and after this six to ten grains (0.4–0.65 Gm.) a day for two weeks. In obstinate cases a full dose of quinine may be exhibited every seventh day, the methylene blue being omitted. The staining action of methylene blue upon any portion of the body or clothing with which it may come in contact, and its color effect upon the urine, should always be explained to the patient.

Dose, two to five grains (0.13–0.32 Gm.).

MEZEREUM. N. F.

MEZEREUM [Mezereon]

"Mezereum is the dried bark from aerial portions of *Daphne Mezereum* Linné, *Daphne Gnidium* Linné, or of *Daphne Laureola* Linné (Fam. *Thymeleaceæ*). Mezereum contains not more than 2 per cent. of foreign organic matter." *N. F.*

Mezerei Cortex, *Br.* 1898; Mezereon Bark; Cortex Mezerei, Cortex Thymeleæ (vel Coccognidii), Dwarf Bay, Wild Pepper, Spurge-flax, Spurge-olive, Magell; Mézéréon, Bois gentil, *Fr.;* Lauréole, Thymelée, *Fr.;* Kellerhals, Seidelbastrinde, Kellerhalsrinde, *G.;* Mezereo, *It.;* Mecereon, *Sp.*

All the species of *Daphne* are possessed of active properties, but three only are official—*D. Mezereum, D. Laureola,* and *D. Gnidium.*

Daphne Mezereum is a very hardy, low shrub, with a branching stem, and a smooth, dark gray bark, very easily separable from the wood. The leaves spring from the ends of the branches, are deciduous, sessile, obovate-lanceolate, entire, smooth, and of a pale green color, somewhat glaucous beneath. They are preceded by the flowers, which appear very early in the spring, and sometimes bloom even amidst the snow. These are of a purple-rose color, rarely white, highly fragrant, and disposed in clusters, each consisting of two or three flowers, forming together a kind of spike at the upper part of the stem and branches. At the base of each cluster are deciduous floral leaves. The fruit is oval, shining, fleshy, of a bright red color, and contains a single round seed. Another variety produces white flowers and yellow fruit. This species of *Daphne* occurs throughout the forests of Europe, and extends in Western Asia from the Caucasus to the Altai. It is cultivated in Europe, and is occasionally found in our own gardens. *D. Mezereum* is locally naturalized from New York and Massachusetts to western Quebec and Ontario.

Daphne Gnidium.—In this species, called *garou* or *sain-bois* by the French, the leaves are linear-lanceolate, acute, entire, smooth, and irregularly but closely set upon the branches. The flowers are white, downy, odoriferous, and disposed in terminal panicled racemes. The fruit is globular, dry, at first green, but ultimately black. *D. Gnidium* grows in dry uncultivated places in the south of Europe, and flowers in June. Its bark, which in France is used indiscriminately with that of the former species, is of a deep purplish-brown color, and hairy in the younger portions. It appears to be equally as active, medicinally, as the other official species.

Besides the species above described, *Daphne Laureola,* or *spurge laurel,* is said to furnish a portion of mezereum of commerce, and is recognized by the N. F., but its product is inferior in acrimony, and consequently in medicinal activity.

The commercial supplies of mezereum come chiefly from southern France.

Properties.—The bark of the root was formerly directed, but the mezereum with which our markets are supplied is evidently the bark of the stem, and the N. F. at present very properly directs the bark, without designating the part from which it must be taken.

Description and Physical Properties.—"*Unground Mezereum.*—In flexible, tough quilled pieces or somewhat flattened strips attaining a length of 90 cm.; from 0.3 to 1 mm. in thickness; outer surface yellowish or olive-brown (*D. Mezereum*) or purplish-brown (*D. Gnidium*) or purplish-gray (*D. Laureola*), smooth, numerous lenticels giving a transversely striated appearance and occasionally with numerous, circular, brownish-black apothecia; outer corky layer easily separable from the middle bark which varies from light green to olive-brown and with more or less detached bast fibers; inner surface yellowish white; satiny lustrous, finely striate; fracture tough, fibrous, the inner bark lamellated. Odor very slight; taste at first slight, becoming gradually and increasingly pungent and acrid.

"*Structure.*—A rather thick cork composed of from 20 to 30 rows of cells, the outer being compressed and with yellowish-brown walls, and the inner more or less tubular with nearly colorless walls; a hypodermis of 3 to 5 rows of collenchymatous cells containing chloroplastids or a yellowish-green resinous substance; an inner bark consisting mostly of nearly colorless non-lignified bast-fibers occurring in loosely united groups, and a few starch-bearing medullary rays one cell in width.

"*Powdered Mezereum.*—Light grayish-brown; bast-fibers numerous, from 0.4 to 3 mm. in length and about 0.015 mm. in width, frequently uneven or irregularly bent and considerably attenuated at the ends, the walls being from 0.001 to 0.005 mm. in thickness, colorless, non-lignified and free from pores; fragments of yellowish-brown cork cells and starch-bearing medullary rays; starch grains relatively few, mostly spherical or elliptical, occasionally 2- to 4-compound, the individual grains from 0.003 to 0.15 mm. in diameter." *N. F.*

British writers state that the bark of the root is the most active. The berries and leaves of the plant are also active, and the former have sometimes proved fatal to children who have eaten them.

Vauquelin discovered a bitter glucosidal principle which has received the name of *daphnin.* Gmelin and Bär found it in the bark of *D. Mezereum,* associated with wax, an acrid resin (*mezerein*), a yellow coloring matter, a reddish-brown extractive, and uncrystallizable and fermentable sugar, a gummy matter containing nitrogen, ligneous fiber, malic acid, and several malates. Mezerein, which is easily changed into *mezereic acid,* may be considered as the substance to which the medicinal properties of the drug are due. *Daphnin* is in prismatic crystals, grouped together, colorless, transparent, brilliant, slightly soluble in cold water, very soluble in boiling water and alcohol, without odor, and of a bitter, somewhat harsh, but not acrid taste. Daphnin is isomeric with æsculin and, like it, yields, on hydrolysis, sugar and dioxycoumarin. (See Will and Jung, *A. J. P.,* 1885.) (For a method of preparing the glucoside daphnin, see *U. S. D.,* nineteenth edition, p. 781.) *Coccognin,* isolated in 1870 by Casselmann from the fruits of *D. Mezereum,* appears to be closely allied to, if not identical with, daphnin. By the dry distillation of an alcoholic extract of mezereum bark, Zwenger obtained umbelliferone.

The medicinal properties of mezereon reside in the resin.

Uses.—The recent bark applied to the skin produces inflammation followed by vesication, and has been popularly used as an epispastic, from time immemorial, in some of the southern countries of Europe; the dried bark, though less active, is possessed of a similar property and is occasionally employed in France by regular practitioners for the purpose of forming issues. It is slow in its operation, generally requiring from twenty-four to forty-eight hours to vesicate. The ointment was formerly used for maintaining the discharge from blistered surfaces, and may be applied advantageously to obstinate, ill-conditioned indolent *ulcers.* It was recognized by the U. S. 1880. (See *U. S. D.,* 19th ed., p. 781, for formula.)

Internally administered, mezereum is a stimulant capable of being directed to the skin or kidneys, and in large doses likely to excite purging, nausea, and vomiting. In overdoses it produces the fatal effects of the acrid poisons, and a case of apparently severe narcotic effects has been recorded. (*Am. J. M. S.,* xxi.) It had at one time much reputation as an alterative in *syphilis, chronic rheumatism,* etc., but is of no value as an internal remedy and is almost never administered save as an ingredient of the compound fluidextract of sarsaparilla.

Dose, ten grains (0.65 Gm.).

Off. Prep.—Fluidextractum Sarsaparillæ Compositum, *N. F.;* Fluidextractum Mezerei, *N. F.;* Linimentum Sinapis Compositum (from Fluidextract), *N. F.*

MISTURA AMMONIACI. Br.

AMMONIACUM MIXTURE

Emulsum Ammoniaci, *U. S.* 1890, Emulsion of Ammoniac; Ammoniac Mixture; Emulsio Ammoniaci, Lac Ammoniaci; Milk of Ammoniac; Mixture de Gomme ammoniaque, *Lat.;* d'ammoniaque, *Fr.;* Ammoniak-Emulsion, *G.*

"Ammoniacum, in coarse powder, 30 *grammes;* Syrup of Tolu, 60 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Triturate the Ammoniacum thoroughly with a little of the Distilled Water so as to form a thin paste; gradually add the remainder of the Distilled Water and the Syrup of Tolu, triturating until the mixture assumes a uniform milky appearance; strain through muslin." *Br.*

In this emulsion the resinous and oily constituents are suspended by means of the gum of the ammoniac, imparting a milky appearance to the preparation, which from this circumstance was formerly called *lac ammoniaci,* or *milk of ammoniac.* The greater portion of the resin subsides upon standing. This emulsion is no longer official; that of the U. S. 1890 was slightly stronger, representing 4 per cent. of ammoniac as against 3 in the British.

Dose, one-half to a fluidounce (15–30 cc.).

MISTURA AMYGDALÆ. Br.

ALMOND MIXTURE

Emulsum Amygdalæ, *U. S. IX;* Emulsion of Almond; Milk of Almond; Emulsio Amygdalæ, s. Amygdalarum, Emulsio Simplex; Milk of Almonds; Simple Emulsion; Look Album, *Fr. Cod.;* Emulsion d'Amande, Lait d'Amande, *Fr.;* Mandelemulsion, Mandelmilch, *G.;* Emulsione di mandorle dolci, Looch Bianco, *It.;* Emulsion comun, *Sp.*

"Compound Powder of Almonds, 125 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Triturate the Powder with a little of the Distilled Water so as to form a thin paste; gradually add the remainder of the Distilled Water; strain through fine muslin." *Br.*

The Emulsion of Almond of the U. S. IX was practically the same as the above. The gum arabic in these formulas is introduced not so much for its demulcent properties as to assist in the suspension of the insoluble ingredients of the almonds. The same formula will answer for the preparation of an *emulsion of bitter almonds* from bitter almond or peach kernels. The oleaginous matter of the almonds is suspended in the water by means of their albumen, gum, and sugar, forming a milky emulsion. Great care should be taken to select the almonds perfectly free from rancidity. The emulsion is not permanent and compound powder of almonds often has a taint of rancidity when kept too long. Upon standing, the oil rises like thick cream to the surface, and the separation is effected more quickly by heat, alcohol or acids, which coagulate the albumen. In warm weather the preparation is likely to become sour.

Uses.—This preparation has no medicinal value outside of its nutritive properties and pleasant flavor. It is employed as an addition to the diet, sometimes as a vehicle for more active and disagreeable drugs; and occasionally as an external demulcent. Its use for the latter purpose is to be deprecated because of the sugar in it.

Dose, one-half to one fluidounce (15–30 cc.).

MISTURA CRETÆ. U. S., Br.

CHALK MIXTURE Mist. Cret.

Mixture avec la Craie, *Fr.;* Kreidemixtur, *G.*

"Prepared Chalk, 6 Gm.; Glycerin, 10 cc.; Cinnamon Water, 40 cc.; Distilled Water, a sufficient quantity, to make 100 cc. Gradually add the glycerin to the prepared chalk, in a mortar, triturating until a smooth, uniform mixture is produced. Add the cinnamon water with trituration, transfer the mixture to a graduated vessel, and rinse the mortar with enough distilled water to make the product measure 100 cc. Mix thoroughly.

"This preparation must not be dispensed unless it has been recently prepared." *U. S.*

"Prepared Chalk, 30 *grammes;* Tragacanth, in powder, 5 *grammes;* Refined Sugar, 60 *grammes;* Cinnamon Water sufficient to produce 1000 *millilitres.* Triturate the Prepared Chalk with Tragacanth and Refined Sugar, and gradually add, with constant trituration, sufficient Cinnamon Water to produce the required volume." *Br.*

The direction that this mixture be prepared extemporaneously is a decided improvement. Unsuccessful attempts have been repeatedly made to devise a formula which would yield a permanent product, and much injury has been done through the dispensing of chalk mixture in an incipient fermentative condition. The trifling amount of glycerin present in the chalk mixture official in 1870 was totally inadequate to preserve it during the warm summer months, when it is in greatest vogue. Compound Chalk Powder is official (see *Pulvis Cretæ Compositus*); it will keep indefinitely, and, besides being itself a valuable addition to the materia medica, is quickly made into chalk mixture by rubbing it with the water and cinnamon water, so that there can be no excuse for not dispensing a fresh mixture.

This mixture is a convenient form for administering chalk, and is much employed as a gastric or intestinal antacid in *hyperchlorhydria* and *diarrhea.* Laudanum and kino or catechu are very often added to increase its astringency.

Dose, four fluidrachms (15 cc.), frequently repeated.

MISTURA FERRI COMPOSITA. Br.

COMPOUND IRON MIXTURE [Griffith's Mixture]

Mixture ferrugineuse de Griffith, *Fr.;* Griffithsche Eisenmixtur, *G.*

This mixture was dropped from the U. S. P. IX; but is included in the N. F. (See Part III.)

"Ferrous Sulphate, in powder, 6 *grammes;* Potassium Carbonate, 8 *grammes;* Myrrh, 15 *grammes;* Gum Acacia, in powder, 15 *grammes;* Glucose, 15 *grammes;* Spirit of Nutmeg, 10 *millilitres;* Rose Water, sufficient to produce 1000 *millilitres.* Powder the Myrrh; add the Potassium Carbonate, Glucose, and Gum Acacia; triturate the mixture with a small quantity of the Rose Water so as to form a thin paste; gradually add more Rose Water and the Spirit of Nutmeg; continue the trituration and further addition of Rose Water until one thousand *millilitres* of liquid are produced; add the Ferrous Sulphate and shake until dissolved." *Br.*

This is very nearly the same as the celebrated tonic or *antihectic myrrh mixture* of Griffith. The ferrous sulphate is decomposed by the potassium carbonate, with the production of ferrous carbonate and potassium sulphate, while the excess of the alkaline carbonate forms an emulsion-like mixture with the myrrh. The mixture is green in color. It easily decomposes with the production of a red or brown color due to oxidation of the iron. The official solution may, however, be kept for some time without change, if the vessel in which it is contained be well closed, but the best plan is to prepare it extemporaneously. The sugar contained in it helps somewhat to retard the oxidation of the ferrous salt. The finest pieces of myrrh in lump should be selected for the preparation of this mixture.

This mixture is used in *anemia,* especially when attended with derangement of the menstrual function. It has been also employed in the hectic fever of *phthisis.* It is contra-indicated by the existence of inflammation of the gastric mucous membrane.

Dose, from one-half to two fluidounces (15–60 cc.) two or three times a day.

MISTURA GLYCYRRHIZÆ COMPOSITA. U. S.

COMPOUND MIXTURE OF GLYCYRRHIZA Mist. Glycyrrh. Co. [Brown Mixture]

Mistura Fusca; Mixture de Réglisse, *Fr.;* Zusammengesetzte Lakritzenmixtur, *G.*

"Fluidextract of Glycyrrhiza, 120.00 cc.; Antimony and Potassium Tartrate, 0.24 Gm.; Camphorated Tincture of Opium, 120.00 cc.; Spirit of Nitrous Ether, 30.00 cc.; Glycerin, 120.00 cc.; *Water,* a sufficient quantity, to make 1000 cc.

"Dilute the fluidextract with the glycerin and 500 cc. of water, add the antimony and potassium tartrate, dissolved in 12 cc. of hot water, then the other ingredients, and enough water to make the product measure 1000 cc." *U. S.*

The spirit of nitrous ether is probably useful by somewhat retarding decomposition. It has been suggested many times that this preparation be filtered and dispensed clear but the revisers of the Pharmacopœia have not considered it of sufficient importance to change the well-known appearance of the mixture and there are no advantages in making a *mixture* transparent. (See *A. J. P.*, 1892, 563; *M. R.*, 1910, 253.)

Uses.—The compound mixture of glycyrrhiza is used very frequently as a vehicle, especially in conjunction with the ammonium salts in the early stages of acute bronchitis. Its use in such manner, however, is not to be encouraged because of the presence of the antimony and opium. While the dose of the latter ingredients is so small that in a teaspoonful there will scarcely be sufficient to exercise any perceptible effect in the adult, yet their exhibition in unsuitable cases is certainly unwise. In large dose it acts as a nauseating expectorant and is sometimes given, especially in children, for its active effects in *bronchitis*. In our opinion, however, the combination is not a very happy one for this purpose.

Dose, from two to four fluidrachms (8–15 cc.) for an adult; one fluidrachm (3.75 cc.) for a child eight years old. It should be well shaken when administered.

MISTURA GUAIACI. Br.

GUAIACUM MIXTURE

Emulsio Resinæ Guaiaci; Mixture de Résine de Gayac, ait de Gayac, *Fr.;* Guajak-Emulsion, Guajakharzmixtur, *G.*

"Guaiacum Resin, 25 *grammes;* Refined Sugar, 25 *grammes;* Tragacanth, in powder, 5 *grammes;* Cinnamon Water, sufficient to produce 1000 *millilitres.* Triturate the Guaiacum Resin with the Refined Sugar and the Tragacanth; add gradually, with constant trituration, sufficient Cinnamon Water to produce the required volume." *Br.*

For the changes of color which the Guaiac in this mixture undergoes, and which it produces in other substances, see *Guaiaci Resina,* p. 539. A similar preparation under this title is official in the N. F. (See Part III).

Dose, one-half to two fluidounces (15–60 cc.), repeated two or three times a day, or more frequently.

MISTURA OLEI RICINI. Br.

CASTOR OIL MIXTURE

Emulsion of Castor Oil; Emulsion d'Huile de Ricin, *Fr.;* Ricinusoelmixtur, *G.*

"Castor Oil, 375 *millilitres;* Gum Acacia, in powder, 100 *grammes;* Orange-flower water of commerce, undiluted, 150 *millilitres;* Cinnamon Water, sufficient to produce 1000 *millilitres.* Triturate the Castor Oil with the Gum Acacia in a dry mortar; add, in one portion, two hundred *millilitres* of Cinnamon Water, and continue the trituration until the oil is completely emulsified; then, with constant trituration, add the orange-flower water and sufficient Cinnamon Water to produce the required volume." *Br.*

Under the title *Emulsum Olei Ricini* a similar preparation is official in the N. F. (See Part III.)

Dose, from one-half to two fluidounces (15–60 cc.).

MISTURA SENNÆ COMPOSITA. Br.

COMPOUND MIXTURE OF SENNA

Black Draught; Mixture de Séné composée, *Fr.;* Zusammengesetzte Senna-Aufguss, Zusammengesetzte Sennamixtur, *G.*

"Magnesium Sulphate, 250 *grammes;* Liquid Extract of Liquorice, 50 *millilitres;* Compound Tincture of Cardamoms, 100 *millilitres;* Aromatic Spirit of Ammonia, 50 *millilitres;* Infusion of Senna, sufficient to produce 1000 *millilitres.* Dissolve the Magnesium Sulphate in five hundred *millilitres* of the Infusion of Senna; add the mixed Liquid Extract of Liquorice, Compound Tincture of Cardamoms, and Aromatic Spirit of Ammonia, and sufficient infusion of Senna to produce the required volume." *Br.*

This is a form of Compound Infusion of Senna, called commonly *black draught,* which term should never be used, as death has occurred through misreading prescriptions and dispensing *"black drop"* or vinegar of opium. The Compound Mixture of Senna is an active, but rather unpleasant, cathartic.

Dose, from one to two fluidounces (30–60 cc.).

MISTURÆ

MIXTURES

Mixtures, *Fr.;* Mixturen, *G.;* Mixtura, *Sp.*

This term should be restricted, in the language of pharmacy, to those preparations in which insoluble substances, usually solid, are suspended in aqueous fluids, by the intervention of gum arabic, sugar, yolk of egg, or other viscid matter. When the suspended substance is of an oleaginous nature, the preparation is preferably called an *emulsion,* and the U. S. Pharmacopœia has recognized these as a special class. (See *Emulsa.*) The object of mixtures is usually to facilitate the administration, to conceal the taste, or to obviate the nauseating effects of unpleasant medicines, and their perfection depends upon the intimacy with which the ingredients are blended. Some skill and care are requisite for the production of uniform and perfect mixtures. As a rule, the body to be suspended should be thoroughly mixed by trituration with the substance intended to act as the suspending medium, before the aqueous vehicle is added. In Great Britain, and to some extent in this country, the term mixture is used indiscriminately for aqueous medicinal liquids having more than one ingredient, and for aqueous liquids which cannot be easily classified. Many of such liquids are perfectly transparent and should be in the class appropriate to each.

A study of the principles of colloid chemistry has been brought to bear upon the subject of pharmaceutical mixtures and their preparation, with great advantage (see *Emulsa*).

MITCHELLA. N. F.

MITCHELLA Mitchel. [Squaw Vine]

"Mitchella is the dried plant of *Mitchella repens* Linné (Fam. *Rubiaceæ*). Mitchella contains not more than 5 per cent. of foreign organic matter." *N. F.*

Squaw Vine; Twin Berry; Squaw Berry; Partridge Berry; Checkerberry; Winter Clover; (*Fam.* Rubiaceæ.)

This beautiful little trailing, evergreen herb is characterized by its creeping habit, its round ovate opposite leaves which are usually variegated with whitish lines, and which remain green through the winter. The dimorphic flowers occur in pairs and are white and fragrant, but less conspicuous than the scarlet, berry-like, edible fruit which remains on the vine through the winter. The plant is native to North America being found in coniferous woods from Nova Scotia to Minnesota, south to Florida and Mexico. Abundant supplies of this drug are collected in New Hampshire.

Description and Physical Properties.—"*Unground Mitchella.*—In loosely matted masses consisting of much branched rhizomes with their fine roots together with the stems and leaves; rhizomes light yellowish to dark brown; filiform, with slender fibrous roots; stems quadrangular or flattened, light green with surface finely striated, bearing opposite leaves; leaves green, coriaceous, opposite, rounded ovate, entire up to about 2 cm. in length and with a short petiole, upper surface smooth, dark green with prominent mid-rib and veins, lower surface smooth, light and somewhat shiny. Odor faint; taste slightly bitter.

"*Powdered Mitchella.*—Light grayish-green; numerous raphides of calcium oxalate from 0.020 to 0.055 mm. in length; greenish fragments of epidermal cells with broadly elliptical stomata the latter from 0.020 to 0.027 mm. in length associated with chlorenchyma cells, some of the latter containing a yellowish amorphous content; tracheæ with spiral or reticulate markings; fragments composed of cortical parenchyma some of the cells containing raphides of calcium oxalate; starch grains, mostly simple, spheroidal or ellipsoidal and up to about 0.010 mm. in diameter." *N. F.*

E. Breneiser (*A. J. P.*, 1887, 228) found it to contain some resin, wax, mucilage, dextrin, and what appeared to be a saponin. Mitchella was employed, in decoction, by the Indian squaws, to facilitate parturition. It has been esteemed to be diuretic, tonic, and alterative like the pipsissewa, for which it is often substituted. It is used in *dysmenorrhea* and in irritation of the bladder but is of very questionable value.

Dose, from thirty to sixty grains (2–4 Gm.).

Off. Prep.—Fluidextractum Mitchellæ, *N. F.;* Elixir Aletridis Compositum, *N. F.;* Elixir Heloniadis Compositum, *N. F.*

MORPHINA

MORPHINE

"An alkaloid [$C_{17}H_{19}O_3N + H_2O = 303.18$] obtained from opium." *U. S. IX.*

Morphia, *U. S.* 1870; Morphinum, Morphium; Morphine, *Fr. Cod.;* Morphin, *G.;* Morfina, *It.*, *Sp.*

Although the base morphine is no longer official, for convenience the chemical and therapeutic properties are considered under this title and the various salts under their separate official names.

Various processes for preparing morphine have been employed. In the older processes the morphine was extracted from opium by maceration with water (either pure or acidulated), then precipitated by ammonia, and the crystals afterwards purified by the agency of alcohol, or by repeated solution in a diluted acid and precipitation. Sertürner, the discoverer of morphine, made an infusion of opium in distilled water, precipitated the morphine by ammonia in excess, dissolved the precipitate in diluted sulphuric acid, precipitated anew by ammonia, and purified by solution in boiling alcohol, and crystallization. In evaporating aqueous solutions containing morphine a temperature of 40° C. should not be exceeded.

Morphine is now produced by making opium into a thin paste with calcium chloride solution which converts the alkaloids into hydrochlorides and holds back the meconic and other acids of the drug as calcium salt. Water is then used for extraction, sodium sulphite being employed to prevent oxidation. A concentrated solution of sodium acetate is then added which precipitates narcotine and papaverine. To the filtrate a small amount of alcohol is added and the morphine then precipitated by the careful addition of ammonium chloride and slaked lime. The filtrate after the precipitation and removal of the morphine is shaken out with benzene or chloroform to recover codeine. The morphine is subsequently purified by solution in hydrochloric acid and reprecipitation.

Properties.—Morphine crystallizes from alcohol in the form of small, colorless, shining crystals. It was officially described as follows: "Colorless or white, shining, rhombic prisms, in fine needles, or as a crystalline powder; odorless; permanent in the air. One Gm. of Morphine dissolves in 3340 mils of water, 210 mils of alcohol, 1220 mils of chloroform, 6250 mils of ether, and in 100 mils of lime water, at 25° C.; also in 1075 mils of boiling water and 98 mils of boiling alcohol; insoluble in benzene. A saturated aqueous solution of Morphine is alkaline to litmus. One mil of sulphuric acid added to about 0.05 Gm. of Morphine produces either no color or at most only a red or yellow tint; on heating, a brown color is developed. Sulphuric acid containing 0.005 Gm. selenous acid in each mil gives with Morphine a blue color, changing to green and then to brown. (Codeine yields a green color, changing to blue, and afterwards to grass-green; narcotine gives a green color, changing to brown and then to cherry-red.) Nitric acid produces with Morphine an orange-red color fading to yellow. Sulphuric acid containing 0.005 Gm. of molybdic acid in each mil gives a purple color, changing to blue. Sulphuric acid containing in each mil one drop of solution of formaldehyde yields an intense, purple color. Add a few drops of ferric chloride T.S. to a neutral solution of Morphine (1 in 100), made by the careful addition of diluted sulphuric acid; a blue color is produced which is destroyed by acids, alcohol, or by heating. Morphine solutions, when mixed with an aqueous solution of potassium ferricyanide containing a drop of ferric chloride T.S., yield deep blue solutions from which, after standing, a blue precipitate separates (difference from *codeine*). Morphine loses not more than 6.5 per cent. of its weight when dried to constant weight at 100° C. (*moisture*). No weighable ash remains on incinerating 0.5 Gm. of Morphine. Dissolve about 0.1 Gm. of Morphine in 10 mils of diluted hydrochloric acid; no red coloration is produced by the addition of a few drops of ferric chloride T.S. (*meconic acid or meconates*). Warm about 0.2 Gm. of Morphine with 4 mils of potassium hydroxide T.S.; the odor of ammonia is not noticeable (*ammonium salts*). Dissolve 1 Gm. of Morphine in 10 mils of sodium hydroxide T.S., shake out the solution with three successive portions of 15, 10, and 10 mils of chloroform, passing the chloroform solutions through a small filter previously moistened with chloroform. Evaporate carefully the combined chloroform solutions to dryness on a water bath, dissolve the residue in 10 mils of fiftieth-normal sulphuric acid V.S., add a few drops of methyl red T.S. and titrate the excess of acid with fiftieth-normal potassium hydroxide V.S. Not less than 7.5 mils of the latter is required (*foreign alkaloids*)." *U. S. IX.*

Despite the immense amount of labor which has been expended by chemists we are still uncertain as to the exact structure of the morphine molecule. It may be regarded as established that morphine is a tertiary base derivative from phenanthrene; it contains two hydroxyl groups, one being phenolic and the other a secondary alcohol, and also a methyl radical. For an excellent summary of the work that has been done on the structure of morphine see T. A. Henry, *Plant Alkaloids,* 1924, p. 266.

Heated in the open air, morphine burns with a bright flame, and at a red heat is wholly dissipated. In the products resulting from the combustion of opium or morphine this alkaloid may be detected, proving that it is partly volatilized when burned. Morphine in solution is to a considerable extent absorbed by animal charcoal, which, though it will part with most of the alkaloid to alcohol, cannot be wholly deprived of it by repeated washings with that liquid, either cold or hot. It is also adsorbed when filtered through kaolin or fuller's earth. Its solution restores the blue color of litmus paper reddened by acids, and turns the yellow of turmeric to brown. Morphine is a powerful reducing agent, acting upon silver nitrate and gold chloride even in cold solutions. In the presence of sulphuric acid morphine best exhibits its powers as a reducing agent. Among the most notable instances of deoxidation may be mentioned those of silver oxide, hydrated bismuth oxide, the acids of tin, tungsten, vanadium, titanium, and molybdenum. With the acids morphine forms salts, which are generally soluble, and are decomposed by the alkalies. It is dissolved also by the fixed and volatile oils. The solutions of potassium and sodium hydroxides also dissolve morphine, which is precipitated slowly from them on exposure to the air, in consequence of the absorption of carbon dioxide. Solution of ammonia has to a certain extent the same solvent power, and hence the necessity, in precipitating morphine by this alkali, not to employ it in great excess. Solution of iodine with potassium iodide precipitates the salts of morphine in aqueous solution.

With chlorine water morphine and its salts assume an orange color, and the same effect is produced on them by solution of chlorinated soda. By the contact of nitric acid they assume a blood red color, which ultimately changes to yellow, and this is one of the tests for morphine; but, as the same change of color is produced with brucine, it cannot be relied on in the absenec of other evidence. Nitric acid also produces a red color with oil of cloves, but in this case the red does not change to yellow. For other identifying tests which have been used to detect morphine, see *U. S. D.,* xx, p. 703, also papers by Lantenschlaeger (*D. C.,* 1919, lxiii, p. 352), Palet (*Anales Soc. Quim. Argentina,* through *Chem. Abst.,* 1919, xiii, p. 216) and *J. Soc. Chem. Ind.,* 1919, xxxviii, 438a.

A delicate reaction for morphine has been reported by T. H. Oliver, which is sensitive to 0.00002 Gm. morphine. It is as follows: To the solution of the suspected substance, add a few cc. of hydrogen dioxide solution and a few drops of strong ammonia water. Then stir the solution with a piece of copper wire, whereupon the previously colorless solution becomes of a deep port wine color in the presence of morphine. Codeine and dionine do not give the reaction. (*J. A. M. A.,* 1914, 63, p. 513.)

Morphine and its salts assume a fine blue color with ferric chloride; at least this is true of the alkaloid, its sulphate, acetate, and oxalate, and the same effect will be produced by the other salts, if previously decomposed by an alkali, but that this test should be satisfactory it is necessary to operate on morphine either in powder or in concentrated solution.

Formaldehyde reacts with both morphine and codeine to form medicinally active condensation products by the union of two molecules of the base with one molecule of the formaldehyde, with elimination of water; a methylene group, CH_2, uniting with two alkaloidal residues each of which loses an H atom. That formed from morphine is an amorphous base, difficultly soluble in water, but easily soluble in alkaline solution and in alcohol. It melts at 270° C., and forms a hydrochloride soluble in water. (*Proc. A. Ph. A.*, 1897, 702.)

Uses.—There can be no doubt that morphine is the chief narcotic principle of opium, from which, however, it differs somewhat in its mode of action. The effects of morphine are so protean that they can best be considered by taking the different functions of the body seriatim.

Nervous System.—Morphine is a cerebral depressant but a spinal stimulant. The relative predominance of one or the other of these actions depends upon the relative degree of development of the brain or spinal cord; thus in the frog it produces violent convulsions of the strychnic type, but in man the spinal symptoms are usually imperceptible and for medical purposes we may regard it as a general depressant as far as the nervous system is concerned. The primary action upon the cerebrum seems to be a diminution in the powers of perception, especially of pain, although there is often an evident lowering in the acuity of the special senses. With somewhat larger doses intellection becomes depressed and a tendency to drowsiness is manifest, and after toxic doses a deep comatose sleep may follow. When locally applied in sufficient concentration morphine lowers the functional activity of the peripheral nerve endings both motor and sensory. In this way it may, under certain conditions as shown by Wiki (*J. de P. P.*, 1913, xv, p. 848), exercise a local anesthetic action. It is, however, less active in this regard than some of the other allied alkaloids, notably ethyl-morphine or methyl-morphine (codeine). Among the other actions of morphine which are to be attributed to its influence on nerve centers is the contraction of the pupil, due to stimulation of the oculo-motor center, slowing of the pulse from stimulation of the cardio-inhibitory center, slowing of the respiration from depression of the respiratory center, and overcoming the action of nauseants from its action on the emetic center.

Cushny and Lieb (*J. P. Ex. T.*, 1915, vi, p. 450) have found that in the period of respiratory depression produced by morphine there is not the same sort of insensibility to carbon dioxide that is caused by some other respiratory depressants, and according to Macht (*J. P. Ex. T.*, 1915, vii, 339) small doses of morphine may lessen the sensitiveness of the respiratory center to carbon dioxide without reducing the normal volume of air breathed. Cohen and McGuigan (*J. P. Ex. T.*, 1924, xxxiii, 145) believe that the diminution of respiration is not due to a true depression of the respiratory center but simply to a blockage of the afferent impulses which ordinarily excite this center. These observations are obviously of considerable importance in connection with the clinical use of this remedy in dyspneic states.

The influence upon the unstriped muscles, especially upon the intestines, is so complex that its accurate analysis is still somewhat doubtful. Macht (*J. P. Ex. T.*, 1918, xi, p. 389) has shown that morphine has an exciting action upon unstriped muscle. On the other hand, it is well known that morphine, in the human being at least, lessens intestinal peristalsis—a fact which Macht in an earlier communication admitted and attributed to an action upon the central nervous system. In dogs defecation is a very frequent sequela after the administration of morphine. This, however, is probably due to the difference in dosage employed in dogs and man; Uhlmann and Abelin (*Zeit. E. P. T.*, 1920, xxi, 75) from experimental studies have found that while small doses of opium diminish intestinal peristalsis, larger quantities increase. Morphine causes, certainly in the lower animals and probably also in humans, a spasmodic contraction of the pylorus, which may perhaps explain the nausea that often follows its use.

Circulation.—The action of morphine upon the circulation is quite subsidiary to its effects upon the nervous system. In therapeutic doses the only manifestation of its effects on the part of the circulatory apparatus is slowing of the pulse, due, as mentioned above, to stimulation of the inhibitory center, and flushing of the skin which appears to be the result of a special action on the cutaneous blood vessels. After large doses the blood pressure is generally somewhat lowered, probably from the combined weakening of the heart and vasomotor system.

Nutrition.—Morphine affects the nutrition both through its action upon the digestive processes and through a direct influence on the bodily chemistry. It appears to lessen all the digestive secretions including salivary, gastric, and enteric, also to diminish the peristaltic movements. The direct influence of morphine upon metabolism is not clearly understood, but there is reason to believe that it has some such action.

Elimination.—A large part of the morphine is detoxicated in the body passing out as a dioxymorphine. Some of it, however, is eliminated unchanged, more through the intestinal glands than the kidneys.

Clinical Uses.—Morphine may be used in medicine to fulfil any of seven indications: (1) In its power to relieve *pain* morphine is without rival. Because, however, of its unpleasant action upon the digestive organs and the ever-present danger of formation of the habit, it should be reserved for the more severe degrees of suffering, such as in *gall-stone* or *renal colic*, or when other analgesics have failed. In this connection it should be noted that the analgesic action of morphine is greatly enhanced by combining it with even relatively feeble synergists, such as the coal tar series or scopolamine, and by recourse to this principle of combination the physician is often able to assuage the suffering with comparatively small doses of the alkaloid. (2) As a hypnotic morphine is useful, especially when the *insomnia* is due to suffering. In the purely nervous types of sleeplessness it is less valuable than the aliphatic narcotics, but is often of service as an adjuvant. (3) As a sedative to the respiratory center it is a remedy of much value in *asthma* and certain types of *cough,* such as *whooping cough.* In true *bronchitis,* however, it must be used with circumspection. In the acute stage or where the mucous membranes are dry, it often does great harm by a further checking of the bronchial secretions; on the other hand, when the secretions are very profuse it may so benumb the respiratory center as to stop their expectoration and thereby lead to a dangerous retention of fluid in the chest. (4) In intestinal conditions it is used for its influence both on secretion and peristalsis. For the latter action it is of much service in serous *diarrheas,* but when the diarrhea is due to irritation of the intestinal tract it is generally to be avoided, as it defeats nature's purpose to get rid of the irritant. For its influence upon the muscular movements of the bowel it is useful in various forms of intestinal spasm, such as *lead colic,* and also to keep the bowels at rest in certain types of *peritonitis* and other inflammatory conditions. Whole opium is usually preferred to morphine when an action upon the intestines is desired. (5) For the purpose of aiding in the production of diaphoresis it is used, especially in the form of Dover's powder, in the early stages of *colds,* in *rheumatism, influenza,* etc. (6) To allay *vomiting,* especially of reflex origin. (7) By its calmative effect it protects the system against exhaustion in debilitated conditions, as certain forms of *typhoid fever.* For the same purpose it is also a very valuable drug in the treatment of *internal hemorrhage.*

In cases where it is desired to make a profound impression upon the general system, morphine should be given hypodermically. The dose varies enormously, according to the susceptibility of the patient and the purpose for which it is used. In a general way the dose of the morphine salts, by mouth, may be given as from one-eighth to one-half grain (0.008–0.032 Gm.), and one-twelfth to one-fourth grain (0.005–0.016 Gm.) hypodermically.

In consequence of its insolubility in water, morphine in its pure state is less convenient than its salts, which are therefore always preferred. The acetate, sulphate, and hydrochloride, which have been employed, act precisely alike therapeutically, and differ from opium chiefly in being less disposed to constipate the bowels. They are also somewhat less likely to cause disagreeable after-effects than is opium, but the deodorized tincture is certainly preferable to them for many purposes. They are further adapted for hypodermic use. Oleic acid has also been proposed as a vehicle for morphine externally used, as it dissolves both the alkaloid and its salts perfectly in considerable proportion. A liniment of oleate of morphine has been proposed, consisting of 300 parts of oleic acid and 1 part of morphine scented with a little oil of bergamot.

As the proportion of acid necessary to neutralize morphine is very small, the dose of the alkaloid is practically the same as that of its salts.

Dose, one-fifth of a grain (0.012 Gm.), equivalent to a grain of powdered opium.

MORPHINÆ ACETAS. Br.

MORPHINE ACETATE

"Morphine Acetate, $C_{17}H_{19}NO_3,C_2H_4O_2,3H_2O$, is the acetate of an alkaloid, morphine, obtained from opium." *Br.*

Morphiæ Acetas, *Br.* 1867, *U. S.* 1870; Acetate of Morphia; Morphinum Aceticum; Acetas Morphicus; Acétate de Morphine, *Fr.;* Essigsaures Morphium, Morphinacetat, *G.*

No process for this salt is official; that of the U. S., 1870, may be found in the *U. S. D.,* 20th ed., p. 706.

Properties.—It is officially described in the British Pharmacopœia as "a white, crystalline or amorphous powder. Taste bitter. Almost entirely soluble in 2.5 parts of *water.* Loses acetic acid when exposed to the air. Yields the reactions for morphine described under 'Morphinæ Hydrochloridum,' and the *reactions* characteristic of acetates. 2 grammes form with 5 millilitres of warm *morphinated water* a slightly turbid solution which is rendered clear by the addition of 0.1 millilitre of *acetic acid,* and this solution, when mixed with a slight excess of *solution of ammonia,* yields a white precipitate which, after washing and drying as described under 'Morphinæ Hydrochloridum,' weighs from 1.41 to 1.44 grammes. No appreciable ash." Br.

Uses.—This and the other official salts of morphine are of identical medicinal value. (See *Morphina.*) The solutions for hypodermic use should be freshly prepared, as morphine salts, especially the acetate, are very prone to undergo decomposition, through the growth of a fungus.

Dose, one-twelfth to one-half grain (0.005–0.032 Gm.).

Off. Prep.—Liquor Morphinæ Acetatis, *Br.*

MORPHINÆ HYDROCHLORIDUM.
U. S., Br.

MORPHINE HYDROCHLORIDE Morph. Hydrochl.

"The hydrochloride [$C_{17}H_{19}O_3N.HCl.3H_2O$] of an alkaloid obtained from opium." *U. S.* "Morphine Hydrochloride, $C_{17}H_{19}NO_3,HCl,3H_2O$, is the hydrochloride of an alkaloid, morphine, obtained from opium." *Br.*

Morphinæ Hydrochloras; Morphine Hydrochlorate; Morphine Chloride; Morphiæ Murias; Murias (Hydrochloras) Morphicus; Morphiæ Hydrochloras; Muriate of Morphia; Chlorhydrate de Morphine, *Fr. Cod.;* Morphinum Hydrochloricum, *P. G.*; Morphinhydrochlorid, Salzsaures Morphin, *G.*

A process for this salt is no longer official. The British process (1885) will be found in *U. S. D.*, 17th ed., 882. See also *U. S. D.*, 19th ed., 790.

Description and Physical Properties.—"White, silky, glistening needles or cubical masses, or a white, crystalline powder. It is odorless, and is stable in the air. One Gm. of Morphine Hydrochloride is soluble in 17.5 cc. of water and in 52 cc. of alcohol, at 25° C. One Gm. is soluble in 0.5 cc. of boiling water and in 46 cc. of alcohol at 60° C. It is soluble in glycerin, but insoluble in chloroform and in ether.

"Silver nitrate T.S. added to an aqueous solution of the salt produces a white precipitate, insoluble in nitric acid. Morphine Hydrochloride responds to the tests for identity for morphine under *Morphinæ Sulphas*.

"Morphine Hydrochloride loses not more than 15 per cent. when dried to constant weight at 100° C. (*water*).

"Add 2 cc. of potassium carbonate T.S. to 5 cc. of an aqueous solution of the salt (1 in 30), and gently shake the mixture: a white precipitate is produced, which does not become green on exposure to air, nor color chloroform when shaken with it (*apomorphine*). Morphine Hydrochloride also complies with the tests for purity under *Morphinæ Sulphas*. Preserve in well-closed containers, protected from light." *U. S.*

"Acicular crystals, or a white microcrystalline powder. Taste bitter. Soluble in 25 parts of *water*. 1 drop of *solution of ammonia* added to 5 millilitres of an aqueous solution (1 in 30) produces a white crystalline precipitate easily soluble in *solution of sodium hydroxide*, but soluble with difficulty in excess of *solution of ammonia;* this precipitate yields mere traces to *benzene* (absence of certain other alkaloids). Yields, when moistened with *nitric acid*, an orange-red color; with *T. Sol. of ferric chloride*, a dull greenish-blue. A trace added to 5 millilitres of a very dilute solution of *potassium ferricyanide* to which 1 drop of *T. Sol. of ferric chloride* has been added produces a deep blue color. 0.1 gramme dissolves in 2 millilitres of *sulphuric acid* without coloration, or with the production of not more than a faint pink color; if a portion of this solution is heated on a water-bath for fifteen minutes, cooled, and treated with a few drops of *diluted nitric acid*, a violet coloration, rapidly changing to blood-red, is produced; the addition of *sodium arsenate* to another portion of the original solution produces a bluish-green color. 1 drop of *solution of potassium carbonate* added to 5 millilitres of an aqueous solution (1 in 30) yields a pure white precipitate which does not become colored on exposure to the air, and does not color *chloroform* when shaken with it (distinction from and absence of apomorphine). When 0.5 millilitre of an aqueous solution (1 in 100) is mixed on a white porcelain tile with 0.5 millilitre of *mucilage of starch* in which 0.005 gramme of *iodic acid* has been dissolved, a blue coloration is immediately produced (distinction from morphine esters). Yields the reactions characteristic of chlorides. 2 grammes dissolved in 50 millilitres of warm *morphinated water* give, on the addition of a slight excess of *solution of ammonia*, a white, crystalline precipitate which, when washed with a little cold *morphinated water* and dried, first at 55° to 60° C., and finally for fifteen minutes at 115° C., weighs from 1.50 to 1.52 grammes. Loses about 14 per cent. of its weight when dried at 100° C. No appreciable ash." *Br.*

A saturated solution in boiling water forms a solid crystalline mass on cooling. The solution of morphine hydrochloride, when kept several months, has been known to produce vomiting, through the formation of traces of apomorphine. (*Ph. Centralh.*, 1885, 93.) Potassium hydroxide throws down from its solution a precipitate which is redissolved by an excess of the alkali. The salt is affected by heat, nitric acid, iodic acid, ferric chloride, and chlorine followed by ammonia, in the same manner as morphine. Sugar is said to have been used largely in the adulteration of this salt. It may be detected most readily by the deep red color produced when the adulterated salt is dissolved in strong sulphuric acid. (See *Saccharum*.)

This preparation of morphine is much used in Great Britain, but in this country less than the sulphate. For medicinal properties, see *Morphina*.

Dose, one-twelfth to one-half grain (0.005–0.032 Gm.).

Off. Prep.—Liquor Morphinæ Hydrochloridi, *Br.;* Suppositoria Morphinæ, *Br.;* Tinctura Chloroformi et Morphinæ Composita, *Br.;* Trochiscus Morphinæ, *Br.;* Syrupus Morphinæ et Acaciæ, *N. F.;* Trochiscus Morphinæ et Ipecacuanhæ, *Br.*

MORPHINÆ SULPHAS. U. S.

MORPHINE SULPHATE Morph. Sulph.

"The sulphate [$(C_{17}H_{19}O_3N)_2.H_2SO_4.5H_2O$] of an alkaloid obtained from opium." *U. S.*

Morphiæ Sulphas, *Br.* 1867, *U. S.* 1870; Morphinum Sulphuricum, Sulphas Morphicus; Sulphate of Morphia; Sulfate de Morphine neutre, *Fr. Cod.;* Schwefelsaures Morphium, Morphinsulfat, *G.;* Sulfato morifico, *Sp.*

No process is given in the present U. S. P.; for that of the U. S. P., 1870, see *U. S. Dispensatory*, 19th ed., p. 791. Morphine sulphate is no longer official in the British Pharmacopœia, 1898, the hydrochloride being used in Great Britain, as in Germany, almost exclusively.

Morphine sulphate is prepared from morphine alkaloid, by neutralization with sulphuric acid and careful subsequent concentration of the solution to the crystallizing point. The crystalline masses are then cut into the rectangular blocks so characteristic of this alkaloidal salt. For details of the process as applied on the commercial scale see Calvert (*Pac. Drug.*, June, 1893).

By exposure to a heat of 120° C. it loses 9.66 per cent. of the water, but cannot be deprived of the remainder without decomposition.

The *solution of morphine sulphate* formerly official was made by dissolving 1 grain of morphine sulphate in 1 fluidounce of distilled water, and, although the solution is more stable than that of any other of the morphine salts in common use, it will in time become weakened through the presence of microscopic plants belonging to the Confervoideæ, and hence it is not desirable to keep it on hand.

Description and Physical Properties.—"White, feathery, silky crystals, or cubical masses, or a white, crystalline powder. It is odorless, and is stable in the air. One Gm. of Morphine Sulphate is soluble in 15.5 cc. of water and in 565 cc. of alcohol, at 25° C. One Gm. is soluble in 0.7 cc. of water at 80° C. and in 240 cc. of alcohol at 60° C. It is insoluble in chloroform and in ether.

"Add a few drops of ammonia T.S. to 5 cc. of an aqueous solution of Morphine Sulphate (1 in 30), and gently shake the mixture: a white precipitate is formed, which dissolves upon the subsequent addition of a few cc. of sodium hydroxide T.S. Sulphuric acid containing 0.005 Gm. of selenous acid in each cc. gives with Morphine Sulphate a blue color, changing to green and then to brown. *Codeine* yields a green color changing to blue and afterwards to grass-green. Sulphuric acid containing 0.005 Gm. of molybdic acid in each cc. gives a purple color, changing to blue. Sulphuric acid containing in each cc. one drop of formaldehyde T.S. yields an intensely purple color. With nitric acid Morphine Sulphate produces an orange-red color fading to yellow. The addition of a few drops of freshly prepared ferric chloride T.S. to an aqueous solution of Morphine Sulphate (1 in 100) produces a blue color, which is destroyed by acids, alcohol, or by heating. Add potassium ferricyanide T.S., containing 1 drop of ferric chloride T.S. in each cc. to an aqueous solution of the salt (1 in 100); a deep blue color is produced at once (*difference from codeine*). Barium chloride T.S. produces in an aqueous solution of the salt a white precipitate, insoluble in hydrochloric acid.

"A solution of 0.5 Gm. of the salt in 15 cc. of distilled water requires not more than 0.5 cc. of fiftieth-normal sodium hydroxide for neutralization, using one drop of methyl red T.S. as indicator. Dried to constant weight at 130° C., Morphine Sulphate loses not more than 12 per cent. (*water*). The ash from 0.5 Gm. is negligible. Warm 0.2 Gm. of Morphine Sulphate with 5 cc. of sodium hydroxide T.S.: the odor of ammonia is not noticeable (*ammonium salts*). Add a few drops of ferric chloride T.S. to 5 cc. of an aqueous solution of the salt (1 in 30), previously mixed with 5 cc. of diluted hydrochloric acid: no red color is produced (*meconate*). Dissolve 1 Gm. of Morphine Sulphate in 10 cc. of sodium hydroxide T.S. in a separator, and shake the solution with three successive portions of 15, 10 and 10 cc. of chloroform, passing the chloroform solutions through a small filter previously moistened with chloroform. Shake the combined chloroform solutions with 5 cc. of distilled water, separate the chloroform, and evaporate it carefully to dryness on a water bath. Add to the residue thus obtained 10 cc. of fiftieth-normal sulphuric acid, heat gently until dissolved, cool, add two drops of methyl red T.S., and titrate the excess of acid with fiftieth-normal sodium hydroxide: not less than 7.5 cc. of the latter is required (*foreign alkaloids*).

"Preserve in well-closed containers, protected from light." *U. S.*

In the United States this salt of morphine is used almost to the exclusion of all others. For medicinal properties, see *Morphina.*

Dose, from one-twelfth to one-half grain (0.005–0.032 Gm.).

Off. Prep.—Mistura Chloroformi et Morphinæ Composita, *N. F.;* Syrupus Pini Albæ Compositus cum Morphina, *N. F.*

MORPHINÆ TARTRAS. Br.

MORPHINE TARTRATE

"Morphine Tartrate, $(C_{17}H_{19}NO_3)_2,C_4H_6O_6,3H_2O$, is the tartrate of an alkaloid, morphine, obtained from opium." *Br.*

Morphinum Tartaricum; Tartrate de Morphine, *Fr.;* Morphintartrat, Weinsaures Morphium, *G.*

This salt of morphine was brought into notice by Erskine Stuart (1880), and recommended for hypodermic injection because of its greater solubility in water over the other salts of morphine. (See *Injectio Morphinæ Hypodermica* and *Liquor Morphinæ Tartratis*). It is officially described as "minute acicular crystals, efflorescent at 20° C. Taste bitter. Soluble in 11 parts of *water,* forming a clear solution neutral to litmus. Yields the reactions for morphine described under 'Morphine Hydrochloridum,' and the *reactions* characteristic of tartrates. 2 grammes dissolved in 20 millilitres of warm *morphinated water* give, on the addition of a slight excess of *solution of ammonia,* a precipitate which, after washing and drying as described under 'Morphinæ Hydrochloridum,' weighs from 1.46 to 1.49 grammes. No appreciable ash." *Br.*

A. E. Tanner (*P. J.,* 1903, 134) found morphine tartrate in the English market of low solubility; he investigated the subject and stated that an acid tartrate of morphine was sparingly soluble, that this was found in commerce and that it required 100 parts of cold water for its solution.

Dose, one-twelfth to one-half grain (0.005–0.032 Gm.).

Off. Prep.—Injectio Morphinæ Hypodermica, *Br.;* Liquor Morphinæ Tartratis, *Br.*

MUCILAGO ACACIÆ. U. S., Br.

MUCILAGE OF ACACIA *Mucil. Acac.*
[*Mucilage of Gum Arabic*]

Mucilage of Gum Arabic; Mucilage of Gum Acacia; Mucilage de Gomme, *Fr. Cod.;* Mucilage arabique, *Fr.;* Mucilago Gummi Arabici, *P. G.;* Gummischleim, *G.;* Mucilagine di gomma arabica, *It.;* Mucilago de goma arabica, *Sp.*

"Acacia, in small fragments, 350 Gm.; Sodium Benzoate, 1 Gm.; Distilled Water, a sufficient quantity, to make 1000 cc. Place the acacia in a graduated bottle having a wide mouth and a capacity not exceeding 1000 cc., wash the drug with cold water, allow it to drain, and add enough warm distilled water, in which the sodium benzoate has been dissolved, to make the product measure 1000 cc. After stoppering, lay the bottle on its side, rotating it occasionally, and when the acacia is dissolved, strain the mucilage. Mucilage of Acacia must not be dispensed if it has become sour or mouldy." *U. S.*

"Gum Acacia, 100 *grammes;* Distilled Water, 150 *millilitres.* Rapidly rinse the Gum Acacia with a little *water;* then dissolve it in the Distilled Water in a closed vessel and strain. The Mucilage should be recently prepared. In India and the Eastern Division of the Empire, Mucilage of Indian Gum may be employed in making the official preparations for which Mucilage of Gum Acacia is directed to be used (see 'Gummi Indicum')." *Br.*

This is a very unstable preparation. Numerous suggestions have been made for preserving it. Lime water was employed as a solvent in the U. S. P. VIII, but while the stability of the preparation was improved the incompatibilities of the lime water worked havoc in extemporaneous prescriptions when the physician had forgotten its presence. The only way to have good fresh sweet mucilage of acacia is to make it frequently and use it up rapidly. The addition of sodium benzoate, in the new U. S. formula, while it may serve a useful purpose as a preservative, has objections on the similar ground of incompatibility.

MUCILAGO GUMMI INDICI. Br.

MUCILAGE OF INDIAN GUM

"Indian Gum, 50 *grammes;* Distilled Water, 150 *millilitres.* Rapidly rinse the Indian Gum with a little *water;* then dissolve it in the Distilled Water in a closed vessel and strain. The Mucilage should be recently prepared. In India and the Eastern Divisions of the Empire, Mucilage of Indian Gum may be employed in making the official preparations for which Mucilage of Gum Acacia is directed to be used (see 'Gummi Indicum')." *Br.*

This mucilage was made official in the British Pharmacopœia (1914); it is not as adhesive as the mucilage of acacia.

MUCILAGO TRAGACANTHÆ. U. S., Br.

MUCILAGE OF TRAGACANTH *Mucil. Trag.*

Mucilage de Gomme Adragante, *Fr. Cod.;* Mucilage adragant, *Fr.;* Traganthschleim, *G.;* Mucilagine di gomma adragante, *It.*

"Tragacanth, 6 Gm.; Glycerin, 18 Gm.; Water, a sufficient quantity, to make 100 Gm. Mix the glycerin with 75 cc. of water in a tared vessel, heat the mixture to boiling, remove the heat, add the tragacanth, and macerate during twenty-four hours, stirring occasionally. Then add enough water to make the mixture weigh 100 Gm., stir actively until of uniform consistence, and strain forcibly through muslin." *U. S.*

"Tragacanth, in powder, 1.25 *grammes;* Alcohol (90 per cent.), 2.50 *millilitres;* Distilled Water, sufficient to produce 100.00 *millilitres.* Mix the Tragacanth with the Alcohol; add the Distilled Water as quickly as possible, and shake vigorously." *Br.*

A part only of tragacanth is soluble in water. The remainder swells up and forms a soft tenacious mass, which may be mechanically mixed with water, but does not form a proper solution. Hence trituration is necessary to complete the incorporation of the ingredients. This mucilage is thick and very viscid, but not permanent, as the water separates from the insoluble portion of the tragacanth on standing. It is chiefly used in making pills and troches. The addition of glycerin renders it more serviceable as an excipient. From its great tenacity, it may be advantageously employed for the suspension of heavy insoluble substances, such as the metallic oxides, in water. When kept long, it is apt to undergo decomposition, and to become offensive, but it will keep well if phenol be added. Lyon (*P. J.*, 1901, 600) recommends the use of chloroform water as a preservative in making this mucilage; this is preferred in all cases if the mucilage is not to be used internally. The alcohol in the British process facilitates the quick production of the mucilage, and in addition acts as a preservative.

MYRICA. N. F.

BAYBERRY BARK *Myric.* [*Wax Myrtle Bark*]

"Bayberry Bark is the dried bark of the root of *Myrica cerifera* Linné or *Myrica carolinensis* Miller (Fam. *Myricaceæ*). Bayberry Bark contains not more than 5 per cent. of adhering wood or other foreign organic matter." *N. F.*

Wax Myrtle; Bayberry; Candle Berry; Wax Berry; Candlewood; Candle Tree; Tallow-shrub; Sweet Oak; Tallow Bayberry; Arbre à suif, *Fr.;* Wachsbaum, Wachsgagel, *G.*

Myrica cerifera L. varies from a low, evergreen, diœcious shrub to a tree attaining a height of 12 m. It is found growing in brackish marshes, in sandy soil on the border of brackish ponds and (usually) near the sea, from New Jersey south to Florida, west to Texas and northward to the valley of the Washita River in Arkansas. It possesses crooked branches which form a round-topped head, fragrant, lanceolate-cuneate, coriaceous, evergreen leaves, covered on both surfaces with numerous orange-red and golden-yellow glands, and glandular-dotted catkins of small, apetalous flowers which appear below the leaves on the previous year's wood. The fruits are small, spherical, bluish-white ceriferous nuts, the waxy coating of which has been used along with that from the fruits of the Bayberry (*M. Carolinensis* Mill.) and the hybrids between the Wax Myrtle and Bayberry (*M. Macfarlanei* Youngken) in the production of myrtle wax (see *Vegetable Wax*).

The commercial supplies of the drug come from the states bordering the south Atlantic seaboard. The root bark has been adulterated with the rhizome and aerial stem barks. For distinctions between these three barks see Youngken (*Jour. A. Ph. A.*, 1923, p. 484).

Description and Physical Properties.—"*Unground Bayberry Bark.*—In transversely curved pieces, strips or quills of varying length and breadth and usually 2.5 mm. or less in thickness, rarely up to 5 mm. in thickness (aerial stem bark); outer surface varying from silvery gray to grayish brown or reddish brown, scaly in rhizome and root barks, bearing occasional warts or slight transverse ridges, that of the aerial stem bark exhibiting a number of raised oval lenticels; inner surface reddish brown to brown, finely longitudinally striated, somewhat roughened (rhizome and root barks); fracture short, weak and uneven, the fractured surface reddish brown with short projecting fibers near and along the inner margin of root bark. Odor characteristic; taste astringent, mildly bitter and slightly acrid.

"*Structure.*—Root bark; an outer cork of several layers of suberized cells many of which possess lignified walls, a phellogen, a secondary cortex of cortical parenchyma, some of the cells of which contain tannin, others starch, others rosette crystals or monoclinic prisms of calcium oxalate, while some are more or less filled with a yellowish brown gummy lignin, a broad phlœm separated into a number of phlœm patches by starch-containing medullary-rays which frequently broaden out toward the cortex; phlœm parenchyma with contents similar to those found in the cortical parenchyma; among the cells of both phlœm and cortex numerous fibers and stone cells arranged both singly and in groups, the former often accompanied by crystal fibers containing monoclinic prisms of calcium oxalate. Aerial stem bark similar to the root bark, chiefly distinguished from the latter by possessing a continuous or nearly continuous band of fibers and cells in the pericycle. Rhizome bark differs mainly by the absence of sclerenchyma elements in the cortex, fewer sclerenchyma elements in the phlœm and further by the presence of a discontinuous zone of widely separated islets of narrow, comparatively thin-walled fibers in the pericycle.

"*Powdered Bayberry Bark.*—Reddish brown; numerous simple or 2- to 3- or rarely 4-compound starch grains, the individual grains being spheroidal or plano-convex, often with a central cleft and up to 0.012 mm. in diameter; calcium oxalate crystals chiefly in monoclinic prisms from 0.007 to 0.025 mm. in length, some in the form of rosettes from 0.011 to 0.045 mm. in diameter; numerous strongly lignified fibers with walls up to about 0.038 mm. in thickness; numerous stone cells of varying shape up to 0.125 mm. in length, with thick, lignified, lamellated and porous walls; cork cells polygonal in surface view and frequently with lignified walls; numerous fragments of parenchyma some of the cells rich in starch, others containing gummy lignin which is insoluble in cold or boiling water, cold concentrated sodium hydroxide solution, ammonia, alcohol or xylol but soluble in boiling nitric acid, boiling concentrated sodium hydroxide solution and hot solution of sodium hypochlorite; tracheæ from adhering wood few or absent." *N. F.*

For a detailed study of the *Myricaceæ* of the Eastern United States, see Youngken. (*Contrib. Bot. Lab. U. of Pa.*, 1919, iv, No. 2, p. 339.) *M. Gale* L. (*Sweet Gale, Dutch Myrtle*) has been used as a substitute for hops, and the volatile oil from the green overground portions is known as *Dutch Myrtle Oil.*

The leaves have been used in France as an emmenagogue and abortifacient, and were formerly official in that country under the name of *Herba Myrti Rabantini.* They contain a poisonous volatile oil.

George M. Hambright found in Bayberry bark volatile oil, starch, lignin, gum, albumen, extractive, a red coloring substance, tannic and gallic acids, an acrid resin soluble in alcohol and ether, an astringent resin soluble in alcohol and not in ether, and a peculiar acrid principle having acid properties, *myricinic acid,* which seems to be allied to the saponins. (*A. J. P.*, 1863, 193.)

From the bark of *Myrica Nagi* Thunb., of Japan, the yellow coloring matter of which is known as *myricetin,* A. G. Perkin has separated a glucoside, *myricetrin,* closely resembling *quercitrin.* (See *Proc. Chem. Soc.*, xviii, 11.) For analysis of the rhizome, *Myrica asplenifolia* L., see *A. J. P.*, 1892, 303.

Uses.—Wax Myrtle bark appears to be moderately stimulating and astringent, and in large doses emetic. It has been considerably used by the eclectics in *diarrhea, jaundice, scrofula,* etc. Externally the powdered bark is used as a stimulant to indolent *ulcers,* and the decoction as a gargle and injection in chronic *inflammation of the throat, leucorrhea,* etc.

Dose, of the powder, ten to thirty grains (0.6–2.0 Gm.).

Off. Prep.—Pulvis Myricæ Compositus, *N. F.*

MYRISTICA. U. S., Br.

MYRISTICA Myrist. [Nutmeg]

"Myristica is the dried ripe seed of *Myristica fragrans* Houttuyn (Fam. *Myristicaceæ*), deprived of its seed coat and with or without a thin coating of lime. Myristica yields not less than 25 per cent. of non-volatile, ether-soluble extractive and not more than 0.5 per cent. of acid-insoluble ash." *U. S.* "Nutmeg is the dried kernel of the seed of Myristica fragrans, *Houtt.*" *Br.*

Nux Moschata; Muscade; Noix muscade, *Fr.;* Semen Myristicæ, *P. G.;* Muskatnuss, *G.;* Noce moscata, *It.;* Nuez moscada, *Sp.*

The nutmeg tree is about thirty feet high, with numerous branches, and an aspect somewhat resembling that of the orange tree. The leaves are alternate, petiolate, oblong-oval, pointed, entire, bright green and somewhat glossy on their upper surface, whitish beneath, and of an aromatic taste. The staminate and pistillate flowers are upon different trees. The former are disposed in axillary, peduncled, solitary clusters; the latter are single, solitary, and axillary; both are minute and of a pale yellowish color. The fruit, which appears on the tree mingled with the flowers, is round or oval, of the size of a small peach, smooth, yellow when ripe, and marked with a longitudinal furrow. The external covering, which is at first thick and fleshy and abounds in an austere, astringent juice, afterwards becomes dry and coriaceous, and, separating into two valves from the summit, discloses a scarlet reticulated membrane or arillus, commonly called *mace* (see Part II), closely investing a thin, brown, shining shell, which contains the seed or *nutmeg.*

The tree is produced from the seed. It does not flower until the eighth or ninth year, after which it bears flowers and fruit together, without intermission, and is said to continue bearing for seventy or eighty years. Little trouble is requisite in its cultivation. A branch of the staminate tree is grafted into all the young pistillate plants when about two years old, so as to insure their early fruitfulness. J. H. Hart presented an interesting report (*Bull. Bot. Dept.,* Trinidad, 1907, p. 202) showing that 16-year-old nutmeg trees growing in Trinidad bear both staminate and pistillate flowers. Indeed, he found both kinds of flowers on the same branch of the tree, and he therefore suggests that an attempt should be made to perpetuate this variety by grafting.

The nutmeg tree is a native of the Moluccas and other neighboring islands, and abounds especially in that small cluster distinguished by the name of Banda, whence the chief supplies of nutmegs were long derived. But numerous varieties of the plant are now cultivated in Sumatra, Java, Singapore, Penang, Ceylon, and other parts of the East Indies, and have been introduced into the Isles of France and Bourbon, Cayenne, and several of the West India islands. Various species of the genus *Myristica,* other than the official one, yield commercial seeds or products. The larger part of the nutmegs of commerce is said still to come from the Dutch Banda Islands. The Penang nutmegs are distinguished by not being limed.

In the Moluccas the tree yields three crops annually. The fruit is gathered by hand, and the outside covering rejected. The arillode, constituting the mace of commerce, is then carefully separated, so as to break it as little as possible. It is flattened, dried in the sun, and afterwards sprinkled with salt water, with the view of contributing to its preservation. The nuts are dried in the sun or by ovens, and exposed to smoke until the kernel rattles in the shell. They are then broken open, and the kernels, having been removed and steeped for a short time in a mixture of lime and water, in order to preserve them from the attacks of worms, are next cleaned, and packed in casks or chests for exportation. Lumsdaine has found them to keep better if rubbed over with dry lime than when prepared in the moist way. Tschirch confirms the value of liming as a preservative against the attacks of insects. (*Ph. Rev.,* 1898, 196.) This is, however, not sufficient protection, as the commercial nutmegs are sometimes "wormy." Nutmegs are brought to this country from the British West Indies and either directly from the East Indies or indirectly from England and Holland. About half of the nutmegs entering this country in 1924 came from Grenada in the West Indies, and 40 per cent. was from Java. The other important nutmeg centers are, Sumatra, Banda, Penang, Macassar, Amsterdam, Rotterdam and London. Nutmegs from the East Indies are usually limed while those from the West Indies are not limed.

Shrivelled nutmegs and nutmegs in the shell (whole seeds deprived of arillodes) are imported for distilling purposes.

Description and Physical Properties.—"*Unground Myristica.*—Ovoid or ellipsoidal, from 20 to 30 mm. in length and about 20 mm. in thickness; externally light brown to dark brown; reticulately furrowed, the broad end with a large, circular, upraised scar from which arises a groove extending to a depression at the opposite end; the cut surface having a waxy luster and mottled brown appearance; odor characteristically aromatic, taste pungently aromatic. Perisperm thin, dark brown, penetrating by many wavy branches or folds into the light brown endosperm; embryo small and more or less shrunken, in an irregular cavity near the base.

"*Powdered Myristica.*—Dark reddish-brown; consisting of irregular yellowish-brown and blackish-brown fragments; perisperm with large, circular or elliptical volatile-oil reservoirs, small thin-walled parenchyma cells with brown contents and occasional spiral tracheæ; endosperm with more or less polygonal parenchyma cells containing starch and aleurone grains and occasionally brown pigment; fixed oil globules numerous; starch grains single or compound, the individual grains spherical, plano-convex or polygonal, from 0.003 to 0.020 mm. in diameter, with a distinct, sometimes cleft hilum.

"**Assay.**—Proceed as directed under non-volatile ether-soluble extractive." *U. S.*

"Broadly oval or rounded, rarely more than twenty-five millimetres long; greyish-brown externally, marked with reticulated furrows, and minute black points and lines; internally greyish-red with darker brownish-red veins. Transverse section marbled. Strong aromatic odor; taste aromatic, warm and somewhat bitter." *Br.*

The microscopical structure of nutmeg and mace have been well illustrated by Winton and Moeller in the *"Microscopy of Vegetable Foods."* Spaeth has made an interesting contribution to the pharmacognosy of nutmeg and the detection of the prevalent adulterations in *Ph. Zentralh.*, xlix, p. 627. The quality of present commercial supplies varies considerably. Some shipments arrive which are quite moldy and insect infested. It has been stated that much of the ground nutmeg of commerce has been made from small, stunted and worthless nutmegs, so-called "grinding nutmegs." The powdered drug is sometimes adulterated with corn meal, powdered beans, curcuma and various nut-shells.

Nutmegs have been punctured and boiled in order to extract their essential oil, and the orifice afterwards closed so carefully as not to be discoverable unless by breaking the kernel. The fraud may be detected by their lightness. They are also apt to be injured by worms, which, however, attack preferably the parts least impregnated with the volatile oil. The Dutch were formerly said to heat them in a stove in order to deprive them of the power of germinating and thus prevent the propagation of the tree. The largest nutmegs now command the highest prices. They should be rejected when very light in weight, with a feeble taste and odor, worm eaten, musty, or marked with black veins.

Constituents.—Nutmeg contains from 5 to 15 per cent. of a volatile oil to which it owes its medicinal value (see *Oleum Myristicæ*), from 25 to 40 per cent. of a fixed oil and from 5 to 15 per cent. of an ash; the remainder being starch, fiber, water, etc.

The *concrete* or *expressed oil of nutmeg* (*Oleum Myristicæ Expressum,* Br., 1885, *Oleum Nucistæ,* P. G.), often called *oil of mace,* or *nutmeg butter,* is obtained by bruising nutmegs, exposing them in a bag to steam, and then compressing them strongly between heated plates. A liquid oil flows out, which becomes solid when it cools. This oil may also be obtained by treating nutmeg, thoroughly comminuted, with three times its weight of well-rectified carbon disulphide, agitating the mixture frequently for twenty-four hours, expressing, repeating the process with two parts only of the menstruum, mixing the products of the two macerations, filtering in a covered vessel, and then distilling off the disulphide until the residue is entirely deprived of the solvent. It would seem difficult to prevent the retention of a little of the solvent. The best nutmeg butter is imported from the East Indies in stone jars, or in rectangular blocks 10 inches long by 2½ inches wide, wrapped in palm leaves. It is solid, soft, unctuous to the touch, of a yellowish or orange-yellow color, more or less mottled, with the odor and taste of nutmeg. It is a brownish solid with specific gravity of 0.995 and melting at about 45° C. In 1874 Playfair separated from this a crystallizable fat, *myristin,* which is the glyceride of *myristic acid,* $C_{14}H_{28}O_2$. Power and Salway (*Tr. Chem. Soc.*, 1908, p. 1653) found the expressed oil of nutmeg to contain 73 per cent. of trimyristin, 12.5 per cent. of essential oil, smaller quantities of oleic acid, linoleic acid, resinous material with traces of formic, acetic and cerotic acids, with 8.5 per cent. of unsaponifiable residue. Myristin is also found in spermaceti, in cocoanuts, and in the fixed oil of linseed and poppy oil. It may be obtained directly from nutmeg by exhausting it by means of benzene, filtering the liquid, and allowing it to crystallize by spontaneous evaporation. To purify the product, it may be dissolved in a mixture of two parts of absolute alcohol and three of benzene with the aid of heat, then filtering the liquid while hot, and setting it aside. An inferior kind of the fat is prepared in Holland, and sometimes found in commerce. It is in hard, shining, square cakes, lighter-colored than that from the East Indies, and with less odor and taste. It is supposed to be derived from nutmegs previously deprived of most of their volatile oil by distillation. An artificial preparation is sometimes sold for the genuine oil. It is made by mixing various fatty matters, such as suet, palm oil, spermaceti, wax, etc., adding some coloring substance, and giving flavor to the mixture by the volatile oil.

Allied Products.—Under the names of *long, female,* or *wild nutmeg, Macassar nutmeg, Papua nutmeg, New Guinea nutmeg, horse nutmeg,* certain seeds have long been known in European commerce. These seeds have been variously ascribed to *M. fatua* Houtt. (*M. tomentosa* Thumb., *M. macrophylla* Roxb.), and other species of the genus *Myristica,* but by Bassermann and Warburg have in all their varieties been traced to the *M. argentea* Warburg, of New Guinea, from which country they are often taken to Macassar to finally enter commerce as Macassar nutmegs. (*P. G.*, 1898, 97.) The numerous varieties of these false nutmegs are readily reducible to two, which differ chiefly in size, the larger being commonly known as the Papua nuts, the smaller as the Macassar nuts. They are distinguished from the nutmeg by their greater length, their elliptical shape, their comparatively feeble odor and disagreeable taste, and by the absence of the dark brown veins. (Holmes, *P. J.*, lxxxii, p. 459.) Heckel has described two new so-called wild nutmegs from Madagascar. (*Rep. d. Pharm.*, 1909, p. 49.) Bombay nutmegs from the *M. mala-*

barica Lam. are also long and narrow. They do not possess the characteristic aroma of true nutmegs.

Ucuhula nut is a round or oval seed of *Myristica surinamensis* Roland. It is one-half to two-thirds of an inch in diameter, light brown, but usually covered by a blackish, thin, friable testa. Internally it resembles the nutmeg, but is distinguished by the presence of extraordinarily large and handsome albuminous crystalloids. These seeds are said to contain over 70 per cent. of a solid yellow fat, melting at 36° C. (See *A. J. P.*, 1886; also *A. Pharm.*, July, 1888.) The kernel of the fruit of the Brazilian *Myristica officinalis* Mart. (*M. Bicuhyba* Schott) resembles the nutmeg in form and structure, but is covered with a black shell marked with broad furrows. It contains crystals like those above spoken of, but less splendid and regular, and apt to be in three forms. It yields a fat (*bicuhyba fat,* or *bicuhyba balsam*) very much like that of the ordinary nutmeg, but having a rather sour, sharp taste, melting at 47° C. It contains a peculiar fatty acid, *bicuhybastearic* acid.

The *otoba fat,* sometimes called *american nutmeg butter,* is expressed from the fruit of the *Myristica otoba* H. B. K. which grows in the mountains of Colombia. It is almost colorless and when fresh has a nutmeg-like odor. It consists, according to Baughman and Jamieson (*J. Am. C. S.,* 1921, xliii, p. 199) of more than 50 per cent. of the glyceride of myristic acid with smaller quantities of the glycerides of lauric, oleic and palmitic acids, about 9 per cent. of volatile oil and 9.4 per cent. of an unsaponifiable substance, *otobite.* The latter principle crystallizes in shiny, colorless crystals, melting at 133° C. The fruit of *Virola sebifera* Aubl. (*Myristica sebifera* Sw.) of South America also yields a fatty substance which is known as *ocuba wax,* which is used in the manufacture of candles.

The so-called *California nutmeg* is not a nutmeg at all but the seed of a coniferous tree, *Torreya californica* Torr. It is oblong, with a smooth, thin, brownish testa and exhibits a marbled surface in cross section. Its odor and taste are terebinthinate. Neither are the *Jamaica* or *calabash nutmeg,* from *Monodora Myristica* Dun., the New Holland or *plum nutmeg,* from *Atherosperma moschatum* Labill., and the *clove nutmeg,* from *Ravensara aromatica* J. F. Gmel., true nutmegs.

Uses.—Nutmeg owes its medicinal and toxic properties solely to the volatile oil which it contains. For the consideration of the effects and uses of this, see *Oleum Myristicæ.* Powdered nutmeg is rarely used in medicine alone, although it has been used in *dysentery* (see Leidy, *N. Y. M. R.,* March 1, 1919). It enters into the composition of a number of galenicals. The expressed oil is occasionally used as a gentle external stimulant and was an ingredient in the *Emplastrum Picis* of the 1885 British Pharmacopœia. *Mace* possesses properties essentially the same as those of nutmeg.

Dose, five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Pulvis Aromaticus, *N. F.;* Tinctura Lavandulæ Composita, *U. S., Br.;* Pulvis Catechu Compositus, *Br.;* Pulvis Cretæ Aromaticus, *N. F., Br.;* Spiritus Armoraciæ Compositus, *Br.*

MYROBALANUM. Br.

MYROBALANS

"Myrobalans are the dried immature fruits of Terminalia Chebula, *Retz.,* usually distinguished in commerce as Chebulic myrobalans." *Br.*

Five varieties of these East India fruits are distinguished by authors. The most important are as follows: (1) *Myrobalani Chebulæ.* This is the only variety which is official. It is produced by the *Terminalia Chebula* Retz. (*Buceras Chebula*). This by some is believed to be identical with the *T. Bellerica* Roxb. noted below. The fruit is roundish or ovate, varying in size from that of a hazel nut to that of a walnut. It consists of an exterior firm fleshy portion and an interior kernel which is light brown, inodorous and with a bitterish, astringent taste.

(2) *Myrobalani Bellericæ.* This is obtained from the *T. Bellerica* Roxb. It closely resembles the previous variety but is of a more grayish-brown color and is sometimes supplied with a short thick foot stalk which is lacking in the official form.

(3) *Myrobalani citrinæ* vel *flava.* These are from a variety of the same tree which affords the chebula myrobalans, from which they differ only in being somewhat smaller, of a light brown or yellowish color, and of a taste rather more bitter. They were formerly sometimes sold in the shops of Philadelphia, under the name of *white galls,* to which, however, they bear no other resemblance than in taste.

(4) *Myrobalani indicæ* vel *nigræ.* These are thought to be the unripe fruit of *T. Buceras* Wright (*Bucida Buceras* L.). They are ovate-oblong, from four to eight lines long and from two to three lines thick, of a blackish color, wrinkled longitudinally, and presenting, when broken, a thick brown mass, without kernel, but with a small cavity in the center. They are sourish and very astringent.

(5) *Myrobalani emblicæ.* This variety is wholly different from the preceding, and derived from a plant having no affinity to the Terminaliæ, of the Fam. *Combretaceæ*—namely, the *Phyllanthus Emblica* L. (Fam. *Euphorbiaceæ*).

Myrobalans are officially described in the Br. Pharm., 1914, as "irregularly ovoid or fusiform, from ten to thirty millimetres or more long and from five to fifteen millimetres wide; strongly shrivelled longitudinally, dark brown or nearly black; in transverse section dark, with a small central cavity; hard. No odor; taste very astringent." *Br.*

When the fruit is entire, it is blackish, spherical depressed, of the size of a cherry, presenting six obtuse ribs with as many deep furrows, and separating into six valves, and has a strongly astringent and acidulous taste. It is often in segments, as found in commerce.

These fruits contain about 30 per cent. of an astringent substance which has been considered to be gallo-tannic acid. According to Freudenberg and Fick (*B. Chem. G.*, 1920, liii, 1728), the astringency is due to a characteristic principle, *chebulinic acid,* which splits up into a crystalline tanning substance, digalloylglucose, and a dibasic acid.

The greenish oleoresin obtained from these fruits is sometimes called *myrobalanin.*

Uses.—Myrobalans were in high repute with the Arabians, and were long employed by European practitioners, as primarily laxative and secondarily astringent, in various complaints, particularly *diarrhea* and *dysentery.* Pierre Apery states that when roasted they are still used in Turkey with excellent results in *intestinal* catarrhs. (*R. T.*, Dec., 1887.) Under the name of *Eutannin* a product asserted by Thoms to be chebulinic acid has been used as an intestinal astringent in dose of from four to ten grains (0.25–0.65 Gm.).

The ointment is used as a local astringent.

The internal *dose* of myrobalans is one-half to one drachm (2.0–3.9 Gm.), given in the form of a powder.

Off. Prep.—Unguentum Myrobalani, *Br.;* Unguentum Myrobalani cum Opio, *Br.*

MYRRHA. U. S., Br.

MYRRH Myrrh. [Gum Myrrh]

"Myrrh is a gum-resin obtained from *Commiphora Myrrha* (Nees) Baillon or from other species of *Commiphora* (Fam. *Burseraceæ*). Myrrh yields not less than 30 per cent. of alcohol-soluble extractive and not more than 4 per cent. of acid-insoluble ash." *U. S.* "Myrrh is an oleo-gum-resin obtained from the stem of Commiphora Myrrha, *Holmes,* and probably other species." *Br.*

Arabian or Somali Myrrh, Herabol Myrrh; Gummi Resina Myrrha; Myrrhe, *Fr. Cod.;* Myrrha, *P. G.;* Myrrhe, *G.;* Mirra, *It., Sp.;* Murr, *Ar.;* Bowl, *Hindost.*

Though *myrrh* has been employed from the earliest times, all the plants yielding it have not been definitely determined. The *Amyris Kataf* of Forskhal, seen by that traveller in Arabia, was supposed by him to be the myrrh tree, but without sufficient proof. Afterwards, in 1820, Ehrenberg discovered myrrh-yielding trees along the eastern shore of the Red Sea in Arabia, at Ghizan and surroundings. From the bark of several of these he collected a gum-resin precisely similar to the myrrh of commerce. From the specimens of the plant taken by Ehrenberg to Germany, Nees von Esenbeck referred it to the genus *Balsamodendron* of Kunth, and named it *Balsamodendron Myrrha.* This has since proven to be the *Commiphora Myrrha* (Nees) Engler or one of the true Myrrh trees. It was not thought by De Candolle sufficiently distinct, but is now generally recognized under the name of *Commiphora,* first given it by Jacquin in 1797, and therefore preceding the name of Kunth by some 27 years. Berg found another species in Ehrenberg's collection, to which was attached a label by the discoverer, stating that he had collected myrrh from it, and proposed to call it *Balsamodendron ehrenbergianum.* (*A. J. P.*, 1873, 314.) Both Oliver and Trimen agree that this plant is not specifically distinct from *B. Opobalsamum.* Gum resins from several species of *Commiphora* furnish commercial myrrh. Hildebrand (*P. J.*, 1878, ix, p. 893) collected the *C. Myrrha* on the north Somali coast in 1873, and presents evidence to show that it yields myrrh. Although this view has been disputed, E. M. Holmes (*Y. P. B.*, 1913, p. 453) supports it and this species is recognized by the British Pharmacopœia. Deflers and Schweinfurth (*B. P. G.*, 1893), however, believe that genuine myrrh is yielded by *Commiphora abyssinica* (Berg.) Engl., which is found in Southern Arabia, Erithrea, and Northern Abyssinia. *C. Schimperi* (Berg.) Engl., occurring in the Yemen, Abyssinia, and from Kern to Tigré, is likely also to yield some of the commercial Arabian myrrh. It appears to be established that *C. Myrrha* produces myrrh, but it is probable that it is also yielded by other trees belonging to the genus *Commiphora,* which genus includes more than 60 species, natives of Arabia and Africa.

Commiphora Myrrha (Nees) Engler (Syn. *C. Myrrha* Holmes) is a small tree, with a stunted trunk, covered with a whitish-gray bark, and furnished with rough abortive branches terminating in spines. The leaves are ternate, consisting of obovate, blunt, smooth, obtusely denticulate leaflets, of which the two latter are much smaller than the one at the end. The fruit is oval-lanceolate, pointed, longitudinally furrowed, of a brown color, and surrounded at its base by the persistent calyx. The tree grows along the Red Sea in Arabia in the neighborhood of Gison, in dwarfish thickets, interspersed among the *Acaciæ* and *Euphorbiæ.* It also thrives in Somaliland. The juice concretes spontaneously upon the bark.

Myrrh is now collected in Somaliland and Arabia by making incisions into the bark of the trees, when a yellowish oleoresin exudes. Upon hardening this exudate becomes reddish-brown and is gathered. Some of the oleoresin which collects within the secretion reservoirs of the bark exudes spontaneously. This represents but a small proportion of the drug collected. Other gums and resins as well as considerable bark is found in the crude article which is more or less removed before it is sent into commerce. The greater bulk of the drug comes from Somaliland (Northeast Africa). This is sent to Aden whence it is shipped to Europe and America either direct or through Bombay. It is usually imported in chests containing between one and two hundred-weight. Sometimes the different qualities are brought separate, but oftener more or less mingled. Only the best kind should be selected for medicinal use.

There are several varieties of myrrh recognized in commerce. The official description corresponds to that of that known as the Arabian myrrh or Somaliland myrrh.

Another variety of myrrh coming from Arabia known as the *Fadhli* (*Fahdi*) *myrrh* is described in the *Pharmacographia* as "occurring in irregular masses, seldom exceeding 1½ inches long, and having a somewhat gummy-looking exterior. The larger lumps seem formed by the cohesion of small, rounded, translucent, externally shining drops or tears. The fracture is like that of common myrrh, but less unctuous, and has not the whitish markings. The odor and taste are those of the ordinary drug." This myrrh is said to be collected on the hills about Shugraeea and Sureeae, east of Aden. "*Meetiyu*," or *Arabian Myrrh of Dymock*, is said to be sold in India as true myrrh. It has a dull surface, a dark reddish-brown color, a more unctuous and waxy fracture, and has white marks like Somali myrrh, which it resembles in taste, but its odor is rather less fragrant. *Yemen Myrrh*, which is said by Hanbury to contain a resin, which differs from that of Somali myrrh and the Arabian myrrh, or Fahdi, in that its solution in petroleum spirit does not give a violet color on the addition of bromine. This myrrh is said to enter commerce chiefly from Makulla via Aden and Bombay. It occurs in large pieces 1 to 3 inches long, irregularly rounded and characterized by a dark reddish-brown color with a similarly colored fracture free from white streaks. Odor and taste similar to Somali myrrh, but stronger and more rank. *Heerabol* (or *Herabol*) myrrh is a variety obtained from a tree known locally as *Didthin*, which is probably the *C. Playfairii* (Hook. f.) Engl. *Bissabol*, or *East Indian Myrrh* seems to be the perfumed bdellium (see *Bdellium*, Part II).

Mecca balsam, according to G. Schweinfurth, is yielded by *Commiphora Opobalsamum*, from which it is collected in the valleys near Mecca. It is said to be the myrrh of the Bible, the error of translation having been made on account of the similarity of the old Hebrew word "mar" with the modern Arabic word "morr," the name of the true myrrh.

Description and Physical Properties.—"*Unground Myrrh.*—Rounded or irregular tears or masses of agglutinated tears, brownish-yellow or reddish-brown and more or less covered with a grayish or yellowish dust; fracture waxy, granular, conchoidal, internally deep yellowish or reddish-brown, sometimes marked with nearly white spots or lines, oily, translucent at the edges; odor balsamic, aromatic; taste aromatic, bitter and acrid.

"*Powdered Myrrh.*—Yellowish-brown; consisting of numerous angular fragments of resin and gum, a few fragments of lignified tissue and a very few starch grains.

"**Assay.**—Proceed as directed under alcohol-soluble extractive." *U. S.*

"In rounded or irregular tears, or masses of agglutinated tears, varying much in size; reddish-brown or reddish-yellow externally, dry, and more or less covered by a fine powder; brittle, the fractured surface irregular, somewhat translucent, of a rich brown color, oily, and frequently exhibiting whitish marks. Aromatic odor; taste aromatic, bitter and acrid. Not more than 70 per cent. insoluble in *alcohol* (90 per cent.). The solution obtained by boiling 0.1 gramme of coarsely powdered Myrrh with 2 millilitres of *alcohol* (90 per cent.), evaporated in a porcelain dish so as to leave a thin film, yields a residue which assumes a violet color in contact with *nitric acid* diluted with an equal volume of *water*. Ash not more than 5 per cent." *Br.*

Under the teeth it is at first friable, but soon softens and becomes adhesive. It is inflammable, but does not burn vigorously, and is not fusible by heat. Its sp. gr. is stated as 1.36. The inferior kind is in pieces much darker, more opaque, less odorous, and often abounding with impurities. We have seen pieces of India myrrh enclosing large crystals of sodium chloride, as if the juice had fallen from the tree and concreted upon the ground where this mineral abounds. Pieces of *bdellium*, and other gummy or resinous substances of unknown origin, are often mixed with it. Among these is a product which may be called *false myrrh*. It is in irregular pieces, of a dirty reddish-brown color, a vitreous brownish-yellow fracture, semi-transparent, of a faint odor of myrrh, and a bitter balsamic taste. Myrrh is best purchased in mass, as in powder it is liable to adulterations not easily detected. It is sometimes admixed with small stones which are added when the myrrh is in a moist state. It has been adulterated with senegal gum and chestnuts.

George F. Merson (*P. J.*, Jan., 1900, 42) proposes as a test of the quality of myrrh that it should yield not more than 5 per cent. of ash, which should be almost entirely soluble in diluted hydrochloric acid, and that when exhausted with 90 per cent. alcohol and dried at 100° C. one gramme should not afford more than 0.6 Gm. of residue.

Myrrh is partially soluble in water, alcohol, and ether. Triturated with water it forms an opaque yellowish or whitish emulsion, which deposits the larger portion upon standing. Its alcoholic tincture is rendered opaque by the addition of water, but throws down no precipitate. According to Neumann, alcohol and water severally extract the whole of its odor and taste. By distillation a volatile oil arises, having the peculiar flavor of myrrh, and leaving the residue in the retort simply bitter. The gum-resin is soluble in solutions of the alkalies, and, when triturated with them in a crystalline state, forms a tenacious liquid. Hence potassium carbonate may be used to facilitate its suspension in water. Hirschsohn recommends as a reagent for myrrh, trichlor-acetal-chloroform, which is obtained by conducting chlorine into seventy-five per cent. alcohol until turbidity ensues and two layers are formed; the lower of these is shaken with an equal volume of water and then with calcined magnesia and filtered. In one part by weight of the trichloracetal thus obtained, four parts by weight of hydrated chloral are dissolved by heating. The syrupy reagent thus made, which fumes slightly in the air, gives a violet color with the smallest quantity of pure Herabol myrrh. Hirschsohn failed to get a similar reaction with any other resin, not even with Bisabol myrrh. (*Ph. Centralh.*, 1903, 809.)

According to Bley and Diesel myrrh containing a little volatile oil always has an acid reaction, which they ascribe to the oxidation of the oil. They propose as a test of myrrh the production of a transparent dirty-yellow liquid with nitric acid, while false myrrh affords a bright-yellow solution in the same fluid, and bdellium is not dissolved, but becomes whitish and opaque. (*A. J. P.*, xviii, 228.) According to Righini, if powdered myrrh, rubbed for fifteen minutes with an equal weight of ammonium chloride, and fifteen times its weight of water gradually added dissolves quickly and entirely, it may be considered pure.

Constituents.—The chemistry of myrrh is in a very unsatisfactory state; the various constituents reported as present must be looked on as questionable and the formulas assigned to them as purely empirical. In a general way myrrh consists of about 25 to 45 per cent. of resin, 30 to 40 per cent. of gum, 3 to 8 per cent. of volatile oil, with traces of free acetic, formic and *myrrholic* acids and small amounts of water and inorganic salts.

The volatile oil has been called *myrrhol* or *myrrhenol*, and, according to Ruickoldt, has the formula $C_{10}H_{14}O$. Koehler (*A. J. P.*, 1890, p. 346) confirms this formula, and states that this body, while isomeric with thymol and carvol, is distinct from them. He found 7 or 8 per cent. of essential oil. Gladstone (*J. Chem. S.*, [2], 2, 1) found that the oil had a sp. gr. of 1.0189 at 7.5° C., a boiling point of 266° C., and was lævorotatory. Friedrichs (*A. Pharm.*, 1907, ccxlv, 427) found 8.8 per cent. of essential oil having a sp. gr. 1.011 and an optical rotation 73.86°. He also reported a new tricyclic sesquiterpene, *heerabolene*, $C_{15}H_{24}$.

The resin Gladstone suggested to call *myrrhin.* He gave the formula $C_{48}H_{32}O_{10}$; it is neutral, but becomes acid when kept for a short time in fusion. In the latter state Ruickoldt proposes to call it *myrrhic acid.* (*A. Pharm.*, lxi, 1.) Koehler has found in the portion soluble in alcohol an indifferent soft resin, to which he gave the formula $C_{26}H_{34}O_5$, containing three replaceable OH groups, and two dibasic resin acids, of the formulas $C_{26}H_{32}O_{16}$ and $C_{26}H_{32}O_9$. Friedrichs gives the following constituents: *Commiphorinic acid,* $C_{28}H_{36}O_8$; *alpha-heerabomyrrhol,* $C_{18}H_{26}O_5$; *beta-heerabomyrrhol,* $C_{20}H_{26}O_6$; *heeraboresene,* $C_{42}H_{56}O_8$; *alpha-myrrholdic acid,* $C_{15}H_{22}O_7$; *beta-myrrholdic acid,* $C_{25}H_{32}O_6$; an unidentified monatomic alcohol, $C_{14}H_{22}O_2$.

An investigation of the essential oil of Bissabol myrrh from the interior of the Somali country was made by W. Tucholka. (*Schim. Rep.*, Oct., 1897, 36.) He obtained by distillation 7.8 per cent. of an oil of 0.8836 sp. gr., boiling at from 220° to 270° C. From this was separated, by means of the crystalline hydrochloride, a terpene boiling at from 259° to 260.2° C., which the author calls *bissabolene,* and an oxygenated portion to which he gives the rather strange formula $C_{56}H_{96}O$.

The gum appears to consist largely of arabin and yields a good mucilage; when making tincture of myrrh, the residue insoluble in the alcoholic menstruum should be saved for that purpose.

Uses.—Although myrrh has been an important article of commerce from times of the greatest antiquity, it was cherished chiefly as a constituent of incense and perfumes, rather than for medicinal properties. By the ancient Greek physicians it was used as a local remedy and apparently, to some extent, also internally. It probably, however, does not possess any important therapeutic virtues which are not found in many other resinous substances. Like so many of the resins it is locally stimulating and may, perhaps, for this reason excite peristalsis in the alimentary tract; it is therefore used as an ingredient of certain cathartic pills and occasionally in atonic *dyspepsia.* The older writers believed that it was capable of absorption and useful in chronic *bronchitis* and certain types of *amenorrhea.* Its most important use today is as an aromatic stimulant mouth wash.

Myrrh may be given in the form of powder or pill, or suspended in water, as in the famous antihectic mixture of Griffith. (*Mistura Ferri Composita.*) The infusion is also sometimes given, and an aqueous extract has been recommended as milder than myrrh in substance. The tincture is used chiefly as a local application.

Dose, five to twenty grains (0.3–1.2 Gm.).

Off. Prep.—Decoctum Aloes Compositum, *Br.;* Mistura Ferri Composita, *Br.;* Pilulæ Aloes et Myrrhæ, *N. F.* (*Br.*)*;* Pilulæ Rhei Compositæ, *N. F.* (*Br.*)*;* Tinctura Myrrhæ, *U. S., Br.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloe, *N. F.;* Tinctura Aloes et Myrrhæ, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.;* Tinctura Capsici et Myrrhæ, *N. F.*

NEOARSPHENAMINA. U. S.

NEOARSPHENAMINE Neoarsphen.

"Neoarsphenamine is a product obtained by the action of sodium methanol sulphoxylate on arsphenamine, and consists partially of sodium

3-diamino 4-dihydroxyarsenobenzene methanol sulphoxylate [$NH_2.OH.C_6H_3As:AsC_6H_3.OH.NH(CH_2O)OSNa$]. It contains not less than 19 per cent. of As, and complies with the requirements of the United States Public Health Service. Neoarsphenamine is distributed in sealed containers of colorless glass, from which the air has been excluded either by the production of a vacuum or by displacement with a nonoxidizing gas." *U. S.*

Neosalvarsan; Novarsenobenzol; Neokharsivan.

The difficulties and inconvenience involved in preparing arsphenamine for injection directed research toward the discovery of a soluble derivative which would be neutral and still retain its effectiveness. The most satisfactory derivative tried was the methylene sulphinate which was prepared by acting upon a compound of arsphenamine with sodium formaldehyde sulphoxylate.

It is prepared as follows: Arsphenamine dihydrochloride is dissolved in ten times its weight of water and is treated with an equal volume of a ten per cent. solution of sodium formaldehyde sulphoxylate. After allowing the mixture to stand for an hour a 10 per cent. solution of sodium carbonate is added to make a clear solution. The subsequent addition of a 12 per cent. hydrochloric acid solution precipitates a methylene sulphinic acid derivative of arsphenamine, containing one CH_2SO_2H group. This derivative is converted into the normal sodium salt by the careful addition of solution of sodium hydroxide and the resulting neoarsphenamine is precipitated by the addition of a large volume of strong alcohol or of acetone and is then washed and dried under reduced pressure.

In another method the reaction between arsphenamine base and sodium formaldehyde sulphoxylate is carried out in ethylene glycol as a solvent.

Neoarsphenamine may also be prepared directly from 3-nitro-4-hydroxyphenyl-arsenic acid.

According to Roth (*U. S. Pub. Health Rep.*, 1921, xxxvi, 2523), it is not a definite chemical compound.

Description and Physical Properties.—" A yellow powder. It is odorless or has a slight odor. In the dry state or in solution it is readily oxidized by exposure to the air, becoming darker and more toxic. Higher temperatures accelerate the oxidation. It is very soluble in water, soluble in glycerin, slightly soluble in alcohol and almost insoluble in acetone, chloroform, and in ether.

" An aqueous solution of Neoarsphenamine (1 in 100) is neutral or slightly alkaline to litmus paper (*difference from arsphenamine*). An aqueous solution of Neoarsphenamine (1 in 100) is precipitated by diluted mineral acids (*difference from arsphenamine*), but yields no precipitate with solutions of alkali hydroxides or carbonates, and is not precipitated by mercuric potassium iodide T.S. (*difference from arsphenamine*). The addition of 2 drops of freshly prepared ferric chloride T.S. to 5 cc. of an aqueous solution of Neoarsphenamine (1 in 1000) produces a purple or purplish-red color, changing to dark red. Add 3 cc. of silver nitrate T.S. to 5 cc. of an aqueous solution of neoarsphenamine (1 in 100): a brown precipitate is immediately formed, rapidly becoming black (*difference from arsphenamine*). To 10 cc. of an aqueous solution of Neoarsphenamine (1 in 100) add 10 cc. of diluted hydrochloric acid, and heat: the odor of sulphur dioxide is perceptible. The solution resulting from the assay for arsphenamine directed below yields with hydrogen sulphide a yellow precipitate soluble in ammonium carbonate T.S. Add 5 cc. of distilled water to 0.5 Gm. of Neoarsphenamine in a test tube, and gently agitate the mixture: a complete solution results in five minutes.

" **Assay.**—Proceed as directed under *Arsphenamine.*

" Preserve in the original sealed tubes in a cool place, preferably not above 10° C.

" *Caution—Solutions of Neoarsphenamine must be freshly prepared when required for use.*" *U. S.*

Roth (*J. A. M. A.*, 1922, lxxxviii, 1191) has found that even in sealed ampules neoarsphenamine undergoes chemical changes, some samples showing obvious deterioration in a few weeks. These changes—which may be manifested by such obvious alterations as lower solubility or difference in color—take place much more rapidly at warmth; he advises, therefore, that the drug be kept under the same storage conditions as biological products. The U. S. recommends that it be stored at a temperature of 10° C.

Uses.—Neoarsphenamine is employed in medicine for the same purposes as arsphenamine (*q. v.*). The question of the relative therapeutic efficiency of the two compounds can not as yet be positively answered. Although it contains two-thirds as much arsenic as arsphenamine according to Schamberg (*J. A. M. A.*, 1919, lxxiii, 1883) it requires about twice the dose to exercise the same degree of spirocheticide action. The comparative value of the two drugs depends, however, not merely on their activity but also on their relative toxicity. This latter point is very difficult to accurately determine; Shamberg, Kolmer and Raiziss (*A. J. M. S.*, 1920, clx, 188) find that for rats neoarsphenamine is less than half as poisonous when injected intravenously, but almost equally toxic when given subcutaneously.

It is administered by the same methods and with the same precautions as arsphenamine.

Dose, from eleven to fourteen grains (0.6–0.9 Gm.).

NITROGENII MONOXIDUM. U. S.

NITROGEN MONOXIDE Nitrogen. Monox.
[Nitrous Oxide]

"Nitrogen Monoxide gas [N_2O]." *U. S.*

Laughing gas; Oxyde nitreux, Potoxide d'Azote, *Fr.;* Stickstoffoxydul, Lachgas, *G.*

This gas was originally discovered by Priestley in 1776, but first brought into general notice in 1800 by Humphry Davy, who discovered and made known the remarkable exhilarating properties which earned for it the name of laughing gas.

Preparation.—In its preparation, pure fused ammonium nitrate is submitted to a heat sufficient to decompose it, not exceeding 204.4° C., and the resulting gas collected and purified. When ammonium nitrate is heated to the point of decomposition, it is wholly resolved into aqueous vapor and nitrogen monoxide, according to the reaction:

$$NH_4.NO_3 = 2H_2O + N_2O$$

It is necessary not to let the heat employed in the process be too high, as otherwise, besides nitrous oxide, there will come over portions of nitric oxide, uncombined ammonia, even nitric acid. At times nitrogen gas is also found in the nitrogen monoxide, probably resulting from a trace of nitrite present or some reducing action upon the nitrate in the moment of its decomposition. When the monoxide is liquefied under pressure this free nitrogen remains as unliquefied gas.

Properties.—Nitrogen monoxide gas is colorless, inodorous, slightly sweetish to the taste, and of the sp. gr. 1.527 compared with air. Cold water will absorb about three-fourths of its bulk of the gas, and, under pressure, much more, and, thus impregnated, has a slight, not unpleasant odor, and a sweetish taste. By the joint influence of cold and pressure the gas may be condensed into a colorless, very mobile liquid. Liquid nitrogen monoxide has a sp. gr. of 0.9367 and a boiling point (at atmospheric pressure) of –89.8° C. Inflammable bodies will generally burn with increased vigor in nitrous oxide gas, but it is entirely incapable of giving oxygen to the blood.

Description and Physical Properties.—"A colorless gas, having a slight characteristic odor and a somewhat sweet taste. It supports the combustion of many substances. For convenience in handling and use, Nitrogen Monoxide is compressed in metallic cylinders.

"It is quite soluble in water at low temperatures; 1 volume of water dissolves about 1.3 volumes of nitrous oxide at 25° C.

"Pass 2000 cc. of the gas, measured under normal atmospheric pressure at about 25° C., through 100 cc. of barium hydroxide T.S. at a rate not exceeding 4000 cc. per hour: the turbidity produced, if any, is not greater than that produced by 1 cc. of a solution prepared by dissolving 0.2 Gm. of sodium bicarbonate in 100 cc. of freshly boiled distilled water (*carbon dioxide*). Pass 2000 cc. of Nitrogen Monoxide, under the conditions described above through a mixture of 100 cc. of distilled water and 1 cc. of silver nitrate T.S.: no opalescence is produced (*halogens*). Pass 2000 cc. of Nitrogen Monoxide through 100 cc. of distilled water, colored with 5 drops of litmus T.S., under the conditions described above: the color of the liquid is not changed (*acids or alkalies*). Pass 2000 cc. of Nitrogen Monoxide through a solution of 0.2 cc. of tenth-normal potassium permanganate in 100 cc. of distilled water: the color of the liquid is not changed (*reducing substances*)." *U. S.*

Uses.—Although Sir Humphrey Davy as far back as 1800 suggested the use of nitrous oxide for the production of anesthesia, the first practical employment of it was in 1844 by Horace Wells, of Connecticut. Nitrous oxide is remarkable among anesthetics in being almost physiologically inert, save in its effect on the cerebrum. While as it is ordinarily administered there are marked alterations in the circulation owing to partial asphyxia, by carefully combining pure oxygen with the gas it is possible to induce with nitrous oxide a state of complete anesthesia without any considerable change in either the rapidity of the pulse, the blood pressure, or the respiration. It differs also from the liquid anesthetics in that it is not depressant to the spinal cord. For operations of short duration, such as extraction of teeth, opening of abscesses, and the like, it should always be the anesthetic of preference, if available. The mortality in this group of operations is almost nil; it has been estimated variously as from one death in a hundred thousand to one in a million. The two great drawbacks to its more frequent employment are its cumbersomeness of transportation and the shortness of the narcosis. By administering it in conjunction with pure oxygen the inhalation may be continued for long periods of time, so that it can be employed in major operations. There is, however, great difference of opinion as to the advisability of its use for this purpose; Crile (*J. A. M. A.*, 1910, liv), who has had a large experience with it, believes that with a skilful anesthetist it is safer than ether, but that in the hands of the inexperienced is more dangerous.

NUX VOMICA. U. S., Br.

NUX VOMICA Nux Vom. [Strychni semen, P. I.]

"Nux Vomica is the dried ripe seed of *Strychnos Nux-vomica* Linné (Fam. *Loganiaceæ*). Nux Vomica yields not less than 2.5 per cent. of the alkaloids of Nux Vomica." *U. S.* "Nux Vomica consists of the dried ripe seeds of Strychnos Nux-vomica, *Linn.*" *Br.*

Semen Nucis Vomicæ; Poison Nut, Quaker Buttons, Dog Buttons; Noix vomique, *Fr. Cod.;* Semen Strychni,, *P. G.;* Krähenaugen, Brechnuss, *G.;* Noce vomica, *It.;* Nuez vomica, *Sp.*

Strychnos Nux-vomica is a tree of a moderate size, with numerous strong branches, covered with a smooth, dark gray bark. The young branches are long, flexuous, smooth, and dark green, with opposite, ovate, petiolate, entire, smooth, and shining leaves. The flowers are small, white, funnel-shaped and in terminal corymbs. The fruit is a round berry, about as large as an orange, with a smooth, yellow or orange-colored, hard, fragile rind, and many seeds in a juicy pulp. It has frequently been asserted that the pulp is innocuous, but Flückiger and Hanbury, and also Dunstan and Short (*P. J.*, 3d series, xv, 1) have demonstrated that it contains strychnine. Dunstan and Short have also proved that of the commercial varieties of nux vomica, Bombay seed stands first in percentage of contained strychnine, then Cochin, and lastly Madras. (*P. J.*, 1883, xiv, 1053.)

The tree is a native of India, growing in Bengal, Malabar, on the Coromandel Coast, in Ceylon, in many islands of the Indian Archipelago, in Cochin China, and in Northern Australia. The fruits are collected when fully mature and the seeds removed from the pulp by washing, or the pulp may be rotted off the seeds. They are then dried in the sun on mats, graded and marketed. Most of the world's supply comes from India, two-thirds of the available supply being furnished by the Madras Presidency. The chief importers are the United States and Great Britain. The drug is largely shipped to the United States in small sacks from Madras, Cochin, Cocanada, Calcutta and Bombay, some coming indirectly through London.

The wood and root are very bitter, and were employed in the East Indies for the cure of intermittents. The *radices colubrinæ* and *lignum colubrinum* of the older writers, long known in Europe as narcotic poisons, have been ascribed to this species of *Strychnos*, under the impression that they were identical with *Strychnos colubrina*, to which Linnæus refers them. They were ascertained by Pelletier and Caventou's researches to contain a large quantity of strychnine. The bark has been mistaken for cusparia, and hence is sometimes referred to as *false angustura*. Gehe & Co. (*Handelsbericht*, 1914, p. 119) state that a new variety of nux vomica, the origin of which is unknown, is being exported from Burma. The seeds are externally light gray, internally yellow and are devoid of strychnine. For a description of commercial varieties of nux vomica seeds, see a paper by Youngken and Slotter in *A. J. P.*, 1920, p. 538.

Description and Physical Properties.—" *Unground Nux Vomica.*—Seed orbicular, nearly flat, occasionally somewhat bent, from 10 to 30 mm. in diameter, and from 4 to 5 mm. in thickness; externally grayish or greenish-gray, covered with appressed hairs, giving it a silky luster; hilum indicated by a circular scar at the center of one of the flattened sides, and connected with the micropyle by a ridge; very hard when dry; internally showing a thin and hairy seed-coat and a large grayish-white endosperm at one end of which is embedded a small embryo with two broadly ovate, 5- to 7-nerved cotyledons; inodorous; taste intensely and persistently bitter.

" *Powdered Nux Vomica.*—Light gray; consisting chiefly of thick-walled endosperm cells containing globules of a fixed oil and a few small aleurone grains; and fragments of strongly lignified, non-glandular hairs, the walls of the latter possessing large, circular, or long, slit-like pores. In the tissues of the adhering pulp occur a few small, nearly spherical starch grains." *U. S.*

" Seeds disc-shaped, nearly flat, but sometimes irregularly bent; rounded or somewhat acute at the margin, from a small prominence on which a raised line passes to the central hilum. Ash-grey or greenish-grey. From two to two and a half centimetres in diameter, and about six millimetres thick. Surface densely covered with short, satiny, radiately arranged and closely appressed hairs. Endosperm large and horny; cotyledons small and leafy. Powdered Nux Vomica exhibits fragments of the endosperm, the cell-walls of which are very thick but not lignified, also slender rod-like fragments of the hairs and their thickened, pitted, lignified basal portions. No odor; taste extremely bitter. Yields not less than 1.25 per cent. of strychnine when tested by the following process." *Br.*

The seeds are destitute of odor, but have an acrid, very bitter taste, which is much stronger in the kernel than in the investing membrane. They impart their virtues to water, but more readily to diluted alcohol. For a method of distinguishing powdered nux vomica from powdered ignatia and other powders, see *Proc. A. Ph. A.*, 1897, 503.

Herder has proposed a detection of the alkaloids in nux vomica by various microchemical means and shows how they may be localized in the seeds and growing plants. (*A. Pharm.*, 1906, p. 129.) Tunmann (*A. Pharm.*, 1910, 644) has studied the distribution of the alkaloids in the germinating seeds of *Strychnos Nux-vomica*, and concludes that the embryo of the seed contained only brucine and that strychnine, which was contained in the endosperm only in the cell plasma of the cell content, appears to act as a protection for the growing plant. Grutterink has also published an illustrated article on the microchemical examination of the several alkaloids of nux vomica. (*Zeit. An. Chem.*, li, p. 187.) Rusby has reported the shipment of nux vomica which consisted of small inferior seeds which had been rolled in some mixture of clay. (*Proc. A. Ph. A.*, 1908, lvi, p. 794.) Powdered nux vomica has been adulterated with ground olive stones and the raspings of vegetable ivory. (See *Rep. d. Pharm.*, 1909, p. 241; *Ann. d. chim. Analyt.*, 1909, p. 261.)

Assay.—" Place 10 Gm. of Nux Vomica, in fine powder, in a 250 cc. flask, add 100 cc. of ether-chloroform mixture, and proceed by Type Process A. Decant 50 cc. of the ethereal solution to complete the assay, using chloroform as the immiscible solvent in shaking out the alkaline liquid, and determine the alkaloids volumetrically. Each cc. of tenth-normal sulphuric acid corresponds to 0.0364 Gm. of the total alkaloids of Nux Vomica (Proximate Assays)." *U. S.*

"Shake 7.5 grammes of Nux Vomica in No. 60 powder frequently during half an hour with a mixture of 25 millilitres of *chloroform,* 50 millilitres of *ether,* and 5 millilitres of *solution of ammonia.* Transfer 50 millilitres of the clear ethereal liquid to a separator, and extract the alkaloids, by shaking with three successive portions, each of 10 millilitres, of *N/1 solution of sulphuric acid,* transferring the acid solutions to a second separator. Make the acid solutions alkaline with *solution of ammonia,* and again extract the alkaloids by shaking successively with 10, 5, and 5 millilitres of *chloroform,* drawing off the chloroformic solutions into a small flask. Recover the chloroform by distillation, dissolve the residue in a mixture of 5 millilitres of *diluted sulphuric acid* and 10 millilitres of water, heat the solution to 50° C., add 3 millilitres of a mixture of equal volumes of *nitric acid* and *water,* and set aside for ten minutes. Transfer the solution to a separator, rinsing the flask with a little *water,* make alkaline with *solution of sodium hydroxide,* and extract the alkaloid by shaking successively with 10, 5, and 5 millilitres of *chloroform.* Wash the mixed chloroformic solutions in a separator with 5 millilitres of *water,* transfer to a tared dish and allow the chloroform to evaporate, adding towards the end 5 millilitres of *alcohol* (90 per cent.). Evaporate to dryness, dry the residue at 100° C., and weigh. This weight, multiplied by 20, is the weight of strychnine in 100 grammes of the powdered Nux Vomica. Powdered Nux Vomica, when used for official purposes other than the production of standardised preparations, must be adjusted, if necessary, by the addition of powdered Milk Sugar to contain in 100 grammes 1.25 grammes of strychnine when tested by the foregoing process. *Limit of error* 0.05 gramme in excess or defect." *Br.*

The U. S. assay determines the total amount of alkaloid but in the Br. method the brucine is destroyed by the treatment with nitric acid and the final result represents the proportion of strychnine. Schweissinger recommended the direct determination of the alkaloids in nux vomica by titration with hydrochloric acid as the best way of ascertaining the strength of pharmaceutical preparations. (*A. Pharm.,* 1885, 579.) Keller's method of estimating the alkaloids in nux vomica (see *Proc. A. Ph. A.,* 1895, 1024) is commended by Sander. (*A. Pharm.,* 1897, 133; see also *A. J. P.,* 1896, 189.) A method of assay for nux vomica and its preparations has been proposed by M. Azadain (*P. J.,* xciii, 371) which involves the precipitation of the alkaloids by silico-tungstic acid.

Constituents.—Pelletier and Caventou discovered in nux vomica two alkaline principles, *strychnine* and *brucine,* united with a peculiar acid which they named *igasuric.* Shenstone (*J. Chem. S.,* 1881, xxxix, 453) has shown that the *igasurine* of Desnoix is a mixture of strychnine and brucine. Boorsma discovered a new alkaloid in the leaves of *S. Nux-vomica* (*Bull. de l'Inst. Bot. de Buitenzorg,* 1902) and he named it *strychnicine;* it is only slightly poisonous. (See also *P. J.,* 1902, 65.)

Hugo H. Schafer (*J. A. P. A.,* 1914, p. 1077) announced a new alkaloid in nux vomica which he has named *struxine,* $C_{21}H_{30}O_4N_2$. It is present only in the drug coming from Cochin China, and in an amount of 0.1 per cent. It is probably a decomposition product of either brucine or strychnine.

Strychnine ($C_{21}H_{22}O_2N_2$) was discovered by Pelletier and Caventou in 1818, in both the nux vomica and the bean of St. Ignatius. It generally constitutes a little less than one-half of the total alkaloids. For account of its chemical properties see *Strychnina.* For valuable practical information about the yield of the alkaloids, extracts, etc., by E. L. Patch, see *Proc. A. Ph. A.,* 1891, 91; also *P. J.,* 1889, 341; *P. J.,* 1890, 493.

Brucine ($C_{23}H_{26}O_4N_2$) was discovered by Pelletier and Caventou, first in the bark in combination with gallic acid, and subsequently, associated with strychnine in the form of igasurates, in the nux vomica and in the bean of St. Ignatius. It is a dimethoxy-strychnine. It may be separated from strychnine by virtue of the lesser solubility of its oxalate in dehydrated alcohol or of its hydriodide in water, or by the insolubility of strychnine chromate in water. Brucine is crystallizable from alcohol, the crystals then containing $4H_2O$. It is without odor, but of a permanent, harsh, very bitter taste; is sparingly soluble in water; very soluble in alcohol, whether hot or cold; it dissolves in 4 parts of chloroform, 440 parts of ether, 60 parts of benzene, and 120 parts of petroleum benzin. It is permanent in the air. The hydrated crystals melt at 105° C., and sublime at 204° C., while the anhydrous base melts at 178° C. changing color, and depositing carbon. It forms crystallizable salts with acids.

Concentrated nitric acid produces with brucine or its salts an intense crimson color, which changes to yellow by heat, and upon the addition of stannous chloride becomes violet. A test for brucine, given by Stanislas Cotton, consists in adding to a warm solution of brucine (from 40° to 50° C.) in nitric acid, a concentrated solution of sodium thiosulphate. The mixture first becomes violet, and then passes to green when the alkaline salt is in excess. (*J. P. C.,* 1869.) These reactions serve to distinguish brucine from strychnine, and, if produced with the latter alkaloid, evince the presence of the former. According to Larocque and Thibierge, auric chloride produces, with solutions of the salts of brucine, precipitates at first milky, then coffee-colored, and finally chocolate-brown. (*Journ. de Chim. Méd.*, 1842.) Chlorine water produces with solution of brucine a rose color, due to the formation of *dichlor-brucine.* This is a reddish-brown, hygroscopic powder. (*A. Pharm.*, 1886, 934.) A *dinitro-brucine,* $C_{23}H_{24}(NO_2)_2N_2O_4$, has also been obtained by the action of nitrogen trioxide upon the brucine in alcoholic solution. According to the analyses of Shenstone and Dragendorff, the bark of the nux vomica contains brucine, with a trace of strychnine, while in the leaves Hooper found only brucine. (*P. J.*, 1890, xxi.)

Brucine may be procured, in a manner essentially the same as that in which strychnine is procured from nux vomica, with this difference, that the alcoholic extract obtained from the precipitate produced by lime or magnesia should be treated with oxalic acid, and subsequently with a mixture of rectified alcohol and ether, which takes up the coloring matter, leaving brucine oxalate. This is decomposed by magnesia, and the brucine is separated by alcohol, which by spontaneous evaporation yields it in the state of crystals. Prescott (*Organic Analysis,* 1887, p. 458) gives two methods for the separation of strychnine from brucine, first, by the use of alcohol of 0.97 sp. gr., which easily dissolved brucine, but has very slight solvent power upon strychnine; second, by Dunstan and Short's method with potassium ferrocyanide. This method has been reported upon by Holst and Beckurts (*Ph. Centralh., N. F.* 1887, p. 119), who find that if the hydrochloric acid solution containing mixed alkaloids is not too dilute, on the addition of potassium ferrocyanide the whole of the strychnine will be precipitated as ferrocyanide, while the brucine salt will remain in solution.

The estimation of strychnine in the presence of brucine is most conveniently effected by exposing the mixed alkaloids to the action of diluted nitric acid, which destroys brucine very rapidly while having no appreciable action on strychnine; this method is used in the British official assay process.

Dunstan and Short (*P. J.*, 1883, xiv, 1025) found in the nux vomica seeds, but more abundantly in the pulp surrounding them, a glucoside *loganin,* $C_{25}H_{34}O_{14}$.

Loganin is present in the pulp to the amount of 4 or 5 per cent. and is contained in small quantity also in the seeds. It was obtained by exhausting the pulp with a mixture of chloroform and alcohol (100:25). The exhaustion was effected in an apparatus for hot repercolation. The percolate, on cooling, deposited crystals, which when recrystallized a number of times from alcohol, and finally from absolute alcohol, were obtained pure. Loganin is easily soluble in water and alcohol, less soluble in ether, chloroform, and benzene. Its aqueous solution is not precipitated by any of the alkaloidal reagents. Its most characteristic reaction is found in its behavior with concentrated sulphuric acid. A very small quantity of loganin, when gently warmed with a few drops of concentrated sulphuric acid, yields a fine red color, which, on standing, develops into a deep purple. By boiling with dilute sulphuric acid, loganin is resolved into glucose (reducing Fehling's solution) and a body for which the name *loganetin* is proposed. This substance, like loganin, gives the characteristic reaction with sulphuric acid, but the purple color does not develop so rapidly. Loganetin is soluble in water and alcohol, less soluble in ether, carbon disulphide and chloroform. (*P. J.*, 1884, p. 1025.)

In addition to these constituents, there are present a yellow coloring matter, a fixed oil, gum, starch. a small quantity of wax, and several earthy phosphates. The unsaponifiable portion of the oil was identified as a mixture of phytosterins. (*A. Pharm.*, 1912, p. 398.) F. Meyer (*In. Dis.*, St. Petersburg, 1875) investigated the fatty oil, and found it to consist of the glycerides of capric, caprylic, caproic, butyric and palmitic acids. (*A. J. P.*, 1874, 405.)

Other species of *Strychnos* contain the poisonous alkaloids, and may some time become a commercial source of them. *Bidara laut* of the Indian bazaars, believed to be obtained from *S. ligustrina* Blume has been analyzed by Russow, who found the wood to contain 2.26 per cent. and the bark 7.38 per cent. of brucine without strychnine. Henry G. Greenish found in the wood and bark respectively of *S. colubrina* L. 0.96 per cent. and 5.54 per cent. of mixed alkaloids; the same analyst obtained from false Angustura bark (*S. Nux-vomica*), young bark 3.10 per cent., old bark 1.68. (*P. J.*, 3d sér., ix, 1014.) According to Bernelot-Moens, the dry seeds of the *S. Tieute* Lesch. contain 1.469 per cent. of strychnine, with a trace of brucine. (*A. J. P.*, 1866, p. 506.) From the seeds of *Strychnos Rheedii* C. B. Clarke, W. R. Dunstan obtained a yield of 0.06 per cent. of brucine and no strychnine. (*Imp. Inst. Rep.*, 1901–1902.) The Congo poison known as *Cupua Apus,* according to Vinci (*A. I. P. T.*, xx), is produced from the *Strychnos Kipapa* Gilg. The bark of the root contains 6 per cent. of strychnine and the wood 0.1 per cent. From the seeds of *Strychnos cinnamomifolia* Thw., native to Ceylon, India, G. R. A. Short obtained a yield of 2.231 per cent. of brucine and 0.342 per cent. of strychnine (*P. J.*, 1924, 97).

Strychnos quadrangularis Hill. yields "*Ipohaker*" or Malayan arrow- poison. *S. Gaultheriana* Pierre yields *Hoangnan bark* which is used in eastern countries as a remedy for leprosy. *Strychnos Nux-blanda* Hill. of Burma produces seeds which contain neither strychnine nor brucine and are devoid of bitterness. According to A. W. Hill this species differs from *S. Nux-vomica* in the long calyx segments, the larger, abruptly acute leaves, larger fruits with more numerous seeds, the latter having a felty-white surface, without the satiny luster of genuine nux vomica seeds (*Kew Bull.*, 1917, p. 121).

Igasuric acid has been regarded as erroneously named, and investigators have stated that it was malic acid and tannic acid, while G. Sander (*A. Pharm.*, 1897, 133) believes that the acid found in nux vomica, heretofore known as igasuric acid, is *caffeo-tannic acid.*

Uses.—The medicinal and toxic properties of nux vomica are those of its alkaloid. (See *Strychnina.*) The belief held by some physicians that it acts more favorably as a bitter upon the stomach has only this much of justification—namely, that it is more slowly absorbed, and therefore acts locally somewhat more persistently.

BRUCINE.—On account of the difficulty of separating strychnine from brucine, it has been found by physiologists difficult to determine the exact action upon the human organism of the pure alkaloid. It was formerly taught that brucine closely resembled strychnine in its physiological action, except that it was less poisonous and that it was depressant to the peripheral sensory nerves. Dickson and Harvey (*P. J.*, 1908, lxxxi, p. 367), however, experimenting with a chemically pure brucine, reach the conclusion that its dominant action is a paralysis of the peripheral motor nerves, and that the convulsive action which is the characteristic effect of strychnine is almost entirely absent in the case of brucine. According to the observation of Mays, brucine is an active paralyzant to the sensory nerves and a 5 or 10 per cent. solution applied to the mouth causes local anesthesia. He has used it for the relief of *pruritus.* Burnett also asserts that a 5 per cent. solution is a valuable local anodyne in inflammations of the external ear.

Dose, of nux vomica, one to four grains (0.065–0.26 Gm.).

Off. Prep.—Extractum Nucis Vomicæ, *U. S.*, *Br.;* Fluidextractum Nucis Vomicæ, *U. S.* (*Br.*)*;* Tinctura Nucis Vomicæ (from Extract), *U. S.* (from Liquid Extract), *Br.*

OLEA
OILS

These are liquid or solid substances, unctuous to the touch and characterized by inflammability. They are divided into two classes, the *fixed* and the *volatile,* because distinguished, as their names imply, most readily by their different behavior on the application of heat.

OLEA FIXA. *Fixed Oils.*

Oleo Pingua; Fats, Fatty Oils; Huiles Graisses, Huiles fixés, *Fr.;* Fette, Fette Oele, *G.;* Olios, *It.;* Aceites, *Sp.*

These are sometimes termed *fatty oils,* because they constitute in part the vegetable and animal fats. The distinction between liquid and solid fats is for the most part a physical one only, as they contain the same chemical compounds, although in relatively different proportions. The fatty oils, though existing in greater or less proportion in various parts of plants, are mainly derived commercially from the fruit, and, as a rule, are most abundant in the dicotyledonous seeds. They are obtained either by submitting the bruised seeds to pressure, or by boiling them in water, and skimming off the oil, as it rises to the surface. When pressure is employed, it is customary to prepare the seeds for the press by exposing them to a moderate heat, so as to render the oil more liquid and thus enable it to flow out more readily. Another mode of extracting certain oils is by extraction with one of the immiscible solvents, ether, carbon disulphide, carbon tetrachloride, or petroleum benzin being used. Fixed oils may be clarified and decolorized by subsidence, by filtration through animal charcoal, fuller's earth, kaolin, or diatomaceous earth, cellulose and asbestos filters are often used, and on the large scale, for separating mechanical impurities, centrifugal machines like those employed for milk. Some oils are given a preliminary treatment with sulphuric acid which is later removed by neutralization with alkali. Fixed oils containing stearin or palmitin are likely to deposit these fats in cold weather, leaving the olein in a liquid condition. The olein may be separated by expression and filtration in the cold.

Hydrogenated Fats and Oils.—A class of solid fats has appeared upon the market which are produced by a process known as hydrogenation, which is carried out commercially by bringing liquid fats into intimate contact with metallic catalyzers (finely divided nickel is usually employed), at elevated temperatures (160°–200° C.). Under these conditions the unsaturated members of the fatty acid series which are usually liquid and are represented by oleic acid, become converted into the solid members of the series, exemplified by stearic acid which is a saturated acid. Several commercial products made in this way are largely used for culinary purposes.

Some fixed oils, in drying, lose their fluid and oily character, and are converted into a transparent, yellowish, flexible solid. These are called "drying oils." Most fixed oils especially when not quite pure or entirely free from moisture, become rancid, acquiring an acrid and an unpleasant odor. This change is usually accompanied by the liberation of free fatty acids. Oils which have become rancid may sometimes be restored by treatment with weak alkalies and subsequent washing and drying.

The fixed oils are insoluble in water, but by the agency of certain factors are capable of forming mixtures with water which are called emulsions. (See *Emulsa.*) They are in general very sparingly soluble in alcohol, but readily dissolved by ether. By the aid of heat they are enabled to dissolve sulphur and phosphorus. The stronger acids effect the hydrolysis of fixed oils under certain conditions, giving rise, among other products, to oleic, palmitic and stearic acids. They are saponified by various alkalies. The compounds which the fatty acids form with potassium and sodium are the common detergent soaps, although strictly speaking, a soap is the combination of a fatty acid with any metal or base. (See *Sapo* and *Eplastrum Plumbi.*) The fixed oils also serve as good vehicles for various metallic bases and subsalts, which form soaps to a certain extent soluble in the oil, and thus become less irritant to the tissues. The fixed oils dissolve many of the alkaloids, the volatile oils, resin, and some other proximate principles of plants. The alkaloids are more readily dissolved in them by being first combined with oleic acid, the oleates being more soluble than the alkaloids themselves. According to Buignet, fixed oils, with very few exceptions, are indifferent to polarized light; of all those used in medicine, the only exceptions are the liver oils of the ray and dog fish, which have a very feeble lævorotatory power, and castor oil, which is decidedly dextrogyrate.

It is very likely that, with the exception of castor oil, whose rotatory power is due to the asymmetric carbon atom of the ricinoleic acid, the rotatory power is not due to the glycerides themselves but to small proportions of optically active substances such as cholesterol. (Lewkowitsch, *Chem. Analysis of Oils, Fats and Waxes,* p. 121.)

The fixed oils, whether animal or vegetable, in their natural state consist in most cases of at least two or three distinct constituents, one liquid at ordinary temperatures, and the other two solid or semi-solid. The liquid is a distinct proximate principle called *olein;* the more solid principles consist of *stearin* and *palmitin,* the former being found most largely in animal and the latter in vegetable oils or fats, and the two in most cases existing together in the same oil. The substance formerly known as *margarin* is now generally recognized to be a mixture of palmitin and stearin. As the most frequent of these proximate constituents of the fixed oils, and existing in many different oleaginous substances, olein, palmitin, and stearin merit a special notice. Preliminarily to their individual consideration, it will be proper to refer to their nature and composition generally.

These three substances, *olein, palmitin,* and *stearin,* together with *butyrin, caprin,* and other minor fat principles, are glycerides; that is, esters or salts of the triatomic alcohol glycerol, $C_3H_5(OH)_3$, and of the several fatty acids, oleic, palmitic, stearic, etc., all of which are monobasic acids. The three mentioned glycerides have the following composition:

Olein (triolein), $C_3H_5(OC_{18}H_{33}O)_3$
Palmitin (tripalmitin), $C_3H_5(OC_{16}H_{31}O)_3$
Stearin (tristearin), $C_3H_5(OC_{18}H_{35}O)_3$

There are also mixed glycerides exemplified by the following formula:

$$\underset{\text{(oleopalmitostearin)}}{C_3H_5}\begin{cases} OC_{18}H_{33}O \\ OC_{16}H_{31}O \\ OC_{18}H_{35}O \end{cases}$$

When these substances, or oils composed principally of them, are treated with alkali with the aid of heat, decomposition takes place, which may be illustrated as follows:

$$C_3H_5(OC_{18}H_{33}O)_3 + 3NaOH = C_3H_5(OH)_3 + 3NaOC_{18}H_{33}O$$

that is, olein is decomposed by sodium hydroxide into glyceryl hydroxide, or glycerin, and sodium oleate, or a sodium soap.

The waxes differ from the fats proper in being esters of the higher monatomic alcohols like *cetyl alcohol,* $C_{16}C_{33}.OH$, and *myricyl alcohol,* $C_{30}H_{61}.OH$, instead of being glycerides. The fatty acids present are partly palmitic and stearic, but more largely still higher ones, like *cerotic acid,* $C_{27}H_{54}O_2$.

Other fatty acids represented in fixed oils may be grouped as follows: (1) Saturated fatty acids, including *butyric acid,* $C_4H_8O_2$; *valeric acid,* $C_5H_{10}O_2$; *caproic acid,* $C_6H_{12}O_2$; *caprylic acid,* $C_8H_{16}O_2$; *capric acid,* $C_{10}H_{20}O_2$; *lauric acid,* $C_{12}H_{24}O_2$; *myristic acid,* $C_{14}H_{28}O_2$; *arachidic acid,* $C_{20}H_{40}O_2$. The first few members of the above list are known as the volatile fatty acids, which serve as the basis for the determination of what is known as the Reichert-Meissl number. (2) Unsaturated acids (Oleic Acid series) including: *crotonic acid,* $C_4H_6O_2$; *angelic* and *tiglic* (*tiglinic*) *acids,* $C_5H_8O_2$; *hypogeic acid,* $C_{16}H_{30}O_2$; *erucic acid,* $C_{22}H_{42}O_2$; *linoleic acid,* $C_{18}H_{32}O_2$, which gives to certain oils the peculiar "drying" properties.

Olein. Elain. Liquid Principle of Oils.—It is extremely difficult to obtain olein pure. Being in most oils associated with the solids stearin and palmitin, it must be separated by pressure and other mechanical means, which separation is not always perfectly effected. As ordinarily procured, therefore, olein contains more or less dissolved palmitin or stearin, or both. In this somewhat impure state it is obtained either by the agency of alcohol or by expression. When one of the oils, olive oil, for example, is dissolved in boiling alcohol, the solution, on cooling, deposits the palmitin and stearin, still retaining the olein, which it yields upon evaporation. The other method consists in compressing one of the solid fats, or one of the liquid oils rendered concrete by cold. Olein is a liquid of oily consistence, congealing at – 6° C., colorless when pure, with little odor and a sweetish taste, insoluble in water, soluble in boiling alcohol and ether. Its formula, as already stated, is $C_3H_5(OC_{18}H_{33}O)_3$, being an oleate of the triad radical *glyceryl,* C_3H_5. By reaction with nitric acid, or, under the influence of nitrous acid fumes, olein is converted into a deep yellow, butyraceous mass. If this be treated with hot alcohol, a deep orange-red oil is dissolved, and a peculiar fatty matter remains, called *elaidin.* This is white, crystalline, fusible at 34° C., insoluble in water, readily soluble in ether, and appears to be isomeric with olein. It is the product which gives the firm consistency to citrine ointment. It is resolved by saponification with the alkalies into *elaidic acid* and glycerin.

Palmitin.—Palmitic acid occurs in the more liquid fats, such as palm oil and cocoa-nut oil, as well as in butter and human fat, as glyceride, while in spermaceti and some forms of wax it is combined with monatomic alcohol radicals. Palmitin is the *palmitic acid glyceride,* or *glyceryl tripalmitate.* It is best obtained from palm oil.

Stearin.—This exists abundantly in tallow and other animal fats. Pure stearin may be obtained by treating the press cake from lard, free from olein, by cold ether so long as anything is dissolved. The palmitin is thus taken up, and stearin remains. Another method is to dissolve suet in heated oil of turpentine, allow the solution to cool, submit the solid matter to expression in unsized paper, repeat the treatment several times, and finally dissolve in hot ether, which deposits the stearin on cooling. This is concrete, white, opaque in mass, but of a pearly appearance as crystallized from ether, pulverizable, fusible at 66.5° C., soluble in boiling alcohol and ether, but nearly insoluble in those liquids cold, and quite insoluble in water. It consists of glyceryl and stearic acid (see *Acidum Stearicum*) in combination as a glyceride, $C_3H_5(OC_{18}H_{35}O)_3$, and has been formed synthetically by heating a mixture of these two materials to 280° to 300° C.

Commercially the fixed oils are frequently sold under the names "summer pressed" and "winter pressed." These were once really seasonal designations, as an oil pressed during the warmer months would contain more dissolved stearin and would consequently congeal or cause a deposit when chilled, while an oil pressed during cold weather would remain transparent at low temperatures, and thus winter pressed oils were more satisfactory for lubricating purposes and commanded a higher price. Artificial refrigeration now makes it possible to make either grade of oil at any season of the year, although the former designations "summer pressed" and "winter pressed" are still commercially used.

The fixed oils are liable to certain spontaneous changes, which have been investigated by Pelouze and Boudet. It appears from their researches that the oils are accompanied, in the seeds which contain them, with principles which act as a ferment and cause the oils to resolve themselves spontaneously into the several fatty acids which they afford on saponification, and into glycerin; that is, become rancid. This change takes place in the seeds as soon as the cells containing the oils are broken, so as to permit the contact of the oil with the fat splitting or lipolytic enzyme. The decomposition of fats by the action of enzymes has been made a working method capable of technical application, by Connstein, Hoyer and Wartenburg. The enzyme contained in the castor oil bean has been found best adapted for this. An emulsion of fats, water, 10 per cent. of ground castor oil beans and a small amount of free acid are used, when the decomposition proceeds rapidly. As rancidity in fats renders them altogether useless in pharmacy, and as it is not always readily discoverable by the senses in its earlier stages, it becomes desirable to possess a test by which it may be detected. Such a test is to be found, according to Thos. B. Groves, in potassium iodide, which is rapidly decomposed by the new principles developed, and the orange-brown discoloration produced by the liberation of the iodine indicates the existence of rancidity, and the degree of that discoloration, approximately, the extent of the change. The alteration of color is said by Groves to be plainly perceptible when only one-twentieth of rancid fat is present. The presence of water in a fatty oil favors the production of rancidity.

It is also extremely important to be able to protect fats against this change. The complete exclusion of air, light, and moisture—and, when in relation to air this may not be entirely practicable, the destruction by heat of the enzyme by which the decomposition is often originated—will go far to effect this object; but it would often be very inconvenient, if not impossible, to carry these measures into complete effect, and hence the discovery of substances which may have the effect of retarding, if not wholly preventing, these fermenting processes, is very desirable. This preservative effect has been known and practically used many years. Thus, benzoin rubbed up with fats is well known to preserve them long against rancidity, and benzoinated lard, made by extracting ten per cent. of benzoin with melted lard, is one of the official preparations, and the buds of the poplar (*Populus nigra*) are perhaps still more effectual, as, according to Deschamps, lard impregnated with their virtues will keep good indefinitely. In the French Codex the poplar buds are employed in the *Pommade de Bourgeon de Peuplier,* in which 8 parts of the dried buds are used to 40 parts of the ointment, consisting of lard impregnated with the virtues of several narcotic substances, the fresh narcotic plants being boiled with lard until all their water is evaporated, and the buds afterwards digested in the strained liquid for twenty-four hours.

The adulteration of the fixed oils may be effected in several ways—by admixture with the fatty oil of substances distinctly foreign to the fats, and by adding a cheaper or inferior oil of the same identity or closely related to one of greater value. In the former case we may have the addition of paraffin wax, ceresine, mineral oils, neutral tar oils, resin oils, resin, and waxes. Of these, the first three are entirely unsaponifiable, resin oils contain but small quantities of saponifiable substances, waxes are partly saponifiable, and resin almost completely saponifiable. The determination of unsaponifiable matter is therefore of great importance. The common method for this is to saponify the suspected sample with alcoholic potassium hydroxide and then to shake out the unsaponifiable matter with ether or petroleum ether. From this solution, on evaporation, will be obtained the mineral, resin, or tar oils that may have been present. For these there are appropriate tests elsewhere noted. In case a cheaper oil or fat has been added for the purpose of adulterating a more valuable one, we must be guided by the determination of certain constants, such as those mentioned below by Cowley, or by the indication of certain qualitative color tests. The constants referred to are much more to be depended upon in such a case.

R. C. Cowley (*P. J.*, 1897, 331) regards the following as the most important determinations in examining fats and fixed oils. 1. Specific gravity. 2. Melting and solidifying points. 3. Melting and solidifying points of fatty acids. 4. Behavior with solvents. 5. The Hehner value. 6. The Reichert-Meissl value. 7. The saponification value. 8. The iodine value. To these have been added during recent years: 9. The refractive index. 10. The acetyl number. 11. The temperature rise with sulphuric acid (Maumené number).

CLASSIFICATION.

The following scheme of classification of the fixed oils, both liquid and solid (Allen, *Com. Org. Anal.*, 3d ed., vol. ii, Part I, pp. 88–102), gives a general view of their essential characters, points of difference, etc.

I. Olive Oil Group. *Vegetable Non-drying Oils.*—The oils of this group solidify on treatment with nitrous acid or mercuric nitrate, but do not lose their power of producing a greasy stain on paper, however long they may be exposed to the air. Their density varies from 0.914 to about 0.920, and hence is less than that of Groups III, IV, and V. Their viscosity is notably greater than that of the drying oils.

This group includes almond oil (from *Amygdalus communis* L.), peach oil (from kernels of *Prunus Persica* Stokes), apricot oil (from kernels of *Prunus Armeniaca* L.), oil of ben (from *Moringa oleifera* Lam.), earth nut oil (from *Arachis hypogæa* L.), and olive oil (from *Olea europæa* L.).

II. Rape Oil Group.—The oils of this group are all derived from seeds of the family *Cruciferæ.* They are non-drying but less distinctly so than the oils of Group I. They show higher saponification values, higher iodine absorption and less solid elaidins than Group I.

This group includes Colza oil and rape seed oil (from *Brassica campestris* L., *B. napus* L. and other species); oil of black mustard (from seeds of *Brassica nigra* Koch.); oil of white mustard (from seeds of *Sinapis alba* L.).

III. Cotton Seed Oil Group.—The oils of this group occupy a position intermediate between the vegetable non-drying and the true drying oils (Groups I and IV). In density they somewhat exceed the oils of Group I, but are lighter than those of Groups IV and V. They form more or less elaidin on treatment with nitrous acid or mercuric nitrate, but do not become wholly solidified. On the other hand, they undergo more or less drying on exposure to the air, but not so markedly as the oils of Group IV.

This group includes beech nut oil (from *Fagus sylvatica* L.), cotton seed oil (from *Gossypium* species), hazel nut oil (from *Corylus Avellana* L. see *Proc. A. Ph. A.*, 1893), sesame or teel oil (from *Sesamum indicum* L.), sunflower oil (from *Helianthus annuus* L.), camelina oil (from *Myagrum sativum* L.), cress seed oil (from *Lepidium sativum* L.), and maize oil (*Corn Oil*).

IV. Linseed Oil Group. *Vegetable Drying Oils.*—These oils are not solidified by treatment with nitrous acid or mercuric nitrate, but become gradually converted into solid masses or varnishes, by exposure to the air. In density the oils of this group vary from about 0.923 to 0.937, and hence are distinctly heavier than the non-drying oils and than most of the oils of Group III. On the other hand, they are lighter than the oils of Group V. The fluidity of the drying oils is also much higher than that of the non-drying oils.

This group includes niger seed oil (from *Guizotia oleifera* DC.), hemp seed oil (from *Cannabis sativa* L.), linseed oil (from *Linum usitatissimum* L.; *L. perenne* L.), poppy seed oil (from *Papaver somniferum* L.), Scotch fir seed oil (from *Pinus sylvestris* L.), tobacco seed oil (from *Nicotiana Tabacum* L.), walnut oil (from *Juglans regia* L.), weld seed oil (from *Reseda Luteola* L.), and soya bean oil (from *Glycine Max* Merr.).

V. Castor Oil Group.—The oils of this group are distinguished from those of Groups I, II, III, and IV, by their very high density and viscosity. They are also remarkable for their ready solubility in alcohol, and their marked purgative properties. In their drying characters and behavior with the elaidin test they resemble the oils of the cotton seed oil group. Both castor and croton oil are miscible in all proportions with glacial acetic acid.

This group includes castor oil (from *Ricinus communis* L.), croton oil (from *Croton tiglium* L.), Japanese or Chinese wood oil (from seeds of *Aleurites cordata* Steud.), boiled linseed oil, blown oils (made by oxidation of rape seed, cotton seed, linseed, lard, and other oils).

VI. Palm Oil Group. *Solid Vegetable Fats.*—This group includes solid fats not containing notable quantities of glycerides of lower fatty acids. The densities for the melted fats at 98° and 99° C. are compared with the density of water at 15.5° C. taken as 1.000, and vary from 0.920 to 0.995.

This group includes palm oil (from fruit of *Elæis guineensis* Jacq.), cacao butter (from nuts of *Theobroma Cacao* L.), nutmeg butter (from nuts of *Myristica fragrans* Houttuyn), and shea butter (from seeds of *Bassia Parkii* G. Don) (*Butyrospermum Parkii* Kotschy).

VII. Cocoanut Oil Group. *Solid Vegetable*

Fats.—This group includes solid fats containing notable quantities of glycerides of lower fatty acids—that is, of acids distilling with more or less facility in a current of steam at 100° C. The group includes cocoanut oil (from the seeds of *Cocos nucifera* L. and *C. butyracea* L.), palm oil (from the kernels of the nuts from *Elæis guineensis* Jacq.), laurel oil (from fruit of *Laurus nobilis* L.), Japan wax (drupes of *Rhus succedanea* L.), myrtle wax (fruits of *Myrica cerifera* L.). For a description with constants of some of the rarer fixed oils belonging to the vegetable group, see papers by J. A. Wijs, *Ph. Ztg.*, 1903, 563; by Pancoast and Graham, *A. J. P.*, 1904, 70; and by Lewkowitsch, *P. J.*, 1904, 492.

VIII. Lard Oil Group. *Animal Oleins.*—This group includes those oils fluid at ordinary temperatures which are obtained from terrestrial animals. They resemble the whale or fish oils in their reaction with chlorine, but are not turned red or brown by boiling with caustic soda. On exposure to air and on treatment with nitrous acid or mercuric nitrate, they behave like the non-drying vegetable oils (Group I). This group includes bone oil, lard oil, tallow oil, and neat's-foot oil. For a paper by P. L. Simmonds on various animal oils, see *Bull. Pharm.*, 1893, 297, 344.

IX. Tallow Oil Group. *Solid Animal Fats.*—This group comprises oils that are solid or semisolid at ordinary temperatures. Their melting points vary somewhat, and are capable of permanent alteration. The group includes bone fat, butter fat, hog's lard, horse fat, beef tallow and mutton tallow.

X. Whale Oil Group. *Marine Animal Oils.*—This group comprises the various fluid oils obtained from fish and cetaceous mammals. They are distinguished as a class by their offensive fishy odor, by the brown color they assume when subjected to the action of chlorine, and by the reddish color which is produced on boiling them with a solution of caustic alkali. With sulphuric acid they give colorations varying from light red to purple or brown. The fish oils do not dry on exposure to air, and mostly yield but little elaidin on treatment with nitrous acid. The term *"train oil"* includes whale, seal, shark, cod, and all similar oils. Cod oil (from *Gadus morrhua* L. and allied species), cod liver oil (from the same), menhaden oil (from *Alosa menhaden* L.), porpoise oil (from *Delphinus phocæna* and allied species), seal oil (from various species of *Phoca*), shark oil (from *Squalus maximus* L. and allied species), and whale oil (from *Balaena mistecetus* L. and allied species) are all members of this group.

XI. Sperm Oil Group. *Liquid Waxes.*—The members of this group differ from all the fatty oils of previous classes in not being glycerides, consisting essentially of esters of monatomic alcohols of the ethylic series, in which respect they resemble the true waxes, but are fluid at ordinary temperatures. They are less dense than glycerides, they do not dry or thicken notably on exposure to air, but they yield solid elaidins on treatment with nitrous acid. The group includes sperm oil (from cranial cavities of *Physeter macrocephalus* L.), doegling or bottlenose oil, and dolphin oil.

XII. Spermaceti Group. *Waxes Proper.*—Spermaceti and the various waxes differ from the true fixed oils and fats in not forming glycerin when saponified, yielding instead certain of the higher monatomic alcohols, the identity of which varies with the nature of the wax. These alcohols are insoluble in water, and dissolve to but a limited extent in alcohol, but they are soluble in ether, chloroform, carbon disulphide, benzene, and petroleum benzin, and are apt to be mistaken for added paraffin wax when the substance is saponified and the soap extracted with a solvent.

This group includes beeswax (from honeycomb of various species of bees), Carnauba or Brazil wax (from the leaf-coverings of *Copernicia cerifera* Mart.), Chinese wax or Pela wax (produced by a species of *Coccus* which punctures the branches of certain trees), myrtle wax from fruits of *Myrica cerifera*), Ocuba wax (from *Myristica sebifera* Sw.), palm wax (from bark of *Ceroxylon andicola* Humb. of the Cordilleras) and spermaceti (deposits from the oil found in the cranial cavities of the sperm whale, *Physeter macrocephalus* L.). Wool fat, which consists largely of cholesterol, belongs to this group.

When oils are decomposed by heat they emit vapors of *acrolein*—which is *allyl aldehyde*, CH_2CHCHO—a highly volatile liquid resulting from the decomposition of glycerin well known for its irritating effects on the eyes and nostrils. Exposed to a red heat, in closed vessels, they yield, among other products of the destructive distillation, a large quantity of combustible and illuminating gases, among which ethylene and acetylene are readily recognized. Heated in the open air, they take fire, burning with a bright flame, and producing water and carbon dioxide. When kept in air-tight vessels, they remain unchanged for a great length of time, but exposed to the atmosphere they absorb oxygen and undergo change.

Effervescent Oils.—K. Dieterich recommends oils and fats which have been supersaturated with carbon dioxide and introduced by him under the name of "effervescent oils." (See *Proc. A. Ph. A.*, 1900, 494.) Under the influence of carbon dioxide, compounds which are easily split with the fatty acids are produced, which, particularly in the case of cod liver oil, permit the more complete absorption of the oil than is the case with oil not treated with carbon dioxide. The latter, moreover, acts as a preservative of the oils and renders them more palatable, destroying the unpleasant taste of cod liver oil, and to a certain extent also that of added medicaments, very materially. The absorbability of carbon dioxide is, however, not the same in all oils. Cod liver oil is capable of absorbing the largest quantity, castor oil the smallest, while olive oil stands intermediate. (*Ph. Centralh.*, 1901, 485.)

OLEA VOLATILIA. [*Olea Destillata.*]

Volatile Oils.

Olea Ætherea, Ætherolea; Ethereal Oils, Essential Oils, Distilled Oils; Huiles Volatiles, Huiles Essentielles, Huiles Distillées, Essences, *Fr.;* Flüchtige Oele, Aetherische Oele, *G.;* Essenze, *It.;* Esencias, Aceite volatil, *Sp.*

These are sometimes called *distilled oils,* from the mode in which they are usually procured; sometimes *essential oils,* from the circumstance that they possess, in a concentrated state, the organoleptic properties of the plants from which they are derived. The word *essence* is used in some countries to designate the volatile oils themselves, but in America this word has unfortunately been largely applied to the alcoholic solutions of the volatile oils, usually called the *spirits,* and the word *soluble essence* has been used to describe hydroalcoholic solutions of volatile oils which possess the property of mixing clear with water.

The term *Ætherolea* is used in some countries to distinguish the volatile oils in general from those which are produced by destructive distillation, like oil of amber, oil of cade, oil of tar, etc., which are given the collective name *pyrolea* (pyroligneous oils).

They exist in most odoriferous vegetable tissues, sometimes pervading the plant, sometimes confined to a single part; in some instances contained in distinct cells, and partially retained after desiccation, in others formed upon the surface, as in many flowers, and exhaled as soon as formed. Occasionally two or more are found in different parts of the same plant. Thus, the orange tree produces one oil in its leaves, another in its flowers, and a third in the rind of its fruit. In a few instances, when existing in distinct cells, they may be obtained by pressure, as from the rind of the lemon and orange; but they are generally obtained by steam distillation. (See page 733.) Some volatile oils, as those of bitter almond and mustard do not pre-exist in the plant issues but are produced by a chemical reaction which takes place between certain constituents in the presence of moisture. (See these oils for further details.)

The volatile oils are usually colorless when freshly distilled, or at most yellowish, but some are brown, red, green, or blue. There is reason, however, to believe that in most instances the color depends on foreign matter dissolved in the oils. Septimus Piesse succeeded, by the fractional distillation of certain volatile oils, in separating a blue liquid, which, by repeated rectification, he has obtained quite pure. In this state it has the sp. gr. 0.910, and a fixed boiling point of 302.3° C., and yields a dense blue vapor having peculiar optical properties. He named this principle *azulene,* and believed that upon it depends the blueness of volatile oils wherever existing. The yellowness of the oils he ascribed to the resin resulting from their oxidation, the green and brown colors to a mixture of azulene and resin in various proportions. The formula of azulene he gave as $C_{16}H_{26}O$. (*Chem. News,* 1863.) Gladstone named this blue coloring constituent *cæruleïn,* and stated that it contains nitrogen and is colored green by acids and alkalies.

Azulene was later investigated by Sherndal, who assigns to it the formula $C_{15}H_{18}$, which places it in the class of hydrocarbons. He states that it yields a dihydrosesquiterpene, $C_{15}H_{23}$, upon reduction and believes it to be related to alpha gurjunene, $C_{15}H_{24}$, a tricyclic compound existing in gurjun balsam.

The volatile oils have a strong odor, resembling that of the plants from which they were procured, though generally less agreeable. Their taste is hot and pungent, and, when they are diluted, is often gratefully aromatic. The greater number are lighter than water, though some are heavier; their sp. gr. varies from 0.847 to 1.17. They vaporize at ordinary temperatures, diffusing their peculiar odor, and are completely volatilized by heat. When distilled alone, they nearly always undergo partial decomposition. Heated in the open air, they take fire and burn with a bright flame attended with much smoke. Almost all of them are optically active, and advantage may sometimes be taken of this property to detect adulterations of one of these oils with another. The refractive index is another physical constant that is being studied in connection with volatile oils, but the accumulation of data is not yet sufficiently large to give the factor much value as yet. Exposed at ordinary temperatures, some of them absorb oxygen, assume a deeper color, become thicker and less odorous, and are ultimately converted into resin. This change takes place most rapidly under the influence of light. Before the alteration is complete, the remaining portion of oil may be recovered by distillation.

It is said that volatile oils which resinify and assume a turpentine odor, can be kept indefinitely by adding sodium bisulphite in the proportion of 50 grains to 1 pound. (*Pract. Drug.,* 1920, xxxix, 36.) They can also be preserved by the addition of 5 per cent. of a fixed oil, such as cotton-seed or olive oil.

CLASSIFICATION

The volatile oils are sometimes hydrocarbons, although with these are frequently associated alcohol- or ketone-like bodies called *camphors,* and products of oxidation known under the general name of resins, and undoubtedly formed from the hydrocarbons. Phenols, aldehydes, esters, ethers, and sulphides are also represented. The hydrocarbons are generally known as *terpenes,* from oil of turpentine, which is taken as a type. *Olea ætherea sine terpeno* is the name proposed by Schweissinger for concentrated volatile oils made so by the removal of the non-fragrant hydrocarbon, and representing from two to thirty volumes of the ordinary essential oils. Thus, one volume of the concentrated oil represents two volumes of the oils of anise, cassia, fennel, ginger grass, mentha crispa, mentha piperita, cloves, sassafras, and star anise; two and one-half volumes of the oils of bergamot, caraway, and lavender; four volumes of cumin and rosemary; five volumes of thyme; six volumes of coriander; eight volumes of calamus; ten volumes of absinthe; twenty volumes of juniper; thirty volumes of angelica, lemon and orange. It is asserted that these concentrated oils are more permanent, more soluble in alcohol and in water, have a finer odor, and are of constant composition, thus enabling the specific gravity and boiling point to be used as tests of purity. They should be kept in the dark. (*Ph. Centralh.*, 1888, No. 25. Under the name of *"terpeneless volatile oils,"* similar products can now be found in the market especially for use in perfumery and in the manufacture of flavoring extracts; they are undoubtedly superior to the ordinary volatile oils in odor and strength, but are not medicinally equivalent.

Wallach, to whom much of our knowledge on volatile oils is due, divides the hydrocarbons into classes, as follows:

1.—**True terpenes,** of the formula $C_{10}H_{16}$, of which there are two main groups: (*a*) the *terpane* group, uniting with two molecules of haloid acid or four atoms of bromine; this group includes *limonene, dipentene, sylvestrene, terpinolene, terpinene, thujene,* and *phellandrene,* and its members boil between 175° and 185° C.; (*b*) the *camphane* group, uniting with one molecule of haloid acid or two atoms of bromine; this group includes *pinene, bornylene, camphene,* and *fenchene,* and its members boil between 151° and 161° C.

2.—**Hemiterpenes,** of the formula C_5H_8, such as *isoprene.*

3.—**Polyterpenes,** such as *cedrene, cubebene, cadinene,* etc., of the formula $C_{15}H_{24}$ (*sesquiterpenes*); *colophene,* of the formula $C_{20}H_{32}$; and *caoutchouc,* of the formula $(C_{10}H_{16})_x$.

Hydrocarbons other than those of the terpene class, or derivable from them, occur very sparingly in the natural oils. Thus there is of the paraffin series of saturated hydrocarbons, *heptane,* C_7H_{16}, occurring in the oil from the *Pinus sabiniana,* or California *digger pine,* and solid hydrocarbons of the same series in oil of rose, and probably in oils of wintergreen and sweet birch. Of the benzene series there is a single representative in *cymene,* $C_{10}H_{14}$, found in the oils of the *Thymus* and *Monarda* species.

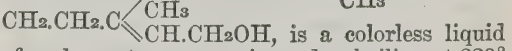
In addition to these naturally occurring hydrocarbons, there is a class of artificially prepared hydrocarbons known as *hydroterpenes,* such as dihydrodipentene from dipentene, menthene and carvomenthene from menthol and carvone.

The terpenes in general are practically insoluble in water, but soluble in alcohol, ether, chloroform, benzene, petroleum benzin, and the fixed and volatile oils.

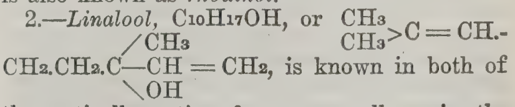
Many of the essential oils, however, owe their essential character and their value to other constituents than hydrocarbons. We shall briefly notice the most important of these either describing them or referring to other places in the text where they are already described, and shall then give a classification of the commonly known essential oils based upon the character of the most important compounds present in them.

In adition to the terpenes already mentioned, the chemical constituents of the volatile oils may be divided into seven groups as follows:

I. Alcohols and Their Esters.—This is an interesting group of open chain, unsaturated alcohols, which, with their esters and aldehydes, play a very important part in the composition of many essential oils. It is the geraniol, linalool and citronellol group.



1.—*Geraniol,* $C_{10}H_{17}OH$, or $\begin{matrix}CH_3\\CH_3\end{matrix}\!>C=OH.$-$CH_2.CH_2.C\begin{matrix}\diagup CH_3\\ \diagdown CH.CH_2OH\end{matrix}$, is a colorless liquid of a pleasant rose geranium odor, boiling at 229° to 230° C., under ordinary pressure, and at 129° C., under a pressure of 16 mm. Its specific gravity is about 0.881 and its refractive index 1.478. It is optically inactive. By careful oxidation with chromic trioxide it yields its aldehyde, citral, and by heating it in an autoclave with water to 200° C., it is partly converted into its isomer, linalool. It is a monatomic, primary, open chain alcohol, and is the principal constituent of true geranium (pelargonium) oil, as well as of the so-called *"Turkish geranium oil,"* or *oil of palmarosa.* It is a constituent of rose oil, of citronella oil and in very small proportions of a number of other oils. Of the esters of geraniol the most important is the *geranyl acetate.* This is a fragrant oil of specific gravity 0.917, boiling at from 128° to 129° C., under a pressure of 16 mm. It occurs naturally in several essential oils, and can be made artificially by the action of acetic anhydride upon geraniol. Commercial geraniol is also known as *rhodinol.*



2.—*Linalool,* $C_{10}H_{17}OH$, or $\begin{matrix}CH_3\\CH_3\end{matrix}\!>C=CH.$-$CH_2.CH_2.C\begin{matrix}\diagup CH_3\\ -CH=CH_2\\ \diagdown OH\end{matrix}$, is known in both of the optically active forms as well as in the inactive. It is a liquid having a pleasant odor, and boils under normal pressure at about 198° C., and at from 86° to 87° C. at 14 mm. pressure. Its specific gravity ranges from 0.868 to 0.877, and its refractive index is 1.463. It is a monatomic, tertiary, open chain alcohol, and is an essential constituent of oil of linaloe, and is found in the free state or as an acetic ester in oils of bergamot, coriander, lavender, neroli, etc. The most important of its esters is *linalyl acetate,* which occurs in many essential oils, as in oil of bergamot. It is an odoriferous liquid of the specific gravity 0.912, and boiling at from 105° to 108° C. at 11 mm. pressure. It is so prepared artificially, and the artificial ester is an important commercial article.

3.—*Citronellol*, $C_{10}H_{19}OH$, or $\left.\begin{matrix}CH_2\\CH_3\end{matrix}\right\rangle C—CH_2.CH_2.CH_2.CH\left\langle\begin{matrix}CH_3\\CH_2.CH_2OH\end{matrix}\right.$, is found in oil of rose and in Spanish geranium oil. It is an odoriferous oil, boiling at from 117° to 118° C., under a pressure of 17 mm.; specific gravity, 0.8565 at 17.5° C.; refractive index, 1.457. It is an open chain alcohol closely related to geraniol and is found in oil of rose, oil of geranium, etc. When obtained from oil of rose it is lævogyrate, while when obtained by reducing the aldehyde it is dextrogyrate; in most geranium oils both varieties exist.

A second group comprises the monocyclic alcohols, terpineol, which is unsaturated, and menthol, a saturated compound.

4.—*Terpineol*, $C_{10}H_{17}OH$, $\left.\begin{matrix}CH_3\\CH_3\end{matrix}\right>CH—COH.CH_2.CH_2.CH_2.CH.C—CH_3$, occurs in liquid and solid modifications, inactive, as well as in the two optically active, varieties. Besides occurring naturally it is made artificially by the dehydration of terpin hydrate, and is largely used in the perfume industry because of its lilac odor. It has a sp. gr. of 0.940 at 15° C. Its most important ester is the acetate, which occurs in cajuput and cardamom oils.

5.—*Menthol, menthyl alcohol,* $C_{10}H_{19}OH$, $\left.\begin{matrix}CH_3\\CH_3\end{matrix}\right\rangle CH–CH.CH_2.CHOH.CH_2.CH_2CH—CH_3$, is now official, and will be found described. Two of its esters are recognized as occurring with it in peppermint oil, menthyl acetate and menthyl iso-valerate. Of these the former is the more important. It is an oil having a penetrating odor, boiling at 224° C.

To a third group of compounds known as dicyclic, belongs:

6.—*Borneol*, $C_{10}H_{17}OH$, or $CH.CH_2.CH_2.CH_2.CH_3.C.CH_3.CH_2.CHOH.C—CH_3$. — This compound occurs naturally in both optically active modifications. It also occurs optically inactive. It forms crystalline masses, which, when quite pure, melt at 203° C. Borneol can be prepared artificially by reducing its ketone (camphor) with metallic sodium. In this case, however, there results a mixture of borneol and iso-borneol. Borneol forms a number of esters, of which *bornyl acetate* is the most important. This compound melts at 29° C., and has a specific gravity of 0.991 at 15° C. It is the characteristic constituent of the pine needle oils.

7.—*Nerol* is an alcohol discovered in oil of neroli. It is a stereo-isomer of geraniol. *Santalol,* so called, is found as an alcoholic constituent of oil of sandalwood. It has been given the formula $C_{15}H_{25}OH$, but is probably a mixture of several isomeric or closely related alcohols. It exists in two isomeric forms known as alpha and beta santalol. Alpha santalol has the following characters: b. pt. 300° C.; sp. gr. 0.979; ref. ind. 1.4990; opt. rot. +1° 6′. Beta santalol is as follows: b. pt. 309° C.; sp. gr. 0.989; opt. rot. –56°. Sabinol, $C_{10}H_{15}OH$, is a constituent of oil of savin. It is a secondary alcohol existing in several other oils. Its characters are as follows: b. pt. 208° C.; sp. gr. 0.9518; ref. ind. 1.4895; opt. rot. + 7° 56′.

Fenchyl alcohol, thujyl alcohol, and pulegol, all having the same empiric formula as geraniol, $C_{10}H_{17}OH$, do not occur naturally, but are produced from the respective ketones.

II. Aldehydes.—Of the alcohols just enumerated, only the first group are primary alcohols, and will yield aldehydes. Thus, from geraniol, there is obtained by oxidation, citral, the corresponding aldehyde, and from its isomer, linalool, the same.

1.—*Citral,* $C_9H_{15}COH$, or $(CH_3)_2C.CH.CH_2.CH_2.C(CH_3)CH.COH$.—Although at one time called *geranial,* this compound is now universally known as citral, which indicates its importance in the oils of the *citrus family.* It is obtained most abundantly from lemon grass oil by the aid of the bisulphite process. It is an oily liquid, boiling at from 228° to 230° C., under ordinary pressure, and at 110° C., under 12 mm. Its specific gravity is about 0.89 and its refractive index 1.49. It is optically inactive. Under the influence of alkalies, citral condenses with acetone with the elimination of water to form pseudo-ionone, $C_{13}H_{20}O$, which is converted into its isomer ionone by means of acids. Reduction with sodium produces the alcohol geraniol.

2.—*Citronellal,* $C_9H_{17}OH$, or $C(CH_3)_2CH.CH_2CH_2CH(CH_3)CH_2COH$, the aldehyde of citronellol, occurs in several essential oils, as in citronella oil. It is an oily liquid of characteristic odor; specific gravity 0.8768, refractive index 1.4481. It is dextrogyrate.

Of the class of aromatic aldehydes, there are found in essential oils, salicyl aldehyde, cumic aldehyde, benzaldehyde, and cinnamic aldehyde.

3.—*Salicyl Aldehyde,* $C_6H_4(OH)COH$.—This body is an oily liquid of aromatic odor, boiling at 196° C., and having a specific gravity of 1.172. It occurs in the oils of the several varieties of *Spiræa.* It can also be formed by the oxidation of its alcohol saligenin, or by the action of chloroform and potassium hydroxide on phenol.

4.—*Cumic Aldehyde,* $C_6H_4(C_3H_7)COH$.—This is p-isopropyl-benzaldehyde, and is found in several essential oils, as in cumin oil. It is an aromatic oil, having a specific gravity of 0.973, and boiling at 235° C.

5.—*Benzaldehyde,* $C_6H_5.COH$.—This is now official.

6.—*Cinnamic Aldehyde,* $C_6H_5.CH{:}CH.COH$.—This is described elsewhere (see under *Oleum Cinnamomi*).

Anisic Aldehyde, $C_6H_4(OCH_3)COH$ (oxymethyl-benzaldehyde), is a synthetic product used in artificial hawthorn perfume.

Piperonal or *Heliotropin,* $C_6H_3O_2CH_2COH$, is a synthetic product used in heliotrope perfume.

Santalal, $C_{14}H_{23}COH$, is found in sandalwood oil.

III. Ketones.—This class of chemical compounds is largely represented in essential oils. Of aliphatic saturated ketones there is only one fairly important representative.

1.—*Methyl-nonyl-ketone,* $CH_3.CO.C_9H_{19}$, which is found in oil of rue, is a liquid of strong odor, boiling at 225° C., and specific gravity 0.8295 at 17° C. It solidifies when cooled, and melts at 13° C.

Of aliphatic unsaturated ketones there is also one occurring naturally.

2.—*Methyl-heptenone,* $CH_3.CO.C_6H_{11}$, is found in lemon grass oil and other oils, and results from the oxidation of citral or the distillation of cineolic anhydride. It has a specific gravity of 0.853 at 20° C. and boils at 174° C.

A *methyl-amyl-ketone,* $C_5H_{11}COCH_3$, boiling at 151° C. and having a specific gravity of 0.837 at 50° C., is found as a minor constituent in oil of cloves.

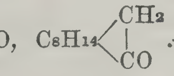
The most commonly occurring ketones, however, belong to the cyclic compounds:

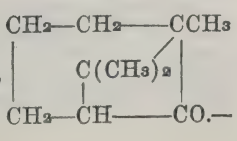
3.—*Carvone,* $C_{10}H_{14}O$, $CH_3C\left\langle\begin{matrix}CH—CH_2\\CO—CH_2\end{matrix}\right\rangle CH—C\left\langle\begin{matrix}CH_3\\CH_2\end{matrix}\right.$.—This compound, found in oils of caraway, fennel, spearmint and dill, is a colorless oil boiling at 225° C. and having a sp. gr. of 0.960 at 18° C. It is optically active, occurring in both forms. Its most interesting addition compound is that with hydrogen sulphide; this is obtained in crystals, decomposing with alcoholic potassium hydroxide and liberating pure carvone. When heated with glacial phosphoric acid, it is changed into the isomeric carvacrol, a phenol compound.

4.—*Pulegone,* $C_{10}H_{16}O$, $CH_3CH\left\langle\begin{matrix}CH_2—CO\\CH_2—CH_2\end{matrix}\right\rangle C{=}C\left\langle\begin{matrix}CH_3\\CH_3\end{matrix}\right.$.—This characteristic ketone of pennyroyal oil is a liquid boiling at 221° C. and having a specific gravity of 0.9323 at 20° C. An isomeric body, iso-pulegone, has been obtained artificially.

5.—*Menthone,* $C_{10}H_{18}O$, $CHCH\left\langle\begin{matrix}CH_2—CH_2\\CH_2—CO\end{matrix}\right\rangle CHCH(CH_3)_2$.—This occurs along with the corresponding secondary alcohol menthol, in oil of peppermint. It is an oily liquid boiling at 206° C., with a specific gravity of 0.897 at 15° C. By the action of oxidizing agents it can be converted into thymol, $C_{10}H_{14}O$.

To the class of dicyclic ketones belong the following isomeric bodies:

6.—*Camphor,* $C_{10}H_{16}O$,  .—This most important compound of the ketone class is official (see *Camphora*).

7.—*Fenchone,* $C_{10}H_{16}O$,  This ketone occurs as dextro-fenchone in oil of fennel, and as lævo-fenchone in oil of thuja. When purified, it forms an oil of camphoraceous odor, boiling at 193° C., and having a specific gravity of 0.9465 at 19° C.

8.—*Thujone,* $C_{10}H_{16}O$, $CH_3—CH\left\langle\begin{matrix}CO—CH_2\\CH—CH_2\end{matrix}\right\rangle C—CH\left\langle\begin{matrix}CH_3\\CH_3\end{matrix}\right.$.—This ketone is found in oils of thuja, tansy, wormwood and sage, and is identical with the bodies formerly known as *tanacetone* and *salvone.* It is an optically active liquid, boiling at from 200° to 203° C. and having a specific gravity of 0.9126 at 20° C.

A more complex ketone yet to be noted is:

9.—*Irone,* $C_{13}H_{20}O$, $(CH_3)_2C\left\langle\begin{matrix}CH(CH{:}CH.CO.CH_3)CH.CH_3\\CH{:}CH—\end{matrix}\right\rangle CH_2$.—The characteristic constituent of orris oil, to which also the violet odor is due, is irone. It is an oil almost insoluble in water, but readily soluble in alcohol, boiling at 144° C. at 16 mm., and having a specific gravity of 0.939 at 20° C. In the attempt to effect the synthesis of irone, Tiemann and Krüger obtained an isomeric body, *ionone,* from citral, which is now used as the artificial violet odor.

IV. Acids and Their Esters.—While esters of several of the fatty acids, both saturated and unsaturated, are found in the essential oils, the compounds are not so distinctive or characteristic, that they require mention here. Some of the esters have been already described under the appropriate alcohols, see geraniol, linalool, etc. Of esters of aromatic acids there are several of importance, however, comprising the most valuable constituents of the oil in which they occur. These include Methyl Salicylate, Methyl Anthranilate, Benzyl Acetate, Linalyl Acetate, Geranyl Acetate, Bornyl Acetate, Menthyl Acetate, Bornyl Valerate, Geranyl Tiglate, most of which are described under their alcohol constituent.

1.—*Methyl Salicylate* is the chief constituent of the oils of wintergreen and sweet birch. It is now official (see *Methylis Salicylas*).

2.—*Methyl Anthranilate* (*Methyl o-amidobenzoate*), $C_6H_4(NH_2)COOCH_3$.—This is the odoriferous constituent of neroli oil. It is an oil solidifying at low temperatures in crystals melting at 24.5° C., and boiling at 127° C. at 11 mm. Its specific gravity is 1.163 at 26° C. It is strongly fluorescent and has a powerful grape-like odor. It is used in imitation grape flavors.

V. Phenols and Phenol Ethers.—This is an important class largely represented in the volatile oils. Of monatomic phenols there are:

1.—*Chavicol* (para-allyl-phenol), $C_6H_4(OH)$-C_3H_5.—This occurs in the *oil of Chavica Betle,* and is a colorless liquid having a strong odor and a specific gravity of 1.035 at 20° C., boiling at 237° C. Still more abundantly formed in nature is its methyl ether, which is:

2.—*Methyl-chavicol,* $C_6H_4(OCH_3)C_3H_5$.—This occurs in the oils of anise, star anise, sweet-basil, bay, etc. It is also known as solid anethol or as *estragol* from its occurrence in *estragon* (*tarragon*) oil, from *Artemisia dracunculus.* It is a colorless liquid of an anise-like odor, boiling at from 215° to 216° C., having a specific gravity of 0.972 and a refractive index of 1.522.

3.—*Anethol,* $C_6H_4(OCH_3)C_3H_5$, is the methyl ether of p-propenyl-phenol, and isomeric with methyl-chavicol. It can be formed from the latter by heating it with alcoholic potassium hydroxide. It is the most abundant constituent of the oils of anise, star anise and fennel. It forms white scales having a specific gravity of 0.786 at 25° C., melting at 21° C., and boiling at 232° C. It is also known as *iso-estragol.*

4.—*Thymol* (*methyl-propyl-phenol*), $C_6H_3.CH_3.(OH)C_3H_7$ 1:3:4.—This is one of the best known of the phenols occurring in volatile oils. As it is official its description will be found under *Thymol.*

5.—*Carvacrol* (methyl-propyl-phenol), $C_6H_3.CH_3(OH)C_3H_7$ 1:2:4.—This important phenol, occurring in oils of marjoram and savory, is isomeric with thymol. It is a thick oil, solidifying at 0° C. and boiling at 236° C. It can be prepared artificially by heating carvone, an isomeric ketone, with phosphoric acid or by heating camphor with iodine.

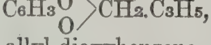
Of diatomic phenols and their ethers, there are the following:

6.—*Eugenol,* $C_6H_3.OH.OCH_3.C_3H_5$ 4:3:1, is the methyl ether of allyl-dioxybenzene. It occurs in the oils of cloves, allspice, bay, Ceylon cinnamon and cinnamon leaves. It is now official.

7.—*Methyl-eugenol,* $C_6H_3.(OCH_3)_2.C_3H_5$, is found together with eugenol in oil of bay. It has a specific gravity of 1.041 at 11° C. and boils at 248° C.

8.—*Iso-eugenol* is the methyl ether of propenyl-dioxybenzene, and is produced from eugenol when the latter is heated with alcoholic potassium hydroxide. It is used in the manufacture of artificial vanillin.

9.—*Chavibetol,* $C_9H_8(OCH_3)OH$, is another isomer of eugenol, and occurs with chavicol in oil of betel leaves.

10.—*Safrol,*  $C_6H_3\genfrac{}{}{0pt}{}{O}{O}\!\!>CH_2.C_3H_5$, is the methylene ether of allyl-dioxybenzene. It is found quite largely in the oils of sassafras, camphor, etc. It was official in the U. S. P. VIII and is described in Part II.

11.—*Iso-safrol* is the methylene ether of propenyl-dioxybenzene, and is produced from safrol by heating the latter with alcoholic potassium hydroxide. It is used in the manufacture of *piperonal* (artificial heliotropin).

12.—*Thymohydroquinone dimethyl-ether,* $C_6H_2.(OCH_3)_2.CH_3.C_3H_7$, constitutes the bulk of the oil of arnica root. It is a liquid distilling at from 248° to 250° C.

Of triatomic phenols and their ethers, the representative is:

13.—*Asarol,* $C_6H_2(C_3H_5)(OCH_3)_3$.—This is the trimethyl ether of propenyl-trioxybenzene. It forms the solid constituent of the oil of *Asarum europæum,* and occurs in prisms melting at 61° C., and boiling at from 295° to 296° C. It has also been made synthetically.

Of tetratomic phenols and their ethers, there is also a representative, as follows:

14.—*Apiol,* $C_{12}H_{14}O_4$, $C_9H_6(OCH_3)_2O_2.CH_2$, is the dimethyl-methylene ether of allyl-tetroxybenzene. It occurs in two isomers—the apiol from oil of parsley and dill apiol from some varieties of oil of dill. Of these, the former is a crystalline solid melting at 30° C. and boiling at 294° C. and the latter is an oily liquid boiling at 288° C.

15.—*Diosphenol,* $C_{10}H_{16}O_2$ or buchu camphor as it is called, is a phenolic ketone. Its properties are as follows: m. pt. 83°; opt. rot. 0° b. pt. 232° (with decomposition). It has been prepared synthetically by several methods.

VI. Neutral Bodies, Oxides, etc.—One important compound of frequent occurrence in volatile oils has not been classified under any of the preceding groups, for the reason that it is relatively inert in a chemical way and is considered as an oxide of neither distinct acid or basic character.

1.—*Cineol* (*Eucalyptol*), $C_{10}H_{18}O$.—This is found in nature in large amounts in eucalyptus oil (hence the name "eucalyptol" sometimes given to it), in cajuput oil (hence the name of "cajuputol"), in lavender, wormseed, and other oils. It is now official under the name of *eucalyptol.*

VII. Sulphides and Sulphur Compounds.—Several of the volatile oils contain compounds of sulphur. Among the latter are:

1.—*Di-allyl disulphide,* $C_6H_{10}S_2$, is a constituent of oil of garlic and occurs in many oils belonging to the *Cruciferæ.* It is a liquid of very unpleasant odor, boiling at 140° C.

2.—*Allyl-isothiocyanate,* $C_3H_5.NCS$, is the principal constituent of the volatile oil of mustard. It is, however, a decomposition product of the glucoside potassium myronate, which breaks up under the influence of the ferment myrosin. The allyl thiocyanate can also be obtained artificially by distilling allyl iodide or bromide with alcoholic potassium thiocyanate. This artificial product is largely sold in place of the natural oil. It is a liquid having a very unpleasant odor, boiling at 151° C., and having a specific gravity of 1.017 at 10° C.

Vinyl sulphide, $(C_2H_3)_2S$, is found in a variety of garlic.

Butylisothiocyanate, $CH(CH_3)C_2H_5NCS$, is found in oil of horseradish, *acrynyl isothiocyanate,* C_7H_7ONCS, is found in white mustard and *phenylethyl isothiocyanate,* $C_2H_4(C_6H_5)-NCS$, is found in oil of mignonette.

CLASSIFICATION.

Classification of the more commonly occurring volatile oils.—In considering the question of classifying the volatile oils, two methods of arrangement naturally suggest themselves, viz.: a classification according to the botanical natural orders to which they belong, and a chemical classification based on the most important chemical constituents of the oils themselves. While the first of these is the more readily made, it suffers from the disadvantage of being cumbrous and less readily understood except by the botanist. On the other hand, the second plan shows at a glance the sources of the valuable odoriferous and medicinally and technically important constituents for which the volatile oils are largely used. That it has not been generally adopted is no doubt due to the fact that many of the oils contain several different constituents of value, and it is therefore difficult to make an assignment of some of them to individual chemical groups. Any chemical system of classifying volatile oils must be either exceedingly complex and cumbersome or, if conciseness is attempted, there are too many inconsistencies and discrepancies. For instance, one of the favored methods of classification is to divide them into four groups, i.e., the terpenes, oxygenated oils, nitrogenerated oils, and sulphurated oils. If this be critically studied it is seen that oil of lemon, which is usually given as a typical example of the terpene class, owes its real identity and value to citral, an aldehyde present in only a very small proportion (less than 5 per cent.), and that oil of bitter almond, which is given as the example of the nitrogenated class, owes its classification in this respect only to the incidental presence of hydrocyanic acid, which is frequently removed from the oil, especially when it is used for flavoring purposes. Moreover the sulphurated class contains only one important member, which the oxygenated class is the repository of over 90 per cent. of oils of diversified character.

It is therefore more suitable to follow the foregoing outline adding such explanatory matter and examples as will serve to make it intelligible and valuable for either study or reference purposes. It is believed that the chemical classification adopted here will be found to have practical value for reference.

Group I.—*Oils containing mainly Terpenes and Sesquiterpenes.*

Oil of Cedarwood; cedrene and cedrol (an oxygenated constituent).
 Copaiba Balsam; caryophyllene.
 Cubeb; cadinene and cubeb camphor (an oxygenated constituent).
 Dog Fennel; pellandrene.
 Fleabane; d-limonene.
 Galbanum; pinene and cadinene.
 Ginger; sesquiterpene and phellandrene.
 Hemp; cannabene and other terpenes.
 Hops; humulene and tetrahydrocymene.
 Myristica; terpenes and myristicol (an oxygenated constituent).
 Orange; limonene with small amount of citral and citronellal (both oxygenated constituents).
 Turpentine; pinene and sylvestrene.

Group II.—*Oils containing mainly Alcohols and their esters.*

a. Aliphatic saturated alcohols:
 Oil of Heracleum; octyl alcohol and octyl ester.

b. Aliphatic unsaturated alcohols:
 Oil of Bergamot; linalool and linalyl acetate.
 Coriander; linalool and d-pinene.
 Geranium; geraniol and geranyl esters.
 Lavender; linalyl acetate and geraniol.
 Lime; linalyl acetate and limonene.
 Linaloes; linalool and geraniol.
 Petit Grain; linalool and linalyl acetate.
 Rose; geraniol and citronellol with esters.

c. Monocyclic and dicyclic alcohols:
 Oil of Angostura; galipol, galipene, and cadinene.
 Fir Cones; bornyl acetate and terpenes.
 Golden Rod; borneol and bornyl esters.
 Juniper Berries; Juniper camphor and cadinene.
 Ledum; ledum camphor.
 Lovage; terpineol.
 Mace; myristicol.
 Patchouli; patchouli camphor and cadinene.
 Peppermint; menthol and menthone.
 Pine Needles; bornyl acetate and terpenes.
 Rosemary; borneol and bornyl acetate.
 Sandalwood; santalol and esters.
 Savin; sabinol and sabinyl acetate.
 Valerian; Borneol and bornyl esters.

d. Aromatic Alcohols and Esters:
 Oil of Jasmine; benzyl acetate and benzyl alcohol.

Group III.—*Oils containing Aldehydes as characteristic constituents.*

a. Aliphatic unsaturated aldehydes:
 Oil of Citron peel; citral and limonene.
 Citronella; citronellal and geraniol.

Lemon; Citral and citronellal (this oil might also properly be classed in Group I, as the terpenes constitute over 90 per cent. of the oils).
Lemon grass; citral, citronellal, and methyl-heptenone.
Verbena; citral.

b. Aromatic aldehydes:
Oil of Bitter Almond; benzaldehyde.
Cassia; cinnamic aldehyde.
Cinnamon; cinnamic aldehyde and eugenol.
Cumin; cumic aldehyde.
Meadow Sweet; salicyl aldehyde.

Group IV.—*Oils containing Ketones as characteristic constituents.*

a. Aliphatic saturated aldehydes:
Oil of Rue; methyl-nonyl-ketone.

b. Aliphatic unsaturated aldehydes:
Oil of Lemon grass; methyl-heptenone.

c. Monocyclic and dicyclic ketones:
Oil of Artemisia; thujone.
Camphor; camphor.
Caraway; carvone and limonene.
Dill; carvone and limonene.
Orris; irone.
Pennyroyal; pulegone.
Peppermint; menthone and menthol.
Sage; thujone with borneol and cineol.
Spearmint; carvone.
Tansy; thujone with borneol.
Thuja; thujone and fenchone.
Wormwood; thujone and thujyl alcohol.

Group V.—*Oils containing Esters.*

a. Aliphatic Acids:
Oil of Angelica; methyl-ethyl-acetic esters.
Calamus; heptylic and palmitic acid and esters.
Cardamom; acetic esters and cineol.
German Chamomile; caproic acid esters.
Roman Chamomile; butyric, angelic and tiglic esters.

b. Aromatic acid esters:
Oil of Neroli; o-amido-benzoic-methyl ester.
Sweet Birch; methyl salicylate.
Gaultheria; methyl salicylate.

c. Undetermined acids:
Oil of Celery; sedanolide and lactone.
Elecampane; alantic acid and lactone.

Group VI.—*Oils containing Phenols and Phenol Ethers.*

a. Monatomic phenols and their ethers:
Oil of Ajowan; thymol and cymene.
Anise; anethol and methyl-chavicol.
Betel; chavicol and methoxy-chavicol.
Fennel; anethol and fenchone.
Marjoram; carvacrol and linalool.
Savory; carvacrol, pinene, and cymene.
Star Anise; anethol, methyl-chavicol and safrol.
Sweet Basil; Methyl-chavicol and d-linalool.

b. Diatomic phenols and their ethers:
Oil of Arnica Root; thymohydroquinone dimethyl-ether.
Bay; eugenol, methyl-eugenol and methyl-chavicol.
Camphor; safrol, eugenol and camphor.
Cascarilla Bark; eugenol and terpenes.
Cinnamon Leaf; eugenol and cinnamic aldehyde.
Cloves; eugenol and sesquiterpene.
Pimenta; eugenol and sesquiterpene.
Sassafras; safrol and camphor.

c. Triatomic phenols and their ethers:
Oil of Asarum; asarol and methyl-eugenol.
Matico; asarol.

d. Tetratomic phenols and their ethers:
Oil of Parsley; apiol.

Group VII.—*Oils containing Neutral Bodies.*
Oil of Cajuput; cineol, terpineol and terpenyl acetate.
Eucalyptus; cineol, pinene, and aldehydes.
Laurel Leaves; cineol and pinene.
Myrtle; cineol, d-pinene and dipentene.
Wormseed; cineol and dipentene.

Group VIII.—*Oils containing Sulphur.*
Oil of Asafœtida; sulphides and pinene.
Garlic; diallyl-disulphide and allylpropyl sulphide.
Mustard; allyl-thiocyanate, allylcyanide and carbon disulphide.
Onion; allyl-propyl sulphide.

Properties.—Volatile oils are slightly soluble in water. Agitated with this fluid they render it milky, but the major portion separates upon standing, leaving the water impregnated with their odor and taste. This impregnation is more complete when water is distilled with the oils, or from the plants containing them. Trituration with insoluble powders, as talc, magnesium carbonate, kieselguhr, etc., renders them more easily soluble, probably in consequence of their minute division. The intervention of sugar also greatly increases their solubility, and affords a convenient method of preparing them for internal use. The hydrocarbon oils are scarcely soluble in diluted alcohol, and, according to De Saussure, the solubility of volatile oils generally in this liquid is proportionate to the oxygen which they contain. The volatile oils dissolve sulphur and phosphorus with the aid of heat, and deposit them on cooling. By long boiling with sulphur they form brown, unctuous, fetid substances, formerly called *balsams of sulphur.* They absorb chlorine, which converts them into resinous oxidation products and then combines with these. Iodine produces a similar effect. They are decomposed by the strong mineral acids, and unite with some organic acids. When treated with a caustic alkali, some of them are saponified or otherwise decomposed. Several of the metallic oxides, and various salts which easily part with oxygen, convert them into resinous oxidation products. The volatile oils dissolve many of the proximate principles of plant and animal tissues, such as the fixed oils and fats, resins, camphor, and many of the alkaloids when in the free state. Exposed to air and light, many of them absorb oxygen and become what are termed ozonized oils which possess oxidizing properties.

Adulterations.—The volatile oils are often sophisticated. Among the greater adulterations are fixed oils, resinous substances, chloroform, hydrocarbon oils, and alcohol, but the most dangerous are those made by mixing the pure oil with the cheaper volatile oils and terpenes and fractions from other oils like limonene. The presence of the fixed oils may be known by the permanent greasy stain which they leave on paper, while that occasioned by a pure volatile oil disappears entirely when exposed to heat. They may also in general be detected by their comparative insolubility in alcohol. Both the fixed oils and resins are left behind when the adulterated oil is distilled with water. If alcohol be present, the oil will become milky when agitated with water in a graduated tube, and after the separation of the liquids the water will occupy more space and the oil less than before. The following method of detecting alcohol was proposed by Beral. Put twelve drops of the suspected oil in a perfectly dry watch-glass, and add a piece of potassium about as large as the head of a pin. If the potassium remains for twelve or fifteen minutes in the midst of the liquid, there is either no alcohol present, or less than 4 per cent. If it disappears in five minutes, the oil contains more than 4 per cent. of alcohol; if in less than a minute, 25 per cent. or more. Borsarelli employs calcium chloride for the same purpose. This he introduces in small pieces, well dried and perfectly free from powder, into a small cylindrical tube, closed at one end, and about two-thirds filled with the oil to be examined, and heats the tube to 100° C., occasionally shaking it. If there is considerable proportion of alcohol, the chloride will be entirely dissolved, forming a solution which sinks to the bottom of the tube; if only a very small quantity, the pieces will lose their form, and collect at the bottom in a white adhering mass; if none at all, they will remain unchanged. (*J. P. C.,* xxvi, 429.) J. J. Bernoulli proposes as a test dry potassium acetate, which remains unaffected in a pure oil, but will be dissolved if alcohol be present, and form a distinct liquid. (See *A. J. P.,* xxv, 82.) Distillation, catching the first portion, and testing for alcohol by the iodoform reaction, will detect very small additions of alcohol. The adulterants most difficult of detection are the synthetic terpenes or alcohols or those occurring as by-products in some departments of the essential oil industry.

Sometimes volatile oils of little value are mixed with the more costly. The taste and odor afford in this case the best means of detecting the fraud. The specific gravity of the oils is rarely of any value as a test of purity.

The optical activity is one of the most valuable of the physical constants used in detecting adulteration and in determining the purity of volatile oils. Thus, the oils of juniper, lavender, and rosemary rotate the plane of polarization to the left, while American oil of turpentine rotates it to the right; and if this should be added to one of the other oils it lowers the optical activity and thus offers one means for its detection. Unfortunately, the French oil of turpentine, obtained from the *Pinus Maritima,* acts strongly in the opposite direction. But the very strength of its left-rotatory power might lead to its detection by the abnormal increase of this power which it would impart to the oils in question. Synthetic or artificial volatile oils are now largely manufactured. They vary greatly at times in their resemblance to the natural products. They will be considered under their respective titles elsewhere, a number having received official recognition.

Volatile oils may be preserved without change in small, well-stoppered amber-colored bottles, entirely filled with the oil, and secluded from the light.

They may also be preserved by mixing with them about 5 per cent. of a bland fixed oil which will remain undissolved when the volatile oil is added to alcohol and for which allowance must be made, of course, in the volume of the oil used in formulas, etc. (LaWall, *Proc. A. Ph. A.,* 1910, 1121.)

Manufacture.—Neither the U. S. nor Br. give any official method for distilling any of the volatile oils. Although some of these require peculiar methods for their proper separation most of the official volatile oils may be prepared by the general formula of the U. S. P. 1870: "Put the substance from which the Oil is to be extracted into a retort or other vessel suited for distillation, and add enough water to cover it; then distil by a regulated heat into a large refrigeratory. Separate the Distilled Oil from the water which comes over with it."

Under the general observations on the *Aquæ,* or *Waters,* will be found remarks upon the use of steam in preparing the Distilled Waters, which are to a considerable extent applicable also to the volatile oils.

The substances from which the volatile oils are extracted may be employed in either the recent or the dried state. Certain flowers, however, such as orange flowers and roses, must be used fresh, or preserved with salt or by means of glycerin, as they afford little or no oil after desiccation. Most of the aromatic herbs, also, as peppermint, spearmint, pennyroyal, and marjoram, are usually distilled while fresh. Dried substances, before being submitted to distillation, require to be macerated in water until they are thoroughly penetrated by this fluid, and to facilitate the action of the water it is necessary that, when of a hard or tough consistence, they should be properly comminuted by slicing, shaving, rasping, bruising or other similar mechanical operation.

The water which is introduced into the still with the substance answers the double purpose of preventing the decomposition of the vegetable matter by regulating the temperature, and of facilitating the volatilization of the oil, which, although in most instances readily rising with the vapor of boiling water, requires, when distilled alone, a considerably higher temperature, and is at the same time liable to be partially decomposed. Some oils, however, will not ascend readily with steam at 100° C., and in the distillation of these it is customary to use water saturated with common salt, which does not boil under 110° C. Recourse may also be had to a bath of strong solution of calcium chloride, or to an oil bath. Other oils, again, may be volatilized with water at a temperature below the boiling point, and, as heat exercises an injurious influence over the oils, it is desirable that the distillation should be effected at as low a temperature as possible. To prevent injury from heat, it has been recommended to suspend the substance containing the oil in a wire basket, or to place it upon a perforated shelf, in the upper part of the still, so that it may be penetrated by the steam, without being in direct contact with the water. Another mode of effecting the same object is to distil it *in vacuo*. Duncan stated that the most elegant volatile oils he had ever seen were prepared in this manner by Barry, the inventor of the process. The employment of steam heat also prevents injury, and the best volatile oils are now prepared by manufacturers in this way. Steam can be very conveniently applied to this purpose by causing it to pass through a coil of tube, of an inch or three-quarters of an inch bore, placed in the bottom of a common still. The end at which the steam is admitted enters the still at the upper part, and the other end, at which the steam and condensed water escape, passes out laterally below, being furnished with a stop-cock, by which the pressure of the steam may be regulated and the water drawn off when necessary. In some instances it is desirable to conduct the steam immediately into the still near the bottom, by which the contents are kept in a state of brisk ebullition. This method is used in the preparation of the oil of bitter almond. The same method is applicable to the preparation of distilled waters.

The quantity of water added is not a matter of indifference. An excess above what is necessary acts injuriously by holding the oil in solution when the mixed vapors are condensed, and if the proportion be very large, it is possible that no oil whatever may be obtained separate. On the contrary, if the quantity be too small, the whole of the oil will not be distilled, and there will be danger of the substance in the still adhering to the sides of the vessel and thus become burnt. Enough water should always be added to cover the solid material and prevent the latter accident. Dried plants require more water than the fresh and succulent. The whole amount of material in the still, should not exceed three-fourths of its capacity, as otherwise there would be danger of the liquid boiling over. The form of the still has an influence over the quantity of water distilled, which depends more upon the extent of surface than upon the amount of liquid submitted to evaporation. By employing a high and rather narrow vessel one may obviate the disadvantage of an excessive quantity of water. Sometimes the proportion of oil in the substance employed is so small that it is wholly dissolved in the water distilled, even though the proportion of the liquid in the still is not greater than is absolutely essential. In this case it is necessary to redistil the same water several times from fresh portions of the plant, until the quantity of oil exceeds the solvent power of the water. This process is called *cohobation*.

The more volatile of the oils pass with facility along with the steam into the neck of the common still, but some which are less volatile are apt to condense in the head and thus return into the still. For the distillation of the latter, a copper still should be employed having a very low head. As, after the distillation of any one oil, it is necessary that the apparatus should be thoroughly cleansed before being used for the preparation of another, it is better that the condensing tubes should be straight, rather than spiral as in the ordinary still. It should be recollected, moreover, that certain oils, such as those of anise and fennel, are rendered solid by a comparatively slight reduction of temperature, and that in the distillation of these the water employed for refrigeration should not be below 5.5° C.

The mixed vapors are condensed into a milky liquid, which is collected in a receiver, and, after standing for some time, separates into the oil and a clear solution of it, the former floating on the surface, or sinking to the bottom, according as it is lighter or heavier than water. The distillation should be continued so long as the liquid coming over has a milky appearance.

The last step in the process is to separate the oil from the water. For this purpose the *Florentine receiver* may be used. For illustrations of this, and other forms of receivers, for collecting and separating immiscible liquids, see Remington's *Practice of Pharmacy*, 6th edition, p. 250. This is a conical glass vessel, broad at the bottom and narrow towards the top, and very near its base furnished with a tubulure or opening, to which is adapted, by means of a pierced cork, a bent tube so shaped as to rise perpendicularly to seven-eighths of the height of the receiver, then to pass off from it at right angles, and near the end to bend downward. The condensed liquid being admitted through the opening at the top of the receiver, the oil separates, and, rising to the top, occupies the upper narrow part of the vessel, while the water remains at the bottom, and enters the tube affixed to the receiver. When the surface of the liquid attains in the receiver a higher level than the top of the tube, the water will necessarily begin to flow out through the latter, and may be received in bottles. The oil thus accumulates as long as the process continues, but it is evident that the plan is applicable only to the oils lighter than water. For the heavier oils, cylindrical vessels may be employed, to be renewed as fast as they are filled; but, as all the water cannot be removed by these plans, it is necessary to resort to some other method of effecting a complete separation. An instrument called a *separator* is usually employed for this purpose. It consists of a glass funnel, or a globular vessel, furnished with a stopper, and prolonged at the bottom into a very narrow tube. The lower opening being closed, the mixed liquids are introduced and allowed to stand until they separate. The orifice at the bottom is then opened, and, the stopper at the top being a little loosened, so as to admit the air, the heavier liquid slowly flows out, and may be separated to the last drop from the lighter, which floats above it. If the oil is heavier than the water, it passes out of the separator; if lighter, it remains within. According to George Leuchs, all oils obtained by distillation with water, even when perfectly clear, contain some water.

The water saturated with oil should be preserved for use in future distillations, as it can dissolve no more of the oil. One or more volatile acids are frequently found in the distilled water, as acetic, butyric, or valerianic, and Wunder has detected all three of these acids in the water distilled from chamomile flowers. (*J. Pr. Chem.*, lxiv, 499.) For an illustration of a cheap apparatus for distilling volatile oils by steam under slight pressure, see *Proc. A. Ph. A.*, 1894, 680.

When first procured, some volatile oils have a disagreeable somewhat empyreumatic odor, from which they may be freed by allowing them to stand for some days in vessels loosely covered with paper. They should then be filtered and introduced into small opaque bottles, which should be well stoppered so as to exclude the air. When altered by exposure to air, they may sometimes be restored to their original appearance and quality by agitation with a little recently heated animal charcoal, and the same method may be employed for freeing them from adhering water.

They may be administered upon a lump of sugar; or triturated with at least ten times their weight of sugar, forming *oleosaccharates*, which are then dissolved in water; or made into emulsions with water, sugar, and gum arabic. In making emulsions with volatile oils, it has been recommended first to dissolve them in one of the fixed oils, the oil of almond for example, and then to emulsionize the oleaginous solution with syrup and gum arabic. For 100 parts of water, 15 of the almond oil in which the volatile oil is to be dissolved, 10 of powdered gum arabic, and 25 of syrup may be taken. The following suggestions on preparing emulsions of the volatile oils may be useful. Oil of turpentine and other volatile oils, to be emulsionized in quantity, are most successfully treated by rubbing them with one-half their weight of powdered gum arabic, and, when intimately mixed, adding at once, with rapid trituration, water in the proportion of one and a half times the weight of the gum used. Such an emulsion is more permanent when a little fixed oil is used. The volatile oils are often kept dissolved in alcohol under the name of essences.

Enfleurage.—This term is applied by the French to the impregnation of fixed oils and fatty matters with the odors of certain sweet scented plants, such as jasmine, tuberose, and mignonette, the oils of which are so delicate and fugitive that they cannot well be separated by distillation. The process consists in exposing the fatty matter, placed in layers, in suitable frames, to the exhalations from the flowers, which are absorbed, and give their characteristic odor to the fat. Another plan is to expose alternate layers of the flowers, and of cotton impregnated with bland fixed oil, to the sun, and afterwards to express the oil from the cotton. (*A. J. P.*, xxix, 551.) The French sometimes give to the spirituous solutions made by extracting the odors from fats and oils with alcohol the name of *Essences.*

Uses.—While substances differing so widely in their source and in their chemical composition must manifestly exercise dissimilar effects upon the body, there are certain properties common to so many of the volatile oils that a word concerning the therapeutic effects of this group of principles may be in place. Practically all of the official volatile oils are more or less irritant; some of them only feebly so and some very actively so. By virtue of this action when taken into the intestinal tract they excite peristalsis and are therefore used for the expulsion of flatus in *colic* as well as to enhance the effect of cathartic drugs. Although the direct action of the volatile oils upon muscle tissue as shown by Gunn (*J. P. Ex. T.*, 1920, xvi, p. 39) is to relax rather than stimulate, Plant (*J. P. Ex. T.*, 1920, xvi, p. 311) has shown that when applied to the mucous membrane of the intestines, they increase both the tone and peristaltic contraction. That these effects are due to an action upon the sensory nerve endings is strongly indicated by the fact that they are abolished by local application of cocaine. He finds considerable variation in the carminative power of the volatile oils, the most powerful of these tested by him including mustard, cinnamon, peppermint and clove. In a subsequent paper (*J. P. Ex. T.*, 1923, xxi, p. 203) he reported that cinnamon water lessened the muscular contractions of the stomach, although it increased those of the intestines. It is probably also to this local irritant effect that their uses as expectorants, diaphoretics, and diuretics is to be attributed. A large number of them are powerful germicides and nearly all of them more or less antiseptic. The antibacterial property of the volatile oils has been investigated especially by Martindale (*Perfume and Essential Oil Record,* 1910, i, p. 266), by Gilmore (*P. J.*, 1910, p. 844), and by Peck (*J. A. M. A.*, 1899, xxxii, p. 6). According to Martindale the oil of origanum is twenty-five times as actively germicidal as phenol and the oil of cloves about 9 times; while Peck finds that the oil of cloves prevents the multiplication of bacteria when present in about 1 part to 1100. The following volatile oils are powerfully germicidal: origanum, thyme, cinnamon, cassia, cloves, bay, and sassafras. Of considerable disinfectant power but weaker than the preceding are: peppermint, eucalyptus, cajuput, bitter almond, sandal wood, spearmint and lavender. The following are feeble in their antibacterial properties: anise, bergamot, juniper, cade, and turpentine. Concerning most of the other oils figures are lacking. While the cost of the volatile oils precludes their use for many disinfectant purposes yet for others they are very valuable agents, especially are they employed for their antibacterial properties in the mouth and nose. Morel and Rochaix (*C. R. S. B.*, 1921, lxxxv, p. 861) found that the vapors given off at a temperature of 37° C. by some of the volatile oils had a feeble germicidal effect, but that none but the most sensitive bacteria were killed and these only after several hours.

OLEATA.

OLEATES

Oléates, *Fr.;* Oleate, *G.*

The *oleates* are a class of preparations which were introduced to the medical profession by John Marshall, F.R.S., in 1872. They are usually solutions of certain bases in oleic acid, and are made by triturating the solid substance with the oleic acid until it is dissolved. Whenever it is possible, the application of heat should be avoided, and it has been observed that the freshly precipitated oxides of the metals dissolve more readily than those which are old. The title oleate is probably the best that could be devised, although it must be understood that, as found in the Pharmacopœias, they are not pure chemical compounds, but merely compounds of the oxides or the alkaloids, as the case may be, with oleic acid dissolved in an excess of the latter or in a fixed oil.

Oleates may be made either by direct combination of the ingredients or by double decomposition. When made by the latter method, a good quality of oleic acid should be treated with the proper quantity of solution of sodium hydroxide, to saponify it, any excess of the alkali being neutralized with a little tartaric acid. This soap solution is preferably used diluted.

J. M. Good, in making the oleates of the alkaloids, proposes the use of sufficient oleic acid to dissolve the alkaloid and then diluting the solution with a bland fixed oil, such as almond oil. (*Proc. Missouri Pharm. Association*, 1891, p. 65.)

The *medicinal properties* of the oleates are, of course, dependent upon the base, so that these preparations may be considered the equivalents of the corresponding ointments, over which, however, they have certain advantages. They are much cleaner and more elegant in appearance. They seem to be more irritating than the ointments, and, unless diluted with an equal bulk of cottonseed, olive, or other bland oil, are, when applied with friction, likely to provoke a cutaneous eruption or even pustulation. Marshall recommends that they be applied with a brush, or gently spread over the part with the finger.

OLEATUM HYDRARGYRI. U. S. (Br.)

OLEATE OF MERCURY Oleat. Hydrarg.

Hydrargyrum Oleatum, *Br.;* Mercuric Oleate; Hydrargyrum Oleicum; Oléate de Mercure, *Fr.;* Oelsaures Quecksilber, Quecksilberoleat, Mercurioleat, *G.*

"Yellow Mercuric Oxide, in very fine powder, 25 Gm.; Oleic Acid, a sufficient quantity, to make 100 Gm.

"Mix the yellow mercuric oxide with 75 Gm. of oleic acid, warm the mixture to a temperature not exceeding 50° C., stir constantly for five minutes, and then continue the heat, stirring frequently until the mercuric oxide is dissolved. Add sufficient oleic acid to make the product weigh 100 Gm. and mix thoroughly. In the preparation of this Oleate avoid all contact with metallic utensils. Preserve Oleate of Mercury in tightly-closed containers, protected from light, and do not dispense it if globules of mercury are visible at the bottom of the container." *U. S.*

"Yellow Mercuric Oxide, 20 *grammes; Liquid* Paraffin, 5 *grammes;* Oleic Acid, 75 *grammes.* Triturate the Mercuric Oxide with the Liquid Paraffin until it is thoroughly subdivided; add the Oleic Acid with vigorous stirring. Heat the mixture to 50° C. triturating occasionally until combination is effected, and, when cool, a yellowish unctuous preparation is obtained." *Br.*

This oleate is now made with 25 per cent. of mercuric oxide; that of the British Pharm. contains 20 per cent. Water was used in this oleate in order to facilitate combination in the U. S. P. VIII, alcohol in the U. S. P. IX, but neither in the U. S. P. X.

If made from oleic acid which has been purified from the usual contaminations (palmitic and stearic acids), it is a clear yellowish liquid of a thick consistence and having the peculiar odor of oleic acid. As usually seen, however, it is of the consistence and appearance of petrolatum, due to the presence of small quantities of mercuric palmitate and stearate. (See *Acidum Oleicum.*) The formula of a normal oleate of mercury would be $(C_{18}H_{33}O_2)_2Hg$. Free oleic acid is intentionally present in this U. S. preparation, which is known frequently as "25 per cent. oleate of mercury." In making this preparation, care must be exercised in the selection of the oleic acid, and to avoid exceeding the degree of heat directed in the official process; indeed, our experience has been that it keeps better if made by the cold process—*i.e.*, by simply mixing the freshly precipitated yellow oxide with the oleic acid, and allowing them to stand at ordinary temperatures until the precipitate has dissolved. The British preparation (1898) was modelled after Shoemaker's process, but in the Br. Pharm., 1914, the mercuric oxide is triturated with liquid paraffin. The precipitated mercuric oleate is difficult to free from water, and is prone to change. In time, even with the best oleic acid that can be procured, some decomposition will take place, and metallic mercury will be found at the bottom of the containing bottle. The rapidity of the change will be in proportion to the impurities in the oleic acid and the degree of heat employed. Beringer's process, by the double decomposition of potassium oleate and mercuric nitrate, is commended by Edel. (See *West. Drug.*, 1894, 85.)

Uses.—This preparation may often be substituted with advantage for mercurial ointment, which it closely resembles in its medicinal properties; it has been asserted that it is more readily absorbed, and therefore more effective. Mercury oleate has been especially commended by Marshall in cases of *chronically inflamed joints,* and in *hordeolum, indurations after abscesses,* and various other forms of superficial local inflammations of a slow type; also in *sycosis, tinea, psoriasis, eczema,* and as a constitutional alterative in *hereditary syphilis.*

Dose, one-half to two drachms (2–8 Gm.) applied externally.

Off. Prep.—Massa Hydrargyri, *U. S.;* Unguentum Hydrargyri Fortius, *U. S.;* Unguentum Hydrargyri Oleati, *Br.*

OLEORESINA ASPIDII. U. S. (Br.)

OLEORESIN OF ASPIDIUM Oleores. Aspid. [Oleoresin of Male Fern]

"Oleoresin of Aspidium yields not less than 24 per cent. of crude filicin." *U. S.* "Liquid Extract of Male Fern contains in 100 grammes not less than 20 grammes of filicin." *Br.*

Extractum Filicis Liquidum, *Br.;* Oleoresina Filicis, *Pharm.* 1870; Liquid Extract of Male Fern, Oil of Fern; Oleum Filicis Maris; Extrait de Fougère Mâle, *Fr. Cod.;* Extractum Filicis, *P. G.;* Farnextrakt, Wurmfarnextrakt, Wurmfarnöl, *G.;* Estratto de felce maschio etero, *It.;* Extracto etereo de helecho macho, *Sp.*

"Aspidium, recently reduced to coarse powder, 500 Gm.; Ether, a sufficient quantity. Place the aspidium in a cylindrical glass percolator provided with a stop-cock, and arranged with a cover and a receptacle suitable for volatile liquids. Pack the powder firmly, and percolate slowly with ether added in successive portions until the drug is exhausted. Recover the greater part of the ether from the percolate by distillation on a water bath, and, having transferred the residue to a dish, allow the remaining ether to evaporate spontaneously in a warm place, remote from a naked flame." *U. S.*

"Male Fern, in No. 20 powder, 1000 *grammes;* Ether, *a sufficient quantity.* Exhaust the Male Fern by percolation with the Ether; from the clear percolate recover the ether by distillation and finally evaporate on a water-bath until an oily extract remains. Specific gravity not less than 1.000. *Refractive index* at 40° C. not less than 1.490. Contains in 100 grammes not less than 20 grammes of filicin as determined by the following process." *Br.*

The requirement of the U. S. that not more than 15 per cent. of the oleoresin shall be insoluble in petroleum ether is directed against the presence of castor oil.

This is the only preparation of male fern which should be used; in its making aspidium which is green in color and recently collected should be employed. It is a thick, dark green liquid, having the odor of the fern and a nauseous bitter and somewhat acrid taste. It usually contains a granular deposit of crystalline *filicic anhydride,* often erroneously called *filicin* or *filicic acid,* which is regarded as an active ingredient and should not be separated. Wm. G. Greenawalt found both the liquid and the sediment effective tenicides, the sediment somewhat the more active. According to Hayes, when an absolutely dry root and an anhydrous ether (containing but little alcohol) of a specific gravity below 0.728 are used, the oleoresin remains clear. Oleoresin of male fern is sometimes found in the market containing noticeable proportions of copper, and in many cases it is colored green artificially.

Description and Physical Properties.—"A dark green, thick liquid, usually depositing a granular, crystalline substance, which must be thoroughly mixed with the liquid portion before use. Not less than 85 per cent. of the Oleoresin is soluble in purified petroleum benzin. Specific gravity: not less than 1.00 at 25° C. Preserve in well stoppered bottles." *U. S.*

Assay.—It is unfortunate that the U. S. and British Pharmacopœias both use the term "filicin" as indicative of the important principles of this drug, for the activity of the substance to which this name is applied in scientific literature (filicic anhydride) is very doubtful (see under *Aspidium*). The composition of the ethereal extraction—as in the official assay—is reputed to be about as follows: 100 parts of oleoresin contain 3.5 of filicic acid, 2.5 of flavaspidic acid, 6.00 of filicic nigrine, 5.00 of filmaron (by some believed to be the true active principle), 0.05 of albaspidin, 0.10 each of flavaspidin and aspidinol, and 5.00 of amorphous acids.

The official methods of standardization are as follows:

"Warm the Oleoresin on a water bath and stir until it is thoroughly mixed. Transfer about 5 Gm., accurately weighed, to a 200 cc. flask, dissolve in 40 Gm. of ether, add 100 Gm. of an aqueous solution of barium hydroxide (3 in 100), and shake vigorously for five minutes. Allow the liquids to separate, and filter off 86 Gm. of the aqueous fluid. Transfer this to a separator, add sufficient hydrochloric acid to produce a distinctly acid reaction, and extract with three successive portions of 30 cc., 20 cc., and 15 cc. of ether. Draw off and combine the ethereal solutions, filter, wash the filter with ether, evaporate, and dry the residue to constant weight at 100° C. This residue weighs not less than 0.96 Gm., corresponding to not less than 24 per cent. of crude filicin." *U. S.*

"Dissolve 5 grammes of the Liquid Extract in 40 millilitres of *ether,* transfer to a separator, add 100 grammes of *solution of barium hydroxide* and shake vigorously and continuously for five minutes. Allow the liquids to separate and filter off 86 grammes of the aqueous liquid. Acidify this with *hydrochloric acid* and extract with three successive portions of 30, 20, and 15 millilitres of *ether.* Filter the mixed ethereal solutions, wash the filter paper with *ether,* evaporate, dry the residue at 100° C. and weigh. It weighs not less than 0.8 gramme, equivalent to not less than 20 grammes of filicin in 100 grammes of the Liquid Extract. This Liquid Extract contains not less than 20 per cent. of filicin." *Br.*

The assay of oleoresin of aspidium is likely to give very discrepant results because of lack of homogeneity of the sample.

For therapeutic properties of this oleoresin, see *Aspidium.*

Dose, from one-half to one fluidrachm (1.8–3.75 cc.), administered in emulsion.

OLEORESINA CAPSICI. U. S.

OLEORESIN OF CAPSICUM Oleores. Capsic.

Oléorésine (Extrait éthéré) de Capsique, *Fr.;* Spanischpfeffer-Oelharz, Aetherisches Spanishpfeffer-extrakt, *G.*

"Capsicum, in coarse powder, 500 Gm.; Ether, a sufficient quantity. Place the capsicum in a cylindrical glass percolator provided with a stop-cock, and arranged with a cover and a receptacle suitable for volatile liquids. Pack the powder firmly, and percolate slowly with ether added in successive portions until the percolate measures 800 cc. Recover the greater part of the ether from the percolate by distillation on a water bath, and, having transferred the residue to a dish, allow the remaining ether to evaporate spontaneously in a warm place, remote from a naked flame. Then pour off the liquid portion, transfer the remainder to a glass funnel provided with a pledget of cotton, and, when the separated fatty matter (which is to be rejected) has been completely drained, mix the liquid portions.

"Oleoresin of Capsicum should meet the requirements of the following test: Dissolve 0.2 Gm. of the Oleoresin in 50 cc. of alcohol in a stoppered flask, dilute 0.1 cc. of the clear separated solution with 140 cc. of distilled water containing 10 per cent. of sucrose: five cc. of this dilution, swallowed at one time, will produce a distinct sensation of pungency in the mouth and throat of at least two out of three individuals. Preserve in well stoppered bottles." *U. S.*

One of the active principles of capsicum, called *capsaicin,* $C_9H_{14}O_2$, is very soluble in ether, and is wholly extracted in the process. Its precise nature has not been determined. Another principle, even still more pungent than *capsaicin,* is *capsicutin* which is also extracted by the official solvent in making this oleoresin. (See *Capsicum.*) After the concentration of the acetone solution, a solid fatty matter separates on standing, but a portion of fixed oil probably still remains. The preparation is a very thick liquid, capable, however, of being dropped, of a dark reddish-brown color, and, though opaque in mass, yet transparent in thin layers. It has not very decidedly the odor of capsicum, but to the taste is intensely pungent. W. C. Alpers found a capsicum which yielded 16 per cent. of oleoresin; the statement has been frequently made that 5 per cent. is the usual yield. (*M. R.,* 1896, 593.)

Uses.—It may be usefully employed to give locally stimulant properties to substances administered internally in a pilular form, in cases of *gastric insensibility* and excessive *flatulence,* and the relaxing type of serous *diarrhea.* One drop given three times a day has produced cystic irritation and strangury. It may be used also as a powerful rubefacient, in strengths of from one to two per cent., diluted with olive oil or soap liniment.

Dose, from one-fourth to one grain (0.015–0.065 Gm.).

Off. Prep.—Unguentum Capsici, *N. F.*

OLEORESINÆ

OLEORESINS

Oléo-résines, Extraits éthérés, *Fr.;* Oelharze, Aetherische Extrakte, *G.*

The oleoresins, as a class of preparations, were introduced into the U. S. Pharmacopœia at the revision of 1860, having been previously classed with the fluidextracts; only two were admitted to the U. S. X. Their peculiarity is that they consist of principles which, when extracted by means of ether, alcohol, or acetone, retain a liquid or semi-liquid state upon the evaporation of the menstruum. They are decidedly more potent than the fluidextracts because they retain none of the solvent, and differ from them also in not having a definite relation of strength to the drug. They consist chiefly, as their name implies, of oil, either fixed or volatile, holding resin and sometimes other active matter in solution. Their preparation is very simple, consisting in the exhaustion of the drug with ether by means of percolation, and the subsequent evaporation of the menstruum. In consequence of the great volatility of the solvent, it may in great measure be recovered by distillation, thus very materially diminishing the costliness of the process. It is proper not to continue the heat necessary for the recovery of the solvent by distillation until the whole of the solvent is driven over, lest, towards the close, a portion of the volatile matters also should pass, and the strength of the oleoresin be impaired. Hence in every instance the last portions of the menstruum are allowed to separate by spontaneous evaporation. Petroleum benzin and acetone have been proposed as a substitute for other solvents in these preparations, but are not at present officially sanctioned. It is difficult, if not impossible, to remove the last traces of this solvent without loss of volatile oil. Acetone replaced ether in most of the formulas of the U. S. P. VIII on account of economy, but as ether is again the cheaper solvent because of the use of denatured alcohol in its manufacture, it is again officially directed in the U. S. P. X.

OLEUM ABIETIS. Br.

OIL OF SIBERIAN FIR [Oil of Pine]

"Oil of Siberian Fir is the oil distilled from the fresh leaves of Abies sibirica, *Ledeb.*" *Br.*

Abies sibirica Ledeb. is a coniferous tree indigenous to Eastern Europe and Asia. It attains a height of 60 to 100 feet and possesses dark yellowish-green leaves and slender, cylindrical, brownish-yellow cones up to 3 inches long.

The oil which is distilled from the leaves is described as:

"Colorless or nearly so. Aromatic odor; taste pungent. Specific gravity 0.900 to 0.920; *optical rotation* −32° to −42°; *refractive index* at 25° C. about 1.474. Contains from 30 to 40 per cent. of *esters,* calculated as bornyl acetate, $C_{10}H_{17}C_2H_3O_2$." *Br.*

This is practically the same in its properties and uses as pine needle oil. (See *Oleum Pini Pumilionis.*)

OLEUM AJOWAN. Br.

AJOWAN OIL [Ptychotis Oil]

"Ajowan Oil is the oil distilled from the fruit of Carum Copticum, *Benth. and Hook. f.*" *Br.*

For description of the plant from which this oil is obtained, see *Ajowan,* Part II. The fruits resemble in size the fruits of the ordinary parsley and are of a grayish-brown color and have a tubercular surface with five prominent ridges to each mericarp. The odor and taste resemble that of thyme. These fruits yield from 4 to 6 per cent. of an agreeably aromatic volatile oil. Ajowan oil is "colorless, with an odor and taste resembling thyme. Specific gravity 0.910 to 0.930. *Optical rotation* + 1° to + 2°. When 10 millilitres with 100 millilitres of *solution of sodium hydroxide* in a flask with a narrow graduated neck are heated on a water-bath, well shaken, and allowed to stand, the uncombined oil, cooled to 15.5° C., measures not more than 6 millilitres (presence of not less than 40 per cent. of thymol)." *Br.*

This oil, besides containing thymol, contains a terpene and also the cyclic hydrocarbon, cymene.

The oil of ajowan is one of the most important commercial sources of thymol. Its medicinal virtues are due entirely to this ingredient.

Dose, one-half to five minims (0.03–0.3 cc.).

OLEUM AMYGDALÆ AMARÆ. U. S.

OIL OF BITTER ALMOND Ol. Amygd. Amar. [Bitter Almond Oil]

"The volatile oil obtained by maceration with water and subsequent distillation with steam from the dried ripe kernels (deprived of fixed oil) of *Amygdalus communis* Linné (Fam. *Rosaceæ*), or from other kernels containing amygdalin. The botanical source from which the Oil is derived must be stated on the label. Oil of Bitter Almond yields not less than 85 per cent. of benzaldehyde [C_7H_6O] and not less than 2 per cent. and not more than 4 per cent. of hydrocyanic acid [HCN]. Oil in which crystals have formed must not be dispensed. NOTE—This Oil is intended for medicinal use and neither it nor its solution should be used or sold for flavoring foods." *U. S.*

Oleum Amygdalarum (Amararum) Æthereum; Oleum Amygdalæ Volatile; Volatile Oil of Almond; Huile volatile d'Amande amère, *Fr. Cod.;* Essence d'Amandes amères, *Fr.;* Bittermandelöl, *G.;* Esencia de almendras amargas, *Sp.*

When bitter almonds are expressed, they yield a bland fixed oil, and the residuary cake, reduced to powder by grinding, and submitted to distillation with water, yields oil of bitter almond. This does not pre-exist in the almond, but is produced by the action of water upon the l-mandelonitrile glucoside contained in it, through the intervention of an enzyme called emulsin (see *Amygdala Amara*).

Much of the "bitter-almond oil" of commerce comes from apricot kernels.

Oil of bitter almond has a yellowish color, a bitter, acrid, burning taste, and the odor of the kernels in a high degree. It is heavier than water, soluble in alcohol and ether, according to Flückiger soluble in 300 parts of hot or cold water, and deposits, upon standing, a white crystalline substance consisting chiefly of benzoic acid.

Description and Physical Properties.—"A clear, colorless or yellow, strongly refractive liquid, having the characteristic odor and taste of benzaldehyde. When first prepared, the Oil is neutral to moistened litmus paper, but afterward develops an acid reaction, due to the formation of benzoic acid.

"The Oil is slightly soluble in water and is soluble in all proportions in alcohol and in ether. It forms a clear solution with 2 volumes of 70 per cent. alcohol, by volume. Specific gravity: 1.038 to 1.060 at 25° C. Optical rotation: varies from inactive to $+0° 10'$ in a 100 mm. tube at 25° C. Refractive index: 1.5428 to 1.5439 at 20° C. The Oil meets the requirements of the test for *heavy metals in volatile oils.* Rinse the interior surface of a well-cleaned, 1000 cc. beaker with distilled water, and pass the washings through a small filter until the addition of 1 drop of silver nitrate T.S. to a portion of the filtrate, acidulated with 1 drop of nitric acid, shows no turbidity. Place 3 or 4 drops of the Oil on a clean watch glass supported on a triangle, ignite, and immediately cover with the moistened beaker. Wash the products of combustion from the sides of the beaker through the washed filter with 10 to 20 cc. of distilled water, and acidulate the filtrate with 1 drop of nitric acid: the addition of 1 drop of silver nitrate T.S. produces no turbidity (*chlorinated products*). Add 10 drops of Oil of Bitter Almond to 5 cc. of alcohol, then add a small amount of zinc dust and 2 cc. of acetic acid, and boil the mixture for about ten seconds: no odor of phenylisocyanide develops after rendering the liquid strongly alkaline with sodium hydroxide T.S. and then adding a few drops of chloroform and heating (*nitrobenzene*). Preserve in small, well-stoppered, completely filled, amber-colored bottles, in a cool place, protected from light." *U. S.*

Besides benzaldehyde, it contains also hydrocyanic acid, with usually a small proportion of benzoic acid produced by oxidation of the aldehyde. The characteristic odor of this oil is due chiefly to the benzaldehyde and although slightly modified by the prussic acid. The U. S. provides assays for benzaldehyde and also for hydrocyanic acid.

Benzoic aldehyde is now made synthetically from toluene, C_7H_8. (See *Benzaldehydum.*) To prevent the formation of benzoic acid in oil of bitter almond, Schimmel & Co. recommended the addition of 10 per cent. of alcohol to the oil. Wm. A. Tilden (*P. J.*, 1866) has found that the introduction of a little fused calcium chloride into purified oil of bitter almond contributes to its preservation, probably by the absorption of the last traces of water contained in it.

Schimmel & Co. (*Semi-Annual Report,* April, 1893) state that an oil of high specific gravity should be carefully examined for benzo-nitrile, C_6H_5CN, which may form by condensation from benzaldehyde and hydrocyanic acid, and when distilled even *in vacuo* will decompose into the same components.

Nitrobenzene was at one time a frequent adulterant of oil of bitter almond. It may best be detected by the U. S. P. test given above, for additional tests see *U. S. D.*, 19th ed., p. 830–831.

Hager's test may be used quantitatively for the estimation of the amount of nitrobenzene present. Oil of bitter almond requires for solution sixteen to seventeen times its volume of 45 per cent. alcohol. Two cc. of the oil are agitated with 34 cc. of the 45 per cent. alcohol, and the mixture set aside. After the lapse of a day, the nitrobenzene (all but a trace which remains in solution) will be found collected at the bottom. An important indication of the presence of a sophistication is the cloudiness produced at the first moment. (*N. R.*, Oct., 1880.)

Assay for Benzaldehyde.—"Dissolve about 3 cc. of freshly redistilled phenylhydrazine in about 60 cc. of alcohol, and titrate 25 cc. of this solution, which must be freshly prepared, with half-normal hydrochloric acid, using 1 drop of methyl orange T.S. as indicator. To about 1 Gm. of Oil of Bitter Almond, accurately weighed, add another 25 cc. portion of the phenylhydrazine solution, and allow the mixture to stand thirty minutes. Add 1 drop of methyl orange T.S., and acidify the mixture by adding a measured excess of half-normal hydrochloric acid. Filter the mixture, and wash the precipitate with small portions of distilled water until the washings cease to redden moistened blue litmus paper. Then titrate the excess of hydrochloric acid in the combined filtrates with half-normal sodium hydroxide, and subtract the number of cc. of half-normal hydrochloric acid consumed from the number of cc. of half-normal hydrochloric acid used in titrating 25 cc. of the phenylhydrazine solution. The difference multiplied by 0.05304 gives the weight of benzaldehyde." *U. S.*

Assay for Hydrocyanic Acid.—"Dissolve 0.75 Gm. of magnesium sulphate in 45 cc. of distilled water, add 5 cc. of half-normal sodium hydroxide and 2 drops of potassium chromate T.S., and titrate the solution with tenth-normal silver nitrate to the production of a permanent reddish tint. Pour this mixture into a 100 cc. flask containing about 1 Gm. of Oil of Bitter Almond, accurately weighed, mix well, and titrate again with tenth-normal silver nitrate until a red tint, which does not disappear on shaking, is reproduced. Conduct this titration as rapidly as possible. Each cc. of tenth-normal silver nitrate corresponds to 0.002702 Gm. of hydrocyanic acid." *U. S.*

Uses.—The unpurified volatile oil of bitter almond, which is the product directed by the Pharmacopœia, acts physiologically like hydrocyanic acid. Death is said to have occurred in a man ten minutes after taking two fluidrachms (7.5 cc.) of the oil. It might be substituted for medicinal hydrocyanic acid, if it always contained a uniform percentage of the acid, as the acid contained in the oil is much less liable to decomposition, remaining for several years unaltered, provided the oil be preserved in well-stoppered bottles. But the proportion is not constant; the U. S. official standard is not less than 2 per cent. and not more than 4 per cent. It has been employed externally, dissolved in water in the proportion of one minim (0.06 cc.) to a fluidounce (30 cc.), in *prurigo senilis* and other cases of troublesome *itching*. To facilitate the solution in water, the oil may be previously dissolved in spirit. Oil of bitter almond is sometimes used to conceal the taste of cod liver oil and of castor oil.

Dose, one-fourth to one minim (0.015–0.06 cc.).

Off. Prep.—Spiritus Amygdalæ Amaræ, *N. F.;* Elixir Amygdalæ Compositum, *N. F.;* Elixir Anisi (from Spirit), *N. F.;* Elixir Aromaticum Rubrum, *N. F.*

OLEUM AMYGDALÆ EXPRESSUM. U. S. (Br.)

EXPRESSED OIL OF ALMOND Ol. Amygd. Exp. [Oil of Sweet Almond]

"The fixed oil obtained from the kernels of varieties of *Amygdalus communis* Linné (Fam. *Dosaceæ*)." *U. S.* "Almond Oil is the oil expressed from the Bitter or Sweet Almond." *Br.*

Oleum Amygdalæ, *Br.;* Almond Oil; Oleum Amygdalæ Dulcis, *U. S.* 1860; Sweet Almond Oil; Huile d'Amande douce, *Fr. Cod.;* Huile d'Amandes, *Fr.;* Oleum Amygdalarum, *P. G.*; Mandel öl, *G.;* Olio di mandorle dolci, *It.;* Aceite de almendras dulces, *Sp.*

This oil is obtained equally pure from sweet and from bitter almonds. In its preparation, the almonds, having been deprived of a reddish-brown powder adhering to their surface, by being rubbed together in a piece of coarse linen, are ground in a mill resembling a coffee-mill, or bruised in a stone mortar, and then pressed in canvas sacks between plates of iron slightly heated. The oil, which is at first turbid, is clarified by rest and filtration. Sometimes the almonds are steeped in very hot water, deprived of their cuticle, and dried in a stove, previous to expression. The oil is thus obtained free from color, but in no other respect better, while it is more likely to become rancid on keeping. Bitter almonds treated in this way impart an odor of hydrocyanic acid to the oil. The yield of oil from the sweet almond is from 40 to 55 per cent. and slightly less from the bitter. Though sometimes expressed in this country from imported almonds, the oil is generally brought from Europe.

Description and Physical Properties.—"A clear, pale straw-colored or colorless, oily liquid. It is almost odorless, and has a bland taste. It is slightly soluble in alcohol, but is miscible with ether, chloroform, benzene, and with petroleum benzin.

"Specific gravity: 0.910 to 0.915 at 25° C. The Oil remains clear at −10° C., and does not congeal until cooled to nearly −20° C. (*olive* or *lard oil*). Shake vigorously for five minutes: 2 cc. of the Oil with a mixture of 1 cc. of fuming nitric acid and 1 cc. of distilled water: the mixture is not more than slightly colored. (*Oil of peach kernels and oil of apricot kernels* yield a red color, and *sesame oil and cottonseed oil* yield a brown color.) Heat 10 cc. of the Oil with 15 cc. of an aqueous solution of sodium hydroxide (1 in 6) and 30 cc. of alcohol on a water bath in a flask, having a small funnel inserted in the neck, and occasionally agitate the mixture until it becomes clear. Transfer the solution to a shallow dish, and evaporate the alcohol on a water bath: the residue, when mixed with 100 cc. of distilled water, produces a clear solution (*paraffin oil*). Add an excess of hydrochloric acid to this solution: a layer of oleic acid rises to the surface which, when separated, washed with warm water, clarified by heating on a water bath, and cooled to 15° C. remains clear for thirty minutes (*various foreign oils.*) One volume of the oleic acid obtained in the preceding test, when mixed with an equal volume of alcohol, yields a clear solution, which, at 15° C., does not deposit any fatty acids, or become turbid upon the further addition of 1 volume of alcohol (*difference from olive, peanut, cottonseed, sesame, and other fixed oils*). Saponification value: not less than 191 and not more than 200. Iodine value: not less than 93 and not more than 100. Preserve in well-closed containers." *U. S.*

"Pale yellow. Nearly inodorous; taste bland and nutty. Specific gravity 0.915 to 0.920. *Saponification value* 188 to 196; *iodine value* 93 to 100; *acid value* not more than 6.0; *refractive index* at 40° C. 1.4624 to 1.4640. Remains clear after exposure for three hours to a temperature of −10° C., and does not congeal till the temperature has been reduced to about −18° C. When 1 millilitre of a freshly prepared mixture of equal parts by weight of *sulphuric acid, fuming nitric acid,* and *water,* kept cool while cautiously mixed, is vigorously shaken with 5 millilitres of the Oil for one minute, a whitish mixture with not more than the very slightest tinge of red or brown is produced; after some hours a white solid, sometimes tinged with green, separates, the lower acid layer remaining colorless (absence of peach oil and apricot oil)." *Br.*

Expressed oil of almond consists chiefly of olein with traces of linolein; there is no stearin present. It belongs among the "non-drying" oils.

It is sometimes adulterated with oils from peach or apricot kernels; these are excluded by the test of the U. S.

Uses.—The expressed oil of almonds possesses the emollient properties of the other fixed oils over most of which it has the advantage of comparative tastelessness, and freedom from odor and its lack of tendency to become gummy.

It is widely employed as an emollient for *chapped hands* and other inflamed conditions of the skin. It is also used to aid the emulsification of the volatile oils.

Dose, one fluidrachm to one fluidounce (3.75–30 cc.).

OLEUM ANETHI. Br.

OIL OF DILL

"Oil of Dill is the oil distilled from Dill Fruit." *Br.*

Huile volatile d'Aneth, Essence d'Aneth, *Fr.;* Dill, Dillöl, *G.*

Oil of dill is of a pale yellow color, with the odor of the fruit, and a hot, sweetish, acrid taste. Its sp. gr. varies between 0.895 and 0.915. The fruit yields about 3.5 per cent. of it.

"Colorless or pale yellow, darkening on keeping. Odor that of Dill Fruit; taste at first sweet and aromatic, but subsequently pungent. Specific gravity 0.900 to 0.915; *optical rotation* +70° to +80°; *refractive index* at 25° C. 1.483 to 1.488. Soluble in 3 parts of *alcohol* (90 per cent.)." *Br.* Dill oil contains from 40 to 60 per cent of carvone, considerable d-limonene and smaller amounts of other terpenes; English and Spanish oils contain phellandrene which, it is said, does not occur in oil of German origin.

East Indian dill oil, which is occasionally used as an adulterant or substitute, comes from a different plant (*Peucedanum Sowa* Kurz.). It differs from the genuine in containing less carvone; small amounts of an apiol are also present.

Dose, from one to three minims (0.065–0.2 cc.).

OLEUM ANISI. U. S., Br.

OIL OF ANISE Ol. Anisi [Anise Oil]

"The volatile oil distilled from the dried ripe fruit of *Pimpinella Anisum* Linné (Fam. *Umbelliferæ*) or from the dried ripe fruit of *Illicium verum* Hooker filius (Fam. *Magnoliaceæ*). The botanical source from which the Oil is derived must be stated on the label. If solid material has separated, carefully warm the Oil until completely liquefied, and mix it thoroughly before dispensing." *U. S.* "Oil of Anise is the oil distilled from Anise Fruit; or from the fruit of the star-anise, Illicium verum, *Hook. f.*" *Br.*

Huile volatile d'Anis vert (Badaine), *Fr. Cod.;* Essence d'Anis, *Fr.;* Oleum Anisi, *P. G.;* Anethol, Anisöl, *G.;* Essenza di anice, *It.;* Esencia de anis, *Sp.*

The product of oil from anise is variously stated at from 1.56 to 3.12 per cent. The oil employed in this country is imported. It is colorless or yellowish, with the peculiar odor and taste of the seed. At 10° C. it crystallizes in flat tables, and it does not melt under 16.6° C. Its sp. gr. increases with age, and is variously given at from 0.9768 to 0.9903. It is miscible in all proportions with ether or dehydrated alcohol.

Description and Physical Properties.—"A colorless or pale yellow, strongly refractive liquid, having the characteristic odor and taste of anise.

"The Oil is soluble with not more than a slight cloudiness in 3 volumes of 90 per cent. alcohol, by volume. Specific gravity: 0.978 to 0.988 at 25° C. Optical rotation: varies from +1° to −2° in a 100 mm. tube at 25° C. Refractive index: 1.5440 to 1.5600 at 20° C. A solution of the recently distilled Oil in 90 per cent. alcohol (1 in 3) is neutral to moistened litmus paper, and develops no blue or brownish color upon the addition of 1 drop of ferric chloride T.S. to 5 cc. of the solution (*phenols*). The Oil meets the requirements of the test for *heavy metals in volatile oils.* The congealing point of Oil of Anise does not fall below 15° C. as determined by the method described on page 1536. Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

"Colorless or pale yellow. Odor that of Anise Fruit; taste sweet and aromatic. Specific gravity at 20° C. (compared with *water* at 15.5° C.) 0.975 to 0.990; *optical rotation* −2° to +1°; *refractive index* at 25° C. 1.552 to 1.558. Congeals, when stirred, at about 15.5° C., and does not again liquefy below 17° C. Not less than 80 per cent. distils between 225° and 235° C. Soluble in 3 parts of *alcohol* (90 per cent.)." *Br.*

Oil of anise contains a small quantity of terpenes, but consists mainly (about 85 per cent.) of methyl-p-propenyl-phenol. This is present both in the solid form, known as estragol, and in the liquid form, anethol. Some samples have been reported as showing traces of safrol. The solidification test of the U. S. P. X is based upon the anethol content. Oil of anise, by exposure to air, is oxidized with the formation of anisic aldehyde, acetic aldehyde and anisic acid, and becomes less disposed to congeal.

The so-called *Japanese star anise oil* (from *Illicium religiosum*) which is from the leaves instead of the fruit. This latter oil contains eugenol and safrol as well as much less anethol than the oil from the fruit. (See *Illicium,* Part II.)

In consequence of its high price, Oil of Anise is frequently adulterated with spermaceti, wax, or camphor. The first two may be detected by their insolubility in cold alcohol, the last by its odor. In one instance as much as 35 per cent. of spermaceti was found. Schimmel & Co. have found fennel stearoptene in commercial oil of anise. (*Ph. Rev.,* 1897, 94). Much of the oil of anise of commerce is the *oil of star aniseed* (*Oleum Badiani,* or *Oleum Illicii*). Oil of anise has also been distilled from the sweet cicely, *Osmorrhiza longistylis* (Torr.) DC., of the United States and Canada. (*Ph. Rund.,* July, 1887.) For description and analysis of Russian oil of anise, see *P. J.,* 1896, 164, also

243. Anisic acid is said to be antiseptic, resembling salicylic acid in its action.

Uses.—As a flavoring agent the oil of anise rivals any of the aromatic oils in the extent of its applicability. It is especially enjoyed by young children. Therapeutically it is useful to stimulate peristalsis in *colic* and, according to Kobert, also as an *expectorant.* It has also been recommended as a means of destroying body lice. Parutz (*Schim. Rep.,* 1920) has used a 1 per cent. ointment for *scabies.*

Dose, from three to five minims (0.2–0.3 cc.).

Off. Prep.—Aqua Anisi, *U. S.;* Elixir Aromaticum (from Spirit), *U. S.;* Spiritus Anisi, *U. S., Br.;* Spiritus Aurantii Compositus, *U. S.*

OLEUM ANTHEMIDIS. Br.

OIL OF CHAMOMILE

"Oil of Chamomile is the oil distilled from Chamomile Flowers." *Br.*

Oleum Chamomillæ Romanæ; Essence de Camomille romaine, *Fr.;* Römisch-Kamillenöl, *G.*

The yield of this oil by chamomile flowers ranges from 0.8 to 1.5 per cent. It has the peculiar odor of chamomile, with a pungent somewhat aromatic taste.

It is "blue when freshly distilled, but gradually becoming greenish or brownish-yellow under the influence of air and light. Odor that of Chamomile Flowers; taste aromatic, characteristic. Specific gravity 0.905 to 0.915. *Optical rotation* –1° to +3°; *refractive index* at 25° C. about 1.445. Soluble in less than 1 part of *alcohol* (90 per cent.)." *Br.*

For account of the chemistry of this oil see under *Anthemidis Flores.* It has sometimes been employed in spasm of the stomach, and as an adjunct to purgative medicines. Its chief use, however, appears to be as an ingredient of the extract of chamomile of the British Pharmacopœia, to which it is added in order to supply the place of the oil driven off by the heat used in its preparation. This oil must not be confounded with that of *Matricaria Chamomilla* L. employed on the continent of Europe under the name of oil of chamomile. (See *Matricaria.*)

Dose, one to three minims (0.06–0.2 cc.).

OLEUM ARACHIS. Br.

ARACHIS OIL

Arachis Oil is the oil expressed from the seeds of Arachis hypogæa, *Linn.*

Earth-nut Oil, Ground-nut Oil, Pea-nut Oil.

For description of the pea-nut plant (*Arachis hypogæa*), see *Ground-nuts,* Part II. The oil consists of the glycerides of oleic acid and in smaller amount of linoleic, hypogeic, arachidic and lignoceric acids. It should be obtained by expression without heat. It is usually of a pale yellowish or green color with a faint odor, and a more distinct taste of the nuts, although on clarification a nearly colorless and tasteless oil may be obtained. Upon exposure to the air the oil slowly thickens and becomes rancid. It is soluble in all proportions in ether, chloroform, and petroleum benzin, but insoluble in alcohol.

"Pale yellow or greenish-yellow. Faint, nutlike odor; taste bland, nutty. Specific gravity 0.916 to 0.921; *saponification value* 190 to 196; *iodine value* 83 to 101; *acid value* not more than 6; *refractive index* at 40° C. 1.4628 to 1.4645. When 1 millilitre of the Oil and 15 millilitres of *N/1 alcoholic solution of potassium hydroxide* are boiled for twenty minutes in a flask provided with a reflux condenser, set aside for twenty-four hours at a temperature not exceeding 15.5° C., and afterwards heated on a water-bath for three minutes, the solution deposits crystals on standing. When a mixture of 2 millilitres of the Oil and 1 millilitre of *hydrochloric acid* containing 1 per cent. of *refined sugar* is shaken for half a minute, and allowed to stand for five minutes, the acid layer does not become pink (absence of sesame oil). When 2 millilitres of the Oil are mixed with 1 millilitre of *amylic alcohol* and 1 millilitre of a solution (1 in 100) of *precipitated sulphur* in *carbon disulphide,* and the mixture heated in a test-tube immersed in boiling *water,* no red color is developed within fifteen minutes (absence of cotton seed oil)." *Br.*

At 3.3° C. it thickens, solidifies at about –5° C., and at 326.6° C. is decomposed, giving out spontaneously inflammable vapors. Winter made experiments to ascertain how far it might be employed with advantage in pharmacy, and found that it answered well in the preparation of cerates and ointments, but would not serve as a substitute for olive oil in the preparation of lead plaster. (See *Proc. A. Ph. A.,* 1897, 179.) Its use is permitted, by the British Pharmacopœia, in India, and in the Eastern, African, and Australasian Divisions of the Empire, for making the official Liniments, Ointments, Plasters, and Soaps for which Olive Oil is directed to be used. It is a non-drying oil, and therefore will not answer for painting; but it has been enormously used for adulteration (particularly of French olive oils) and for various purposes in the arts, as for lubricating machinery, and in the manufacture of woollen cloths; in lamps it burns with a bright light. It saponifies slowly, but yields an excellent firm, white, and odorless soap.

OLEUM AURANTII. U. S.

OIL OF ORANGE Ol. Aurant. [Orange Oil, Oil of Sweet Orange]

"The volatile oil obtained by expression from the fresh peel of the ripe fruit of *Citrus Aurantium* var. *sinensis* Linné (Fam. *Rutaceæ*). Oil of Orange which has a terebinthinate odor must not be dispensed." *U. S.*

Oleum Aurantii Corticis, *U. S. VIII;* Oleum Aurantiorum; Essential Oil of Orange Peel, Essence of Orange; Huile volatile d'Orange, *Fr. Cod.;* Essence de Portugal, *Fr.;* Apfelsiunencharenöl, Pomeranzenschalenöl, *G.;* Essenza di arancio amara, Essenza della corteccia, *It.*

This oil is used only for flavoring purposes, and has been introduced principally because of its employment in elixirs and in *Spiritus Aurantii Compositus.*

The oil of orange is obtained either by expression or distillation. One method which has been employed in Sicily from very early times is to remove the pulp of the fruit and press the rind by hand against a sponge which absorbs the oil as it is expressed. Sometimes the oil is expressed by machinery. The "écuelle" process (see under *Oleum Limonis*) is largely employed in France and also in Jamaica (*D. C.*, 1918, lxii, p. 196); the oranges are rolled in vessels thickly studded with sharp points and the oil collected as it oozes out of the wounds.

Oil of orange peel consists, as has been shown by Wallach, of d-limonene to the extent of at least 90 per cent.; of the remainder, about 5 per cent. are the odorous constituents, among which are citral, traces of citronellal, and the methyl ester of anthranilic acid. (See under *Indigo,* Part II.) The inner thick part of the rind contains also a bitter principle, called hesperidin (see under *Limonis Cortex*).

Description and Physical Properties.—"A yellow liquid, having the characteristic odor and taste of the outer part of sweet orange peel.

"The Oil does not form a clear solution with 2 volumes of 90 per cent. alcohol, by volume, (*washed citrus oils*). It is soluble in all proportions in dehydrated alcohol and in carbon disulphide, and in an equal volume of glacial acetic acid. Specific gravity: 0.842 to 0.846 at 25° C. Optical rotation: not less than + 94° and not more than + 99° in a 100 mm. tube at 25° C. Refractive index: 1.4723 to 1.4737 at 20° C. A solution of recently expressed Oil of Orange in dehydrated alcohol is neutral to moistened litmus paper. The Oil meets the requirements of the test for *heavy metals in volatile oils.* A 25 Gm. portion of Oil of Orange evaporated to dryness at a temperature not exceeding 100° C. yields not less than 2 per cent. of residue (*washed citrus oils*). Place 50 cc. of Oil of Orange in a 250 cc. three-bulb Ladenburg flask of approximately the following dimensions: The lower or main bulb, 6 cm. in diameter, with the smaller condensing bulbs 3.5 cm., 3.0 cm. and 2.5 cm., respectively, in diameter; the distance from the bottom of the flask to the side arm, 20 cm. Distil the Oil at the rate of 1 drop per second until the distillate measures 5 cc.: the angle of rotation of the distillate is equal to that of the original Oil, or does not differ more than 2 degrees from it, and the refractive index of the distillate is not less than 0.0008 and not more than 0.0015 lower than that of the original Oil at 20° C.

"Preserve in small, completely filled, well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

A waxy non-volatile substance is present in oil of orange, which interferes with the transparency of solution made with 90 per cent. alcohol. This oil is one of the most difficult to preserve. A method for its preservation, which we have used for years, is to shake the oil briskly with one-eighth of its volume of distilled water, and allow it to separate, then remove the essential oil, filter rapidly if necessary, and mix the filtered oil with 95 per cent. alcohol in the proportion of one volume of the oil to seven volumes of alcohol.

It may be preserved indefinitely by adding 10 per cent. of its volume of olive oil.

The oil of orange is used chiefly as a flavoring agent but Zickgraf (*M. M. W.*, 1910, lvii, p. 1070) speaks very highly of its effect in *chronic bronchitis* for the same class of cases in which oil of turpentine is used. It has the advantages over the latter of being much more pleasant to take and non-irritant to the kidneys.

Dose, three to five minims (0.2–0.3 cc.).

Off. Prep.—Elixir Aromaticum (from Compound Spirit), *U. S.;* Spiritus Aurantii Compositus, *U. S.;* Elixir Cardamomi Compositum (from Compound Spirit), *U. S.;* Elixir Pepsini Compositum, *N. F.;* Spiritus Cardamomi Compositus, *N. F.;* Spiritus Myrciæ Compositus, *N. F.;* Spiritus Vanillini Compositus, *N. F.*

OLEUM AURANTII AMARÆ. N. F.

OIL OF BITTER ORANGE Ol. Aurant. Amar.

"A volatile oil obtained by expression from the fresh peel of the bitter orange, *Citrus Aurantium* Linné (Fam. *Rutaceæ*)." *N. F.*

Oil of Orange; Oil of Bigarade; Essence de Bigarade, *Fr.;* Oleum Aurantii Corticis, *G.*

Description and Physical Properties.—"Oil of Bitter Orange is a pale yellow liquid, having the characteristic, aromatic odor of the Seville orange, and an aromatic somewhat bitter taste. Soluble in 4 volumes of alcohol, the solution being neutral to litmus paper. Also soluble in all proportions in dehydrated alcohol and in an equal volume of glacial acetic acid.

"Specific gravity: 0.842 to 0.848 at 25° C. It is dextrorotatory, the angle of rotation varying from +88 to +98°, in a 100 mm. tube, at 25° C. Introduce 50 cc. of Oil of Bitter Orange into a 200 cc. three-bulb, fractionating flask of approximately the following dimensions; the lower or main bulb 6 cm. with smaller condensing bulbs 3.5 cm., 3.0 cm. and 2.5 cm. in diameter, respectively; with the distance from the bottom to the side arm 20 cm. Distil the Oil at the rate of 2 cc. per minute until a distillate measuring 6 cc. has been collected. The angle of rotation of this distillate is equal to, or only slightly lower than, that of the original Oil.

"Preserve it in small, well-stoppered, amber-colored bottles, in a cool place, protected from light. Oil of Bitter Orange having a terebinthinate odor is not to be dispensed." *N. F.*

Dose, from three to five minims (0.2–0.3 cc.).

Off. Prep.—Elixir Aurantii Amari, *N. F.*

OLEUM AURANTII FLORUM. N. F.

OIL OF ORANGE FLOWERS Ol. Aurant. Flor.
[Oil of Neroli]

"A volatile oil distilled from the fresh flowers of the bitter orange, *Citrus Aurantium* Linné (*Citrus vulgaris* Risso, *Citrus Bigaradia* Risso) (Fam. *Rutaceæ*)." *N. F.*

Oleum Neroli; Oil of Neroli; Oleum Naphae; Pomerantzenblüthenöl, *G.;* Esencia de Azahar, Esencia de Flor de Naranjo, *Sp.*

Various sweet-smelling oils have been prepared from different species of oranges. From the flowers of the sweet orange is obtained a very fragrant oil known as *néroli petale.* From the flowers of the bitter orange a similar although somewhat inferior perfume which is called *néroli bigarade;* this is the oil official in the N. F. The *oil of petit grain* (*huile de petit grain citronnier, essence de petit grain*) was originally obtained from the unripe fruits but is now distilled from the twigs and leaves of the lemon tree. It is often used for adulterating the true orange flower oil. (*C. D.*, 1897, p. 53.)

Description and Physical Properties.—"Oil of Orange Flowers is a pale yellow, slightly fluorescent, neutral liquid, having a distinctive fragrant odor, similar to that of orange blossoms, and an aromatic, at first sweet then somewhat bitter taste.

"It is soluble in an equal volume of alcohol, the solution having a violet fluorescence and a neutral reaction to litmus paper. Also soluble in two volumes of 80 per cent. alcohol, the solution becoming cloudy on the further addition of alcohol of the same percentage. Specific gravity: 0.868 to 0.880 at 25° C. It is dextrorotatory, the angle of rotation varying from +1° 30′ to +5° in a 100 mm. tube, at 25° C.

"Preserve it in small, amber-colored, well-stoppered bottles in a cool place, protected from light." *N. F.*

Neroli oil is one of the most complex of all of the volatile oils in its constitution. It contains the following constituents: l-a-pinene, l-camphene, limonene, dipentene, decyl aldehyde, phenyl-ethyl alcohol, nerol, linalool, d-terpineol, nerolidol, geraniol, acetic esters of the various alcohols mentioned, indol, traces of benzoic, palmitic and phenylacetic acids in the form of esters, linalyl acetate, and several paraffin hydrocarbons. A fluorescent substance, methyl o-amido benzoate, is also present. Noel distinguishes the different volatile oils of the orange tribe by shaking five drops of the oil with one cc. of pure concentrated hydrochloric acid. After one minute seven or eight cc. of 90 per cent. alcohol are added, whereby the color is changed, and increased or decreased according to the extent of the adulteration. It is obvious that to use effectually such a test requires special education. (See *Proc. A. Ph. A.*, 1887.)

Under the name of *nerolin* an artificial product has been placed upon the market in the form of a white crystalline powder, soluble in alcohol and fixed oils and almost insoluble in water. It is used by soap makers as a substitute for oil of neroli, and is said to be ten times as strong. This compound is said to be the *ethyl ether of β-naphthol.* (*B. Chem. G.*, 1893, 2706.) It is also used in the manufacture of eau-de-Cologne with advantage instead of neroli oil. (*Schim. Rep.*, April, 1893.) Oil of neroli of excellent quality is now produced artificially; Schimmel & Co. state that it contains pinene, camphene, dipentene, terpineol, phenyl-acetic acid, benzoic acid, decylic aldehyde, and linalool.

Oil of orange flowers is used only as a perfuming agent.

Off. Prep.—Spiritus Odoratus, *N. F.*

OLEUM BERGAMOTTÆ. N. F.

OIL OF BERGAMOT Ol. Bergam.

"A volatile oil obtained by expression from the rind of the fresh fruit of *Citrus Aurantium* Linné var. *Bergamia* (Risso et Poiteau), Wight et Arnott (Fam. *Rutaceæ*), and containing not less than 36 per cent. of ester, calculated as linalyl acetate." *N. F.*

Oleum Bergami; Essentia Bergamothæ; Bergamottol, *G.;* Essence de Bergamotte, *Fr.*; Esentia de Bergamota, *Sp.*

The bergamot tree has oblong-ovate, dentate, acute, or obtuse leaves, somewhat paler on the under than on the upper surface, and with winged petioles. The flowers are white, and usually small; the fruit is a pyriform or globular, thin skinned hesperidium, about three inches in diameter. The pulp of the fruit is sour, somewhat aromatic, and not disagreeable. The rind is shining, and of a pale-yellow color, and abounds in volatile oil. This may be obtained by expression or distillation. In the former case it preserves the agreeable flavor of the rind, but is somewhat turbid; in the latter it is limpid but less sweet. The mode of procuring it by expression is exactly the same as that used for oil of lemon. (See *Oleum Limonis.*) The bergamot tree is extensively cultivated in Calabria for its essential oil which is used in the preparation of Eau de Cologne and various perfumes. It is brought from Italy, the south of France, and Portugal.

Description and Physical Properties.—"Oil of Bergamot is a green or greenish-yellow liquid, neutral or only faintly acid, having a characteristic fragrant odor and an aromatic bitter taste. Two volumes of the Oil, when mixed with 1 volume of alcohol, give a clear solution and this does not become turbid on the further addition of alcohol. It is soluble in 2 volumes of 80 per cent. alcohol with not more than a slight cloudiness, and no separation of oil globules. Also soluble in all proportions in glacial acetic acid.

"Specific gravity: 0.875 to 0.880 at 25° C. It is dextrorotatory, the angle of rotation varying from +8° to +24°, in a 100 mm. tube at 25° C. Evaporate in a tared dish on a water bath about 2 Gm. of the Oil, accurately weighed, until the odor has completely disappeared; a soft green residue remains, corresponding to not more than 6 per cent. of the Oil (*fixed oils*). To 2 Gm. of Oil of Bergamot add 10 cc. of half normal alcoholic potassium hydroxide, free from chloride, evaporate to dryness and incinerate. Extract the ash with distilled water and acidify with diluted nitric acid; no cloudiness is produced on the addition of silver nitrate T.S. (*chlorinated compounds*).

"**Assay.**—To 2 Gm. of the Oil add 20 cc. of half-normal alcoholic potassium hydroxide, and heat the mixture in a flask on a water bath, under a reflux condenser, for a half hour. Cool the mixture, add 100 cc. of distilled water and titrate with half-normal sulphuric acid, using phenolphthalein T.S. as indicator. Not more than 12.6 cc. of half-normal sulphuric acid is required, corresponding to not less than 36 per cent. of ester, calculated as linalyl acetate, in the Oil. Each cc. of half-normal potassium hydroxide consumed corresponds to 0.09808 Gm. of ester, calculated as linalyl acetate.

"Preserve it in small, amber-colored, well-stoppered bottles in a cool place, protected from light." *N. F.*

The oil of bergamot contains limonene, dipentene, linalool, a solid greasy compound called *bergaptene*, or *bergamot camphor*, and linalool acetate, which latter makes up about 40 per cent. of the expressed oil, but is decomposed in large part by the process of steam distillation. Bergaptene has been very fully studied by Pomeranz. (*M. Chem.*, 1891, 379.) It melts at 188° C., and has the composition $C_{12}H_8O_4$, being the lactone or inner anhydride of *bergaptenic acid*, $C_{12}H_{10}O_5$. By fusion with potassium hydroxide, bergaptene yields phloroglucin. (See *Schim. Rep.*, April, 1893, and 1895, 24; also *Proc. A. Ph. A.*, 1897, 630.) The oil is distinguished from lemon and orange oils by readily dissolving in solution of potassium hydroxide and forming with it a clear solution.

Though possessed of the stimulant properties of the volatile oils in general, it is employed chiefly as a perfume. According to Galewsky (*Ph. Ztg.*, 1915, lx, p. 55), the oil of bergamot is an extraordinarily active insecticide and useful to protect the body against lice and other vermin.

It is often adulterated. (See *C. D.*, 1908, 383; also 1910, 52.)

Off. Prep.—Spiritus Odoratus, *N. F.*

OLEUM BETULÆ EMPYREUMATICUM RECTIFICATUM. N. F.

RECTIFIED OIL OF BIRCH TAR Ol. Bet. Empyr. Rect.

"The pyroligneous oil obtained by the dry distillation of the bark and wood of *Betula alba* Linné (Fam. *Betulaceæ*), rectified by steam distillation." *N. F.*

Rectified Empyroligneous Oil of Birch; Oleum Rusci Rectificatum; Oleum Muscoviticum; Pix Betulina; Oleum Fagi; Oleum Betulinum; Lithanei Balsamum; Dagget; Birkentheer, Birkenöl, *G.*

From the bark of the European white birch there is obtained, especially in Russia, by a process of destructive distillation a tar-like product. From this by distillation is obtained the liquid recognized by the N. F. It is, however, not certain whether the rectification has removed some of the valuable constituents. (For description of the white birch, see *Betula*, Part II).

Description and Physical Properties.—"Rectified Oil of Birch Tar is a limpid, dark brown liquid having a penetrating, empyreumatic odor resembling that of Russia leather. It yields clear solutions with 3 volumes of dehydrated alcohol, and with ether, chloroform, glacial acetic acid, amyl alcohol, oil of turpentine, benzene or carbon disulphide. When mixed with 3 volumes of alcohol or purified petroleum benzin, the solution is not more than slightly turbid, but a decided turbidity is produced when mixed with the same volume of methyl alcohol.

"Specific gravity: 0.886 to 0.950 at 25° C. Warm 2 cc. of the Oil with 10 cc. of distilled water, agitate and allow the mixture to cool; separate and filter the aqueous liquid. The filtrate is colorless, has a strong, empyreumatic odor and an acid reaction. Add two drops of potassium dichromate T.S. to 4 cc. of the aqueous filtrate; it produces a bright yellow solution which soon becomes darker and turbid. Add one drop of dilute ferric chloride solution (1 in 100) to 4 cc. of the filtrate; it produces a green coloration which changes to brown and becomes turbid (distinction from *oil of cade*)." *N. F.*

It contains guaiacol, creosol, cresol, xylenol and traces of phenol. Dutch and German *oil of birch* are quite different from the Russian oil. (See *P. J.*, xv, 769.)

Uses.—This oil has been found useful as a local application in *chronic eczema* and other *skin diseases* in strengths varying between 1 and 20 per cent. Its medicinal properties closely resemble those of oil of cade. (See *Oleum Cadini.*)

Off. Prep.—Unguentum Resorcinolis Compositum. *N. F.*

OLEUM CADINUM. U. S., Br.

OIL OF CADE Ol. Cadin. [Cade Oil, Oleum Juniperi Empyreumaticum]

"The empyreumatic volatile oil obtained from the wood of *Juniperus Oxycedrus* Linné (Fam. *Pinaceæ*)." *U. S.* "Oil of Cade is an empyreumatic oily liquid obtained by the destructiye distillation of the woody portions of Juniperus Oxycedrus, *Linn.*" *Br.*

Oil of Juniper Tar; Juniper Tar Oil; Huile de Cade, *Fr.*; Kadeöl, Kadiöl, *G.*

The *Juniperus Oxycedrus* Linné, *prickly cedar*, or *large brown-fruited juniper*, is a common tree in the waste places and stony hill-sides of the Mediterranean districts of northern Africa, Spain, Portugal, and France, reaching up in its distribution as high as 3000 feet in the Apennines. It commonly attains a height of from ten to twelve feet, with long spreading branches and slender drooping branchlets, covered with light-green scattered and spreading leaves of medium size, lanceolate or awl-shaped, sharply pointed, having two white lines on their upper surface. The fruits are numerous, large (one-fourth to one-third of an inch in diameter), globular, shining, reddish or chestnut-brown, and marked on the apex with three white scars indicating the separation of the carpels.

From the heart wood of this tree the oil of cade is prepared by destructive distillation. Pieces of the wood are placed on a concave slab from the center of which a pipe leads downward and over them is inverted an iron pot and heated by means of small pieces of the wood. According to Huerre (*J. P. C.*, 1921, xxiii, p. 441) in this process much of the volatile oil of the wood is distilled over—some after partial decomposition—which acts as a solvent for the heavier tar-like bodies.

Oil of cade is a brown liquid, much more mobile and less thick than tar, having a tar-like but distinct odor, and a smoky, acrid, bitterish, disagreeable taste. In mass it is dark and opaque, but in very thin layers clear.

Description and Physical Properties.—"A dark brown, clear, thick liquid, having a tarry odor, and a warm, faintly aromatic, bitter taste. The Oil is very slightly soluble in water, but imparts to it an acid reaction shown by moistened blue litmus paper. It is only partially soluble in alcohol and in petroleum benzin, but completely soluble in 3 volumes of ether and soluble in all proportions in amyl alcohol, chloroform, glacial acetic acid, and in oil of turpentine.

"Specific gravity: 0.980 to 1.055 at 25° C. Shake 1 part of Oil of Cade with 20 parts of warm distilled water, and filter: separate portions of 5 cc. each of the aqueous filtrate give a red coloration with 3 drops of ferric chloride solution (1 in 1000), blacken silver ammonium nitrate T.S. in the cold, and give a red precipitate with alkaline cupric tartrate T.S. on heating. Agitate 1 cc. of Oil of Cade with 15 cc. of purified petroleum benzin, filter the solution, add an equal volume of copper acetate solution (1 in 100), shake the mixture, and allow it to separate. Decant the benzin layer into a test tube, and add to it an equal volume of ether: no intensely green coloration is produced, nor does the liquid become more than light yellow to brown (*rosin* or *rosin oils*)." *U. S.*

"A dark reddish-brown or nearly black, oily liquid. Empyreumatic odor; taste aromatic, bitter and acrid. Specific gravity about 0.990. Soluble in *ether*, and in *chloroform;* partially soluble in cold, almost wholly soluble in hot *alcohol* (90 per cent.); very slightly soluble in *water*, the filtered aqueous solution being almost colorless and acid to *litmus*. Yields no reaction for pine tar when tested as follows: Shake 1 millilitre of the Oil vigorously with 15 millilitres of *petroleum spirit*, and filter; to 10 millilitres of the filtrate add 10 millilitres of *solution of copper acetate*, shake vigorously, and set aside until separation into two layers is complete; 5 millilitres of the upper layer, when mixed with 10 millilitres of *ether*, become pale brownish-yellow, but not green (absence of pine tar)." *Br.*

This oil contains phenols and a sesquiterpene termed *cadinene*, $C_{15}H_{24}$, the latter boiling at from 274° to 275° C., and having a sp. gr. of 0.918 at 20° C., also acetic acid, hydrocarbons boiling from 210° to 400° C., resin phenolic bodies, derivatives of pyrocatechin, such as guaiacol and its ethyl and propyl derivatives, and creosol.

Yaucher recommends acetone for disguising the odor of oil of cade, and proposes an *oil of cade collodion* in which acetone is used to dissolve the pyroxylin instead of the usual solvents. (*C. D.*, 1897, 16.)

Uses.—Oil of cade has been used locally, by the peasantry, in the treatment of the cutaneous diseases of domestic animals almost from time immemorial. More recently it has been largely employed in the treatment of *chronic eczema, psoriasis,* and other skin diseases of man, and has also been found to be an efficient parasiticide in *psora* and *favus*. It is applied, sometimes of full strength, sometimes diluted with a bland oil, well rubbed into the affected parts with the fingers, or with a cloth, and is also made into ointments, and especially into soaps. A glycerite is also prepared. It is very rarely, if ever, used internally, but probably resembles oil of tar in its physiological action.

Dose, one to three minims (0.06–0.2 cc.).

Off. Prep.—Linimentum Saponis Mollis Compositum, *N. F.;* Petroxolinum Cadinum, *N. F.;* Petroxolinum Sulphuratum Compositum, *N. F.;* Unguentum Sulphuris Compositum, *N. F.*

OLEUM CAJUPUTI. U. S., Br.

OIL OF CAJUPUT Ol. Cajup. [Cajuput Oil Oil of Cajeput]

"The volatile oil distilled from the fresh leaves and twigs of several varieties of *Melaleuca Leucadendron* Linné, especially the var. *Cajeputi* (Roxburgh) Niedenzu and the var. *minor* (Smith) Duthie (Fam. *Myrtaceæ*), rectified by steam distillation." *U. S.* "Oil of Cajuput is the oil distilled from the leaves of Melaleuca Leucadendron, *Linn.*, and other species of Melaleuca." *Br.*

Oleum Cajeputi; Essence de Cajeput, Huile volatile de Cajeput, *Fr.;* Cajeputöl, *G.;* Essenza di Cajeput, *It.;* Esencia de Cayeput, *Sp.;* Kayuputieh, *Mal.*

It was long supposed that the *oil of cajuput* was derived only from *Melaleuca Leucadendron*, but it is now well established that it is derived chiefly from one or more varieties of this species. They are trees indigenous to upper India, the Islands of the Indian Ocean, northern Australia, Queensland and New South Wales. (See *The Volatile Oils*, Gildemeister and Hoffmann.)

Stickel of Jena, succeeded in procuring from the leaves of *M. hypericifolia* Sm., cultivated in the botanical garden of that place, a specimen of oil not distinguishable from the cajuput oil of commerce, except by a pale-green color. (*Ann. Pharm.*, xix, 224.)

Melaleuca Leucadendron Linné (*M. Cajuputi* Roxb.)—commonly known as *cajuput tree, punk tree* and *swamp tea tree*—is a large tree with crooked trunk, thick, pale-buff, spongy bark and scattered branches bearing pendulous twigs. The leaves are alternate, elliptic or oblong, when young sericeous, when full-grown smooth, deep green, 3 to 7 nerved, slightly falcate, entire, from three to five inches long, from one-half to three-quarters of an inch broad, and when bruised exhale a strong aromatic odor. The flowers are small, white, varying to pink and purple in Australia, inodorous, sessile, and disposed in terminal and axillary downy spikes, with solitary, lanceolate, three-flowered bracts. The filaments are three or four times longer than the petals, and both are inserted in the rim of the calyx. The oil is obtained from the leaves by distillation. It is prepared chiefly in Amboyna and Bouro, and is exported from the East Indies in glass bottles. The small proportion yielded by the leaves and the extensive use made of it in India render it somewhat costly.

Description and Physical Properties.—"A colorless or yellowish liquid, having a peculiar, agreeable distinctly camphoraceous odor, and an aromatic, slightly bitter taste.

"The Oil is soluble in 1 volume of 80 per cent. alcohol. Specific gravity: 0.912 to 0.925 at 25° C. Optical rotation: does not exceed –4° in a 100 mm. tube at 25° C. Refractive index: 1.4660 to 1.4710 at 20° C. Oil of Cajuput meets the requirements of the test for *heavy metals in volatile oils*.

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

"Green or bluish-green. Agreeable, camphoraceous odor; taste aromatic, bitter and camphoraceous. Specific gravity 0.919 to 0.930; *optical rotation* not more than –4°; *refractive index* at 25° C. 1.460 to 1.467. When 10 millilitres of the Oil are mixed with 4 to 5 millilitres of *syrupy phosphoric acid* in a vessel surrounded by a freezing mixture, and then pressed strongly in a piece of fine calico between folds of blotting-paper, the pressed cake, decomposed by warm *water* in a graduated vessel, yields an oily layer, which, on cooling to 15.5° C., measures not less than 4.5 millilitres (presence of not less than 45 per cent. of cineol)." *Br.*

The U. S. requires the oil to be colorless or yellow, but according to the Br. it has a greenish tint. When it is distilled, a light, colorless liquid first comes over, and afterwards a green and denser one. The green color is due to a salt of copper derived from the vessels in which the distillation is performed, and Guibourt obtained two grains and a half of copper oxide from a pound of the commercial oil. The oil may be obtained colorless by redistillation.

Constituents.—This oil contains as its chief ingredient about from 40 to 65 per cent. of *cajuputol,* which is identical with cineol (see *Eucalyptol*). There is present also a small amount of the solid terpineol, both in the free state and as an acetic ester, also l-pinene and traces of butyric, valeric and benzoic aldehydes (*Schim. Rep.*, April, 1897).

Oil of cajuput is said to be often adulterated with oils derived from other than the official species of *Melaleuca.* Oil of rosemary, and oil of turpentine, impregnated with camphor and colored with the resin of milfoil, are also said to be employed as adulterants. The best test, according to Zeller, is iodine; this, after a moderately energetic reaction, with little increase of temperature and but a slight development of orange vapors, occasions immediate inspissation into a loose coagulum, which soon becomes a dry, greenish-brown, brittle mass.

Uses.—This oil is highly stimulant, producing when swallowed, a sense of heat, with an increased fulness and frequency of pulse, and exciting in some instances profuse perspiration. It is much esteemed by the Malays and other people of the East, who consider it a panacea. Formerly the oil of cajuput was used internally in *chronic rheumatism, low fevers,* and various other complaints, but is rarely employed at present for its alterative effects. It is useful internally as a stimulating expectorant in *chronic laryngitis* and *bronchitis,* and as an anthelmintic especially against the *round worm.* Its most frequent uses, however, are externally in the treatment of various skin diseases. For this latter group of affections it is used for its antiparasitic effect in such diseases as *scabies, tinea versicolor,* etc., and for its stimulating action in *acne rosaceæ, psoriasis,* and other chronic conditions. It is also used externally as a counter-irritant in *chronic rheumatism* and other painful conditions. Like many other essential oils it *relieves toothache* if introduced into the hollow carious tooth.

Dose, from three to ten minims (0.2–0.6 cc.).

Off. Prep.—Linimentum Crotonis, *Br.;* Spiritus Cajuputi, *Br.;* Linimentum Tiglii, *N. F.*

OLEUM CARDAMOMI. N. F.

OIL OF CARDAMOM Ol. Cardam.

"A volatile oil distilled from the seeds of *Elettaria Cardamomum,* (Linné) Maton (Fam. *Zingiberaceæ*)." *N. F.*

This oil has been introduced into the National Formulary as an ingredient of compound spirit of cardamom, which is an ingredient in compound elixir of cardamom. It is also used as a flavor in other elixirs. It is to be regretted that cardamom seeds were not used instead of this oil which is largely adulterated. In fact oil of cardamom has been found in the market made from oils which contain no oil of cardamom whatsoever. The high price of cardamom seeds and the small percentage of volatile oil found in them offers an extraordinary inducement to adulterators. Care must therefore be used to employ only the oil which complies strictly with the requirements of the National Formulary. It is described as follows:

Description and Physical Properties.—"Oil of Cardamom is a colorless or very pale yellow liquid having the characteristic aromatic, penetrating and somewhat camphoraceous odor of cardamom, and a persistent, pungent, and strongly aromatic taste. It is very soluble in alcohol and readily soluble in four volumes of 70 per cent. alcohol, forming a clear solution.

"Specific gravity: 0.924 to 0.947 at 25° C. It is dextrorotatory, the angle of rotation varying from +22° to +44°, in a 100 mm. tube at 25° C.

"Preserve it in small, well-stoppered amber-colored bottles, in a cool place, protected from light." *N. F.*

For further description of this oil see *Cardamomi Semen.*

Oil of cardamom is not used medicinally but solely for pharmaceutical purposes.

Off. Prep.—Spiritus Cardamomi Compositus, *N. F.*

OLEUM CARI. U. S. (Br.)

OIL OF CARAWAY Ol. Cari. [Caraway Oil]

"The volatile oil distilled from the dried ripe fruit of *Carum Carvi* Linné (Fam. *Umbelliferæ*). Oil of Caraway yields not less than 50 per cent. by volume of carvone [$C_{10}H_{14}O$]." *U. S.* "Oil of Caraway is the oil distilled from Caraway Fruit, and rectified." *Br.*

Oleum Carui, *Br.;* Huile volatile de Carvi, *Fr. Cod.;* Essence de Carvi, *Fr.;* Oleum Carvi, *P. G.*; Kümmelöl, Carvon, *G.*

This oil is prepared to a considerable extent by our distillers. The fresh fruit as cultivated in Holland yields nearly 6 per cent. of oil, while the German fruit yields about 4 per cent.

Description and Physical Properties.—"A colorless or pale yellow liquid, having the characteristic odor and taste of caraway.

"The Oil is soluble in 8 volumes of 80 per cent. alcohol, by volume. Specific gravity: 0.900 to 0.910 at 25° C. Optical rotation: varies from + 70° to + 80° in a 100 mm. tube at 25° C. Refractive index: 1.4840 to 1.4880 at 20° C. Oil of Caraway meets the requirements of the test for *heavy metals in volatile oils.*

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

"Colorless or pale yellow. Odor and taste those of Caraway Fruit. Specific gravity 0.910 to 0.920; *optical rotation* + 75° to + 82°; *refractive index* at 25° C. 1.485 to 1.497. Soluble in 1 part of *alcohol* (90 per cent.), and in 10 parts of a mixture of equal volumes of *alcohol* (90 per cent.) and *alcohol* (70 per cent.). When fractionally distilled from a distillation flask at the rate of one drop per second, not less than 50 per cent. distils at a temperature above 200° C." *Br.*

Assay.—"Place 10 cc. of Oil of Caraway, measured from a pipette, in a 100 cc. cassia flask and add 50 cc. of a saturated solution of sodium sulphite, which has been carefully rendered neutral to 2 drops of phenolphthalein T.S. by means of a 5 per cent. sodium bisulphite solution. Heat the mixture in a bath containing boiling water, and shake the flask repeatedly, neutralizing the mixture from time to time by the addition of a few drops of the 5 per cent. sodium bisulphite solution. When no coloration appears upon the addition of a few more drops of phenolphthalein T.S. and heating for fifteen minutes, cool to room temperature, and, when the liquids have separated completely, add sufficient sodium sulphite solution to raise the lower limit of the oily layer within the graduated portion of the neck. Note the volume of the residual liquid. This measures not more than 5 cc., indicating the presence of not less than 50 per cent. by volume of carvone." *U. S.*

For additional tests, see *Schim. Rep.*, 1893, 10; also *Bull. Pharm.*, 1894, 257. Kremers and Schreiner (*Ph. Rev.*, xiv, 67) recommend a method of determining the value of oil of caraway based on the conversion of carvone into its oxime, and the separation of the carvoxime from the terpenes by steam distillation; it is as follows: "To a solution of 10 Gm. of oil, dissolved in 25 cc. of alcohol, 5 Gm. of hydroxylamine hydrochloride and 6.5 Gm. of sodium bicarbonate are added. This mixture is boiled on a water bath for half an hour in a flask connected with a reflux condenser, 25 cc. of water are then added, and the alcohol is distilled off on the water bath. Steam is then passed through the liquid until traces of carvoxime come over. The last portions of the distillate are collected separately in test tubes, and when traces of crystals of carvoxime appear on the surface, the operation is interrupted. The tube of the condenser is washed with a little hot water, and this, as well as the last collected distillate, containing some carvoxime, is returned to the flask. The contents of the flask are allowed to cool, and after the carvoxime has completely solidified, it is removed from the sides of the flask by means of a loop of stiff wire, thrown upon a force filter, washed, and dried by suction. The air-dried carvoxime is transferred to a tared glass dish and heated for 1 hour on a water bath, and when cool, weighed. To the weight thus obtained 0.100 Gm. is added, as this is about the quantity lost during heating. From the weight of the carvoxime that of the carvone may be readily calculated, 164.67 parts of the former corresponding to 149.66 parts of the latter, or the weight of carvoxime obtained, expressed in Gm., when multiplied by 0.9088, gives the weight of the equivalent amount of carvone."

Oil of caraway is essentially a mixture of the ketone carvone—of which it contains from 50 to 60 per cent.—with a terpene formerly called *carvene* but now recognized to be d-limonene. Traces of carvacrol have been also reported. The carvone can be isolated from the oil and prepared in a pure state by taking advantage of the formation of a crystalline compound of carvone and hydrogen sulphide, which can then be decomposed by treatment with alcoholic potassium hydroxide.

Oil of caraway is used to impart flavor to medicines, and to correct their nauseating and griping effects.

Gmeiner (*B. Their. W.*, 1909, p. 695) recommends the use of oil of caraway in the treatment of *scabies*. He employs a solution in castor oil containing five parts of alcohol and oil of caraway in seventy-five parts of castor oil.

Dose, from one to five minims (0.06–0.3 cc.).

Off. Prep.—Pilula Aloes, *Br.;* Elixir Cardamomi Compositum (from Compound Spirit), *N. F.;* Mistura Carminativa, *N. F.;* Spiritus Cardamomi Compositus, *N. F.*

OLEUM CARYOPHYLLI. U. S., Br.

OIL OF CLOVE Ol. Caryoph. [Clove Oil Oil of Cloves]

"The volatile oil distilled from the dried flower-buds of *Caryophyllus aromaticus* Linné (Fam. *Myrtaceæ*). Oil of Clove yields not less than 82 per cent. by volume of eugenol $[C_{10}H_{12}O_2]$." *U. S.* "Oil of Cloves is the oil distilled from Cloves." *Br.*

Huile volatile de Girofle, *Fr. Cod.;* Oleum Caryophyllorum, *P. G.;* Nelkenöl, Eugenol, *G.;* Essenza di garofani, *It.;* Esencia de clavo, *Sp.*

This oil is obtained by distilling cloves with water, to which it is customary to add common salt, in order to raise the temperature of ebullition, and the water should be repeatedly distilled from the same cloves, in order completely to exhaust them. Scharling has found advantage from the application of superheated steam to the distillation of this oil. (*P. J.*, xi, 469.) It is essential also to use the same water over and over again, in order to avoid loss by the solution of the oil in the water. The product of good cloves is about one-fifth or one-ninth of their weight. The oil was formerly brought from Holland or the East Indies, but since the introduction of the Cayenne cloves into our markets the reduced price and superior freshness of the drug have rendered the distillation of oil of clove profitable in this country, and the best now sold is of domestic extraction.

Description and Physical Properties.—"A colorless or pale yellow liquid, becoming darker and thicker by age or exposure to the air, and having the characteristic odor and taste of clove.

"The Oil is soluble in 2 volumes of 70 per cent. alcohol, by volume. Specific gravity: 1.038 to 1.060 at 25° C. Optical rotation: does not exceed –1° 10′ in a 100 mm. tube at 25° C. Refractive index: 1.5300 to 1.5350 at 20° C. The Oil meets the requirements of the test for *heavy metals in volatile oils.* A solution of the recently distilled oil in 70 per cent. alcohol (1 in 2) is slightly acid to moistened blue litmus paper. Shake 1 cc. of the Oil with 20 cc. of hot distilled water: the water shows not more than a scarcely perceptible acid reaction with blue litmus paper. Cool the mixture, and pass the aqueous layer through a wetted filter: the clear filtrate, with 1 drop of ferric chloride T. S. yields only a transient, grayish-green color, but not a blue or violet color (*phenol*).

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light.

"**Assay.**—Place 10 cc. of Oil of Clove, measured from a pipette, in a 100 cc. cassia flask, add 50 cc. of potassium hydroxide T.S., shake the mixture for five minutes, and heat it for ten minutes in a bath containing boiling water. Remove it from the bath, and cool to room temperature. When the liquids have separated completely, add sufficient potassium hydroxide T.S. to raise the lower limit of the oily layer within the graduated portion of the neck, and note the volume of the residual liquid. This measures not more than 1.8 cc., indicating the presence of not less than 82 per cent. by volume of eugenol." *U. S.*

"Colorless or pale yellow when fresh, darkening with age and on exposure to air. Odor and taste those of Cloves. Specific gravity 1.047 to 1.065; *refractive index* at 25° C. 1.528 to 1.540. Soluble in 3 parts of *alcohol* (70 per cent.), the solution yielding a blue color with *T. Sol. of ferric chloride.* When 10 millilitres of the Oil are well shaken with 100 millilitres *of solution of sodium hydroxide,* heated on a water-bath in a flask with a narrow graduated neck, and then allowed to stand, the uncombined oil, cooled to 15.5° C., measures not more than 1.5 millilitres (presence of not less than 85 per cent. of eugenol)." *Br.*

Oil of clove is one of the least volatile of the essential oils and requires for congelation a temperature from –17.8° to –20° C. According to the observations of H. C. Wood, Jr. (*J. A. Ph. A.*, 1920, ix, 878), the solubility of this oil in 70 per cent. alcohol corresponds more nearly with that given in the Br. (1 in 3) than that in the U. S. P. (1 in 2).

Oil of clove contains small amounts of vanillin, methyl alcohol and furfurol, but is mainly composed of an unsaturated phenol termed eugenol—which is now an official product (see *Eugenol*)—and its acetic derivative and a sesquiterpene *caryophyllene.* Eugenol acetyl salicylate has also been reported. The eugenol content is the most important criterion of its quality and purity.

For the estimation of eugenol in the form of its crystalline benzoyl compound, see *A. J. P.*, 1892, 26 and 508; also *Schim. Rep.*, April, 1892, 28. The characteristic aromatic odor of oil of clove is due to *methylamylketone*, $CH_3.CO.C_5H_{11}$, which has been isolated by the chemists of Schimmel & Co., and found to be present only in minute quantity. (*Ph. Rev.*, 1897, 115.)

Uses.—By virtue of its local irritant effect oil of clove stimulates peristalsis and is frequently a useful remedy in the treatment of *flatulent colic.* It is also an active local anesthetic and is a favorite remedy for *toothache;* for this purpose a small pledget of cotton is saturated with oil and inserted into the carious cavity. It is a powerful germicide, far exceeding phenol in activity, but is not frequently used for this purpose because of its irritant properties. Eugenol has been used internally in doses of forty-five grains (3 Gm.) *per diem* as an antiseptic antipyretic. Little, however, is known of its physiological action. According to Leubuscher (*W. M. Bl.*, 1889), it is a feeble local anesthetic. Landis (*T. G.*, 1909, xxxiii, 386) has used oil of clove as a stimulant expectorant in *tuberculosis* and *bronchiectasis* with good results.

Dose, from two to six minims (0.12–0.4 cc.).

Off. Prep.—Elixir Cardamomi Compositum (from Compound Spirit), *N. F.;* Acetum Aromaticum, *N. F.;* Nebula Aromatica, *N. F.;* Spiritus Cardamomi Compositus, *N. F.*

OLEUM CHAULMOOGRÆ. U. S., Br.

CHAULMOOGRA OIL Ol. Chaulmoog.

"The fixed oil expressed from the seeds of *Taraktogenos Kurzii* King (Fam. *Flacourtiaceæ*). The fixed oil from the seeds of certain species of *Hydnocarpus,* when designated as such and when agreeing in physical and chemical characters with Chaulmoogra Oil, may be used in its place." *U. S.* "Chaulmoogra Oil is the fatty oil expressed from the seeds of Taraktogenos Kurzii, *King.*" *Br.*

Oleum Gynocardiæ, Gynocardia oil, Chaulmugra oil.

Under the name of Chaulmoogra Oil there has long been used in southeastern portions of Asia a semi-solid fat produced from the seeds of a tree known by the natives as *Kalaw.*

It was at one time believed that the chaulmoogra oil was derived from *Gynocardia odorata* R. Br., but Desprez in 1899 demonstrated the fallacy of this belief. In the following year Prain attributed the seeds to *Hydnocarpus heterophylla* Bl., which is more properly known as the *Taraktogenos Kurzii* King. (Fam. *Flacourtiaceæ*). In 1922 J. F. Rock (*Bull.* 1057 *U. S. Dept. Agriculture*) published the results of an extensive exploration through Burma and Assam. He found that the seed sold in Burma as from the kalaw was from the fruit not only of *Taraktogenos Kurzii* but also of *Hydnocarpus castanea* Hf. and Th. and perhaps other allied species. He described the *Taraktogenos* as a large tree reaching a height of from 50 to 60 feet, with a smooth pale yellowish bark. The fruits are about the size of a large orange of a light fawn color and velvety, containing numerous seeds irregularly imbedded in the fleshy pulp. The chaulmoogra seeds are brownish yellow, from one to one and a quarter inches long, more or less angular or flattened, and yield upon expression from 25 to 30 per cent., to ether about 50 per cent. of oil.

The process of extracting the oil as reported by Rock is as follows: The seeds are washed, and after drying in the sun, shelled, crushed and submitted cold to hydraulic pressure. The cold drawn oil is then filtered.

Description and Physical Properties.—"A yellow or brownish-yellow liquid, or, at temperatures below about 25° C., a whitish, soft solid. It has a characteristic odor, and a somewhat acrid taste. Chaulmoogra Oil is sparingly soluble in alcohol; soluble in benzene, chloroform, ether, and in petroleum benzin.

"Specific gravity: about 0.950 at 25° C. The specific rotation $[\alpha]_D$ of Chaulmoogra Oil determined at 25° C., in chloroform, containing about 10 Gm. of the Oil in each 100 cc. of the solution, and using a 100 mm. tube, is not less than + 48° and not more than + 60°.

"Dissolve 1 Gm. of the Oil in 15 cc. of a mixture of equal volumes of alcohol and ether, previously neutralized with tenth-normal sodium hydroxide, using 5 drops of phenolphthalein T.S. as indicator, and titrate the solution with tenth-normal sodium hydroxide to the production of a pink color which persists for fifteen seconds: not less than 1.8 cc. and not more than 5 cc. of tenth-normal sodium hydroxide is required (*free acid*). Saponification value: not less than 196 and not more than 213. Iodine value: not less than 98 and not more than 104.

"Preserve in well-closed containers, in a cool place, protected from light." *U. S.*

The Br. describes it as "a brownish-yellow oil or soft fat. Characteristic odor; taste somewhat acrid. Melting point about 22° to 30° C. Specific gravity at 45° C. about 0.940; *saponification value* 198 to 213; *iodine value* 96 to 104; *acid value* 21 to 27. Soluble in *ether,* in *chloroform,* and in *carbon disulphide;* partially soluble in cold *alcohol* (90 per cent.); almost entirely soluble in hot *alcohol* (90 per cent.)." *Br.*

Constituents.—Oil of Chaulmoogra contains small amounts of palmitin and linolein but is made up chiefly of the glycerides of two acids, which do not belong to any of the common types of fatty acids, chaulmoogric and hydnocarpic acid. For our knowledge of these principles, we are chiefly indebted to F. B. Power and his collaborators (*J. Chem. S.*, 1904, lxxxv and 1905, lxxxvii) whose work has been confirmed and extended by Dean and Wrenshall (*J. Am. C. S.*, 1920, xlii, 2626). Both acids are optically active and differ from the ordinary fatty acids in containing a five atom carbon ring with an unstable hydrogen atom. The acids can be readily converted into the ethyl esters, which seem to possess certain therapeutic advantages over chaulmoogra oil, and the mixture of them is official (see *Æthylis Chaulmoogras*).

Chaulmoogric acid, $C_{18}H_{32}O_2$, forms beautiful crystals which melt at 68.5° C. and have an optical rotatory power of +62.1°. Chaulmoogric acid has also been found by Goulding and Akers (*Proc. Chem. Soc.*, 1913, xxix, 97) in the African *gorli seeds*, from *Oncoba echinata* Oliver (Fam. *Flacourtiaceæ*).

Hydnocarpic acid, $C_{16}H_{28}O_2$, also crystallizable, melts at 60° C. and has an optical rotation of +68°.

Sir Leonard Rogers (*Ind. Med. Gaz.*, 1919, liv, p. 165; *Pract.*, 1921, cvii, p. 77) introduced the sodium salts of the fatty acids under the names of *sodium gynocardate* (more properly *sodium chaulmoograte*) and *sodium hydnocarpate*, these having the advantage of being water soluble. He also employed *sodium morrhuate* which, however, is prepared from the unsaturated fatty acid of cod liver oil, not chaulmoogra. (See *Oleum Morrhuæ.*)

It is stated that the seeds of the *Hydnocarpus Wightiana* Blume and of the *H. anthelmintica* Pierre under the name of *lukrabo* are also employed for similar purposes to the chaulmoogra. According to Power (*J. Chem. S.*, 1905, lxxxvii, p. 884), this oil is very similar both in physical properties and chemical composition to the true chaulmoogra oil.

The *Oil of Gynocardia* is optically inactive and contains none of the acids peculiar to the genuine chaulmoogra oil. It consists of glycerides of linolic, palmitic, linolenic, isolinolenic and oleic acids and a phytosterol, as well as a cyanogenetic glucoside, *gynocardin*, $C_{13}H_{19}O_9N$, which resembles amygdalin and which is associated in the seeds with an enzyme, gynocardase. (Power, *J. Chem. S.*, 1905, lxxxvii.)

Uses.—Chaulmoogra oil has been used by the natives of India since time immemorial. An Indian legend relates that a King of Benares, by the name of Rama, some 3000 years ago, afflicted with leprosy retired to the jungles, where he lived largely on the fruit of the Kalaw tree and became cured of his leprosy. In England it is very widely used as a counter-irritant application in *bruises, sprains*, and similar local inflammations both of man and beast as well as in *open sores* and *wounds*. Its most important use, however, is in the treatment of *leprosy*. There seems to be little doubt that it is the most useful remedy known for this intractable infection, indeed many authorities have claimed that it will often produce complete and permanent cures. It should be used freely both internally and externally. Donato (*Leprosy in the Philippines and Its Treatment*, Manila, 1915) believes that its action is due to the stimulation of leucocytosis, but Walker and Sweeny (*J. Inf. D.*, 1920, xxvi) find that it has a powerful germicidal effect on the lepra bacillus. Although the experience of the ancient Indians would seem to demonstrate that the absorption from the alimentary tract can take place sufficiently to exert some beneficial action, all recent writers have preferred the intramuscular injection. The Heiser formula for this injection, at one time largely employed, was as follows: Resorcin 4 Gm., camphor 6 Gm., olive oil 60 cc., chaulmoogra oil 60 cc.; of this solution 1 cc. weekly is the beginning dose, the amount of the injections being gradually increased. Since the work of Power on its chemistry the crude drug has been largely abandoned in favor of the mixed ethyl esters of hydnocarpic and chaulmoogric acids. The advantage of these esters appears to be chiefly in their fluidity. The sodium salts of these acids have also been employed by a number of investigators with favorable results (see *Indian Med. Gaz.*, 1920, lv, pp. 121 to 134). For extensive bibliography of chaulmoogra see Morrow, Walker and Miller (*J. A. M. A.*, 1922, lxxix, 434).

On the ground that both the lepra bacillus and tubercle bacillus are acid-fast organisms, various authors have experimented with the effects of chaulmoogra oil in *tuberculosis*. Kolmer, Davis and Jaeger (*J. Inf. D.*, 1921) found that the oil had no destructive action on the tubercle bacillus and Voegtlein (*J. A. M. A.*, 1921, lxxvii, 1017) found that it was of no value in experimental tuberculosis in the guinea pig. Although some benefit has been reported from the local application in *tuberculous ulcers of the larynx* (see Peers and Shipman, *J. A. M. A.*, 1922, lxxix, 461) it does not appear probable that the drug has any real curative value in tuberculous diseases.

Read (*J. P. Ex. T.*, 1924, xxiv, p. 221) has studied the toxic effects of chaulmoogra on dogs and rabbits. In the former whether given by mouth or by injection it causes vomiting and loss of appetite, which appears to be chiefly of central origin. Large doses also have a marked hemolytic effect. In fatal intoxications there were fatty changes of the liver and evidences of irritation of the kidneys. As far as we know serious poisoning in human beings has not been reported except two cases of fatty embolism of the lung reported by Castel, from hypodermic injection.

Dose, five to ten minims (0.3–0.6 cc.) gradually increased to one fluidrachm (3.75 cc.).

Off. Prep.—Unguentum Chaulmoogræ, *Br.*

OLEUM CHENOPODII. U. S.

OIL OF CHENOPODIUM Ol. Chenopod.
[Oil of American Wormseed]

"The volatile oil distilled with steam from the fresh, over-ground parts of the flowering and fruiting plant of *Chenopodium ambrosioides* var. *anthelminticum* (Linné) A. Gray (Fam. *Chenopodiaceæ*). Oil of Chenopodium yields not less than 65 per cent. of ascaridol [$C_{10}H_{16}O_2$]." *U. S.*

Huile volatile d'Ansérine vermifuge, *Fr. Cod.*; Essence de Chénopode anthelmintique, *Fr.*; Amerikanisches Wurmsamenöl, Chenopodiumöl, *G.*

For description of the plant from which this oil is derived see *Chenopodium*, Part II. The oil is largely distilled in Maryland. It is of a light-yellow color when recently distilled, but becomes deeper yellow and even brownish by age. Its reaction is neutral. It has in a high degree the peculiar odor of the plant.

Description and Physical Properties.—"A colorless or pale yellowish liquid, having a peculiar, disagreeable odor, and a bitter, burning taste.

"The Oil is soluble in not more than 8 volumes of 70 per cent. alcohol, by volume. Specific gravity: 0.955 to 0.980 at 25° C. Optical rotation: varies from –4° to –10° in a 100 mm. tube at 25° C. Refractive index: 1.4723 to 1.4770 at 20° C. The Oil meets the requirements of the test for *heavy metals in volatile oils.*

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

Assay.—"Place 10 cc. of Oil of Chenopodium, measured from a pipette, in a 100 cc. cassia flask, add 50 cc. of a solution of acetic acid, made by diluting 60 cc. of glacial acetic acid with distilled water, to measure 100 cc. Shake the mixture well, add sufficient of the acetic acid solution to raise the lower limit of the oily layer within the graduated portion of the neck, and allow the liquids to separate, rotating the flask from time to time. Note the volume of the oily layer. It measures not more than 3.5 cc., indicating the presence of not less than 65 per cent. by volume of ascaridol." *U. S.*

This assay process was suggested by Nelson (*J. A. Ph. A.*, 1921, x, 836).

In 1907 Kremers, in attempting the fractional distillation of oil of chenopodium, found that a large part consisted of a liquid which could not be distilled because it underwent an explosive decomposition when heated. Schimmel and Co. (*Schim. Rep.*, April, 1908) succeeded in isolating this fraction by distillation at reduced pressure and gave to it the name of ascaridol. *Ascaridol,* which makes up from 45 to 70 per cent. of the oil, is an unstable organic peroxide which, according to Wallach, is neither an alcohol, ketone, aldehyde or acid. It has the formula $C_{10}H_{16}O_2$: a specific gravity of 0.9985 at 20° C. and is lævorotatory. It is liable to explode with considerable violence, either when heated or by treatment with certain organic acids. Henry and Paget (*J. Chem. Soc.*, 1921, cxix, 1714) find the oil consists of at least 60 per cent. of ascaridol with about 5 per cent. of the corresponding glycol and 30 to 40 per cent. of a mixture of hydrocarbons made up approximately of cymene 15 per cent., α-terpinene, and a new lævorotatory terpene 10 per cent. They report also minute traces of butyric acid and less than 0.5 per cent. of methyl salicylate.

The conclusion of Nelson (*J. Am. C. S.*, 1920) that ascaridol is the active principle of the oil of chenopodium, although called into question by Hall and Hamilton (*J. P. Ex. T.*, 1918, xi, 231) has been confirmed by Molloy (*J. P. Ex. T.*, 1923, xxi, 390) and by Smillie and Pessoa (*J. P. Ex. T.*, 1924, xxiv, 359) and is generally accepted.

Uses.—The oil of chenopodium is used in medicine almost exclusively as an anthelmintic. Although it has been official in the Pharmacopœia for many years, it owes its modern popularity to the investigations of Brunning. (*Z. E. P. T.*, 1905, i, and 1906, iii, p. 564). This author showed that one part in five thousand paralyzed, although it did not kill, the round worm of dogs, and that one part in two hundred had a distinct antiseptic action. In mammals, if given in sufficient dose, it depresses the spinal cord and finally kills by arrest of respiration. According to Salant and Livingston (*A. J. Phys.*, 1915, xxxviii) the oil of chenopodium in doses of 0.02 cc. per kilo, or more, produces a lowering of the blood pressure through a cardiac action and diminution in the amplitude and rate of respiration.

Since the investigations of Brunning oil of chenopodium has been widely used in all sorts of intestinal parasites and with generally satisfactory results. Originally it was employed chiefly against the *ascarides* and still remains the remedy of choice against this parasite, but both Schuffer and Verwoort (*M. M. W.*, 1913, lx, p. 129) and Rousis and Bishop (*J. A. M. A.*, 1920, lxxiv, p. 1768), from comparative studies, range it as more efficient than thymol in uncinariasis. Several authors, including Barnes and Cort (*J. A. M. A.*, August 3, 1918), have also found it useful in the treatment of *amebic dysentery.*

While with proper care oil of chenopodium is a relatively safe anthelmintic, it is not a drug to be used carelessly. In a not inconsiderable proportion of cases mild toxic symptoms occur and Levy (*J. A. M. A.*, 1914, lxiii, p. 1946) has collected from the literature twelve cases of serious poisoning of which nine ended fatally. The smallest dose in this series was four drops three times a day for two days, which caused death in a baby one year old. In another case a child of two recovered from a dose of two teaspoonfuls given in the course of one afternoon. The symptoms of poisoning by oil of chenopodium—which may not appear for several hours after taking the oil—are nausea, vomiting, headache followed by drowsiness, ringing in the ears, and sometimes deafness. In the fatal cases there develop coma and convulsions.

The experiments of Zeigler (*Interstate Med. Jour.*, October, 1917) and of Salant (*J. A. M. A.*, 1917, lxix, p. 2016) show very distinctly an accumulative tendency in the toxicity of this drug. In Salant's experiments an increased sensitiveness to a second dose persisted 5 to 9 days after the first dose. Oil of chenopodium differs from most vermifuges in that its use should not be preceded with a period of starvation. There is no evidence that this preliminary fasting enhances the vermicidal efficiency of the oil and the original observations of Salant that fasting or poorly-nourished animals are more susceptible to the toxic effects have been abundantly confirmed for human beings.

The physiological studies of Salant and of Zeigler show that its toxic effects are partly the result of local irritation, not only of the alimentary tract, but also of the eliminating organs especially of the kidney and liver, and partly due to a direct depressant effect on the circulation and respiration. In the milder cases of chenopodium poisoning the symptoms usually pass off within a few hours spontaneously; in the severe cases circulatory stimulants, especially digitalis, epinephrin and atropin, are recommended.

The *dose* and method of administration of oil of chenopodium differs according to the weight, age and nutritive state of the patient as well as with the type of infection. It is most conveniently administered enclosed in gelatin capsules and should be always followed with a purgative dose of castor oil. For round worm infestation two or three doses of from 3 to 5 minims (0.2–0.3 cc.) each at intervals of one or two hours may be administered to well-nourished adults but in hook worm considerably larger quantities have been used. For children and poorly-nourished persons the doses should be reduced in proportion to the weight. It is important that the dose should be measured by minims and not by drops as the drop is approximately equal to one-half minim.

OLEUM CINNAMOMI. U. S., Br.

OIL OF CINNAMON Ol. Cinnam.
[Oleum Cassiæ, U. S. IX]

"The volatile oil distilled from the leaves and twigs of *Cinnamomum Cassia* (Linné) Blume (Fam. *Lauraceæ*), rectified by steam distillation. Oil of Cinnamon yields not less than 80 per cent. by volume of cinnamic aldehyde [C_9H_8O]." *U. S.* "Oil of Cinnamon is the oil distilled from Cinnamon Bark." *Br.*

Essence de Cannelle, Huile volatile de Cannelle, *Fr.;* Oleum Cinnamomi, *P. G.;* Zimmtöl, Zimmtkassienöl, *G.;* Essenza di Cannella, *It.*

There are two oils of cinnamon in commerce, one procured from the Ceylon cinnamon, the other from the Chinese cinnamon, and often distinguished by the name of *oil of cassia.* There is no essential difference in the two oils, and that of the Chinese cinnamon, as much the cheaper and more abundant of the two, will probably continue to be generally employed, notwithstanding that the Ceylon product has the finer flavor. The U. S. P. X and the German Pharmacopœia recognize as oil of cinnamon only that obtained from cassia. The British Pharmacopœia and French Codex make Oil of Ceylon Cinnamon official. The oil of the Br. has a lower specific gravity and a lower content of cinnaldehyde than the U. S.

Oil of Chinese Cinnamon.—*Cassia oil* is imported from Canton and Singapore it is pale yellow, becoming red with age. Its flavor is similar to that of the Ceylon oil, though inferior, and it commands a much lower price.

The researches of Schimmel & Co. seem to show that the Chinese cassia oil of commerce is distilled from the leaves, leaf-stalks, and young twigs of the cassia plant—probably with broken bark and various refuse products from the tree; also that much of the oil is adulterated with rosin and petroleum. Besides cinnamic aldehyde cinnamyl acetate and cinnamic acid are also present as well as small amounts of phenylpropyl acetate and orthocumaric aldehyde.

In the distillation by Schimmel & Co. the various portions of the cassia plant obtained from China yielded the following results. 1. Cassia bark (*Cassia lignea* of commerce): yield of essential oil 1.5 per cent.; aldehyde in oil 92 per cent.; sp. gr. 1.035. 2. Cassia buds (*Flores Cassiæ* of commerce): yield of essential oil 1.550 per cent.; aldehyde in oil 80.4 per cent.; sp. gr. 1.026. 3. Cassia budsticks: yield of essential oil 1.64 per cent.; aldehyde in oil 92 per cent.; sp. gr. 1.046. 4. Cassia leaves, leaf-stalks, and young twigs mixed: yield of essential oil 0.77 per cent.; aldehyde in oil 93 per cent.; sp. gr. 1.055. Zeller states that oil of cassia is heavier, less liquid, and sooner rendered turbid by cold, and that in the Ceylon oil, iodine dissolves rapidly, with a considerable increase of heat, and the production of a tough residue, like an extract, while in oil of cassia and reaction is slow, quiet, and with little heat, and the residue is soft or liquid.

Description and Physical Properties.—"A yellowish or brownish liquid, becoming darker and thicker by age or exposure to the air, and having the characteristic odor and taste of cassia cinnamon.

"The Oil is soluble in an equal volume of alcohol, in 2 volumes of 70 per cent. alcohol, by volume, and in an equal volume of glacial acetic acid. Specific gravity: 1.045 to 1.063 at 25° C. Optical rotation: varies from $+1°$ to $-1°$ in a 100 mm. tube at 25° C. Refractive index: 1.6020 to 1.6060 at 20° C. A solution of the recently rectified oil in 70 per cent. alcohol (1 in 2) is slightly acid to moistened blue litmus paper. The Oil meets the requirements of the test for *heavy metals in volatile oils.* Shake 2 cc. of the Oil in a test tube with from 5 to 10 cc. of purified petroleum benzin, allow the liquids to separate, and decant the benzin layer into another test tube: this liquid is but slightly colored, and does not assume a green color upon shaking with an equal volume of copper acetate solution (1 in 1000) (*rosin* or *rosin oils*). Rinse the interior surface of a well-cleaned, 1000 cc. beaker with distilled water, and pass the washings through a small filter until the addition of 1 drop of silver nitrate T.S. to a portion of the filtrate, acidulated with 1 drop of nitric acid, shows no turbidity. Place 3 or 4 drops of the Oil on a clean watch glass supported on a triangle, ignite, and immediately cover with the moistened beaker. Wash the products of combustion from the sides of the beaker through the washed filter with from 10 to 20 cc. of distilled water, and acidulate the filtrate with 1 drop of nitric acid: the addition of 1 drop of silver nitrate T.S. produces no turbidity (*chlorinated products*).

"Preserve in well-stoppered, amber-colored bottles, in a cool place protected from light.

"**Assay.**—Proceed as directed under *Oleum Cari,* using 10 cc. of Oil of Cinnamon, measured from a pipette. The volume of the residual oily layer measures not more than 2 cc., indicating the presence of not less than 80 per cent. by volume of cinnamic aldehyde." *U. S.*

H. C. Wood, Jr. (*J. A. Ph. A.*, 1920, ix, 878) finds the solubility of oil of cinnamon in 70 per cent. alcohol is much less than that stated in the Pharmacopœia.

Oil of Ceylon Cinnamon.—Oil of cinnamon of Ceylon is distilled from inferior grades of bark, of insufficient value to pay the export duty. The following account of the method of extraction is given by Marshall. The bark, having been coarsely powdered, is macerated for two days in sea water, and then submitted to distillation. A light and a heavy oil come over with the water, the former of which separates in a few hours and floats upon the surface, the latter falls to the bottom of the receiver, and continues to be deposited for ten or twelve days. In future distillations, the saturated cinnamon water is employed with sea water to macerate the cinnamon. Eighty pounds of the freshly prepared bark yield about 2.5 ounces of the lighter oil, and 5.5 of the heavier.

Oil of Ceylon cinnamon is of a light-yellow color, becoming deeper by age, and ultimately red. Pereira stated that the London druggists redistilled the red oil, and thus obtained two pale-yellow oils, one lighter and the other heavier than water, with a loss of about 10 per cent. in the process. The oil has the flavor of cinnamon, and when undiluted is excessively hot and pungent. It is said sometimes to have a peppery taste, ascribable to an admixture of the leaves with the bark in the preparation of the oil. Oil of Ceylon cinnamon has a slightly acid reaction. Cinnamic aldehyde is the chief constituent, but eugenol is present to the extent of over 5 per cent., and phellandrene has also been reported.

The British Pharmacopœia gives the following description and tests: "Yellow when freshly distilled, gradually becoming reddish. Odor and taste those of Cinnamon Bark. Specific gravity 1.000 to 1.030; *optical rotation* –0.5° to –1°; *refractive index* at 25° C. 1.565 to 1.580. Soluble in from 3 to 4 parts of *alcohol* (70 per cent.). 1 drop dissolved in 5 millilitres of *alcohol* (90 per cent.) assumes a pale green, but not a blue or brown coloration, on the addition of 1 drop of *T. Sol. of ferric chloride* (absence of cinnamon leaf oil and cassia oil). Contains from 55 to 65 per cent. of cinnamic aldehyde as determined by the following test: To 10 millilitres of the Oil add 70 millilitres of an aqueous solution (1 in 5) of *sodium sulphite* and sufficient *solution of phenolphthalein* to give a well marked pink coloration. Heat the mixture on a water-bath, shake well, and neutralise with *acetic acid* diluted with twice its volume of *water;* repeat the heating and neutralisation until no further pink coloration is developed, the time occupied being from thirty to forty-five minutes. The oily layer which separates on standing, cooled to 15.5° C., measures not more than 4.5 or less than 3.5 millilitres (presence of 55 to 65 per cent. of cinnamic aldehyde)." *Br.*

The *cinnamon leaf oil,* as formerly imported into Great Britain, was of two kinds, one containing a considerable quantity of a fatty fixed oil, perhaps cinnamon-suet from the fruit, the other a pure volatile oil. The oil was said to be obtained by distilling the leaves after maceration in sea water. Cinnamon leaf oil contains much eugenol and very little cinnamic aldehyde, safrol and benzaldehyde being present as minor constituents. It resembled the oil of clove and pimento in sensible properties, having a brownish color, a penetrating, fragrant odor, and a very pungent taste. Schimmel & Co. found it to have a sp. gr. 1.056 to 1.060, and contained 87 per cent. of eugenol, and about 0.1 per cent. of cinnamic aldehyde.

When exposed to the air oil of cinnamon absorbs oxygen, and is slowly converted into cinnamic acid, two distinct resins, and water. Of the two resins, one is soluble both in hot and in cold alcohol; the other readily in the former, but sparingly in the latter. Oil of cinnamon is almost wholly converted by nitric acid, slowly added, into a crystalline mass, producing a compound of the oil and the acid. These several facts are explained when it is found that oil of cinnamon contains from 75 to 90 per cent. of *cinnamic aldehyde.*

Cinnamic aldehyde, C_9H_8O, was official in the U. S. VIII under the title *Cinnaldehydum.* "It is a colorless liquid, having a cinnamon-like odor and a sharp, burning, aromatic taste. Specific gravity about 1.047 at 25° C. Optically inactive. It boils at about 250° C., with partial decomposition. Cinnamic aldehyde should partially solidify when the temperature is reduced by a freezing mixture of ice and salt and should melt again at 7.5° C. It is sparingly soluble in water, soluble in all proportions in alcohol, ether, and fixed and volatile oils." *U. S. VIII.* By moderate oxidation it yields the corresponding cinnamic acid, but by more energetic oxidation yields benzoic acid. Cinnamic aldehyde has been produced artificially by Strecker from styrone, a derivative from styrax (see *Styrax*), and more recently from benzaldehyde and acetaldehyde, a mixture of which is saturated with hydrochloric acid gas, when a condensation takes place, as follows:

$$C_6H_5COH + CH_3COH = C_6H_5.CH : CH.CHO + H_2O$$

Ordinary sodium hydroxide will also bring about the reaction between the two aldehydes, and is to be preferred to hydrochloric acid for this purpose.

Uses.—Although a very powerful germicide the oil of cinnamon, because of its irritant properties, is rarely used in medicine as an antibacterial. It has the cordial and carminative properties of cinnamon, without its astringency, and is much employed as an adjuvant to other medicines, the taste of which it corrects or conceals, while it conciliates the stomach. As a powerful local stimulant, it is sometimes prescribed in *gastrodynia, flatulent colic,* and *gastric debility.* Drummond (*B. M. J.,* 1918) states that it is useful as an internal remedy in *coryza.* Mitscherlich found six drachms to kill a moderate-sized dog in five hours, and two drachms one in forty hours. Inflammation and corrosion of the gastro-intestinal mucous membrane were observed after death.

Dose, one to three minims (0.06–0.2 cc.).

Off. Prep.—Aqua Cinnamomi, *U. S.;* Spiritus Cinnamomi, *U. S., Br.;* Elixir Cardamomi Compositum (from Compound Spirit), *N. F.;* Elixir Vanillini Compositum (from Compound Spirit), *N. F.;* Mistura Oleo-Balsamica, *N. F.;* Nebula Aromatica, *N. F.;* Nebula Mentholis Composita, *N. F.;* Spiritus Cardamomi Compositus, *N. F.;* Spiritus Vanillini Compositus, *N. F.;* Odontalgicum, *N. F.*

OLEUM COPAIBÆ. Br.

OIL OF COPAIBA

Oil of Copaiva; Oleum Balsami Copaivæ; Essence de Copahu, *Fr.;* Copaivaöl, *G.*

Oil of copaiba is no longer official in the U. S. P. The oil constitutes from one-third to one-half of the Maracaibo copaiba and from one-half to three-fourths of the Para copaiba. It is prepared largely by steam distillation. As it first comes over it is colorless, but the later product is of a fine greenish hue. By redistillation it may be rendered wholly colorless. It has the odor and taste of copaiba, a neutral reaction, solidifies, partly crystalline, at –26.1° C. (Gmelin), is soluble in ether and in an equal weight of absolute alcohol. The oil consists chiefly of caryophyllene. "Colorless or pale yellow. Odor and taste those of Copaiba. Specific gravity 0.896 to 0.910; *optical rotation* –7° to –35°; *refractive index* at 25° C. 1.494 to 1.500. Distils between 250° and 275° C. A solution of 1 millilitre of the Oil in 5 millilitres of *glacial acetic acid* does not develop more than a faint violet coloration on the addition of 4 drops of *nitric acid* (absence of gurjun oil). When distilled in a vacuum the first 10 per cent. of the distillate has an *optical rotation* lower than that of the original Oil (absence of oil of African copaiba)." *Br.*

From its want of oxygen, it answers even better than naphtha for preserving potassium, a fact first observed by Durand, of Philadelphia. It dissolves sulphur and phosphorus.

Its effects on the system are those of copaiba. From the experiments of C. Mitscherlich, it is one of the least injurious of the volatile oils to the animal system, six drachms of it having been introduced into the stomach of a rabbit without causing death. Externally it produces much less irritation than does oil of turpentine. It may be used for the same purposes as copaiba.

Dose, five to fifteen minims (0.3–0.9 cc.).

OLEUM CORIANDRI. U. S., Br.

OIL OF CORIANDER Ol. Coriand. [Coriander Oil]

"The volatile oil distilled from the dried ripe fruit of *Coriandrum sativum* Linné (Fam. *Umbelliferæ*)." *U. S.* "Oil of Coriander is the oil distilled from Coriander Fruit." *Br.*

Essence de Coriandre, *Fr.;* Korianderöl, *G.*

This oil may be obtained by distillation with water from the bruised fruit in the manner directed in the U. S. Pharm. 1870, for volatile oils. The average yield of oil from coriander is from 0.5 to 1 per cent. It boils at about 150° C., and consists chiefly (45 to 65 per cent.) of *coriandrol,* $C_{10}H_{18}O$. According to Semmler (*B. Chem. G.,* xxiv, 206), coriandrol boils between 194° and 198° C., is optically dextrogyrate, and has a sp gr. of 0.8679 at 20° C. Coriandrol is now known as dextrogyrate linalool. The other constituents of oil of coriander are pinene, terpinene, decyl aldehyde, geraniol and borneol. The characteristic odorous principle, or principles, is not known. (See *Schim. Rep.,* April, 1892.)

Description and Physical Properties.—"A colorless or pale yellow liquid, having the characteristic odor and taste of coriander.

"The Oil is soluble in 3 volumes of 70 per cent. alcohol, by volume. Specific gravity: 0.863 to 0.875 at 25° C. Optical rotation: varies from +8° to +13° in a 100 mm. tube at 25° C. Refractive index: 1.4630 to 1.4760 at 20° C. Oil of Coriander meets the requirements of the test for *heavy metals in volatile oils.*

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

"Colorless or pale yellow. Odor and taste those of Coriander Fruit. Specific gravity 0.870 to 0.885; *optical rotation* +8° to +14°; *refractive index* at 25° C. 1.463 to 1.467. Soluble in 3 parts of *alcohol* (70 per cent.)." *Br.*

Oil of coriander is extensively adulterated with colorless rectified oil of orange, which can be detected by its insolubility in 90 per cent. alcohol, in which pure coriander oil dissolves in every proportion; equal parts of oil of orange and 90 per cent. alcohol make a turbid mixture. The oil has the medicinal properties of the fruit, and, like the aromatic oils generally, may be used to cover the taste or correct the nauseating or griping properties of other medicines. It has the great advantage of being more stable and retaining its agreeable odor longer than any other oil of its class.

Dose, one to three minims (0.06–0.2 cc.).

Off. Prep.—Spiritus Aurantii Compositus, *U. S.;* Elixir Aromaticum (from Spirit), *U. S.*

OLEUM CUBEBÆ. Br.

OIL OF CUBEBS

"Oil of Cubebs is the oil distilled from Cubebs." *Br.*

Oleum Cubebarum; Cubeb Oil; Huile volatile (Essence) de Cubèbe, *Fr.;* Kubebenöl, *G.*

The oil is obtained from cubeb by grinding the berries, and then distilling with water. The yield is from 10 to 18 per cent. When recently distilled from the fruit, the oil is somewhat greenish, becoming yellowish by age, but when carefully redistilled it is colorless. It has the odor of cubeb, a warm, aromatic, camphoraceous taste, and a neutral reaction, is of a consistence approaching that of almond oil, is lighter than water, and when exposed to the air is said to thicken without losing its odor.

"Colorless, pale green, or greenish-yellow. Odor and taste those of Cubebs. Specific gravity 0.910 to 0.930; *optical rotation* −25° to −40°; *refractive index* at 25° C. 1.486 to 1.500. Not less than 60 per cent. distils between 250° and 280° C." *Br.*

The oil consists chiefly of sesquiterpenes which distil over between 250° and 280° C., one of which is cadinene, $C_{15}H_{24}$, with some dipentene, and probably pinene or camphene. Upon standing, it sometimes deposits rhomboidal prismatic crystals of a stearopten. The *camphor of cubeb* is a crystalline substance having the formula $C_{15}H_{26}O$, is fusible at from 66° to 68° C., and volatilizes without change at from 148° to 150° C. It appears to occur only in old specimens of the oil and is probably a product of the oxidation of a sesquiterpene.

The oil has the aromatic properties of cubeb, but it is much less pungent than the fluidextract or the oleoresin and does not, therefore, completely represent the crude drug. It may, however, often be advantageously substituted for the powder, the dose to be gradually increased until its effects are obtained, or until it proves offensive to the stomach. It may be given suspended in water by means of sugar, in the form of emulsion, or enclosed in capsules of gelatin.

Dose, five to fifteen minims (0.3–0.9 cc.).

OLEUM EUCALYPTI. U. S., Br.

OIL OF EUCALYPTUS Ol. Eucalypt.

[Eucalyptus Oil]

"The volatile oil distilled from the fresh leaves of *Eucalyptus Globulus* Labillardière, and from some other species of *Eucalyptus* (Fam. *Myrtaceæ*). Oil of Eucalyptus yields not less than 70 per cent. of eucalyptol (cineol) [$C_{10}H_{18}O$]." *U. S.* "Oil of Eucalyptus is the oil distilled from the fresh leaves of Eucalyptus Globulus, *Labill.,* Eucalyptus dumosa, *A. Cunn.,* and other species of Eucalyptus, and rectified." *Br.*

Oil of Eucalyptus Globulus; Huile volatile (Essence) de Eucalyptus, *Fr. Cod.;* Eucalyptusöl, *G.;* Esencia de eucalipto, *Sp.*

Various species of the genus *Eucalyptus,* grown in Australia and Algeria, yield volatile oils in sufficient quantity to be commercial products. There are more than one hundred different kinds of eucalyptus oil known. These are classified according to the predominant constituent as follows: Eucalyptus-pinene oils of which fifty-one varieties have been described; eucalyptus-pinene oils containing no phellandrene, of which there are seven varieties; pinene-sesquiterpene oils, containing no phellandrene, of which there are fourteen varieties; oils containing *aromadendral* but no phellandrene of which there are nine varieties; phellandrene containing oils with *piperotone* present, of which there are eleven varieties; phellandrene containing oils with sesquiterpene present, of which there are twenty-two varieties and unclassified oils containing geraniol and its acetic ester, citral, citronellal, etc., of which there are four varieties.

Aromadendrol is an aldehyde-like body which Baker and Smith reported along with *australol,* a phenolic compound. (*Ph. Ztg.,* 1922, lxvii, 611.) *Cryptol,* a lævorotatory compound, is responsible for the optical activity of certain eucalyptus oils according to Read and Smith. These oils differ radically in therapeutic properties (see *Eucalyptus*). The oils officially intended are those containing preponderating proportions of cineol. There are very few species which produce an oil as rich in cineol as required by the U. S. X (70 per cent.) but the standard of the Br. is considerably lower (55 per cent.). Oils reaching the latter figure have been distilled from the *E. incinata* Turcz., and *E. cneorifolia* DC., in addition to those named by the Pharmacopœia. The oils from *E. odorata* Behr. and *E. amygdalina* Labill. also yield oils fairly rich in cineol but rarely, if ever, reach the proportion official.

Description and Physical Properties.—"A colorless or pale yellow liquid, having a characteristic, aromatic, somewhat camphoraceous odor, and a pungent, spicy, cooling taste.

"The Oil is soluble in 4 volumes of 70 per cent. alcohol, by volume. Specific gravity: 0.905 to 0.925 at 25° C. Optical rotation: varies from −10° to +10° in a 100 mm. tube at 25° C. Refractive index: 1.4600 to 1.4690 at 20° C. A solution of the recently distilled Oil in 70 per cent. alcohol (1 in 4) is neutral to moistened litmus paper. Mix 2 cc. of Oil of Eucalyptus with 4 cc. of glacial acetic acid, and gradually add 3 cc. of a 20 per cent. aqueous solution of sodium nitrite. When the mixture is gently stirred with a glass rod, crystals of phellandrene nitrite do not form (*eucalyptus oils containing large amounts of phellandrene*). The Oil meets the requirements of the test for *heavy metals in volatile oils.*

"The congealing point of Oil of Eucalyptus does not fall below −15.4° C. as determined by the method described on page 1536.

"Preserve it in well-stoppered amber-colored bottles in a cool place protected from light." *U. S.*

"Colorless or pale yellow. Aromatic, camphoraceous odor; taste pungent, leaving a sensation of cold. Specific gravity 0.910 to 0.930; *optical rotation* −10° to +10°. Soluble in 5 parts of *alcohol* (70 per cent.). Contains not less than 55 per cent. by volume of cineol as determined by the process described under 'Oleum Cajuputi.' When 1 millilitre is mixed with 2 millilitres of *glacial acetic acid* and 5 millilitres of *petroleum spirit,* 2 millilitres of a saturated aqueous solution of *sodium nitrite* being added, and the mixture gently shaken, no crystalline precipitate forms in the upper layer (absence of oils containing much phellandrene)." *Br.*

Assay.—The assay of oil of eucalyptus for its cineol content has long been a matter of research. The earlier methods depended upon fractional distillation, freezing the proper fraction and subsequently weighing the crystallized cineol. Later a method was used in which strong phosphoric acid was added to the oil. This produced a crystalline magma of cineol phosphate, which was collected, pressed between sheets of filter paper and subsequently decomposed with hot water in a graduated tube which enabled the proportion of separated cineol to be read off. This was the test used in the U. S. P. VIII. This test was subsequently changed by the substitution of arsenic acid for the phosphoric acid previously used, the cineol arsenate being believed to be more easily separated and purified. This was known as Turner and Holmes' modification. (*Perf. and Essent. Oil Rec.,* 1915, p. 21.)

Schimmel and Co. later recommended the use of a cassia flask and the absorption of the cineol by a 50 per cent. aqueous solution of resorcinol. Still another method was proposed by Dodge in which potassium permanganate was employed as the reagent.

Parry reviewed the arsenic acid method and condemned it as not satisfactory as to its accuracy.

The U. S. P. Revision Committee, finding no method of assay for cineol that can be considered reliable, has included none in the tenth revision, simply relying on the congealing point of the oil for an approximate idea of its value.

The assay process of the U. S. IX was as follows: "Measure 10 mils of the Oil, from a pipette, into a round-bottom glass dish of 50 mils capacity, which is embedded in finely broken ice. Add 10 mils of arsenic acid T.S. and stir until precipitation is complete. When the mixture ceases to congeal further, allow it to stand for ten minutes in the ice bath. (If at this point a hard mass is formed, add 5 mils of purified petroleum benzin, and mix the mass well before proceeding with the assay.) Then transfer it immediately to a hardened filter paper, about 18.5 cm. in diameter, by means of a pliable horn spatula; spread it evenly over the surface of the paper and lay a second hardened filter paper over the top. Wrap several thicknesses of absorbent or filter paper around the hardened filters, and place the whole between the plates of a press and bring to bear all the pressure possible for about one minute. Change the outside absorbent papers and press again, repeating the operation, if necessary, until the eucalyptol arsenate is apparently dry, and separates readily when touched with a spatula. The pressing is not complete until a hard mass remains which is broken up with difficulty; and usually two changes of filter paper are required, pressing each time for about two minutes; if left too long in the press the compound may decompose. Now, transfer the compound completely by means of the horn spatula to a glass funnel inserted into a 100 mil cassia flask with a neck graduated to 10 mils into tenths. Wash the last portions of the precipitate into the flask with a stream of hot distilled water from a wash bottle, assisting the disintegration with a glass rod, place the flask in boiling water and rotate it until the compound is thoroughly broken up. Then add enough distilled water to cause the eucalyptol to rise into the neck of the flask, cool it to room temperature and read its volume. This volume, multiplied by 10, shows the percentage of eucalyptol (cineol) in the Oil." *U. S. IX.*

Power has modified the test for phellandrene so as to make it more delicate. According to his directions, 1 cc. of the oil is mixed with 5 cc. of petroleum benzin, 1 or 2 cc. of a concentrated solution of sodium nitrite added, and subsequently glacial acetic acid added, a drop or two at a time, with vigorous agitation after each addition. If phellandrene is present in any considerable amount, its crystalline nitrosite, $C_{10}H_{16}(NO)NO_2$, will separate from the benzin solution.

The oil from *Eucalyptus Globulus* contains pinene, $C_{10}H_{16}$, and *eucalyptol* (or *cineol*). Schimmel & Co. also state (*B. Chem. G.,* April, 1888) that they have obtained several of the aldehydes of the fatty series, notably valeraldehyde, and probably butyraldehyde and capronaldehyde, in their distillation of the oil from *Eucalyptus Globulus.*

Eudesmol, $C_{10}H_{16}O$ (possibly a ketone), is the name given to a crystalline camphor obtained from the oil from *E. piperita* Smith, by H. G. Smith and R. T. Baker. It also occurs in the oil from *E. Globulus.* It is isomeric with camphor, but has its oxygen atom combined in a different way.

Whether or not the medicinal virtues of the official oil are due entirely to its cineol is uncertain, but many prefer to use the pure eucalyptol to the oil itself.

Uses.—Oil of eucalyptus is an active germicide, although surpassed in power by many of the other volatile oils. Cineol is probably a less efficient antibacterial agent than oil of eucalyptus. It is absorbed from the intestinal tract, eliminated partially through the breath to which it imparts its odor, and also, as an oxidation product, through the urine to which it gives an odor resembling that of violets.

A number of cases of poisoning from oil of eucalyptus have been reported. Barker and Rowntree (*J. H. H. B.*, 1918, xxix, 215) have collated 29 cases of eucalyptus poisoning of which 7 were fatal. The smallest fatal dose was 3.5 cc. (57 minims), but doses of 5 fluidrachms and in one case 1 fluidounce were recovered from. The most common symptoms were epigastric burning with nausea and usually vomiting; dizziness and muscular weakness also occurred almost uniformly. The skin was pale, or sometimes cyanotic, the extremities cold, pulse rapid and small, pupils generally much contracted; the intellection almost always affected, in most instances the patients were dazed and usually drowsy. In the very severe types delirium was common and occasionally associated with convulsions. One of the earliest symptoms is a feeling of suffocation. The odor of the drug was strong on the breath, often remaining for one or two days, and was sometimes also perceptible in the urine and feces. There are some people with idiosyncrasies in whom ordinary therapeutic doses give rise to dermatitis.

The oil of eucalyptus is used locally as an antiseptic, especially in the treatment of infections of the upper respiratory tract and in certain forms of *skin disease.* Internally it is used as a stimulating expectorant in *chronic bronchitis* and *tuberculosis.* In these conditions it is also frequently given by inhalation; a few drops of the oil may be added to boiling water and the mixed vapors and steam inhaled. It has been especially praised in *asthma,* given internally or preferably by inhalation by means of cigarettes, which may be made by rolling up the dried leaves, or the vapor from boiling water containing the oil may be inhaled. It is also used as a remedy against the *hookworm,* but is probably of inferior value. It possesses also some antiperiodic power and may be used in *malarial fever* when for any reason quinine or methylthionine are not available.

Dose, three to ten minims (0.2–0.6 cc.), best administered in emulsion.

Off. Prep.—Unguentum Eucalypti, *Br.;* Curatio Paraffini, *N. F.*

OLEUM FŒNICULI. U. S.

OIL OF FENNEL Ol. Fœnic. [Fennel Oil]

"The volatile oil distilled from the dried ripe fruit of *Fœniculum vulgare* Miller (Fam. *Umbelliferæ*). If solid material has separated, carefully warm the Oil until completely liquefied and thoroughly mix it before dispensing." *U. S.*

Huile volatile de Fenouil, *Fr. Cod.;* Essence de Fenouil, *Fr.;* Oleum Fœniculi, *P. G.;* Fenchelöl, *G.*

Fennel seeds yield about 2.5 per cent. or, according to Zeller, from 3.4 to 3.8 per cent., of oil. That used in this country is imported.

Description and Physical Properties.—"A colorless or pale yellow liquid, having the characteristic odor and taste of fennel.

"The Oil is soluble in 8 volumes of 80 per cent. alcohol, by volume, and in 1 volume of 90 per cent. alcohol by volume. Specific gravity: 0.953 to 0.973 at 25° C. Optical rotation: varies from +12° to +24° in a 100 mm. tube at 25° C. Refractive index: 1.5280 to 1.5380 at 20° C. A solution of the recently distilled Oil in 80 per cent. alcohol (1 in 8) is neutral to moistened litmus paper. The Oil meets the requirements of the test for *heavy metals in volatile oils.* The congealing point of Oil of Fennel does not fall below 3° C. when determined by the method described on page 1536.

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

It congeals below 10° C. into a crystalline mass—especially if a small crystal of solid anethol be added—separable by pressure into a solid and a liquid portion, the former heavier than water, and less volatile than the latter, which rises first when the oil is distilled. It contains anethol (see *Oleum Anisi*), usually in amounts of about 60 per cent., d-pinene, phellandrene, dipentene, *fenchone,* $C_{10}H_{16}O$ (a liquid ketone), chavicol, anisic aldehyde, and anisic acid. Fenchone is the constituent which when present gives the disagreeable bitter taste to many of the commercial oils. *Schimmel's Report* for April, 1897, mentions limonene as also at times present as a constituent. The proportion of the different ingredients in oil of fennel varies considerably according to its source. Umney (*Proc. A. Ph. A.*, 1897, p. 516) finds that the Japanese oil contains about 75 per cent. of anethol and 10 per cent. of fenchone. The French (sweet or Roman) oil is practically free from fenchone, that from the Russian and Saxon fruits contains from 18 to 22 per cent. of fenchone. It is slightly dextrogyrate.

Dose, three to five minims (0.2–0.3 cc.).

Off. Prep.—Aqua Fœniculi, *U. S.;* Elixir Anisi, *N. F.;* Elixir Catariæ et Fœniculi, *N. F.;* Mistura Carminativa, *N. F.*

OLEUM GAULTHERIÆ. Br.

OIL OF GAULTHERIA [Oil of Wintergreen]

"Oil of Gaultheria is the oil distilled from the leaves of Gaultheria procumbens, *Linn.*, or from the bark of Betula lenta, *Linn.*" *Br.*

Oil of Teaberry; Huile volatile (Essence) de Winter-green, *Fr. Cod.;* Essence de Gaulthérie, *Fr.;* Wintergrünöl, Bergtheeöl, *G.*

Oil of gaultheria is no longer official in the U. S. P. Under *Methylis Salicylas* the U. S. Pharmacopœia directs that oil of gaultheria and oil of betula or sweet birch may be used.

The volatile oil of gaultheria is largely obtained in the United States by distillation of the plant. It probably does not exist in the plant, but is formed by a reaction between water and a neutral principle analogous to amygdalin, to which Procter has given the name of *gaultherin.* (*A. J. P.*, xv.) This substance, which was called by Schneegans *bétulase,* probably exists in all the numerous plants which yield methyl salicylate on distillation. The oil occurs in various of our native plants, and has been detected in *Polygala paucifolia* Willd., *Spiræa Ulmaria* L., *Spiræa lobata* Jacq., and *Chiogenes hispidula* Torr. and Gray. T. E. de Vrij found it in considerable proportion in the *Gaultheria leucocarpa* Blume. and *G. fragrantissima* Wall., plants which are abundant in the volcanic regions of Java (*A. J. P.*, 1879); while Bourquelot (*C. R. S. B.*, iii, 1896) detected it in *Monotropa Hypopitys* Walt., in *Polygala Senega* L., and in other species of Polygala. (See also *A. J. P.*, 1898, 412.) Much of the so-called oil of wintergreen is obtained from the sweet birch, *Betula lenta* L., which yields a product physically and chemically indistinguishable from methyl salicylate. It is mostly distilled in rather crude receptacles in those parts where the plants are abundant, as the mountains of North Carolina and Tennessee. For description of these stills see *U. S. D.*, 20th ed., p. 764.

Occasionally the oil is very highly colored, and the wholesale dealers have three ways of "cleaning" it—redistillation, filtration, and decolorization. In the last method the oil to be decolorized is put into a bottle, crystals of citric acid are added, and the whole is allowed to stand, agitating occasionally, until the oil is colorless, or nearly so.

Oil of gaultheria when freshly redistilled is nearly colorless, but as found in commerce has a brownish-yellow or reddish color.

"Colorless or nearly colorless. Strong, characteristic odor; taste pungent. Specific gravity 1.180 to 1.187; *optical rotation* at 25° C. 0° to −1°; *refractive index* 1.537 to 1.539. Soluble in 6 parts of *alcohol* (70 per cent.) at 25° C. Contains not less than 99 per cent. of esters, calculated as methyl salicylate, $CH_3C_7H_5O_3$." *Br.*

Cahours found in addition to methyl salicylate a peculiar hydrocarbon, which he called *gaultherilene.* Trimble and Schroeter (*A. J. P.*, 1889, 398) found that the amount of the hydrocarbon *gaultherilene* was about 0.3 per cent. By analysis and vapor density determination they fixed its formula as $C_{15}H_{24}$, but they state that it may consist of a solid and a liquid portion. Power and Kleber (*Fritzsche Bros. Circ.*, No. 7) assert that this hydrocarbon belongs to the paraffin series, and state that it is probably triacontane, $C_{30}H_{62}$. They also find in the oil an aldehyde or ketone, with an odor like enanthic aldehyde, an apparently secondary alcohol, $C_6H_{16}O$, and an ester, $C_{14}H_{24}O_2$. To the alcohol and the ester are attributed the characteristic odor of the oil. True oil of gaultheria contains about 99 per cent. of methyl salicylate. (For methods of distinguishing the natural from synthetic oil see under *Methylis Salicylas.*)

Uses.—The therapeutic properties of this oil are precisely the same as those of methyl salicylate.

Dose, ten to twenty minims (0.6–1.3 cc.).

OLEUM GOSSYPII SEMINIS. U. S.

COTTONSEED OIL Ol. Gossyp. Sem. [Cotton Seed Oil]

"A fixed oil obtained from the seeds of cultivated varieties of *Gossypium herbaceum* Linné, or of other species of *Gossypium* (Fam. *Malvaceæ*)." *U. S.*

Oleum Gossypii; Cotton Oil; Huile de Semences de cotonnier, *Fr.*; Baumwollsamenöl, Baumöl, *G.*

This oil is produced in large quantities by the expression of cotton seed either hot or cold. The annual production amounts to upwards of 230,000,000 gallons. The residue left after the expression of the oil is known as *oil-cake* and is largely used as a food for cattle; the latter sometimes produces toxic effects which is due to the presence of a plant pigment of the phenol group called *gossypol* (see Carruth, *J. Am. Chem. S.*, 1918, xl, p. 647, and Alsberg and Schwartze, *J. P. Ex. T.*, 1921, xvii, p. 344). For a description of the process of extraction, see *A. J. P.*, 1896, 42; also 1898, 497.

This oil is obtained by expression from the seeds previously deprived of their shells. In this state they yield two gallons of oil to the bushel. As first obtained, it is thick and turbid, but it deposits a portion of its impurities on standing.

Besides this crude oil, there are three varieties in commerce, more or less purified, recognized as the *clarified,* the *refined,* and the *winter bleached.* The last mentioned corresponds to the official requirements.

The oil is clarified by first boiling it with water, to separate the mucilage, and then heating it with a weak solution of sodium hydroxide, which combines with the coloring matter and saponifies a part of the oil. The mixture becomes filled with black flecks, which deposit on standing and leave the oil but slightly colored. The loss in refining is usually from 4 to 7½ per cent., but occasionally amounts to 12 or 15.

Among the improvements in the purification of cottonseed oil are the processes of Chisholm using silicate of soda for clarifying and of Baskerville using a paper pulp or cellulose fiber.

The oil is used in the preparations of woollen cloth and morocco leather, and for oiling machinery. It has been found to be an excellent substitute for almond and olive oils in most pharmaceutical preparations in which they are employed, but it does not answer so well in the formation of lead plaster. Citrine ointment carefully prepared with it, too great heat being avoided, retains a rich orange color and proper unctuous consistence.

Cotton-seed oil belongs among the semi-drying group.

Description and Physical Properties.—"A pale yellow, oily liquid. It is odorless or nearly odorless, and has a bland taste. Cottonseed Oil is slightly soluble in alcohol, but is miscible with ether, chloroform, petroleum benzin, and with carbon disulphide.

"Specific gravity: 0.915 to 0.921 at 25° C. At a temperature below 12° C. particles of solid fat separate from the Oil, and at about 0° to –5° C. it becomes solid or nearly so. Dilute Cottonseed Oil with an equal volume of carbon disulphide, and add sulphuric acid (specific gravity 1.6 to 1.7): a reddish-brown color is rapidly produced. Mix 2 cc. of the Oil in a test tube with 2 cc. of a mixture of equal volumes of amyl alcohol and a 1 per cent. solution of precipitated sulphur in carbon di-sulphide, and immerse the test tube to one-third of its depth in a boiling, saturated aqueous solution of sodium chloride: a red color develops in from ten to fifteen minutes. Saponification value: not less than 190 and not more than 198. Iodine value: not less than 105 and not more than 114.

"Preserve in well-closed containers." *U. S.*

As this oil has been much used for adulterating olive oil, tests to distinguish it are very desirable. The test most depended upon is that known as *Halphen's test,* a mixed solution of amyl alcohol and carbon disulphide containing 1 per cent. of dissolved sulphur. This is given in the official test. It is stated that cotton seed oil, which has been heated to 250° C. no longer gives many of the characteristic reactions for detecting the oil.

Cottonseed oil possesses the nutritive and emollient properties of the fixed oils. Its value for some purposes is lessened by its flavor and its tendency to become gummy on exposure to the air.

Dose, two to six fluidrachms (7.5–22.5 cc.).

Off. Prep.—Linimentum Camphoræ, *U. S.;* Linimentum Ammoniæ, *N. F.*

OLEUM GRAMINIS CITRATI. Br.

OIL OF LEMON GRASS

"Oil of Lemon Grass is the oil distilled from Cymbopogon citratus, *Stapf,* and Cymbopogon flexuosus, *Stapf.*" *Br.*

Lemon-grass Oil; Malabar- or Cochin-grass Oil.

Both of these grasses are awnless and indigenous to India. *Cymbopogon citratus* is the genuine *Lemon grass* while *Cymbopogon flexuosus,* also called *Lemon grass,* is more properly designated *Malabar-* or *Cochin-grass.* The latter is claimed to yield the oil of best quality.

The *East Indian Lemon Grass Oil* comes from Malabar, Cochin, India and the Malay Peninsula. A product of the *C. citratus* comes from Ceylon, Burma and adjacent countries, as well as from Java, West Africa, Tonkin, Brazil and the West Indies.

It is officially described in the British Pharmacopœia, 1914, as "Dark yellow. Odor resembling that of verbena. Specific gravity 0.880 to 0.905; *optical rotation* –3° to +3°. Contains not less than 70 per cent. of aldehydes as determined by the process described under 'Oleum Cinnamomi.'" *Br.*

The chief aldehyde present is citral, of which it contains 70 to 85 per cent. Linalool, geraniol and methyl heptenone are also reported present in small amounts. The principal use of the oil is as a source for manufacturing ionone and in perfuming cheap soaps. (See also *Oil of Citronella,* Part II.)

Oil of lemon grass is sometimes used in Eastern countries as a carminative and stimulant in *doses* of one-half to three minims (0.03–0.2 cc.).

OLEUM JUNIPERI. U. S., Br.

OIL OF JUNIPER Ol. Junip. [Juniper Oil]

"The volatile oil distilled from the ripe fruit of *Juniperus communis,* Linné (Fam. *Pinaceæ*)." *U. S.* "Oil of Juniper is the oil distilled from the ripe fruit of Juniperus communis, *Linn.,* and rectified." *Br.*

Oleum Fructus (vel Baccæ) Juniperi; Oil of Juniper Berries; Huile volatile (Essence) de Genièvre, *Fr.;* Oleum Juniperi, *P. G.;* Wachholderöl, Wachholderbeeröl, *G.;* Essenza di ginepro, *It.*

The proportion of oil which juniper berries afford is variously given as from 0.3 to 2.3 per cent.; the usual yield is probably about 1 per cent.

Description and Physical Properties.—"A colorless or faintly green or yellow liquid, having the characteristic odor and taste of juniper berries.

"The Oil is soluble in 4 volumes of alcohol, with not more than a slight cloudiness. Specific gravity: 0.854 to 0.879 at 25° C. Optical rotation: varies from 0° to –15° in a 100 mm. tube at 25° C. Refractive index: 1.4790 to 1.4840 at 20° C. A solution of the recently distilled Oil in alcohol (1 in 4) is neutral or only slightly acid to moistened litmus paper. The Oil meets the requirements of the test for *heavy metals in volatile oils.*

"Preserve in well-stoppered, completely filled, amber-colored bottles, in a cool place, protected from light." *U. S.*

"Colorless or pale yellowish-green. Odor that of the fruit; taste warm, aromatic and bitter. Specific gravity 0.862 to 0.890, increasing with age; *optical rotation* –3° to –15°; *refractive index* at 25° C. 1.472 to 1.488. Soluble, when freshly distilled, in 4 parts of a mixture of equal volumes of *alcohol* (90 per cent.) and *absolute alcohol,* becoming less soluble with age." *Br.*

Oil of Juniper consists chiefly of pinene and cadinene. Its characteristic aroma, however, is due to small quantities of some unknown ingredient. It was at one time believed that this was an ester, but this cannot be the case as the odor persists after the complete saponification of the small amount of ester. On cooling the oil deposits a crystalline substance known as *juniper camphor;* this has a melting point of 165° to

166° C. Oil of turpentine is often fraudulently added, but may be detected by the specific gravity of the mixture being less than that of the unadulterated oil of juniper.

Uses.—In its medicinal properties oil of juniper apparently resembles the oil of turpentine. It is chiefly used for its stimulant action in chronic disorders of the genito-urinary tract. It is sometimes employed as a diuretic in certain forms of *dropsy* especially in conjunction with other drugs. On account, however, of its local irritant action, it may exercise injurious effects upon the kidneys, especially when these organs are inflamed. Its widespread use as an ingredient of patent medicines intended for disorders of the kidney is greatly to be deprecated. It is frequently combined with potassium bitartrate.

Dose, one to five minims (0.06–0.3 cc.).

Off. Prep.—Spiritus Juniperi, *Br.;* Acetum Aromaticum, *N. F.*

OLEUM LAVANDULÆ. U. S., Br.

OIL OF LAVENDER Ol. Lavand.

" The volatile oil distilled from the fresh flowering tops of *Lavandula Spica* Linné (*Lavandula officinalis* Chaix, *Lavandula vera* DeCandolle) (Fam. *Labiatæ*). Oil of Lavender yields not less than 30 per cent. of esters calculated as linalyl acetate $[C_{10}H_{17}.C_2H_3O_2]$." *U. S.* " The oil distilled from the flowers of Lavandula vera, *DC.*" *Br.*

Oleum Lavandulæ Florum, *U. S. VIII;* Oil of Lavender Flowers; Huile volatile de Lavande officinale, *Fr. Cod.;* Essence de Lavande, *Fr.;* Oleum Lavandulæ, *P. G.;* Lavandelöl, *G.;* Essenza di lavanda, *It.;* Esencia de espliego, *Sp.*

This oil is usually distilled from the flowers (see *Lavender Flowers,* Part II) and flower stems conjointly, though of finer quality when obtained from the former exclusively. Dried lavender flowers are said to yield from 1 to 1.5 per cent. of oil According to Zeller, the fresh flowers yield 1.03, the dried 4.3, the whole fresh herb in flower 0.76 per cent. It is said that the portion of oil first distilled is most fragrant, and is often kept separate, and sold at a higher price.

Description and Physical Properties.—" A colorless or yellow liquid, having the characteristic odor and taste of lavender flowers.

" The Oil is soluble in 3 volumes of 70 per cent. alcohol, by volume. Specific gravity: 0.875 to 0.888 at 25° C. Optical rotation: varies from –3° to –10° in a 100 mm. tube at 25° C. Refractive index: 1.4600 to 1.4640 at 20° C. Shake 5 cc. of Oil of Lavender with an equal volume of distilled water in a narrow, graduated, 10 cc. glass-stoppered cylinder: the volume of the Oil does not diminish (*alcohol*). Shake 20 cc. of the Oil with 40 cc. of 5 per cent. alcohol in a 100 cc. glass-stoppered cylinder. When the mixture has cleared, withdraw 30 cc. of the alcoholic solution, by means of a pipette, and place it in a 125 cc. Erlenmeyer flask. Neutralize the solution with half-normal potassium hydroxide, using 2 drops of phenolphthalein T.S. as indicator, add 5 cc. of half-normal potassium hydroxide, and heat the mixture on a bath of boiling water under a reflux condenser during one hour. Allow the mixture to cool, remove the flask from the bath, and titrate the excess of alkali with half-normal hydrochloric acid: not less than 4.7 cc. is required for neutralization (*acetins*).

" Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

" Pale yellow or yellowish-green. Odor that of the flowers; taste pungent, slightly bitter. Specific gravity 0.883 to 0.900; *optical rotation* –3° to –10°. Soluble in 4 parts of *alcohol* (70 per cent.). Contains from 7 to 11 per cent. of *esters* (Engish oil), or not less than 30 per cent. of *esters* (foreign oil), calculated as linalyl acetate, $C_{10}H_{17}C_2H_3O_2$." *Br.*

The principal constituent is linalool. It also contains linalyl acetate (from 30 to 45 per cent. in the oil from French flowers, and from 7 to 10 per cent. in the oil from English flowers), the butyric ester of the same alcohol, geraniol, a very small amount of cineol (more in the English than in the French oil), and sometimes traces of pinene, limonene, and a sesquiterpene.

Oil of Spike is procured from the broad-leaved variety of lavender which grows wild in Europe, the *Lavandula Spica* of De Cavanilles. Its odor is less fragrant than that of common oil of lavender, and is somewhat analogous to that of oil of turpentine, with which it is said to be often adulterated. It is used by artists in the preparation of varnishes. The oil of spike contains about 30 per cent. of cineol and but small quantities of esters.

Oil of lavender is used chiefly as a perfume, though possessed of carminative and stimulant properties, and sometimes useful in cases of *nervous languor* and *headache.*

Dose, from one to five minims (0.06–0.3 cc.).

Off. Prep.—Spiritus Lavandulæ, *U. S., Br.;* Tinctura Lavandulæ Composita, *U. S., Br.;* Acetum Aromaticum, *N. F.;* Spiritus Odoratus, *N. F.;* Mistura Oleo-balsamica, *N. F.*

OLEUM LIMONIS. U. S., Br.

OIL OF LEMON Ol. Lemon. [Lemon Oil]

" The volatile oil obtained by expression from the fresh peel of the fruit of *Citrus Medica* var. *Limonum* (Risso) Hooker filius (Fam. *Rutaceæ*). Oil of Lemon yields not less than 4 per cent. of the aldehydes of Oil of Lemon calculated as citral $[C_{10}H_{16}O]$. Oil of Lemon having a terebinthinate odor must not be dispensed." *U. S.* " Oil of Lemon is the oil obtained from Lemon Peel by various methods of expression." *Br.*

Oleum Limonum; Huile volatile de Citron, *Fr. Cod.;* Essence de Citron, *Fr.;* Oleum Citri, *P. G.;* Citronenöl, *G.;* Olio de limone, *It.;* Esencia de limon, *Sp.*

The exterior rind of the lemon abounds in a volatile oil, which, being contained in distinct cells, may be separated by simple expression. The rind is first grated from the fruit, and then submitted to pressure in a bag of fine cloth. The oil thus obtained is allowed to stand till it becomes clear, when it is decanted, and kept in stoppered bottles. By a similar process, the oil called by the French *huile de cédrat* is procured from the citron. These oils may also be obtained by distillation, but thus procured, though clearer, and, in consequence of the absence of mucilage, less liable to change on keeping, they have less of the peculiar flavor of the fruit, and the mode by expression is generally preferred. A third method of separating the oil, used in Calabria and Sicily, is to put the grated rind into hot water and skim off the oil as it rises to the surface. (*A. J. P.*, 1868, p. 27.) The method employed to obtain the finest oil is, however, that known as the écuelle process. The écuelle is an instrument usually made of tinned copper, bowl-shaped, and armed with concentric rows of short spikes. Attached to the bottom of the bowl is a hollow handle, closed at the bottom. This acts as a reservoir for the oil as the fruit is rubbed by the workmen over the sharp teeth. The oils are brought from Italy, Portugal, or Southern France.

The oils of lemons and oranges, as well as those of the other *Aurantiaceæ,* will keep indefinitely upon admixture with a small proportion of alcohol (one ounce to a pound of the oil). When wanted for use, a quantity of water equal to that of alcohol, added to the mixture, will unite with the alcohol, and subside, leaving the oil free of the alcohol for all practical purposes. The best method of preservation is to add 10 per cent. of a bland fixed oil such as olive or cottonseed, which must subsequently be allowed for in measuring the oil for use.

Description and Physical Properties.—" A pale yellow or greenish-yellow liquid, having the characteristic odor and taste of the outer part of fresh lemon peel.

" The Oil is soluble in 3 volumes of alcohol, and in all proportions in dehydrated alcohol, carbon disulphide, and in glacial acetic acid. Specific gravity: 0.851 to 0.855 at 25° C. Optical rotation: varies from +57° to +64° in a 100 mm. tube at 25° C. Refractive index: 1.4744 to 1.4755 at 20° C. A solution of the recently expressed Oil in alcohol (1 in 3) is neutral or only slightly acid to moistened litmus paper. Oil of Lemon when distilled as described under *Oleum Aurantii,* gives the following results: The angle of rotation of the first 5 cc. is not more than 5 degrees less than that of the original Oil. The refractive index of this same portion is not less than 0.0020 and not more than 0.0027 lower than that of the original Oil.

" Preserve in completely filled, well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

" Pale yellow. Volatile; odor that of lemons; taste warm, afterwards slightly bitter. Specific gravity 0.857 to 0.860: *optical rotation* + 58° to + 64°; *refractive index* at 25° C. 1.473 to 1.476. Contains not less than 4 per cent. by weight of aldehydes, calculated as citral, $C_{10}H_{16}O$, as determined by the following process." *Br.*

Assay.—" Place about 15 cc. of Oil of Lemon in a tared, 250 cc. Erlenmeyer flask, and weigh accurately. Add 10 cc. of an alcoholic solution of phenylhydrazine (1 in 10) (not darker in color than pale yellow), and allow it to stand for thirty minutes at room temperature. Then add 3 drops of methyl-orange T.S., and neutralize the liquid by the addition of half-normal hydrochloric acid. If difficulty is experienced in determining the end point of the reaction, continue the titration until the liquid is distinctly acid, transfer it to a separatory funnel, and after the layers have separated draw off the alcoholic portion. Wash the oil remaining in the funnel with distilled water, adding the washings to the alcoholic solution, and titrate the latter with half-normal sodium hydroxide. Carry out a blank test identical with the foregoing, omitting the Oil of Lemon, and note the amount of half-normal hydrochloric acid consumed. Subtract the number of cc. of half-normal sodium hydroxide from the number of cc. of half-normal hydrochloric acid consumed in the test containing the Oil of Lemon, and this result from the number of cc. of half-normal hydrochloric acid consumed in the test without the Oil of Lemon. Each cc. of this difference corresponds to 0.07609 Gm. of aldehydes calculated as citral." *U. S.*

" To 20 grammes of the Oil contained in a flask add 20 millilitres of *N/2 solution of hydroxylamine hydrochloride,* 8 millilitres of *N/1 alcoholic solution of potassium hydroxide* and 20 millilitres of *alcohol* (90 per cent.). Attach a reflux condenser, boil for thirty minutes, cool, and dilute with 250 millilitres of *water,* rinsing the condensing tube into the flask with part of this quantity. Neutralise the solution thus obtained with *N/1 alcoholic solution of potassium hydroxide, solution of phenolphthalein* being used as indicator, and then titrate with *N/2 solution of sulphuric acid, solution of methyl orange* being used as indicator. Repeat the experiment, omitting the Oil of Lemon. The quantity of *N/2 solution of sulphuric acid* required in the second experiment exceeds that required in the first experiment by not less than 10.5 millilitres (presence of not less than 4 per cent. of aldehydes, calculated as citral, $C_{10}H_{16}O$)." *Br.*

Constituents.—Oil of lemon consists chiefly of dextrogyrate limonene, which, together with phellandrene, makes up nearly 90 per cent. of the oil. Its pleasant aroma is due to the presence of about 7 or 8 per cent. of the aldehyde citral and a small amount of citronellal, $C_{10}H_{18}O$. Pinene, higher aldehydes, as octyl and nonyl, terpineol, octylene, camphene, methyl heptenone, citronellal, linalyl acetate, bisabolene, cadinene, methyl anthranilate and geranyl acetate have also been reported in small amounts.

Also a lemon-camphor, *citraptene*, which appears to be *dimethoxy coumarin*, is present to the extent of 2 per cent. This constituent has been found to be identical with *limettin*. Of these the citral is the constituent to which the oil chiefly owes its aroma and value. Umney and Swinton (*P. J.*, 1898, 196) state that citral, citronellal, and an ester of geraniol are all necessary to form the true odor of oil of lemon. Citral boils under normal atmospheric pressure at from 228° to 229° C. without decomposition if pure, and, like aldehydes, forms stable compounds with alkaline bisulphites. Schimmel & Co. now prepare the citral in a pure state, and recommend its use for enriching the ordinary oil of lemon.

For use in perfumery there have been placed on the market oils of lemon from which the terpenes have been removed. Parry (*Ch. & Dr.*, 1913, p. 378) discusses at some length the relative advantages of terpeneless and sesquiterpeneless oils and normal oils. The ordinary terpeneless oils contain from 42 to 45 per cent. of citral, while those that are sold as sesquiterpeneless contain from 65 to 72 per cent. citral. He states that the latter products lack the sweetness and softness of odor of those containing less citral, the overpowering odor of the latter constituent destroying the balance of harmony in the odor of the oil. He states that users of these products claim to get the best results from oils containing slightly less than 40 per cent. of citral and from which the whole of the terpenes have not been removed. The characters of the commercial terpeneless oils are as follows: sp. gr. at 15° C., 0.8935 to 0.899; optical rotation, $-5°$ to $-8° 30'$; refractive index, 1.4810; citral, 42 to 48 per cent. The sesquiterpeneless oils are slightly higher in specific gravity, lower in optical rotation and always run above 65 per cent. of citral.

Oil of lemon is often adulterated by the fixed oils and by alcohol, and sometimes with purified oil of turpentine, which is difficult of detection, from its similar composition and specific gravity, except with the polariscope. One of the tests for the presence of this oil is the terebinthinate odor produced when the adulterated oil is evaporated from heated paper; the official quantitative test defining the percentage of citral will be of service in detecting these adulterations. The most insidious adulteration of oil of lemon is the use of *citrene*, the terpene left after the extraction of citral from oil of lemon which has been used in making terpeneless oil.

Parry (*Schim. Rep.*, Apr., 1912, p. 78) reports several shipments of lemon oil which upon investigation were found to be adulterated with Greek turpentine oil. They were noted by their low optical rotation, $+50°$ to $+54°$, and their low citral content, 3.3 to 4.1 per cent.

In consequence of some seizures of lemon oil alleged to be adulterated with turpentine, in 1906, a number of importers stated their belief that pinene was normally present in appreciable amounts in some lemon oils. In consequence of this the U. S. Dept. of Agriculture undertook a special investigation of the subject, sending a trained observer and analyst to the producing countries, and published the results of the investigation in a special bulletin called "Circular 46, by E. M. Chace." The investigation showed conclusively that lemon oil shows no appreciable amount of pinene.

Spirit of Lemon (*Spiritus Limonis, U. S.* 1890) was made by dissolving 50 cc. of oil of lemon in 900 cc. of deodorized alcohol, to which 50 Gm. of freshly grated lemon peel were added, the whole macerated for twenty-four hours, filtered, and enough deodorized alcohol added through the filter to make the whole measure 1000 cc.

Uses.—The oil of lemon is much less active than most of the other official volatile oils, and is used almost exclusively for its flavoring properties.

Dose, two to five minims (0.12–0.3 cc.).

Off. Prep.—Elixir Aromaticum (from Spirit), *U. S.;* Spiritus Aurantii Compositus, *U. S.;* Acetum Aromaticum, *N. F.;* Spiritus Odoratus, *N. F.;* Mistura Oleo-balsamica, *N. F.*

OLEUM LINI. U. S., Br.

LINSEED OIL. Ol. Lini. [Oil of Flaxseed, Raw Linseed Oil]

"A fixed oil obtained from Linseed. Linseed Oil which has been 'boiled' must not be used nor dispensed." *U. S.* "Linseed Oil is the oil expressed from Linseed." *Br.*

Huile de Semence de Lin, *Fr.;* Oleum Lini, *P. G.;* Leinöl, Leinsamenöl, *G.;* Olio di lino, *It.;* Aceite de linaza, *Sp.*

This oil is obtained by expression from the seeds of *Linum usitatissimum*, or common flax, which contain from 30 to 40 per cent. In its preparation for commerce, the seeds are usually roasted before being pressed, in order to destroy the gummy matter contained in their coating, and expressed hot. The oil is thus obtained more free from mucilage, but more highly colored and acrid than when procured by cold expression. For medicinal use, therefore, it should be prepared without heat, and, as it is apt to become rancid quickly on exposure, it should be used as soon after expression as possible. It is said to be obtained purer and in larger proportion by treating the crushed seeds with carbon disulphide than by expression.

Description and Physical Properties.—"A yellow, oily liquid, having a peculiar odor, and a bland taste. When exposed to the air, it gradually thickens, darkens in color, and acquires a more pronounced odor and taste. Linseed Oil is slightly soluble in alcohol, but is miscible with ether, chloroform, petroleum benzin, carbon disulphide, and with oil of turpentine.

"Specific gravity: 0.925 to 0.935 at 25° C. Linseed Oil, when spread in a thin layer on a glass plate and allowed to stand in a warm place, is gradually converted into a hard, transparent film (*non-drying oils*). Dissolve 2 Gm. of Linseed Oil in 20 cc. of a mixture of equal volumes of alcohol and ether, which has previously been neutralized with tenth-normal sodium hydroxide, using 5 drops of phenolphthalein T.S. as indicator, and titrate with tenth-normal sodium hydroxide to the production of a pink color, which persists for fifteen seconds: not more than 1.5 cc. of tenth-normal sodium hydroxide is required (*free acid*). To 10 cc. of the Oil, add 3 Gm. of potassium hydroxide, 10 cc. of alcohol and 10 cc. of distilled water, and heat the mixture on a water bath with frequent agitation until a clear solution results: the addition of 100 cc. of distilled water to this solution yields a clear liquid, free from oily drops (*mineral* or *rosin oils*). Warm 2 cc. of the Oil with an equal volume of glacial acetic acid in a test tube, agitating frequently, and after cooling add to the mixture 1 drop of sulphuric acid: a greenish color is produced (a violet color under these circumstances indicates the presence of *rosin* or *rosin oils*). Unsaponifiable matter: not more than 1.5 per cent. Saponification value: not less than 187 and not more than 195. Iodine value: not less than 170.

"Preserve in well-stoppered containers." *U. S.*

"Yellowish-brown. Characteristic odor; taste bland. Specific gravity 0.930 to 0.940; *saponification value* 187 to 195; *iodine value* not less than 170; *acid value* not more than 3.0; *unsaponifiable matter* not more than 1.0 per cent.; *refractive index* at 40° C. 1.4725 to 1.4748. Does not congeal at temperatures higher than $-20°$ C. Gradually thickens on exposure to the air, forming, when spread in thin layers, a hard transparent varnish. A mixture of 2 millilitres of the Oil with an equal volume of *acetic anhydride,* warmed and shaken, and then cooled to 15.5° C., is not colored violet by the addition of 2 drops of a cooled mixture of 2 parts by weight of *sulphuric acid* and 1 part by weight of *water* (absence of resin and resin oils)." *Br.*

It has the property of drying or becoming solid on exposure to the air, acquiring during the process a strong odor and taste, and increasing as much as 12 per cent. of its weight, owing to the formation of *linoxyn* by atmospheric oxidation. The drying property resides in a constituent which, to distinguish it from the olein of the non-drying oils, is named *linolein,* and is the glyceride of *linoleic acid.* Linseed oil contains about 10 to 15 per cent. of glycerides of solid fatty acids, palmitic, myristic, and stearic, and 85 to 90 per cent. of liquid glycerides. Hazura (*J. Soc. Chem. Ind.,* 1888, 506) states that the liquid fatty acids consist of about 5 per cent. of oleic acid, $C_{18}H_{34}O_2$, 15 per cent. of *linoleic acid,* $C_{18}H_{32}O_2$, 65 per cent. of *isolinolenic acid,* $C_{18}H_{30}O_2$, and 15 per cent. of *linolenic acid,* $C_{18}H_{30}O_2$. Boiled with litharge, red lead, manganese dioxide, and other so-called "driers," it absorbs oxygen still more rapidly, and gains 14 per cent. in weight. Its acridity is owing to the presence of a small portion of an acrid oleoresin. From its drying property, it is useful in painting and in making printers' ink and in linoleum and oil cloth manufacture. The chief adulteration of linseed oil is with mineral oils and rosin oil. For their detection, see official tests already given.

The prohibition of the use of boiled linseed oil for medicinal purposes has its origin in the fact that much of the boiled linseed oil of commerce contains a compound of lead or manganese as a drying agent. Instances are on record where lead-containing boiled linseed oils caused the death of cattle to which the oil had been administered.

Uses.—The oil is laxative in the dose of a fluidounce (30 cc.), but, on account of its disagreeable taste, is seldom given internally. It has, however, been highly recommended as a cure for *piles,* in the dose of two fluidounces (60 cc.) of the fresh oil, morning and evening. It is sometimes added to purgative enemata. Particular care must be observed not to use boiled linseed oil for any medicinal purposes, as the latter frequently contains compounds of lead which give it poisonous properties.

Dose, one to two fluidounces (30–60 cc.).

Off. Prep.—Linimentum Calcis, *U. S.;* Ceratum Resinæ Compositum, *N. F.*

OLEUM MENTHÆ PIPERITÆ. U. S., Br.

OIL OF PEPPERMINT Ol. Menth. Pip. [Peppermint Oil]

"The volatile oil distilled from the fresh, over-ground parts of the flowering plant of *Mentha piperita* Linné (Fam. *Labiatæ*), rectified by steam distillation. Oil of Peppermint yields not less than 5 per cent. of esters, calculated as menthyl acetate [$C_{10}H_{19}.C_2H_3O_2$], and not less than 50 per cent. of total menthol [$C_{10}H_{19}.OH$], free and as esters." *U. S.* "Oil of Peppermint is the oil distilled from fresh flowering peppermint, Mentha piperita, *Sm.,* and rectified, if necessary." *Br.*

Huile volatile de Menthe poivrée, *Fr. Cod.;* **Essence de Menthe poivrée,** *Fr.;* **Oleum Menthæ piperitæ,** *P. G.;* **Pfefferminzöl,** *G.;* **Essenza di menta,** *It.;* **Escencia de menta piperita,** *Sp.*

For account of the peppermint plant and its cultivation see *Mentha Piperita.*

Peppermint varies considerably in the quantity of oil which it affords. Zeller gives as the product of the fresh herb, from 0.37 to 0.68 per cent., of the dried 1.14 per cent. The yield is generally less than 1 per cent. This oil is largely distilled in the States of Michigan, Indiana, and New York, Michigan producing the largest quantity. The oil is also largely produced in Japan. (See illustrated paper, *C. D.,* 1896, 601.)

Description and Physical Properties.—"A colorless liquid, having a strong, penetrating odor of peppermint, and a pungent taste, followed by a sensation of cold when air is drawn into the mouth.

"The Oil is soluble in 4 volumes of 70 per cent. alcohol, by volume, showing not more than a slight opalescence and no separation of oil globules (*dementholized or impure peppermint oil*). Specific gravity: 0.896 to 0.908 at 25° C. Optical rotation: varies between −23° and −33° in a 100 mm. tube at 25° C. Refractive index: 1.4600 to 1.4710 at 20° C. A solution of the recently rectified Oil in 70 per cent. alcohol (1 in 4) is neutral to moistened litmus paper. Distil 1 cc. from 25 cc. of Oil of Peppermint, and carefully superimpose the distillate on 5 cc. of mercuric chloride T.S. in a test tube: a white film does not form at the zone of contact within one minute (*dimethyl sulphide found in non-rectified peppermint oils*).

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

"Colorless, pale yellow, or greenish-yellow. Odor that of peppermint herb; taste pungent and aromatic followed by a sensation of cold. Specific gravity 0.900 to 0.920; *optical rotation* −20° to −35°. Soluble in 4 parts of *alcohol* (70 per cent.). Contains not less than 50 per cent. of total *alcohols*, free and combined, calculated as menthol, $C_{10}H_{20}O$, and not less than 5 per cent. of esters, calculated as menthyl acetate, $C_{10}H_{19}O_2H_3O_2$." *Br.*

"**Assay for Esters.**—Place 10 cc. of Oil of Peppermint in a tared, 125 cc. Erlenmeyer flask, and weigh accurately. Add 25 cc. of half-normal alcoholic potassium hydroxide, connect the flask with a reflux condenser, and boil the mixture on a water-bath for one hour. Allow the mixture to cool, disconnect the flask from the condenser, and titrate the excess of alkali with half-normal sulphuric acid, using 10 drops of phenolphthalein T.S. as indicator. Subtract the number of cc. of half-normal sulphuric acid required for neutralization from the 25 cc. of half-normal alcoholic potassium hydroxide taken, multiply the difference by 9.912, and divide this product by the weight of Oil of Peppermint taken: the result shows the per cent. of esters calculated as menthyl acetate.

"**Assay for Total Menthol.**—Place 10 cc. of Oil of Peppermint in an acetylization flask of 100 cc. capacity, add 10 cc. of acetic anhydride and 1 Gm. of powdered anhydrous sodium acetate. Boil the mixture gently for one hour, cool, disconnect the flask from the condenser, transfer the mixture to a small separatory funnel, rinsing the acetylization flask with three successive 5 cc. portions of warm distilled water, and add the rinsings to the separatory funnel. When the liquids have completely separated, remove the aqueous layer, and wash the remaining oil with successive portions of sodium carbonate T.S., diluted with an equal volume of distilled water, until the mixture is alkaline to 2 drops of phenolphthalein T.S. Dry the resulting Oil with fused calcium chloride, and filter. Transfer 5 cc. of the dry acetylized oil to a tared, 100 cc. Erlenmeyer flask, note the exact weight, add 50 cc. of half-normal alcoholic potassium hydroxide, connect the flask with a reflux condenser, and boil the mixture on a water bath for one hour. Allow the mixture to cool, disconnect the flask from the condenser, and titrate the excess of alkali with half-normal sulphuric acid using 10 drops of phenolphthalein T.S. as indicator. Calculate the per cent. of menthol by the following formula:

$$\text{Per cent. of total menthol} = \frac{A \times 7.811}{B - (A \times 0.021)} \times [1 - (E \times 0.0021)]$$

"A is the result obtained by subtracting the number of cc. of half-normal sulphuric acid required in the above titration from the number of cc. of half-normal alcoholic potassium hydroxide originally taken, B is the weight of acetylized oil taken, and E is the per cent. of esters calculated as menthyl acetate." *U. S.*

Upon cooling or long standing it deposits a stearopten called *peppermint camphor* or *menthol*, $C_{10}H_{19}OH$. (See *Menthol.*) A complete summary of the composition of American peppermint oil, on the authority of Power and Kleber, given in *Schimmel & Co.'s Report* for April, 1897, shows the following constituents: acetaldehyde, isovaleraldehyde, dimethyl sulphide, amyl alcohol, isovaleric acid, pinene, phellandrene, cineol, limonene, *menthone*, $C_{10}H_{18}O$, menthol, the acetate and isovalerate of menthyl, *a-lactone*, $C_{10}H_{16}O_2$, and cadinene. Menthol, its oxidation product menthone, and the acetic and isovaleric esters of menthol have been identified as present in English and French peppermint oils, which probably also contain most of the other constituents mentioned above. Menthol and its esters are regarded as the main constituents of oil of peppermint and an official assay for determining the percentage of menthol will be found above. The dimethyl sulphide and some of the other constituents are objectionable from the flavoring standpoint, and are largely removed by the steam distillation which is required for rectification. The polariscope has been shown to be an uncertain guide in determining the quality of oil of peppermint. (A. B. Stevens, *Proc. A. Ph. A.*, 1888, p. 97.)

Power and Kleber first proposed (*Ph. Rund.*, 1894, 157) to estimate the menthol in oil of peppermint by acetylizing a sample and saponifying an exactly weighed portion of the acetylized oil after washing, drying, and filtering the same. Kebler (*A. J. P.*, 1897, 192) proposed to take instead a weighed quantity of the oil, acetylize it, and then saponify the product after washing and neutralizing it. In *Schimmel & Co.'s Report* for October, 1897, Kleber criticizes Kebler's modification, and claims greater accuracy for the original method. Of course, this determination gives the total menthol; a determination of the combined menthol is had by titrating with alcoholic alkali.

Peppermint oil has been variously mixed and adulterated with the following substances: alcohol, oil of turpentine, oil of copaiba, oil of erigeron (from the erigeron plant growing with the peppermint plant, and being collected with it for distillation), oil of eucalyptus, oil of pennyroyal, and others. Most of these are detectable by the official tests, or when present lower the assay strength, or are readily recognized by the odor or taste, which they communicate to the oil. For further details concerning some of these adulterants and their detection, see *U. S. D.*, 19th ed., p. 854, 855.

Uses.—Oil of peppermint possesses the physiological properties and therapeutic virtues of menthol, and may be used for practically all those conditions in which menthol is of service but is, proportionally, a more active local irritant. It is generally preferred for internal use because of its more pleasant taste. It is an excellent carminative and gastric stimulant, and is widely employed in *flatulence, nausea,* and *gastralgia.* It adds to a stimulating effect upon the alimentary canal an antiseptic and local anesthetic influence. Heinz (*Therap. Halbmonatsh.*, April 1, 1920) asserts that it is an active cholagogue and recommends its use in *gall-stones.* As a local application for *coryza* it may be used in strengths of from three to ten minims to an ounce of liquid petrolatum or olive oil. Incorporated into a lozenge it offers a pleasant and efficient antiseptic and anesthetic in *pharyngitis.* Internally it may be given either rubbed up with sugar and then dissolved in water, or more commonly in the form of the spirit. It is extremely popular as a flavoring agent.

Dose, one to five minims (0.06–0.3 cc.).

Off. Prep.—Aqua Menthæ Piperitæ, *U. S., Br.;* Spiritus Menthæ Piperitæ, *U. S., Br.;* Acetum Aromaticum, *N. F.;* Lavatis Ori, *N. F.;* Mistura Carminativa, *N. F.;* Liquor Sodæ et Menthæ, *N. F.;* Tabellæ Sodii Bicarbonatis, *N. F.;* Oleum Hyoscyami Compositum, *N. F.*

OLEUM MENTHÆ VIRIDIS. U. S., Br.

OIL OF SPEARMINT Ol. Menth. Vir. [Spearmint Oil]

"The volatile oil distilled from the fresh, overground parts of the flowering plant of *Mentha spicata* Linné (*Mentha viridis* Linné) (Fam. *Labiatæ*). Oil of Spearmint yields not less than 43 per cent. by volume, of carvone [$C_{10}H_{14}O$]." *U. S.* "Oil of Spearmint is the oil distilled from fresh flowering spearmint, Mentha viridis, *Linn.*, or Mentha crispa, *Roth.*" *Br.*

Huile volatile (Essence) de Menthe verte, *Fr.;* Römischminzöl, Krauseminzöl, *G.*

According to Lewis, ten pounds of spearmint yield an ounce of oil; by others the product is stated not to exceed one part from five hundred. The oil is largely distilled in this country, the whole plant being used. It is pale yellow or greenish when recently prepared, but becomes red with age, and ultimately almost of a mahogany color.

Description and Physical Properties.—"A colorless, yellow or greenish-yellow liquid, having the characteristic odor and taste of spearmint.

"The Oil is soluble in 1 volume of 80 per cent. alcohol, by volume, forming a clear solution, which becomes cloudy on dilution with more of the alcohol. Specific gravity: 0.917 to 0.934 at 25° C. Optical rotation: varies from $-38°$ to $-56°$ in a 100 mm. tube at 25° C. Refractive index: 1.4820 to 1.4900 at 20° C. A solution of the recently distilled Oil in an equal volume of 80 per cent. alcohol is neutral or only slightly acid to moistened litmus paper.

"**Assay.**—Proceed as directed under *Oleum Cari,* using 10 cc. of Oil of Spearmint. The oily layer measures not more than 5.7 cc., indicating the presence of not less than 43 per cent. by volume, of carvone.

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

"Colorless, pale yellow, or greenish-yellow, becoming darker on keeping. Odor and taste those of spearmint herb. Specific gravity 0.925 to 0.940; *optical rotation* $-30°$ to $-50°$. Soluble in 3 parts of *alcohol* (90 per cent.). Forms a clear solution with 1 part of a mixture of equal volumes of *alcohol* (90 per cent.) and *alcohol* (70 per cent.), the solution becoming turbid on further dilution." *Br.*

Oil of spearmint contains a terpene, l-limonene, $C_{10}H_{16}$, and l-carvone, $C_{10}H_{14}O$. Baeyer found the l-carvone in both German and American oils to the amount of from 35 to 56 per cent. (*A. Pharm.*, ccxii, 238.) Schimmel & Co., in an investigation of Russian oil, found from 5 to 10 per cent. of carvone only, but 50 to 60 per cent. of linalool, together with some cineol and l-limonene. (*Schim. Rep.*, April, 1898.) It is used chiefly for its flavor, especially in chewing gum.

The peculiar odor of spearmint oil has not yet been definitely associated with any of its constituents. It was for a time thought to be due to an acetic derivative of dihydrocuminyl, but this has recently been denied so far as the oil of American origin is concerned.

Dose, one to six minims (0.06–0.4 cc.).

Off. Prep.—Aqua Menthæ Viridis, *U. S. Br.;* Spiritus Menthæ Viridis, *U. S.*

OLEUM MORRHUÆ. U. S., Br.

COD LIVER OIL Ol. Morrh.

"The fixed oil obtained from the fresh livers of *Gadus morrhua* Linné and of other species of *Gadus.* Cod Liver Oil may be assayed for its vitamine A potency, and should then contain at least 50 units per Gm. Cod Liver Oil so assayed must be labeled 'This unit is not a measure of the antirachitic activity of Cod Liver Oil.'" *U. S.* "Codliver Oil is the oil expressed from the fresh liver of the cod, Gadus morrhua, *Linn.*, at a temperature not exceeding 85° C., and from which solid fat has been separated by filtration at about −5° C." *Br.*

Oleum Jecoris Aselli; Oleum Hepatis Morrhuæ; Cod Oil; Huile de Foie de Morue, *Fr. Cod.;* Huile de Morue, *Fr.;* Oleum Jecoris Aselli, *P. G.;* Leberthran, Stockfischleberthran, Dorschleberthran, Kablianleberthran, *G.;* Olio di fegato di merluzzo, *It.;* Aceite de higado de bacalao, *Sp.*

Gadus morrhua Linn.; *Morrhua vulgaris* Storer.—The *common cod* is between two and three feet long, with brown or yellowish spots on the back. The body is moderately elongated and somewhat compressed, and covered with soft, rather small scales, being quite conspicuous also on the head. Of the fins, which are soft, there are three on the back (dorsal), two anal, and a distinct caudal, and the fin (ventral) under the throat is narrow and pointed. The jaws are furnished with pointed irregular teeth, in several ranks. The gills are large, with seven rays. This species of cod inhabits the cold waters of the northern Atlantic, and is especially abundant on the Banks of Newfoundland, where it finds food adapted to its wants.

Besides the common cod, several other species of *Gadus,* frequenting the seas of northern Europe and America, contribute to furnish the cod liver oil of commerce. Among these De Jongh mentions *Gadus callariaus* L., or *dorsch* (*Morrhua americana* of Storer), *G. molva* L., or *ling, G. carbonarius* L., or *coal fish,* and *G. pollachius* L., or *pollack,* as affording the oil on the coast of Norway, where from 17,000,000 to 35,000,000 of codfish are annually taken. For an account of the mode of fishing for cod and of preparing the oil practised in Norway and Denmark, see *Ph. Ztg.,* 1900, 261; *Ph. Era,* 1904, 111; *C. D.,* 1904, 21.

Holmes (*J. Metab. R.,* 1922, ii, No. 1) has experimentally found that the oil obtained from the livers of the pollack, hake and haddock are equal in vitamin content to that from the true cod.

On the American coast, in addition to the pollack above mentioned, it is obtained also from the *hake* (*G. merluccius* L.) and the *haddock* (*G. æglefinus* L.). It is produced on our coast north of Boston. The oil is also largely produced in Newfoundland, Great Britain, Norway, and to some extent in Iceland.

The exact habits of the codfish still remain to be discovered. It is known that annually enormous schools or shoals of codfish visit the northern seas and are found along the coasts of Norway, Scotland, Iceland, Newfoundland and New England, Alaska, Japan and Siberia. The most noted fishing grounds are along the coast of Norway. In the vicinity of the Lofoten Islands the fish appear in February and remain for about two months. At Finmarken the fish do not appear until June and seem to be much less mature and are accompanied by other varieties of fish which are also caught by the fishermen for the sake of their livers. For this reason the Lofoten oil is of better quality than any other Norwegian oil. The codfishing industry originally had for its object the "cured" meat of the fish and the livers were at first thrown away with other putrescible and non-edible portions of the fish. From the empiric use of the oil which naturally exuded from the heaps of decomposing livers has risen an industry in which many thousands of barrels of the oil are produced annually, and from a small Norwegian district it has spread to all the countries bordering the Northern seas. The fish are usually caught by hook and line, rarely by nets or traps. The head of the fish is severed, the abdomen split and the liver removed by a deft twist of the operator's wrist.

Preparation.—In the early days of the industry the livers were allowed to accumulate in tanks or barrels and underwent a process of spontaneous decomposition in which the cells were ruptured and the oil exuded. The oil thus obtained was contaminated with basic decomposition products and possessed a disagreeable odor and a nauseating taste. Later the oil was obtained by steaming or by pressure and as sanitary conditions improved and scientific knowledge advanced the effort has been made to extract the oil from the livers while they are in as fresh a condition as possible. For this reason some of the former grades of cod liver oil such as the "raw" oil and "brown" oil are no longer seen or heard of. For a detailed description of the earlier methods of production and of the properties of the oil thus obtained see *U. S. D.,* 20th ed., p. 773.

The first high quality medicinal oil was obtained by treating the livers with steam to rupture the cell membranes, much in the same manner in which lard is "rendered." In the best equipped establishments the livers are "extracted" immediately after being taken from the fish, it having been found that exposure even if only for a few hours is very detrimental to the quality of the oil that is obtained. The livers are carefully sorted, all stained or abnormal livers being rejected. They are then placed in tin lined tanks provided with open steam coils and low pressure steam is blown through the mass which causes an immediate separation of oil. Patents have been obtained for the application of vacuum extraction methods or the extraction in an atmosphere of carbon dioxide but the steam extraction method just described is used in the majority of establishments.

The oil separated as described is filtered to separate cellular tissue fragments and is then bleached by treatment with fuller's earth or by exposure to sunlight. The oil thus prepared will congeal at low temperatures owing to the presence of stearin. In some establishments this is removed by chilling to −10° C. and expression, the separated stearin being sold for soap making, and the oil being called "non-congealing oil."

Some lower grades of oil are produced from livers which are unsuitable for the production of the high grade medicinal oil, and from livers which are mixed with other fish livers.

Cod liver oil prepared by the putrefactive method had a brown color and a strong offensive odor and flavor. It contained a large proportion of free fatty acids and of animal bases of the ptomaine type. The color of the modern oil is from the slightest tint of transparent yellow to a fine golden yellow. It is of a rather thin consistence, and has a characteristic odor and taste, by which it may be distinguished from other oils. When a decided odor of ordinary fish oil is perceived, the genuineness may always be suspected; it is quite distinct from that peculiar to the cod liver oil.

Description and Physical Properties.—"A pale yellow, thin, oily liquid. It has a peculiar, slightly fishy, but not a rancid odor, and a fishy taste.

"Cod Liver Oil is slightly soluble in alcohol, but is soluble in ether, chloroform, carbon disulphide, and in ethyl acetate.

"Specific gravity: 0.918 to 0.927 at 25° C. A solution of 1 drop of the Oil in 1 cc. of chloroform, when shaken with 1 drop of sulphuric acid, acquires a violet-red tint, gradually changing to reddish-brown. Dissolve 2 Gm. of Cod Liver Oil in 20 cc. of a mixture of equal volumes of alcohol and ether, which previously has been neutralized with tenth-normal sodium hydroxide, using 5 drops of phenolphthalein T.S. as indicator, and titrate with tenth-normal sodium hydroxide to the production of a pink color which persists for fifteen seconds: not more than 1 cc. of tenth-normal sodium hydroxide is required (*free acid*). Unsaponifiable matter: not more than 1.5 per cent. Saponification value: not less than 180 and not more than 190. Iodine value: not less than 140 and not more than 180.

"Preserve in a cool place, in well-closed containers which have been thoroughly dried before filling.

"**Assay.**—Proceed as directed under the vitamine A assay for *Cod Liver Oil.*" *U. S.* (See Part III.)

"Pale yellow. Slight, fishlike, but not rancid odor; taste bland, fishlike. Specific gravity 0.920 to 0.930; *saponification value* 179 to 192; *iodine value* 155 to 173; *acid value* not more than 2.5; *refractive index* at 40° C. 1.4704 to 1.4745; *unsaponifiable matter* not more than 1.5 per cent. When exposed for three hours to a temperature of 0° C., no solid fat separates." *Br.*

Composition.—The chemical composition of cod liver oil is very complicated. It consists in larger part of the glycerides of two unsaturated fatty acids, *jecoleic* ($C_{19}H_{36}O_2$) and *therapic* ($C_{17}H_{26}O_2$); smaller amounts of the glycerides of palmitic and stearic acids are present. But the so-called "stearin" separating from cod liver oil on cooling contains some unknown unsaturated compounds, as the cod liver stearin has a very high iodine value (113.4, Heyerdahl; 94, Lewkowitsch). The glycerides of the lower fatty acids, such as acetic, butyric, valeric, and capric acids, stated by various authors to occur in cod liver oil, are, according to Salkowski and Steenbuch, secondary products due to the putrefaction of the livers. The researches of Heyerdahl (*Cod Liver Oil and Chemistry,* P. Möller, London, 1895) give as present in the mixed fatty acids about 4 per cent. of palmitic acid, 20 per cent. of jecoleic acid, and 20 per cent. of therapic acid; *morrhuic acid,* $C_9H_{13}O_3N$, and *asellic acid,* $C_{17}H_{32}O_2$, have also been reported. Bull has stated (*B. Chem. G.,* 1906, xxxv, 70) that Heyerdahl's jecoleic acid does not exist, but that it is a mixture of *dihydroxystearic acid* and *dihydroxygadoleic acid.* Heyerdahl states that in the fresh state cod liver oil contains no hydroxy-acids.

A characteristic constituent of cod liver oil is *cholesterol,* which can be isolated by saponifying the oil and exhausting the soap with ether. The quantity of cholesterol, according to Allen and Thomson, is from 0.46 to 1.32 per cent. By reaction with ammonia in distillation the oil yields a volatile alkaloid, trimethylamine (see Part II), which has a strong pungent odor, recalling that of herring pickle, of which the same alkaloid is an ingredient. No other official fatty oil yields a similar product. (See *A. J. P.,* xxiv, 343.) Gautier has obtained from cod liver oil the leucomaines *butylamine, iso-amylamine, hexylamine,* and *dihydrolutidine,* and two fixed bases, *aselline,* $C_{25}H_{32}N_4$, and *morrhuine,* $C_{19}H_{27}N_3$. Aselline was found by its discoverer to be relatively feeble physiologically; morrhuine, of which about 2 milligrammes are believed to exist in a tablespoonful of ordinary cod liver oil, is affirmed to have the properties of exciting the appetite and acting as a powerful diuretic and diaphoretic. Besides these bases, an acid containing nitrogen has been found. This acid, *morrhuic acid,* $C_9H_{13}NO_3$, is probably identical with De Jongh's *gaduine. Gaduol* and *Morrhuol* are names which have been applied to the inspissated alcoholic extract of cod liver oil or of the alcoholic extraction of the livers themselves. It is described as a brown oily liquid, possessing a bitter, acrid taste. It was formerly claimed to possess the therapeutic virtues of cod liver oil and to contain iodine, bromine, phosphorus and alkaloids.

Some have been disposed to ascribe the virtues of cod liver oil to its iodine and bromine, but these are in too small proportion for any effect, and the oil has produced results which have never been obtained from iodine and bromine themselves. The presence of iodine cannot be detected by the usual tests. It is necessary to convert the oil into a soap and to carbonize this, before it will give evidence of iodine. The proportion never exceeds 0.05 per cent., or 1 part in 2000, and it is by no means certain that iodine is always, if ever, present in pure oil. The proportion of iodine present has been investigated by E. C. Stanford (*P. J.* [3], xiv, 353), who found it to be extremely minute, ranging from 0.00138 to 0.00433 per cent. with an average of 0.00322 per cent. The oil is capable of dissolving a larger proportion of iodine, and, if any specimen contain more than 0.05 per cent., there is reason to suspect that iodine has been added. Cod liver oil becomes rancid so easily that it contains varying amounts of free fatty acids, frequently showing their presence, even when freshly rendered. Medicinal oils, however, should not show more than from 0.3 to 0.7 per cent. of free acid, calculated as oleic acid.

The so-called active principles of cod liver oil which are found in the market under various names indicative of their origin are usually made by alcoholic extraction of the oil or of the livers themselves. They consist almost entirely of crude fatty acids, no iodine, bromine or phosphorus is detectable, the bases which are sometimes present are in very minute amount, and are probably of the ptomaine type, derived from partly decomposed products. These so-called alcoholic extracts or active principles are themselves scarcely soluble in diluted alcoholic menstrua, such as are used in preparing the so-called "tasteless" preparations of cod liver oil, so that such preparations can possess little or no activity due to cod liver products.

A preparation derived from cod liver oil, called *sodium morrhuate* has appeared in commerce. It is said to be prepared by the following method: Boil 100 Gm. of cod liver oil, 20 Gm. of sodium hydroxide (dissolved in the same volume of water), and 200 cc. of rectified spirit on a water bath under a reflux condenser for about four hours. The solution is then mixed with a little water, and exactly neutralized with dilute sulphuric acid. Some of the alcohol is then recovered and the solution mixed with nearly 200 Gm. of fairly large grained sand (washed with hydrochloric acid and water), and the whole quickly evaporated to dryness on the water bath. The dry residue is then extracted with ether in Soxhlet's apparatus (using ice water in the condenser), and the fatty acids liberated by a slight excess of the calculated quantity of dilute sulphuric acid (say, a diluted solution of nearly 18 cc. of strong sulphuric acid of sp. gr. 1.82). The fatty acids liberated are washed several times with water to free them from sulphuric acid, and then neutralized with an alcoholic solution of pure sodium hydroxide, using phenolphthalein as indicator. The neutral solution of sodium morrhuate is quickly evaporated to dryness at as low a temperature as possible. A three per cent. solution is used hypodermically and intravenously. Sodium morrhuate was suggested by Rogers (*B. M. J.*, 1919, i, 146) as a remedy for tuberculosis; it has since been tried with more or less success by a number of physicians, especially in India both in *tuberculosis* and in *leprosy* (see Davies, *Ind. Med. Gaz.*, 1921, lvi, 283).

Tests of Purity.—In consequence of the great demand for this oil, it has not infrequently been adulterated with other fixed oils, and occasionally others have been fraudulently substituted for it. The importance, therefore, of ascertaining some mode of testing its purity and genuineness is obvious.

There is reason to believe that all the oils from the livers of the *Gadidæ* have analogous properties. They have been indiscriminately used, and upon the results of their employment is based, in part, the present reputation of the medicine. They may, therefore, be considered as in fact one oil, so far as their medicinal use is concerned. Unfortunately, chemistry has yet discovered no perfectly reliable test. The furthest it has gone is to point out certain reactions which may be considered as evidences of the presence of biliary principles in the oil, thus indicating its hepatic origin. Among these probably the most characteristic is that of Hager and Salkowski, in which a drop of sulphuric acid, added to fresh cod liver oil, on a porcelain plate, causes a centrifugal movement in the oil, and gives rise to a fine violet color soon passing into a yellowish or brownish-red. Sometimes, instead of assuming the violet hue, the color immediately becomes a clear red or a dark brownish-red. This is said to be especially the case with those specimens of the oil which have been prepared by boiling the livers with water. Shark liver oil responds in like manner to the test of sulphuric acid, but is said to have the sp. gr. 0.866, which is much lower than that of any variety of the genuine oil. Rauitz (*Ph. Ztg.*, 1900, 261) states that Norwegian oil prepared by the cold process is often adulterated with the oil from a species of shark, *Scymnus vulgaris*. According to Kremel, fuming nitric acid causes instantly, when agitated with cod liver oil, a pinkish or rose-red color, which soon becomes brown, while no such effect is produced on other animal or vegetable oils. According to Winckler, the oil should afford the odor of herring pickle when heated with potassium hydroxide, lime and ammonium chloride. But the most reliable tests are the sensible properties of odor and taste. If there be none of the peculiar shoe leather odor and taste, or if a strong lamp oil odor be perceptible, the oil may be suspected. Little of importance can be inferred from the color.

Uses.—Although cod liver oil had been used as a folk remedy by the Dutch peasants for a long time, its introduction into regular medicine is attributable chiefly to the researches of Professor Bennett of Edinburgh in the middle of the nineteenth century. While its therapeutic value is not open to question, we are still ignorant as to what its medicinal properties are due. The idea, at one time quite prevalent, that its virtues resided in the small amount of iodine or phosphorus it contained, is scarcely tenable today; equally fallacious is the view that would attribute its efficacy to the organic bases such as morrhuine, etc. In 1914 Osborne and Mendel (*J. Bi. Chem.*, xvii, p. 401) showed that cod liver oil is very rich in fat soluble Vitamin-A, and a number of authorities have attempted to explain its value on the ground of its vitamin content. While this may be true of certain uses, it will not explain all the purposes for which the oil has been found useful. A most reasonable statement is that of Kirschner (*Amer. Rev. Tuberculosis,* 1922, vi, p. 401); he believes that the peculiar value is due in part to the fact that the unsaturated fatty acids are not only more completely absorbed in the intestines but also promote the absorption of other fats, and in part to the effects of some vitamin; he suggests also that there is some evidence that the unsaturated fatty acids directly increase the bodily resistance against tubercle bacilli.

The conditions in which cod liver oil is most frequently of service are: diseases of the bone, especially *rickets;* various forms of *tuberculosis;* and many forms of general *malnutrition.* That cod liver oil encourages the deposition of calcium salts in rickety bones has been demonstrated beyond cavil by researches of Hess (*J. A. M. A.,* 1921, lxxvi, p. 698), McCollum (*J. Bi. Chem.,* 1921, xlv, p. 343) and many others. Brown, MacLacklen and Simpson (*Amer. Journ. Dis. Child.,* June, 1920) have found that the use of cod liver oil in conjunction with calcium salts is of much benefit in the treatment of *tetany.*

While our faith in its usefulness in *phthisis* and other forms of tuberculosis must at present be based chiefly on empirical evidence, it seems, nevertheless, well established. The view commonly held today is that its benefit in these states is owing to its being a readily absorbed food stuff, but Williams (*B. M. J.,* 1912, ii, p. 700) believes that the unsaturated fatty acids have a direct inhibiting effect on the growth of the tubercle bacilli which may in part explain its action in tuberculosis. The idea of a specific influence in this infection is probably incorrect, but in the reaction against its use the pendulum has swung too far and it is ofttimes neglected or even condemned in cases in which it might be well employed. Cod liver oil is valuable in many conditions of undernourishment. Thus it is of service in those types of *chronic rheumatism* or *gout* which are associated with malnutrition, in some cases of *neurasthenia* and *neuralgia,* in infantile *marasmus* and nearly all wasting diseases in which it is acceptable to the digestive tract. It is unique among the oils in that it is absorbable through the skin, at least by young infants, in sufficient quantity to have a perceptible influence upon nutrition.

Various measures have been recommended for overcoming the objectionable taste which is a great obstacle to the wider use of this remedy. None of these, however, are entirely successful. It is most frequently exhibited in the form of one of the numerous emulsions upon the market, of which that with malt extract is one of the best. It is sometimes given in flexible capsules, but these have the objection that they can only hold comparatively small doses.

Dose, one to four fluidrachms (3.75–15 cc.).

Off. Prep.—Emulsum Olei Morrhuæ, *U. S.;* Emulsum Olei Morrhuæ cum Malto, *N. F.;* Emulsum Olei Morrhuæ cum Hypophosphitibus, *N. F.;* Emulsum Olei Morrhuæ cum Vitello, *N. F.*

OLEUM MYRCIÆ. N. F.

OIL OF MYRCIA

"A volatile oil distilled from the leaves of *Pimenta Acris* (Swartz) Wight (Fam. *Myrtaceæ*)." *N. F.*

Oil of Bay; Bayöl, *G.;* Essence de Bay, *Fr.*

This oil is obtained from the *Pimenta acris* Wight. The common name of "oil of bay" is very unfortunate as it is liable to lead to confusion with the aromatic oil obtained from the sweet bay (*Laurus nobilis*) or with that from the bay laurel (*Umbellularia Californica*). The official name of oil of myrcia is not much better, for it has long been recognized that the plant from which it is derived does not belong to the genus *Myrcia.*

The *Pimenta acris,* from the leaves of which this oil is obtained, is a small tree, native in the West India Islands. The flowers are white and borne in cymes. The fruit is a small globular berry resembling allspice. The large leathery leaves yield in the neighborhood of 3 per cent. of volatile oil. Two varieties of *P. acris* occur in coastal districts where the pure species abounds, and which are locally known as "Bois d'Inde Citronelle" and "Bois d'Inde Anise." The leaves of these are said to be frequently admixed with the leaves of the true bay to the great detriment of the oil subsequently distilled. The oil from the "Citronelle" variety (*P. acris* var. *citrifolia*) contains citral and possesses the flavor of lemon (*Kew Bull.,* No. 5, p. 158, 1918). According to the account of Franck (*P. J.,* 1921, cvi, 318), "The picking is best done in June, when men and boys break off smaller branches and carry them to the distilleries. Here the leaves are cooked in immense brass decanters, from which the bay oil is drawn off, and the leaves tossed out, apparently unchanged, except from green to coppery brown. One hundred and thirty pounds of leaves are required to produce a quart of oil."

Proper *bay rum* is the product directly distilled from the leaves of the bay tree. As described by Fishlock (*C. D.,* 1912, lxxxi, 714) either the fresh or dried leaves are employed; 200 pounds of the dried leaves are mixed with 65 gallons of rum and about 100 gallons of water, containing a little salt, and the whole of the distillate from this collected.

The commercial oil of bay is a mixture of both heavy and light oils, as G. M. Beringer found the specific gravity of two samples of undoubted purity to be 0.975 and 0.994. (*A. J. P.*, 1887, 286.) This is due to the complex character of the oil and the erratic manner in which it is distilled in the West Indies. The loss of the heavier fraction produces an inferior oil.

Description and Physical Properties.—"Oil of Myrcia is a yellow or brownish yellow liquid having a pleasant, aromatic odor and a pungent, spicy taste. With an equal volume of alcohol, glacial acetic acid, or carbon disulphide, it yields slightly turbid solutions. An alcoholic solution is slightly acid to litmus paper.

"Specific gravity: 0.962 to 0.990 at 25° C. It is lævorotatory, the angle of rotation not exceeding −3°, in a 100 mm. tube, at 25° C. When mixed with an equal volume of a concentrated solution of sodium hydroxide it forms a semi-solid mass. Dissolve 2 drops of the Oil in 4 cc. of alcohol, and add a drop of ferric chloride T.S.; a light green color is produced; if the same test is made with a drop of dilute ferric chloride T.S., prepared by diluting the test solution with 4 times its volume of distilled water, a light bluish coloration is produced, which soon disappears. Shake 1 cc. of the Oil with 20 cc. of hot distilled water and filter; the filtered aqueous solution does not give more than a scarcely perceptible acid reaction with litmus paper and on adding a drop of ferric chloride T.S. it yields only a transient, grayish green but not a blue or violet color (*phenol*).

"Preserve it in small, well-stoppered amber-colored bottles, in a cool place, protected from light." *N. F.*

Mittmann (*A. Pharm.*, 1889, 529) reported the following constituents: 1, pinene; 2, possibly dipentene; 3, a polyterpene, probably diterpene (insoluble in alcohol); these three in small quantity only; 4, eugenol, the chief constituent; and, 5, methyl-eugenol, in smaller quantity. It has since been examined by Power and Kleber (*Ph. Rund.*, 1895, 60) who state that it contains from 60 to 65 per cent. of phenols, of which two were identified: eugenol and chavicol, two phenol esters, methyl-eugenol, $C_{11}H_{14}O_2$, and methyl-chavicol, phellandrene and a newly discovered terpene which they named *myrcene*, $C_{10}H_{16}$, and citral, $C_{10}H_{16}O$. (*Ph. Rund.*, 1895, 60.)

Uses.—The oil of bay is an active antiseptic, 1 part in 1000, according to Peck (*J. A. M. A.*, 1899, xxxii, p. 6) being sufficient to prevent the growth of bacteria. It is, however, almost never employed in its unmixed state. In the form of the compound spirit, which is practically equivalent to bay-rum, it affords a pleasant perfume for various external medicines. It has also been used in cases of *nervous headache, faintness* and other *nervous disorders*, either held to the nostrils, or applied on soft linen to the head and forehead. According to Berger (*Th. M.*, 1907, xxi, p. 221), it is a valuable local application in various diseased conditions of the skin, especially in *seborrhea* of the scalp. It is also grateful to the feeble and convalescent patient, by being sprinkled on the bed covering or otherwise made to impregnate the air of the chamber. The oil of bay is often adulterated, and is frequently sold by smugglers.

Off. Prep.—Spiritus Myrciæ Compositus, *N. F.*

OLEUM MYRISTICÆ. U. S., Br.

OIL OF MYRISTICA Ol. Myrist. [Myristica Oil Oil of Nutmeg]

"The volatile oil distilled from the dried kernels of the ripe seed of *Myristica fragrans* Houttuyn (Fam. *Myristicaceæ*)." *U. S.* "Oil of Nutmeg is the oil distilled from Nutmeg and rectified." *Br.*

Volatile oil of Nutmeg; Oleum Myristicæ Æthereum, Oleum Nucis Moschati, Oleum Nucistæ Æthereum; Huile volatile (Essence) de Muscade, *Fr.*; Oleum Macidis, *P. G.*; Aetherisches Muskatöl, Aetherisches Muskatnussöl, *G.*

This oil is obtained from nutmegs, after powdering them, by distillation with water, usually after the removal of their fat. Schimmel & Co. (1899) state that oil of nutmeg is made from the light, worm-eaten nuts, of which large quantities are rejected in sorting the different qualities in Holland; the worm robs the nutmeg of its fat oil, while the essential oil remains in the nut in full. According to Cushny (*Proc. Royal Soc. Med.*, 1908), nutmeg yields from 3 to 8 per cent. of volatile oil.

Description and Physical Properties.—"A colorless or pale yellow liquid, having the characteristic odor and taste of nutmeg.

"The oil is soluble in an equal volume of alcohol and in 3 volumes of 90 per cent. alcohol, by volume. Specific gravity: 0.859 to 0.924 at 25° C. Optical rotation: varies from +12° to +30° to a 100 mm. tube at 25° C. Refractive index: 1.4780 to 1.4895 at 20° C. A solution of the recently distilled Oil in an equal volume of alcohol is neutral or only slightly acid to moistened litmus paper. Evaporate 3 Gm. of the Oil in a small tared dish on a bath of boiling water: the weight of the residue does not exceed 0.006 Gm.

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

"Colorless or pale yellow. Odor and taste those of Nutmeg. Specific gravity 0.870 to 0.925; *optical rotation* +13° to +30°; *refractive index* at 25° C. 1.474 to 1.484. Soluble in 3 parts of *alcohol* (90 per cent.). Leaves not more than 5 per cent. of residue when evaporated on a water-bath." *Br.*

Power and Solway (*Tr. Chem. Soc.*, 1907, 2037) have analyzed the volatile oil of nutmeg and find that about 80 per cent. of it is dextro-pinene and dextro-camphene with about 8 per cent. of dipentene, besides small proportions of eugenol and iso-eugenol, linalool, borneol, terpineol, geraniol and safrol; they found about 4 per cent. of *myristicin*, small amounts of free myristic acid, and traces of esters of this and other fatty acids. Semmler (*B. Chem. G.*, 1890,

1803) examined an oil of myristica of sp. gr. 0.8611 which contained only terpenes; these boiled at about 50° C. under a pressure of 8 mm.

Myristicin, $C_{12}H_{14}O_3$, is of interest as the poisonous ingredient of nutmeg (see under *Uses*). It is the 3:4:5-trioxybenzene-methyl-methylene ether and has a melting point of 30° C.

Uses.—The oil of nutmeg unites to the common properties of the aromatics considerable narcotic power. It causes in the lower animals dilatation of the pupils, unsteadiness of the gait followed by sleepiness, with slow respiration, and, if the dose be large enough, loss of reflexes. According to Dale (*Proc. Royal Soc. Med.*, Feb., 1909), doses large enough to produce narcosis in the cat are invariably fatal through fatty degeneration of the liver. A number of fatal cases of nutmeg poisoning have been reported in human beings. For references to cases of nutmeg poisoning see Power and Solway (*A. J. P.*, 1908, 563). Cullen (quoted by above) reports a case in which 2 drachms of powdered nutmeg produce drowsiness deepening into stupor, the patient continuing for several hours alternately delirious and sleeping. Dale found that dose of 1.9 Gm. per kilo caused in a cat a semi-comatose condition with death in 24 hours with fatty degeneration of the liver.

The toxic ingredient in oil of nutmeg is undoubtedly myristicin. Dale found that myristicin caused similar symptoms but the quantity required was much larger than would be contained in a toxic dose of powdered nutmeg, the fatal dose of myristicin for a cat being between 0.5 and 1 cc. per kilo; Power and Solway suggest that this difference may be due to imperfect absorption and state that 2 minims (0.12 cc.) hypodermically, will produce in the cat extensive degeneration of the liver.

The oil of nutmeg is used to correct the taste of various drugs and as a local stimulant to the gastro-intestinal tract. It probably has also some value as a nerve sedative.

Dose, one-half to three minims (0.03–0.2 cc.).

Off. Prep.—Spiritus Myristicæ, *Br.;* Elixir Pepsini et Rennini Compositum, *N. F.;* Mistura Oleo-Balsamica, *N. F.*

OLEUM OLIVÆ. U. S., Br.

OLIVE OIL Ol. Oliv.

"The fixed oil obtained from the ripe fruit of *Olea europæa* Linné (Fam. *Oleaceæ*)." *U. S.* "Olive Oil is the oil expressed from the ripe fruit of Olea europæa, *Linn.,* and refined." *Br.*

Sweet Oil; Huile d'Olive, *Fr. Cod.;* Olivarum Oleum, *P. G;* Olivenöl, *G.;* Olio di olive, *It.;* Aceite de olivas, *Sp.*

Olea europæa L. is one of the leading fruit trees of the world. It is usually from fifteen to twenty-five feet in height, though sometimes much larger, especially in Greece and the Levant. It has a solid, erect, unequal stem, with numerous straight branches, covered with a grayish bark. The leaves are evergreen, firm, oblong or lanceolate, entire, two or three inches in length, smooth and of a dark green color on their upper surface, whitish and almost silvery beneath. The flowers are small, yellowish white, and disposed in opposite axillary clusters, about half as long as the leaves, and accompanied with small, obtuse, hoary bracts. The fruit, or olive, is a smooth, oblong or oval drupe, greenish at first, but of a deep violet color when ripe, with a fleshy mesocarp and a very hard endocarp. Clusters of not less than thirty flowers yield only two or three ripe olives.

The olive tree, which is probably native to western Asia or the eastern Mediterranean district, flourishes at present in all the countries bordering on the Mediterranean, and has been cultivated from time immemorial in Spain, the south of France, and Italy. It begins to bear fruit after the second year, is in full bearing at six years, and continues to flourish for a century. There are forty varieties, distinguished by the form of the leaves and the shape, color, and size of the fruit. The variety *longifolia* of Willdenow is said to be chiefly cultivated in Italy and the south of France, and the *latifolia* in Spain. The latter bears much larger fruit than the former, but the oil is less esteemed. The olive is largely cultivated in the north of Africa, especially in the vicinity of Tunis, southern California and other warm regions.

Olives are cultivated especially in Spain in the district of Cadiz. Two classes are produced, the one known as the "Queen olive," a large olive, which is mostly exported to the United States; the other the Manzanillo, or small olive, which is chiefly consumed in Spain, South America and Cuba.

Pickled olives, made by soaking green olives first in dilute solution of sodium hydroxide and then in salt water, are largely used as an article of food; the ordinary green olive of commerce has been picked before ripening. The ripe olive, which, in the United States, is chiefly obtained from California, is dark-purple, often almost black, very different in taste from the ordinary unripe pickled fruit, and is said to contain about 50 per cent. of olive oil, so that it affords an excellent method of administering fat.

There have been reported several epidemics of a peculiar form of food poisoning, known as *botulism,* from the eating of ripe olives which had been improperly preserved. This disease is caused by the *Bacillus botulinus,* or the toxins produced by it. It follows the use not only of olives, but of many other foods which have not been properly sterilized. The most prominent symptoms, which usually begin a few hours after the ingestion of the peccant food, are: Nausea, vomiting and diarrhea, with abdominal cramps, followed by constipation: there are severe nervous disturbances, especially of the visual apparatus—dilatation of the pupils, diplopia, and ptosis—loss of voice, dryness of the throat and great thirst, followed by exhaustion and, in many cases, death, sometimes preceded by delirium.

The leaves and bark of the olive tree have an acrid and bitter taste, and have been employed as substitutes for cinchona, though with no great success. In hot countries, a substance resembling the gum-resins exudes spontaneously from the bark. It was thought by the ancients to possess useful medicinal properties, but is not now employed. Analyzed by Pelletier, it was found to contain resin, a little benzoic acid, and a peculiar principle analogous to gum, which has been named *olivile*. But the fruit is by far the most useful product. In the unripe state the fruit is hard and insupportably acrid, but when macerated in water or an alkaline solution, and afterwards introduced into a solution of common salt it loses these properties, and becomes a pleasant and highly esteemed article of diet. Mannite has been found in all parts of the tree while in vital activity, as in the green leaves and unripe fruit, but cannot be detected in the yellow fallen leaves or in the perfectly ripe fruit.

The pericarp, or fleshy part of the ripe olive, abounds in a fixed oil, from 10 to 20 per cent., which constitutes its greatest value, and for which the tree is chiefly cultivated in southern Europe. The olives ripen from November to March, and the oil is obtained by first bruising them in a mill and then submitting them to pressure. The product varies much, according to the state of the fruit and the circumstances of the process. The best, called *virgin oil*, is obtained from the fruit picked before perfect maturity, and immediately pressed. It is distinguished by its greenish hue. The common oil used for culinary purposes and in the manufacture of soaps is procured from very ripe olives, or from the pulp of those which have yielded the virgin oil. In the latter case the pulp is thrown into boiling water, and the oil removed as it rises. An inferior kind, employed in the arts, especially in the preparation of the coarser soaps, plasters, unguents, etc., is afforded by fruit which has been thrown into heaps, and allowed to ferment for several days, or by the marc left after the expression of the finer kinds of oil, broken up, allowed to ferment, and again introduced into the press.

Description and Physical Properties.—" A pale yellow, or light greenish-yellow, oily liquid, having a slight, peculiar odor and taste, with a faintly acrid after-taste. Olive Oil is slightly soluble in alcohol, but is miscible with ether, chloroform, and carbon disulphide.

" Specific gravity: 0.910 to 0.915 at 25° C. When cooled to from 10° to 8° C., the Oil becomes somewhat cloudy from the separation of crystalline particles, and at 0° C. it usually forms a whitish granular mass. Mix 5 cc. of the Oil in a test tube with 5 cc. of a mixture of equal volumes of amyl alcohol and carbon disulphide, the latter containing 1 per cent. of precipitated sulphur in solution, and immerse the test tube to one-third of its depth in boiling, saturated aqueous solution of sodium chloride: no reddish color develops in fifteen minutes (*cottonseed oil*). Mix 2 cc. of the Oil with 1 cc. of hydrochloric acid containing 1 per cent. of sucrose, shake the mixture for half a minute, and allow it to stand for five minutes: on adding 3 cc. of distilled water to the mixture and shaking it, the acid layer shows no pink color (*sesame oil*). Saponify 10 Gm. of Olive Oil by heating it under a reflux condenser with a solution of 4 Gm. of potassium hydroxide in 80 cc. of alcohol for one hour. Neutralize exactly with diluted acetic acid, using phenolphthalein T.S. as indicator, and wash into 120 cc. of boiling lead acetate T.S. Boil the mixture for one minute, and cool by immersing the flask in cold water, occasionally rotating the contents to cause the precipitate to adhere to the sides of the flask. Decant the liquid, wash the precipitate with cold water to remove excess of lead acetate, then wash with 90 per cent. alcohol (by volume). Add 100 cc. of ether, cork well, and allow to stand until the precipitate is disintegrated. Connect with a reflux condenser, boil for five minutes, cool to about 15° C. and allow to stand over night. Filter, and thoroughly wash the precipitate of lead soaps with ether. Wash the precipitate into a 500 cc. separator by means of a jet of ether, alternating with diluted hydrochloric acid at the end, if a little of the precipitate adheres to the filter paper. Add enough diluted hydrochloric acid to make the total acid layer about 100 cc., and enough ether to make the total ether layer about 100 cc. and shake vigorously for several minutes. Allow the layers to separate, draw off the acid layer, and wash the ether once by shaking with 50 cc. of diluted hydrochloric acid and then with several portions of water until the water washings are no longer acid to methyl orange T.S. Transfer the ether solution to a dry flask, evaporate the ether, add a little dehydrated alcohol and evaporate on a steam bath. Dissolve the dry fatty acids by warming with 50 cc. of 90 per cent. alcohol (by volume), slowly cool the solution to 15° C., shaking frequently to aid crystallization, and allow the mixture to stand at 15° C. for thirty minutes. No crystals separate (*peanut oil*). Saponification value: not less than 190 and not more than 195. Iodine value: not less than 79 and not more than 90.

" Preserve in well-closed containers, in a cool place." *U. S.*

" Pale yellow or greenish yellow. Faint but not rancid odor; taste bland. Frequently assumes a pasty consistence when maintained for some time at a temperature of 10° C., and at a lower temperature may become a soft granular mass. Specific gravity 0.915 to 0.918; *saponification value* 188 to 197; *iodine value* 79 to 87; acid value not more than 6.0; *refractive index* at 40° C. 1.4605 to 1.4635. A mixture of 2 millilitres of the Oil with 1 millilitre of *amylic alcohol* and 1 millilitre of a solution (1 in 100) of *precipitated sulphur in carbon disulphide,* placed in a test-tube immersed in boiling *water*, does not assume a red color within thirty minutes (absence of cottonseed oil). When a mixture of 2 millilitres of the Oil and 1 millilitre of *hydrochloric acid* containing 1 per cent. of *refined sugar* is shaken for half a minute, and allowed to stand for five minutes, the acid layer does not become pink (absence of sesame oil). When 1 millilitre of the Oil and 15 millilitres of *N/1 alcoholic solution of potassium hydroxide* are boiled for twenty minutes in a flask provided with a reflux condenser, set aside for twenty-four hours at a temperature not exceeding 15.5° C., and afterwards heated on a water-bath for three minutes, the solution does not deposit crystals on standing for twenty-four hours further (absence of arachis oil)." *Br.*

The concrete portion, about 28 per cent of the oil, which separates at a freezing temperature, consists chiefly of the glyceride of palmitic acid, together with a smaller amount of glyceride of arachidic acid (stearic acid is stated by Hehner and Mitchell to be absent entirely); the liquid portion is essentially olein, with a small amount (seven parts for ninety-three of olein) of the glyceride of the less saturated linoleic acid. According to Braconnot, the oil contains 72 per cent. of olein and 28 of palmitin. A small quantity of phytosterin has also been found in the oil. Olive oil is solidified by nitrous acid and mercuric nitrate, and converted into *elaidin.* (See under *Olea Fixa.*)

The greenish color is owing to the presence of a trace of chlorophyll, and a trace of cholesterin is also extracted by repeated agitation with glacial acetic acid.

For discussion of the spectra of olive oil, see *P. J.*, 3d series, vii, 22, 110.

Olive oil, when exposed to the air, is prone to become rancid, acquiring a disagreeable odor, a sharp taste, and a thicker consistence; it also loses its color, and the change is promoted by heating it.

It is frequently adulterated with the cheaper fixed oils, especially with cottonseed oil, peanut oil, sesame oil and poppy seed oil. Of these, sesame is easily recognized; for peanut oil there is as yet no reliable color reaction, and while Bechi's reaction may, under certain conditions, answer well for the detection of cottonseed oil, this, under others, has also proven unreliable. (*Ph. Ztg.*, 1904, 104.) According to Kreis and Grob (*S. W. P.*, 1901, 88), Billier's test is very sensitive. It is carried out by shaking the suspected oil with a solution of resorcinol in benzene and afterwards with nitric acid. Olive oil under these circumstances remains unchanged in color, cottonseed and nut oil become red violet and maw seed oil is turned brown red. (See also official test for peanut oil.) Bechi's test for ascertaining the admixture of cottonseed oil with olive oil has received the approval of the Commission of Florence after most exhaustive experiments, and is as follows: One grain (0.065 Gm.) of silver nitrate is dissolved in fifteen minims (0.9 cc.) of water, and six and a half fluidounces (195 cc.) of alcohol are added. Two fluidounces (60 cc.) of ether may be added to render the solution more easily miscible with the oil, but it is not absolutely necessary. A solution of eighty-five parts of amyl alcohol and fifteen parts of rape seed oil is prepared. These reagents should not be kept on hand any length of time. To ten cc. of the oil to be examined one cc. of the solution of silver nitrate is added, and then from eight to ten cc. of the amyl alcohol reagent; the mixture is agitated strongly, and heated on a water bath for five or ten minutes. In the case of pure oils the color is unaltered by the addition of the reagents; if cottonseed oil be present, a brownish color or turbidity, varying from a light brown to a deep maroon or black (according to the extent of the adulteration), will be produced. (*A. J. P.*, 1887.) Milliau's test is a modification of the foregoing. If the fatty acids instead of the oil itself are treated with the same reagents, the same reduction of the silver salts occurs and the same brown color as in the Bechi test. Halphen's test with a mixture of amyl alcohol and carbon disulphide containing about 1 per cent. of sulphur in solution is now regarded as the most distinctive for cottonseed oil. For details see the official test. Lewkowitsch (*Chemical Analysis of Oils, Fats, and Waxes,* 2d ed., 1898, 462) says that the color reactions proposed by various authors are altogether unreliable and yield no definite results, with the exception of the color test (Baudoin's test, see *Oleum Sesami*) for sesame oil and perhaps Bechi's and Milliau's or Halphen's for cottonseed oil. Bulletin 77 (1905), of the Bureau of Chemistry, United States Department of Agriculture, showed that most of the spurious and adulterated olive oil in the United States was of domestic origin and that the oil as imported in original packages was mostly genuine. This has been verified by numerous other investigators during recent years. Since the passage of the Food and Drugs Act in 1906 it is rare to find a labelled container of olive oil adulterated, although much that is sold in bulk is still found to be spurious. In several states it has been judicially decided that the synonyms "sweet oil" and "salad oil" when unqualified mean olive oil. A low grade of olive oil used for soap making and other technical purposes is imported at a less rate duty than is collected on edible olive oil. The frequent use of such low grade oil for table purposes by those who are not particular about quality and flavor led to the requirement on the Part of the U. S. Treasury Department that such "technical oil" must be denatured for admission. There are three alternative and optional methods of denaturing. They consist in adding to the oil a small portion of oleoresin of capsicum, of oil of rosemary or of kerosene. Arachis oil, which is produced in large quantities in Marseilles, has been found in numerous samples of imported olive oil. According to

Tambon, the present-day adulterations do not consist in the addition of a single cheaper oil, but of ingeniously prepared mixtures of different oils in such proportions to each other that on analysis it becomes difficult or impossible to distinguish the adulterated from the genuine oil by the chemical and physical constants accepted for the latter.

Uses.—Olive oil is nutritious and mildly laxative and is often used in milder cases of chronic *constipation*, especially when associated with malnutrition. (See *J. A. M. A.*, 1919, lxxiii, 1441.) In the form of enema it is often a useful remedy in *fecal impaction*. It was formerly largely used in the treatment of *gall stones* with the idea that it stimulated the secretion of bile. The concretions which were passed by these patients, however, were shown to be masses of hardened soap and it is extremely questionable whether the oil has any real value in this disease. Externally it is useful to soften and relax the skin and to protect it against the action of the air. The most extensive use of olive oil is in pharmacy as a constituent of liniments, ointments, cerates, and plasters.

Dose, as a laxative, from one-half to two fluidounces (15–60 cc.).

Off. Prep.—Linimentum Ammoniæ, *Br.;* Linimentum Calcis, *Br.;* Linimentum Camphoræ, *Br.;* Oleum Phenolatum, *N. F.;* Unguentum Fuscum, *N. F.*

OLEUM PHOSPHORATUM. Br.

PHOSPHORATED OIL

"Phosphorated Oil contains 1 per cent. by weight of Phosphorus. It should be freshly prepared." *Br.*

Huile phosphorée, *Fr. Cod.;* Liniment phosphoré, *Fr.;* Phosphorhaltiges Oel, *G.;* Aceite fosforado, *Sp.*

"Phosphorus, 1 *gramme;* Almond Oil, previously heated to 150° C., cooled and filtered, 98 *grammes;* Oil of Lemon, 1 *gramme.* Add the Phosphorus to the Almond Oil contained in a stoppered bottle capable of holding rather more than the required quantity; warm to about 80° C., and shake until the Phosphorus is entirely dissolved; cool, and add the Oil of Lemon. A clear, pale-yellow liquid, phosphorescent in the dark." *Br.*

Phosphorated oil was not retained in the U. S. P., but has been admitted to the N. F. (see Part III).

The object of heating the oil is to expel air and traces of water, which would oxidize the phosphorus. The ether not only assists in the preservation of the finished preparation, but is also of use in rendering the oil less disagreeable to the taste. E. R. Squibb passes a current of carbon dioxide through the oil contained in the bottle in which it is to be kept, to expel the air and prevent oxidation.

This is a clear and colorless or but slightly colored oil, phosphorescent in the dark, and having the odor and taste of phosphorus quite distinctly. It should be perfectly free from any particles of undissolved phosphorus. It may be administered in the form of an emulsion, like the official almond emulsion, and flavored with oil of bitter almond, or preferably in capsules; each minim contains a little less than one one-hundredth of a grain of phosphorus.

Dose, one to two minims (0.06–0.13 cc.).

OLEUM PICIS RECTIFICATUM. U. S.

RECTIFIED OIL OF TAR Ol. Pic. Rect. [Oleum Picis Liquidæ Rectificatum, U. S. P. IX]

"The volatile oil from pine tar rectified by steam distillation." *U. S.*

Rectified Tar Oil; Oil of Tar; Oil of Pine Tar; Huile volatile de Goudron, *Fr.;* Theeröl, Pechöl, *G.*

This oil is prepared by distilling wood tar, the residue left in the still being known as pitch. It represents thoroughly the medicinal properties of tar, and is preferable on account of its less offensive taste.

Description and Physical Properties.—"A thin liquid, having a dark reddish-brown color, and a strong, empyreumatic odor and taste.

"The oil is soluble in all proportions in alcohol. Specific gravity: 0.960 to 0.990 at 25° C. An alcoholic solution of the Oil is acid to moistened blue litmus paper." *U. S.*

For composition of this oil see *Pix Pini.*

The thick tarry oil of high viscosity and almost black color, found upon the market and frequently supplied for oil of tar, does not comply with the U. S. P. requirements of sp. gr., as it is usually much heavier than water, while the U. S. P. is lighter.

Uses.—The oil of tar is used chiefly in the treatment of *chronic bronchitis.* Its action is practically the same as that of creosote, which is indeed its most important constituent. It may be administered either in emulsion or by dropping it on sugar. It is often added to boiling water for inhalation in the proportions of five to ten minims to a pint. It is also used externally in various *skin diseases.*

Dose, one to five minims (0.06–0.3 cc.), administered in capsule or in emulsion.

Off. Prep.—Unguentum Picis Compositum, *N. F.;* Syrupus Picis Pini, *U. S.*

OLEUM PIMENTÆ. N. F.

OIL OF PIMENTA Ol. Piment. [Oil of Allspice Pimento Oil]

"A volatile oil distilled from the fruit of *Pimenta officinalis* Lindley (Fam. *Myrtaceæ*), yielding not less than 65 per cent., by volume, of eugenol [$C_{10}H_{12}O_2$ (164.15)]." *N. F.*

Oleum Amomi; Oil of Pimento; Huile volatile (Essence) de Piment de la Jamaïque, *Fr.;* Nelkenpfefferöl, Pimentöl, *G.*

Oil of pimenta was deleted from the British Pharmacopœia 1914, and from the U. S. X, but is recognized by the N. F. V.

The berries of the allspice (see *Pimenta*) yield from 1 to more than 4 per cent. of the volatile oil, which as found in commerce is brownish-red, and has the odor and taste of pimenta, though warmer and more pungent. It has a slightly acid reaction.

Description and Physical Properties.—"Oil of Pimenta is a colorless, yellow or reddish liquid, becoming darker with age and having the characteristic odor and taste of allspice. It is soluble in an equal volume of 90 per cent. alcohol; also soluble in 2 volumes of 70 per cent. alcohol.

"Specific gravity 1.018 to 1.048 at 25° C. The optical rotation varies from 0° to –4° in a 100 mm. tube at 25° C.

"**Assay.**—Introduce 10 cc. of the oil into a flask with a long graduated neck (cassia flask) add 50 cc. of sodium hydroxide T.S., shake the mixture for five minutes and then heat it on a water bath during ten minutes, cool and when the liquids have separated completely add sufficient sodium hydroxide T.S. to raise the lower limit of the oily layer within the graduated portion of the neck and note the volume of the residual liquid. The residual liquid measures not more than 3.5 cc. indicating the presence of not less than 65 per cent. by volume, of eugenol.

"Preserve it in well-stoppered amber-colored bottles, in a cool place, protected from light." *N. F.*

Oil of pimenta contains from 60 to 75 per cent. of eugenol; the remainder is chiefly a sesquiterpene, whose exact composition has not been determined. There is present also a small amount of resin and an unknown odorous principle. Oil of pimenta, therefore, is analogous in its constitution to oil of clove (see *Oleum Caryophylli*). Nothing is known of the constituents which give oil of pimenta its characteristic odor.

Oil of pimenta is given for the same purposes as are the other stimulant aromatic oils.

Dose, from one to five minims (0.06–0.3 cc.).

Off. Prep.—Liquor Pepsini Aromaticus, *N. F.;* Spiritus Myrciæ Compositus, *N. F.*

OLEUM PINI PUMILIONIS. U. S.

OIL OF DWARF PINE NEEDLES Ol. Pin. Pumil.

"The volatile oil distilled from the fresh leaves of *Pinus montana* Miller (*Pinus Pumilio* Haenke) (Fam. *Pinaceæ*). Oil of Dwarf Pine Needles yields not less than 5 per cent. of esters calculated as bornyl acetate [$C_{10}H_{17}.C_2H_3O_2$]." *U. S.*

Oleum Pini, *Br., 1898;* Oil of Pine; Dwarf Pine Oil; Pine Needle Oil; Latchenkieferöl, Krummholzöl, *G.;* Oleum templinum, Pumiline.

Beissner, in his *Handbuch der Nadelholzkunde,* considers *P. Pumilio* Haenke, a synonym of *P. montana* Mill., whereas in the *Index Kewensis* the latter is brought under the former. Most authors agree with De Candolle and Beissner in bringing *P. Pumilio* Haenke, under *P. montana* Mill. The latter known as *Swiss Mountain Pine* varies in habit from a low shrub to a pyramidal tree which attains a height of 40 feet. Its branchlets are brownish and bear bright green acute leaves in fascicles of 2 and up to 2 inches in length. Its cones are ovate or conic-ovate and from ¾ to 2¼ inches long. It is a native of the mountains of Central Europe. The exudate obtained by cutting off the branches is called *Hungarian Balsam.*

The volatile oils of several of the coniferous trees are used for medicinal purposes and different ones have from time to time been official in several countries.

The Br. 1885 recognized, under the name of *Oleum Pini,* an oil from the leaves of the *P. sylvestris* L. but this has been replaced by a similar product from the Siberian Fir (see *Oleum Abietis*). The U. S. P. recognizes that from the leaves of the *mountain pine.*

Description and Physical Properties.—"A colorless or faintly yellowish liquid, having a pleasant, aromatic odor, and a bitter, pungent taste.

"The Oil is soluble in 10 volumes of 80 per cent. alcohol, by volume. Specific gravity: 0.853 to 0.869 at 25° C. Optical rotation: varies from –4° 30′ to –9° in a 100 mm. tube at 25° C. Refractive index: 1.4750 to 1.4800 at 20° C. A solution of the recently distilled Oil in 80 per cent alcohol (1 in 10) is neutral or only slightly acid to moistened litmus paper. Less than 1 per cent. of the Oil distils below 165° C.

"**Assay.**—Proceed as directed for esters under *Oleum Menthæ Piperitæ,* using 10 cc. of Oil of Dwarf Pine Needles. Multiply the number of cc. of half-normal alcoholic potassium hydroxide consumed in the saponification, by 9.811, and divide the product by the weight of the Oil taken. The result shows the per cent. of esters calculated as bornyl acetate.

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

Pine oil contains lævo-pinene, lævo-phellandrene, sylvestrene, *bornyl acetate,* and in the last portions of the distillate, cadinene. (Gildemeister and Hoffmann, *Aetherische Oele,* p. 338.) It is supposed that the pine oil owes its odor to the presence of the acetic ester of borneol, which is ordinarily present to the amount of about 3.5 per cent., and Schimmel & Co. (*Schim. Rep.* for Oct., 1897) found in a sample of American fir oil as much as 12.1 per cent.

Under the name of *templin oil* a volatile oil from the cones is sold. It is much lighter in density than the leaf oil and has a higher optical rotation, and contains a greater proportion of esters. (*Perf. & Ess. Oil Rec.,* 1915, vi, p. 165.) Both the cones and leaves of *Abies Picea* yield oils known respectively as *pine cone oil* and *pine needle oil.* According to *Schimmel's Report* for April, 1897, they both contain pinene, limonene, and bornyl acetate. The oil from *Pinus sylvestris,* known as *fir oil,* also contains bornyl acetate to the amount of 12 per cent. according to *Schimmel's Report* for October, 1897, 47. On the other hand, the oil from *Larix Europæa,* known as *larch needle* *oil,* contains 8.1 per cent. of bornyl acetate and 6.14 per cent. of free borneol. (*Ibid.,* 61.)

Uses.—In medicine it may be employed for many of the purposes for which oil of turpentine has been used. As an expectorant in *chronic bronchitis* it may be administered by the mouth but is especially prized as an inhalant because of its pleasant odor. For this purpose a few drops may be placed in boiling water and the vapors inhaled. It has also been employed internally in the treatment of *chronic rheumatism.*

The leaves of the *Pinus sylvestris,* with those of other European firs and pines, by pounding are converted into a fibrous substance, known as *fir wool* (*Fichtenwolle*), which is used in Germany as a local application in *chronic rheumatism,* the affected part being enveloped in a thick batting of the fir wool, which is also sometimes made into clothing for rheumatic persons. An extract of the leaves is also sold under the name of *fir wool extract,* for use in rheumatism.

Dose, of oil of pine needles, five to ten minims (0.3–0.6 cc.).

OLEUM RICINI. U. S., Br.

CASTOR OIL Ol. Ricin.

"The fixed oil obtained from the seeds of *Ricinus communis* Linné (Fam. *Euphorbiaceæ*)." *U. S.* "Castor Oil is the oil expressed from the seeds of Ricinus communis, *Linn.*" *Br.*

Huile de Ricin, *Fr. Cod.;* Oleum e semine Ricini, *Fr.;* Ricinusöl, *G.;* Olio di ricino, *It.;* Aceite de ricino; Oleum Palmæ Christi, *Sp.*

The castor oil plant, or *palma Christi,* is a native of India and is now extensively cultivated in the warmer regions throughout the world. In India there are about seventeen different varieties grown which are grouped into two types: The first consists of tall shrubs or small trees, being usually planted as a shade for other crops and yielding large seeds which contain an abundance of inferior oil. The second type includes the herbaceous annuals, which, while they produce small yields, yield a much better grade of fixed oil.

The following description applies to the plant as cultivated in cool latitudes. The stem is of vigorous growth, erect, round, hollow, smooth, glaucous, somewhat purplish towards the top, branching, and from three to eight feet or more in height. The leaves are alternate, peltate, palmately six to eleven lobed, the lobes acute or acuminate and serrate, smooth on both sides, and of a bluish-green color. The flowers are monœcious, stand upon jointed peduncles, and form a pyramidal terminal raceme, of which the lower portion is occupied by the male flowers, the upper by the female. Both are destitute of corolla. In the staminate flowers the calyx is divided into five oval, concave, pointed, reflected, purplish segments, and encloses numerous stamens, united into fasciculi at their base. In the pistillate the calyx has three or five narrow lanceolate segments, and the ovary, which is roundish and three-sided, supports three linear, reddish stigmas, forked at their apex. The fruit is a roundish, glaucous capsule, with three projecting sides, covered with tough spines, and divided into three loculi, each containing one seed, which is expelled by the bursting of the capsule. The seeds are now produced in commercial quantities in India, the Islands of West Indies, South America, and southern, middle and western United States. Those supplies received from India have contained less impurities than the supplies of castor seeds from the West Indies and South America. The impurities found in commercial supplies include hulls, sand, stones, pebbles, black, broken, decorticated and immature castor seeds. Black "beans" (seeds) are those whose kernels have become discolored as a result of the seeds having been wet. Black, decorticated and broken beans, if not removed from the stock, have the effect of increasing the acidity of the oil produced therefrom. An interesting and valuable article on the cultivation of the castor bean in the United States appears in the *Proc. P. Ph. A.,* 1916, p. 209, by Joseph L. Lemberger. The flowers appear in July, and the seeds ripen successively in August and September. A decoction or poultice of the leaves is sometimes used as a local galactagogue, and an infusion has been given internally for a similar purpose.

1. The Seeds.—These are from 8 to 18 mm. long and 4 to 12 mm. broad, oval, compressed, obtuse at the extremities, very smooth and shining, and of a grayish or ash color, marbled with reddish-brown spots and veins. At one end of the seed is a small yellowish caruncle, from which an obscure longitudinal ridge proceeds to the opposite extremity, known as the raphe. In its general appearance the seed is thought to resemble the insect called the *tick,* the Latin name of which has been adopted as the generic title of the plant. Its variegated color depends upon a very thin pellicle closely investing a hard, brittle, blackish, tasteless, easily separated shell, within which is the kernel, highly oleaginous, of a white color, and of a sweetish taste succeeded by a slight degree of acrimony. The seeds easily become rancid, and are then unfit for the extraction of the oil, which is acrid and irritating. G. J. Scattergood found the odor of castor oil to be developed in the beans when bruised with water, and much more powerfully in those long kept than in the fresh. The water distilled from the seeds has a peculiar nauseous odor, quite distinct from that of the oil.

The seeds are active poisons; three have produced fatal gastro-enteritis in the adult. Their poisonous action, as first shown by Stillmark in 1889, is due to an albumose called *ricin.* This has been obtained as a white amorphous powder soluble in water, neutral in reaction. It is so actively poisonous that 0.002 milligramme is sufficient to kill a rabbit. It is a peculiarly interesting substance because when injected in small doses the body produces an antitoxin precisely analogous to those produced against bacteria. Commercially ricin has been employed for the detection of pepsin. For details of the method see Solms. (*Z. K. M.*, 1907.)

The most important constituent of the castor bean is the fixed oil, of which they yield about 50 per cent. The cake left after the expression of the oil known as *castor pomace* contains a nitrogenous crystallizable body which differs from the alkaloids in not forming salts with acids. This substance, which was first described by Tuson in 1864 and named by him *ricinine,* has been reinvestigated by Phillippe and Maquerme (*Proc. A. Ph. A.*, 1904, 950); they regard it as a dimethyl-ester of ricinic acid and assign a formula $C_8H_8O_2N_2$. Böttcher who prepared 450 grammes of the alkaloid from 300 kilos of castor beans finds the pure alkaloid to melt at 200° C. and upon hydrolysis with potassium carbonate to yield ricininic acid melting at 298° C. He questions the formula assigned by Phillippe and Maquerme. A typical zymogen is also present. It is soluble in fats and in a mixture of fats and ethyl ether, and is activated by acids.

Castor seeds consist of 20 per cent. of husks, which are rich in mineral constituents but contain no oil, and 80 per cent. of kernels. The whole seeds contain about 50 per cent. of oil. One of the early methods of obtaining castor oil was boiling the seeds with water and skimming off the separated oil. This has long since been abandoned for less wasteful methods. Two methods may be economically used—extraction with an appropriate solvent, or expression. Some oil has been produced in European countries by extracting the ground seed with petroleum benzin or alcohol but the oil as obtained by extraction is not as satisfactory for medicinal use as that obtained by expression.

The expression may be hot or cold. The seeds are first decorticated by being passed between properly adjusted rollers and the kernels are separated from the husks by an air blast. The medicinal oil is expressed cold, or with the kernels not warmer than 50° C. as above this temperature ricinine is dissolved. The residue is sometimes expressed a second or even a third time, with elevation of the temperature. These later fractions of oil are used for industrial or soap making purposes. The press cake called *castor pomace* is unfit for feeding animals as it contains the poisonous constituents of the seed. Attempts have been made to free the press cake from these poisonous principles by different methods of treatment, but no castor press cake has been produced on the large scale that is safe for feeding purposes. The press cake therefore finds its principal use as a fertilizer. About 40 per cent. of oil is obtained by expression, 33 per cent. in the first pressing and the balance in the later pressings. A "cage" hydraulic press is used in the pressing operation. Extraction of the remaining oil from the press cake is frequently accomplished by the use of very elaborate extraction apparatus known as a "rotary extractor."

The albuminous principles which may have accompanied the oil are then removed by steaming, which also destroys any of the enzyme that might be present and it is finally filtered. If not of satisfactory color it may be bleached by treatment with fuller's earth and filtration.

India was for many years the world's principal production point for castor oil, Marseilles, France, coming next. During the World War castor oil was used extensively as a motor lubricant for aeroplanes. The supplies from India were cut off in the early part of the war by the destruction of shipping and a great scarcity was threatened. In both Great Britain and the United States all stocks of high grade castor oil were seized, the lower grades being left for medicinal use. Its qualities as an aeroplane lubricant are discussed by C. Frabot, *Ann. Chim.,* 1918, 81. The cultivation of the castor plant was urged in many parts of the United States, particularly in the southern States, but the attempts were usually unsuccessful. See Grosh, *D. C.,* 1914, p. 197 and J. L. Lemberger, *Proc. Penna. Ph. A.,* 1920, p. 155. In 1918 supplies began to come in more rapidly. India furnished eight million pounds to Great Britain alone and the rest of the world was supplied principally by Japan, and Java, each of which countries exported nearly two million pounds. The United States produced some but not very much.

Properties.—Pure castor oil is a thick, viscid, colorless liquid, with little odor, and a mild though somewhat nauseous taste, followed by a slight sense of acrimony. As found in commerce it is often tinged with yellow and has an unpleasant odor, and parcels are sometimes, though rarely, met with of a brownish color and hot acrid taste. It does not readily congeal by cold. When exposed to the air it slowly thickens, without becoming opaque. When exposed to the air in a thin layer, it slowly dries to a varnish-like film. It is heavier than most of the other fixed oils. It differs also from most other fixed oils in being miscible in all proportions with cold absolute alcohol.

It is officially described as: "A pale yellowish or almost colorless, transparent, viscid liquid. It has a faint, mild odor, and a bland, afterwards slightly acrid and usually nauseating taste. Castor Oil is miscible with dehydrated alcohol and with glacial acetic acid.

"Specific gravity: 0.945 to 0.965 at 25° C. Castor Oil is only partly soluble in petroleum benzin (*difference from most other fixed oils*), but it yields a clear liquid with an equal volume of alcohol (*foreign fixed oils*). Dissolve 2 Gm. of Castor Oil in 20 cc. of alcohol, which previously has been neutralized with tenth-normal sodium hydroxide, using 5 drops of phenolphthalein T.S. as indicator, and titrate with tenth-normal sodium hydroxide to the production of a pink color which persists for fifteen seconds: not more than 1.5 cc. of tenth-normal sodium hydroxide is required (*free acid*). Saponification value: not less than 179 and not more than 185. Iodine value: not less than 83 and not more than 88.

"Preserve in well-closed containers." *U. S.*

"Nearly colorless, or with a yellowish tinge, viscid. Liable to solidify at low temperatures. Slight odor; taste at first bland, but afterwards acrid and unpleasant. Specific gravity 0.958 to 0.970; *saponification value* 177 to 187; *iodine value* 83 to 90; *acid value* not more than 4.0; *refractive index* at 40° C. 1.4695 to 1.4730. Soluble in all proportions of *absolute alcohol,* and in 3.5 parts of *alcohol* (90 per cent.). 10 millilitres shaken with 7 millilitres of *petroleum spirit* in a stoppered glass cylinder form a clear mixture at 15.5° C.; on shaking with a further addition of 3 millilitres of *petroleum spirit* a turbid mixture is formed, which becomes clear when maintained for five minutes at 21° C., but again becomes turbid when the temperature falls below 18° C. (absence of other fixed oils)." *Br.*

The bulk of castor oil is *ricinolein,* which is the *ricinoleic acid* ($C_{18}H_{34}O_3$) glyceride. At the same time it also contains a small quantity of tristearin and of the glyceride of dihydroxystearic acid, together with from 0.30 to 0.37 per cent. of unsaponifiable matter. Ricinoleic acid, as obtained from the decomposition of the glyceride is a viscid oil, which solidifies below 0° C., does not solidify in contact with the air by absorption of oxygen, and is not homologous with oleic or linoleic acid, neither of which is found in castor oil. On warming with 1 part of starch and 5 parts of nitric acid (sp. gr. 1.25) castor oil thickens, owing to the formation of *ricinelaidin.* From this *ricinelaidic acid* may be obtained in brilliant crystals. Ricinoleic acid is converted by potassium hydroxide into caprylic alcohol and sebacic acid, with disengagement of hydrogen, and the same products are obtained by the reaction of potassium hydroxide with the oil itself. (See *J. P. C.,* 1885, 113.) Castor oil differs from most other fixed oils in turning the plane of polarized light to the right.

By the action of concentrated sulphuric acid upon castor oil is formed a valuable product known as "*Turkey-red oil,*" much used in dyeing and printing with madder and alizarine (See *Sodium Sulphoricinate,* Part II.)

Castor oil which is acrid to the taste may sometimes be rendered mild by boiling it with a small proportion of water. If turbid, it should be clarified by filtration through coarse paper. On exposure to the air it is apt to become rancid, and is then unfit for use.

Twombly finds that the best method for removing the odor and taste of castor oil is by washing a cold pressed oil several times with boiling water. After separating, the oil is filtered cold very slowly through a thick layer of powdered animal charcoal. Any effort to quicken the method gives poor results. Several manufacturers are now producing a castor oil which is practically free from the characteristic unpleasant flavor and which appears to be equally efficacious as a medicine.

Uses.—The cathartic effects of castor oil are due to its ricinoleic acid which is split off in the intestinal tract. This, by gentle irritation of the mucous membrane, excites active peristalsis in the upper bowel and probably also somewhat increases the intestinal secretions, although the main action appears to be due to the increased peristalsis. Because of the thoroughness with which it empties the enteric canal there is on the following day an insufficient accumulation of intestinal contents and hence constipation is liable to follow. Because it cleans out the whole alimentary system and that with relatively small degree of irritation, it is especially valuable in conditions of irritation or inflammation of the bowels, as *colic, enteritis,* or *dysentery;* on account of the tendency to subsequent constipation it is not to be recommended as a habitual laxative. It is frequently resorted to in cases of *pregnant* and *puerperal women,* and is decidedly, as a rule, the best and safest cathartic for children. Infants usually require a larger relative dose than adults.

Externally it is useful for its emollient effects in *seborrhea* and other *skin diseases,* having the advantage over other oils of being soluble in alcohol.

The *dose* for an infant is from one to three fluidrachms (3.75–11.25 cc.). It is difficult of administration from its peculiarly disagreeable taste and from its oleaginous and viscid character. In a few cases, the disgust which it excites is utterly unconquerable by any effort of resolution. A common method of disguising the taste is to give it floating in cinnamon water or orange-juice but that which we have found, upon the whole, the least offensive is to give it floating on the froth of sarsaparilla syrup mixed with carbonic acid water. It is sometimes administered advantageously in a sweetened, aromatized emulsion. It is stated (*Bull. Pharm.,* 1920, xxxiv, p. 479) that the Arabs successfully mask the taste of castor oil by stirring it with heated milk, which forms a perfect emulsion, and flavoring this with syrup of orange flowers. Another method of disguising its taste is to add a drop of one of the aromatic oils, as cloves or wintergreen, and pour the oil in a chilled spoon which is laid on a cake of ice, when the oil becomes semi-solid and can be swallowed in a mass before it melts. Tragacanth has been recommended as producing a better emulsion than gum arabic. Castor oil may also be used as an enema, in the quantity of two or three fluidounces (60 or 90 cc.), mixed with some mucilaginous liquid.

Dose, from one-half to two fluidounces (15–60 cc.).

Off. Prep.—Mistura Olei Ricini, *Br.;* Emulsum Olei Ricini, *N. F.;* Oleum Ricini Aromaticum, *N. F.*

OLEUM ROSÆ. Br.

OIL OF ROSE

"Oil of Rose is the oil distilled from the fresh flowers of Rosa damascena, *Linn.*" *Br.*

Oleum Rosarum; Attar or Otto of Rose; Huile volatile de Rose pâle, *Fr. Cod.;* Essence de Rose, *Fr.;* Oleum Rosae, *P. G.;* Rosenöl, *G.;* Essenza de rose, *It.*

Fats and oils saturated with the rose perfume have been used since the earliest times. Of the seven thousand or more cultivated varieties of rose only a few are used for the production of oil. The chief of these is *Rosa damascena* or *damask rose,* a shrub whose habitat is unknown but which was introduced to Europe from Asia Minor in the 16th century. It attains a height of 5 feet and is further characterized by possessing stems covered with many stout, hooked prickles and glandular bristles, imparipinnate leaves with 5 to 7 ovate-oblong, serrate leaflets, pubescent on their lower surfaces, prickly petioles, red, pink or white flowers, borne in corymbs, and obovate hip fruits. The volatile oil from this species is commonly called *attar, otto,* or *essence of roses.* It is prepared on a large scale in Europe, especially in the Balkan Mountains, in Egypt, Persia, Cashmere, India, and other countries of the East, but European and American commerce is at present supplied chiefly from the region constituting the southern slope of the Balkans in Bulgaria, the town of Kizanlik being the most important center of production. The roses are gathered in May, and are distilled with the green leaves of the calyx. From thirty to sixty pounds are put into a tinned copper boiler, of the capacity of about 150 pounds, nearly filled with water. The heat is applied over an open fire, and a boiling temperature is continued for two hours, when the first part of the distilled fluid is returned to the boiler, and the process is continued to completion. The oil collects on the top of the water in the receiver, when it is removed from time to time as it accumulates. In the south of France a small quantity of oil of rose is prepared by distilling the petals with water and separating the oil which floats to the surface. The annual output of oil is small, most of it being marketed in the form of rose water.

The quantity of oil yielded by roses is very small, from 150 to 300 pounds being required to produce a single ounce of the oil. The price is correspondingly high; at present (1924) it is about $20 to $30 an ounce.

The experiments of Schimmel are said to indicate that the oil of rose can be prepared from German-grown flowers with commercial success. It is affirmed that the product is superior to the Turkish oil in fineness and strength of aroma, and also that it differs in having a higher congealing point, German oil solidifying at 32° C., Turkish oil at 20° C. For an account of its production, see *P. J.,* 1893, 262; also *J. S. C. I.,* 1919, xxxix, 43A.

For accounts of the modern rose industry see Tschirch, *Seifenseider Ztg.,* 1921, xlviii, and Chipkoff, *Bull. Sc. Pharm.,* 1921, xxviii, 389. Srivastava and Sinha give an account of the manufacture of otto from Indian rose. (*Perf. & Ess. Oil Rec.,* 1921, xii, 14.) Lorgues (*C. D.,* 1920, xciii, 1629) describes the French rose industry.

Oil of rose is nearly colorless, or presents some shade of green, yellow, or red, but, according to Polier, the color is no criterion of its value. Its odor is very powerful and diffusive. Alcohol dissolves it, although not freely when cold. Although described by the Br. as a "semi-solid," at the temperatures ordinarily met with in the United States it is liquid.

"A pale yellow or yellowish-green crystalline mass, semi-solid at ordinary temperatures. Strong, fragrant, rose-like odor; taste sweetish. Specific gravity at 30° C. (compared with *water* at 15.5° C.) 0.854 to 0.862; *optical rotation* –2° to –4°; *refractive index* at 25° C. 1.456 to 1.465; melting point 20° to 23° C." *Br.*

Oil of rose consists of two portions, one liquid, the other solid at ordinary temperatures. These may be separated by freezing the oil and compressing it between folds of blotting paper, which absorbs the liquid oil and leaves the concrete stearopten. The liquid portion is oxygenated, while the solid portion, which is odorless when pure, consists of a mixture of several hydrocarbons, one of which melts at from 35.5° to 36.5° C., and is a paraffin of the formula $C_{16}H_{34}$. "The addition of 70 per cent. alcohol precipitates the paraffin hydrocarbons of the oil, but forms a clear solution with its other constituents, the solution being slightly acid to litmus T.S." *U. S. VIII.* The oxygenated portion consists of the two alcohols, geraniol, and citronellol, together constituting 75 per cent. of the oil. The *rhodinol* of Eckart was a mixture of these two alcohols. (*Schim. Rep.,* April, 1898, 40.) While these two alcohols are mainly found in rose oil in the free state, esters of the same are also present in amounts varying from 2.5 to 3.5 per cent. (Gildemeister and Hoffmann, *Aetherische Oele,* p. 565.) Linalool, citral and phenyl ethyl alcohol are also present in small amounts as are also nerol, farnesol, eugenol, linalol and nonylic aldehyde.

The U. S. P. VIII considered the saponification value as of sufficient importance to incorporate it as an official test, as follows:

Assay.—"Place in a weighing-bottle about 2 cc. of the Oil of Rose, and weigh accurately. Transfer it, with the aid of a little alcohol, to a 100 cc. flask, and add 20 cc. of half-normal alcoholic potassium hydroxide V.S. Connect the flask with a reflux condenser, and boil the mixture during thirty minutes on a water-bath. When cool, add 50 cc. of distilled water and a few drops of phenolphthalein T.S., and titrate with half-normal sulphuric acid V.S. Subtract the number of cc. of half-normal sulphuric acid V.S. required, from 20 (the 20 cc. of half-normal alcoholic potassium hydroxide V.S.

taken), multiply the difference by 27.87, and divide by the weight of the Oil to obtain the saponification value." *U. S. VIII.*

Oil of rose is frequently, one might almost say usually, adulterated with various fixed or volatile oils; among those most commonly met are spermaceti, oil of rose-geranium (see *Pelargonium,* Part II) and oil of palmarosa (see *Oil of Citronella,* Part II). Some of these falsifications are very difficult of detection. An adulteration with a fixed oil produces a permanent greasy stain upon paper, and spermaceti is left behind on the evaporation of a few drops of the oil from a watch crystal in a water bath. Massatsch (*Ph. Ztg.,* 1923, lxviii, 832) states that to be certain of the purity of rose oil, the following characters must be determined: specific gravity, optical rotation, congealing point, refractive index, stearopten content, saponification number and alcohol content. He gives the following constants for a good oil: sp. gr. 0.849–0.862, congealing point 18–23.5° C., acid number 0.5–3.0, ester number 7–16, saponification number 7.5–19, alcohol content 66–75 per cent., stearopten 17–21 per cent.

Tedermann (*Zeit. An. Chem.,* 1895, 5) reached the conclusion, after much experimenting that there is no reliable chemical or physical test for the adulteration of oil of rose with geranium oil. The sense of smell, according to Conroy, furnishes the best means of determining the quality; he recommends the dissolving of one drop of oil of rose in twenty drops of alcohol, pouring the solution in one fluidounce of warm water, shaking, and comparing the odor with that of a standard sample treated in the same way. (*P. J.,* 1896 474; see also *C. D.,* 1897, 53.) For other tests which have been suggested see *U. S. D.,* 20th ed., p. 787.

Synthetic rose oils are now manufactured and sold on a large scale. Most of them contain a certain proportion of true rose oil, for the reproduction of the odor by synthetic constituents alone has never been achieved. *Rhodinol* is the trade name for the principal constituent in most of these formulas. It consists of citronellol and geraniol in the proportion of about two of the former to one of the latter. Nerol and terpeneless oil of rose are other constituents of importance. An indispensable ingredient is *phenyl-ethyl alcohol* $C_6H_5CH_2CH_2OH$ (*benzyl carbinol*), which contributes to the similarity of the odor. Other constituents the names of which appear in formulas for synthetic rose oil, intended to imitate one or the other of special types of rose are as follows: Alpha ionone, ethyl cinnamate, benzyl acetate, isobutyl acetate, isoeugenol, cinnamic aldehyde, citronellyl acetate, nonyl aldehyde and citral.

A rose oil is said to be distilled in Germany which contains 75 per cent. of phenyl-ethyl alcohol, which is present in only small proportions in ordinary rose oil, in which it ordinarily occurs as a benzoic ester or combined with phenylacetic acid. Hjort and Kaufman (*J. P. Ex. T.,* 1920, xv, 129) have shown this oil to be a powerful local anesthetic, but its instability is said to interfere with its practical usefulness.

A rose oil obtained in the yield of 0.015 per cent. by extraction of the petals with volatile solvents was found by F. Elze to have the following constants: Sp. gr. 0.9844 at 20° C., specific rotation +0.6°; acid value 3.15; ester value 2.9; acetylation value 317.5. Phenylethyl alcohol was the chief constituent of this oil which also contained geraniol, citronellol, nerol, and farnesol (*J. Soc. Chem. Ind.,* 1919, xxxix, 43A).

Oil of rhodium (*Oleum ligni Rhodii, Aspalathum*). This oil was attributed by Lewis to the *Convolvulus Scoparius* L. but according to Holmes (*Perfume and Essential Oil Record,* 1911, ii, p. 29) is the product of a species of *Genista,* either *G. canariensis* L. or *G. virgata* Link. It is used to adulterate oil of rose. Guaiac wood oil is also occasionally used for the same purpose. A factitious oil of rhodium is sometimes sold as a lure for rats and other animals. It is made from oil of copaiba flavored with a trace of oil of rose. The synthetic oil of rose has largely replaced that obtained by distillation.

Oil of rose may be added, as a grateful perfume, to various spirituous preparations for internal use, and to cerates and ointments. It is both too expensive and too powerful for most pharmaceutic purposes.

Off. Prep.—Unguentum Aquæ Rosæ, Br.

OLEUM ROSMARINI. U. S., Br.

OIL OF ROSEMARY Ol. Rosmar. [Rosemary Oil]

"The volatile oil distilled from the fresh flowering tops of *Rosmarinus officinalis* Linné (Fam. *Labiatæ*). Oil of Rosemary yields not less than 2.5 per cent. of esters calculated as bornyl acetate [$C_{10}H_{17}.C_2H_3O_2$], and not less than 10 per cent. of total borneol [$C_{10}H_{17}OH$] free and as esters." *U. S.* "Oil of Rosemary is the oil distilled from the flowering tops of Rosmarinus officinalis, *Linn.*" *Br.*

Oleum Rorismarini, Oleum Anthos; Huile volatile de Romarin, *Fr. Cod.;* Essence de Romarin, *Fr.;* Oleum Rosmarini, *P. G.;* Rosmarinöl, *G.;* Essenza di rosmarino, *It.;* Esencia de romero, *Sp.*

For description of the plant from which this oil is obtained see under *Rosemary,* Part II. The fresh leaves of rosemary yield, according to Baumé, 0.26 per cent. of volatile oil, but the percentage is rated much higher by others. Schimmel & Co. obtained by distillation from dry French rosemary flowers 1.4 per cent. of oil.

This oil is colorless, with an odor similar to that of the plant, though less agreeable. Its sp. gr. is said to be 0.911, but reduced to 0.8886 by rectification (0.894 to 0.912, *U. S.*). Buignet gives the sp. gr. of the rectified oil at 0.896, and states that it is moderately dextrogyrate. Its reaction is neutral. It is soluble in all proportions in alcohol of 0.830, but requires for solution at 17.7° C. forty parts of alcohol of 0.887. (Berzelius.)

Description and Physical Properties.—" A colorless or pale yellow liquid, having the characteristic odor of rosemary, and a camphoraceous taste.

" The Oil is soluble in 10 volumes of 80 per cent. alcohol, by volume. Specific gravity: 0.894 to 0.912 at 25° C. Optical rotation: varies from 0° to +15° in a 100 mm. tube at 25° C. Refractive index: 1.4660 to 1.4720 at 20° C. A solution of the recently distilled Oil in 80 per cent. alcohol (1 in 10) is neutral or only slightly acid to moistened litmus paper." *U. S.*

" Colorless or pale yellow. Odor that of rosemary; taste warm, camphoraceous. Specific gravity 0.895 to 0.920; *optical rotation* –2° to +15°; *refractive index* at 25° C. 1.463 to 1.473. Soluble in 1 part of *alcohol* (90 per cent.), and in 5 to 10 parts of a mixture of equal volumes of *alcohol* (90 per cent.) and *alcohol* (70 per cent.). Contains not less than 10 per cent. of total *alcohols,* calculated as borneol, $C_{10}H_{18}O$, and not less than 1.8 per cent. of *esters,* calculated as bornyl acetate, $C_{10}H_{17}C_2H_3O_2$." *Br.*

Kept in bottles imperfectly stoppered, it deposits a stearopten, sometimes amounting, according to Proust, to one-tenth of the oil.

Both Gladstone and Flückiger find that most of the oil consists of a hydrocarbon, which Schimmel & Co. (*Schim. Rep.,* Oct., 1889) identified as pinene, but there is a smaller fraction boiling at from 200° to 210° C., which at low temperatures deposits a camphor, identified as borneol. Weber examined oil of rosemary in Wallach's laboratory (*Ann. Ch. Ph.,* ccxxxviii, 89), and found that the fraction boiling between 176° and 182° C. contains cineol. The oil is therefore recognized at present as containing d-pinene, camphene, cineol, borneol (10–15 per cent.), and camphor. It is said to be sometimes adulterated with oil of turpentine, which may be detected by mixing the suspected liquid with an equal volume of pure alcohol, the oil of rosemary is dissolved, and that of turpentine left.

Assay for Esters.—" Proceed as directed for esters under *Oleum Menthæ Piperitæ,* using 10 cc. of Oil of Rosemary. Multiply the number of cc. of half-normal alcoholic potassium hydroxide consumed in the saponification of the Oil by 9.811, and divide the product by the weight of the Oil taken. The result shows the per cent. of esters, calculated as bornyl acetate.

" **Assay for Total Borneol.**—Proceed as directed for total menthol under *Oleum Menthæ Piperitæ,* using 10 cc. of Oil of Rosemary. Use the following formula in calculating the per cent. of total borneol.

Per cent. of total borneol =

$$\frac{A \times 7.710}{B - (A \times 0.021)} \times [1 - (E \times 0.0021)]$$

" *A* is the result obtained by subtracting the number of cc. of half-normal sulphuric acid required in the titration from the number of cc. of half-normal alcoholic potassium hydroxide originally taken, *B* is the weight of the acetylized oil taken, and *E* is the per cent. of esters calculated as bornyl acetate.

" Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

Oil of rosemary is used, chiefly in combination with other drugs, as a carminative. It is also employed as an ingredient in rubefacient liniments. For a case of fatal poisoning, see *A. J. P.,* xxiii, 286.

Dose, three to six minims (0.2–0.4 cc.).

Off. Prep.—Spiritus Rosmarini, *Br.;* Tinctura Lavandulæ Composita, *U. S., Br.;* Spiritus Odoratus, *N. F.*

OLEUM SANTALI. U. S., Br.

OIL OF SANTAL Ol. Santal. [Oil of Sandalwood Santalwood Oil]

" The volatile oil distilled from the dried heart-wood of *Santalum album* Linné (Fam. *Santalaceæ*). Oil of Santal yields not less than 90 per cent. of alcohols calculated as santalol [$C_{15}H_{24}O$]." *U. S.* " Oil of Sandal Wood is the oil distilled from the wood of Santalum album, *Linn.*" *Br.*

Oleum Ligni Santali; Oleum Santali Flavi; Oil of Sandal Wood; Huile volatile (Essence) de Santal, *Fr.;* Oleum Santali, *P. G.;* Ostindisches Sandelholzöl, Santelöl, *G.;* Esencia de sandalo, *Sp.*

Sandalwood has been used medicinally since the middle of the 15th century.

Santalum album, or *yellow sandalwood,* is a small, evergreen, parasitic tree with opposite, elliptic-ovate or ovate-lanceolate leaves, and panicles of straw colored to blood red flowers, and black globular drupaceous fruits about the size of a cherry. It is indigenous to the mountainous districts of India and the Malay archipelago and has been cultivated in southern India for its wood and oil. For an interesting account of the cultivation of the plant see J. L. Pigot in *Schimmel's Report,* 1900.

Nearly all the sandalwood of commerce is obtained in Mysore, India. Here the tree is torn up and deprived of its bark and a portion of its sapwood. The trunks are then sawed into segments of about a metre, and trimmed, and the roots deprived of their bark.

A quantity of the oil is distilled in Mysore but most of the wood is exported to Great Britain and other countries directly from Mysore or Bombay, where it is used alike for the production of the volatile oil of santal and the manufacture of various articles.

Other varieties of sandalwood are collected in the Hawaiian Islands from *Santalum Freycinetianum* Gaud., and *S. pyrularium* A. Gray; in the Fiji Islands from *S. Freycinetianum* Gaud. (*S. Yasi* Seem.), in New Caledonia from *S. austrocaledonicum* Vieillb.; in Queensland from *Eremophila Mitchelli* Benth. (Fam. *Myoporaceæ*); and in East Africa from *Osyris tenuifolia* Engl.

Australian Sandalwood Oil.—Under this title there has appeared in commerce a variety of products, some of which seem to bear little relation to the true santal oil. From western Australia come two oils, one, also called *oil of amyris,* is obtained from the *Amyris balsamifera* L. (Fam. *Rutaceæ*) and does not contain any santalol, its most important constituent being a sesquiterpene alcohol called *amyrol,* $C_{15}H_{26}O$ (Vansoden, *Ph. Ztg.,* 1900, xlv, 878). It is used as an adulterant of santal oil from which it differs in its physical properties, especially in not being soluble in 70 per cent. alcohol. The second West Australian oil is from the *Fusanus spicatus* R. Br. (Fam. *Santalaceæ*); according to Rao and Sudborough (*J. Soc. Chem. Ind.,* 1923, xlii, 575A) it yields from 70 to 80 per cent. of santalol but will not meet the physical constants required by the British Pharmacopœia.

In Southern Australia a sandalwood is obtained from the *Santalum Preissianum* Miq. (*Fusanus acuminata* R. Br.), which yields an oil with a rose-like odor.

Venezuelan, or *West Indian Sandalwood* according to Holmes (*P. J.,* xii) is from the *Schimmelia oleifera* Holmes (*Amyris Balsamifera* L.).

Oil of santal is distilled in the United States, Germany, England, and India, the ordinary method of steam distillation being applied after the wood has been reduced to small particles by chipping or grinding. According to the Indian Pharmacopœia the yield of oil is about 2.5 per cent.

Description and Physical Properties.—"A pale yellow, somewhat viscid, oily liquid, having the characteristic odor and taste of sandalwood.

"The Oil is soluble in 5 volumes of 70 per cent. alcohol, by volume. Specific gravity: 0.965 to 0.980 at 25° C. Optical rotation: varies from –15° to –20° in a 100 mm. tube at 25° C. Refractive index: 1.5040 to 1.5080 at 20° C. A solution of the recently distilled Oil in 70 per cent. alcohol (1 in 5) is slightly acid to moistened blue litmus paper.

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

"Pale yellow or nearly colorless, somewhat viscid in consistence. Aromatic odor; taste unpleasant. Specific gravity 0.973 to 0.985; *optical rotation* –13° to –21°; *refractive index* at 25° C. 1.498 to 1.508. Soluble in 6 parts of *alcohol* (70 per cent.) at 20° C. Contains not less than 90 per cent. of total *alcohols,* calculated as santalol, $C_{15}H_{24}O$." *Br.*

Oil of santal is habitually adulterated, castor oil and other fixed oils being added, and on the continent of Europe by the volatile oil of cedar. Holmes states that the presence of more than 10 per cent. of the cedar oil can be recognized through the different solubilities of the oils in alcohol. (See *P. J.,* xvi, 820.) R. A. Cripps, after a thorough examination of the oils in the London market (see *P. J.,* 1892, 461), gives this test: "Two drops of the oil added to six drops of nitric acid, sp. gr. 1.5 on a white tile, should give a yellow to bright reddish-brown coloration, without any green, indigo, or violet tint at the edges during five minutes. For complete saponification in alcoholic solution, it requires not more than 1 per cent. of potassium hydrate." (See also *A. J. P.,* 1893, 20; *Schim. Rep.,* Oct. 1893; *P. J.,* 1895, 118; *West. Drug.,* 1897, 262.)

Assay.—"Proceed as directed for total menthol under *Oleum Menthæ Piperitæ,* page 262, using 10 cc. of Oil of Santal. Use the following formula in calculating the per cent. of santalol:

$$\text{Per cent. of santalol} = \frac{A \times 11.01}{B - (A \times 0.021)}$$

"*A* is the result obtained by subtracting the number of cc. of half-normal sulphuric acid required in the titration from the number of cc. of half-normal alcoholic potassium hydroxide originally taken, and *B* is the weight of the acetylized oil taken." *U. S.*

The following equations represent the reactions involved in the official assay:

$$C_{15}H_{25}OH + (C_2H_3O)_2O = C_{15}H_{25}OCOCH_3 + CH_3CO_2H$$

santalol + acetic anhydride = santalol acetate + acetic acid

$$C_{15}H_{25}O.COCH_3 + KOH = C_{15}H_{25}OH + CH_3CO_2K.$$

santalol acetate + potassium hydroxide = santalol + potassium acetate.

Constituents.—In the oil from *Santalum album* there exist two isomeric sesquiterpene alcohols having the formula $C_{15}H_{26}O$. One is bi-cyclic and is called *alpha-santalol,* the other is tri-cyclic and is called *beta-santalol.* The two *santalols* may be separated by careful fractional distillation and conversion of the fractions into the phthalates and subsequently into the strychnine salts of these compounds, which are finally separated by repeated recrystallizations until the melting point and rotatory power of each is constant. By the oxidation of the santalols, isomeric aldehydes are obtained called *santalals,* $C_{15}H_{24}O$.

Semmler regards nor-tricyclo-ecsantalane, $C_{10}H_{16}$, as the parent body of santalol.

Uses.—The oil of sandalwood is used largely as a perfume. In medicine its chief use is in *gonorrheal urethritis,* although it is sometimes employed in *chronic bronchitis* and *cystitis.* Its general antibacterial power is comparatively weak, but it has special relations towards certain micro-organisms; thus in the experiments of Jordan (*B. M. J.,* Sept. 13, 1913) twenty minims of oil of sandalwood three times a day had practically no effect on the growth of *B. coli* in the urine, but markedly retarded the multiplication of staphylococci. It was first recommended in medicine by Thomas B. Henderson who, however, is said to have used the oil of *S. myrtifolium.* Under the name of *arheol* a proprietary form of santalol is recognized by the *N. N. R.,* 1924. It is asserted to be less liable to upset the stomach than the whole oil. Numerous esters of this alcohol have been put on the market; these are described in Part II.

Dose, five to twenty minims (0.6–1.3 cc.), in emulsion, or in capsule, three or four times a day.

OLEUM SASSAFRAS. U. S.

OIL OF SASSAFRAS Ol. Sassaf. [Sassafras Oil]

"The volatile oil distilled from the root of *Sassafras variifolium* (Salisbury) O. Kuntze (Fam. *Lauraceæ*). If the oil has solidified in whole or in part, carefully warm it until liquefied, then thoroughly mix it before dispensing." *U. S.*

Huile volatile (Essence) de Sassafras, *Fr.;* Sassafrasöl, *G.;* Esencia de sasafras, *Sp.*

The proportion of oil yielded by the root of sassafras averages between 1 and 2 per cent.

Description and Physical Properties.—"A yellow or reddish-yellow liquid, having the characteristic odor and taste of sassafras.

"The Oil is soluble in 2 volumes of 90 per cent. alcohol, by volume. Specific gravity: 1.065 to 1.077 at 25° C. Optical rotation: varies from +3° to +4° in a 100 mm. tube at 25° C. Refractive index: 1.5250 to 1.5350 at 20° C. A solution of the recently distilled Oil in 90 per cent. alcohol (1 in 2) is neutral to moistened litmus paper. Oil of Sassafras meets the requirements of the test for ***heavy metals in volatile oils.***

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

Variation in the sp. gr. of oil of sassafras may often arise through the congelation and separation of safrol, or through stratification. (LaWall and Pursel, *A. J. P.,* 1898, 340.)

The most complete investigation of sassafras oil is that made by Power and Kleber in 1896. (*Schim. Rep.,* April, 1896.) They find it to have the following composition: safrol about 80 per cent.; pinene and phellandrene, about 10 per cent.; dextrogyrate camphor about 6.8 per cent.; eugenol, about 0.5 per cent.; a high boiling portion, consisting of cadinene and residue, 3 per cent. They say that the hydrocarbon constituent of sassafras oil, to which Grimaux and Ruotte gave the name of *safrene,* is, as just stated, a mixture of pinene and phellandrene. Safrol is described in Part II.

Uses.—The oil of sassafras is much less irritant to mucous membranes than many of the other volatile oils, and is therefore of less service as a carminative. It is, however, a very powerful antiseptic. While chiefly esteemed at present for its pleasant flavor, it has a real therapeutic usefulness for its disinfectant properties. It has been highly praised by Peck (*J. A. M. A.,* 1899, xxxii, p. 6) for the disinfection of root canals in dentistry and is coming into considerable use in the treatment of nasal *catarrhs.* For the latter purpose it is generally employed dissolved in liquid petrolatum in strengths of about 1 per cent.

A teaspoonful of it produced in a young man vomiting, collapse, somewhat dilated pupils, and pronounced stupor. (*Cincinnati Lancet-Clinic,* Dec., 1888.) According to the experiments of A. Heffter (*Atti Dell' XI. Congres. Med. Internaz.,* iii, 1894), safrol is slowly absorbed from the alimentary canal, and escapes through the lungs unaltered and through the kidneys oxidized into *piperonalic acid.* When taken in sufficient dose, it quickly kills by a centric paralysis of respiration, preceded by great depression of the circulation, and when taken in smaller yet toxic amount, it causes death by widespread fatty degeneration of the heart, liver, kidneys, etc. Its isomer, *isosafrol,* is in warm-blooded animals much less active as a poison than is safrol, and is chiefly eliminated as *piperonalic acid.*

Dose, of oil of sassafras, two to six minims (0.12–0.4 cc.).

OLEUM SESAMI. N. F., Br.

SESAME OIL Ol. Sesam. [Teel Oil, Benne Oil]

"A fixed oil obtained from the seeds of one or more cultivated varieties of *Sesamum indicum* Linné (Fam. *Pedaliaceæ*)." *N. F.*

"Sesame Oil is the oil expressed from the seeds of Sesamum indicum, *Linn.*" *Br.*

Sesame oil is reputed by many pharmacists to resist rancidity better than other fixed oils of its class. For description of the plant yielding it see *Sesamum,* Part II.

Description and Physical Properties.—"Sesame Oil is a pale yellow, oily liquid, almost odorless, and having a bland taste. It is slightly soluble in alcohol, miscible with ether, chloroform, petroleum benzin, or carbon disulphide.

"Specific gravity: 0.916 to 0.921 at 25° C. Shake 1 cc. of the Oil for half a minute with a solution of 0.1 Gm. of sugar in 10 cc. of hydrochloric acid; the acid layer becomes bright red and changes to dark red on standing. Blue litmus paper previously moistened with alcohol is not more than slightly reddened by 2 cc. of the Oil (*free acid*). Mix 5 cc. of the Oil in a test tube with 5 cc. of a mixture of equal volumes of amyl alcohol and a 1 per cent. solution of sulphur in carbon disulphide, and immerse the test tube to one-third of its depth in a boiling saturated aqueous solution of sodium chloride: no reddish color develops in fifteen minutes (*cotton-seed oil*). Saponification value: not less than 188 nor more than 193. Iodine value: not less than 103 nor more than 112.

"Preserve it in well-closed containers." *N. F.*

"Pale yellow. Faint odor; taste bland. Specific gravity 0.921 to 0.924; *saponification value* 189 to 193; *iodine value* 103 to 114; *acid value* not more than 8; *refractive index* at 40° C. 1.4650 to 1.4675. When a mixture of 2 millilitres of the Oil and 1 millilitre of *hydrochloric acid* containing 1 per cent. of *refined sugar* is shaken for half a minute, and allowed to stand for five minutes, the acid layer becomes pink.

When 1 millilitre of the Oil and 15 millilitres of *N/1 alcoholic solution of potassium hydroxide* are boiled for twenty minutes in a flask provided with a reflux condenser, set aside for twenty-four hours at a temperature not exceeding 15.5° C., and afterwards heated on a water-bath for three minutes, the solution does not deposit crystals on standing for a further twenty-four hours (absence of arachis oil). When 2 millilitres of the Oil are mixed with 1 millilitre of *amylic alcohol* and 1 millilitre of a solution (1 in 100) of *precipitated sulphur* in *carbon disulphide,* and the mixture heated in a test-tube immersed in boiling *water,* no red color is developed within fifteen minutes (absence of cottonseed oil). In India, and in the Eastern, African, and North American Divisions of the Empire, Sesame Oil may be employed in making the official Liniments, Ointments, Plasters, and Soaps for which Olive Oil is directed to be used." *Br.*

The color reaction with sugar and hydrochloric acid was suggested as a distinguishing test from other oils by Schaedler (*A. Pharm.,* 1887).

Sesame oil is a non-drying oil. It contains about 75 per cent. of olein with smaller amounts of the glycerides of linoleic, palmitic, stearic, and myristic acids. Villavecchia and Fabris (*Zeit. für Ang. Chem.,* 1893, 505) found in addition: a higher alcohol of the formula $C_{25}H_{44}O$, fusing at 137° C., a finely crystallizing substance of the formula $C_{11}H_{12}O_3$, fusing at 123° C., which substance they name *sesamin,* and a thick uncrystallizable oil, non-nitrogenous, which is the cause of the cherry-red coloration which sesame oil shows with hydrochloric acid and sugar. Tocher (*P. J.,* 1893, 700), after analyzing *sesamin* and determining its molecular weight by Raoult's method in benzene and glacial acetic acid, maintains that its formula should be $C_{18}H_{18}O_5$. Tocher, as quoted by Lewkowitsch (*Chem. Anal. of Oils, Fats, and Waxes,* 2d ed., 389), also believes that the higher alcohol mentioned is cholesterol. *Sesamol* is a phenolic substance isolated by Kreis from sesame oil (*Chem. Ztg.,* 1903, p. 1030). Later investigations indicate that it does not occur in the oil in a free state but as a complex body from which sesamol is liberated by the addition of mineral acids.

Benne oil was known to the ancient Persians and Egyptians, and is esteemed by the modern Arabs and other people of the East both as food and as an external application to promote softness of the skin. In India it is generally used for cooking and anointing. It is laxative in large doses.

The name sesame oil is also sometimes applied to the oil from the cruciferous seed of *Camelina sativa.*

Sesame oil is used for pharmaceutical purposes.

Off. Prep.—Linimentum Ammoniæ, *N. F.;* Olea Infusa, *N. F.*

OLEUM SINAPIS VOLATILE. U. S., Br.

VOLATILE OIL OF MUSTARD Ol. Sinap. Vol. [Mustard Oil]

"The volatile oil obtained by maceration with water and subsequent distillation of the dried ripe seed (freed from fixed oil) of *Brassica nigra* (Linné) Koch or of *Brassica juncea* (Linné) Cosson (Fam. *Cruciferæ*), or prepared synthetically. The label must state the botanical source, or that it was made synthetically. Volatile Oil of Mustard yields not less than 93 per cent. of allyl isothiocyanate [C_3H_5NCS]. *Caution—Great care must be exercised in smelling this Oil. It should be tasted only when highly diluted." U. S.* "Volatile Oil of Mustard is the oil obtained by distillation from black mustard seeds, deprived of most of their fixed oil and macerated in water for several hours." *Br.*

Oleum Sinapis, *Br.* 1885; Oleum Sinapis Æthereum; Oil of Mustard; Huile volatile (Essence) de Moutarde, *Fr.;* Oleum Sinapis, *P. G.;* Senföl, Aetherisches Senföl, *G.;* Essenza di senape, *It.;* Esencia de mostaza negra, *Sp.*

After mustard seeds have been deprived of their fixed oil by hydraulic pressure, the cake—retaining its sinigrin and enzyme (see *Sinapis*)—when macerated in water gives rise to the characteristic volatile oil which may be collected by distillation. Most of the commercial supply of volatile oil of mustard, however, is of synthetic origin. According to Zeller mustard seeds yield from 0.33 to 0.63 of volatile oil.

Description and Physical Properties.—"A colorless or pale yellow, strongly refractive liquid, having a very pungent odor, and an acrid taste.

"Volatile Oil of Mustard is soluble in all proportions in alcohol, ether, and carbon disulphide. Specific gravity: 1.013 to 1.020 at 25° C. Optical rotation: inactive. Refractive index: 1.5268 to 1.5280 at 20° C. An alcoholic solution of the recently distilled oil is neutral to moistened litmus paper. The addition of 1 drop of ferric chloride T.S. to 1 cc. of the Oil, diluted with 5 volumes of alcohol, does not produce a blue coloration (*phenols*). The Oil distils completely between 148° and 154° C. Both the first and last 10 per cent. portions of the distillate have practically the same specific gravity as the original Oil (*alcohol, chloroform, petroleum or fatty oils*).

"Preserve in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

"Colorless or pale yellow. Intensely penetrating odor. Produces almost immediate vesication when applied to the skin. Specific gravity 1.014 to 1.025. Distils between 148° and 156° C. Contains in 100 millilitres not less than 92 grammes of allyl isothiocyanate, C_3H_5NCS, as determined by the following process." *Br.*

Assay.—"Dilute about 4 cc. of Volatile Oil of Mustard, accurately weighed, with sufficient alcohol to make exactly 100 cc. Transfer 5 cc. of this solution by means of a pipette to a 100 cc. measuring flask, and add 50 cc. of tenth-normal silver nitrate and 5 cc. of ammonia T.S. Connect the flask to a reflux condenser, and heat it on a bath of boiling water for one hour. Allow the liquid to cool to room temperature, disconnect the flask from the condenser, add sufficient distilled water to measure 100 cc., mix well, and filter. To 50 cc. of the filtrate, accurately measured, add about 5 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S., and titrate the excess of silver nitrate with tenth-normal potassium thiocyanate. Each cc. of tenth-normal silver nitrate corresponds to 0.004957 Gm. of allyl isothiocyanate." *U. S.*

"With *alcohol* (90 per cent.) prepare a solution containing 1 gramme of the Oil in 50 millilitres. To 5 millilitres of this solution in a 100 millilitre flask add 30 millilitres of *N/10 solution of silver nitrate* and 5 millilitres of *solution of ammonia.* Heat on a water-bath to 80° C. for thirty minutes, shaking frequently; cool to 15.5° C., make up to exactly 100 millilitres with *water,* and filter. To 50 millilitres of the filtrate add 4 millilitres of *nitric acid,* a few drops of *solution of ferric sulphate,* and sufficient *N/10 solution of ammonium thiocyanate* to produce a permanent red color. Not more than 5.7 millilitres of the latter reagent are required (presence of not less than 92 grammes of allyl isothiocyanate in 100 millilitres of the Oil)." *Br.*

Volatile oil of mustard consists chiefly of *allyl isosulphocyanate,* $CSNC_3H_5$ (*allyl isothiocyanate*); sometimes containing allyl cyanide and traces of carbon disulphide. This was first produced artificially by Berthelot and S. de Luca, by treating allyl iodide, C_3H_5I, with an alcoholic solution of potassium sulphocyanate. It is now extensively manufactured by this method. What first forms is allyl thiocyanate, which is not identical, but isomeric, with mustard oil (allyl isosulphocyanate). But if the sulphocyanate be heated to its boiling point 161° C., the thermometer sinks rapidly to 150° C., because of the change into the isosulphocyanate, or mustard oil. This change also takes place spontaneously at summer temperature. A small quantity of carbon disulphide seems always to be produced at the same time.

Ammonia converts the mustard oil into *thiosinamin* (see Part II), according to the reaction

$$CSNC_3H_5 + NH_3 = C_4H_8N_2S$$

The reaction is stated by Flückiger (*Pharm. Chem.,* 2d ed., 1888, p. 20) to be quantitative. Oil of mustard naturally contains about 0.56 per cent. of carbon disulphide. (*A. J. P.,* 1881, p. 572.)

Uses.—Oil of mustard is a powerful rubefacient, although liable to blister unless used with much caution. Diluted, either with alcohol or lard, it is used as a counter-irritant application in *sprains, rheumatism* and like conditions. It may be employed in strengths of from one to four per cent. According to Sollman (*J. P. Ex. T.,* 1918, xi, p. 229), the irritant effect of oil of mustard upon the skin is inverse to its solubility in the solvent employed; thus a 1 per cent. solution in olive oil caused practically no irritation, in dilute alcohol marked irritation, as an emulsion in mucilage still more.

The volatile oil of mustard has been employed as a substitute for the mustard plaster. For this purpose one part may be mixed with sixty parts of alcohol, and the mixture sprinkled, not too thickly, on muslin and covered with waxed paper. It acts speedily and efficiently.

The oil is too pungent and irritating to be given internally.

Off. Prep.—Linimentum Sinapis, *Br.;* Linimentum Sinapis Compositum, *N. F.;* Spiritus Sinapis, *N. F.;* Unguentum Sinapis, *N. F.*

OLEUM TEREBINTHINÆ. U. S.

OIL OF TURPENTINE Ol. Tereb. [Turpentine Oil "Spirits of Turpentine"]

"The volatile oil distilled from the oleoresin obtained from *Pinus palustris* Miller and other species of *Pinus* (Fam. *Pinaceæ*) which yield exclusively terpene oils." *U. S.*

Essence de Térébenthine, *Fr. Cod.;* Huile volatile de Térébenthine, *Fr.;* Oleum Terebinthinæ, *P. G.;* Terpentinöl, *G.;* Essenza di trementina, *It.;* Esencia de trementina, Aceite volatil de trementina, *Sp.*

This oil is commonly erroneously called *spirits of turpentine.* It is prepared by distillation from our common turpentine, though equally afforded by other varieties. It may be distilled either with or without water, but in the latter case a much higher temperature is required, and the product is liable to be empyreumatic. To obtain it quite pure it should be redistilled from a solution of potassium hydroxide. The turpentine of *Pinus palustris* is said to yield about 17 per cent. of oil, while that from *Pinus Pinaster* Ait. affords 25 per cent. and that from *Pinus sylvestris* L. 32 per cent.

Description and Physical Properties.—"A colorless liquid, having a characteristic odor and taste, both of which become stronger and less pleasant on aging or exposure to air. The Oil is soluble in 5 volumes of alcohol. Specific gravity: 0.854 to 0.868 at 25° C. Optical rotation: active, but variable. Refractive index: 1.4680 to 1.4780 at 20° C. An alcoholic solution of the recently distilled Oil (1 in 5) is neutral or only slightly acid to moistened litmus paper. Evaporate 5 cc. of the Oil in a small tared dish on a bath of boiling water: the weight of the residue does not exceed 0.1 Gm. (*petroleum, paraffin, or rosin oils*). Three drops of the Oil placed on white unsized paper and exposed to the air, evaporates without leaving a permanent stain (*fixed oils*). A 5 cc. portion of the Oils shaken with an equal volume of potassium hydroxide T.S. does not become darker than a light straw-yellow after standing twenty-four hours. A 5 cc. portion of the Oil shaken vigorously with an equal volume of hydrochloric acid in a glass-stoppered cylinder and allowed to stand for five minutes does not develop a color darker than a light straw yellow in either the acid or the oil layer. Place 100 cc. of Oil of Turpentine in a standard 100 cc. Engler flask, having the side tube 8 cm. above the top of the bulb, and distil the Oil at the rate of 2 drops per second: 90 per cent. of the Oil distils between 154° and 170° C., the temperature being read with the bulb of the thermometer opposite the side tube of the flask, and the top of the mercury column of the thermometer remaining within the neck of the flask. Place 20 cc. of fuming sulphuric acid in a graduated narrow-necked Babcock bottle, stopper, and place in an ice bath to cool, and then add slowly, drop by drop, from a pipette, 5 cc. of the Oil of Turpentine. Mix the acid and Oil, as added, by gently shaking or rotating the bottle, keeping the temperature at about 60° to 65° C. by continued immersion in the ice bath. When the mixture no longer becomes warm on shaking, agitate thoroughly by vigorously shaking for about one-half minute. Place the bottle in a water bath and heat at 60° to 65° C. for ten minutes, keeping the contents of the bottle thoroughly mixed by frequent vigorous shaking, not less than six times during the heating period. (*If the shaking at first is too prolonged and vigorous, there is danger of the escaping SO_2 forcing some of the mixture out of the neck of the bottle.*) Cool to room temperature, and fill the bottle with sulphuric acid (specific gravity about 1.83) until the oily layer rises into the graduated neck. Centrifuge for five minutes at 1200 revolutions per minute, or for fifteen minutes at 900 revolutions per minute, or allow to stand, lightly-stoppered, for twelve hours. The reddish or straw colored viscous layer which separates on top of the dark acid does not exceed 1 per cent. (0.05 cc.) of the volume of Oil taken (*mineral oil*). *Caution —The addition of Oil of Turpentine to the fuming sulphuric acid, must be made only drop by drop, because of the violence of the reaction.*

"Preserve in well-stoppered containers, in a cool place." *U. S.*

As found in commerce, it is always somewhat ozonized, but when perfectly pure it consists exclusively of carbon and hydrogen, and is composed of one or more terpenes, among which are pinene, which constitutes the major portion of the oil, and small amounts of camphene and fenchene with derivatives of pinene. (See p. 730.) The English or American oil (prepared from *Pinus palustris*) is composed of *dextro-pinene*, while the French oil (prepared from *Pinus Pinaster* Ait.) is composed of *lævo-pinene*. On the other hand, the Russian turpentine contains, in addition to pinene, *dipentene* (or *cinene*) and *sylvestrene*, and the Swedish turpentine contains pinene and sylvestrene. Both the American and the French oil of turpentine boil at about 156° C. On heating oil of turpentine to about 300° C. in a sealed tube for several hours it is converted into a polymer called *isoterebenthene*, $C_{20}H_{32}$, which is so oxidizable that it is converted into a viscid mass on exposure to the air for a few hours. This has a marked odor, resembling oil of lemon, and boils at 176° to 177° C. On treatment with a small portion of sulphuric acid, oil of turpentine yields an optically inactive liquid, which boils at 160° C. This is a mixture resolvable by repeated fractional distillation into *terebene*, $C_{10}H_{16}$, boiling at 150° C., *cymene*, $C_{10}H_{14}$, boiling at 175° C.; a small quantity of a camphor-like body, boiling at 200° C.; *colophene*, $C_{20}H_{32}$, boiling at 318° C., and a mixture of semi-solid products of higher boiling point. Oil of turpentine absorbs hydrochloric acid gas, forming with it two compounds, one a red dense liquid, the other a white crystalline substance resembling camphor, and hence called *artificial camphor*. Both are monohydrochlorides, $C_{10}H_{16}.HCl$, but the latter is much more stable, and can be purified by crystallization from alcohol or ether. When turpentine oil is left in contact with concentrated hydrochloric acid a dihydrochloride is formed, $C_{10}H_{16}.2HCl$. This forms rhombic plates, insoluble in water, and decomposed by boiling with alcoholic potash, with formation of *terpinol* $(C_{10}H_{16})_2.H_2O$. (Allen, *Com. Org. Anal.*, vol. ii, p. 51.) Nitric acid converts oil of turpentine into resin, and by long boiling into *terebic acid*, $C_7H_{10}O_4$. Turpentine oil and other terpenes unite with water to form crystals of *terpin hydrate*, $C_{10}H_{18}(OH)_2.H_2O$, which sublimes often from turpentine oil which has long stood in contact with water and has then been heated to water-bath temperature. These crystals are sometimes found in the natural oil also. The presence of alcohol with the water and turpentine oil facilitates their formation. Thus, a mixture of 1 part of nitric acid, 1 part of alcohol, and 4 parts of turpentine oil, spread out in flat dishes, will yield within a few days crystals amounting to 20 per cent. of the oil taken. If these crystals be fused at 116° C. they will lose water, and *terpin*, $C_{10}H_{18}(OH)_2$, will remain in crystalline needles, fusing at 104° C., and boiling at 258° C. If either of the hydrates just mentioned be boiled with sulphuric, phosphoric, or glacial acetic acid, *terpineol*, $C_{10}H_{17}OH$, will be formed along with hydrocarbons of the formula $C_{10}H_{16}$, such as terpinene, terpinolene, and dipentene. Terpineol is a thick, colorless, optically inactive liquid, with a pleasant hyacinthine odor and a bitter, feebly pungent taste. It is used extensively in perfumery. Baeyer (*B. Chem. G.*, xxvi, p. 826) has also prepared the methyl ether of terpineol. Oil of turpentine may be made to yield cymene identical with that existing in the oil of cumin and with that obtained by dehydrating camphor. (See *Cumin Seed*, in Part II; also see under *Olea Volatilia*.)

Exposed to the air the oil absorbs oxygen, becomes thicker and yellowish, and loses much of its activity, owing to the formation of resin. Hence the older Pharmacopœias directed the oil to be rectified by distilling it with about four measures of water. But the process is difficult, in consequence of the great inflammability of the vapor, and its rapid formation, which causes the liquid to boil over. In the present U. S. Pharmacopœia the oil is rectified by washing with sodium hydroxide, which saponifies the resin.

C. T. Kingzett has shown that the atmospheric oxidation of turpentine is accompanied by the formation of a body having the formula $C_{10}H_{14}O_4$, which he regards as *camphoric peroxide*. This substance, by the action of water, is converted into hydrogen peroxide and camphoric acid. The disinfectant known as *"sanitas"* is produced by passing air through Russian oil of turpentine in contact with warm water.

In this country the oil of turpentine is frequently adulterated with petroleum distillates. The adulteration is best detected by the treatment with sulphuric acid followed by steam distillation of the oil layer remaining above the sludge acid; this treatment with acid and after-distillation to be repeated if necessary. The sulphuric acid will thus completely polymerize the essential oil, leaving the paraffin hydrocarbons unaffected in the residual oily layer. A shorter and more readily executed test with sulphuric acid, though not so complete, is now given in the official test of the U. S. P. X.

Considerable quantities of a turpentine obtained by steam distillation of the so-called "lightwood," or resin saturated stumps and pieces of pine wood, have been offered in recent years. For an experimental study of this process and an account of the product see an article by Walker, Wiggins and Smith. (*Chemical Engineer,* Dec., 1905, p. 78.)

The presence of rosin oil in oil of turpentine may be detected by treating one drop of the distillate from 5 Gm. of the sample with sulphuric acid and acetic anhydride. A blue purple color indicates the presence of the impurity. Pine oil may be detected by the Heyfeld reaction, which consists of treating the sample with a few cc. of 10 per cent. sodium sulphate solution, followed by acidulation with sulphuric acid. A green-yellow fluid indicates pine oil, pure oil of turpentine remaining colorless. Hydrocarbons can best be detected by the bromine absorption test; 2.5 cc. of pure oil of turpentine decolorizing at least 25 cc. of standard bromine solution. (*Schweiz. Apoth. Ztg.,* 1915, 198.)

The several species of pine indigenous to California and the slopes of the Sierra Nevada appear to yield quite different products. Wenzell (*A. J. P.,* March, 1872) described, under the name of *abietene,* an oil distilled from the exudation of the *Pinus sabiniana* Dougl. (*Nut Pine* or *Digger Pine*). He found it to have a sp. gr. of 0.694, and to boil at 101° C. Sadtler (*A. J. P.,* April, 1879, p. 176) examined an oil of turpentine from California said to have been obtained from the *Pinus ponderosa* Dougl. (*Yellow-* or *Bull-Pine*), and found it to agree substantially with Wenzell's abietene. It was shown by Thorpe (*A. J. P.,* 1879, p. 293), and later confirmed by Schorlemmer, that the exudation of the California pine is almost pure *heptane,* C_7H_{16}, one of the chief constituents of American petroleum. It differs materially in its properties from the official oil.

Uses.—The oil of turpentine is locally irritant and feebly antiseptic. It is absorbed through the mucous membrane of the alimentary canal and apparently also of the respiratory tract, and is eliminated partly with the breath to which it imparts its own odor, and through the urine to which it gives an odor resembling that of violets. After the ingestion of large doses it produces a sense of warmth in the stomach, accelerates the circulation, and causes a feeling of exhilaration associated with more or less vertigo and a sense of fullness in the head. These symptoms are attended frequently with nausea and frequently, although not always, succeeded by brisk catharsis. When given in small doses frequently repeated it at first stimulates the kidneys, augmenting the secretion of urine, but if the administration is continued too long it produces painful irritation of the urinary vessels amounting at times to violent strangury and may cause inflammation of the kidney with scanty, albuminous, or even bloody urine. In some constitutions it produces, even when taken internally, an erythematous eruption of the skin. Apparently enough may be absorbed after the inhalation of its vapor to irritate the urinary organs and it is stated that seamen of vessels loaded with turpentine sometimes develop strangury and hematuria.

Most of the therapeutic uses of the oil of turpentine may be attributed to its local irritant influence; thus during its elimination through the mucous membrane of the lungs it acts as a stimulant expectorant and is a useful remedy in *chronic bronchitis.* In the same way it acts as a stimulant to the kidney and is occasionally used as a diuretic, although this employment has largely passed out of vogue. As a carminative in *flatulent colic* it is one of the most valuable remedies we possess. It is sometimes of service for its local stimulant action for *chronic diarrheas* or *dysentery.* In *typhoid fever* it is useful not merely in tympanitic states for its carminative effects, but appears to have a direct influence upon the disease itself. According to the observations of Omelchenko (*B. G. T.,* 1891), while it is very feeble in its general antibacterial properties it has a special toxicity for the typhoid bacillus and this organism will not grow in an atmosphere saturated with turpentine vapor.

Oil of turpentine has been used for many years in the treatment of *hemoptysis.* Of its mode of action we have no knowledge, but there is considerable clinical evidence as to its power to check bleeding; Smith (*B. M. J.,* 1908, i,

p. 1218) has even recommended it in *purpura hemorrhagica.* Among other conditions in which it has been from time to time recommended with more or less reasonableness, are *helminthiasis, leucorrhea, chronic rheumatism, amenorrhea,* and *puerperal fever.*

For ordinary purposes the dose of the rectified oil is from 5 to 10 minims (0.3–0.6 cc.) repeated every two to six hours as may be necessary. As a remedy against the *tapeworm* the dose is from one-half to one fluidounce (15–30 cc.), followed in half an hour by castor oil; the safety of these large doses is dependent upon the catharsis sweeping out the bowel before the turpentine can be absorbed. It is best administered in the form of an emulsion, although it is frequently given by dropping into a teaspoonful of sugar. The use of gelatin-coated capsules is not to be recommended because as soon as the gelatin dissolves in the stomach the undiluted oil comes in contact with the gastric mucosa and is liable to produce an undue degree of irritation.

In the form of an enema the oil of turpentine is highly useful in obstinate *constipation, tympanitis,* and *seat worms.* From one-half to two fluidounces (15–60 cc.) may be added to a pint of warm soapsuds.

Externally it is an excellent rubefacient and is widely employed in the form of liniments in various rheumatic affections as *lumbago, arthritis, neuralgias,* and the like. For this purpose it should be diluted with from one to three parts of cottonseed or other bland oil. In the form of turpentine stupe it is advantageously employed as a counter-irritant in various deep seated inflammations, especially of the abdomen. The turpentine stupe is made as follows: a piece of flannel is wrung out in hot water and then either sprinkled with or dipped in previously warmed turpentine, quickly wrung out and applied to the part. It was also formerly employed as a local application to *burns* in which it was supposed to allay the pain and promote healing. For this purpose it was usually mixed with the rosin cerate so as to form a liniment capable of being spread upon linen (see *Linimentum Terebinthinæ*).

The following is the formula adopted many years ago by the Philadelphia College of Pharmacy for the rubefacient liniment known as *British Oil,* which is still in use in some parts of the country as a popular remedy. Oil of Turpentine, Linseed Oil, of each, 8 fl. oz., Oil of Amber, Oil of Juniper, of each, 4 fl. oz., Barbados Petroleum 3 fl. oz., Crude American Petroleum 1 fl. oz.

Oil of turpentine has likewise been recommended as a local application in parasitic *skin diseases,* especially *pediculus capitis.* The inhalation of its vapors has been employed in *chronic bronchitis* and has been especially recommended by Skoda in *gangrene of the lungs.*

For internal use the rectified oil should be used. (See *Oleum Terebinthinæ Rectificatum.*)

Off. Prep.—Oleum Terebinthinæ Rectificatum, *U. S.;* Linimentum Opii Compositum, *N. F.;* Linimentum Terebinthinæ Aceticum, *N. F.;* Petroxolinum Sulphuratum Compositum, *N. F.;* Linimentum Terebinthinæ, *N. F.*

OLEUM TEREBINTHINÆ RECTIFICATUM. U. S., Br.

RECTIFIED OIL OF TURPENTINE Ol. Tereb. Rect.
[Rectified Turpentine Oil]

"Rectified Oil of Turpentine is the oil distilled from the oleo-resin (turpentine) obtained from various species of Pinus, and rectified." *Br.*

Essence de Térébenthine purifiée, *Fr.;* Oleum Terebinthinæ Rectificatum, *P. G.;* Gereinigtes Terpentinöl, *G.*

"Oil of Turpentine, a convenient quantity. Solution of Sodium Hydroxide, an equal quantity. Mix the two liquids thoroughly in a suitable still provided with a well-cooled condenser. Recover about three-fourths of the Oil by distillation, and separate the clear oil from the water. Dry the Oil by shaking with anhydrous calcium chloride or anhydrous sodium sulphate, and filter.

"NOTE.—Rectified Oil of Turpentine is to be dispensed when Oil of Turpentine is required for internal use. Oil that has become turbid should not be dispensed." *U. S.*

When oil of turpentine is distilled in contact with sodium hydroxide solution, the distillate comes over purified and freed from the decomposition products which give the commercial oil the disagreeable odor and taste which are inseparable by ordinary distillation without alkali; hence this rectified oil is much preferable for internal administration. It has in other respects the same properties as Oleum Terebinthinæ.

Description and Physical Properties.—"A colorless liquid which conforms to the properties and tests under *Oleum Terebinthinæ,* specific gravity and non-volatile residue excepted. Specific gravity: 0.853 to 0.862 at 25° C. Evaporate 5 cc. of Rectified Oil of Turpentine rapidly in a tared dish on a bath of boiling water: the weight of the residue does not exceed 0.015 Gm.

"Preserve in well-stoppered, amber-colored bottles in a cool place protected from light." *U. S.*

"A colorless, limpid liquid. Characteristic odor; taste pungent, somewhat bitter. Specific gravity 0.860 to 0.870; *refractive index* at 25° C. 1.465 to 1.480. Distils almost entirely between 156° and 180° C., leaving no appreciable residue." *Br.*

For uses see under *Oleum Terebinthinæ.*

Dose, five to ten minims (0.3–0.6 cc.).

Off. Prep.—Emulsum Olei Terebinthinæ, *U. S.;* Linimentum Terebinthinæ, *Br.;* Linimentum Terebinthinæ Aceticum, *Br.*

OLEUM THEOBROMATIS. U. S., Br.

OIL OF THEOBROMA Ol. Theobrom. [Cacao Butter]

"The fat obtained from the roasted seeds of *Theobroma Cacao* Linné (Fam. *Sterculiaceæ*)." *U. S.* "Oil of Theobroma is a solid fat expressed from the seeds of Theobroma Cacao, *Linn.*" *Br.*

Oleum Theobromæ, *U. S.* 1880; Butter of Cacao; Cocoa butter (improperly); Beurre de Cacao, *Fr. Cod.*; Oleum concretum e semine Theobromæ Cacao, *Fr.*; Oleum Cacao, *P. G.*; Kakaobutter, *G.*; Manteca de coco, Aceite de coco, *Sp.*

For description of this tree see under *Cacao Præparata.*

Oil of theobroma is extracted either by expression, decoction, or the action of a solvent. Soubeiran recommends that the seeds, previously ground, be mixed with one-tenth of their weight of water and then pressed between hot plates of tinned iron. It is advisable that the heat should not exceed that of boiling water, and even a lower heat will answer. When the method of decoction is used, the cacao should be slightly roasted before boiling. As a solvent, carbon disulphide has been found to answer well, as recommended in the preparation of the expressed oil of nutmeg. (See *Oleum Myristicæ.*) Upon the whole, the method of expression is perhaps preferable. The presence of water in the ground seeds is said greatly to facilitate the process. The commercial supply is largely a by-product in the manufacture of cocoa. It occurs usually in the shape of oblong cakes, weighing about half a pound each.

Description and Physical Properties.—"A yellowish-white solid, having a faint, agreeable odor, and a bland, chocolate-like taste. It is usually brittle at temperatures below 25° C. Oil of Theobroma is slightly soluble in alcohol; soluble in boiling dehydrated alcohol; freely soluble in ether, chloroform, petroleum benzin, and in benzene.

"Specific gravity: about 0.973 at 25° C. It melts between 30° and 35° C. Refractive index: 1.4537 to 1.4578 at 40° C. Dissolve 1 Gm. of Oil of Theobroma in 3 cc. of ether in a test tube at a temperature of 17° C., and immerse the tube in water having the temperature of melting ice: the liquid does not become turbid or deposit white flakes in less than three minutes. After congealing, raise the temperature to 15° C.: a clear liquid is gradually formed (*wax, stearin,* or *tallow*). Saponification value: not less than 188 and not more than 195. Iodine value: not less than 33 and not more than 38." *U. S.*

"A yellowish-white solid, breaking with a smooth fracture. Odor resembling that of cocoa; taste bland, agreeable. Somewhat brittle at ordinary temperatures, but softening at 25° C. Specific gravity 0.990 to 0.998; melting point 30° to 33° C.; *saponification value* 188 to 195; *iodine value* 35.5 to 37.5; *acid value* not more than 2.0; *refractive index* at 40° C. 1.4565 to 1.4575. In ascertaining the melting point and specific gravity, seventy-two hours should be allowed to elapse between the time of melting and the time of determining the constants. When 1 gramme is dissolved at 17° C. in 3 millilitres of *ether* in a test-tube, and the tube placed in *water* at 0° C., the solution neither becomes turbid nor deposits a granular or flaky mass in less than three minutes; and if, after congealing, it is exposed to a temperature of 15.5° C., a clear solution is gradually formed (absence of certain other fats)." *Br.*

Cacao butter consists chiefly of the glycerides of stearic, palmitic, and lauric acids, with small quantities of the glycerides of arachidic, linoleic, formic, acetic, and butyric acids. The percentage of stearic acid obtainable is from 39.9 to 40.6. Kingzett believes it to contain in addition a peculiar acid which he calls *theobromic,* and to which he gives the formula $C_{64}H_{128}O_2$, but his results have not been confirmed by subsequent investigators. From its large proportion of stearin, it is one of the best fats for the preparation of stearic acid. It is said to be frequently adulterated with animal fats, which are excluded by the official tests.

Uses.—Butter of cacao is used as an ingredient in cosmetic ointments, and in pharmacy for coating pills and preparing suppositories. For the last purpose it is well adapted by its blandness, and the fact that although liquefying at a temperature below that of the body, it is of firm consistence at 20° C. It is also valuable for the reason that easily decomposable substances like silver nitrate, potassium permanganate, etc., may be incorporated in it without material change and it is therefore valuable as an excipient. It has the emollient properties of the fats and is used to soften and protect *chapped hands* or *lips.*

OLEUM THYMI. N. F.

OIL OF THYME Ol. Thymi. [Thyme Oil]

"A volatile oil distilled from the flowering plant of *Thymus vulgaris* Linné (Fam. *Labiatæ*), and containing not less than 20 per cent., by volume, of phenols." *N. F.*

Huile volatile de Thym, *Fr. Cod.*; Essence de Thym, *Fr.*; Oleum Thymi, *P. G.*; Thymianöl, *G.*; Esencia de tomillo, *Sp.*

In the south of France thyme grows wild in great abundance, and is largely collected for distillation. The oil is taken from France to England, and thence reaches this country under the name of *oil of origanum,* having, probably from its greater cheapness, been substituted for the latter. (See Part II.)

Thymus vulgaris is a common plant, indigenous to Southern Europe, and cultivated in our gardens. It possesses a subcampanulate two-lipped calyx, villous in the throat; corolla limb two-lipped, the upper erect and emarginate, the lower spreading, three-cleft. It is a low undershrub, procumbent at the base, with ovate-linear, revolute leaves, the flowers occurring in a whorled spike. The herbaceous portion, which should be gathered when the plant is in flower, has a peculiar, strong, aromatic, agreeable odor, not lost by drying, and a pungent, aromatic camphoraceous taste. The dried herb yields on distillation about 1 or 2 per cent. of volatile oil.

The oil, as prepared in Southern France, is, after one distillation, of a reddish-brown color, and called the *red oil,* but when again distilled is colorless, and in this condition is distinguished as the *white oil;* this colorless oil, however, usually reddens again on keeping.

Description and Physical Properties.—"Oil of Thyme is a colorless or red liquid, having a characteristic odor and taste. It is soluble in 2 volumes of 80 per cent. alcohol.

"Specific gravity: 0.894 to 0.930 at 25° C. It is slightly lævorotatory. Shake 1 cc. of the Oil with 10 cc. of hot distilled water, and, after cooling, pass the aqueous layer through a wetted filter; the filtrate does not assume a blue or violet color upon the addition of a drop of ferric chloride T.S.

"**Assay.**—Introduce 75 cc. of sodium hydroxide T.S. into a flask with a long graduated neck (cassia flask), add 10 cc. of the Oil to be assayed, stopper the flask tightly, shake the mixture thoroughly, and set it aside for from twelve to twenty-four hours. Then add sufficient sodium hydroxide T.S. to raise the lower limit of the oily layer within the graduated portion of the neck of the flask, and, after the alkaline solution has become clear, adjust it to the temperature at which it was measured, and note the volume of the residual liquid. This measures no more than 8 cc., indicating the presence of not less than 20 per cent., by volume, of phenols.

"Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *N. F.*

The more volatile portion, that coming over below 180° C. in distillation, is a mixture of cymene and pinene. The less volatile and most valuable portion is chiefly thymol, a white crystalline solid, which constitutes from 20 to 30 per cent. of the oil. (See *Thymol.*) Carvacrol is also present, at times replacing part or all of the thymol, and in addition linalool and bornyl acetate have been found in small amount. (See *Proc. A. Ph. A.*, 1897, 637.)

The *Spanish oil of thyme* according to Dorronsow (*Ph. Era,* 1921, liv, p. 102) is obtained not only from the official species but also from the *T. Zygis* L., *T. Liemalis* Lg. and *Corydothymus capitatus* Robb. It differs in its composition from the official oil in containing considerable amounts of carvacrol.

The oil is commonly adulterated with the oil of turpentine, the *white oils* being especially impure. The presence of oil of turpentine, according to Duyk (*J. P. A.*, 1899, 41), is due to the fact that the French peasants place in the body of the still as a foundation for the herbs a layer of pine and fir branches.

Oil of thyme has been largely replaced in medicine by thymol. According to Camperdon, in doses of from three to fifteen grains (0.2–1.0 Gm.), oil of thyme causes mental excitement, and is a valuable diffusible stimulant in *collapse.* It is powerfully germicidal. (See *Thymol.*)

Dose, one to five minims (0.06–0.3 cc.).

Off. Prep.—Liquor Antisepticus, *N. F.;* Mistura Oleo-Balsamica, *N. F.;* Oleum Hyoscyami Compositum, *N. F.*

OLEUM TIGLII. U. S. (Br.)

CROTON OIL. Ol. Tiglii

"The fixed oil expressed from the seeds of *Croton Tiglium* Linné (Fam. *Euphorbiaceæ*). *Caution—It must be handled carefully as it causes pustular eruptions when applied to the skin.*" *U. S.* "Croton Oil is the oil expressed from the seeds of Croton Tiglium, *Linn.*" *Br.*

Oleum Crotonis, *Br.;* Huile de Croton Tiglium, *Fr. Cod.;* Huile de Graines de Tilly, *Fr.;* Oleum Crotonis, *P. G.;* Krotonöl, *G.;* Olio di crotontiglio, *It.;* Aceite de croton tiglio, Aceite de grano tiglio, *Sp.*

Croton Tiglium Willd. is a small tree or shrub, with a few spreading branches, bearing alternate petiolate leaves, which are ovate, acuminate, serrate, smooth, of a metallic green to bronze and orange or variegated color on the upper surface, paler beneath. The flowers are in erect terminal racemes, scarcely as long as the leaf—the lower being pistillate, the upper staminate—with straw-colored petals. The fruit is a smooth capsule, about the size of a filbert, with three cells, each containing a single seed.

The tree is a native of Hindostan, Ceylon, and other parts of India. It is pervaded by an acrid purgative principle, probably analogous to that found in other plants belonging to the family of *Euphorbiaceæ.* Rumphius says that the root is employed in Amboyna, in the dose of a few grains, as a drastic purge in dropsy, and, according to the same author, the leaves are so acrid that when chewed and swallowed they excite inflammation in the lips, mouth, and throat, and along the whole course of the alimentary canal. The wood is said in small doses to be diaphoretic, in larger, purgative and emetic. But the seeds are the most active part. These have been long used in India as a powerful purgative, and were employed so early as 1630 in Europe, under the names of *grana Molucca* and *grana tiglia.* But in consequence of their violent effects they fell into neglect, and had ceased to be ranked among medicines, when, at a comparatively recent period, attention was again called to them by the writings of some English physicians in India. They are now imported for their oil, which is the only official product of the plant.

It is probable that most if not all of the *Crotons* are purgatives. The oil of the Mexican *Croton morifolius* Willd. is said to be mildly purgative in doses of two or three minims (0.12–0.2 cc.). In India, under the name of *Kowli seeds* (*Kuli seeds*), are used certain beans, which have been referred by authorities to *Croton oblongifolius* Roxb., and also to the *C. persimilis* Müll.-Arg. (See *Ph. Rev.*, Oct., 1896.) Kowli seeds reach a length of 2.1 cm., a breadth of 1.2 cm., a thickness of 0.8 cm., ovate, having pointed ends with a marked caruncle. The outer side shows the grayish-brown crusty seed coat with irregular rough longitudinal stripes; the cross-section shows a large endosperm, in the middle the embryo of considerable size with flat cotyledons. Besides the fatty oil and protoplasm, the cells of the endosperm show longitudinally very large aleurone grains, which contain a considerable number of small globoids and badly formed crystalloids. Cash and Dilling (*J. P. Ex. T.*, 1914, v, p. 235) have also found a purgative oil in the seeds of the *Croton Elliottii* Chapm. which grows in British East Africa.

The seeds of the *C. Tiglium* resemble castor beans in general structure. They are oblong, rounded at the extremities, with two faces, the dorsal considerably more convex than the ventral, separated from each other by longitudinal ridges, and each divided by a similar longitudinal ridge, so that the whole seed presents an irregular quadrangular figure. Sometimes their ventral surface is flat, with a longitudinal groove, owing to the presence of only two seeds in the capsule, the groove being produced by the central column or axis. The shell is covered with a soft, yellowish-brown epidermis, beneath which the surface is black and smooth, and, as the epidermis is often partially removed by friction during their carriage, the seeds as they come to us are frequently mottled, and sometimes nearly black. The kernel or endosperm is yellowish-brown, and abounds in oil.

The commercial supplies of croton seeds come to the United States chiefly from Colombo, Ceylon. Smaller amounts are obtained from Bombay and London. In India the seeds are prepared for use by submitting them to slight torrefaction, by which the shell is rendered more easily separable. In the dose of one or two grains (0.065 or 0.13 Gm.) the kernel purges severely.

Both the U. S. and Br. direct the oil be obtained by expression from the seeds, but commercially it is also separated by decoction in water, or by the action of ether, or carbon disulphide, which dissolves the oil and leaves it behind when evaporated. It is open to question whether the oils obtained by expression and extraction are of exactly the same composition.

The seeds consist of 64 per cent. of kernel and 36 of envelope. From the seeds imported into England, about 22 per cent. of oil is obtained by simple expression. Guibourt, by his process, obtained 52 per cent. from the kernels, equivalent to about 35 per cent. from the seeds. They contain also a toxic mixture of globulin and albumose, analogous to ricin (see *Oleum Ricinus*), which is known as crotin.

Crotin is described as a yellowish powder, yielding about 21 per cent. of ash, soluble in water, and possessed of such active poisonous properties that the subcutaneous lethal dose for the rabbit is from 0.05 to 0.08 Gm. per kilo. It attacks the blood corpuscles as well as the central nervous system, and, indeed, probably affects all protoplasm. (*On Some Toxic Albumins,* Upsala, 1897.)

Croton oil, as found in commerce, varies greatly in color, from a pale yellow to a dark reddish-brown. That imported from India is usually pale, that expressed in Europe dark, like the deepest-colored sherry. Its consistence is rather viscid, and is increased by time. Its odor is faint, but peculiar, its taste hot and acrid leaving in the mouth a disagreeable sensation which continues for many hours.

Description and Physical Properties.—"A pale yellow or brownish-yellow, somewhat viscid and slightly fluorescent liquid, having a slight, characteristic odor. Croton Oil is slightly soluble in alcohol, the solubility increasing with age; freely soluble in ether, chloroform, and in fixed or volatile oils.

"When gently heated with twice its volume of dehydrated alcohol, it forms a clear solution from which the Croton Oil separates, either partially or completely, on cooling. It is acid to litmus paper previously moistened with alcohol. Specific gravity: 0.935 to 0.950 at 25° C.

"Add 1 cc. of fuming nitric acid and 1 cc. of distilled water to 2 cc. of the Oil, and shake the mixture vigorously for a few minutes: it does not solidify either completely or partially after standing for twenty-four hours (*foreign oils*). Saponification value: not less than 200 and not more than 215. Iodine value: not less than 104 and not more than 110.

"Preserve in small, well-stoppered bottles, protected from light." *U. S.*

"Brownish-yellow to dark reddish-brown; viscid, slightly fluorescent. Disagreeable odor; when cautiously tasted, acrid. Blisters the skin and mucous membrane. Specific gravity 0.940 to 0.960; *saponification value* 210 to 215; *iodine value* 102 to 106. Freely soluble in *ether* and in *chloroform*. Miscible with half its volume of *absolute alcohol*. Thickens slightly but does not solidify, either completely or partially, when vigorously shaken with half its volume of *fuming nitric acid* and the same proportion of *water* (absence of other non-drying oils)." *Br.*

Croton oil may be detected when present in admixture with other oils by the following reaction: The sample of oil is shaken with twice its volume of dehydrated alcohol; the clear solution is superimposed upon a highly concentrated solution of potassium hydroxide in a test tube, which is then carefully warmed for thirty minutes on a water bath and then examined. If croton oil is present, an intense reddish-brown or reddish-violet ring forms at the junction of the two liquids. (*J. P. C.*, 1916, xiv, 38.)

Croton oil has been often adulterated with other fixed oils, which having a different saponification and iodine number can usually be detected by those tests. There is reason to believe that the oils of allied plants such as *Jatropha Curcas* (see *Barbados Nuts,* Part II) or other species of *Croton* are sometimes substituted for it.

Constituents.—Croton oil consists chiefly of the glycerides of stearic, palmitic, myristic, lauric, and oleic acids. There are also present, in the form of glycerin ethers, the more volatile acids, as formic, acetic, isobutyric, and isovalerianic acids. The volatile part of the acid yielded by croton oil contains, moreover, an acid of the oleic series, named by Geuther and Frölich *tiglic* or *tiglinic acid,* $C_5H_8O_2$. It is isomeric with angelic acid, but the melting points (angelic acid 45° C., tiglic acid 64° C.) and the boiling points (angelic acid 185° C., tiglic acid 198.5° C.) differ. *Crotonic acid,* $C_4H_6O_2$, was thought by Schlippe to be present, but later investigation does not confirm the statement. *Crotonol,* announced by Schlippe as the vesicating principle of the oil, has likewise been found only by the discoverer.

In 1873 Buchheim found in croton oil an alcohol-soluble, oily substance which he called *crotonoleic acid* and to which he attributed the cathartic powers of the oil. (For method of its preparation see *U. S. D.,* 20th ed., p. 801.) Dunstan and Boole (*Proc. Royal Soc. of London,* 1895, lxiii) state that this is a mixture of inert oily acids and that the true active ingredient is a resinous substance for which they suggest the name of *croton resin.* This conclusion has been confirmed by Boehm (*A. E. P. P.,* 1915, lxxix, p. 138); by repeated extraction with methyl alcohol and treating the extract with barium hydroxide to get rid of the fatty acids, he obtained an intensely irritant and poisonous resin which was optically active. He suggests that a polarimetric examination of the oil would afford a useful criterion for its valuation.

Uses.—Croton oil is a powerful drastic purgative, in large doses apt to excite vomiting and severe griping pains, and capable, if immoderately taken, of producing fatal effects. It acts with great rapidity, frequently evacuating the bowels in less than an hour, and generally exciting a rumbling sensation in half that period. It possesses also great advantage in the minuteness of the dose, on account of which it may frequently be given when we should fail with more bulky medicines, as in *mania, coma,* and the cases of children. A drop placed on the tongue of a comatose patient will generally operate. Though long used in India, and known for two centuries to the Dutch physicians, it did not attract general notice till about 1820, when it was introduced into England by Conwell. It is employed in cases of *obstinate constipation,* in which other cathartics have failed or when violent or speedy purging is demanded. The seeds are said to have been used successfully in India, in *amenorrhea.* Applied externally, the oil produces inflammation of the skin, attended with pustular eruption, and has been used as a counter-irritant in *rheumatism, gout, neuralgia, bronchitis* and other inflammations. It should be diluted with three parts of olive oil, soap liniment, oil of turpentine, or other convenient vehicle, and applied as a liniment twice or oftener in twenty-four hours. It has been said that four drops, used externally by friction, will produce a purgative effect, but this is denied by Barlai of Tuscany, who states that it is only when the oil is applied to the skin divested of the cuticle that it will operate upon the bowels.

The oil is most conveniently administered in the form of pill. A safe and convenient plan is to make two drops into four pills with a crumb of bread, and to give one every hour until they operate. The oil may also be given in emulsion.

According to Kobert crotonoleic acid is a very active irritant poison, much more harsh and severe in its influence than croton oil itself. He maintains, therefore, that old, acid croton oil must be more irritant than the fresher and nearly neutral oil, and asserts that the neutral oil should always be preferred in practice, and that the acid oil should be rejected.

Dose, one-half to two minims (0.03–0.12 cc.).

Off. Prep.—Linimentum Crotonis, *Br.;* Linimentum Tiglii, *N. F.;* Pilulæ Aloes, Hydrargyri et Scammonii Compositæ, *N. F.*

OLIVERI CORTEX. Br.

OLIVER'S BARK [Black Sassafras]

"Oliver's Bark is the dried bark of Cinnamomum Oliveri, *Bailey.*" *Br.*

The genus *Cinnamomum* comprises some fifty-four species which are mostly tropical or subtropical evergreen shrubs or trees. They are mostly aromatic and comprise two principal groups: The one yielding camphor, and the other aromatic cinnamon-like barks. The tree which furnishes oliver bark is *Cinnamomum Oliveri* Bailey (Fam. *Lauraceæ*). It is indigenous to New South Wales and Queensland, where it is sometimes called *Black Sassafras.* It is much of the same habit as the trees yielding cinnamon and the bark is used as a substitute for this spice in the Australian Colonies.

"In flat pieces usually about twenty centimetres long, four centimetres wide and one centimetre thick. Cork greyish-brown, very warty. Inner surface umber-brown, satiny. Fracture short, slightly fibrous. In transverse section, umber-brown, a pale line separating the cork from the inner tissues. Aromatic odor; taste aromatic, bitter, camphoraceous." *Br.*

Oliver bark yields a yellow volatile oil which contains safrol, eugenol, cineol and cinnamic aldehyde. It also contains tannin. It is used as a substitute for cinnamon.

Off. Prep.—Tinctura Oliveri Corticis, *Br.*

OPIUM. U. S., Br.

OPIUM

"Opium is the air-dried, milky exudation obtained by incising the unripe capsules of *Papaver somniferum* Linné or its variety *album* De Candolle (Fam. *Papaveraceæ*). Opium in its normal, moist condition yields not less than 9.5 per cent. of anhydrous morphine." *U. S.* "Opium is the juice obtained by incision from the unripe capsules of Papaver somniferum, *Linn.*, inspissated by spontaneous evaporation. Any suitable variety of opium may be employed as a source of Tincture of Opium and Extract of Opium, provided that when dry it contains not less than 7.5 per cent. of anhydrous morphine; but, when used for official purposes other than the preparation of the alkaloids or their salts, opium must be of such a strength that when dried, and powdered, the resulting powder dried at 60° C. yields not less than 9.5 per cent., and not more than 10.5 per cent., of anhydrous morphine. Opium yielding when dried more than 10 per cent. of anhydrous morphine must be diluted to that percentage either with powdered Milk Sugar or with any opium containing when dried between 7.5 and 10 per cent. of anhydrous morphine." *Br.*

Lachryma Papaveris, Meconium, Succus Thebaicus, Thebaica; Opium, *Fr. Cod.;* Opium, *P. G.;* Mohnsaft, *G.;* Oppio, *It.;* Opio, *Sp.;* Affioni, *Turk.;* Ufyoon, *Arab.;* Sheerikhaskash, *Pers.;* Ufeem, *Hindost.*

Opium is generally believed to be derived exclusively from *Papaver somniferum,* though every species of poppy is capable of yielding it to a greater or less extent. The United States, British and French Pharmacopœias recognize only the first mentioned species and its varieties.

Papaver somniferum L., or *Opium Poppy,* is an annual, glabrous and glaucous herb up to four feet in height, indigenous to Asia but cultivated in many tropical, subtropical and temperate countries. It possesses large, oblong, sinuate to dentate-serrate leaves, clasping at the base, and long peduncles, with nodding buds that expand into erect flowers which while usually purplish are sometimes white, pink or red in color. Each flower consists of a receptacle bearing two green sepals, four colored petals, numerous stamens and a syncarpous pistil composed of a globose ovary showing many projecting parietal placentæ bearing the ovules and a compound, radiate, sessile stigma. The fruits are globose capsules each with an 8–12 rayed sessile stigma and containing numerous small oily seeds. There are several varieties of this species, of which the two most prominent are distinguished by the titles of the white and the black poppy, derived from the color of their seeds. The *Papaver somniferum* var. *album* DC., *white poppy,* is annual, with a cylindrical smooth, erect, glaucous, often branching stem, usually rising two or three feet in height, but sometimes five or even six feet in favorable situations. The leaves are large, variously lobed and toothed, and alternately disposed on the stem, which they closely embrace. The flowers are terminal, very large, and of a white or silver-gray color. In India they appear in February, in Europe and the United States not earlier than June, July, or August. The calyx is smooth and composed of two sepals, which fall when the four petals expand. The ovary is smooth and globular, supports a radiate stigma, and is surrounded by numerous stamens with short, slender filaments and erect, oblong, compressed anthers. The capsule is smooth and glaucous, rounded, from two to four inches in diameter, somewhat flattened at the top and bottom, and crowned with the persistent stigmas, the diverging segments of which are arranged in a circle upon the summit. It contains numerous minute white seeds, which when perfectly ripe escape through small openings between the stigma. In the *black poppy,* the flower, though sometimes white, is usually violet-colored, the capsule somewhat smaller and more globular, and the seeds of a brown or blackish color.

There occur two additional varieties, *Papaver somniferum* var. *setigerum* Elk. and *P. somniferum* var. *glaucum* O. Kuntze, which, however, are not cultivated as sources of opium.

All parts of the poppy contain a white opaque, narcotic juice, but the leaves analyzed by Blondeau, yielded none of the active principles by which opium is characterized. (*J. P. C.,* vii, 214.) It is in the capsule that the juice most abounds and the virtues of the plant chiefly reside, hence this part is sometimes employed medicinally and was official in the British Pharmacopœia of 1898 as *Papaveris Capsulæ* and in the N. F. IV as *Papaveris Fructus.* The dried poppy capsules vary in size from 5 to 7.5 cm. in diameter, and in shape from ovoid to globular, according to the variety of the poppy from which they are procured. Those commonly found in commerce are spheroidal, flattened below, and surrounded by a crown-like expansion—the persistent stigma—which is marked by numerous diverging rays that rise somewhat above the surface and appear to be prolongations of partial septa or partitions, proceeding along the interior circumference of the capsule from the top to the bottom. They are of a dirty white or purplish brown color, of a consistency somewhat like that of paper, inodorous and with little taste unless long chewed when they are decidedly bitter. They contain the same principles as opium but in much smaller amounts. The seeds are destitute of narcotic properties, and are even used as food. The Romans employed them in the preparation of various dainties. They are commercially known as *maw seed* (probably a corruption of the German *mohnsamen*) and frequently used for culinary purposes. They abound with a bland oil, called commercially *poppy seed oil,* or maw oil, which may be extracted by expression. The latter is of a straw-yellow color, without odor, and of a pleasant almond taste. It is without narcotic properties, and much resembles olive oil, as a substitute for which and an adulterant of which it is very largely used on the continent of Europe. It has a low congealing point, thickening only at –15° C. and solidifying at –20° C. The black variety is specially used for the expression of oil, as its culture is easier, and the oil percentage in both varieties is practically the same, ranging between 50 and 60 per cent. As the oil cake generally retains about 8 per cent. of the oil, the yield by expression is from 42 to 50 per cent. Poppy oil contains the glycerides of stearic and palmitic acids, together with those of linoleic, linolenic, and oleic acids. Of the liquid fatty acids, linoleic constitutes about 65 per cent., oleic 30 per cent., and linolenic 5 per cent. Myristic and lauric acid seem to be absent. The oil is an article of much importance on the continent of Europe, particularly in France and Germany, where it is employed for culinary and pharmaceutical purposes, in painting and the manufacture of soap, and in other ways, as substitute for olive oil.

The poppy does not appear to elaborate the milky fluid in which its narcotic properties reside before a certain period of its growth, for we are told that, in Persia, the young plants which are pulled up to prevent too thick a crop, are used as potherbs, and the *μήκων* of the Greeks, which is believed to be identical with the *Papaver somniferum,* is said by Hippocrates to have been nutritive.

Though generally believed to be a native of Asia Minor, this species of poppy grows wild in the south of Europe, and even in England, whither its seeds are supposed to have been brought at a very early period. It was cultivated by the ancient Greeks, and is mentioned by Homer as a garden plant. It is at present cultivated very extensively in India, Persia, Turkey, Macedonia, Bulgaria, China, and Asia Minor, for opium, and in certain parts of Europe chiefly for its seeds. Attempts have been made both in Europe and the United States to produce opium from the poppy, but although it is possible to obtain the product, commercial success has not been, and probably never will be, achieved because of the cost of labor.

For further details on this subject see *U. S. D.,* 20th ed., p. 808. True reports on some experiments in the cultivation of opium poppy in the United States and states that it yields a good crop in Vermont, and a bumper crop in the dry climate of the state of Washington. (*Proc. N. W. D. A.,* 1911, p. 17.) He also outlines a plan for converting the waste product of the poppy seed industry, the capsule, into a valuable source of opium alkaloids. (*Oil, Paint, and Drug Rep.,* 1906, lxx, p. 37.)

The following articles are of interest in connection with the cultivation of the opium poppy: Stahl "On Persian Opium" (*Chem. Zeit.,* xxxii, p. 804); van Itallie and Kerbosch "On Opium in Northern China" (*Arch. Pharm.,* 1910, p. 614); "Opium Cultivation in Turkey" (*C. D.,* lxxxiii, p. 134); "On the Cultivation of Opium at Dorpat" (Muszynski in *Apoth. Zeit.,* xxvi, p. 431).

The opinion that a hot climate is not necessary for the production of the narcotic principles would seem to be established by the facts that the opium of Anatolia is richer in morphine than that of the much hotter regions of Bengal and Upper Egypt, and that good quality of opium has been produced in the northern United States as well as in France and Germany.

Opium is obtained from the capsule of the poppy in a manner almost the same as that described by Dioscorides eighteen hundred years ago. A few days after the petals have fallen from the flower, when the capsule is approaching maturity, horizontal, vertical or spiral incisions into the capsule are made, usually with a several-bladed knife, care being taken not to penetrate the cavity. The white juice which exudes is allowed to harden for twenty-four hours, when it is scraped off by means of a large, blunt knife, a portion of the epidermis of the capsule being removed and constituting about six to ten per cent. of the product. In some places the poppy-head yields opium but once, but in Persia and probably other very hot countries the operation is repeated two or three times after periods of rest. The quality of the product depends largely upon the weather; if this is very hot and dry, the juice will be scanty and very thick, but if the weather is moist the product will be larger but more aqueous. After gathering, the poppy juice is worked up into opium in a manner which differs in different producing countries. An opium-like substance has been in past times, and perhaps even is at present in some districts, produced by making an aqueous extract from the nearly ripe capsule of the poppy. According to the writings of Dioscorides the ancient Greeks were acquainted with both processes of producing the drug from the poppy capsule. The term *ὀπίον,* derived from *ὀπος, juice,* they applied to the substance procured by incisions, which answers precisely to the modern opium. The inspissated expressed juice they called *μηκωνιον,* from *μήκων,* the name of the plant.

Commercial History.—Commerce is supplied with opium chiefly from Turkey, Asia Minor, Macedonia, Jugo-Slavia, Bulgaria, Persia and India. Turkey opium constitutes the principal commercial article. Since the passage of the Narcotic Drugs Import and Export Act in 1922 which established the Federal Narcotics Control Board, the quantities of opium imported into the United States have decreased annually. In 1924, only 87,344 pounds entered this country through legitimate channels.

The commercial opiums may be classified into the following varieties: (1) Turkey opium also known as Asia Minor, Smyrna or Constantinople opium; (2) Macedonian opium, (3) Bulgarian opium, (4) Persian opium, (5) Indian opium, (6) Chinese opium, (7) Egyptian opium.

TURKEY OPIUM (*Smyrna, Asia Minor,* or *Constantinople Opium*).—This opium is produced in the central and northwestern districts of European Turkey, Asia Minor and to a smaller extent also includes some drug sent into Turkey from Bulgaria and Macedonia.

It represents the most important and abundant opium on the American market and is imported chiefly from Constantinople and Smyrna in tin or zinc lined wooden cases.

As seen on our markets it occurs as compressed spheroidal or flattened masses of variable size, usually from half a pound to two or three pounds in weight. These masses usually possess a hard crust on the outside but are soft, plastic, and reddish brown within. They are covered externally with the remains of poppy leaves and with adhering reddish winged fruits of a species of Rumex, the latter being placed in packing between the masses to prevent their cohering. The odor is quite characteristic and the taste bitter.

Two important varieties of Turkish opium now occur in commerce, *viz.,* "Soft shipping opium" and "Druggist's opium." The former opium occurs in masses having a somewhat uniform pasty texture within and containing 25 per cent. to 30 per cent. or more of moisture. The latter variety occurs in harder masses possessing a granular internal appearance, and varies in moisture content from 10 per cent. to 25 per cent.

Considerable soft shipping opium comes from southern Serbia and Malatia; Karahissar, Boghaditz and Giveh supply much of the druggist's opium.

Little of the opium is produced in the immediate neighborhood of Smyrna, the greater portion being brought, on the backs of camels, from a distance of from ten to eighteen days' journey.

In Turkey the district of Anatolia has been a large producing center. The various towns in the Sanjak, or Province of Samsun, which are engaged in the growing of this plant, use Samsun as a port of shipment to Constantinople and European ports. Planting takes place usually in the month of January, and six months must elapse before the plant develops and reaches a height of approximately 3½ feet to 4½ feet. Towards the end of May capsules appear on the plant, and the end of July finds them completely matured. The capsules are then slit and latex is scraped off, which is allowed to dry, and is then exported in round-shaped balls preserved with leaves. After the latex has been completely withdrawn from the unripe capsules, which is allowed to remain on the plant, a new period of ripening sets in; the paste which remains in the capsules, after the latex has been removed, dries and becomes granulous. The buds are then picked and the poppy seeds are withdrawn. These are either white, blue, or greyish in color. Poppy seeds are purchased by Samsun export commission agents from the various centers of production in the interior, and are sent to the coast on the backs of horses, oxen or camels. From there they are exported to various countries where they are used as a food or as a source of oil. Curiously enough, the United States only provides a market for blue seeds, seeming never to be interested in white. According to the opinion of local shippers, this preference on the part of the United States is only one of habit or custom, as there is absolutely no difference between the two kinds of seeds. (*P. J.,* 1921, cvi, 320.)

MACEDONIAN OPIUM.—The opium poppy is cultivated in Greek Macedonia, largely in the regions of Langaza and the peninsula of Chalchidice. While the output of Macedonian opium is comparatively small, this opium has been in great demand by drug manufacturers.

According to Valdegrice, the opium produced in Salonica and environs is free from capsule fragments and contains in the moist condition from 13 per cent. to 17 per cent. of morphine, 0.464 per cent. codeine, and 0.075 per cent. of narceine. (*J. P. C.,* 1918, xviii, 81). The opium produced in Serbian Macedonia according to Brunetti (*P. J.,* 1918, ci, 107) is collected in a number of localities—the most esteemed coming from Kavadar, Veles and Chtap—and is richer in codeine than the opium from Asia Minor.

PERSIAN OPIUM.—This variety of opium is produced chiefly in the vicinity of Shiraz, Ispahan and Mesched, Persia. The latex is collected by the natives from the poppy capsules and kneaded, frequently with added gum, into a homogeneous mass, after which it is cut into brick-shaped masses weighing about a pound, dried in the sun, and wrapped in red or less often white paper and tied with red or yellow string. Occasionally the Persian opium is found in wrapped cones or sticks. It contains less moisture than the Turkey opium and its interior has a homogeneous texture. Its odor is musty and its taste very bitter.

The most important local varieties of Persian opium appear to be the so-called *Mesched opium,* which occurs in grayish-brown shining sticks, wrapped in paper, and *Ispahan opium,* of similar appearance, but of a purer brown color. According to the investigations of Schindelmeiser (*Ap. Ztg.,* 1904, 19) the Mesched opium, when freed from moisture, yields from 5.9 to 8.7 per cent. of morphine; while Ispahan opium has in it from 11.9 to 19 per cent. of the alkaloid. *Tschakida* of the Persians is a dark brown, blackish impure opium occurring in cakes prepared for smoking, and according to Schindelmeiser contains not more than 0.4 per cent. of morphine. W. D. Howard examined a sample of the Persian opium sent to England as "perfectly pure," which yielded to him on analysis, without previous drying—morphine, 10.40 per cent.;

codeine, anhydrous, 0.29 per cent.; narcotine, 2.50 per cent.; thebaine, 0.57 per cent.; cryptopine, 0.09 per cent.; papaverine, a trace. He is unable to say whether it contained any narceine.

Ordinarily but little of the Persian opium enters commerce, most of it being consumed in that country for smoking, but during the world war the Powers, Weightman and Rosengarten Co., of Philadelphia, imported a considerable quantity; they found it to run about 10 per cent. of morphine.

India Opium.—The opium of Hindostan is distributed extensively through continental and insular India, where it is habitually employed as a narcotic. Great quantities were also sent to China, into which it found an easy entrance, notwithstanding prohibitory laws. Much was formerly imported by the East India Company into England, through which a small proportion reached our own country. For various reasons India opium no longer enters Western commerce to any extent. India opium is usually relatively poor in morphine; in many samples the proportion of narcotine is higher than morphine. It is stated that the quality of India opium has much improved since 1914.

There appear to be two chief varieties of it—one produced in Bahar and Benares, in the Bengal Presidency, and called *Bengal opium,* the other in the interior provinces, and designated by the name of *Malwa opium.* For minute description of Indian opium, see *P. J.,* xi, xii, abstracted in *A. J. P.,* xxiv, 118; also *Pharmacographia.*

Bengal Opium, Benares Opium, Patna Opium.—This is produced in Hindostan chiefly under government supervision. The drug as first obtained is semi-liquid, owing to the excessive dews, but is allowed to drain and dry by spontaneous evaporation until only 30 per cent. of moisture is left, when it is taken to the government factories. Great care is exercised to prevent adulteration. In the factories it is worked up with the drainings (known as *passēwā*), poppy petals, and ground poppy plant into balls of standard strength. These are called *"cakes,"* are about six inches in diameter, and are prevented from adhering by being rolled in the ground poppy plant. It is in round balls, weighing three pounds and a half, invested by a coating half an inch thick, composed of agglutinated leaves and poppy petals. The interior of the mass is of a brownish-black color, of the consistence of a stiff paste, and possessed in a high degree of the characteristic odor and taste of opium.

Malwa Opium.—Malwa opium is a variety not made by licensed cultivators on the tablelands of Malwa, northeast of Bengal. Its quality varies greatly. It occurs in round balls. It seems never to be encased in poppy remnants. The masses are commonly quite hard, dry, and brittle, of a light-brown color, a shining fracture, a compact homogeneous texture, and free from mechanical impurities.

Indian Medicinal Opium.—This grade of Indian opium occurred on the markets during the World War, in the form of cubes each weighing about two pounds. It is wrapped in paper that was frequently oiled.

Chinese Opium.—This variety is produced in China and largely used by the Chinese; occasional lots, however, are smuggled into other countries. It occurs in flattened globular cakes that are frequently wrapped in white paper.

Egyptian Opium.—Much opium was formerly produced in Upper Egypt, especially in the district of ancient Thebes, which was supposed to yield it in greatest perfection, hence the term *Opium Thebaicum,* and the old name of laudanum, *Tinctura Thebaica.* The cultivation of the opium poppy in Egypt was prohibited in 1918 in order to increase the area under food cultivation. (*C. D.,* 1918, xc, 846). This variety occurred in flat roundish cakes, of various dimensions, sometimes as much as six inches in diameter and a pound in weight, usually, however, much smaller, and sometimes not weighing more than half an ounce. These cakes were either wrapped in a poppy leaf, so placed that the mid-rib divided the surface into two equal parts, or exhibited vestiges of such a covering. Occasionally the brown color of the opium was seen through the leaf, and the surface appeared as if uncovered, while the leaf was still present. The fracture was conchoidal and of a waxy luster and small fragments of it were translucent. Its color was usually redder than that of Smyrna opium, though sometimes dark. Some of the pieces, on exposure to the air, became damp and sticky on the surface, indicating the fraudulent addition of a deliquescent substance. The odor was similar to that of Smyrna opium, but weaker. It was an inferior variety, as the best of it, examined by Merck, yielded only 6 or 7 per cent. of morphine.

Adulterations.—The adulteration of opium has given rise to much complaint on the part of pharmacists, and various plans of customs legislation have been suggested by which it has been thought that these adulterations could be prevented. It is, however, obviously impossible to pronouncedly affect the action of the semi-barbarians who are engaged in the cultivation of opium, by any American legislation. Usually the substances which are used to adulterate the drug are inert, and therefore do no harm except by weakening its activity. The U. S. Custom House requires that opium, in order to enter the United States as opium, shall conform to the U. S. P. standard and contain not less than 9.5 per cent. of anhydrous morphine.

Sand, ashes, the seeds of different plants, extracts of the poppy, *Lactuca virosa, Glycyrrhiza glabra,* and *Chelidonium glaucum,* gum arabic, tragacanth, salep, aloes, even small stones and minute pieces of lead and iron, are mentioned among the substances employed in the sophistication of the drug. Tschirch (*A. J. P.*, 1898, 488) proposes the use of the Roentgen ray in detecting such adulterations.

Masson described a product which was sold under the name of "Smyrna" or "manipulated," and which consisted of a mixture of the natural juice with substances more or less inert. The samples varied very widely in composition, and in some cases were so altered that the active ingredients could not be readily dissolved. (*J. P. C.*, 1905, p. 529.) Stahl found in some samples of Turkish opium the possible admixture of fruit pulp or fruit extracts. (*Ph. Zentralh.*, xlix, p. 958.) Dried grape-juice mixed with flour was at one time frequently added to the opium juice.

Opium is regarded as inferior when it has a blackish color, a weak or empyreumatic odor, a sweet or slightly nauseous and bitter taste, a soft, viscid, or greasy consistence, a dull fracture, or an irregular, heterogeneous texture, from the intermixture of foreign substances. It should not impart a deep-brown color to the saliva, nor leave a dark uniform trace when drawn over paper, nor form with water a thick viscid solution. The best test is the assay for alkaloids.

Description and Physical Properties.—Good opium has a strong, peculiar odor, and a bitter, somewhat acrid taste. It is officially described as: "In more or less rounded, somewhat flattened, masses, usually about 8 to 15 cm. in diameter; externally dark brown, covered with fragments of poppy leaves and at times with fruits of a species of rumex adhering from the packing; more or less plastic when fresh, becoming hard and brittle or tough on keeping; internally dark brown, interspersed with lighter areas, somewhat lustrous; odor characteristic, narcotic; taste very bitter, characteristic." *U. S.*

"Usually in rounded, irregularly formed, or flattened masses, varying in weight, but commonly weighing from about 250 to 1000 grammes. When fresh, plastic, and internally somewhat moist, coarsely granular, or nearly smooth, and reddish or chestnut-brown; but becoming harder on keeping, and darkening to blackish-brown. Strong and characteristic odor; taste bitter." *Br.*

When long chewed it excites much irritation in the lips and tongue, and may even blister the mouths of those unaccustomed to its use. Its color is reddish-brown or deep fawn; its texture compact; its sp. gr. 1.336. When drawn over paper it usually leaves an interrupted trace of a light-brown color. It is often soft in the interior of the mass, and in this state is tenacious; but when exposed to the air it gradually hardens, and ultimately becomes brittle, breaking with a shining fracture, and affording, when pulverized, a yellowish-brown powder, which becomes adhesive upon a slight elevation of temperature. It readily inflames upon the application of a lighted taper. On heating opium on a watch crystal and collecting the sublimate on a slide, Rosenthaler found the sublimate to give the characteristic red color reaction for narcotine. (*Ph. Zentralh.*, liv, p. 1250; *Apoth. Zeit.*, xxviii, p. 991.)

Opium yields its virtues to water, alcohol, and diluted acids, but not to ether, benzine and some of the other immiscible solvents. To all these menstrua it imparts a deep-brown color. Alcohol dissolves about four-fifths of it. Pelletier stated that the proportion taken up by water varies in the specimens. He never found the quantity of extract prepared with cold water to exceed 12 parts out of 16.

The proportion of morphine which any particular specimen of opium will furnish is considered the best test of its value. The U. S. Pharmacopœia directs that opium, in its normal, moist condition should contain not less than 9.5 per cent. of anhydrous morphine, and powdered or granulated opium, dried at a heat not exceeding 85° C., should contain not less than 10 nor more than 10.5 per cent. of anhydrous morphine when assayed by the official process, which is as follows:

"Place 8 Gm. of Opium, which if fresh should be in very small pieces, and if dry in fine powder, into an Erlenmeyer flask having a capacity of about 250 cc., add 80 cc. of distilled water, stopper the flask, and agitate it every ten minutes (or continuously in a mechanical shaker) during three hours. Then pour the contents as evenly as possible upon a wetted filter having a diameter of not over 12 cm., and, when the liquid has drained off, wash the residue with distilled water, carefully dropped upon the edges of the filter and its contents until a filtrate of 120 cc. has been obtained. Carefully transfer the moist Opium to a mortar by means of a spatula, and rub to a smooth paste, then rinse into the original flask with 50 cc. of distilled water, agitate it thoroughly, and return the whole to the filter. When the liquid has drained off, wash the residue with 75 cc. of distilled water. Evaporate the mixed filtrates and washings on a water bath to about 40 Gm., transfer the extract to a 50 cc. graduated flask, and wash the evaporating dish with sufficient distilled water to make the entire volume measure exactly 50 cc. when cooled to room temperature. Place in a small mortar 4 Gm. of freshly slaked lime, add about 10 cc. of the Opium extract and rub to a smooth paste, then add the remainder of the extract, and rinse the flask with exactly 10 cc. of distilled water, adding the rinsings to the mortar, and stir frequently during fifteen minutes, avoiding unnecessary loss by evaporation. Filter through a dry filter, about 10 cm. in diameter, and transfer exactly 30 cc. of the filtrate, representing 4 Gm. of Opium, to an Erlenmeyer flask of suitable capacity. To this add 2 cc. of alcohol and 15 cc. of ether, and after shaking the mixture add 1 Gm. of ammonium chloride, stopper the flask, and shake it frequently during

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half an hour, then set it aside in a cool place for twelve hours or over night. Remove the stopper, and brush any adhering crystals back into the flask. Decant the ethereal layer into a small funnel, the neck of which has been previously closed with a pledget of purified cotton. (A small filter paper may be used if preferred.) Rinse the flask and contents with 15 cc. of ether, and, when the ether has passed through, wash the funnel and cotton with a small quantity of ether, and then pour the aqueous liquid into the funnel without trying to remove the crystals. Wash the crystals in the flask and the contents of the funnel with distilled water previously saturated with morphine, until the washings are colorless. Then add a few drops of distilled water to replace the morphinated water. Incline the edge of the funnel over the mouth of the flask, and by means of a glass rod carefully transfer the cotton with adhering crystals to the flask. Insert the funnel into the neck of the flask, and wash the funnel with 20 cc. of tenth-normal sulphuric acid, followed by 10 cc. of distilled water applied, drop by drop, around the edge of the funnel. Remove the funnel, replace the cork, warm gently, and agitate until the crystals are dissolved. Rinse the cork with distilled water, and titrate the excess of acid with fiftieth-normal sodium hydroxide. Each cc. of tenth-normal sulphuric acid corresponds to 0.02853 Gm. of anhydrous morphine." *U. S.*

Assay of Opium, Br.—" Opium, in No. 50 powder, dried at 60° C., 8 *grammes;* Calcium Hydroxide, freshly prepared, 2 *grammes;* Ammonium Chloride, 2 *grammes;* Alcohol (90 per cent.), Ether, Distilled Water, of each, *a sufficient quantity.* Triturate together the Opium, *calcium hydroxide,* and 20 millilitres of *water,* in a mortar until a uniform mixture results; add 60 millilitres of *water* and stir occasionally during half an hour. To 51 millilitres of the filtered liquid (representing 5 grammes of Opium) in a convenient vessel add 5 millilitres of *alcohol* (90 per cent.), and 25 millilitres of *ether;* shake the mixture; add the *ammonium chloride,* shake well and frequently during half an hour; set aside for twelve hours for the morphine to separate. Counterbalance two small filters; place one within the other in a small funnel in such a way that the triple fold of the inner filter shall be superposed upon the single fold of the outer filter; wet them with *ether;* remove the ethereal layer of the liquid in the vessel as completely as possible by means of a small pipette, transferring the liquid to the filter; rinse the vessel with 10 millilitres of *ether,* again transferring the ethereal layer, by means of the pipette, to the filter; wash the filter with a total of 5 millilitres of *ether,* added slowly and in portions. Let the filter dry in the air, and pour upon it the contents of the vessel in portions, in such a way as to transfer the granular crystalline morphine as completely as possible to the filter. When all the liquid has passed through, wash the remainder of the morphine from the vessel with *morphinated water,* until the whole has been removed. Wash the crystals with *morphinated water* until the washings are free from color; allow the filter to drain, and dry it, first at 60° C. and finally, for two hours, at 115° C. Weigh the crystals in the inner filter, counter-balancing by the outer filter. Dissolve 0.2 gramme of the crystals in 10 millilitres of *N/10 solution of sulphuric acid,* and titrate back with *N/10 solution of sodium hydroxide, solution of methyl orange* being used as indicator. Each millilitre of the acid neutralised by the alkaloid corresponds to 0.0285 gramme of pure anhydrous morphine. The weight of pure anhydrous morphine obtained, as indicated by the titration, plus 0.051 gramme, the average loss of morphine during the process, together amount to 0.5 gramme, representing in 100 grammes of the dry powdered Opium 10 grammes of morphine, calculated as anhydrous. *Limit of error* 0.5 gramme in excess or defect." *Br.*

Morphinated Water.—" Prepared by digesting pure morphine in chloroform water for seven days at a temperature of 15.5° C., with shaking occasionally, so as to obtain a saturated solution of the alkaloid, and filtering from the undissolved morphine." *Br.*

The U. S. and Br. methods of assay are practically identical in principle, belonging to the class of assays known as " lime processes." Experience has proved that the " lime processes " have some objectionable features. They all depend upon the principle that opium in the presence of lime is treated with a definite quantity of water until the latter has extracted as much as possible of the soluble portions, after which a certain portion of the solution, which is *assumed to represent* a corresponding fraction of the weight of the opium, is weighed or measured off, the morphine determined in it. The strength is calculated from the quantity of morphine found in this fraction or aliquot part. The " lime processes," in the hands of ordinary operators, " register too low," the assay being applied to a proportion of the opium which may or may not be an aliquot part of the whole, but is generally less than it is assumed to be, because no allowance is made for the increase in volume due to the solution of the solid constituents of the opium. The British Pharmacopœia overcomes this objection by requiring 104 cc. of liquid to be taken instead of 100 cc. Want of space prevents our giving a critical review of the many methods of assay in use at various times. (Extensive references to the older methods are found in the *U. S. Dispensatory,* 19th ed., p. 905.) See also *J. I. E. C.,* 1912, p. 514; *Gehes. Rep.,* 1912; *Year Book of Pharm.,* 1913, 443.

Chemical Constituents.—It was through the researches into the nature of this substance that chemists were led to the discovery of the alkaloids. To Sertürner, an apothecary at Eimbeck, in Germany, belongs the credit of having opened the important field of alkaloidal research. The development of the alkaloids in opium has been the object of the studies of A. Müller. (*Ph. Ztg.*, lix, p. 600.) He found the seeds to be alkaloid-free, but that the sprouts, after two weeks, show the presence of alkaloids. The alkaloidal content of the plant slowly increases until the flowers appear, when there is a sharp increase lasting until the floral leaves fall. After the ripening of the capsule, the alkaloidal nitrogen content of the entire plant was found to be 0.0094 per cent.; of the stem and leaves alone, 0.0085 per cent.; and of the capsule walls only 0.0168 per cent. The alkaloidal content was found to vary from day to day, being less on cloudy than on sunny days. His conclusions were that the alkaloids of the poppy plant are not excretion material intended to protect the plant from animal enemies, as has been suggested, but that they are present to afford a source of nitrogen for the synthesis of reserve protein. A comprehensive study of the market conditions of the more important opium alkaloids was contributed by L. E. Warren, *A. J. P.*, 1915, p. 439.

In the year 1803 Derosne made known the existence of a crystallizable substance which he had discovered in opium, and which he erroneously believed to be the active principle. In the following year Seguin discovered another crystallizable body, which experience has proved to be the true narcotic principle of opium, but he did not fully investigate its nature, and no immediate practical advantage accrued from his excellent analysis. About the same time, Sertürner was engaged in a similar investigation, the results of which, very analogous to those obtained by Seguin, were published in a German journal, without, however, attracting general attention. In this state the subject remained until 1817, when Sertürner announced the existence of a saline compound in opium, consisting of a peculiar alkaline principle united with a peculiar acid, and clearly demonstrated the precise nature of a substance which, though discovered both by Seguin and himself, had been hitherto but vaguely known. To the alkaloid, in which he correctly conceived the narcotic powers of opium to reside, he gave the name of *morphium,* which has been since changed to *morphine,* in order to render it conformable with the titles of the other alkaloids. The acid he called *meconic,* a term derived from the Greek name of the poppy. The correctness of the statements of Sertürner was confirmed by Robiquet, who also satisfactorily demonstrated that the substance obtained by Derosne and called by him the *salt of opium* was a principle altogether distinct from morphine, though supposed to possess considerable influence over the system. In the belief in its narcotic powers, Robiquet denominated it *narcotine,* a title which it still retains. A number of other alkaloids have since been discovered in opium, although most of these are in very limited amount, and the existence of some is not quite definitely established as it is possible that they are decomposition products, due to the fact that they were reported in mother liquors from which the more valuable alkaloids had previously been extracted.

According to the views of its constitution at present accepted, it contains some twenty-five alkaloids, namely: morphine, codeine, thebaine, papaverine, protopapaverine, pseudopapaverine, papaveramine, laudanine, laudanidine, laudanosine, meconidine, codamine, narceine, narcotine, oxynarcotine, hydrocotarnine, lanthopine, protopine, cryptopine, neopine, tritopine, pseudomorphine and rhœadine. In addition to the above list, *Deuteropine, Opianine, Papaverosine,* and *Porphyroxine* are possible alkaloids that have been announced, but not sufficiently established as yet. Of these several are official and described elsewhere in this work; the remainder are described below in alphabetical order.

There are present also at least two organic acids, lactic and meconic, and three neutral principles, meconin, meconoisin and opionin; these are described on p. .

Of the principles above mentioned, morphine is by far the most important. It is generally admitted to exist in opium united in part with meconic acid in the state of meconate, and to a certain extent also as a sulphate, although A. R. L. Dohme (*A. J. P.*, 1891, p. 168) believes that the results of a dialysis of opium show that the morphine is combined with sulphuric acid alone.

The relative proportion of the various alkaloids differs considerably in samples of opium. The ordinary ranges of the more important alkaloids are: morphine 5 to 15 per cent.; narcotine 2 to 8 per cent.; codeine 0.1 to 2 per cent.; papaverine 0.5 to 1 per cent.; thebaine 0.15 to 0.5 per cent.; narceine 0.1 to 0.4 per cent. The other reported bases are present in only very small proportions. The amount of labor that has been expended in attempting to determine the chemical structure of the opium alkaloids is so enormous that it can not even be summarized here; the interested reader will find an excellent epitome of the subject in Henry's *Plant Alkaloids,* 1924.

CODAMINE.—*Codamina,* $C_{20}H_{25}O_4N$, is isomeric with laudanine, but is readily distinguished from it by the effect of ferric chloride and nitric acid, both of which color it deep green. According to Allen, codamine also gives a dark green coloration with sulphuric acid and, in the presence of a minute quantity of ferric chloride, a greenish-blue. It can be purified by taking advantage of the feeble solubility of its iodide. Codamine crystallizes also from petroleum benzin; but thus obtained it melts at 126° C., while that procured through ether melts at about 120° C. The acid iodide, tartrate, and oxalate are crystallizable.

CODEINE, $C_{18}H_{21}O_3N$ (or $C_{17}H_{17}NO(OH)$.-

OCH_3), and its phosphate and sulphate are now official and are described under *Codeina.* For a paper on the determination of codeine in opium, by Chas. E. Caspari, see *Proc. A. Ph. A.*, 1904, 386.

COTARNINE, $C_{12}H_{15}O_4N$, was first obtained by Wöhlu by the oxidation of narcotine with manganese dioxide in the presence of sulphuric acid. It is also produced from the same source by oxidation with nitric acid. (See *Cotarnine hydrochloride.*)

CRYPTOPINE, $C_{21}H_{23}NO_5$.—This alkaloid was discovered by T. and H. Smith, of Edinburgh. (*P. J.*, 1867.) They obtained it from the weak alcoholic washings of crude morphine after precipitation, by precipitating with milk of lime, and separating from the thebaine by fractional crystallization. (For details of their method, see *U. S. D.*, 19th ed., p. 895.)

The quantity of cryptopine in opium is extremely small but commercial papaverine has been found to contain as much as 4 per cent. of cryptopine. A most exhaustive research on this alkaloid was reported by W. H. Perkin (*Tr. Chem. Soc.*, 1916, cix, 815; 1919, cxv, 713) in which the mystery of its constitution was finally solved.

Cryptopine is without color or odor, and its salts, though at first bitter to the taste, afterward cause a sense of coolness in the mouth, like that produced by peppermint. It melts at 217° C., and, on cooling, crystallizes in radiated forms at 171° C. It is insoluble in water and in ether, very sparingly soluble in alcohol, requiring 1265 parts of that liquid when cold to dissolve it. Chloroform dissolves it almost as freely as narcotine. It has very strong alkaline powers, and forms crystallizable salts with the acids, which are distinguishable from all the other salts of the opium alkaloids by a strong tendency to gelatinize. From all the constituents of opium, except the alkaloids, morphine, codeine, and thebaine, it is distinguished by its strong alkaline properties. From morphine it differs in the effect of strong sulphuric acid, which produces a blue color with the minutest quantity of cryptopine, a blood-red with thebaine, and none with morphine or codeine.

DEUTEROPINE, $C_{20}H_{21}O_3N$, according to Allen, is an alleged homologue of protopine and cryptopine. It requires further examination.

GNOSCOPINE, $C_{22}H_{23}O_7N$, was found by T. and H. Smith in 1878. It is now regarded as optically inactive narcotine. It is crystallizable, melts at 229° C., is soluble in chloroform and carbon disulphide, slightly so in benzene, not in ether. The salts have an acid reaction.

HYDROCOTARNINE, $C_{12}H_{15}O_3N$, is obtained from the mother waters of thebaine, after the removal of cryptopine and protopine with warm petroleum benzin, by precipitation with ammonia; laudanosine, which is also precipitated, is removed by treatment of the benzin solution with sodium bicarbonate. The hydrocotarnine is retained in solution by the benzin, from which the laudanosine has been deposited on cooling. Hydrochloric acid gas being made to pass through this solution, hydrocotarnine hydrochloride crystallizes out. This alkaloid, as the name indicates, can be formed from cotarnine, by the action of zinc and hydrochloric acid. It is a basic hydrolytic product of narcotine (which see). This alkaloid is very soluble in alcohol, acetone, chloroform, benzin, and ether. It melts at 50° C., and loses at 57° C. the half molecule of water with which it crystallizes. Sulphuric acid dissolves it, coloring it yellow in the cold, and crimson red if heated. Nitric acid colors it yellow; ferric chloride does not affect its color. It has been physiologically studied by Stockman and Dott (*B. M. J.*, Jan., 1891), who find that it produces in the lower animals symptoms similar to those caused by narcotine.

LANTHOPINE, $C_{23}H_{25}O_4N$, differs from pseudomorphine in not becoming blue with ferric chloride, and in giving, when entirely pure, with sulphuric and nitric acids, colorless solutions. It forms colorless microscopic prisms, which fuse at about 200° C. Its acid oxalate and tartrate are crystallizable. The alkaloid is crystallizable, does not have an alkaline reaction, is sparingly soluble in hot or cold alcohol, ether, or benzene, but readily soluble in chloroform. (See *U. S. Dispensatory*, 19th ed., p. 896.) According to Allen, it is obtained from the mother liquor, left from the preparation of morphine by the Robertson-Gregory process. It is a weak base, and is colored orange-red by nitric acid, and pale violet by sulphuric acid, the latter color changing to a dark brown on heating.

LAUDANINE, $C_{20}H_{25}O_4N$, as first prepared, is mixed with cryptopine, from which it is separated by dissolving it in acetic acid, and adding a slight excess of diluted solution of sodium hydroxide, by which the cryptopine is entirely precipitated. The liquid being filtered, and treated with ammonium chloride, lets fall the laudanine, which soon assumes the crystalline form. The acetate, with the addition of potassium iodide, gives rise to laudanine hydriodide, from which ammonia separates the base perfectly pure. It crystallizes from its solution in boiling alcohol in transparent granules or hexagonal prisms melting at 166° C. It is lævorotatory, tasteless, and poisonous, the hydrochloride resembling strychnine in its effects. It is dissolved at 18° C. by 647 parts of ether. With ferric chloride it gives a green coloration and with sulphuric acid and ferric oxide, a deep red color. It contains three methoxy groups and one hydroxyl group. It is sometimes accompanied by its isomeride *laudanidine,* which is probably the lævo form. (Hesse, *Ann. Chem.*, 1894, cclxxxiv.) Laudanine is an energetic base, and with potassium hydroxide forms a crystallizable compound. Its salts, except the neutral sulphate, oxalate, and tartrate, are crystallizable.

LAUDANOSINE, $C_{21}H_{27}O_4N$, exists in the mother waters of thebaine, with cryptopine and protopine. It is itself insoluble in water and the alkalies, but it is soluble in alcohol, acetone, and chloroform. It melts at 89° C., and is decomposed at 110° C. Ferric chloride does not color it. Sulphuric acid gives it a rose color in the cold, and violet when heated. Nitric acid transforms it into a nitrobase. The crystals are anhydrous. It forms crystallizable salts, which are soluble and bitter. The complete synthesis of laudanosine has been effected by Pictet and Finkelstein (*C. R. A. S.*, 1909, cxlviii).

MECONIDINE, $C_{21}H_{23}O_4N$, was discovered by Hesse in 1870. It is brownish-yellow, amorphous, alkaline, melts at 58° C., and is not stable, the salts also being easily altered. It is easily soluble in alcohol, ether, benzene, chloroform, and acetone. It is dissolved by sulphuric acid with an olive-green color, and by nitric acid with an orange-red.

MORPHINE, $C_{17}H_{19}O_3N + H_2O$, and its preparations are treated under another head. (See *Morphina.*)

NARCEINE, *Narceina*, $C_{23}H_{27}O_8N.3H_2O$, discovered by Pelletier in 1832, is in white, silky crystals, inodorous, of bitter taste. E. Merck has shown (*Chem. Ztg.*, 1889, p. 525) that the melting point of the ordinary commercial alkaloid of English manufacture is between 150° and 160° C. and the pure base at 170° to 171° C. Out of water at 60° C. it crystallizes with 2 molecules of water, which it loses at 100° C. and at 140° C. another molecule of water escapes, leaving in the fused residue a mixture of bases. Soluble in 375 parts of cold and 220 of boiling water, soluble also in alcohol, and insoluble in ether. It forms a bluish compound with iodine, the color of which is destroyed by heat and the alkalies. It is rendered blue by the action of mineral acids so far diluted as not to decompose it, but it does not, like morphine, become blue by the action of ferric salts, nor red by that of nitric acid. Narceine is a feeble mono-acidic tertiary base, containing three methoxy groups.

Dragendorff announced that solution of narceine gives a crystalline precipitate with the double zinc and potassium iodide. This reaction may be employed with iodine as a test of narceine. If a solution of this salt, with a little iodized water, be added to solutions of narceine, and the mixture then agitated with ether to remove the iodine in excess, a solution containing a very small quantity of narceine will distinctly assume a blue color. The other alkaloids of opium are destitute of this property. (*J. P. C.*, April, 1870, p. 346.) For method of isolating it see Hope and Robinson (*Tr. Chem. Soc.*, 1914, cv, 2085); and for study of its constitution, Freund and Oppenheimer (*B. Chem. G.*, 1909, xlii, 1084).

The discordancy of the statements of physiologists and clinicians concerning the action of narceine can only be explained by the presence of impurities in the specimens used. The pure alkaloid would seem to be very feeble in its influence, Mitchell having taken five grains without any other effect than causing some headache. The narceine of commerce has been used in doses of one-third to three-fourths of a grain (0.021–0.048 Gm.) as a mild narcotic, probably acting through contaminating morphine.

NARCOTINE. *Narcotina*, $C_{22}H_{23}O_7N$.—It exists in opium, chiefly, at least, in the free state, and is left behind in considerable quantity when the drug is macerated with water. It is white, tasteless, and inodorous, and crystallizes in silky flexible needles, usually larger than the crystals of morphine, fusible at 175° C., and decomposes at higher temperaure with evolution of ammonia. Heated to 220° C., the residue which remains is *hemipinic acid*, $C_{10}H_{10}O_6$, insoluble in cold water. With acids narcotine forms unstable salts that are dissociated by water. The alkaloid can be extracted by immiscible solvents from acid solutions. Its salts are dextrorotatory. It is a weak mono-acidic tertiary base which is convertible into narceine. It has been synthesized by Perkin and Robinson (*Tr. Chem. Soc.*, 1911, xcix) by the union of meconin and cotarnine. It is decomposed by long boiling, or by heating with nitric acid, into cotarnine and meconin, $C_{10}H_{10}O_4$, and by heating with water to 100° C. in sealed tubes, into hydrocotarnine and opianic acid, $C_{10}H_{10}O_5$, while, on the other hand, the action of nascent hydrogen (from zinc and hydrochloric acid) converts it into hydrocotarnine and meconin, and that of oxidizing agents into cotarnine and opianic acid.

It may be distinguished from morphine by its insipidity, by its solubility in ether and insolubility in alkaline solutions, by not affecting vegetable colors, by assuming a yellowish instead of a blood-red color under the action of strong nitric acid, by not decomposing iodic acid, and by not producing a blue color with ferric salts. It is, however, reddened by a mixture of nitric and sulphuric acids. Hence, if to a mixture of it with strong sulphuric acid a small piece of potassium nitrate is added, a deep blood-red color is produced; while morphine, under the same circumstances, yields a brownish or olive green color. It gives a greasy stain to paper when heated upon it over a candle. Water extracts narcotine partially from opium, in consequence of the acid which the latter contains, either free or combined with the narcotine. It may be separated by the action of ether, which dissolves it without affecting the morphine, and yields it upon evaporation. It may also be obtained by digesting opium in ether, and slowly evaporating the ethereal solution, which deposits crystals of narcotine. The proportion of narcotine in opium varies extremely in the different varieties, and in different specimens of the same variety. Thus, in Smyrna opium it has been found by different observers, in quantities varying from 1.30 to nearly 11 per cent. Though narcotine itself is tasteless, its salts are very bitter, even more so than those of morphine. (Berzelius.) Their solution reddens litmus, and yields precipitates with the alkalies and infusion of galls. For physiological study of the methylamide derivatives of narcotine (*narcotine methylamide*), see *V. A. P. A.*, 142, 1895.

Anarcotine, described as an alkaloid especially abundant in the India opium (Roberts, *B. M. J.*, 1895, ii), appears to be simply impure narcotine. (*Merck's Jahresber.*, 1896, 101.)

The substance described as *opianine* is probably an impure narcotine.

For account of the physiological properties of narcotine see *Uses.*

NEOPINE, $C_{18}H_{21}O_4N$, was discovered by T. and H. Smith in the final mother liquors obtained in the extraction of opium alkaloids and was confirmed by Dobbie and Lander. (*Trans. Chem. Soc.*, 1911, 34.)

It gives color reactions and an absorption spectrum similar to codeine of which it is believed by some authorities to be an isomeride.

OXYNARCOTINE. *Oxynarcotina,* $C_{22}H_{23}O_8N$.—This alkaloid accompanies narceine, from which it can be separated by treating the mixture with dilute sulphuric acid. According to Beckett and Wright (*J. Chem. S.*, 1876), it crystallizes out of alcohol in very fine needles, which are difficultly soluble in boiling water and boiling alcohol, insoluble in other neutral solvents. Heated to 140° or 150° C. it is carbonized. It is oxidized by ferric chloride to *hemipinic acid* and *cotarnine,* thus proving its close relationship to narcotine. It is a monacid base, and forms crystallizable salts. There is some doubt as to its chemical individuality.

PAPAVERAMINE, $C_{21}H_{25}O_6N$.—This alkaloid was also obtained by Hesse (*J. P. C.*, 1903, lxviii) in purifying papaverine. It gives an intensely violet blue coloration with sulphuric acid.

PAPAVERINE. *Papaverina,* $C_{20}H_{21}O_4N$.—The discovery of this alkaloid was announced by G. Merck in 1848. It is crystallizable in needles, fusing at 147° C., insoluble in water, very sparingly soluble in cold alcohol or ether, more soluble in these liquids boiling hot, and deposited by them on cooling. It behaves as a monoacidic base and with acids it forms salts, most of which are very sparingly dissolved by water. By the action of hydrochloric acid at 130° C., however, it is decomposed into methyl chloride and homopyrocatechol. By the action of concentrated nitric acid there is formed, on heating, the nitrate of nitropapaverine, $C_{20}H_{20}(NO)_2O_4.NHNO_3$, which separates in crystals. The nitro-base can be separated in clear yellow flocks by the addition of ammonia. By the action of tin and hydrochloric acid there is formed a tetrahydropapaverine, $C_{20}H_{25}O_4N$. Cold concentrated sulphuric acid does not color it, but on warming a violet color is obtained.

For account of its physiological properties see under *Uses.*

PORPHYROXINE, $C_{19}H_{23}O_4N$, was discovered in Indian opium by Rakshit (*Tr. Chem. Soc.*, 1919, cxv) after the name had previously been applied by Merck on 1837 to a product which was subsequently found to be a mixture of alkaloids. According to K. L. Dey (*P. J.*, 1882, xii, p. 397), it is a definite basic substance, always present in Indian opium, but absent from Turkey or Smyrna opium.

Solutions of this alkaloid become red upon exposure to air.

PROTOPINE, $C_{20}H_{19}O_5N$ (*Macleyine, Fumarine*).—Hesse separated it from cryptopine. Both are precipitated as insoluble hydrochlorides by hydrochloric acid in excess; but if the precipitate be dissolved by an excess of oxalic acid, the acid cryptopine oxalate will crystallize, and protopine remain in the mother waters. The liquid is separated, precipitated by ammonia, and agitated with ether, and the ethereal solution is taken up by hydrochloric acid. Protopine hydrochloride being dense and granular, while cryptopine hydrochloride is very light, the two are separated by levigation—eighty grammes of crude cryptopine furnishing one and a half of protopine. Separated from the hydrochloride by ammonia, protopine constitutes a crystalline powder, insoluble in water, soluble in alcohol and in hot petroleum benzin and acetone, more soluble in chloroform, insoluble in the alkalies generally, but slightly soluble in ammonia. It melts at 202° C., undergoing decomposition, and is in anhydrous crystals. Ferric chloride does not color it; nitric acid colors it yellow; sulphuric acid dissolves it, coloring it first yellow, then red, and lastly violet. The alcoholic solution has an alkaline reaction. The salts are neutral and crystallizable.

For studies of its structure see Perkin, *Tr. Chem. Soc.*, 1916, cix, 875 and 1023.

E. Schmidt (*A. Pharm.*, 1893, ccxxxi, 136) states that protopine is identical with *macleyine,* an alkaloid, which has been found by Eykman in *Macleya cordata,* and that it is also found in *Sanguinaria canadensis, Stylophorum diphyllum, Eschscholtzia californica,* and other plants. (See Danckwortt, *A. Pharm.*, 1912, ccl, 590.)

PSEUDOMORPHINE.—*Pseudomorphina,* $C_{34}H_{36}O_6N_2$, was discovered by Pelletier in 1835, and is said by Hesse to be identical with Polstorff's *oxydimorphine;* but, as it exists in small quantities, and was thought to be only an occasional ingredient in opium, little attention has been paid to it. It has also been termed *dehydromorphine.* An interesting fact, however, in relation to it, and one of some toxicological importance, is that it possesses two properties considered characteristic of morphine, those, namely, of being reddened by nitric acid and of producing a blue color with ferric salts, and yet it is without any poisonous influence upon the animal economy. (*J. P. C.*, xxi, 575.) It is prepared from morphine by oxidation with the presence of potassium permanganate in the presence of sodium bicarbonate. It is tasteless, insoluble in water, alcohol, ether, chloroform, and diluted sulphuric acid, but easily soluble in solution of potassium and sodium hydroxide, and lime, and in alcoholic solution of ammonia, though sparingly in an aqueous solution of ammonia. It does not neutralize hydrochloric acid, dissolves in concentrated sulphuric acid with the production of an olive-green color, in concentrated nitric acid with an intense orange-red, and in solution of ferric chloride with a blue color. At 120° C. it loses two molecules of water of crystallization, and at higher temperatures is decomposed without melting. It forms sparingly soluble salts with sulphuric, nitric, oxalic, and tartaric acids, and a crystalline deposit, very slightly soluble in hydrochloric acid, with solution of corrosive sublimate. (*Chem. News,* 1867, p. 188.) Hesse is of the opinion that pseudomorphine is identical with the oxymorphine prepared by the action of oxidizing agents upon morphine by Schutzenberger.

PSEUDOPAPAVERINE, $C_{21}H_{21}O_4N$, was obtained by Hesse (*J. P. C.,* 1903, lxviii) from commercial papaverine. It gives no coloration with sulphuric acid.

RHŒADINE, $C_{21}H_{21}O_6N$, discovered by Hesse in 1865, is described under *Rhœados Petala.*

THEBAINE (*Paramorphine*), $C_{19}H_{21}O_3N$ (or $C_{17}H_{15}ON(OCH_3)_2$), was discovered by Thiboumery (1835) in the precipitate thrown down from an infusion of opium treated with milk of lime. It occurs to the extent of from 0.1 to 1.0 per cent. in opium. It is white, crystallizable, and of an acrid and styptic rather than bitter taste, fusing at 193.4° C., and, according to Hesse, confirmed by D. B. Dott, is not sublimable. Other observers state that it sublimes at 135° C. without fusing, and is deposited in minute crystals resembling caffeine. It is scarcely soluble in water, very soluble in alcohol and ether when cold, and still more so when heated, and capable of combining with the acids, with which it forms salts not crystallizable from their aqueous solution. Alkalies precipitate it from its acid solutions, and unless in very concentrated solution, do not dissolve it when added in excess. It is not like morphine, reddened by nitric acid, nor does it become blue with solutions of ferric salts. Its distinguishing color reaction is a blood-red color with sulphuric acid which changes to orange yellow and eventually to olive green on warming. (See Reichard, *Ph. Centralh.,* 1906, xlvii, 623.)

In its chemical structure thebaine is closely related to morphine and codeine, probably being, like them, a phenanthrene derivative. For account of its physiological properties see under *Uses.*

Thebaine salicylate is practically insoluble in water; hence in the assay of opium the German Pharmacopœia directs the addition of sodium salicylate to the aqueous solution, thus removing the thebaine before precipitating the morphine.

TRITOPINE, $C_{42}H_{54}O_7N_2$, was discovered in 1890 by Klauder. (*A. Pharm.,* 1890, ccxxviii, 419.) It resembles morphine and laudanine in being soluble in sodium hydroxide solution, but is precipitated in the form of an oil by a large excess of the reagent. Tritopine crystallizes in characteristic, anhydrous, transparent, needle-like plates, melting at 182° C., easily soluble in chloroform, but only slightly so in ether. With sulphuric acid it behaves like laudanine. It appears to be a divalent base.

XANTHALINE, $C_{37}H_{36}O_9N_2$, is a base obtained by T. and H. Smith (*P. J.,* 1893, 772) from the acid mother liquors resulting from the crystallization of morphine or codeine hydrochloride, and purification of the product.

The non-nitrogenous principles in opium include two acids and three neutral bodies. One of the acids, which was discovered by T. and H. Smith, of Edinburgh, and at first named by them *thebolactic acid* under the supposition that it differed from ordinary lactic acid, was shown by Buchanan (*B. Chem. G.,* 1870) to be identical with it. Lactic acid appears to be a constant ingredient in opium.

MECONIC ACID, $C_7H_4O_7 + 3H_2O$, is in white crystalline scales, of a sour taste followed by bitterness, fusible and volatilizable by heat, soluble in four parts of boiling water, soluble also in cold water and alcohol, with the property of reddening vegetable blues and forming salts. Its compounds with the earths and heavy metallic oxides are generally insoluble in water. Its characteristic properties are that it produces a blood-red color with ferric salts, which is not destroyed by mercuric chloride as is the similar reaction produced by sulphocyanates, a green precipitate with a weak solution of ammoniated copper sulphate and white precipitates—which are soluble in nitric acid—with lead acetate, silver nitrate and barium chloride. It is obtained by macerating opium in water, filtering the infusion, and adding a solution of calcium chloride. Calcium meconate and sulphate are precipitated. The precipitate, having been washed with hot water and with alcohol, is treated with diluted hydrochloric acid at 82.2° C. The calcium meconate is taken up, and, upon the cooling of the liquid, calcium bimeconate is deposited. This is dissolved in warm concentrated hydrochloric acid, which deposits pure meconic acid when it cools. It may be freed from coloring matter by neutralizing it with potassium hydroxide, decomposing the meconate thus obtained by hydrochloric acid, and again crystallizing. When heated, it loses first its water of crystallization, and then at 120° C. a molecule of CO_2, and yields *comenic acid,* $C_6H_4O_5$; this at 260° C., or over, loses another molecule of CO_2, and yields *pyrocomenic acid,* $C_5H_4O_3$. By the action of nascent hydrogen (from sodium amalgam) it yields *hydromeconic acid,* $C_7H_{10}O_7$. Meconic acid has little or no action on the system, and is not used separately in medicine; but its natural relation to morphine requires that it should be understood. The three related compounds, meconic acid, comenic acid, and pyrocomenic acid, are now considered to be derivatives of the fundamental compound *pyrone,* $\mathrm{CO}<\genfrac{}{}{0pt}{}{\mathrm{CH}=\mathrm{CH}}{\mathrm{CH}=\mathrm{CH}}>\mathrm{O}$. Thus, from pyrone, $C_5H_4O_2$, are obtained *oxypyrone* (pyromeconic acid), $C_5H_3O_2(OH)$, and *oxypyrone-carboxylic* (comenic) *acid,* $C_5H_2O_2(OH)COOH$, and *oxypyrone dicarboxylic* (meconic) *acid,* $C_5HO_2(OH)(COOH)_2$. Pyrone itself is formed when comenic and chelidonic acids are heated to 250° C. Most of the pyrone derivatives are converted by the action of ammonia into pyridone and pyridine compounds.

Meconic acid was formerly recognized by the British Pharmacopœia, but was dropped at the 1898 revision. It appears to be nearly free from active physiological properties. Sertürner took 4.5 grains of sodium meconate, and Grape and Loewer 12 grains of the pure acid, without the production of any symptoms, while, according to Mulder, Pereira, Lange, and others, 20 grains of the acid cause no sensible effect in the dog.

Meconin (*Opianyl*), $C_{10}H_{10}O_4$, a neutral principle before referred to, the existence of which was announced in 1832, by Couërbe, is identical with a substance discovered several years previously by Dublanc, Jr., but of which no account was published. It occurs also in *Hydrastis* and has been synthesized from guaiacol by Fritsch (*Ann. Chem.*, 1898, ccci). It may also be produced by the oxidation of narcotine with nitric acid. It is perfectly white, in the form of acicular crystals, soluble in about 265 parts of cold and 18 of boiling water, very soluble in alcohol, chloroform, and the essential oils, but only sparingly in ether; fusible under water at 77° C., *per se* at 110° C., sublimable on careful heating, and possessed of a degree of acrimony which favors the supposition that it may not be without action upon the system. It is neither acid nor alkaline, and contains no nitrogen. The method by which it was obtained from opium is described in the *U. S. D.*, 20th ed., p. 816.

Meconoisin, $C_8H_{10}O_2$, was discovered by T. and H. Smith in 1878. Meconin, upon being left to itself for some days, sets into a mass of crystals. These crystals, upon being drained and cautiously washed with cold weak spirit, are to be boiled in a large quantity of water. The filtered liquid gives a crystallization of meconin, and the mother liquor, when concentrated, and yields crystalline masses of meconoisin, associated with meconin. It is a crystallizable neutral body which has a melting point of 88° C. It may be distinguished from meconin by the following test of T. and H. Smith. "When heated with slightly diluted sulphuric acid, and when the evaporation has reached a certain point, meconin produces a beautiful green color. With meconoisin, under the same circumstances, the coloration is deep red, becoming purple." This substance has been found by Stockman and Dott (*B. M. J.*, Jan., 1891) to be a tetanizant.

Opionin was found by Hesse in small quantities in Smyrna opium. It forms white needles, which melt at 227° C. These are insoluble in water, but dissolve in alkalies, alcohol, and ether.

Tests for Opium.—It is sometimes highly important to be able to ascertain the presence or absence of opium in any suspected mixture. As meconic acid and morphine have been found only in the products of the poppy, if either or both of them be shown to exist in any substance, very strong evidence will be afforded of the presence of opium. The test should, therefore, be applied in reference to the detection of these two principles. If an aqueous infusion of the substances examined yields a red color with the tincture of ferric chloride, there is presumptive evidence of the presence of meconic acid. Greater certainty may be obtained by the following process. Add in excess to the filtered liquor a solution of lead acetate. If opium be present, there will be a precipitate of lead meconate, and the morphine and lead acetates will remain in solution. The precipitate is then to be suspended in water, and decomposed, either by adding a little diluted sulphuric acid, which forms lead sulphate and leaves the meconic acid in solution, or by passing through it a stream of hydrogen sulphide, removing by filtration the precipitated lead sulphide, and heating the clear liquor, so as to drive off the hydrogen sulphide. With the clear liquor thus obtained, if it contain meconic acid, the tincture of ferric chloride will produce a striking red color, ammoniated copper sulphate a green precipitate, and lead acetate, silver nitrate, and barium chloride, white precipitates soluble in nitric acid. Potassium sulphocyanate, which, according to Wright, is an invariable constituent of saliva (*Simon's Chemistry,* ii, 6), produces a red color with ferric salts, resembling that produced by meconic acid, but, according to Everitt, this color is entirely and at once destroyed by a solution of corrosive sublimate, which has no effect on the red color of iron meconate. (*A. J. P.*, xii, 88.) On the contrary, gold chloride reddens a solution of sulphocyanic acid or a sulphocyanate, but not of meconic acid. Pereira says the acetates also redden ferric salts, but do not afford the results just mentioned with lead acetate and barium chloride. To test for the presence of morphine, the liquid from which the lead meconate has been precipitated, and which may be supposed to contain the morphine and lead acetates, must be freed from the lead by a stream of hydrogen sulphide, the hydrogen sulphide driven off by heat, the solution then alkalized and extracted with a mixture of three parts of chloroform with one part of alcohol; after evaporation of the solvent tests for identity may be applied to separate portions of the residue: such as general alkaloidal reagents for the detection of an alkaloid; and the specific identity tests given under *Morphina*, viz., nitric acid, which colors the morphine red.

Incompatibles.—The substances which produce precipitates with opium do not all necessarily affect its medicinal virtues, but the alkalies, and all vegetable infusions containing tannic acid, are incompatible, the former separating and precipitating the free alkaloids, the latter forming with it an insoluble compound.

Uses.—The use of opium as a medicine can be clearly traced back to Diagoras, who was nearly contemporary with Hippocrates, and it was probably employed before his time.

Opium owes its activity chiefly to the alkaloid morphine and the physiological actions and therapeutic uses of the whole drug are very similar to those of its dominant alkaloid. Sufficient has been said on this subject under *Morphina*. Certain of the other alkaloids present in opium differ somewhat in their action from that of morphine, and to a certain extent modify the effects of opium, and we shall therefore consider here the medical properties of some of these secondary alkaloids, and point out the conditions in which opium is preferred to morphine.

The most abundant of the alkaloids after morphine is *narcotine;* indeed, in some varieties of opium it is said to be present in larger quantities than morphine. This alkaloid appears to be almost, if not entirely, free of the characteristic narcotic properties of morphine. In large doses it is a spinal stimulant and produces in the lower animals convulsions. According to Macht (*J. P. Ex. T.*, 1915, vii, p. 339), narcotine differs essentially from morphine in its action upon the respiratory center, acting as a stimulant rather than a depressant. He finds also that because of this antagonistic action upon respiration very much larger doses of morphine can be given if combined with narcotine, without dangerous respiratory depression. It was at one time recommended as an antiperiodic, but is probably of no value; the *dose* employed was from two to three grains (0.13–0.2 Gm.).

Papaverine is the only other alkaloid which occurs naturally in opium in large enough quantity to perceptibly modify the effect of the crude drug. Although much less potent than morphine it possesses distinct narcotic powers. According to Pal (*D. M. W.*, 1914, xl, p. 164) papaverine is an active local anesthetic and is especially valuable because of its power in allaying spasm of the involuntary muscles. Macht (*loc. cit.*) finds that papaverine, like narcotine, antagonizes morphine in its effect upon the respiratory center. In 1892 Lebuscher showed that papaverine lessened intestinal peristalsis and more recently Macht has shown that it is a depressant to all unstriped muscles. Papaverine has been recommended in clinical medicine in *diarrhea*, various forms of *gastric* or *intestinal spasms, asthma, biliary colic,* and other conditions of excitability of the involuntary muscles. It, as well as its hydrochloride and sulphate, are recognized by the *N. N. R.*, 1924. The *dose* recommended is usually from one-half to one and one-half grains (0.032–0.096 Gm.), although it is stated that much larger quantities may be given without any evil effects.

Thebaine.—This is chiefly of interest because of its action on the spinal cord. In the lower animals it produces convulsions closely simulating those caused by strychnine. In large quantities it seems to be paralyzant to the peripheral motor nerves. It does not appear to possess narcotic properties.

Codeine being official is considered elsewhere. The other alkaloids occur in such small quantities and are mostly of such feeble powers that it is improbable that they play any part in the effects of opium. For further information on the minor alkaloids of opium, see Crawford and Dohme (*Proc. A. Ph. A.*, 1902, p. 472); Leubuscher (*D. M. W.*, 1892); Macht (*J. P. Ex. T.*, 1915, vii, and 1916, viii); and Pal (*D. M. W.*, 1913, xxxix, and 1914, xl).

In a general way it may be said that opium is more constipating and more nauseating in proportion to its narcotic power than is morphine. According to the experiments of Macht, which have received clinical confirmation from the observations of Sahli and others, it would appear that it is also less dangerous because relatively less depressing to the respiratory center. The fact that opium is more constipating than morphine is probably attributable to its papaverine. Although capable of fulfilling all the indications for which morphine is employed, when used as an analgesic or somnifacient, the alkaloid is usually preferred because of its lesser liability to disturb digestion. On the other hand in *diarrhea* and *spasmodic colic* the whole drug is superior to the alkaloid. Opium is frequently a valuable remedy in *diabetes mellitus*. How it acts is uncertain, but the whole drug is to be preferred to any of its alkaloids. Because of its peculiar power in dilating the vessels of the skin opium tends to increase the sweat and is therefore useful in minor infections, such as *colds, grippe, muscular rheumatism,* and the like. As a sudorific it is generally combined with ipecac in the form of Dover's Powder.

Opium is largely used locally in the form of its tincture either in combination with a solution of lead subacetate or by itself. While it possesses feeble counter-irritant and anesthetic powers the freedom with which it is used as a local application verges on the superstitious.

Recognizing the superior advantages of opium over morphine in some conditions, and the desirability of hypodermic administration, a number of manufacturing chemists have put upon the market preparations which profess to represent all of the alkaloids of opium in approximately their natural proportions; among these may be mentioned *pantopon, alcopon,* *glykopon* and *toponal. Holopon* is an opium preparation asserted to be prepared by dialysis and representing, therefore, only the crystallizable constituents of opium. *Opon* is asserted to contain all the other active ingredients of opium except morphine.

Poisoning.—In moderately large doses opium produces, generally, a pleasurable feeling of languor followed by drowsiness. In toxic dose the most prominent symptom is sleep, from which, in the moderate degrees of poisoning, the patient can easily be awakened by loud noises, shaking, etc. At this stage of the poisoning the respirations are generally slower than normal but of good depth, the pulse is slow and full, the skin warm and flushed and moist, the pupil contracted. As the intoxication deepens the respirations become slower and shallower and often irregular, and the skin is frequently more or less cyanotic from imperfect aeration of the blood; the pupils grow smaller and are eventually reduced in size to almost complete invisibility; the patient can be aroused only with difficulty and when left to himself immediately sinks back into a comatose sleep. The reflexes are generally not greatly affected. When the dose has been very large there may develop, late in the poisoning, failure of the circulation with rapid, feeble pulse and cold, clammy, cyanotic skin. The quantity required to take life varies enormously according to the individual susceptibility of the patient. On the one hand, several fatalities have been reported from less than one-half a grain of morphine and from four or five grains of opium. On the other hand, we have seen an opium habitué take 8 grains of morphine at a dose with no serious effect, and Fell has reported recovery following 33 grains of morphine.

Treatment of Opium Poisoning.—For the evacuation of the stomach, unless the drug has been taken in solid form, the stomach tube is preferable to emetics, the latter often failing to act because of the effect of the drug upon the vomiting centre. In the absence of a stomach tube, however, twenty or thirty grains of zinc sulphate may be given as an emetic. The best chemical antidote is potassium permanganate, which oxidizes the active principle of the drug to a harmless compound; four or five grains of the permanganate may be given at a dose. Where the stomach tube is employed it is well to wash out the stomach with a 1 to 500 solution of potassium permanganate leaving 3 or 4 ounces of this solution in the stomach to neutralize any alkaloid which may be later excreted. If this antidote be not at hand tannic acid may be used as a partial but less satisfactory antidote; it is well to follow this with a saline cathartic as the tannate of morphine is slowly absorbable. Fantus has obtained favorable results in experimental morphine poisoning with the use of fuller's earth (see *Terra Silicea Purificata*). Aside from the prevention of absorption, the most important measures are those directed towards maintaining respiratory function. As this is always in abeyance during sleep the patient should, if possible, be kept awake. Many of the measures, however, which have been employed for preventing sleep have done as much harm in exhausting the patient's strength as the wakefulness has done good. By far the best means for this purpose is the faradic battery, using either a brush electrode or a bare metal upon the skin; with this apparatus an exquisite pain can be caused without any injury to the body. Slapping the skin with the fringe of a wet towel is also useful, but care must be exercised not to bruise. Alternate dashes of hot 40.5° C. and cold water 10° C. upon the bare chest may also be of service. Occasionally by repeated shouting the patient may be kept from going to sleep. We do not believe that the advice, so often given, to keep the patient constantly walking is sound. Among the respiratory stimulants the most useful is probably cocaine or strychnine; caffeine and atropine are also of much service. There was at one time a wide-spread belief that atropine was a complete physiological antagonist to morphine. This, however, is erroneous; while the drug may be useful for its stimulating effects upon the respiratory center, it must be remembered that large doses of atropine are depressant, and if used too freely may injure rather than benefit. If, despite these measures, respiration remains dangerously insufficient, recourse should be had to artificial respiration either by the Sylvester or Schaefer method, or preferably with one of the apparatuses for forced artificial respiration, such as the pulmotor. By means of a simple bellows apparatus Fell (*Medical Examiner,* June, 1899) succeeded in maintaining life for seventy-three hours with the eventual recovery of the patient. The intravenous injection of salt solution has also been recommended with the idea of diluting the poison in the blood. Cardiac stimulants, as ammonia, may occasionally be required in severe cases.

Opium Habit.—The use of opium or one of its various derivatives, especially morphine and diacetyl morphine, is one of the most common and one of the most injurious of drug addictions. In the Orient it has been commonly employed by smoking but among the European peoples the hypodermic needle has been the favorite method of the morphine addict; diacetylmorphine is usually taken as a snuff. Owing to the vigorous campaign which has been waged against these habits in the United States, they seem to be rapidly diminishing. The amount of opium imported into the U. S. reached a maximum in 1911 of over 600,000 pounds. Since then, however, it has been continually decreasing and now (1924) amounts to less than 50,000 pounds annually. Of course, this does not take into consideration the quantities which are smuggled into this country. For study of drug addiction in the U. S. and reference to the literature on the subject, see Kolb and DuMez, *U. S. Pub. Health Rep.*, May 23rd., 1924. For elaborate study of the chemistry of smoking opium see *Ap. Ztg.*, 1903.

Dose, from one to two grains (0.065–0.13 Gm.).

Off. Prep.—*From opium.*—Extractum Opii Liquidum (from Dry Extract), *Br.;* Extractum Opii Siccum, *Br.;* Linimentum Opii (from Tincture), *Br.;* Opium Pulveratum, *U. S.;* Opium Granulatum, *U. S.;* Tinctura Camphoræ Composita (from Tincture), *Br.;* Tinctura Opii, *Br.;* Tinctura Opii Ammoniata (from Tincture), *Br.;* Extractum Opii, *N. F.* (see also preparations under *Tinctura Opii*).

From powdered opium.—Pilula Plumbi cum Opio, *Br.;* Pilula Saponis Composita, *Br.;* Pulvis Cretæ Aromaticus cum Opio, *Br.;* Pulvis Ipecacuanhæ et Opii, *U. S.* (*Br.*)*;* Pulvis Kino Compositus, *Br.;* Pulvis Opii Compositus, *Br.;* Suppositoria Plumbi Composita, *Br.;* Tinctura Opii Camphorata, *U. S.;* Unguentum Myrobalani cum Opio, *Br.;* Unguentum Gallæ cum Opio, *Br.;* Pilulæ Opii et Camphoræ, *N. F.;* Pilulæ Opii et Plumbi, *N. F.;* Pulvis Cretæ et Opii Aromaticus, *N. F.*

From granulated opium.—Tinctura Opii, *U. S.;* Tinctura Opii Crocata, *N. F.*

OPIUM GRANULATUM. U. S.

GRANULATED OPIUM Opium Gran.

"Opium dried at a temperature not exceeding 70° C., and reduced to a coarse powder. Granulated Opium yields not less than 10 per cent. and not more than 10.5 per cent. of anhydrous morphine. Granulated Opium of a higher morphine percentage may be brought within the required limits of strength by admixture with granulated opium of a lower percentage, or with some inert diluent.

"**Assay.**—Proceed as directed under *Opium.*" *U. S.*

This form of opium was introduced into the U. S. P. because, on account of its being in coarse powder, it is better fitted for use in making the liquid preparations of opium. (See *Opium.*)

Granulated opium is prepared by a special milling and sifting process, the finer portions being separated and used in the preparation of powdered opium. Cocoanut shells, coarsely ground, have been found satisfactory as a diluent for reducing granulated opium of a high assay strength to the U. S. standard.

Dose, one to two grains (0.065–0.13 Gm.).

OPIUM PULVERATUM. U. S.

POWDERED OPIUM Opium Pulv. [Opii Pulvis U.S.P. IX, Opii pulvis P.I.]

"Opium dried at a temperature not exceeding 70° C. and reduced to a very fine powder. Powdered Opium yields not less than 10 per cent. and not more than 10.5 per cent. of anhydrous morphine. Powdered Opium of a higher morphine percentage is to be reduced to the official standard by admixture with powdered opium of a lower percentage, or with some inert diluent." *U. S.*

Poudre d'Opium, *Fr. Cod.;* Opiumpulver, *G.;* Polvo de opio, *Sp.*

Description and Physical Properties.—"Light brown, consisting chiefly of yellowish-brown to brownish-red, more or less irregular and granular fragments, varying from 0.015 to 0.150 mm. in diameter; a few fragments of strongly lignified, thick-walled, 4- to 5-sided or narrowly elongated, epidermal cells of the poppy capsule; very few fragments of tissues of poppy leaves, poppy capsules, and rumex fruits. In addition, there will be the microscopic characters of the diluent, if any has been used in the preparation of the powder.

"**Assay.**—Proceed as directed under *Opium.*

"Preserve in well-closed containers." *U. S.*

For chemistry, uses, etc., see under *Opium.*

Under the name of *Opium Deodoratum* (*Deodorized Opium, Denarcotized Opium*) the U. S. P. formerly recognized a preparation freed from certain nauseating constituents. This was prepared as follows:

"Powdered Opium, *five hundred grammes;* Purified Petroleum Benzin, *a sufficient quantity.* Macerate the powdered opium for twenty-four hours in a wide-mouthed, well-closed bottle with sufficient purified petroleum benzin to cover it completely, shaking the mixture occasionally. Then decant the clear benzin layer as closely as possible and repeat the maceration for twenty-four hours with another portion of purified petroleum benzin. Again decant the clear benzin layer and transfer the remaining contents of the bottle to a plain filter. Closely cover the funnel, allow the mixture to drain and then slowly percolate the residue with purified petroleum benzin until the latter passes through without color. Remove the filter containing the Opium from the funnel, expose the powder to the open air, so that it may dry thoroughly, and add sufficient sugar of milk to restore the original weight. Care should be used to guard against the danger due to the inflammability of the benzin. Granulated opium may also be deodorized in the manner directed above." *U. S. IX.*

ORTHOCRESOL. N. F.

ORTHOCRESOL

"The ortho variety of cresol [$C_6H_4.CH_3OH$-1:2 (108.10], obtained from coal tar." *N. F.*

For description of the origin and general properties of this substance see under *Cresol.*

Description and Physical Properties.—"Orthocresol occurs as white crystals or as a colorless or yellow to brown, highly refractive liquid, becoming darker with age and exposure, and having a phenol-like odor. Slightly soluble in water; soluble in alcohol, ether, and chloroform. Miscible with an equal volume of solution of formaldehyde with the production of a transparent solution.

"Specific gravity about 1.05; melting point about 30° C.; boiling point about 190° C. A saturated solution of Orthocresol is neutral or slightly acid to litmus and becomes blue-violet on the addition of ferric chloride T.S.

"Preserve it in well-closed containers, protected from light." *N. F.*

Off. Prep.—Formaldehydum Cresolatum, *N. F.*

OVI ALBUMEN RECENS. N. F.

FRESH EGG ALBUMEN Ovi Album.

"The freshly separated liquid white, or albumen, of the recently laid egg of the hen, *Gallus domesticus* Temminck (Fam. *Phasianidæ*)." *N. F.*

Fresh Egg Albumen, Egg Albumen, Egg white; Eiweiss, *G.*

OVI VITELLUM RECENS. N. F.

FRESH EGG YOLK Ovi Vitel.

"The freshly separated yolk of the recently laid egg of the hen, *Gallus domesticus* Temminck (Fam. *Phasianidæ*)." *N. F.*

Fresh Egg Yolk, Egg Yolk; Dotter, Eidotter, *G.*; Tuorlo, *It.*

Off. Prep.—Glyceritum Vitelli, *N. F.*

OVUM GALLINACEUM. N. F.

FRESH EGG Ovum. Gallin.

"The recently laid egg of the hen, *Gallus domesticus,* Temminck (Fam. *Phasianidæ*)." *N. F.*

Egg, Hen's Egg; Ei, Hühnerei, *G.*; Oeuf, *F.*; Uovo, *It.*

The egg of the ordinary hen consists of an exterior covering, the shell; a white, semi-opaque membrane; the white; and the yolk.

The *shell*—*testa ovi* or *putamen ovi*—consists chiefly of calcium carbonate, with animal matter, and a minute proportion of calcium phosphate, magnesium carbonate, ferric oxide, and sulphur. When exposed to a high degree of heat in the open air, the carbon dioxide is driven off, the animal matter consumed, and the lime left nearly pure.

The *white* is a glairy, viscid liquid, contained in very delicate membranes, without odor or taste, readily soluble in water. It is 85 per cent. water, containing in solution approximately 12 per cent. of a protein belonging to the group of albumins (formerly the word album*e*n was applied to all the proteins of this group, but the tendency among modern writers has been to spell the generic word albumi*n* and to apply the word albume*n*, to the special form of albumin found in egg white); about 2.5 per cent. of a mucin-like substance, called *ovomucoid,* and traces of mineral salts. Albumen may be precipitated from solution without chemical alteration by saturation with certain neutral salts, such as ammonium sulphate. Many of the salts of the heavy metals such as gold chloride, lead subacetate, copper sulphate, mercuric chloride, etc., form insoluble compounds with albumen which leads to a precipitation. Tannic acid, acetic acid and most of the mineral acids if in sufficiently concentrated solutions likewise coagulate the egg albumen by chemical union. When heated above 75° C. the albumen is precipitated. This precipitation must be accompanied with some change in the chemical structure as the cooked albumen does not redissolve on cooling. Albumen is markedly lævo-rotatory, its specific power being about −35.5°. Exposed in thin layers to a current of air, it becomes solid, retaining its transparency and solubility in water. Dried white of egg occurs in the form of pale yellowish translucent scales soluble in eight parts of water. By coagulation it is rendered white, opaque, and insoluble. At a temperature of 100° C., one part of it renders opaque one thousand parts of water in which it has been dissolved. When kept in the fluid state it soon putrefies; but if carefully dried without coagulation it may be preserved unaltered a long time, and may be readily redissolved in water.

The *yolk* is inodorous, of a bland oily taste, and forms an opaque emulsion when agitated with water. By heat it is coagulated into a granular solid, which yields a fixed oil by expression. The constitution of the yolk is about as follows: water, 51.8 per cent.; vitellin, 15.8 per cent.; nuclein, 1.5 per cent.; palmitin, stearin, and olein, 20.3 per cent.; cholesterin, 0.4 per cent.; phosphoglyceric acid, 1.2 per cent.; lecithin, 7.2 per cent.; cerebrin, 0.3 per cent.; coloring matter, 0.5 per cent.; salts, 1.0 per cent. (König, *Nahrungs- und Genussmittel,* 180.)

Vitellin belongs to the class of proteins known as globulins which differ from the albumins in not being soluble in pure water, although they do dissolve in the presence of small amounts of certain neutral salts. From the solution they may be precipitated by saturation with magnesium or ammonium sulphate. The coloring matter is known as *lipochrome,* but of its true chemical structure we have no knowledge.

Cholesterin or *cholesterol* is a monatomic alcohol; the most recent investigations give it the formula of $C_{27}H_{45}OH$. Lecithin is described in Part II. It is said that the yolk may be kept for a considerable time without observable change by adding to it 5 per cent. of sodium sulphate, in powder or concentrated solution. Granules have been found, with the aid of the microscope, in the yellow of the egg, which are rendered blue by iodine, and have all the other properties of the starch granules.

Uses.—The value of eggs as a food-stuff cannot be here discussed in detail. It may be pointed out, however, that they are esteemed by many physicians not merely as a source of energy but for their large proportion of lecithin.

The yolk affords an excellent emulsifying agent and is widely employed in pharmacy for this purpose.

Under the name of *Glyconin* there has been employed in France for many years both for medicinal purposes and for those of the toilet, an emulsion made of glycerin and the yolk of egg. It is now recognized by the N. F. under the name of *Glyceritum Vitelli.* When these two substances are rubbed together, they unite to form a very intimate mixture, which does not separate. It has the consistence of honey, and forms an opaque emulsion with water. It may be preserved almost indefinitely. The usual proportions of the ingredients are four parts of the yolk of egg and five parts of pure glycerin.

The *white* of egg is used frequently for the clarification of liquids, which it effects by involving, during its coagulation, the undissolved particles, and rising with them to the surface, or subsiding. It has been recommended as an antidote for corrosive sublimate, copper sulphate, and other caustic poisons, with which it forms insoluble compounds; the practical value of this treatment of metallic poisons has been gravely questioned in recent years. It is sometimes also used for the suspension of insoluble substances in water, but is inferior for this purpose to the yolk, and even to mucilage of gum arabic. Agitated briskly with a lump of alum, it coagulates, at the same time dissolving a portion of the alum, and thus forming the so-called *alum curd,* which is used between folds of gauze over the eye, in some states of *ophthalmia.* It is also used in the official pepsin valuation.

OXYGENIUM. U. S.

OXYGEN Oxygen.

"Oxygen contains not less than 98 per cent. by volume of O. For convenience it is usually furnished in compressed form in metallic cylinders." *U. S.*

Oxygène, *Fr.;* Sauerstoff, *G.;* Ossigeno, *It.*

Oxygen was discovered about 1774 almost simultaneously by Priestley and Scheele. Both evolved it from metallic oxides or calces as they were called. Priestley called it *dephlogisticated air,* and Scheele called it *fire air,* it not then being recognized as a gaseous element, but was thought to be a kind of air. It is the most abundant of the elemental substances constituting, according to the calculations of some authorities, one-half of the weight of the earth and its atmosphere.

For experimental and laboratory purposes it is usually prepared by heating a mixture of potassium chlorate and manganese dioxide, the latter substance acting as a catalyst and remaining unchanged at the end of the operation, possessing the property of allowing the reaction $KClO_3 = KCl + O_3$ to take place at lower temperatures and without danger. Industrially it is usually prepared by the continuous process known as Brin's, in which BaO is heated in porcelain tubes to 500° C. in a current of carbon dioxide-free air. This produces BaO_2, which upon further heating to 800° C. again evolves the oxygen ($BaO_2 = BaO + O$). Upon lowering the temperature to 500° C. the absorption of oxygen again occurs and the alternate absorption and liberation may be repeated many times until, as is found in practice, the barium oxide loses its activity. Oxygen is also produced commercially from liquid air, taking advantage of the facts that the nitrogen is more volatile, and that the oxygen has a tendency to liquefy first.

G. Kassner has described a method for producing oxygen from the air by the use of a mixture of *sodium metaplumbate,* Na_3PbO_3, and *sodium manganate,* Na_2MnO_4. This combination, which is emerald-green in color, he calls *plumboxan.* The mixture is placed in a combustion tube and heated to between 430° C. and 450° C. Air freed from CO_2 is then passed through it and the oxygen is absorbed by the plumboxan while pure nitrogen passes through unchanged. Steam is then passed into the mass, which liberates the oxygen in an exceedingly pure condition. By alternately injecting air and steam, nitrogen and oxygen can be evolved in the order given indefinitely. The reactions, as given by the author, to account for the changes, are very complex. (*A. Pharm.*, ccli, p. 596.)

Oxygen has also been produced commercially by heating sodium permanganate or by liberating it from sodium peroxide by the action of water. Oxygen comes into commerce for laboratory or medicinal purposes compressed into steel cylinders provided with a valve and outlet tube.

Description and Physical Properties.—"A colorless, odorless, and tasteless gas. It supports combustion more readily than air. One volume of Oxygen dissolves in about 34 volumes of water and in about 3.6 volumes of alcohol, at 25° C.

"A glowing splinter of wood held in Oxygen bursts into flame.

"Pass 2000 cc. of the gas, measured under normal atmospheric pressure at about 25° C., through 100 cc. of barium hydroxide T.S. at a rate not exceeding 4000 cc. per hour: the turbidity produced, if any, is not greater than that produced by 1 cc. of a solution prepared by dissolving 0.2 Gm. of sodium bicarbonate in 100 cc. of freshly boiled and cooled distilled water (*carbon dioxide*). Pass 2000 cc. of Oxygen, under the conditions described above, through a mixture of 100 cc. of distilled water and 1 cc. of silver nitrate T.S.: no opalescence is produced (*halogens*). Pass 2000 cc. of Oxygen through 100 cc. of distilled water, colored with a few drops of litmus T.S., under the conditions described above: the color of the liquid is not changed (*acids* or *alkalies*). Pass 2000 cc. of Oxygen through 100 cc. of a freshly prepared starch-potassium iodide T.S.: the color of the liquid is not changed (*oxidizing substances*)." *U. S.*

Assay.—"Mix about 50 cc. of Oxygen, accurately measured in a calibrated tube, with

10 cc. of alkaline pyrogallol T.S.: not less than 98 per cent. by volume is absorbed, corresponding to not less than 98 per cent. by volume of O." *U. S.*

Uses.—Pure oxygen is so irritant locally that it is difficult to respire it; the statements sometimes made, however, that it is impossible to live in an atmosphere of pure oxygen do not seem to be well supported, at least as far as human beings are concerned. In normal health it is doubtful whether the respiring of pure oxygen has any marked effect upon the bodily processes except that which is due to the irritation of the mucous membrane. It must be remembered that the oxygen-carrying power of the blood is due to the chemical change of hemoglobin in the corpuscles, and enough oxygen is, ordinarily, absorbed by the lungs from the atmosphere to fully oxidize the hemoglobin, so that the blood leaving the lungs contains almost entirely oxyhemoglobin. The only increase in the amount of oxygen the blood will carry is in the relatively small proportion which is dissolved in the blood plasma. While this quantity may be notably increased by inhaling oxygen, in conditions of health its proportion to the oxygen in oxyhemoglobin is so small that it does not greatly affect oxidative processes in the body. On the other hand when the oxygen-carrying power of the blood is reduced—as, for instance, in *carbon monoxide poisoning* or *nitrite poisoning*—through chemical change in the hemoglobin, the amount of oxygen which may be dissolved by the plasma becomes a matter of practical importance and Haldane has experimentally shown (*J. P.*, 1897, xxi, p. 160) that animals will survive a supra-fatal dose of nitrites in an atmosphere of pure oxygen. Again in cyanotic conditions due to insufficiency of the circulation, as in cases of *heart failure,* the small increase in the oxygen of the blood may be sufficient to supply the need of the body and clinical improvement is often seen from the use of oxygen in such instances. In cases where the passage of air in and out of the lungs is obstructed, as in *asthma* or *pneumonia,* the use of oxygen is still more rational because of the small amount of air which comes in contact with the blood. Therefore in practically all cases in which cyanosis indicates a deficient amount of oxygen being carried by the blood, the inhalation of this gas is a reasonable procedure and clinically has in many cases given great relief. It must be remembered, however, that the oxygen does not act by stimulating any vital function, in the sense that strychnine or ammonium might, but it merely supplies a deficient necessity of life. The custom of having a patient inhale oxygen for ten or fifteen minutes at a time three or four times a day, is foolish; the inhalation of the gas must be kept up more or less continuously as long as the symptoms indicate the need of it.

OXYMEL. Br.

OXYMEL

"Acetic Acid, 100 *millilitres;* Distilled Water, 100 *millilitres;* Purified Honey, 500 *millilitres.* Mix." *Br.*

Oxymel Simplex; Mellitum; Mel Acetatum; Mellite de Vinaigre, Oxymelite simple, Acétomel, *Fr.;* Sauerhonig, *G.;* Oximiel simple, *Sp.*

"Specific gravity 1.27. 25 grammes require for neutralisation not less than 32 millilitres of *N/2 solution of sodium hydroxide.* The liquid obtained by mixing 25 grammes of Oxymel with 1 millilitre of *solution of lead subacetate,* diluting to 100 millilitres with *water,* adding 1 gramme of *animal charcoal,* and filtering until bright, has an *optical rotation* at 15.5° C. of not more than −3.9° in a tube 200 millimetres long." *Br.*

This mixture of honey and vinegar forms a pleasant addition to gargles, and is sometimes used as a vehicle of expectorant medicines and to impart flavor to drinks in febrile diseases.

Dose, from one to two fluidrachms (3.75–7.5 cc.).

OXYMEL SCILLÆ. Br.

OXYMEL OF SQUILL

"Vinegar of Squill, 200 *millilitres;* Purified Honey, 500 *millilitres.* Mix." *Br.*

Mellitum Scillæ; Mellite de Vinaigre Scillitique, Oxymel Scillitique, *Fr.;* Oxymel Scillæ, *P. G.;* Meerzwiebelhonig, *G.;* Ossimiele scillitico, *It.;* Oximiel escilitico, *Sp.*

"Specific gravity 1.29. 25 grammes require for neutralisation not less than 11.9 millilitres of *N/2 solution of sodium hydroxide.* The liquid obtained by mixing 25 grammes of Oxymel of Squill with 1 millilitre of *solution of lead subacetate,* diluting to 100 millilitres with *water,* adding 1 gramme of *animal charcoal,* and filtering until bright, has an *optical rotation* at 15.5° C. of not more than −3.9° in a tube 200 millimetres long." *Br.*

After a long vogue, this preparation fell into such neglect that it was abandoned by the Pharmacopœias. Its reintroduction, however, into the Br. Pharmacopœia indicates that it is still prescribed; it has also been introduced into the N. F. IV (see Part III). It has the virtues of syrup of squill, but no advantages. It is chiefly used as an expectorant in those states of the pulmonary organs in which the bronchial tubes are loaded with a viscid mucous of difficult expectoration.

Dose, from one-half to one fluidrachm (1.8–3.75 cc.). In large doses it is emetic, and as such is sometimes used in *infantile croup.*

OXYMEL URGINEÆ. Br.

OXYMEL OF URGINEA [Oxymel of Indian Squill]

"Vinegar of Urginea, 200 *millilitres;* Purified Honey, 500 *millilitres.* Mix." *Br.*

"Specific gravity 1.29. 25 grammes require for neutralisation not less than 11.9 millilitres of *N/2 solution of sodium hydroxide.* The liquid obtained by mixing 25 grammes of Oxymel of Urginea with 1 millilitre of *solution of lead subacetate,* diluting to 100 millilitres with *water,* adding 1 gramme of *animal charcoal,* and filtering until bright, has an *optical rotation* at 15.5° C. of not more than $-3.9°$ in a tube 200 millimetres long." *Br.*

This is a new preparation of the British Pharmacopœia, 1914. It is used for the same purposes as the *oxymel scillæ.*

Dose, from one-half to one fluidrachm (1.8–3.75 cc.).

PANCREATINUM. U. S.

PANCREATIN Pancreat.

"Pancreatin is a substance containing enzymes, principally amylopsin, trypsin, and steapsin, obtained from the fresh pancreas of the hog, *Sus scrofa* var. *domesticus* Gray (Fam. *Suidæ*) or of the ox, *Bos taurus* Linné (Fam. *Bovidæ*). It converts not less than 25 times its weight of starch into soluble carbohydrates and not less than 25 times its weight of casein into proteoses. Pancreatin of a higher digestive power may be brought to this standard by admixture with lactose." *U. S.*

Pancréatine médicinale, *Fr.;* Pancreatina, *Sp.*

The term "pancreatin" has been variously used for many different preparations from the pancreatic gland, and has long been popularly employed for the purpose of distinguishing preparations more or less of the nature of extracts made from the gland. The *pancreatic juice* is an albuminous, transparent liquid, odorless, alkaline, and containing about eight per cent. of organic matter. It is now generally recognized that there are present in the pancreatin secretion three distinct enzymes: *trypsin,* whose function it is to convert albuminous matters into peptone, and probably also peptones into their aminoacids; *amylopsin* or *amylase,* a ferment closely allied if not identical with the ptyalin of the saliva, which hydrolizes starch into maltose and dextrin; and *steapsin* (*lipase, pialyn*), which has the power of splitting up fats into glycerin and fatty acids. Besides these ferments there is apparently present also another substance which has the property of curdling milk. Because of its fat splitting properties the pancreatic juice has a strong emulsifying effect, the viscous agent being the soap formed through the splitting of the fat. The activity of the lipase is greatly increased by the presence of bile. This emulsifying action takes place very rapidly; according to Rachford (*J. Chem. S.,* 1891, 948) a spontaneous emulsion may be formed in two minutes at room temperature. The proteolytic enzyme of the pancreas can be separated to a large extent from the other digestive ferments and various manufacturing pharmacists have placed such preparations on the market under the names of *trypsin* (see *N. N. R.,* 1924). These are not, however, the pure enzyme but contain varying proportions of inert protein. The proteolytic power of some of these preparations far exceeds the pharmacopœial requirements; but they are much less potent than the same amount of pepsin.

All of the pancreatic ferments are active in neutral or mildly alkaline media, but the most favorable reaction is not the same for all of them, thus trypsin is best with an alkalinity corresponding to about 1 per cent. of sodium carbonate, but amylopsin acts most rapidly in the presence of 0.01 per cent. of hydrochloric acid, and the action of the fat splitting ferment is also accelerated by a faintly acid reaction.

The pancreatin of the U. S. Pharmacopœia contains all of these ferments, with more or less extraneous matter.

Various methods of manufacturing pancreatic extracts are employed. Water readily dissolves all the ferments and the French Codex directs that pancreas gland purified by separating foreign matter is to be cut into small pieces, macerated in chloroform water, then expressed, the liquid filtered and rapidly evaporated at a temperature not exceeding 45° C. Choay (*P. J.,* 1898, 505) criticizes the temperature for evaporation and recommends evaporation *in vacuo* at 38° C. Precipitation by the use of strong alcohol is the method used for purification. Biernacki (*A. J. P.,* 1892) previously stated that digestive ferments require for their efficient action a temperature little over that of the human body, 39°. A useful and permanent extract may also be obtained by exhausting the finely divided pancreas with water containing about 2 per cent. of boric acid and 1 per cent. of borax. (Allen, *Com. Org. Anal.,* 2d ed., vol. iv, 354.) The mixed pancreatic enzymes may also be extracted by means of glycerin which gives an active extract which may be preserved indefinitely, but one which cannot be reduced to the dry state. For this purpose the gland is finely minced, rubbed up with some clean sand, shaken with from 10 to 20 parts of glycerin and allowed to stand for about two weeks, then filtered. Another method of extracting its activity is by macerating the minced gland with four times its weight of 25 per cent. alcohol for four or five days. If the pancreas be allowed to stand for two or three days before extracting the resulting pancreatin will be richer in the trypsin and amylopsin, but will have very little fat splitting powers. Where it is desirable to make a pancreatin containing active lipase it should be made from the fresh gland.

Description and Physical Properties.—"A cream colored, amorphous powder, having a faint, characteristic, but not offensive odor. Pancreatin is slowly and incompletely soluble in water; insoluble in alcohol. Pancreatin changes proteins into proteoses and derived substances, and converts starch into dextrins and sugars. Its greatest activities are in neutral or faintly alkaline media; more than traces of mineral acids or large amounts of alkali hydroxides render it inert. An excess of alkali carbonates also inhibits its action.

"Introduce 2 Gm. of Pancreatin into a flask of about 50 cc. capacity, add 20 cc. of ether, stopper, and set it aside for several hours, mixing by rotating at frequent intervals. Decant the supernatant ether by means of a guiding rod into a plain filter of about 7 cm. diameter, previously moistened with ether, and collect the filtrate in a tared beaker. To the residue remaining in the flask add a further portion of 10 cc. of ether, proceeding as directed before, then a third portion of 10 cc. of ether, and transfer the ether and the remainder of the pancreatin to the filter. Allow to drain, evaporate the ether spontaneously, and dry the beaker and residue to constant weight at 100° C.: the residue weighs not more than 0.06 Gm. (*fat*).

"**Assay for Starch Digestive Power.**—Shake 10 Gm. or more of powdered potato starch with about 10 times its weight of cold distilled water, and, after draining the mixture on a filter, wash it with the same quantity of distilled water. Place the washed starch at once in an air bath, and maintain a temperature of about 50° C. until the starch is sensibly dry. Reduce it to a fine powder, and place it in a well-stoppered bottle. Determine the percentage of water remaining in the starch by drying about 0.5 Gm. of it in an air bath, gradually raising the temperature to 120° C. and maintaining it at that temperature for four hours. Of the washed and partially dried starch, mix a quantity equivalent to 7.5 Gm. of dry starch in a 400 cc. beaker with 10 cc. of cold distilled water, add 190 cc. of boiling distilled water, and boil the mixture gently with constant stirring for five minutes or until a translucent, uniform paste is obtained. Replace the water lost by evaporation, and cool the paste to 40° C. in a water bath previously adjusted to this temperature, and add a solution of 0.3 Gm. of Pancreatin in 10 cc. of distilled water, just previously made at 40° C. Mix well, and maintain the same temperature for exactly five minutes, when a thin, nearly clear liquid is produced. At once add 0.1 cc. of this liquid to a previously made mixture of 0.2 cc. of tenth-normal iodine and 60 cc. of distilled water. No blue, red or violet color is produced.

"**Assay for Casein Digestive Power.**—Place 0.1 Gm. of finely powdered casein in a 50 cc. volumetric flask, add 30 cc. of distilled water, and shake well to bring the casein into suspension. Add exactly 1 cc. of tenth-normal sodium hydroxide, and heat the mixture at 40° C. until the casein is completely dissolved, which should not require more than thirty minutes. Cool, add sufficient distilled water to make 50 cc., and mix well. Dissolve 0.1 Gm. of Pancreatin in 500 cc. of distiled water. Mix 1 cc. of glacial acetic acid with 9 cc. of distilled water and 10 cc. of alcohol. Place 5 cc. of the casein solution in a test tube, add to it 2 cc. of the well-shaken Pancreatin solution and 3 cc. of distilled water, and mix by gentle agitation. Immediately immerse the test tube in a water bath at 40° C., and keep it at this temperature for one hour. Then remove from the bath, and add 3 drops of the acetic acid mixture. No precipitate is produced.

"Preserve in well-closed containers." *U. S.*

Uses.—Pancreatin was first used in medicine on account of its emulsifying properties. Horace Dobell, noticing that consumptives are very likely to have a dislike for fat, conceived the idea that this was due to lack of pancreatic digestion, and administered an emulsion made with the fat of beef stirred in milk with the pancreatic juice of the pig. A little later, pancreatic preparations of cod liver oil were prepared, and still have much vogue. Besides this employment, pancreatin has two distinct uses; first, as a ferment to be administered in dyspepsia; second, as a valuable means for the predigestion of food. It is probable that when given internally pancreatin may escape from the stomach into the intestines and the combination of pepsin and pancreatin in *dyspepsia* is not unphilosophical.

Any attempt to make a practical evaluation must bear in mind certain elementary facts: (1) The tryptic ferment is most active in a feeble alkaline medium. It exerts, however, some digestive power in neutral solutions but the presence of free acids not only hinders the ferment action of trypsin but actually destroys the enzyme itself. (See Long and Hull, *J. Am. C. S.*, 1916, xxxviii, and 1917, xxxix, p. 162.) (2) Trypsin is destroyed by artificial gastric juice but Long and Hull have shown that it may resist peptic digestion for considerable time, provided there be enough other protein present to unite with the free hydrochloric acid. (3) Amylopsin acts well in a neutral or faintly acid medium. According to Meltzer's observations the optimum reaction is equivalent to 0.01 per cent. HCl (*In. Dis.*, 1894.) (4) The fat splitting enzyme, steapsin, is the least stable of all pancreatic ferments and is especially susceptible to the action of acids. From the above facts it is manifest that the digestive powers of pancreatin in the stomach must be very limited because of the acidity of the gastric secretions. On the other hand, in the early stages of gastric digestion before the acidity has fully developed, there may be some digestion of starches and perhaps also of proteins by the pancreatic ferment. This, however, cannot continue long and the pancreatic ferments are liable themselves to be eventually destroyed by the rising tide of acid pepsin.

In the predigestion of food by pancreatin, five grains of commercial pancreatin of good quality, with twenty grains of sodium bicarbonate, in an ounce of warm water, may be added to a pint of milk, and kept at the temperature of 43.3° C. for from twenty minutes to an hour. As the thoroughly peptonized or predigested food is very bitter, when the milk is to be given by the mouth it is better to arrest the peptonizing process by boiling the milk after digestion has continued for twenty to thirty minutes, unless the milk can be used at once. Nutritive enemata should be thoroughly pancreatized.

Trypsin has been used in medicine in a variety of conditions. Beer (*Lancet*, 1905) has recommended it as a local treatment for *inoperable cancers,* Schiller (*K. T. W.*, 1910) in the treatment of *tuberculous abscesses,* and Lamballe (*N. Y. M. R.*, 1913) asserts that the intramuscular injection of solutions of trypsin have curative value in *malaria.*

For other uses of the pancreas and its peculiar hormone insulin, see under *Organotherapy,* Part II.

Dose, of pancreatin, eight to fifteen grains (0.5–1.0 Gm.).

Off. Prep.—Liquor Pancreatis, *Br.;* Liquor Pancreatini, *N. F.;* Pulvis Pancreatini Compositus, *N. F.*

PARAFFINUM. U. S. (Br.)

PARAFFIN Paraff.

"A purified mixture of solid hydrocarbons, obtained from petroleum." *U. S.* "Hard Paraffin is a mixture of solid hydrocarbons." *Br.*

Paraffinum Durum, *Br.;* Hard Paraffin; Paraffin Wax; Solid Paraffin; Ceresinum; Paraffinum solidum, *P. G.;* Festes Paraffin, Gereinigtes Erdwachs, *G.;* Parafina, *Sp.*

The name *paraffin,* often spelled *paraffine,* was originally bestowed by Baron von Reichenbach upon a waxy substance obtained through the destructive distillation of wood. He derived it from *parum affinis,* and thus intended to indicate its very neutral character. The name is now popularly applied to a solid white diaphanous substance, resembling white wax, which is procured from petroleum or bituminous shales by distillation, or from ozokerite by purification. (See *Ozokerite, Ceresin,* in Part II.) In the manufacture from petroleum, as carried out in the United States, the residuum from the distillation of crude petroleum for illuminating oil is taken. This is redistilled from what are called "tar stills," in which the distillation is pushed until only coke remains. The paraffin oil distillate obtained in this way is treated with from 4 to 5 per cent. of sulphuric acid, washed, and treated with caustic soda, the mixture being kept liquid by the aid of steam coils. After settling, the paraffin oil goes to the "chill-rooms," where, by the aid of the refrigerating machines the whole mass is brought to a semi-solid condition. This is subjected to powerful pressure, and the refined heavy oil which drains off is collected as lubricating oil. Its specific gravity should be about 32° B. The press cake may be broken up, melted, and allowed to solidify, and then submitted to still greater pressure at a higher temperature 21.1° C. than before, when the product is known as "refined wax." To convert it into block paraffin it must be washed with petroleum benzin, pressed, melted, and filtered through bone black or other medium, when it solidifies in a hard, translucent, colorless condition.

Description and Physical Properties.—Paraffin, in its pure condition, is a white, waxy, inodorous, tasteless substance, harder than tallow, softer than wax, with a specific gravity of 0.900. Its melting point is variable, depending somewhat upon its origin; it ranges between 43° and 65° C. An ultimate analysis yields, on the average, carbon 85 per cent. and hydrogen 15 per cent. It is indifferent to most acids and alkalies, and can be distilled unchanged with strong sulphuric acid. Warm alcohol, ether, oil of turpentine, olive oil, benzene, chloroform, and carbon disulphide dissolve it readily. It can be mixed in all proportions with wax, stearin, palmitin, and resin. As stearin is less soluble in benzene than paraffin, Vogel proposes this reaction as a method for detecting the adulteration of paraffin with stearin. (Joy.)

"A colorless, or white, more or less translucent mass, frequently showing a crystalline structure. It is without odor or taste, and is slightly greasy to the touch. Paraffin is insoluble in water and in alcohol; slightly soluble in dehydrated alcohol; freely soluble in chloroform, ether, benzene, petroleum benzin, carbon disulphide, volatile oils, and in most warm fixed oils.

"Specific gravity: about 0.900 at 25° C. It melts between 50° and 57° C. When strongly heated, Paraffin ignites, burns with a luminous flame, and deposits carbon. Heat about 0.5 Gm. of Paraffin in a dry test tube with an equal weight of sulphur: the mixture becomes black from separated carbon, and hydrogen sulphide gas is evolved. Paraffin is not acted upon or colored by concentrated sulphuric or nitric acid in the cold. Shake melted Paraffin with an equal volume of hot alcohol; the separated alcohol does not redden moistened blue litmus paper (*acids*)." *U. S.*

The Br. Pharm. describes it as "colorless, crystalline, more or less translucent; wax-like, slightly greasy to the touch. No odor or taste. Melting point 50° to 60° C. 5 millilitres of *alcohol* (90 per cent.) shaken with 5 grammes of the melted Paraffin are not acid to *litmus.* 5 grammes, when heated, burn with a luminous flame, leaving no appreciable ash." *Br.*

The fact that solid paraffin wax is essentially made up of a mixture of hydrocarbons of the series C_nH_{2n+2} was established by Gill and Meusel, who studied the action of bromine upon it. The fact that when paraffin wax is oxidized by concentrated nitric acid or by chromium trioxide mixture we obtain *paraffinic acid,* $C_{24}H_{48}O_2$, and *cerotic acid,* $C_{27}H_{54}O_2$, shows that it is essentially made up of hydrocarbons between $C_{24}H_{50}$ and $C_{27}H_{56}$. For *Soft Paraffin,* or *Paraffinum Molle,* see *Petrolatum.*

Uses.—In the arts paraffin is used for many purposes, especially in the manufacture of candles, and sealing various vessels to exclude air. Lemons and eggs coated with paraffin may be kept for long periods of time without decomposition. It is also valuable to saturate paper, rendering it impervious to moisture. In pharmacy it is used chiefly to give stiffness to ointments. It was at one time employed in cosmetic surgery by injecting melted paraffin for filling out undesirable hollows. The treatment resulted in a number of cases, however, in extensive sloughing and has been largely abandoned.

For the use of paraffin as a protective dressing for burns see *Ambrine,* Part II.

Off. Prep.—Curatio Paraffini, *N. F.*

PARAFFINUM CHLORINATUM. U. S.

CHLORINATED PARAFFIN

Paraff. Chlorinat. [Chlorcosane]

"A chlorinated paraffin." *U. S.*

This preparation was suggested by Dakin and Dunham (*B. M. J.,* 1918) as a solvent for dichloramine. They made it by passing chlorine gas into melted paraffin, maintaining the temperature at 125° C. to 140° C., until the liquid increased in weight from about 50 per cent. This liquid, still warm, is then agitated with 5 per cent. of its weight of dry sodium carbonate and filtered. It contains from 30 to 40 per cent. of chlorine which is so firmly bound that it can scarcely be removed with boiling solutions of the alkalies; it yields its chlorine, however, when boiled with aniline.

Description and Physical Properties.—"A light yellow to light amber, clear, thick, oily liquid. It is odorless, and is stable in the air. Chlorinated Paraffin is insoluble in water; slightly soluble in alcohol, but miscible with benzene, carbon tetrachloride, chloroform, and with ether.

"Specific gravity: 1.00 to 1.07 at 25° C. Boil 5 drops of Chlorinated Paraffin with 10 cc. of alcoholic potassium hydroxide T.S. under a reflux condenser for thirty minutes, cool, dilute with 10 cc. of distilled water, and acidulate with diluted nitric acid: the liquid becomes turbid from the separation of small, oily drops. Shake the mixture with an equal volume of ether, allow the liquids to separate, draw off the clear aqueous layer, and add to it a few cc. of silver nitrate T. S.: a white precipitate is formed.

"Ash: not more than 0.1 per cent. Shake about 5 Gm. of Chlorinated Paraffin with 25 cc. of warm distilled water for five minutes, and filter through a filter paper moistened with distilled water: the filtrate is neutral to litmus paper (*acids or alkalies*), and on adding a few drops each of potassium iodide T.S. and of starch T.S. to 5 cc. of the filtrate, no blue color is produced (*free chlorine*). Another 5 cc. portion of the filtrate shows no more *chloride* than corresponds to 0.05 cc. of fiftieth-normal hydrochloric acid. Dissolve 10 Gm. of Chlorinated Paraffin in 10 cc. of carbon tetrachloride in a 50 cc. volumetric flask, dissolve in this solution about 0.5 Gm. of powdered dichloramine, accurately weighed, and allow the mixture to stand at 40° C. for four hours protected from light. Cool, and dilute with sufficient carbon tetrachloride to measure 50 cc. Transfer 10 cc. of this dilution to a glass-stoppered flask, add 10 cc. of glacial acetic acid and 5 cc. of potassium iodide T.S., and tightly stopper the flask. Allow to stand for ten minutes, add 25 cc. of distilled water, and titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Make a blank test with the same quantity of the same dichloramine and the other reagents, but omitting the Chlorinated Paraffin and using sufficient carbon tetrachloride to measure 50 cc. The difference between the amount of tenth-normal sodium thiosulphate consumed in the blank test and that required for the original test is not greater than 0.6 cc. (*completeness of chlorination*)." *U. S.*

Uses.—Chlorcosane is employed solely as a means of applying dichloramine, the latter being rapidly decomposed by liquid petrolatum. It is too viscid to be readily sprayed with an atomizer; when used for this purpose it may be thinned by the addition of carbon tetrachloride or eucalyptol.

PARAFORMALDEHYDUM. U. S.

PARAFORMALDEHYDE Paraform. [Paraform, Trioxymethylene]

"Paraformaldehyde contains not less than 95 per cent. of $(HCHO)_3$." *U. S.*

Triformal; Trioxymethylenum; Formaldehydum Polymerisatum.

Paraformaldehyde is always produced to a greater or lesser extent when solutions of formaldehyde are allowed to evaporate. The change from the ordinary into the polymeric form also takes place at low temperatures, especially when the solution is free from methyl alcohol. This is the way in which it is now produced commercially.

Description and Physical Properties.—"White friable masses, or a white powder, having a slight odor of formaldehyde. Paraformaldehyde is very slowly soluble in cold water, more readily soluble in hot water with the formation of formaldehyde; insoluble in alcohol and in ether; soluble in solutions of fixed alkali hydroxides. Paraformaldehyde, when heated, is partly converted into formaldehyde and partly sublimed unchanged.

"Add 10 drops of sulphuric acid to a mixture of about 0.01 Gm. each of Paraformaldehyde and morphine sulphate: a violet color is produced. Gently warm about 0.02 Gm. of Paraformaldehyde with 5 cc. of sulphuric acid in which about 0.1 Gm. of salicylic acid has been dissolved: a deep red color develops.

"Shake 0.5 Gm. of Paraformaldehyde, finely powdered, with 10 cc. of distilled water: the water remains neutral to litmus paper. Ash: not more than 0.1 per cent.

"**Assay.**—Mix about 1 Gm. of Paraformaldehyde, finely powdered and accurately weighed, with 50 cc. of normal sodium hydroxide in a 250 cc. flask, and add immediately, but slowly, through a small funnel, 50 cc. of solution of hydrogen dioxide which has been previously rendered neutral to litmus T.S. with sodium hydroxide T.S. When the reaction has ceased and the foam subsided, rinse the funnel and the sides of the flask with distilled water, allow the liquid to stand for half an hour, and then determine the excess of alkali with normal sulphuric acid, using litmus T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.03002 Gm. of $(HCHO)_3$.

"Preserve in well-closed containers, in a cool place, protected from light." *U. S.*

Uses.—Although trioxymethylene appears to possess some antibacterial properties *per se,* it is used chiefly as a source for the generation of formaldehyde. The especial utility of the substance for this purpose lies in the fact that by simply heating it is converted into the active gas. Special lamps are upon the market in which a small alcohol flame serves to at once depolymerize the paraform while the moisture from the combustion of the alcohol increases the activity of the formaldehyde. Rideal (*Disinfection and the Preservation of Food,* 1903, p. 309) finds that 10 Gm. of paraformaldehyde per thousand cubic feet of air space in a properly sealed room, is sufficient to destroy the vitality of most pathogenic organisms, but will not certainly kill those enclosed in bedding or similarly protected. The room should be left closed for twenty-four hours. Because of the comparative cost, however, this method is not to be recommended for disinfection of large spaces, but is very convenient for the sterilization of various surgical materials which might be injured by boiling. For this purpose small airtight chambers are employed in which from 1 to 2 Gm. (15–30 grains) for each cubic yard of air space is evaporated.

Paraformaldehyde is also occasionally used internally as a gastro-intestinal disinfectant. Pauchet and Sourdat (*B. A. M.,* 1914) highly laud gauze impregnated with paraform for the treatment of gunshot and other *wounds.* For the preparation of this the gauze is placed in a tin box with a few tablets of trioxymethylene and the box closed, and then put in a warm place, about 50° C. for an hour. It is also used externally as a caustic, for the destruction of *warts,* in 10 per cent. solution. Under the trade name of *formoforin* a mixture of paraform and talc has been employed in Germany for various forms of *hyperidrosis.*

Dose, five to fifteen grains (0.3–1.0 Gm.).

PARALDEHYDUM. U. S., Br.

PARALDEHYDE Paraldehyd. [Paracetaldehyde]

"A polymer $[(CH_3CHO)_3]$ of acetaldehyde." *U. S.* "Paraldehyde, $C_6H_{12}O_3$, is a product of the polymerisation of acetaldehyde." *Br.*

Paraldéhyde, Elaldéhyde, *Fr. Cod.;* Paraldehydum, *P. G.;* Paraldehyd, *G.;* Paraldehido, *Sp.*

Small quantities of acids like hydrochloric and sulphuric, and of certain salts like zinc chloride, convert ethyl, or acetic, aldehyde at ordinary temperatures into its polymer paraldehyde. Commercially it is prepared by the action of hydrochloric upon *acetaldehyde* until the resulting product is no longer soluble in its own volume of water, and then purifying by redistillation and freezing and expressing.

Description and Physical Properties.—"A colorless, transparent liquid. It has a strong, characteristic, not unpleasant or pungent odor, but a disagreeable taste. One cc. of Paraldehyde is soluble in about 8 cc. of water at 25° C. One cc. is soluble in 17 cc. of boiling water. It is miscible with alcohol, chloroform, ether, and with volatile oils.

"Specific gravity: about 0.990 at 25° C. It boils between 120° and 125° C. Congealing point: not below 9° C. When heated with a small quantity of sulphuric acid, Paraldehyde is converted into acetaldehyde, recognizable by its odor.

"Heat 5 cc. of Paraldehyde on a water bath: no disagreeable odor is noticeable as the last portions evaporate (*impurities derived from fusel oil*) and not more than 0.003 Gm. of residue remains. One cc. of Paraldehyde forms with 10 cc. of distilled water at 25° C., a clear solution, free from oily drops (*amyl alcohol*). A 5 cc. portion of this solution, acidulated with a drop of hydrochloric acid, yields no turbidity on the addition of 3 drops of barium chloride T.S. (*sulphate*). Another 5 cc. portion, acidulated with 1 drop of nitric acid, yields no opalescence at once on the addition of three drops of silver nitrate T.S. (*chloride*). A mixture of 6 cc. of Paraldehyde and 8 cc. of alcohol with 1 drop of phenolphthalein T.S. acquires a pink color upon the addition of 0.5 cc. of normal sodium hydroxide (*free acid*). Shake 5 cc. of Paraldehyde with 5 cc. of potassium hydroxide T.S. and allow the mixture to stand at 20° C.: the aqueous layer is not colored yellow or brown within thirty minutes (*acetaldehyde*).

"Preserve in well-closed containers, in a cool place, protected from light." *U. S.*

The British Pharmacopœia gives the following properties and tests: "A clear, colorless liquid. Characteristic, ethereal odor; taste acrid, afterwards cool. Soluble in 9 parts of *water;* less soluble in hot *water.* Miscible in all proportions with *alcohol* (90 per cent.), and with *ether.* Aqueous solution neutral or only slightly acid to *litmus.* Specific gravity 0.998 to 1.000. Solidifies at a low temperature; melting point not under 10° C. Not more than 5 per cent. distils under 123° C., and the remainder distils between 123° and 125° C. When 5 millilitres are shaken with 5 millilitres of *solution of sodium hydroxide* and allowed to separate, the aqueous layer does not exhibit more than a faint yellow coloration within one hour (limit of acetaldehyde). An aqueous solution (1 in 10) yields no characteristic *reactions* for chlorides or for sulphates." *Br.*

Uses.—In moderate doses paraldehyde causes, both in man and the lower animals, sleep which is indistinguishable from natural sleep and is unaccompanied with any marked change in the circulation, respiration, or sensibility. After large quantities the sleep becomes of a more comatose character, there is diminution of reflex activity and considerable slowing of the respiration, the circulation, however, being scarcely affected. It is asserted by Quinquaud that after fatal doses methemoglobin appears in the blood. Death is alleged to have been produced by four ounces in man, but Probst reports a case in which five ounces were taken within a period of sixty hours, causing a profound coma, lividity, and slight fall of bodily temperature, but with no pronounced circulatory disturbances and recovery on the seventh day. It is eliminated partly through the urine and partly with the breath in each of which it may be detected by its odor.

Paraldehyde is a promptly acting somnifacient of moderate power, useful in those types of *sleeplessness* which are not dependent upon pain. Its effects are generally manifest within fifteen to thirty minutes and last two or three hours. Its chief disadvantages are its occasional tendency to cause gastric disturbance and the unpleasant odor which it imparts to the breath. It has also been recommended for the relief of *asthma.*

Dose, one-half to one and one-half fluidrachms (1.8–5.5 cc.).

PAREIRA. N. F.

PAREIRA Pareir. [Pareira Brava]

"Pareira is the dried root of *Chondodendron tomentosum* Ruiz et Pavon (Fam. *Menispermaceæ*). Pareira contains not more than 5 per cent. of its stems or more than 2 per cent. of other foreign organic matter." *N. F.*

Pareira Brava, Pareiræ Radix, *Br. Add.;* Pareira Root.

This root was for a long time attributed to the *Cissampelos Pareira* L., but Hanbury in 1873 demonstrated its true source. *Chondrodendron tomentosum* is a climbing, woody vine, which often attains a considerable height, and is remarkable for the size of its leaves. These are about a foot long, broadly ovate or rounded, slightly cordate, with a smooth upper surface, and on the under surface, between the veins, covered with a fine close wool of an ashy hue. The racemose fruits are of the size of large grapes, oval and black. This plant inhabits both Brazil and Peru where it thrives in a wild state. The roots are dug up at various seasons of the year, cleaned, cut into transverse segments and dried. The commercial supplies come chiefly from Rio de Janeiro and Bahia, Brazil.

Description and Physical Properties.—"*Unground Pareira.*—Nearly cylindrical, more or less tortuous, of variable length and from 1 to 6 cm. in diameter; externally brownish black with transversed ridges on knot-like projections, occasionally fissured and longitudinally wrinkled or even furrowed; hard, heavy and tough; when freshly cut having a waxy luster; the transverse surfaces exhibiting several successive concentric zones of fibro-vascular bundles, each from 2 to 4 mm. in width with crenated borders and separated by distinct zones of parenchyma and stone cells, the zones radially marked by prominent medullary rays. Stems deeply furrowed, grayish in color, usually covered with foliaceous patches of lichens; internally grayish yellow, with a prominent development of wood with a tendency to separate fibro-vascular bundles and without a waxy luster. Odor slight; taste very bitter.

"*Powdered Pareira.*—Dark brown, containing numerous starch grains and a few woody fragments; starch grains mostly simple, occasionally unequally 2- to 4-compound, the individual grains ellipsoidal or oblong, 0.005 to 0.030 mm. in diameter and occasionally with central clefts or irregular markings; fragments with large, wide tracheæ, the walls with numerous slit-like pores and associated with long, thick-walled, strongly lignified, porous wood fibers; stone cells in small groups, with thick porous walls and in form resembling those of the fruits and seeds; fragments of starch-bearing parenchyma; the cells of the root being thick-walled, strongly lignified and with large longitudinal, elliptical pores: occasional fragments of blackish brown cork." *N. F.*

Recent adulterants and substitutes of Pareira have consisted of the roots and stems of *Cissampelos Pareira* L. (Fam. *Menispermaceæ*) and the stems of the *Chondrodendron tomentosum* Ruizet Pavon. The roots of *Cissampelos Pareira* are dark brown externally, light brown internally, are devoid of a waxy luster on their cut surfaces and show but one circle of fibrovascular bundles. The stems of this plant are usually less than an inch in diameter, show spirally furrowed or wrinkled, light brown bark, a coarse fibrous fracture and but one circle of bundles. Both root and stem are bitter but not astringent. The stems of true pareira may be distinguished by having a distinct pith, concentrically arranged bundles often separated from adjacent tissue, the absence of a waxy luster on their cut surfaces and by often possessing foliaceous lichens with black apothecia on their outer surface. The *Chondrodendron platyphyllum* Miers appears to have been, at times, substituted for the genuine root.

Constituents.—The chemistry of pareira is much confused on account of the uncertainty of the botanical origin of the roots which various chemists have investigated. Wiggers in 1838 found in the *Cissampelos Pareira* an alkaloid which he called *pelosine.* Flückiger (*P. J.,* 1870, xi, 192) subsequently showed that pelosine was identical with *bebeerine* of nectandra (see *Bebeeru bark,* Part II) and with the alkaloid that he had previously found in *Chondrodendron tomentosum.*

The substance known commercially as bebeerine sulphate, and said to be obtained from pareira, according to Scholtz (*A. Pharm.,* 1914, cclii, p. 513) is really a mixture of at least five alkaloids, bebeerine, *iso-bebeerine,* beta-bebeerine, bebeerine-b and *chondrodine.* The name *chondrodendine* has also been suggested for bebeerine. Ringer and Brooke (*A. J. P.,* 1892, 255) proved that the true chondrodendron root contained a larger quantity of both alkaloidal and extractive principles than do the substitutes. (See also Dohme's paper, *D. C.,* 1896, 296.)

Uses.—Pareira is supposed to have a diuretic effect and to act as an antiseptic in the bladder. It is chiefly employed for the relief of *chronic inflammations of the urinary passages.* In Brazil it is used in the cure of the *bites of poisonous serpents,*—a vinous infusion of the root being taken internally, while the bruised leaves of the plant are applied to the wound.

Dose, thirty to sixty grains (2.0–3.9 Gm.).

Off. Prep.—Fluidextractum Pareiræ, *N. F.*

PASSIFLORA. N. F.

PASSION FLOWER Passiflor. [Passion Vine]

"Passion Flower is the dried flowering and fruiting top of *Passiflora incarnata* Linné (Fam. *Passifloraceæ*). Passion Flower contains not more than 5 per cent. of stems over 8 mm. in diameter or other foreign matter." *N. F.*

Wild Passion Flower; May-pop.

The *Passiflora incarnata* is a climbing perennial herb, indigenous to the southern United States, with broadly cordate-ovate, palmately three-lobed leaves and solitary large flowers, the calyx bearing in its throat five white petals and a fringe, called the corona, which is of a purplish or pinkish color. The fruit is a yellowish berry about the size of a hen's egg. The whole of the overground portions are employed. Commercial supplies of this drug come from North Carolina and Virginia.

Description and Physical Properties.—"*Unground Passion Flower.*—Stems glabrous or slightly pubescent above, striate, from 6 to 8 mm. in diameter, of variable length, woody, hollow, the cavity about one-half the diameter; bark very thin, greenish or purplish; wood very porous and bordered on the inner side by a thin layer of pith; fracture of the wood uneven, of the stem smooth, of the bark coarsely fibrous. Leaves more or less broken, rather thick, glabrous or often pubescent, when entire nearly orbicular in outline, base cordate, deeply three- to five-lobed, lobes ovate, finely serrate, petioles from 1 to 5 cm. in length, with two glands near the apex. Tendrils numerous and closely coiled. Flowers solitary, axillary, peduncles as long as the petioles, usually three bracted; calyx cup-shaped, with four to five lobes; lobes linear, imbricated, cuspidate, corona of the fresh flowers purplish; petals four to five, yellow; ovary oblong, stalked; stamens monadelphous in a tube about the stalk of the ovary, separated above, anthers narrow, versatile. Fruit from 4 to 5 cm. in length, an ovoid, many-seeded berry; externally green or yellow, shriveled and wrinkled; seeds flat, ovate, yellowish to brown arilled. Odor and taste slight.

"*Powdered Passion Flower.*—Light green; numerous thin-walled non-glandular hairs, 1- to several celled, up to about 0.450 mm. in length; numerous fragments of stem tissue composed of pith and wood parenchyma, tracheæ with spiral and reticulate markings or simple pores and fibers; fragments of leaf tissue composed of chlorenchyma and epidermal cells with stomata from 0.020 to 0.035 mm. in length; calcium oxalate rosettes from 0.010 to 0.030 mm. in diameter." *N. F.*

We have no knowledge of the nature of the active principle of this drug.

Uses.—The passion-flower was introduced into medicine about 1840 by Doctor Phares of Mississippi. It is used as a nerve sedative to allay general *restlessness,* to relieve *insomnia,* and in the relief of certain types of *convulsions* and spasmodic disorders. It is also attributed with anodyne properties and is used in the treatment of various *neuralgias.* While there is considerable evidence that this drug possesses some therapeutic virtue, it has not been carefully studied. J. Ott (*Medical Bulletin,* Dec., 1898) finds that it is a depressant to the motor side of the spinal cord, but increases the rate of the respiration, and that it has very little effect upon the circulation, only temporarily reducing the arterial pressure.

Dose, three to ten grains (0.2–0.65 Gm.).

Off. Prep.—Tinctura Passifloræ, *N. F.*

PELLETIERINÆ TANNAS. U. S., Br.

PELLETIERINE TANNATE Pellet. Tann.

"A mixture of the tannates of the several alkaloids obtained from pomegranate." *U. S.* "Pelletierine Tannate is a mixture of the tannates of the alkaloids obtained from the bark of the root and stem of Punica Granatum, *Linn.*" *Br.*

Pelletierinum Tannicum, Punicinum Tannicum; Punicine Tannate; Tannate de Pelletiérine, *Fr.;* Gerbsaures Pelletierin, Punicin, *G.*

Preparation.—This preparation is a mixture of the various alkaloids of pomegranate bark (see *Granatum*). The bark is ground, and mixed with milk of lime; the mixture is percolated with water, the percolate shaken with chloroform, and the separated chloroformic liquid which contains in solution the mixed alkaloids, is treated with a weak solution of sulphuric acid; upon the addition of a solution of tannic acid to the neutral solution of the sulphates, tannates are precipitated; these are washed and dried.

Description and Physical Properties.—" A light yellow, odorless, amorphous powder, having an astringent taste. One Gm. of Pelletierine Tannate is soluble in about 250 cc. of water at 25° C. It is soluble in alcohol, slightly soluble in ether, and insoluble in chloroform. It is dissolved by warm dilute acids.

" Its saturated, aqueous solution is acid to litmus paper. A saturated aqueous solution of the salt is colored blue-black by ferric chloride T.S.

" The ash from 0.2 Gm. is negligible. Platinic chloride T.S. produces no precipitate in a cold solution of about 0.1 Gm. of Pelletierine Tannate in a mixture of 4 cc. of distilled water and 1 cc. of diluted hydrochloric acid (*many foreign alkaloids*). Dissolve about 0.5 Gm. of Pelletierine Tannate, accurately weighed, in 5 cc. of sodium hydroxide T.S., and shake the solution with four successive portions of 10, 5, 5, and 5 cc. of chloroform. Acidulate the combined chloroform solutions with 0.1 cc. of hydrochloric acid, evaporate to apparent dryness on a water bath, dissolve the residue in 5 cc. of alcohol, again evaporate, and dry for one hour at 60° C. The weight of the residue is not less than 20 per cent. of the weight taken. Stir about 0.001 Gm. of the residue obtained in the preceding test on a white, porcelain surface with 2 drops of sulphuric or nitric acid: no other than a light yellow or slightly brown color is produced.

" Preserve in small, well-closed containers, protected from light." *U. S.*

" A light yellow, amorphous powder. Slightly soluble in *water,* more soluble in *alcohol* (90 per cent.). An aqueous solution gives with *T. Sol. of ferric chloride* a bluish-black color; with *solution of silver nitrate* a brown color rapidly deepening, with separation of metallic silver; and with *solution of auric chloride* a deep purple color, with separation of metallic gold. When heated, Pelletierine Tannate turns brown at about 150° C., softens at about 165° C.; and at a higher temperature decomposes without melting. No appreciable ash." *Br.*

Uses.—For account of the physiological and therapeutic properties of this substance see under *Granatum.* It is chiefly used as a tænifuge.

Dose, three to five grains (0.2–0.3 Gm.).

PEPO. U. S. (Br.)

PEPO [Pumpkin Seed]

" Pepo is the dried ripe seed of cultivated varieties of *Cucurbita Pepo* Linné (Fam. *Cucurbitaceæ*). Pepo contains not more than 5 per cent. of broken or defective seed or other foreign organic matter." *U. S.* " Melon Pumpkin Seeds are the prepared fresh ripe seeds of cultivated plants of Cucurbita maxima, *Duch.* Melon Pumpkin Seeds must not be more than one month old, and when required for use about 100 grammes are bruised with a little water or milk to a creamy consistence and administered as a single dose." *Br.*

Cucurbitæ Semina Præparata, *Br.;* Melon Pumpkin Seeds; Semen Peponis, Semina Cucurbitæ; Semences de Potirons ou de Courge, *Fr.;* Kürbissamen, Kürbiskörner, Graumontsamen, *G.;* Calabaza (Semilla), *Sp.*

Cucurbita Pepo L. is an annual, long running, monœcious herb with prickly stems and petioles indigenous to tropical America, having been cultivated in fields of maize by the aborigines when the first settlers arrived on the American continent. It is further characterized by possessing 3- to 5-lobed, dark dull green leaves, large yellow axillary flowers and pepo fruits, the latter differing in size and shape in the numerous varieties and strains cultivated. Much confusion exists in the usage of the terms " pumpkin " and " squash," these terms having been applied almost indiscriminately to varieties of several species of *Cucurbita.* The various field or pie pumpkins and the summer squashes represent cultivated varieties of *C. Pepo.* The Hubbard, Turban, Marblehead and Sibley squashes are cultivated varieties of *C. maxima* Duchesne. The Canada Crookneck, Winter Crookneck and China squashes are cultivated varieties of *C. moschata.* The seeds of *C. Pepo* are recognized by the U. S. and of *C. maxima* by the Br.

Description and Physical Properties.—" *Unground Pepo.*—Broadly elliptical or ovate, from 15 to 23 mm. in length and from 2 to 3 mm. in thickness; externally yellowish-white, very smooth, occasionally with thin, transparent fragments of adhering pulp and with a shallow groove parallel to and within 1 mm. of the margin; fracture short; seed-coat consisting of a white coriaceous outer layer and a membranous inner layer occasionally of a dark green color; embryo whitish, straight, with a small conical hypocotyl and 2 plano-convex cotyledons; slightly odorous when contused; taste bland and oily.

" *Structure.*—An outer epidermal layer consisting of palisade-like cells, the radial walls attaining a length of 1 mm., the outer walls being usually torn off so that it appears as though the seeds were covered with very long hairs; a sub-epidermal layer consisting of from 5 to 12 rows of cells with slightly thickened, lignified and porous walls; a layer of strongly lignified stone cells, elliptical in outline and about 0.075 mm. in length; a single layer of small cells resembling those of the sub-epidermal layer; several rows of parenchyma cells with characteristic, reticulate markings and separated from each other by large intercellular spaces; several layers of parenchyma cells, the inner layer being more or less collapsed and bounded on the inside by a single epidermal layer, the cells having rather thick walls; the perisperm cells usually more or less collapsed and the endosperm consists of a single layer of cells filled with small, aleurone grains; the cotyledons consist of thin-walled, isodiametric, elongated or palisade-like cells containing a fixed oil and numerous small, aleurone grains." *U. S.*

The British Pharmacopœia recognizes the *melon pumpkin* seeds, under the title of *Cucurbitæ Semina Præparata.* These are derived from a closely related species, *Cucurbita maxima* Duch., which closely resembles *C. Pepo* and differs in that the margins of the leaves possess rounded teeth, whereas in *C. Pepo* they are acute. The British definition and description are as follows: "Flat, ovate, white, and exalbuminous, consisting of two fleshy, easily separable cotyledons, freshly deprived of the yellowish outer, and brownish inner integument. Faint odor; taste very slight. Before preparation, the seeds measure from eight to twenty millimetres in length, and from nine to twelve millimetres in breadth." *Br.*

Although Dorner and Wolkowich reported an alkaloid, *cucurbitine,* in pumpkin seed in 1862, subsequent chemists have not been able to confirm its presence. Power and Solway (*J. Am. C. S.*, 1910, xxxii, p. 346) obtained by expression about 19 per cent. of a reddish fixed oil. This had a specific gravity at 20° C. of 0.922, acid value 3.4, saponification value 189.4, iodine value 119.7; it was composed of 45 per cent. of the glyceride of linoleic acid, the remainder being olein, palmitin and stearin (see also Graham, *A. J. P.*, 1901, p. 352).

In 1875 Heckel obtained a resin which he believed was the active principle. Power and Solway tested both the resin and the oil from pumpkin seed but were unable to find evidence of any vermifuge effect. We must at present, therefore, consider that we have no knowledge of the real active principle of this remedy.

W. E. Miller (*A. J. P.*, 1891, 585) analyzed both the shells and the kernels of pumpkin seed. He also found a resin soluble in alcohol, and a dark reddish fixed oil.

Uses.—The seeds of various species of cucurbita have been used for more than a century in the treatment of *tapeworm.* The use of pumpkin seems to have been introduced into the United States by Soule (*B. M. S. J.*, 1851). Because of its harmlessness it became, and has continued, a favorite vermifuge for this purpose although from time to time its efficacy is denied. De Jongh (*P. J.*, 1917, xcviii, p. 307) reports satisfactory results in the case of infection by the *Tænia nana.* Sollmann (*J. P. Ex. T.*, 1918, xii, 129) has offered a plausible explanation of the varying esteem of this drug; he finds that the infusion of fresh pumpkin seed has a very markedly toxic action on earth worms but that a similar preparation from old seeds is much less efficient.

In treating tapeworm with this drug the patient should be allowed only a light supper of bread and milk, in the morning early should take an ounce and a half of the seeds, a cup of tea or coffee an hour later, but no food; at 10 A. M. a brisk cathartic, and two hours later a substantial meal. We have obtained excellent results from the exhibition of the beaten seeds in the form of an electuary strongly flavored with oil of cinnamon or of gaultheria.

Dose, one to two ounces (31–62 Gm.).

PEPSINUM. U. S., Br.

PEPSIN Pepsin.

"Pepsin is a substance containing a proteolytic enzyme obtained from the glandular layer of the fresh stomach of the hog, *Sus scrofa* var. *domesticus* Gray (Fam. *Suidæ*). Pepsin digests not less than 3000 times its own weight of freshly coagulated and disintegrated egg albumen. Pepsin of a higher digestive power may be brought to this standard by admixture with pepsin of a lower digestive strength or with lactose." *U. S.* "Pepsin is an enzyme obtained from the fresh and healthy stomach of the pig, sheep, or calf." *Br.*

Pepsine, *Fr. Cod.;* Pepsinum, *P. G.;* Pepsin, *G.;* Pepsina, *It.;* Pepsina medicinal, *Sp.*

There is secreted by certain glands in the stomach an enzyme which, in the presence of a slightly acid medium, is capable of converting proteins into proteoses and peptones. This ferment, which is known to the physiologists under the name of pepsin, has never been isolated in a pure condition; the substance known in the Pharmacopœias by the name of "pepsin" contains, besides the ferment itself, varying quantities of inert protein matter. Pepsins having much greater digestive capacity than that chosen for the U. S. official standard have been manufactured, but for all practical purposes the official pepsin is sufficiently concentrated, and indeed it is usually diluted for internal administration.

The British Pharmacopœia of 1885 gave a method for the manufacture of pepsin which consisted simply in scraping the cleansed mucous membrane of the stomach and drying the resulting pulp on glass plates. This process can not give the full enzyme content of the mucous membrane as the peptic ferment does not exist as such in the cells of the mucous membrane, but only as a compound known as *propepsin* or *pepsinogen* which, in the presence of hydrochloric acid is converted into active pepsin. The modern methods of manufacturing pepsin may be briefly stated as follows. The inner membranous linings of hogs' stomachs are washed, passed through a mincing machine, and the resulting mass digested with diluted hydrochloric acid; the solution is strained or filtered and evaporated *in vacuo* or placed on shallow trays, so that a syrupy liquid, which has not been subjected to a higher temperature than 44.5° C., is produced; this is spread upon glass plates to dry, and the scales which are formed scraped off. The thickness of the scales may be varied by using more or less concentrated solutions, and the proportion of peptone is increased by extending the length of time in the digestion process and raising the temperature to the utmost safe limit. Pepsin appears to belong to the group of true albumins; that is—those proteins which are soluble in water but may be precipitated from their aqueous solution by various neutral salts. Practical application of this fact has been made in concentrating pepsin.

Three distinct types of pepsin are found in commerce: (1) Pepsins insoluble in water without the addition of traces of acids; (2) Pepsins soluble in water forming transparent solutions: (3) Pepsins not entirely soluble in water or in diluted hydrochloric acid. The objection to the insoluble pepsins is, of course, the inconvenience resulting from their insolubility in water, but, on the other hand, they are not hygroscopic, do not deteriorate so rapidly, and are active in contact with the gastric juice. The objection to the soluble pepsins is that they are hygroscopic, but they are, when good, well suited for making solutions, wines, etc. Most of the pepsin used at the present time is what is known as scale pepsin and contains from 8 to 12 per cent. of hydrochloric acid.

Description and Physical Properties.—"Lustrous, white or pale yellow, transparent or translucent scales, granules or spongy masses, or a fine, white or cream-colored, amorphous powder, free from any offensive odor, and having a slightly acid or saline taste. It is not more than slightly hygroscopic. Pepsin is freely soluble in water, the solution being more or less opalescent. It is nearly insoluble in alcohol, chloroform, and ether. Dry Pepsin is not injured by heating to 100° C. The activity of Pepsin in solution is destroyed by alkalies or by temperatures exceeding 70° C.

"An aqueous solution of Pepsin (1 in 50) is acid to litmus paper. An aqueous solution of Pepsin yields precipitates with solutions of tannic or gallic acid and with solutions of the salts of many heavy metals. On heating a saturated solution of Pepsin in acidulated water to 100° C., it becomes milky or yields a light, flocculent precipitate, and loses all proteolytic power.

"Preserve in well-closed containers." *U. S.*

Assay.—"Mix 25 cc. of normal hydrochloric acid with 275 cc. of distilled water. Dissolve 0.1 Gm. of Pepsin in 150 cc. of this acid. Select a hen's egg, which is not less than five and not more than twelve days old and has been kept in a cool place, and immerse it in boiling water during fifteen minutes. As soon as the egg has sufficiently cooled to handle, remove the shell and pellicle and all of the yolk and at once rub the albumen through a clean, dry, hair or brass, No. 40 sieve, reject the first portion that passes through the sieve, and place 10 Gm. of the succeeding portion in a wide-mouthed bottle of 100 cc. capacity. Immediately add 20 cc. of the acid and stir the mixture well with a rubber-tipped glass rod so as to separate thoroughly the particles of albumen from each other. Rinse the rod with 15 cc. more of the acid and, after warming the mixture to 52° C., add exactly 5 cc. of the acidulated solution of Pepsin. At once cork the bottle securely, invert it three times, and place it in a bath that has been previously regulated to maintain a temperature of 52° C. Keep the bottle at this temperature for two and one-half hours, agitating the contents every ten minutes by inverting at once. Then remove it from the bath, pour the contents into a conical measure having a diameter not exceeding 1 cm. at the bottom, and transfer the undigested egg albumen, which adheres to the sides of the bottle, to the measure with the aid of small portions (about 15 cc. at a time) of distilled water, until the total amount used measures 50 cc. Stir the mixture well and allow it to stand for half an hour. The deposit of undissolved albumen does not measure more than 1 cc.

"The relative proteolytic power of pepsin, stronger or weaker than that just described, may be determined by ascertaining through repeated trials the quantity of the Pepsin solution made as directed in the assay, required to digest, under the prescribed conditions, 10 Gm. of boiled and disintegrated egg albumen. Divide 15,000 by this quantity expressed in cc. to ascertain how many parts of egg albumen one part of Pepsin will digest." *U. S.*

"A light yellowish-brown powder, or pale yellowish, translucent scales, having a faint odor. Tested as follows it dissolves 2500 times its weight of coagulated white of egg in six hours, the resulting solution being faintly opalescent:—Prepare some coagulated white of egg by boiling fresh eggs in water for fifteen minutes, immersing them in cold water until cool, separating the whites, at once rubbing these through a hair-sieve having 12 meshes to a centimetre, and using the product before it has lost moisture by evaporation. Prepare also a Pepsin solution by triturating 0.25 gramme of the Pepsin with 1 gramme of *sodium chloride* in a small mortar until thoroughly mixed, adding by degrees acidified water (prepared by diluting 6.5 millilitres of *hydrochloric acid* to 1000 millilitres with *water*), continuing the trituration, transferring to a litre flask, washing the mortar with acidified water, and adding the washings to the contents of the flask until 1000 millilitres are produced, then shaking frequently during six hours, and again immediately before use. Introduce 20 millilitres of the Pepsin solution so prepared into a 250 millilitre flask. Triturate 12.5 grammes of the freshly prepared coagulated white of egg in a small mortar with 50 millilitres of acidified water until reduced to uniform granules. Transfer to the flask, rinsing the mortar with a further 50 millilitres of acidified water, adding the rinsing to the contents of the flask. Immerse the flask in a water-bath so that its contents are on a lower level than the water in the bath, and digest at a temperature between 40° and 41° C. for six hours, shaking at intervals of fifteen minutes." *Br.*

The conditions that effect the rapidity of peptic digestion are so many that it is necessary to adhere with great strictness to each detail of the assay method. One of the variables which has caused considerable difficulty is the albumin. The present Pharmacopœia attempts to meet this trouble by a strict definition of the conditions for preparation of the egg. A number of authorities have advocated the use of *edestine,* a globulin found in the cereal grains (see *Bull. Sci. Pharm.,* 1915, xxii, p. 24 and *P. J.,* 1915, xciv, p. 389). Chestnut has advocated the use of ricin, the protein of castor beans, and has devised a method which he believes is more accurate than that of the U. S. P. and which involves the comparison with a standard pepsin (see Fuller, *Chemistry and Analysis of Drugs,* 1920, page 898).

Incompatibilities.—The peptic ferment is an extremely unstable body being destroyed by tannins, alcohol, the salts of the heavy metals and strong acids. Tocher, as the result of an experimental study, concludes that: Solutions of sodium bicarbonate, sodium, potassium, and ammonium hydrates when added to solutions of pepsin in the cold have an immediate inhibitory or destructive effect on pepsin, according to the concentration; dilute solutions of caustic alkali immediately destroy the activity of dilute solutions of pepsin; subcarbonate of bismuth precipitates pepsin from aqueous solutions: subnitrate does not; compound mixtures containing solution of bismuth, morphine, carmine, etc., should contain no pepsin, since the activity of the enzyme is much retarded by the morphine and is destroyed proportionately to the amount of alkali present in solution. (*Year Book of Pharmacy,* 1906, pp. 307–313.) The chemical relations of pepsin are so delicate and widespread that it ought to be given by itself, or in combination only with an insoluble substance, or suspended in inert liquids.

Uses.—Gastric juice was used by Dr. P. S. Physick, the celebrated physician of Philadelphia, nearly a century ago as a local application in *cancers* and *sloughing ulcers,* with a view of removing the dead flesh and correcting the offensive odor and affording a healthy stimulus to the diseased surface. The first to have suggested pepsin as a remedy in disturbances of the stomach seems to have been Corvisart. (*J. P. C.,* xxx, p. 169.) It is now very largely used with the idea of improving the digestive powers of the stomach by supplying the essential ferment. Its value in *dyspepsia,* however, is greatly over-estimated. *Pepsinogen*—from which the active peptic enzyme is derived by the action of the hydrochloric acid—is rarely lacking save in cases of cancer and other very severe diseases of the stomach. When gastric digestion fails it is generally because of the absence of hydrochloric acid in sufficient quantity to activate the pepsinogen. Therefore, in our opinion pepsin is not indicated in the ordinary types of *indigestion* or *gastritis.* It appears, however, to have some sedative influence upon the mucous membrane of the stomach, not due to its digestive powers, and is often of service for the relief of certain forms of *nausea* and to lessen the ill effects of such drugs as the iodides and salicylates upon the stomach. Locally it is still used occasionally for the purpose of dissolving the false membrane in *diphtheria* and hastening the sloughing off of dead tissue in *foul ulcers.*

It would seem trite to say that when pepsin is used as a digestive ferment it must be given in an active form and in sufficient dose to have some influence, were it not for the fact that this truism is so often forgotten. The enzymic activity of pepsin is so easily destroyed by heat and chemical agents, that it should be administered always either alone as a powder or in solution with minute quantities of hydrochloric acid only. The dose of four or five grains of pepsin so often recommended is quite inadequate to seriously influence gastric digestion; if the physician is employing the pepsin with any idea of hastening digestion he should give at least from fifteen to thirty grains (1–2 Gm.) at a dose.

Pepsin should preferably be administered in its original form. It is well to combine it with hydrochloric acid, and the powder is often advantageously exhibited in *infantile diarrhea* along with bismuth subnitrate. With these exceptions, it is usually preferable to give it by itself.

Dose, of official pepsin, may be set down as from ten to sixty grains (0.65–3.9 Gm.).

Off. Prep.—Glyceritum Pepsini, *N. F., Br.;* Elixir Pepsini (from Glycerite), *N. F.;* Elixir Pepsini, Bismuthi et Strychninæ, *N. F.;* Elixir Pepsini et Bismuthi, *N. F.;* Elixir Pepsini et Rennini Compositum, *N. F.;* Liquor Pepsini (from Glycerite), *N. F.;* Liquor Pepsini Antisepticus, *N. F.;* Liquor Pepsini Aromaticus, *N. F.;* Pepsinum Saccharatum, *N. F.*

PERSIO. N. F.

CUDBEAR

"Cudbear is a purplish red powder prepared from species of *Rocella* De Candolle, *Lecanora Acharius,* or other lichens. Cudbear yields not more than 12 per cent. of total ash." *N. F.*

Orseille de Terre, *Fr.;* Rothe Indigo, Persio, *G.*

Three purple or blue coloring substances obtained from various lichenous plants are known in commerce under the names of litmus (see Part II), orchil and cudbear. The species of lichens concerned represent various genera; at present the two most important of the lichens are said to be the *Roccella Montagnei* Bel. of Mozambique and the *Dendrographa leucophœa* Darbish of California. In the north of Europe *Lecanora tartarea* Ach., or *Tartarean moss*, and on the Mediterranean coasts the *Roccella tinctoria* Ach., or *orchilla weed*, at one time furnished the great bulk of the orseille of commerce. The chromogenous ethers which constitute the coloring matter of the lichens may be readily detected *in situ* by reagents. (*P. J.*, Nov. 19, 1904.) In some of the lichens these coloring principles are chiefly situated in the cortex; in others they are especially abundant in the gonidial layer.

These lichens are brought into commerce from the coasts of Sweden and Norway; from the Alps, the Pyrenees, and other European mountains; from the European and African coasts of the Mediterranean; from the Canaries, Madeira, and various other rocky islands, especially from Mozambique, Madagascar, and Angola, and from California.

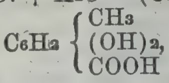
Cudbear is prepared by macerating the lichens with diluted ammonia, probably also with the addition of potassium or sodium hydroxide, for several days. After the proper fermentation has occurred the mixture is dried and powdered.

Orchil (*archil, orseille*) seems to differ in its preparation from cudbear in that, after fermentation, sulphuric acid and sodium chloride are added. It is used as a dye-stuff, especially for modifying the tinctorial effect of other dyes as indigo.

Physical Properties and Tests.—"An aqueous or alcoholic preparation of Cudbear is of a deep red color which is rendered lighter in tint by the addition of acids, and is changed to purplish red on the addition of alkalies. Agitate 2 Gm. of Cudbear occasionally with 200 cc. of water during thirty minutes and then filter; the deep red-colored filtrate conforms to the following tests: Add to 5 cc. of the filtrate 5 drops of glacial acetic acid and boil for one minute; then add 5 drops of stannous chloride T.S., and boil again for one minute; the liquid is only faintly pink (*brazilwood or logwood* which produce solutions of a deep red color); add 25 Gm. of kaolin to 100 cc. of the filtrate in an Erlenmeyer flask, shake frequently during one hour and then filter; the filtrate is almost entirely decolorized in comparison with some of the original filtrate (a number of coal tar colors)." *N. F.*

Constituents.—The principles in these plants upon which their valuable properties depend are themselves colorless, and yield coloring substances by the reaction of water, air, and ammonia. They are generally acids or acid anhydrides, and are named *lecanoric, orsellic, erythric,* etc., according to their origin. *Lecanoric* (*diorsellinic*) *acid*, $C_{16}H_{14}O_7$, the original constituent of most of these plants, when boiled with water or alkaline solutions, is changed into *orsellinic acid*, as follows:

$$C_{16}H_{14}O_7 + H_2O = (C_8H_8O_4)_2$$

Orsellinic acid,  $C_6H_2\begin{cases}CH_3\\(OH)_2\\COOH\end{cases}$, fuses at 176° C., and decomposes into *orcin*, $C_6H_3(CH_3)(OH)_2$, and CO_2. The same decomposition is readily effected by distillation with milk of lime. Orcin combines with ammonia gas to form $C_8H_8O_2.NH_3$, the solution of which exposed to the air becomes colored reddish by the formation of *orcëin*, $C_7H_7NO_3$. This latter compound forms the basis of *orchil*.

Kane described a deep red crystalline substance, *erythrolitmin*, and a brownish-red coloring principle, *azolitmin*, $C_7H_7NO_4$. This latter is considered as the distinctive coloring matter of the commercial litmus, and is now found in commerce under that name and is used as an indicator. It is nearly insoluble in cold water or benzene, but dissolves in alcohol with red, and in ether with yellow color. It appears to have the characters of a weak acid, the salts of which are blue and the potassium and calcium compounds of which exist in litmus.

To test the value of the plants as dye-stuffs, they may be macerated in a weak solution of ammonia, or a solution of calcium hypochlorite may be added to their alcoholic tincture. In the former case a rich violet-red color is produced; in the latter, a deep blood-red color appears, but soon fades.

George M. Beringer has given much attention to cudbear with a view of securing a uniform product. (See *Proc. New Jersey Pharm. Assoc.*, 1912, 56.) He declares that all of the ordinary methods, as color charts, colored yarns, threads, glass, etc., are unsatisfactory and inapplicable to pharmacy. He advocates the preliminary purification of cudbear by washing it with water to remove the sodium chloride so largely used as a diluent and the ammonium salts with their empyreumatic odor and states that if the washing is properly done the cudbear loses scarcely any of its tinctorial power. He believes that the best results would follow the preparation and use of a standard extract. Alexander Gardner gives the name *persionin* to an acetone extract of cudbear made as follows: Percolate commercial cudbear with purified benzin until free from wax, then dry and percolate with acetone to exhaustion—about 2500 cc. being required for 1000 Gm. of cudbear. The acetone is recovered by distillation, the residual extract heated for thirty minutes to 98.8° C. in a porcelain capsule, then pulverized and placed in a sulphuric acid desiccator for three days, during which it loses about 25 per cent. of its weight. So obtained, "persionin" is a black, lustrous powder with an aromatic odor, soluble in alcohol, glycerin, chloroform, ether, and hydroalcoholic liquids, but is only sparingly soluble in water. Five different lots of cudbear yielded, from 5 to 7 per cent. of persionin. Each sample of "persionin" was tested by dissolving 1 part in 100 parts of alcohol and 3 parts of glycerin. One cc. of this was added to 99 cc. of distilled water, and in each particular the color was the same. (*J. A. Ph. A.*, 1913, 51–52.) H. V. Arny (*J. A. Ph. A.*, 1913, 47) proposes to remove a brown pigment present in cudbear (which interferes with the tinctorial power) by macerating an alcoholic extract with chloroform and extracting the residue with acetone. The final product is then "scaled."

Because of the difficulty of completely extracting cudbear the liquid preparations are rarely uniform in color value. For this reason the N. F. uses powdered cudbear in several preparations, allowing it to macerate until all color is extracted. This plan results in more uniform coloring than if the tincture was directed.

Cudbear is used solely for its tinctorial properties.

Off. Prep.—Tinctura Persionis, *N. F.;* Tinctura Persionis Composita, *N. F.*

PETROLATUM. U. S. (Br.)

PETROLATUM Petrolat. [Amber Petrolatum, Yellow Petroleum, Petroleum Jelly]

"A purified, semi-solid mixture of hydrocarbons, obtained from petroleum." *U. S.* "Soft Paraffin is a mixture of semi-solid hydrocarbons." *Br.*

Paraffinum Molle, Soft Paraffin, *Br.;* Adeps Petrolei, Unguentum Paraffinum; Petrolinum; Unguentum Petroleis; Soft Petrolatum, Cosmoline, Vaseline, Paraffin Jelly, Petroleum Jelly, Petroleum Ointment; Vaselinum, *P. G.;* Graisse minérale, Pétréoline, *Fr.;* Weiches Paraffin, Paraffinsalbe, *G.;* Vaselina, *It., Sp.*

Petrolatum is prepared from the residue left in the stills after a distillation of petroleum *in vacuo,* or from the residue or sediment deposited in tanks containing crude petroleum, of which large quantities collect in the storage tanks in the oil districts of western Pennsylvania. It is made on a large scale from residues, but more largely from what are termed "reduced oils," that is, crude oils from which the lighter fractions (those included under the heads of petroleum benzin, naphtha, illuminating and paraffin oils) have been removed by distillation. This process of reducing would leave an increasing amount of black pyrogenous products in the residue, were it not that the reducing is carried out under diminished pressure, by what is termed the "vacuum process," in which, moreover, the heat is not applied directly to the still bottoms, but by means of coils of pipe, through which superheated steam is made to pass. These reduced oils can be brought to 337.7° C. fire-test without acquiring the slightest pyrogenous odor. They are then filtered through well-dried bone black, in chambers kept at a temperature of from 43.3° to 54.4° C., or in some cases higher. The first portions of the filtrate are colorless, and then pass from a light straw or amber color to a red color by transmitted light and light green by reflected light. The latter product is known as "cylinder stock," and is highly prized as a lubricating oil. The crude oil tank residues are purified in a similar manner. The "B. S. Oil," or "rod wax," as it is technically termed, is placed in a still, heat applied, and after the lighter products have distilled over, and indications of congelation are noticed when a portion of the distillate is allowed to cool, the heat is withdrawn, and the contents of the still, after having cooled, are transferred gradually to a percolator which contains recently heated animal charcoal. In place of bone black, clay has in recent years been quite largely used for clarifying purposes, the same being revivified by heat. A somewhat different process is used in Germany; the crude product is derived from crude *ozokerite,* obtained from Alsace and Galicia, or American residue is sometimes used. (1) The oil is heated by steam to about 30° C., mixed, at this temperature, with 10 per cent. of its weight of sulphuric acid of 60° B., stirred for half an hour, and then allowed to stand at rest, so that the carbonized portions may separate. (2) When clear, the oil is washed with an aqueous solution of potassium dichromate, whereby any remaining excess of sulphuric acid is at the same time removed. (3) The residue from the acid treatment is mixed with lime, neutralized, and disposed of to fertilizer factories. (4) The clear oil from the second step of the process, after being washed, is heated by steam to 80° C., mixed with 10 per cent. of its weight of granular animal charcoal, and then allowed to stand at rest, to permit the animal charcoal to settle. (5) After the latter is separated, the liquid portion is filtered through filters heated by steam. (6) The residuary magma of animal charcoal is subjected to hydraulic pressure, the expressed oil filtered, and the solid residue again used in the next operation, a sufficient quantity of fresh animal charcoal being added to make up for any loss or waste.

The commercial varieties of petrolatum may be classed under two heads: (1) Those which, like the American vaseline, are obtained as a ready formed mixture of hydrocarbons of gelatinous consistence; (2) those made by directly mixing solid paraffin of low melting point with heavy lubricating oil, such as are known in Germany as "artificial vaseline." The latter varieties are less homogeneous, and are liable to deposit granules of paraffin on keeping, and hence are not so suited for the preparation of ointments as true American petrolatum.

In warm ether, American petrolatum dissolves freely to a clear solution exhibiting a strong blue fluorescence, and the liquid remains clear, or at most becomes only slightly turbid, on cooling. German petrolatum, on the contrary, is said to form a thick solution with warm ether, and to give a considerable deposit on cooling. Russian petrolatum is stated to dissolve completely in warm ether and give a clear solution which becomes turbid on cooling. (Allen, *Com. Org. Anal.*, 2d. ed., 1887, ii, p.

408.) In the U. S. P. there are three forms of petrolatum as follows: Petrolatum, Petrolatum Album, and Petrolatum Liquidum. In the British Pharmacopœia there are three as follows: Paraffinum Liquidum, Paraffinum Molle, and Unguentum Paraffini. The Petrolatum of the U. S. P. X corresponds with the *Petrolatum Spissum* of the U. S. Pharm., 1890. The Paraffinum Molle of the British Pharmacopœia resembles the *Petrolatum Molle* of the U. S. P. 1890, but is somewhat softer in consistence.

Chemical Constitution.—Petrolatum, as made from American petroleum, consists mainly of the higher members of the paraffin series, but undoubtedly contains also the higher olefines. Puckner (*A. J. P.*, July, 1914) states that American petrolatum is made up of hydrocarbons of the methane series while the Russian oil contains naphthenes. These may possibly alter in time, and give rise to rancidity, although this is not certainly established. The paraffins, which make up the bulk of it, are not capable of direct oxidation, and are therefore not affected by atmospheric influences. Petrolatum contains hydrocarbons of the paraffin series, like $C_{16}H_{34}$, $C_{17}H_{36}$, $C_{18}H_{38}$, etc., up probably to $C_{32}H_{66}$, together with hydrocarbons of the olefine series, $C_{16}H_{32}$, $C_{17}H_{34}$, etc. These latter are less concrete than the corresponding paraffin hydrocarbons, and give petrolatum its oleaginous characters.

Description and Physical Properties.—" An unctuous mass, varying in color from yellowish to light amber. It has not more than a slight fluorescence even after being melted, and is transparent in thin layers. It is free or nearly free from odor and taste. Petrolatum is insoluble in water; almost insoluble in cold or hot alcohol, and in cold dehydrated alcohol. It is freely soluble in benzene, carbon disulphide, chloroform, and oil of turpentine. It is soluble in ether, petroleum benzin, and in most fixed or volatile oils, the degree of solubility in these solvents varying with the composition of the Petrolatum.

" Specific gravity: 0.820 to 0.865 at 60° C. It melts between 38° and 54° C. Heat 2 Gm. of Petrolatum in an open porcelain or platinum dish over a Bunsen flame: it volatilizes without emitting an acrid odor, and on incineration leaves not more than 0.05 per cent. of ash. Shake melted Petrolatum with an equal volume of hot distilled water: the latter remains neutral to litmus paper (*acids or alkalies*). Digest 10 Gm. of Petrolatum, at 100° C., with 10 Gm. of sodium hydroxide and 50 cc. of distilled water for half an hour, then separate the aqueous layer, and supersaturate it with sulphuric acid: no oily or solid substance separates (*fixed oils, fats, or rosin*)." *U. S.*

" White or yellow, translucent, soft, unctuous to the touch, not allowing any liquid to separate on keeping. No odor. Melting point 42° to 46° C. On heating to 80° C. no unpleasant odor is evolved. 10 millilitres of *alcohol* (90 per cent.) boiled with 5 grammes of Soft Paraffin are not acid to *litmus.* When 10 grammes are boiled with 20 millilitres of *solution of sodium hydroxide* for ten minutes and allowed to separate, the aqueous layer yields no precipitate or oily matter when acidified with *sulphuric acid* (absence of fixed oils, fats, and resin). 5 grammes when heated burn with a luminous flame, leaving no appreciable ash." *Br.*

As it is found in the market, petrolatum varies in color, odor, and melting point. The statement frequently made by the manufacturers that it is unalterable in the air is incorrect, as we have frequently noticed that exposure to light and air causes it to assume a disagreeable odor resembling that of crude petroleum. It has been observed to have at times irritating properties. These may be due to imperfect removal of the sulphuric acid or similar agents used, but are more probably caused by rancidity or decomposition.

Uses.—Petrolatum is used almost exclusively as a bland, neutral, protective dressing and as a substitute for the true fats in ointments. For local applications it has the advantage over the fats that it does not so readily become rancid. It is not suited, however, for the preparation of ointments when absorption is desired, for it does not readily penetrate the skin. Although it was at one time suggested as a substitute for butter and animal fats for culinary purposes it has absolutely no food value. Randolph (*T. G.*, 1885, ix, p. 732) appears to have been the first to demonstrate its non-absorbability from the intestinal tract, and Robinson (*M. News*, 1900, lxxvii, p. 56) recovered the entire amount of liquid petrolatum from the feces which was administered by mouth. Randolph also showed that when taken internally, in doses of from one to four drachms (3.9–15.5 Gm.), it acts as a feeble laxative and soothes irritation, so as to be advantageous in inflammations of the gastro-intestinal mucous membrane. (See *Petrolatum Liquidum.*)

Off. Prep.—Unguentum Paraffini, *Br.;* Emulsum Petrolati, *N. F.;* also used as base for several ointments.

PETROLATUM ALBUM. U. S.

WHITE PETROLATUM Petrolat. Alb. [White Petroleum Jelly]

" Petrolatum wholly or nearly decolorized." *U. S.*

In the manufacture of petrolatum, as described in the previous article, the final step is partial decolorization by means of animal charcoal; by carrying this decolorization somewhat further the product may be obtained almost water white. This is the substance which is officially known as *Petrolatum Album.*

An imitation of this ointment base, made by melting together paraffin and white liquid petrolatum has appeared on the market under various descriptive names, such as *snow white mineral jelly,* etc., is extensively used in preparing petrolatum cold creams, but usually separates some of the liquid portion when the attempt is made to incorporate other ingredients by rubbing. This manufactured product is opalescent and usually granular in appearance and is excluded by the official description.

Description and Physical Properties.—"White Petrolatum is a white or faintly yellowish unctuous mass, transparent in thin layers even after cooling to 0° C.

"In other respects White Petrolatum has the characteristics of and responds to the tests for identity and purity under *Petrolatum.*" *U. S.*

Uses.—See *Petrolatum.*

PETROLATUM LIQUIDUM. U. S. (Br.)

LIQUID PETROLATUM Petrolat. Liq. [Liquid Paraffin, White Mineral Oil, Paraffin Oil]

"Liquid Petrolatum is a mixture of liquid hydrocarbons obtained from petroleum." *U. S.* "Liquid Paraffin is a mixture of liquid hydrocarbons." *Br.*

Paraffinum Liquidum, *Br.;* Liquid Paraffin; Vaselinum Liquidum; Oleum Paraffinæ; Paraffine liquide, Huile de Paraffine, *Fr.;* Flüssiges Paraffin, Paraffinöl, *G.;* Aceite de parafina, *Sp.*

Preparation.—*Liquid petrolatum* is made by distilling the residuary liquid boiling between 330° and 390° C., obtained after removing the lighter hydrocarbons from petroleum. It is purified and decolorized by first treating it with sulphuric acid and then with caustic soda and passing it while hot, through animal charcoal. By cooling, some solid paraffins will separate; the liquid is then redistilled, and the portion boiling below 360° C., rejected.

Description and Physical Properties.—"*Heavy Liquid Petrolatum.*—Heavy Liquid Petrolatum has a kinematic viscosity of not less than 0.381 at 37.8° C.

"*Light Liquid Petrolatum.*—Light Liquid Petrolatum has a kinematic viscosity of not more than 0.370 at 37.8° C. Each variety conforms to the following description and tests:

"A colorless, transparent, oily liquid, free, or nearly free, from fluorescence. It is insoluble in water and in alcohol; soluble in ether, chloroform, petroleum benzin, and in fixed or volatile oils. Camphor, menthol, thymol, and many similar substances are soluble in Liquid Petrolatum.

"Specific gravity: 0.828 to 0.905 at 25° C.

"Liquid Petrolatum is odorless and tasteless when cold, and develops not more than a faint petroleum odor when heated. When cooled to 0° C., Liquid Petrolatum does not become more than opalescent (*solid paraffins*). Boil 10 cc. of Liquid Petrolatum with an equal volume of alcohol: the alcohol remains neutral to moistened litmus paper (*acid or alkali*). Pour 5 cc. of Liquid Petrolatum and 5 cc. of colorless sulphuric acid into a glass-stoppered cylinder, which has been previously rinsed with sulphuric acid, and heat in a water-bath for ten minutes, shaking the mixture well at intervals of thirty seconds: the oil remains unchanged in color and the acid does not become darker than pale amber (*carbonizable substances*). Prepare a saturated solution of lead monoxide in an aqueous solution of sodium hydroxide (1 in 5), and mix 2 drops of the clear solution with 4 cc. of Liquid Petrolatum and 2 cc. of dehydrated alcohol: the mixture does not darken after heating at 70° C. for ten minutes and cooling (*sulphur compounds*).

"Preserve in well-closed containers, protected from light." *U. S.*

In the U. S. P. IX two kinds of Liquid Petrolatum were introduced, one being called "heavy," the other "light." The degree of viscosity is the determining factor. For atomizing purposes light liquid petrolatum is used and as a laxative heavy liquid petrolatum is preferred.

The British Pharmacopœia describes it as "transparent, colorless, not fluorescent. No odor or taste. Specific gravity 0.860 to 0.890. A mixture of 4 millilitres of Liquid Paraffin, 2 millilitres of *absolute alcohol,* and 2 drops of a clear saturated solution of *lead oxide* in *solution of sodium hydroxide,* remains colorless when kept at 70° C. for ten minutes (absence of sulphur compounds). When 3 millilitres are heated with an equal volume of *sulphuric acid* in a test-tube placed in boiling *water* for ten minutes, and frequently shaken, the acid layer, after separation, is not darker than pale-brown. 10 millilitres of *alcohol* (90 per cent.) boiled with 5 millilitres of Liquid Paraffin are not acid to *litmus.*" *Br.*

Uses.—Liquid petrolatum is used chiefly for one of two purposes. The first of these is as a demulcent upon the mucous membrane of the upper respiratory tract in acute *coryza, pharyngitis,* and *laryngitis.* It is usually applied by atomization but is sometimes dropped directly into the nostril. It has also been recommended as a dressing for *wounds* and *ulcers.* Chrysopathes (*Cb. Chir.,* 1913, p. 1739) believes that it has an antiseptic effect, but it is more probable that its beneficial action is due to the exclusion of air.

Although vaseline was recommended many years ago by Randolph for its laxative effect, it was not used to any large extent until in 1913 Lane (*B. M. J.,* 1913, ii, p. 1126) introduced the use of the heavy Russian liquid petrolatum in the treatment of *chronic constipation.* Since this time it has become a favorite remedy for this purpose. Its action is purely mechanical rendering the feces soft and perhaps lubricating the bowel. There is a wide-spread belief among the medical profession that where used as a laxative the more viscid petrolatums are preferable. In a comparative study, however, of both the Russian and American oils ranging in specific gravity from 0.857 to 0.885, carried out by eight of the most prominent clinicians in the United States under the auspices of the Council on Pharmacy and Chemistry of the American Medical Association (*J. A. M. A.*, 1915, lxiv, p. 808), the conclusion was reached that as far as the therapeutic results, either as regards the quantity required or the liability to leakage around the anus or other disagreeable effects, there is no difference in the effects of the heavy or light oils. The ordinary quantity required varied from one-half to three ounces, and the effects were the same whether taken in one or three doses. The use of liquid petrolatum hypodermically is a dangerous procedure. Mook and Wander (*J. A. M. A.*, 1919, lxxiii, 1340) report a series of inflamed tumors following the subcutaneous injection of a solution of camphor in liquid petrolatum and point out that fatal emboli have followed the injection of suspensions of mercury in petrolatum.

A formula for an emulsion of liquid petrolatum was contributed by Miles Shimer (*Proc. P. Ph. A.*, 1916, p. 298), as follows: Soft petrolatum, 40 Gm.; white mineral oil, 200 Gm.; powdered acacia, 60 Gm.; syrup, 50 cc.; rum (Jamaica), 50 cc.; water, q. s. ad., 500 cc.

The number of fancy names which have been applied to proprietary brands of liquid petrolatum has become a crying evil. The following are some of the common names and special brands of liquid petrolatum: Adepsine oil, American oil, amilee, atoleine, atolin, bakurol, blandine, crysmalin, deeline, glyco, glycoline, glymol, heavy petroleum oil, interol, lilyolene, liquid abolene, liquid cosmoline, liquid fossiline, liquid geoline, liquid paraffin, liquid petrolatum, liquid saxoline, liquid vaseline, mineral glycerin, mineral oil, minol, muthol, neutralol, nujol, olo, paraffin oil, paroline, petralol, petro, petrolax, petrolia, petronol, petrosio, rock oil, Russian liquid petrolatum, Russian mineral oil, Russian paraffin oil, russol, seneprolin, saxol, stanolax, stanolind, terraline, terralbolia, usoline, water-white mineral oil, white liquid vaseline, white paraffin oil, whiteruss.

Dose, three to six fluidrachms (11–22 cc.).

Off. Prep.—Nebula Aromatica, *N. F.;* Nebula Eucalyptolis, *N. F.;* Nebula Mentholis, *N. F.;* Nebula Mentholis Composita, *N. F.;* Nebula Thymolis, *N. F.*

PHENOBARBITALUM. U. S.

PHENOBARBITAL Phenobarb. [Phenylethylmalonylurea]

"Phenylethyl barbituric acid [$CO(NH.CO)_2C(C_2H_5)(C_6H_5)$]." *U. S.*

This drug differs in its chemical composition from barbital in that one of the ethyl groups has been replaced by a phenyl group. It was originally introduced under the trade name of *luminal*. The sodium salt, *luminal sodium*, is also upon the market and differs in being freely soluble in water.

Phenylethyl barbituric acid is prepared by condensing phenylethyl malonic acid derivatives and urea, or urea compounds, from cyanoacetic acid. The derivatives of the parent acid may be esters, amides, chlorides, nitriles, etc. The condensation may be carried out with urea or its thio, or alkyl derivatives, or with guanidine derivatives.

Description and Physical Properties.—"White, glistening, small crystals, or a white, crystalline powder. It is odorless, and is stable in the air. One Gm. of Phenobarbital is soluble in about 1000 cc. of water, 8 cc. of alcohol, 40 cc. of chloroform, 13 cc. of ether, and in about 700 cc. of benzene, at 25° C. It is soluble in solutions of alkali hydroxides and of alkali carbonates.

"Phenobarbital melts between 172° and 174° C. A saturated aqueous solution of Phenobarbital is acid to litmus paper. Boil about 0.2 Gm. of Phenobarbital with 5 cc. of a 25 per cent. sodium hydroxide solution: ammonia is evolved. Shake about 0.3 Gm. of Phenobarbital for two minutes with 1 cc. of normal sodium hydroxide and 5 cc. of distilled water, filter, and divide the filtrate into 2 portions. To 1 portion add mercuric chloride T.S.: a white precipitate is produced. To the other portion add silver nitrate T.S. a few drops at a time: a white precipitate is produced which at first redissolves but becomes insoluble when an excess of silver nitrate has been added.

"The ash from 0.5 Gm. is negligible. A solution of 0.2 Gm. of Phenobarbital in 2 cc. of sulphuric acid is colorless or only faintly yellow (*readily carbonizable substances*). Boil 2 Gm. of Phenobarbital with 10 cc. of alcohol under a reflux condenser during three minutes: a clear and complete solution results (*phenylbarbituric acid*)." *U. S.*

Uses.—Phenobarbital was originally introduced as a hypnotic for nervous *insomnia* and as a general nerve sedative, but has become of importance chiefly through its use in the treatment of *epilepsy*. Its effects in this disease appear to be, like those of the bromides, merely repressant and not truly curative. While it is undoubtedly of value in reducing the number of convulsions, especially where for any reason the bromides are unsuited, there is no evidence of any permanent curative effect.

According to Gruber and Baskett, large doses of phenobarbital have a marked depressant action on the circulation; they have observed falls of blood pressure of from 10 to 80 per cent.

Although when properly employed phenobarbital is a reasonably safe remedy, there have been a considerable number of cases of more or less serious toxic action, at least one of which ended fatally; Phillips (*J. A. M. A.*, 1922, lxxviii, p. 1199) has collected references to sixteen cases of poisoning. In his own patient, eight doses of 1½ grains taken daily for eight days, produced a violent morbilliform eruption accompanied with high fever and some irritation of the kidneys. Although amaurosis, mental confusion, ataxia and aphasia have been reported in isolated cases, in the majority of instances the symptoms have been of the type just described. In a number of instances quantities of 0.3 Gm. (four and one-half grains) in twenty-four hours have produced active poisoning. Phillips concludes that the single dose should never exceed 0.1 Gm. nor the daily dose 0.2 Gm.

Dose, one-half to three grains (0.03–0.2 Gm.).

PHENOL. U. S. (Br.)

PHENOL [Carbolic Acid]

"Phenol contains not less than 98 per cent. of C_6H_5OH." *U. S.* "Phenol, C_6H_6O, commonly termed carbolic acid, may be obtained from coal-tar oil." *Br.*

Acidum Carbolicum, *Br.*, also *U. S.* 1890; Acidum Phenicum; Acidum Phenylicum Crystallisatum; Phenic Acid, Phenylic Acid, Phenylic Alcohol, Phenic Alcohol, Benzophenol; Phénol, Acide carbolique, Acide Phénique, Hydrate de Phényle, *Fr.;* Acidum carbolicum, *P. G.;* Karbolsaure, Phenylsaure, Phenylalkohol, *G.;* Fenolo cristallizzato, Acido carbolico, *It.;* Acido fenico, *Sp.*

This important medicine was discovered in 1834, in the tar of coal, by Runge, who gave it the name of carbolic acid. When on the subject of its composition, we shall have occasion to show that, although more closely related chemically with the alcohols than the acids, it belongs to a peculiar class known in common as *phenols.* The U. S. P. (8th Rev.) dropped the names of Acidum Carbolicum and carbolic acid and adopted the correct title of Phenol for this substance. The British Pharmacopœia recognizes the name Acidum Carbolicum, but uses "phenol" as the English name for this substance.

Preparation.—For the commercial preparation of phenol the light oil fraction, from the distillation of coal-tar, is collected until a sample of the oil that runs from the still sinks in water. This fraction, with a sp. gr. of from 0.94 to 0.99, boils between 90° and 250° C. and contains from 4 to 10 per cent. of acids, and nearly all the true phenol which boils at 182° C. The oil from which the phenol is to be extracted is agitated with a weak solution of sodium hydroxide, 10 per cent. strength being strong enough. If a stronger solution is used many impurities, like naphthalene, are dissolved and contaminate the finished product. After agitation, the mixture, on standing, separates into two layers, the upper consisting of the extracted oil and the lower the solution of sodium phenolate. To this solution, after separation from the oily layer, an amount of hydrochloric or diluted sulphuric acid calculated from a special test with a small portion, as just sufficient, is then added in order to set the phenol free. It separates as an oily layer upon the surface, and, after being washed with a saturated solution of sodium chloride, is dried over calcium chloride and again distilled. The product thus obtained crystallizes out largely on a cooled surface, and, after removing the crystals from adhering liquid, and drying them by pressure, they are again submitted to the same process of distillation. Only by such a detailed procedure can phenol be separated from its homologues, like cresol (cresylic acid), $C_6H_4(CH_3)OH$, which accompany it, smell much like it, and boil between 185° C. and 200° C.

The unpurified liquors were formerly sold sometimes under the improper name of *coal tar creosote.* They were recognized in the U. S. Pharmacopœia, 1890 (*Acidum Carbolicum Crudum*), which was officially described as "a nearly colorless, or reddish, or brownish-red liquid, of a strongly empyreumatic and creosote-like odor; having a benumbing, blanching, and caustic effect upon the skin or mucous membrane; and gradually turning darker on exposure to air and light. The aqueous solution of Crude Carbolic Acid has a slightly acid reaction on litmus paper. In an aqueous solution of the Acid, bromine water produces a white precipitate. Crude Carbolic Acid should not be soluble in less than 15 parts of water at 15° C., and the aqueous solution should not have an alkaline reaction (absence of *alkalies*). If 50 volumes of the Acid be thoroughly agitated with 950 volumes of water, in a capacious vessel, on allowing the mixture to separate, the undissolved portion should not exceed 5 volumes, or 10 per cent. by volume of the acid (limit of other *less soluble constituents of coal-tar*)." *U. S.*, 1890. It is superior in germicidal power to pure phenol. (See *Cresol.*)

Phenol may be made synthetically in one of two ways—either from benzene, which is converted into *benzene-sulphonic acid,* the sodium salt of which is then fused with an excess of sodium hydroxide, producing sodium phenolate and sodium sulphite, from which, on the addition of sulphuric or hydrochloric acid, the phenol separates and may be distilled off; or a pure aniline oil is taken, neutralized with sulphuric acid, and to the acid solution sodium nitrite is added. The nitrous acid liberated forms at first *diazobenzene sulphate,* but this at once decomposes into phenol, sulphuric acid, and nitrogen, the reactions being as follows:

$$(C_6H_5NH_2)_2H_2SO_4 + 2HNO_2 = (C_6H_5N{=}N)_2SO_4 + 4H_2O$$

$$(C_6H_5N{=}N)_2SO_4 + 2H_2O = 2C_6H_5OH + H_2SO_4 + 4N$$

The practicability of manufacture of synthetic phenol by the above process was made possible by the great increase in price soon after the beginning of the European war. It is made in America by a number of manufacturing firms.

Description and Physical Properties.—Phenol, in its pure state, is a solid at ordinary temperatures, crystallizing in minute plates or long rhomboidal needles, white or colorless, of a peculiar odor recalling that of creosote, and an acrid burning taste. Its sp. gr. is 1.065. (Lemaire.) It is likely to become colored pinkish or brown under the influence of light and air. This reddening has been ascribed to various causes, such as ammonia and ammonium nitrite in the air, rust spots in tinned iron vessels, alkali in glass vessels, organic matter, etc. It is said to be due to oxidation; stannous chloride solution acquires a green color when shaken with the red colored phenol. Demant recommends the removal of the red color by adding to 89 parts of the melted substance 11 parts of alcohol, subjecting the mixture to freezing, and then draining off the portion remaining liquid. Perfectly white crystals can be thus obtained. A slight discoloration does not interfere with any of the medicinal uses of phenol. Phenol deliquesces on exposure, and becomes liquid, and the presence of water in the smallest proportion causes it to liquefy. It is customary to add 10 per cent. of water or glycerin to phenol for dispensing, as it is more convenient to use in a liquid form. Such a form is official (see *Phenol Liquefactum*). Its solution in glycerin is very useful, as the glycerite mixes with water very readily. (See *Glyceritum Phenolis.*) When diluted it has a sweetish taste with a slightly nauseating after-taste, and a faintly acid reaction. Although commonly called carbolic acid, its claims to be considered as an acid are very feeble; while it combines with salifiable bases, it is incapable of neutralizing the alkalies, and does not affect the color of litmus. Although it combines feebly with some bases, its salts are decomposed by carbon dioxide, and those with the alkalies have an alkaline reaction. The potassium phenolate is said to be decomposed even by water. Nitric acid converts it into picric acid, for the manufacture of which it is largely used. It reduces many metallic salts, especially those of silver and copper, and coagulates collodion. Shaken in the liquid form with one-fourth of water, and cooled at 4.5° C., it crystallizes in the form of a hydrate, $C_6H_5.OH + H_2O$, which fuses at 17° C.

" Colorless, interlaced, or separate needle-shaped crystals, or a white or light pink, crystalline mass. It has a characteristic, somewhat aromatic odor. When undiluted it cauterizes and whitens the skin and mucous membrane. One Gm. of Phenol is soluble in about 15 cc. of water at 25° C. It is very soluble in alcohol, glycerin, chloroform, ether, carbon disulphide, and in fixed or volatile oils. Soluble in petrolatum and in liquid petrolatum. When gently heated phenol melts, forming a highly refractive liquid. It is also liquefied by the addition of about 8 per cent. of water. Its vapor is inflammable.

" Congealing point: not below 39° C. Its aqueous solution yields with bromine water a white precipitate of tribromphenol, which at first redissolves, but becomes permanent as more of the reagent is added. Add 1 drop of ferric chloride T.S. to 10 cc. of an aqueous solution of Phenol (1 or 100): the liquid acquires a violet-blue color.

" An aqueous solution of Phenol (1 in 15) is clear, and neutral or only faintly acid to litmus paper. Heat about 5 Gm. of Phenol on a water bath: it is volatilized without leaving more than 0.05 per cent. of residue.

" Preserve in well-closed containers, protected from light." *U. S.*

" Small, colorless, deliquescent crystals; odor peculiar but not fetid or tarry; taste sweetish, pungent. Has a caustic action on skin and mucous membrane. Freely soluble in *alcohol* (90 per cent.), in *ether, chloroform, glycerin,* in the fixed and volatile oils, and in solutions of alkalies. Exposed to moist air it may acquire a pinkish tinge. At 15.5° C., 100 parts of Phenol are liquefied by the addition of 10 parts of *water,* form a clear liquid with 30 to 40 parts of *water,* and are completely dissolved by 1200 parts of *water.* The aqueous solution is clear and colorless. Melting point from 39° to 40° C.; boiling point not higher than 183° C. Specific gravity at the melting point 1.060 to 1.066. Phenol does not immediately redden *blue litmus paper.* Optically inactive. Coagulates *collodion* and *solution of albumen.* An aqueous solution of Phenol becomes deep purple with *T. Sol. of ferric chloride;* yields a white precipitate with excess of *solutions of bromine;* and when mixed with one-fourth of its volume of *solution of ammonia,* and then with a few drops of *solution of chlorinated soda,* becomes blue after a time, or immediately on gently heating. One volume of Phenol liquefied by the addition of 10 per cent. of *water,* forms with 1 volume of *glycerin* a clear liquid which is not rendered turbid by the addition of 3 volumes of *water* (absence of cresol). Evaporated on a water-bath it leaves not more than 0.1 per cent. of residue." *Br.*

Its solubility in water increases on heating the water; at 84° C. both liquids are miscible in all proportions. Its solution is, if pure, colorless, and remains so, but, if impure, is colored brownish by exposure. It is but slightly soluble in cold petroleum benzin.

Assay.—" Dissolve about 1.5 Gm. of Phenol, accurately weighed, in sufficient distilled water to make 1000 cc. Transfer an aliquot portion of this solution, containing from 0.038 to 0.041 Gm. of Phenol, to a 500 cc. glass-stoppered flask having a long, narrow neck, add 30 cc. of tenth-normal bromine, then 5 cc. of hydrochloric acid, and immediately insert the stopper. Shake the flask repeatedly during half an hour, allow it to stand for fifteen minutes, remove the stopper just sufficiently to introduce quickly 5 cc. of an aqueous solution of potassium iodide (1 in 5), being careful that no bromine vapor escapes, and at once stopper the flask. Shake the latter thoroughly, remove the stopper, and rinse it and the neck of the flask with a little distilled water, so that the washings may flow into the flask, then add 1 cc. of chloroform, shake the mixture well, and titrate with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each cc. of tenth-normal bromine corresponds to 0.001568 Gm. of C_6H_5OH." *U. S.*

For other methods of assaying Phenol, see *Chem News,* 1891, 74; *A. J. P.,* 1892, 164; *Ph. Centralh.,* 1892, 479; *D. C.,* 1896, 158; *A. J. P.,* 1898, 369.

The substances with which phenol is most likely to be confounded are cresol or cresylic acid and creosote, the former, like it, extracted from coal tar, the latter from wood tar exclusively. As cresol is incapable of crystallizing at ordinary temperatures, the two cannot be confounded in the solid state, and, as before observed, its presence in the liquid state is of little consequence, as its virtues are of the same kind, and at least equal. Its boiling point, however, is considerably higher than that of phenol, being about 204° C., and it may, therefore, be supposed to be present in any suspected liquid which will not crystallize at any common temperature, or boil under 202° C. to 204° C. It is also distinguished by being less soluble in water, ammonia water, glycerin, and solution of sodium hydroxide than is the case with phenol, but it is more soluble in petroleum benzin. Creosote is distinguished by its lower density, its liquid form, and its higher boiling point; by its insolubility in strong ammonia water, or in 6 per cent. sodium hydroxide solution, as well as its insolubility in pure glycerin (see *Creosotum*); by not coagulating collodion and albumin; and by the different effects on it of strong nitric acid, which with phenol produces pure picric or trinitrophenic acid, and with creosote, oxalic acid, resinous matter, and but a small portion of picric acid. Phenol differs also in having no effect on polarized light.

The commercial antiseptic preparations alleged to contain phenol often contain cresol and also nearly inactive and valueless neutral tar oils, and it is important to be able to determine the percentage of these different classes of constituents in a commercial sample. John Muter (*A. J. P.,* Nov., 1887, p. 581) has worked out a simple method for this, based upon the following four observed facts: (1) Phenol, cresol, and their homologues are completely soluble when shaken up with a 5 per cent. solution of sodium hydroxide; (2) Liquefied phenol and the corresponding cresol are insoluble in a saturated solution of chloride; (3) In the presence of a sufficient excess of alkali even a largely diluted solution may be boiled down without the slightest appreciable loss of phenol or cresol; (4) Tar oils and naphthalene are only very slightly dissolved by alkali, and may be perfectly removed from the solution by agitating it with benzene.

Uses.—Pure phenol is locally irritant, anesthetic and mildly caustic. When applied undiluted to the skin or mucous membrane it causes a sharp pain, followed by numbness, and accompanied by a whiteness and corrugation of the surface due to precipitation of albumen. In dilute solution, up to 3 or 4 per cent., it is only mildly irritant but is actively anesthetic and germicidal. In appropriate strengths phenol is a rapid and certain destroyer of the vegetative forms of bacteria, but against the more resistant spores it is comparatively useless. An 1 per cent. solution will destroy non-sporulating micro-organisms after sufficiently prolonged exposure, and a 2 per cent. solution promptly. On the other hand, the anthrax spores are not killed with certainty even after twenty-four hours' exposure to a 5 per cent. solution. It is antiseptic—that is, inhibits the multiplication of bacteria—when present in the proportion of about 1 to 800. Its peculiar value as a germicide is due largely to the fact that its activity is but slightly diminished by the presence of albuminous material. Although in sufficient concentration phenol precipitates albumen, it does not do so by forming chemical union with it, as does bichloride of mercury, but by changing the character of the solvent; the precipitation is analogous to that which takes place when water is added to an alcoholic solution of resin. Partly because of the wide-spread familiarity with phenol and partly for certain technical reasons it has been adopted by the United States Government as a standard for comparison of disinfectant power. The *phenol coefficient* of the United States Government (*Hygienic Lab. Bulletin* No. 82, April, 1912) represents the amount of phenol required to exercise the same degree of germicidal action against the typhoid bacillus, under certain standard conditions of testing, as one part of the disinfectant to be tested; for instance, if disinfectant X has a phenol coefficient of 2 that means that it would require 2 parts of phenol to equal one of X, or in popular parlance that X is twice as strong as phenol; a phenol coefficient of 0.5 means that the disinfectant is only one-half as active as phenol.

There has been much theorizing concerning the effects of various solvents on the germicidal power of phenol. McMaster has shown that while a solution of phenol in vegetable oil is almost without germicidal power, a 1 per cent. solution in liquid petrolatum is very active. Wilbert (*U. S. Pub. H. Rep.,* April 28th, 1916) finds that the presence of alcohol or glycerin does not lessen the germicidal effects of aqueous solutions.

Phenol is widely used as a disinfectant not only for sanitary but for surgical and medical purposes. For the disinfection of the surgeon's hands its local anesthetic action is a great disadvantage and its uncertain effect upon sporulating organisms almost excludes its use for the disinfecting of surgical instruments. As a dressing for *wounds* it is, however, very widely employed. In *burns* and other painful *ulcerations* its local anesthetic action often makes it peculiarly valuable. When applied continuously for several days it in some way interferes with the nutrition of the part, and a number of cases of local gangrene have followed the use of phenol dressings. Chlunsky (*Cb. I. M.,* 1912, p. 226) asserts that the addition of camphor lessens the caustic action of phenol and has employed a mixture containing 30 parts of phenol, 60 of camphor, and 10 of alcohol, as a local application in the treatment of *erysipelas.* This *phenol-camphor* (which is also known under the name of *kamphenol* and *erypol*), has also been used by a number of surgeons as a local application to infected wounds, furuncles, and as an injection into *cold abscesses,* with asserted excellent results. According to Horowitz (*D. M. W.,* 1913) the diminution of the corrosive action of the phenol is due to the action of the alcohol rather than to the camphor. Phenol is also used to a large extent in the form of oily or watery solutions in the treatment of *coryza, stomatitis,* and other infected conditions of the mucous membranes.

For ordinary surgical purposes it may be used in strengths of from 3 to 5 per cent. The liquid phenol is often applied undiluted as a germicide and caustic in badly infected wounds.

For burns and scalds 1 part of phenol in 6 parts of olive oil may be applied on lint. For the dressing of *cancerous* and other foul *ulcers,* a cerate (ten grains to the ounce) may be used. There is an official ointment.

Phenol is frequently employed as an antiseptic in various forms of gastro-intestinal affections. Because of the rapidity of its absorption as well as the relatively large dose which would be required, it is doubtful whether it exercises any efficient action in the intestines, but in fermentative *gastritis* it is often a useful remedy. It is also of service in *nervous vomiting,* and in *gastrodynia* for its local anesthetic action upon the mucous membrane of the stomach. Externally it is of much service as a local anesthetic in *urticaria, sunburn,* and other conditions attended with *itching* or burning of the skin.

In 1899, Baccelli reported very favorably on the hypodermic injection of phenol for the treatment of *tetanus* (see H. C. Wood, Jr., *M. A.,* 1899, i, p. 191). Although Courmont and Doyon (*Neurol. Centralbl,* 1899) in a research upon experimental tetanus in the lower animals, were unable to note any beneficial action, the method is still reported on favorably by various writers (see *J. A. M. A.,* 1915, lxiv, pp. 278, 1266, and 1918, lxxi, p. 2125).

The method consists in injecting hypodermically two or three cc. (30–45 minims) of a 2 per cent. solution every two or three hours, a total dose of 0.5 to 1.5 Gm. (eight to twenty-three grains) of phenol being given in the twenty-four hours.

Phenol Poisoning.—Because of the ease with which it is obtained and the rapidity and certainty of its effects, phenol is a very frequently used poison for suicidal purposes, and cases of accidental poisoning are also quite common. The symptoms usually develop very rapidly; indeed death has occurred in 2 or 3 minutes, the patient dying in immediate coma and collapse. After small amounts the symptoms are nausea and vomiting, collapse with pallor and cold sweats, feeble pulse, stupor deepening into complete insensibility and disturbances of the breathing, the respirations are usually hurried and shallow, often irregular and sometimes paroxysmally arrested. There is usually paralysis of both sensation and motion, but in some cases violent epileptiform convulsions have occurred. The urine is generally scanty and albuminous and of a greenish or blackish color. The diagnosis is usually not difficult, being made upon the odor, the smoky urine, and the presence of white corrugated spots in the mucous membrane of the mouth or throat. The ordinarily fatal dose of phenol is about half an ounce, but De Vries (*Th. M.,* 1890, iv, p. 644), has reported death in a woman from 22 grains. On the other hand, recovery has followed after the ingestion of an ounce. In the fatal cases death usually occurs in less than 2 hours from respiratory failure, although in some instances weakness of the heart has been the cause of the lethal termination.

In the treatment of carbolic acid poisoning the stomach should be immediately emptied, preferably by means of the stomach pump. There is no efficient chemical antidote known for phenol. Alcohol which is useful for the treatment of local injuries by carbolic acid, probably acts simply because being an excellent solvent it mechanically removes the poison; in the stomach, it may increase the absorption of the phenol and be harmful rather than beneficial. It was at one time supposed that the sulphates would unite with a poison to form innocuous phenol sulphonates. Although there is evidence that the sulphates may be useful in carbolic acid poisoning, their action is not a chemical one. Macht (*J. H. H. B.,* 1915, xxvi, p. 98) advises washing out the stomach with a strong solution of sodium sulphate. Isaacs (*Ohio State M. J.,* 1922, xviii, p. 558) recommends the following treatment: the stomach is washed out with three to six quarts of a 5 per cent. solution of sodium bicarbonate, afterwards from 60 to 120 cc. of a 50 per cent. solution of magnesium sulphate is left in the stomach. The urine is kept alkaline by the administration of bicarbonate and citrate of soda. Pain in the alimentary tract, due to the local caustic action of the drug, is relieved by the use of orthoform or occasionally morphine may be necessary. Stimulation by the use of caffein-sodium benzoate hypodermically, and by the external application of heat, is applied as necessary. The patient should be kept in bed until signs of hemorrhage and renal irritation have disappeared.

Dose, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Glyceritum Phenolis (from Liquefied Phenol), *U. S.* (*Br.*)*;* Phenol Liquefactum, *U. S.* (*Br.*)*;* Unguentum Phenolis (from Liquefied Phenol), *U. S.* (*Br.*)*;* Suppositoria Acidi Carbolici, *Br.;* Trochiscus Acidi Carbolici, *Br.;*

Aqua Phenolata (from Liquefied Phenol), *N. F.;* Liquor Iodi Phenolatus (from Liquefied Phenol), *N. F.;* Liquor Sodii Boratis Compositus (from Liquefied Phenol), *N. F.;* Nebula Aromatica, *N. F.;* Oleum Phenolatum, *N. F.;* Petroxolinum Phenolis, *N. F.;* Petroxolinum Phenolis Camphoratum, *N. F.;* Phenolum Iodatum, *N. F.;* Pulvis Antisepticus, *N. F.;* Odontalgicum, *N. F.*

PHENOL LIQUEFACTUM. U. S. (Br.)

LIQUEFIED PHENOL Phenol Liq. [Liquefied Carbolic Acid]

"Phenol liquefied by mixing with 10 per cent. of water. It contains not less than 88 per cent. of C_6H_5OH." *U. S.*

Acidum Carbolicum Liquefactum, *Br.;* Liquefied Carbolic Acid; Acidum carbolicum liquefactum, *P. G.;* Verflüssigte Karbolsäure, *G.;* Fenolo liquido, *It.;* Acido Fenico liquido, *Sp.*

"Phenol, a convenient quantity, distilled water, a sufficient quantity. Liquefy the phenol by placing the unstoppered container in a water bath and apply heat gradually until it is melted. Transfer the liquid to a tared vessel, weigh, and add 1 Gm. of distilled water for each 9 Gm. of phenol and mix thoroughly." *U. S.* "Phenol, 100 *grammes;* Distilled Water, sufficient to produce 115 *grammes.* Mix." *Br.*

Description and Physical Properties.—"A colorless liquid, which may develop a red tint upon keeping. It has a characteristic, somewhat aromatic odor. When undiluted it cauterizes and whitens the skin and mucous membrane. Liquefied Phenol is miscible with alcohol, ether, and glycerin. When diluted with an equal volume of glycerin, the mixture is miscible with water.

"Specific gravity: about 1.065 at 25° C. When subjected to distillation, the boiling point does not rise above 182° C. In other respects Liquefied Phenol responds to the tests for identity and purity under *Phenol,* omitting the congealing point.

"**Assay.**—Proceed as directed under *Phenol.*" *U. S.*

"NOTE.—When Phenol is to be mixed with collodion, fixed oils, liquid petrolatum, or petrolatum, use melted crystalline phenol instead of Liquefied Phenol.

"Preserve in well-closed containers, protected from light." *U. S.*

"A liquid, at first colorless, but usually acquiring a pinkish hue. Forms a clear solution on the addition of 12 to 20 per cent. by weight of *water* at 15.5° C. Specific gravity 1.067 to 1.069. Boiling point gradually rising to a temperature not higher than 183° C." *Br.*

For uses, etc., see under *Phenol.*

Dose, one to three minims (0.06–0.2 cc.)

Off. Prep.—Glyceritum Phenolis, *U. S.;* Unguentum Phenolis, *U. S.;* Aqua Phenolata, *N. F.;* Liquor Iodi Phenolatus, *N. F.;* Liquor Sodii Boratis Compositus, *N. F.*

PHENOLPHTHALEINUM. U. S., Br.

PHENOLPHTHALEIN Phenolphthal.

"$(C_6H_4OH)_2CO.C_6H_4CO$" *U. S.*

"Phenolphthalein, or dihydroxy-diphenylphthalide, $C_{20}H_{14}O_4$, may be obtained by heating phenol with phthalic anhydride and sulphuric acid, and purifying the product." *Br.*

Phenolphthalein is made by heating phenol, 10 parts, phthalic anhydride, 5 parts, and sulphuric acid, 4 parts, for a number of hours to 120° C. The sulphuric acid acts merely as a dehydrating agent and is subsequently removed by washing with water. The crude phenolphthalein is subsequently purified by dissolving in an alkali, precipitating with an acid and then dissolving in alcohol and decolorizing with animal charcoal. It may be recovered from the alcohol by evaporation or precipitated by diluting the solution with water. The reaction for its formation is as follows:

$$2C_6H_5OH + C_6H_4(CO)_2O = (C_6H_4OH)COC_6H_4CO + H_2O$$

Phenolphthalein has feebly acidic properties and is capable of uniting with metals to form salts. The salts so formed are soluble in water and of a deep red color. For this reason phenolphthalein is widely used in the detection and estimation of alkalies. (See *Phenolphthalein T.S.,* Part III.)

Description and Physical Properties.—"A white or faintly yellowish-white, crystalline powder. It is odorless, and is stable in the air. Phenolphthalein is almost insoluble in water. One Gm. is soluble in 13 cc. of alcohol, and in about 70 cc. of ether, at 25° C.

"Melting point not below 256° C. It is readily dissolved by solutions of alkali hydroxides and by hot solutions of alkali carbonates, yielding a red liquid. These solutions are decolorized by the addition of an excess of acid.

"Ash: not more than 0.05 per cent. A solution of 0.5 Gm. of Phenolphthalein in 30 cc. of neutral alcohol is colorless. One-half Gm. of Phenolphthalein dissolves completely in a mixture of 4 cc. of sodium hydroxide T.S. and 50 cc. of distilled water (*fluorane*). A mixture of 250 cc. of cold, recently boiled, distilled water and 0.5 cc. of a solution of Phenolphthalein (1 in 100) in alcohol, requires not more than 0.25 cc. of fiftieth-normal sodium hydroxide to produce a pink color. Heat 0.5 Gm. of Phenolphthalein with 10 cc. of diluted hydrochloric acid on a water bath for five minutes, filter, and evaporate the filtrate to dryness. The residue dissolved in 25 cc. of distilled water, slightly acidulated with hydrochloric acid, meets the requirements of the test for *heavy metals,* Heat a crucible to redness, and introduce, in small portions, an intimate mixture of 0.2 Gm. of Phenolphthalein, 0.5 Gm. of potassium nitrate, and about 0.3 Gm. of anhydrous sodium carbonate. Maintain a red heat until the reaction ceases, then boil the cooled residue for five minutes with 10 cc. of diluted sulphuric acid, filter, and wash the undissolved residue with 10 cc. of distilled water. Evaporate the filtrate and washings until sulphuric acid vapors begin to evolve. The residue dissolved in 5 cc. of distilled water conforms to the requirements of the test for *arsenic*." *U. S.*

"A white, or yellowish-white, crystalline or amorphous powder. No odor or taste. Soluble in *alcohol* (90 per cent.), the solution being colorless. Almost insoluble in *water*, but soluble in *solution of sodium hydroxide*, forming an intensely red liquid. Melting point 250° to 253° C. Not more than 0.1 millilitre of *N/10 solution of sodium hydroxide* is required to produce a red coloration in 250 millilitres of recently boiled and cooled *water* to which has been added 0.5 millilitre of a solution (1 in 100) of Phenolphthalein in *alcohol* (60 per cent.). No appreciable ash." *Br.*

Uses.—The discovery that phenolphthalein possessed cathartic properties was made accidentally; it was used in Hungary as a means for the ready identification of artificial wines, and the observation that these wines were laxative led to an investigation of its properties. H. C. Wood, Jr. (*J. A. M. A.*, 1911, liv, p. 248), has found that it increases intestinal secretions, and that, when given intravenously to dogs in doses equivalent to 60 grains for a man, it produced no change in circulation or respiration. According to Berthomeau and Daguin (*Press Med.*, 1908, xvi, p. 378), the cathartic effects are due to combined stimulation of secretion and peristalsis. Although it seems to be slightly irritant to the kidneys when introduced into the blood stream, there is little danger of this action because of its slight absorbability by the bowel. It is not uncommon, however, for the urine of patients taking phenolphthalein to give a pinkish reaction with the alkalies.

Hydrick (*J. Bi. Chem.*, 1914, xvii) found albuminuria in every one of twenty experiments after the administration of 1 to 2 grain doses of phenolphthalein, but the results are so contrary to common experience that one is tempted to doubt the accuracy of his observations. Orland (*Med. Klin.*, 1913, p. 257) reported a case of a child aged three years who took 1.8 Gm. (27 grains) in the form of tablets with no more serious effect than violent purgation. The urine for four days showed the presence of phenolphthalein, but showed neither albumin nor sugar.

Several cases of dermatitis following the use of phenolphthalein as a laxative have been reported (see Corson and Sidlick, *J. A. M. A.*, 1922, lxxviii, 882).

Phenolphthalein is a mildly acting cathartic, usually requiring from 4 to 8 hours for catharsis, and producing large, soft discharges without much griping. Although when used continuously the alimentary canal seems to become accustomed to it, it is nevertheless useful as a variant from the vegetable laxatives in chronic as well as in the more occasional types of *constipation*. Phenolphthalein, in a more or less pure state, is the basis of a large number of proprietary aperients. Among these are: *Exlax, laxine, laxoin, laxatol, laxothalen, laxaphen, probilin, phenolax, phenalein, probilin, purgen, purgalax,* etc.

Dose, one-half to three grains (0.032–0.2 Gm.).

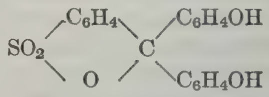
Off. Prep.—Tabellæ Phenolphthaleini, *N. F.*

PHENOLSULPHONPHTHALEINUM. U. S.

PHENOLSULPHONPHTHALEIN Phenolsulphonphthal. [Phenol Red]

"$(C_6H_4OH)_2CO.C_6H_4SO_2$." *U. S.*

This product of the reaction of phenol and sulphobenzoic acid anhydride differs from phenolphthalein in containing an SO_2 group in place of the CO group. It has the following structural formula:



The anhydride of o-sulphobenzoic acid is first prepared by distilling the free acid obtained from the acid ammonium salt with P_2O_5. The acid ammonium salt may be prepared from commercial saccharin. By the fusion of o-sulphobenzoic anhydride with phenol, the phenolsulphonphthalein is produced.

In neutral media, either aqueous or alcoholic it gives yellow solutions, but in the presence of alkalies it forms red solutions similar to those of phenolphthalein but usually not quite so purple.

Description and Physical Properties.—"A crystalline powder, varying in color from bright to dark red. It is stable in the air. One Gm. of Phenolsulphonphthalein is soluble in about 1300 cc. of water, 350 cc. of alcohol, and in 500 cc. of acetone. It is almost insoluble in chloroform and ether.

"It is readily soluble in solutions of alkali hydroxides and carbonates as well as in ammonia water, and in solutions of ammonium carbonate, with a color varying from deep red in concentrated solutions to a violet-tinted red in dilute solutions. The red color is changed to orange or yellow by a slight excess of acid. Its solution in alkali hydroxides is decolorized by warming with zinc dust.

"Dried to constant weight at 110° C., Phenolsulphonphthalein loses not more than 1 per cent. Ash: not more than 0.2 per cent. Fill a 100 cc. glass-stoppered flask with thoroughly boiled and cooled distilled water to within a few cc. of the stopper. Add 1 cc. of an alcoholic solution of Phenolsulphonphthalein (1 in 1000) and 0.5 cc. of fiftieth-normal sodium hydroxide, stopper immediately, and mix well: a strong red color is produced (*sensitiveness*). To about 1 Gm. of Phenolsulphonphthalein, accurately weighed, add a filtered solution of 0.5 Gm. of sodium bicarbonate in 20 cc. of distilled water. Rotate frequently during one hour, dilute to 100 cc., and let stand over night.

Filter through counterbalanced filters or a Gooch crucible, wash at first with 25 cc. of a 1 per cent. solution of sodium bicarbonate, then with 25 cc. of distilled water, and dry to constant weight at 110° C.: the weight of the insoluble residue does not exceed 0.2 per cent. Heat a crucible to redness, and introduce, in small portions, an intimate mixture of 0.2 Gm. of Phenolsulphonphthalein, about 0.5 Gm. of potassium nitrate, and about 0.3 Gm. of anhydrous sodium carbonate. Maintain a red heat until the reaction ceases, boil the cooled residue for five minutes with 10 cc. of diluted sulphuric acid, filter, and wash the undissolved residue with 10 cc. of distilled water. Evaporate the filtrate and washings until sulphuric acid vapors begin to evolve: the residue dissolved in 5 cc. of distilled water meets the requirements of the test for *arsenic.*" *U. S.*

Uses.—Phenolsulphonphthalein is used only as a diagnostic reagent. It was brought forward by Geraghty and Rowntree (*J. A. M. A.,* 1911, lvii, p. 811) as a test for the functional capacity of the kidney. The determination is carried out as follows: Half an hour after having drunk a glass of water the bladder is emptied and one-tenth of a grain (0.006 Gm.) of phenolsulphonphthalein dissolved, with the aid of small amount of sodium bicarbonate in fifteen minims (1.0 cc.) of water is injected intramuscularly. The urine may be collected either by having the patient micturate at the end of fifteen minutes or better by leaving a catheter in the bladder and allowing the urine to drain through the catheter into a vessel containing a drop of a 25 per cent. solution of sodium hydroxide until the appearance of a pinkish tint. This time is noted and the catheter withdrawn. Subsequently the urine is collected at one hour and two hours after the ingestion, and after this it is saved for twenty-four hours. The quantity of the dye in the urine is determined by alkalizing with sodium hydroxide, diluting accurately up to one liter and comparing the depth of color with a standard solution of phenolsulphonphthalein. Various instruments to facilitate this part of the test are on the market. In health the dye appears in the urine within five or ten minutes, about one-half of the dose is eliminated in the first hour and 75 or 80 per cent. in two hours. In cases of *nephritis* the elimination is more or less delayed according to the character of the lesion. While a normally rapid elimination may be accepted as conclusive evidence of the functional capacity of the kidneys, we believe that slight reductions in the rapidity of elimination should be interpreted with some conservatism. It may be remarked in this connection that the preservation of function is no proof that the kidney is perfectly healthy. It simply means that there is enough healthy kidney structure to perform the necessary eliminating functions of this organ.

Dose, one-tenth of a grain (0.006 Gm.).

PHENYLIS SALICYLAS. U. S. (Br.)

PHENYL SALICYLATE Phenyl. Salicyl. [Salol]

"$C_6H_4(OH)COOC_6H_5$ 1:2." *U. S.* "Salol, or phenyl salicylate, $C_{13}H_{10}O_3$, may be obtained by the interaction of salicylic acid and phenol." *Br.*

Salol, *Br., U. S.* 1890; Phenolum Salicylicum, *Fr. Cod.;* Salicylate de Phényle, *Fr.;* Phenylum salicylicum, *P. G.;* Phenylsalicylat, Salicylsaurephenylester, *G.;* Salol, *It.;* Salicilato de fenol, *Sp.*

Preparation.—Phenyl salicylate was first produced by Nencki, of Basel, and introduced to the medical profession by Sahli, of the same place. It is prepared by heating salicylic acid with phenol in the presence of phosphorus pentachloride or phosphorus oxychloride. According to Ernert, nearly the theoretical yield of phenyl salicylate may be obtained by heating salicylic acid to a temperature between 160° and 240° C., and preventing the access of air while water is being disengaged; it is probable that salicylic anhydride is formed, and the phenyl resulting from its decomposition combines with unaltered salicylic acid to produce phenyl salicylate according to the following reaction:

$$2C_6H_4OHCOOH = (C_6H_4OHCO)_2O + H_2O$$

Then

$$(C_6H_4OHCO)_2O = C_{13}H_{10}O_3 + CO_2$$

Description and Physical Properties.—"A white, crystalline powder, having an aromatic odor, and a characteristic taste. One Gm. of Phenyl Salicylate is soluble in 6670 cc. of water and in 6 cc. of alcohol, at 25° C. It is very soluble in chloroform, ether, benzene, and in fixed or volatile oils.

"It melts between 41° and 43° C. Heat about 0.3 Gm. of Phenyl Salicylate with 3 cc. of sodium hydroxide T.S. for a few minutes and then acidify the solution with hydrochloric acid: salicylic acid separates and the odor of phenol is recognizable. The addition of diluted ferric chloride T.S. to an alcoholic solution of the salt (1 in 20) produces a violet color.

"Phenyl Salicylate does not redden moistened blue litmus paper (*free acid*). Ash: not more than 0.05 per cent. Shake 1 Gm. of Phenyl Salicylate with 50 cc. of distilled water and filter the liquid: the addition of 1 drop of ferric chloride T.S. to 10 cc. of the filtrate produces no violet color (*uncombined phenol or salicylic acid*). Ten cc. portions of the filtrate prepared for the preceding test, when tested separately with barium nitrate T.S. and silver nitrate T.S., show no turbidity (*sulphate or chloride*).

"Preserve in well-closed containers, in a cool place." *U. S.*

"Colorless crystals, or crystalline powder. Aromatic odor; taste slight. Almost insoluble in *water;* soluble in 15 parts of *alcohol* (90 per cent.), in 0.3 part of *ether* or of *chloroform,* and in fixed and volatile oils. Melting point from 42° to 43° C. Alcoholic solution neutral to *litmus;* yields a white precipitate with *solution of bromine,* and a violet coloration with dilute *T. Sol. of ferric chloride.* When 0.2 gramme is boiled with 5 millilitres of *solution of sodium hydroxide,* and the cooled solution acidified with *hydrochloric acid,* the odor of phenol is developed and a crystalline precipitate is formed. *Water* which has been shaken with Salol is not affected by *T. Sol. of ferric chloride* (absence of free salicylic acid and of readily soluble salicylates), and yields no characteristic *reactions* for sulphates or chlorides. No appreciable ash." *Br.*

Uses.—In the small intestine phenyl salicylate is broken up by the pancreatic juice, and yields about thirty-six per cent. of phenol and sixty-four per cent. of salicylic acid. The completeness and rapidity of this action depend upon the amount of phenyl salicylate ingested and the alkalinity of the juice in the intestines. The change is, however, sufficient, when phenyl salicylate is freely given, for the production of salicylic acid intoxication, and for the blackening of the urine with educts from phenol. Because this change occurs in the intestines somewhat slowly, the remedy has been used as an internal antiseptic in the treatment of *enteritis* and *intestinal fermentation,* but its value is questionable. It has been largely used in *rheumatism* as a substitute for salicylic acid, but it is much less prompt and certain in its action than is that remedy. Moreover, on account of the large proportion of phenol which it contains, it is much more dangerous than the corresponding dose of salicylic acid. Hesselbach has shown that it is prone to affect the secreting structure of the kidneys, and two fatal cases of poisoning by it have been reported. (*L. L.,* May, 1891.) It is especially dangerous when the kidneys are diseased. Phenyl salicylate is used as a test of gastric motility, the time required for the appearance of salicylic acid in the urine depending largely upon the rapidity with which it passes out of the stomach. It has also been employed as a surgical dusting powder on the basis that it will be slowly decomposed by the wound secretions, liberating its antiseptic constituents.

Dose, from five to fifteen grains (0.3–1.0 Gm.).

PHOSPHORUS. U. S., Br.

PHOSPHORUS Phosphor.

"The yellow allotropic form of phosphorus [P]." *U. S.* "Phosphorus is a solid nonmetallic element. It may be obtained from calcium phosphate." *Br.*

Phosphore, *Fr. Cod.;* Phosphorus, *P. G.;* Phosphor, *G.;* Fosforo, *It., Sp.*

This non-metallic element was discovered in 1669 by Brandt, an alchemist of Hamburg, who obtained it from evaporated urine by a process which remained a secret until 1737. As thus procured, it was exceedingly scarce and costly. In 1769 the Swedish chemist Gahn discovered it in bones, and shortly afterwards published a process by which it might be extracted.

The process in brief consisted in digesting powdered calcined bones with sulphuric acid which changed the basic calcium phosphate into the acid phosphate. The latter by the action of heat was transformed into the metaphosphate $(CaPO_3)_2$ and this by heating in a retort, in the presence of charcoal, was decomposed, the phosphorus passing over as a distillate.

The manufacture of phosphorus by the use of the electric furnace, first brought out by Readman and Parker some years ago, has now practically displaced the older methods for the production of phosphorus. Albright and Wilson, who formerly manufactured phosphorus by the distillation method at Oldbury, England, have built works at Niagara Falls, and practically control the production by the electric furnace method in the United States and England. A mixture of calcium phosphate, carbon, and sand or kaolin is submitted to the temperature of the electric arc while packed in a covered plumbago crucible. The phosphorus is then distilled off in a current of an inert gas. It is very pure, and it is claimed that 86 per cent. is recovered. The native Redonda phosphate, an aluminum phosphate, is also taken for this process instead of the calcium phosphate, and phosphorus obtained from it without any previous purification. The great bulk of the phosphorus is consumed in the manufacture of matches, a smaller amount in the production of phosphor bronze, and another portion in making the chemical compounds of the element.

When perfectly pure it is colorless, but as usually prepared it is yellowish or reddish yellow. It is flexible, and when cut exhibits a waxy luster.

Description and Physical Properties.—"A translucent, nearly colorless solid, having a waxy luster, and a consistence at ordinary temperatures about that of beeswax. After long keeping the surface becomes white or red, and occasionally black. It has a distinctive and disagreeable odor. One Gm. of Phosphorus is soluble in about 400 cc. of dehydrated alcohol, in about 40 cc. of chloroform, 102 cc. of absolute ether, 31.5 cc. of benzene, and in 0.9 cc. of carbon disulphide, at 25° C. It is sparingly soluble in fixed oils, and is practically insoluble in water, to which it imparts its characteristic, disagreeable odor and taste. Specific gravity: about 1.830 at 10° C.

"When exposed to the air, Phosphorus emits white fumes, which are luminous in the dark, and have an odor somewhat resembling that of garlic. On longer exposure to the air, it often takes fire spontaneously.

"Add 1 Gm. of Phosphorus to 10 cc. of nitric acid diluted with 10 cc. of distilled water in a flask having a capacity of 50 cc. Digest the mixture at a gentle heat on a water bath until the Phosphorus is dissolved, maintaining an atmosphere of carbon dioxide in the flask during the heating. Transfer this solution to a dish, evaporate until nitrous vapors are no longer given off, and then dilute the solution to 250 cc. with distilled water. One cc. of this solution meets the requirements of the test for *arsenic.* A 50 cc. portion of the latter solution shows no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid.

"Preserve carefully under water, in strong, well-closed containers, in a secure and moderately cool place, protected from light." *U. S.*

"A semi-transparent, wax-like solid, which emits white vapors and is luminous in the dark when exposed to the air. Insoluble in *water;* soluble in 350 parts of *absolute alcohol,* in 80 parts of *olive oil,* in 80 parts of *ether,* in 25 parts of *chloroform,* and in 0.5 part of *carbon disulphide.* Soft and flexible at ordinary temperatures. Melting point 44° C. Ignites in the air at a temperature a little above its melting point, burns with a luminous flame and produces dense white fumes. 1 gramme is slowly attacked and finally dissolved without residue when boiled with 10 millilitres of *nitric acid* diluted with an equal volume of *water,* and the resulting solution yields not more than the slightest *reaction* for sulphates." *Br.*

Its pulverization may be readily effected by melting it in hot water, and agitating until it is thoroughly cooled; a finer powder is obtained with saline solutions than with pure water.

Phosphorus boils at 287.7° C., air being excluded. During its combustion it combines with the oxygen of the air, and forms phosphoric oxide. On account of its great inflammability, it must be kept under water. When exposed to the air it undergoes a slow combustion, emitting white vapors, which are luminous in the dark. It sometimes contains arsenic, and therefore, when used in forming medicinal preparations, should be tested for that metal. It occasionally contains antimony or sulphur, the latter rendering it brittle.

When phosphorus is kept in ordinary water it becomes covered with a whitish layer. This layer of *white phosphorus,* as it is sometimes called, appears to be due to partial oxidation by the free oxygen held in solution by the water. The change never takes place in water entirely deprived of air, and the water when it has taken place holds phosphorous acid in solution.

Schroetter, of Vienna, in 1845 discovered an allotropic form of phosphorus, which he called *red* or *amorphous phosphorus.* It is formed when ordinary phosphorus is kept long at a temperature between 215° C. and 250° C., in atmospheres which have no action on it, or in closed glass tubes. Red phosphorus is a reddish-brown powder having a sp. gr. of 2.19. It is insoluble in carbon disulphide and in all of the solvents in which ordinary phosphorus is soluble. In marked contrast to the affinity of yellow phosphorus for oxygen, it is practically permanent in the air although it does undergo slight oxidation after sufficiently long exposure. Solidified from the fused state, it is brittle, and breaks with a conchoidal fracture. Its hardness is considerable. Commercial red phosphorus usually contains more or less of the yellow form, from which it may be freed by carbon disulphide—which dissolves the ordinary variety and leaves the allotropic as a deep red amorphous powder—or by boiling in a solution of hydroxide—which dissolves the yellow phosphorus. It may also be purified by shaking it with a solution of calcium chloride of a density intermediate between that of red and that of ordinary phosphorus, and with a little carbon disulphide. The red variety will sink to the bottom, and the ordinary float on top of the solution, dissolved in the disulphide. (E. Nicklés.) Red phosphorus, when pure, is not poisonous and has, therefore, entirely replaced the poisonous yellow variety in the manufacture of friction matches. The use of the yellow for this purpose is legally forbidden in most civilized countries.

There are other allotropic modifications of phosphorus known but are of little practical interest and the reader is referred to works on chemistry.

Phosphorus forms with oxygen two oxides, *phosphoric,* P_2O_5, and *phosphorous,* P_2O_3. Corresponding to the first of these are three acids, known as *orthophosphoric* (tribasic phosphoric), H_3PO_4, *pyrophosphoric,* $H_4P_2O_7$, and *metaphosphoric,* HPO_3. The first of these is formed by dissolving P_2O_5 in boiling water, or by the action of nitric acid upon phosphorus itself; the second by the heating of the tribasic phosphoric acid to 213° C., and the third by the ignition of the tribasic variety, or by dissolving P_2O_5 in cold water. To the second oxide corresponds *phosphorous acid,* H_3PO_3, although it cannot be formed directly from the oxide. This is a dibasic acid, containing one hydrogen atom not replaceable by metal. To the hypothetical *hypophosphorous oxide,* P_2O, corresponds *hypophosphorous acid,* H_3PO_2. It is monobasic, containing two hydrogen atoms which are not replaceable by metal.

Phosphorus is frequently used as an ingredient in rat pastes. A method for the determination of the free phosphorus in such preparations as well as in the phosphoretted resin, tablets, pills, etc., has been described by E'we and Vanderkleed (*J. A. P. A.*, 1914, p. 1684), in which the phosphorus is distilled in an atmosphere of CO_2, and the distillate collected in a silver nitrate solution and the resulting silver compound decomposed and the phosphorus estimated in the ordinary manner.

Uses.—The continued use of small doses of phosphorus stimulates the blood-making organs, but especially the growth of bone. When administered to growing animals the spongy tissue of the bone becomes thickened and the compact tissue more dense. That phosphorus affects the growth of bones in young animals was first proven in 1872 by Wegner who found that the administration to calves caused a thickening of the compact layer of bone especially along the epiphyseal lines. His results as far as the lower animals are concerned have been confirmed by several investigators, and Phemister (*J. A. M. A.*, 1921, lxxvi, p. 850) by means of the X-ray has shown that a similar change occurs in the bones of children. There is some evidence also that it has a tonic effect upon the nervous system. Phosphorus is used in medicine in the treatment of diseases of the osseous tissues, such as *rickets, ununited fracture,* and *osteomalacia.* It is also widely employed in corrections of nervous exhaustion, such as *neurasthenia* and some types of *neuralgia.* It is even believed by some to be of service in degenerative conditions of the nervous system, and has been used in *brain softening,* but with less positive results. Leubuschur (*M. M. W.*, 1913, xxx, p. 494) lauds it in the management of *epilepsy.* It has also been asserted to be of benefit in certain *skin diseases,* notably *acne, psoriasis,* and *chronic eczema.* It might be well to emphasize that the action of elemental phosphorus is not possessed by phosphoric acid and there is no convincing evidence that either the organic or inorganic phosphates possess the same kind of influence over the metabolism.

Phosphorus Poisoning.—Phosphorus is a very virulent poison, as little as one-eighth of a grain having proven fatal, and an infant was killed by eating the heads of two old-fashioned friction-matches. Since the prohibition of the manufacture of yellow phosphorus matches phosphorus poisoning has become very rare but an occasional case from *roach-poison,* or other vermin exterminator may occur. The symptoms usually do not manifest themselves until some hours after the ingestion of the phosphorus. General malaise then becomes very pronounced, and is soon accompanied by nausea, abdominal pain, and vomiting of food, mucus, and bile. On the second and third day the vomiting is likely to cease, but the abdominal tenderness remains, and there is some fever. Later the patient becomes jaundiced and severe vomiting of a coffee-ground liquid, free from bile and similar to the black vomit of yellow fever, may set in; the urine is scanty and albuminous, often with tyrosine and leucine in it, or it may finally be suppressed. Frequently there is wild delirium. The temperature falls markedly, and the patient sinks into a coma which ends in death. After death a peculiar fatty degeneration is found affecting almost all the soft tissues. The parts which suffer first are the liver, the gastro-intestinal mucous membrane, and the kidneys. Both in its symptoms and in its lesions phosphorus poisoning so closely resembles acute atrophy of the liver that only by detecting the phosphorus in the matters vomited, in the excretions, or in the tissues of the body, can a positive diagnosis be made. As the phosphates are normally abundant in the urine it is necessary to find the phosphorus in the elemental state.

For methods of detecting phosphorus in cases of suspected poisoning, see *U. S. D.*, 19th ed., p. 935.

It is evident from the widespread lesions caused by phosphorus that after its absorption no treatment can be of service. It is therefore of the utmost importance that chemical antidotes and emetics be used promptly. Probably the best chemical antidote is potassium permanganate, which acts by oxidizing the poison, but copper sulphate is of great value as it not only forms a non-toxic phosphide of copper but also acts as an emetic. The oil of turpentine has been stated to possess antidotal properties, but this is not true of the American oil. If the stomach tube be at hand probably the best treatment is washing out the stomach with a one-half per cent. solution of potassium permanganate repeatedly and leaving about half a pint of the solution in the stomach. In the absence of the stomach pump, three grains of copper sulphate may be given every five minutes until free emesis, and after the stomach has been thoroughly emptied a dose of four grains of potassium permanganate should be given.

Formerly workers in match factories were frequently attacked with a peculiar form of chronic phosphorus poisoning of which the most characteristic symptom was a necrosis of the jaw, whence the popular name of "phossy jaw." Since the introduction of red phosphorus this condition has become much less common.

Phosphorus should never be exhibited in substance, but the official pill is an eligible preparation. The *elixir* (*Elixir Phosphori,* N. F.) is probably the most eligible of the liquid preparations, but the *oil* (*Oleum Phosphoratum,* N. F. and Br.) is very efficient. Great caution is necessary in the exhibition of phosphorus, and its effects should be closely watched.

Dose, of phosphorus, from 1-100th to 1-80th of a grain (0.0006–0.0008 Gm.). Much larger doses than these have been given, but have in various cases produced unpleasant symptoms.

Off. Prep.—Oleum Phosphoratum, *Br., N. F.;* Pilulæ Phosphori, *U. S.* (*Br.*)*;* Elixir Phosphori, *N. F.;* Liquor Phosphatum Compositum, *N. F.*

PHYSOSTIGMINÆ SALICYLAS. U. S.

PHYSOSTIGMINE SALICYLATE Physostig. Salicyl.
[Eserine Salicylate]

"The salicylate [$C_{15}H_{21}O_2N_3.C_7H_6O_3$] of an alkaloid obtained from the dried ripe seeds of *Physostigma venenosum* Balfour (Fam. *Leguminosæ*)." *U. S.*

Eserinum Salicylicum, *Fr. Cod.;* Salicylate d'Esérine, *Fr.;* Physostigminum salicylicum, *P. G.;* Physostigminsalicylat, Eserinsalicylat, *G.*

The seeds of the *Physostigma venenosum* Balfour (Fam. *Leguminosæ*) were formerly official but were dropped at the 10th revision of the U. S.

Physostigma venenosum is a perennial woody climbing plant indigenous to West Africa, frequenting especially the banks of streams, into which it often drops its fruit when ripe, and it is said that the people of Calabar derive their supply principally from the borders of the streams down which the fruits are carried. The rhizome is spreading, with numerous rootlets, often having attached to them small succulent tubers. The leaves are pinnately-compound, stipulate, each possessing 3 ovate, acuminate leaflets. The flowers are in axillary, multiflorous, pendulous racemes. The corolla is papilionaceous, of a pale pink color with a purplish tinge. The legume when ripe is about seven inches long, and contains two or three reniform or oblong seeds. It ripens at all seasons, but is most abundant during the rainy season from June to September. The seeds are the part used. The plant has been introduced into India and Brazil, and is said to flourish in the latter country. The market supplies are obtained from the regions surrounding the mouth of the Niger and the lower portion of the Calabar River, the chief port of export being Lagos (*Ap. Ztg.*, xxvi, p. 568; xxvii, p. 137). The commercial supply to the United States comes through London. For additional data on the botanical description, history, etc., of *Physostigma venenosum,* see papers by J. U. Lloyd in *West. Drug.*, 1897, 249 and G. Sharp in *Pharm. J.*, 1916, 619.

The seeds (*Physostigma* U. S. IX, *Calabar Bean; Chopnut; Ordeal Bean of Calabar; Esere Nut; Faba Calabarica; Fève du Calabar,* Fr.; *Kalabarbohne,* G.; *Eseve,* Sp.) were officially described as follows: "Oblong or ellipsoidal, somewhat compressed reniform, from 15 to 30 mm. in length and from 10 to 15 mm. in thickness; externally reddish or chocolate brown, smooth, somewhat wrinkled near the brownish-black groove, the latter being about 2 mm. in width and extending almost the entire length of the convex edge and in which are found frequently the remains of the white membranous funiculus, the margins of the seed-coat on both sides of the groove somewhat elevated, of a yellowish-red or brownish-red color and somewhat thickened; embryos large, white, with short hypocotyl and two concavo-convex cotyledons; taste at first starchy, afterwards acrid. The powder is grayish-white, starch grains numerous, from 0.005 to 0.15 mm. in diameter, ellipsoidal or somewhat reniform, and usually with a distinct cleft and frequently with radiating or irregular fissures; fragments of seed-coat with very thick, reddish-brown cells, being either palisade-like or very irregular and resembling stone cells, but the walls are not lignified; an occasional fragment with tracheæ showing reticulate thickenings. Physostigma yields not more than 3 per cent. of ash." *U. S. IX.*

The following assay process was official: "Introduce 15 Gm. of Physostigma in No. 60 powder, into a flask of about 250 mils capacity, and add 150 mils of ether. Stopper the flask, shake it well and allow it to stand ten minutes, then add 10 mils of an aqueous solution of sodium bicarbonate (1 in 20) and shake the mixture vigorously at intervals during four hours. Now add 15 mils of distilled water, again shake the flask well, and, when the drug has settled, decant 100 mils of the ether solution, representing 10 Gm. of Physostigma. Filter the solution through a pledget of purified cotton into a beaker and rinse the graduate and cotton with ether. Add 20 mils of tenth-normal sulphuric acid V.S. and evaporate off the ether, stirring during the evaporation with a rubber-tipped glass rod. After the resinous and fatty matter has agglutinated, pour off the acid solution through a wetted filter into a separator. Redissolve the residue in the beaker in about 15 mils of ether, add 2 mils of tenth-normal sulphuric acid V.S., evaporate off the ether with continued stirring as before and pour the acid solution on the filter. Repeat this operation until all the alkaloid is extracted and then wash the filter with distilled water until it is free from alkaloids. Collect the solution and washings in a separator, add sufficient sodium bicarbonate to make the solution decidedly alkaline to litmus and completely extract the alkaloids by shaking it out repeatedly with ether. Wash the combined ether solutions with 10 mils of distilled water, separate the water completely, and filter the ether solution, washing the container and filter with ether. Evaporate the ether solution to dryness, dissolve the alkaloids from the residue, add exactly 5 mils of tenth-normal sulphuric acid V.S. and titrate the excess of acid with fiftieth-normal potassium hydroxide V.S., using cochineal T.S. as indicator.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 27.52 milligrammes of the alkaloids of Physostigma." *U. S. IX.*

Calabar beans are occasionally substituted by a number of more or less similar seeds of African plants. Hartwich (*S. W. P.*, 1905, p. 441) calls attention to a false physostigma found in the Hamburg drug market which is derived from *Pentaclethra macrophylla* Benth., a leguminous tree indigenous to tropical Africa. The seeds are dark reddish-brown, from 5 to 7 cm. long, about 5 cm. broad and about 1 cm. thick. They are flattened-oval or roundish-triangular. Other substitutes have included the seeds of *Entada scandens* Benth. which are round, flat, brown and shining, about 5 cm. in width and the seeds of *Mucuna urens* De Candolle which are flattened and discoid and about 5 cm. in width.

The seeds of *Physostigma cylindrospermum* Holmes have occurred as an occasional adulterant of calabar beans. These are subcylindrical, up to 4 cm. long and possess a shorter raphe than the genuine article.

In 1864 Jobst and Hesse isolated an alkaloid to which they gave the name of *physostigmine.* The following year Vée and Leven obtained an alkaloid which they called *eserine,* from the African name for the drug. This latter was subsequently shown to be identical with physostigmine. Polonovski (*B. Soc. Chem.,* 1915, xvii; 1923, xxxiii) maintains that this does not occur naturally in the bean but is a reduction product of an alkaloid which he names *geneserine,* $C_{15}H_{21}O_3N_3$. Besides the principal alkaloid, the following other bases have been described: *Calabarine* (now usually known as *eseridine*) discovered by Harnack and Witkowski in 1876. The formula $C_{15}H_{23}O_3N_3$ has been given to it by Eber (*Ph. Ztg.,* 1888, p. 611), which differs from that of physostigmine, it will be seen, by H_2O only, and it is stated that the one can be changed into the other by the action of dilute acids. Salway (*Tr. Chem. Soc.,* 1911, xcix) was unable to confirm its presence. *Eseramine,* $C_{16}H_{25}O_3N_4$, was discovered by Ehrenberg in 1893 (*Verhand. d. Gesellsch. Deutsche Natur. u. Aertzte.,* 1893, ii, p. 102).

Still another alkaloid, announced by Salway (*Tr. Chem. Soc.,* 1911, xcix), is *physovenine,* $C_{14}H_{18}O_3N_2$. It is a powerful myotic like eserine. He believed it to be an intermediate product in the decomposition of eserine by alkalies, which results in the formation of a new base called *eseroline,* $C_{13}H_{18}ON_2$. Another decomposition product of eserine is produced by an excess of ammonia and is called *eserine blue,* $C_{17}H_{23}O_2N_3$.

Isophysostigmine, discovered by Ogiu in 1904, is isomeric with physostigmine and according to its discoverer, similar but more active in its physiological effects.

Basic physostigmine occurs: "In colorless or pinkish crystals, slightly soluble in water, but readily soluble in alcohol and in diluted acids. The aqueous solution has an alkaline reaction, when warmed with or when shaken with dilute solution of potash becomes red, and when evaporated to dryness over a water bath leaves a bluish residue, the acidified solution of which is beautifully dichroic, being blue and red." *Br.,* 1885.

A peculiarity of the alkaloid is that an aqueous solution of it, or of one of its salts, exposed to the air in the presence of potassium or sodium hydroxides, or lime, becomes red, owing to the absorption of oxygen. The coloring matter, sometimes called *rubreserine,* is taken up by chloroform. The color is not permanent, but gradually changes to yellow, green, or blue. This test will detect less than the hundred-thousandth part of the alkaloid. The same property is possessed by the alcoholic extract of the bean. This is the cause of the color changes taking place in solutions dispensed in ordinary glass bottles. The change may be retarded by previously rinsing out the bottle with diluted hydrochloric acid, and subsequently with distilled water, or it may be entirely prevented by coating the inner surface of the dispensing vial with paraffin.

The U. S. recognizes the salicylate in preference to the sulphate of the alkaloid which is in the Br. on account of its greater stability. Its advantage is that it is not deliquescent.

Description and Physical Properties.—"Colorless or faintly yellow, shining, odorless, crystals. It acquires a red tint when long exposed to light and air. *Caution—Physostigmine salicylate is extremely poisonous.*

"One Gm. of Physostigmine Salicylate is soluble in 75 cc. of water, 16 cc. of alcohol, 6 cc. of chloroform, and in 250 cc. of ether, at 25° C. One Gm. is soluble in 16 cc. of water at 80° C., and in 5 cc. of boiling alcohol.

"A cold-saturated aqueous solution of Physostigmine Salicylate is neutral, or only faintly acid to litmus paper. Upon standing, the solution usually acquires a pink color. Evaporate on a water bath about 0.005 Gm. of Physostigmine Salicylate with a few drops of ammonia T.S.: a blue residue is produced which, when dissolved in alcohol, yields a red, fluorescent solution upon the addition of an excess of acetic acid. On adding a few drops of sodium hydroxide T.S. to 5 cc. of a cold-saturated aqueous solution of the salt, a pink color rapidly develops. Ferric chloride T.S. produces a deep violet color in an aqueous solution of Physostigmine Salicylate.

"The ash from 0.1 Gm. is negligible. A solution of 0.1 Gm. of Physostigmine Salicylate in 2 cc. of sulphuric acid does not become darker than yellow within five minutes (*readily carbonizable substances*). Precipitate the salicylic acid from 10 cc. of a cold-saturated aqueous solution of the salt with a slight excess of diluted hydrochloric acid, and filter: the filtrate is not rendered turbid at once by the addition of 5 drops of barium chloride T.S. (*sulphate*).

"Preserve in small, well-closed containers, protected from light." *U. S.*

Uses.—Physostigma was introduced to the medical profession in 1840 by a missionary, Dr. Daniell, who had been laboring in Western Africa. Among the negroes of the Calabar coast this bean was used, under the name of *esere* as an ordeal, and, when given by their head men, usually proves fatal to the accused, unless free vomiting occurs. A draught containing 19 seeds pounded and infused in water is said to have killed a man in an hour. In the experiments of Fraser, it was found that the integuments of the seeds, as well as the shell, are distinctly purgative. It is probable that in the fresh bean they are also emetic, and that the priests or chiefs who administer the ordeal take advantage of this in regulating the effects of the poison to suit their own purposes; sometimes, however, even the pure alkaloid causes vomiting. (Gubler.)

The physiological actions of physostigmine divide themselves into three groups: depression of the central nervous system, increased irritability of the autonomic nerves, and stimulation of unstriped muscles. The depression of the central nervous system is most noticeably manifested in the diminution of reflex activities from depression of the spinal cord. After toxic doses the drug also depresses the respiratory center. Its effects upon the autonomic nerves are antagonistic to those of atropine (see *Atropina*). Among the most important of these actions are the slowing of the pulse by stimulation of the vagus, and the contraction of the pupil by stimulation of the oculomotor nerve. In large doses it also increases secretion, although it is not employed practically for this purpose. Although in sufficient dose physostigmine causes a rise in blood pressure by its stimulating action upon the cardiac and vascular muscles, the only therapeutically important action upon muscle tissue is on the intestinal tract. According to the studies of Magnus (*A. G. P.*, 1905, cviii, p. 1), it increases both the tone and the extent of contraction of the intestinal muscles.

Physostigmine is used in medicine chiefly to meet one of three indications. To contract the pupil in *glaucoma* and other diseases of the eye, it may be directly instilled into the diseased organ in strengths of from one-fourth to one-half of one per cent. As a stimulant to peristalsis it is useful in *chronic constipation, phantom tumor,* post-operative *intestinal atony, flatulent colic* and other conditions of deficient activity of the alimentary muscles. Edmunds (*J. P. Ex. T.*, 1923, xx, p. 405) concludes from his experimental studies that the occasional clinical failure of physostigmine to stimulate the intestinal muscles can be explained because of its action in increasing the output of epinephrin in the body, whose effects upon the intestines are antagonistic. Martin and Weiss (*J. A. M. A.*, 1925, lxxxiv, 1407) have used physostigmine with striking effects in post-operative flatulence. They believe that the reason it has so frequently failed in the hands of others is on account of insufficient dosage; they recommend from 1/20 to 1/16 grain (3 to 4 milligm.) be injected intramuscularly. These doses cause, besides the expulsion of gas, usually perspiration with increase of the pulse rate and frequently a rise in blood pressure. In many cases there was vomiting as well as belching. The drug was not successful in toxic type of case. As a sedative to the spinal cord it has been used in *tetanus* and *strychnine poisoning,* but clinical experience has shown that it is of much less value than chloral or the bromides. It has been recommended by Kaufmann (*W. K. W.*, 1912, p. 1080), by Lian and Welt (*B. Hop. Par.*, 1921, xlv, 559) and others in the treatment of *tachycardia* (*W. K. W.*, 1912, p. 1080).

Poisoning.—Of seventy children poisoned in Liverpool by eating Calabar beans which had been thrown upon a waste heap, vomiting occurred, or was produced by emetics, in all except one, in whom four kernels caused death. The nausea and vomiting came on in about half an hour, the nervous symptoms in less than an hour.

There are generally diminution of reflexes, coarse muscular tremors which may be sufficiently violent to suggest convulsions, contraction of the pupil, and progressive diminution of motor power. In the fatal cases death is generally due to paralytic asphyxia.

In the treatment of physostigma poisoning the stomach should be thoroughly washed out either with an emetic or the stomach pump, and tannic acid or compound solution of iodine given as a chemical antidote. Atropine, which is a partial physiological antagonist, should be given in doses of about one-fiftieth of a grain (0.0013 Gm.), and strychnine and other stimulants employed as indicated.

The *extract of the seeds* (*Extractum Physostigmatis,* U. S. IX) was given in doses of from one-sixth to one-half of a grain and the *tincture* (*Tinctura Physostigmatis,* U. S. IX) in doses of from ten to thirty minims (0.6–2.0 cc.).

Dose, of physostigmine salicylate, one-sixtieth to one twenty-fourth of a grain (0.0011–0.0025 Gm.).

PHYSOSTIGMINÆ SULPHAS. Br.

PHYSOSTIGMINE SULPHATE [Eserine Sulphate]

"Physostigmine Sulphate, $(C_{15}H_{21}N_3O_2)_2$-H_2SO_4, is the sulphate of an alkaloid, physostigmine, obtained from the seeds of Physostigma venenosum, *Balfour.*" *Br.*

Sulfate d'Esérine, *Fr.;* Physostigminum sulfuricum, *P. G.;* Physostigminsulfat, *G.;* Sulfatu de eserina, *Sp.*

This salt is preferred by the Br. to the salicylate on account of its greater solubility, but on exposure to the air it soon assumes an extractive consistence which renders it difficult to dispense; the salicylate is free from this objection.

Petit and Polonovski conducted experiments with the view of discovering salts of eserine which would be stable and non-hygroscopic; they made *eserine benzoate, eserine meta-cresotate, eserine citrate,* and *eserine tartrate.* Processes will be found in *J. P. C.*, 1894, 55.

Properties.—It is officially described as "minute white crystals, becoming yellowish on exposure to air and light; very deliquescent. Readily soluble in *water,* soluble in *alcohol* (90 per cent.). Aqueous solution neutral to *litmus;* yields the *reaction* characteristic of sulphates; yields with dilute *solution of sodium hydroxide* a white precipitate turning pink and forming a red solution with excess of the reagent; when mixed with *solution of ammonia* and evaporated to dryness on a water-bath it leaves a bluish residue, the solution of which in very dilute acids is dichroic, being red by reflected and blue by transmitted light. A minute fragment dissolved in a few drops of *fuming nitric* *acid* forms a yellow liquid, which, on warming on a water-bath, turns orange, then blood-red, and on evaporation to dryness leaves a green residue; this residue turns violet-blue on exposure to the fumes of *nitric acid,* and when moistened with the acid gives gradually a blood-red color, which changes to greenish-yellow on the addition of *water.* A dilute aqueous solution applied to the eye causes contraction of the pupil. No appreciable ash." *Br.*

Physostigmine sulphite has been patented and it is stated that it is more stable than either the salicylate or sulphate.

The medicinal properties, uses, and dose of physostigmine sulphate are the same as those of *Physostigminæ Salicylas.*

Dose, from one-sixtieth to one twenty-fourth of a grain (0.0011–0.0025 Gm.).

Off. Prep.—Lamellæ Physostigminæ, *Br.*

PHYTOLACCA. N. F.

PHYTOLACCA Phytolac. [Poke Root]

"Phytolacca is the dried root of *Phytolacca americana* Linné (Fam. *Phytolaccaceæ*). Phytolacca contains not more than 5 per cent. of its stem bases or more than 2 per cent. of other foreign organic matter." *N. F.*

Poke Root; Phytolaccæ Radix; Phytolacca Root; Racine de Phytolaque, *Fr.;* Kermesbeerenwurzel, *G.*

Phytolacca decandra L. is an indigenous plant, with a large, branching, perennial root, often 20 to 25 cm. in diameter, which is fleshy, fibrous, whitish within, and covered with a thin brownish cork. The stems, which are annual, frequently grow to the height of 6 to 15 dm., and divide into numerous spreading branches, which are green when young, but becoming purple especially in the upper portions after the berries have ripened. The leaves are alternate, short petiolate, ovate-oblong, entire, acute and glabrous. The flowers are small, greenish-white and in long racemes. The raceme of flowers becomes a cluster of dark purple, almost black, shining compound berries flattened above and below, and divided into ten loculi, each containing one seed.

Poke is abundant in all parts of the United States, flourishing in soil containing lime salts, along fences, by the borders of woods, in newly cleared fields, and especially in the muck thrown up from the ditches or swamps. It also grows spontaneously in northern Africa and southern Europe, where, however, it is supposed to have been introduced from America. Its flowers begin to appear in July, and the fruit ripens in autumn. The magnitude of the poke weed, its large rich leaves, and its beautiful clusters of purple berries, often mingled upon the same branch with the green unripe fruit and the flowers still in bloom, render it one of the most striking of our native plants. The young shoots are much used as food early in the spring, boiled in the manner of asparagus. The leaves, berries, and root are used in medicine, but the latter is the most active. It should be dug up late in November, cut into thin transverse slices, and dried with a moderate heat. As its virtues are diminished by keeping, a new supply should be procured every year. The berries should be collected when perfectly ripe, and the leaves about the middle of the summer, when the foot-stalks begin to redden.

Commercial quantities of poke root have been gathered for the market chiefly in Indiana, North Carolina and Virginia.

The berries (*Phytolaccæ Fructus,* U. S., 1890, *Phytolaccæ Baccæ, U. S.,* 1880, *Poke Berry*) contain a succulent pulp, and yield upon pressure a large quantity of fine purplish, red juice. They have a sweet, nauseous, slightly acrid taste, with little odor.

Description and Physical Properties.—"*Unground Phytolacca.*—Cylindrical, or somewhat tapering, sparingly branched, from 3 to 7 cm. in thickness, mostly in transverse or longitudinal slices; externally yellowish brown, finely longitudinally or spirally wrinkled and thickly annulate with lighter colored low ridges; fracture fibrous, characterized by alternating layers of fibrovascular tissue and parenchyma, the layers of the latter being much retracted. Odor slight; taste sweetish, afterwards highly acrid.

"*Powdered Phytolacca.*—Brownish yellow, sternutatory; starch grains simple or compound the individual grains mostly up to 0.025 mm., occasionally up to 0.035 mm. in diameter; calcium oxalate in raphides from 0.015 to 0.050 mm. in length; numerous fragments composed of parenchyma or of tracheæ with scalariform markings or bordered pores and long fibres; fragments of cork tissue." *N. F.*

Constituents.—We have no knowledge of the nature of the active principle of poke root. W. A. Partee (*A. J. P.,* 1888, p. 123) made a proximate examination of poke root and found crystals deposited from a solution of an alcoholic extract in absolute alcohol; he also discovered traces of tannin, glucose, and indications which pointed to the presence of a glucosidal principle. Frankforter and Ranaley (*A. J. P.,* 1897, 281) have again analyzed the root with care. They find nearly 10 per cent. of a non-reducing sugar, free acid, identified as formic acid, but no certain proof of either alkaloid or glucoside. The very bitter resin amounted to 1 per cent.; *phytolaccine,* an alkaloid, has been said to exist in minute quantities in the root. It contains a large amount (5.56 per cent.) of potassium (Frankforter, *A. J. P.,* 1897, p. 134). Claussen (*Pharmacist,* 1879) prepared from the seeds a neutral principle in silky lustrous crystals, insoluble in water, soluble in alcohol, ether, and chloroform, which he named *phytolaccin.* A. Tereil (*C. R. A. S.,* 1880, xci, 856) obtained from the berries an acid (*phytolaccic acid*) as an uncrystallizable yellowish-brown mass of gummy consistency. It was soluble in water and alcohol, slightly soluble in ether, of acid reaction, and gelatinizing with hydrochloric and sulphuric acids. W. F. Wagner (*A. J. P.,* 1887, p. 69) found tannin in the berries, but not in the root.

Uses.—Phytolacca is emetic, purgative and somewhat narcotic. Its properties were known to the American Indians before the arrival of the white man. As an emetic it is very slow in its operation, frequently not beginning to cause vomiting in less than one or two hours after it has been taken, and then continuing to act for a long time upon both the stomach and the bowels. The vomiting produced by it is said not to be attended with much pain or spasm, but narcotic effects have been observed by some physicians, such as drowsiness, vertigo, and dimness of vision. In overdoses it produces excessive vomiting and purging, attended with great prostration of strength, and sometimes with convulsions, and has, in several instances, proven fatal. According to Robert Bartholow, phytolacca causes in the lower animals convulsions and death from paralysis of respiration.

It is not fit for use as an emetic, but has been employed as an alterative in *chronic rheumatism, granular conjunctivitis,* and even in *cancer.* Locally it has been used in the form of ointment (a drachm to the ounce) in the treatment of *psora, tinea capitis, sycosis,* and *favus.* It occasions at first a sense of smarting and heat in the parts to which it is applied. It has been recommended, both internally and as a gargle, in various forms of *sore-throat.*

Dose, emetic, ten to twenty grains (0.6–1.2 Gm.), alterative, one to five grains (0.06–0.3 Gm.).

Off. Prep.—Fluidextractum Phytolaccæ, *N. F.*

PICRORHIZA. Br.

PICRORHIZA

"Picrorhiza is the dried rhizome of Picrorhiza Kurroa, *Royle.*" *Br.*

Kutki, Katki, Kuru, Kuruwa, Kaur, Karru, Kutaki, Kalikutki, or Black Kutki, Katukurogani, Kurroa.

Picrorhiza Kurroa Royle (*P. Kurrooa* Benth.), more properly known as *P. Lindleyana* (Wall. Wettst.), is a low, hairy perennial herb (Fam. *Scrophulariaceæ*), indigenous to the Alpine Himalayas. The rhizome has long been used in India and has been frequently spoken of by European and Mahometan writers as *black hellebore,* but is essentially different.

Properties.—Picrorhiza occurs "in cylindrical pieces two to five centimetres long, and four to eight millimetres thick, sometimes terminating in a stem or scaly leaf-bud; brittle. Cork greyish-brown, wrinkled, with transverse leaf scars and small buds. Fracture short. In transverse section internally dark and porous, with a thin, greyish cork and narrow ring of tangentially elongated wood-bundles. No odor; taste very bitter." *Br.*

Picrorhiza resembles externally the rhizome of *Gentiana Kurroo* Royle (Fam. *Gentianaceæ*), the latter, however, is uniformly brown internally, whereas the rhizome of Picrorhiza is darker or black, whence its name kali or black kutki.

From this rhizome H. Warden has separated a glucoside, *picrorhizin,* which is freely soluble in water and alcohol and appears to be the bitter principle of the drug; also a red-brown, resinous, tasteless body, *picrorhizetin,* and, perhaps, cathartic acid (*Pharmacog. Indica,* vol. 3).

Uses.—The natives of India attribute active antiperiodic power to picrorhiza, which appears to be a powerful bitter tonic with slight laxative action.

Dose, as a tonic, five to twenty grains (0.3–1.3 Gm.); as an antiperiodic, from forty to fifty grains (2.6–3.2 Gm.).

Off. Prep.—Extractum Picrorhizæ Liquidum, *Br.;* Tinctura Picrorhizæ, *Br.*

PILOCARPINÆ HYDROCHLORIDUM. U. S.

PILOCARPINE HYDROCHLORIDE Pilocarpin. Hydrochl.

"The hydrochloride [$C_{11}H_{16}O_2N_2.HCl$] of an alkaloid obtained from the dried leaflets of *Pilocarpus Jaborandi* Holmes, or of *Pilocarpus microphyllus* Stapf (Fam. *Rutaceæ*)." *U. S.*

Pilocarpinæ Hydrochloras, *U. S.* 1890; Chlorhydras Pilocarpinæ; Pilocarpine Hydrochlorate; Pilocarpine Chloride; Pilocarpinum Chlorhydricum, *Fr. Cod.;* Pilocarpinum Hydrochloricum, *P. G.*

Under the titles *Pilocarpus* (U. S. IX) or *Jaborandi Folia* (Br. 1898) the dried leaflets of various species of *Pilocarpus* have been official; at the present neither the Br. nor U. S. recognizes the crude drug although they do salts of the alkaloid. The terms *jaborandi* or *jamguarandi* are still commonly applied in commerce to these leaves although in South America they are used to designate various pungent, sudorific plants, some of which have no botanical relation at all with pilocarpus. What is called jaborandi in this country in South America is known as *Arruda do Mato* or as *Arruda brava* or, rarely, as *Jamguarandi* or *Jaurandi.*

The genus *Pilocarpus* consists of woody shrubs belonging to the *Rutaceæ* and inhabiting tropical and subtropical America, including Cuba, Guadeloupe, Martinique, and probably other islands. For elaborate botanical and histological studies of the commercial species of Pilocarpus, see the articles by A. Duvall, *B. Sc. Pharm.,* iii, pp. 41 and 98; Geiger, *Ber. d. D. Phar. Ges.,* 1897, p. 356; Hartwich, *Apoth. Zeit.,* 1900; Holmes, *P. J.,* 1903, p. 713; and 1904, p. 54; Schneider, *Jour. of Pharmacology* (N. Y. C. P.), 1897, No. 6; Tunman, *S. W. P.,* xlvii, p. 177.

P. Jaborandi Holmes (*P. officinalis* Pohl) yields the commercial variety known as Pernambuco Jaborandi. It inhabits the northern and northeastern part of Brazil. Its leaves are two or three jugate and are especially separated from those of the *P. pennatifolius* by the fact that all of the leaflets except the terminal one have their bases cordate, while the bases of all the leaflets of *P. pennatifolius* are attenuate. This commercial variety is practically no longer obtainable, only occasional lots being imported.

P. pennatifolius Lemaire (*P. simplex* Baillon), which yields Paraguay jaborandi, inhabits the southern portion of Brazil and Paraguay, whence its leaves were formerly largely exported through Buenos Ayres and Rio de Janeiro; at present they seem to have almost disappeared from commerce. The leaflets are grayish-green in color, oval, elliptical, obtuse, attenuate at the summit, which is feebly emarginate, and also attenuate at their base but not petiolated.

P. selloanus Engler appears to be a variety of *P. pennatifolius* Lemaire, from which it differs almost solely in the length of its flower stalk, which is six times as long as the flower bud, while that of *P. pennatifolius* is but three to four times as long as the bud. *P. selloanus* seems to be the more southern plant of the two, and is especially abundant in Paraguay. It has been imported from Rio de Janeiro.

P. microphyllus Stapf, which yields Maranham jaborandi, grows in the northeastern part of Brazil, whence the leaves, much mixed with the débris of the petioles, of the twigs and of the fruit, are sent to Liverpool and Hamburg. These leaves are alternate, imparipinnate having from one to five pairs of leaflets, or are often apparently simple owing to the failure of the lateral leaflets to develop. The leaflets are opposite, slightly pubescent, their petioles being marked by a deep longitudinal furrow. They vary very much in form, the base usually being attenuate and feebly cordate or unequal.

P. spicatus A. Saint-Hilaire (*P. parviflorus* Martius et Nees) inhabits the southern and northern portions of Brazil and can be recognized at once by its having simple leaves which are from 3 to 11 cm. long and from 1 to 4 cm. broad, and are tender or coriaceous and more or less pubescent and dotted. They are brownish-green above, paler beneath, and attached by a short twisted petiole. They appeared in commerce in 1895 under the name of *Arocati Jaborandi*. *P. subcoriaceus* Engler is probably a variety of this species. *P. racemosus* Vahl, a native of Martinique, Cuba, Guadeloupe and probably other of the West Indian Islands, appeared first in commerce in 1903 as a new variety of jaborandi under the name of *Guadeloupe jaborandi*. The leaves are proportionately broader than those of *Pernambuco jaborandi*, more obovate in outline, of a purer green color, and are trifoliate or apparently simple. Considerable diversity of result has been obtained by chemists in the examination of the Guadeloupe jaborandi. See Rocher (*A. J. P.*, 1900) and Cownley (*P. J.*, 1903, lxxii).

Other species, while never official, have appeared in commerce. These include: *P. trachylophus* Holmes whose leaflets are smaller than those of the *P. jaborandi*, and are oblong, elliptical, obtuse, and emarginate at the summit with cordate bases, symmetrically and shortly petiolate. The plant grows in northeastern Brazil, especially in the provinces of Ceará and Maranhoa, and the leaves, although they contain so little of the alkaloid (about 0.2 per cent.) as to be of small value, have been sent into commerce in considerable quantities. Their color upon the upper surface is dark olive green, below yellowish-green. The under surface is covered with short hairs.

The most common adulterant appears to be in lots of *P. microphyllus*, which often contain leaves of the leguminous plant, *Tunatea decipiens* (Holmes), O. Kze. (*Swartzia decipiens* Holmes). In general appearance the two leaves resemble one another, both being imparipinnate and having the leaflets about the same size and shape, but in *P. microphyllus* the leaflets are opposite and the petioles are only slightly pubescent, while in the *Tunatea* the leaflets are alternate, and the petioles very pubescent. Then again, the absence of secreting hairs, the deep green of the upper and lighter green of the lower surface of the leguminous leaf serve easily to distinguish it from the true drug.

The U. S. IX recognized the *P. jaborandi* and *P. microphyllus* which it described as follows: "*Pernambuco jaborandi.*—Leaflets when entire, oval, oblong, or elliptical from 4 to 10.5 cm. in length and from 2 to 4 cm. in breadth and with short, stout petiolules; summits more or less rounded or acute and emarginate; bases rounded or acute and mostly unequal; margins entire and narrowly revolute; very smooth, shiny, coriaceous and glandular-punctate; upper surfaces grayish to brownish-green, midribs mostly depressed, under surfaces yellowish- or greenish-brown and slightly pubescent on the prominent midvein; peculiarly aromatic when crushed; taste bitterish, becoming somewhat pungent and having a sialagogue effect.

"*Maranham Jaborandi.*—Leaflets rhomboidally oval to obovate or elliptical, from 1.5 to 5 cm. in length and from 1 to 3 cm. in breadth, the lateral ones nearly sessile, the terminal ones on margined petiolules, from 0.5 to 1.5 cm. in length; of a nearly uniform grayish or yellowish-green color, rather thin but otherwise resembling Pernambuco Jaborandi.

"Under the microscope, transverse sections of Pilocarpus show the upper epidermal cells with a yellowish layer of cutin from 0.005 to 0.01 mm. in thickness; palisade cells, 1 to 3 rows deep, being filled with chloroplastids; among the palisade cells occur large, nearly circular, oil-secretion reservoirs from 0.08 to 0.15 mm. in diameter; the dorsal pneumatic layer, from 10 to 20 rows in depth, the cells occasionally containing rosette aggregates of calcium oxalate from 0.01 to 0.025 mm. in diameter; distributed in the center of the leaf, are the collateral fibro-vascular bundles each surrounded by a more or less interrupted circle of several rows of thick-walled, slightly lignified bast-fibers; tracheæ associated with strongly lignified wood-fibers;

among the cells of the lower epidermis occur numerous stomata. On surface view the stomata are broadly elliptical, from 0.025 to 0.04 mm. in length, being uniformly smaller in Maranham Jaborandi. Upon both surfaces of Pernambuco Jaborandi occur a number of non-glandular, one-celled hairs, more or less bent or curved, from 0.08 to 0.5 mm. in length, thick-walled and with numerous, slight, centrifugal projections. The powder is dark green or greenish-brown; epidermal cells on surface view 5- or 6-sided; stomata broadly elliptical, from 0.02 to 0.04 mm. in length, usually with four neighboring cells; fragments of fibro-vascular bundles showing tracheæ with simple or bordered pores or spiral thickenings, associated with thick-walled and strongly lignified wood-fibres; bast-fibers few, walls thick and only slightly lignified, calcium oxalate in rosette aggregates, from 0.01 to 0.025 mm. in diameter; fragments of laminæ showing large, oil-secretion reservoirs and usually containing one or more globules of oil; non glandular hairs having thick walls, usually more or less broken, are occasionally found.

"Pilocarpus yields not more than 7 per cent. of ash." *U. S. IX.*

Assay.—"Introduce 15 Gm. of Pilocarpus in No. 60 powder into a 250 mil flask, add 150 mils of chloroform and proceed as directed under *Belladonnæ Radix*, page 222, fifth line of the assay, beginning with the word 'Stopper,' and decreasing the amount of water to be added after maceration to 5 mils. The 100 mils of chloroform solution must be drawn off from the bottom of the flask, and dissolve the alkaloids from the residue in 8 mils of tenth-normal sulphuric acid V.S.

"Each mil of tenth-normal sulphuric acid V.S. corresponds to 20.8 milligrammes of the alkaloids of Pilocarpus." *U. S. IX.*

Constituents.—An alkaloid was isolated in 1875 from jaborandi almost simultaneously by A. W. Gerrard and M. Hardy. To this the name of *pilocarpine* was given. A second base, *jaborine,* was reported by Harnak and Meyer (*Ann. Chem.,* 1880, 67); but Jowett (*Tr. Chem. Soc.,* 1900, 474, 851; 1901, 581, 1331) asserts this to be a mixture. In 1885 Harnak and Meyer (*Chem. Centr.,* 1885, 628) discovered still another alkaloid, *pilocarpidine,* which was confirmed by Jowett, although it cannot be found in the jaborandi of present day commerce. In 1897 still another alkaloid was isolated by Petit and Polonovski (*J. P. C.,* v, 370; vi, 8) from *Pilocarpus microphyllus,* which they also called *pilocarpidine,* under the impression that it was identical with that reported previously by Harnak and Meyer. This has been called *β-pilocarpine* by Brühl, and *isopilocarpine* by Jowett. Still another alkaloid called *pilosine* has been reported by Pyman. Petit and Polonovski later reported *ϕ-pilocarpine* and *ϕ-jaborine* in the leaves of *Pilocarpus spicatus.* He also obtained a volatile oil, tannic acid, a peculiar volatile acid, and potassium chloride.

Isopilocarpine (*betapilocarpine*) seems to be a stereo-isomer of pilocarpine. It is a colorless viscid oil-like liquid, forming crystalline salts, with an optical rotation of + 42.8. On oxidation by potassium permanganate it yields *pilopic acid,* $C_7H_{10}O_4$ and *homopilopic acid,* $C_8H_{12}O_4$.

Pilocarpidine, $C_{10}H_{14}O_2N_2$, is also liquid and forms crystalline salts. It is miscible with water and has an optical rotation of +81.3. Pilosine, $C_{16}H_{18}O_3N_2$, forms colorless crystals melting at 187°. It is sparingly soluble in water, ether or benzene, more soluble in boiling water or alcohol. *ϕ-pilocarpine* and *Φ-jaborine* are both amorphous, optically inactive bases.

An essential oil of sp. gr. 0.875, and boiling between 180° and 290° C., has been obtained by Schimmel & Co., Leipsic. (*B. Chem. G.,* April, 1888.) The portions going over above 260° C. solidified on cooling, and yielded a hydrocarbon, which fuses at 27° to 28° C. As it decolorizes notable amounts of bromine when in solution in petroleum benzin, it probably belongs to the olefine series. The yield of oil in pilocarpus is about 0.4 per cent. In a later report (Oct., 1893) they give dipentene as a probable constituent of the lower boiling portions of the oil. The total amount of essential oil varies, according to the freshness of the plant, from 0.2 to 1.1 per cent.

The alkaloid pilocarpine may be obtained from pilocarpus by the following process: The leaves are exhausted with 80 per cent. alcohol containing 8 grammes of hydrochloric acid in a liter, the tincture is distilled and evaporated to the consistence of a liquid extract, and this is mixed with a small quantity of water, and filtered. The filtrate is treated with a slight excess of ammonium, and then with a large quantity of chloroform. The chloroform solution is agitated with water, to which hydrochloric acid is added, drop by drop, in sufficient quantity to neutralize the alkaloid, the hydrochloride of which is obtained in long needles on evaporating the aqueous solution, while foreign principles remain dissolved in the chloroform. By dissolving the crystals in water, treating the solution with ammonia and chloroform, and evaporating the latter solution, pilocarpine is obtained as a soft viscous mass, which is only slightly soluble in water, but is freely soluble in alcohol, ether, and chloroform.

Kingzett originally assigned pilocarpine the formula $C_{23}H_{34}O_4N_4 + 4H_2O$. Harnack and Meyer, on the other hand, give it as $C_{11}H_{16}O_2N_2$. The latter has been generally accepted, and is recognized by the U. S. Pharmacopœia. When heated pilocarpine is changed into an isomeric compound, *isopilocarpine,* which also occurs naturally in the crude drug, see under *Pilocarpus.* Pilocarpine dissolves in soda solution with partial decomposition. Structurally, it is regarded as the lactone of *pilocarpic acid,*

$C_{11}H_8O_3N_2$ (see Petit and Polonovski, *J. P. C.*, 1897, v; *Bull. Soc. Chim.*, 1922, xxxi). For further studies in its structure see Pyman (*Tr. Chem. Soc.*, 1922, cxxi, 2616).

The nitrate has probably been used most frequently, and it and the hydrochloride are now official. Gerrard tested the solubilities of several of the salts as follows. The nitrate is soluble in water, sparingly in cold but freely in boiling alcohol; it is insoluble in chloroform, benzene, carbon disulphide, and ether. The *phosphate* is soluble in water, sparingly in cold, more freely in boiling, alcohol, from which on cooling it crystallizes in lustrous tables; it is insoluble in ether, chloroform, benzene, and carbon disulphide. The *hydrochloride* is freely soluble in water, alcohol and chloroform; insoluble in ether, benzene, and carbon disulphide. The *acetate* is soluble in water, alcohol, chloroform, benzene, and ether; insoluble in carbon disulphide. The *hydrobromide* is soluble in water, alcohol, and chloroform; insoluble in ether and carbon disulphide.

Description and Physical Properties.—Pilocarpine Hydrochloride occurs as "colorless, odorles, translucent crystals. It is hygroscopic. One Gm. of Pilocarpine Hydrochloride is soluble in 0.3 cc. of water, 3 cc. of alcohol, and in 366 cc. chloroform, at 25° C. One Gm. is soluble in 1.5 cc. of alcohol at 60° C. It is insoluble in ether.

"When dried to constant weight at 100° C., Pilocarpine Hydrochloride melts between 195° and 198° C. Its aqueous solution (1 in 20) is slightly acid to litmus paper. Dissolve 0.01 to 0.02 Gm. of Pilocarpine Hydrochloride in 2 cc. of distilled water in a test tube, add 2 cc. of a faintly acid hydrogen dioxide T.S., and cover the mixture with about 1 cc. of benzene. Add 3 or 4 drops of a solution of potassium dichromate (1 in 300) and shake the mixture gently: the benzene layer acquires a violet color, while the aqueous layer remains yellow (*distinction from other alkaloids*). (If more than 0.02 Gm. of the salt is used, the benzene turns blue and the reaction is no longer characteristic.) Silver nitrate T.S. produces, in an aqueous solution of the salt, a white precipitate, insoluble in nitric acid.

"The ash from 0.1 Gm. is negligible. A solution of 0.1 Gm. of Pilocarpine Hydrochloride in 2 cc. of sulphuric acid is colorless or at most only faintly yellow (*readily carbonizable substances*). The addition of ammonia T.S. or of potassium dichromate T.S. to 10 cc. of an aqueous solution of the salt (1 in 100) produces no turbidity (*various foreign alkaloids*).

"Preserve in well-closed containers, protected from light." *U. S.*

Uses.—The physiological effects of the various bases of pilocarpus have been studied by Harnak (*A. E. P. P.*, 1886, xx) and by Marshall (*J. Phys.*, 1904, xxxi). Jaborine appears to have an atropine-like effect, antagonistic to pilocarpine, and pilocarpic acid to be inert; the others resemble this alkaloid but are less active. The whole drug may be used for the same purposes as pilocarpine but is very little used except occasionally as a local remedy to stimulate the growth of hair for which, however, it is probably of no value.

Pilocarpine is the physiological antagonist of atropine, exciting those nerve endings which are paralyzed by that alkaloid. Thus it causes contraction of the pupil by stimulating the peripheral ends of the oculomotor nerve, increased flow of saliva by acting on the chorda tympani, slowing of the pulse through vagal stimulation (for some unknown reason the pulse rate is often increased in human beings), free sweating, and increased peristalsis of the intestines. The effects upon secretion are especially pronounced, the quantity of sweat brought out by a single dose of the alkaloid has been estimated at from 9 to 15 ounces. Ewing has shown that in the case of the salivary glands at least (*J. P. Ex. T.*, 1911, iii, p. 1) the increase is not merely in the watery constituents, but represents a true excitation of glandular activity because the solid matters and specific ferment of the secretion are also augmented. Usually there is more or less compensatory corollation between the degree of action on the various glandular structures, that is, if the sweat is greatly increased the effects upon the salivary glands, for instance, will be comparatively slight. There has been considerable difference of opinion among clinicians as to whether pilocarpine has any effect upon the kidney, and if so, what is the nature of this action, but the studies of Baco and Plumier (*J. de P. P.*, 1908, x, p. 32) have shown that the changes in the urinary output are secondary to the effects on the circulation; thus if the drug causes a fall of blood pressure the quantity of urine is diminished, but if there is no change in the circulation the kidney activity is unaffected. It is probable that in human beings the loss of water through the skin will also affect the quantity of urine.

Pilocarpine is used in medicine chiefly as a sudorific, either for the purpose of evacuating *dropsies* or aiding in the elimination of toxic substances, as in *uremia, gout, chronic rheumatism* and similar complaints. It should always, if possible, be used in conjunction with some form of external heat so as to determine the blood towards the skin. If used incautiously it may give rise to a very dangerous pulmonary edema. The mechanism of this is three-fold, an increase in the bronchial secretions, a reduction of the force of the circulation, and a spasm of the bronchial muscles. If the action of the drug has been directed towards the skin by other diaphoretic measures and the dose has not been unduly large, the likelihood of this accident is extremely remote. Its occurrence is the signal for the immediate exhibition of atropine. We believe that the doses sometimes employed are much larger than necessary. If properly used more than one-eighth of a grain hypodermically is very rarely needed. Pilocarpine has also been recommended by Reid (*J. A. M. A.*, 1911, lvi, p. 1739) in the treatment of *pruritus.* It is believed by some to have an effect upon the growth of the hair and is used both internally and topically in the treatment of *baldness.* Robinson (*J. A. M. A.*, 1914, lxiii, p. 63) reports favorable results in the treatment of *hypertension.* It is also asserted to be of value in *catarrhal jaundice.* As a local remedy it is employed by ophthalmologists as a myotic in strengths of one-half to one per cent.

When an overdose of jaborandi, or its principal alkaloid, has been taken, the symptoms begin with flushing of the face and neck, soon followed by free sweating and salivation, both of which may be extremely profuse. Frequently there is nausea and sometimes vomiting, the pulse is usually somewhat more rapid than normal, the pupils contracted, and often there is diarrhea. In patients with circulatory disturbances, pulmonary edema may occur, and prove rapidly fatal. The antagonism between pilocarpine and atropine is about as complete as between any two drugs, and the most certain treatment for cases of poisoning by jaborandi, after evacuating the stomach, is the prompt administration of a full dose of atropine, or some substance containing it.

Dose, of pilocarpine hydrochloride, one-twentieth to one-sixth of a grain (0.003–0.01 Gm.).

PILOCARPINÆ NITRAS. U. S., Br.

PILOCARPINE NITRATE Pilocarpin. Nit.

"The nitrate [$C_{11}H_{16}O_2N_2.HNO_3$] of an alkaloid obtained from the dried leaflets of *Pilocarpus Jaborandi* Holmes, or of *Pilocarpus microphyllus* Stapf (Fam. *Rutaceæ*)." *U. S.* "Pilocarpine Nitrate, $C_{11}H_{16}N_2O_2.HNO_3$, is the nitrate of an alkaloid, pilocarpine, obtained from the leaves of Pilocarpus microphyllus, *Stapf,* and other species of Pilocarpus." *Br.*

Pilocarpinum Nitricum, *Fr. Cod.;* Nitrate de Pilocarpine, *Fr.*

Preparation.—This salt may be made by adding pure pilocarpine to diluted nitric acid, carefully evaporating the solution, and purifying the crystals by solution in alcohol and recrystallizing.

Description and Physical Properties.—"Shining, colorless crystals. It is stable in the air. One Gm. of Pilocarpine Nitrate is soluble in 4 cc. of water and in 75 cc. of alcohol, at 25° C. One Gm. is soluble in 21 cc. of alcohol at 60° C. It is insoluble in chloroform and in ether.

"Pilocarpine Nitrate melts between 170° and 173° C. Its aqueous solution (1 in 20) is slightly acid to litmus paper. Dissolve from 0.01 to 0.02 Gm. of Pilocarpine Nitrate in 2 cc. of distilled water in a test tube, add 2 cc. of a faintly acid hydrogen dioxide T.S., and cover the mixture with about 1 cc. of benzene. Add 3 or 4 drops of a solution of potassium dichromate (1 in 300) and shake the mixture gently: the benzene layer acquires a violet color, while the aqueous layer remains yellow (*distinction from other alkaloids*). (If more than 0.02 Gm. of the salt is used, the benzene turns blue and the reaction is no longer characteristic.) Mix an aqueous solution of the salt with an equal volume of ferrous sulphate T.S., and superimpose the mixture upon 5 cc. of sulphuric acid, contained in a test tube: the line of contact becomes brown.

"The ash from 0.1 Gm. is negligible. A solution of 0.1 Gm. of Pilocarpine Nitrate in 2 cc. of sulphuric acid is colorless or at most only faintly yellow (*readily carbonizable substances*). The addition of a few drops of silver nitrate T.S. to 5 cc. of an aqueous solution of the salt (1 in 50), acidulated with nitric acid, does not at once produce an opalescence (*chloride*). The addition of ammonia T.S. or of potassium dichromate T.S. to 10 cc. of an aqueous solution of Pilocarpine Nitrate (1 in 100) produces no turbidity (*various foreign alkaloids*).

"Preserve in well-closed containers, protected from light." *U. S.*

"A white crystalline powder. Soluble in 8 parts of *water.* Melting point about 176° C. Yields with *sulphuric acid* a colorless solution slowly becoming green on the addition of *potassium bichromate.* When a solution of 0.01 gramme in 5 millilitres of *water* is mixed with 2 drops of *diluted sulphuric acid* and then with 1 millilitre of *solution of hydrogen peroxide,* 1 millilitre of *benzene,* and 1 drop of *solution of potassium chromate,* and the mixture well shaken and allowed to separate, the benzene is colored bluish-violet. No appreciable ash." *Br.*

The medicinal properties and dose are the same as those of *Pilocarpinæ Hydrochloridum.*

Dose, from one-twentieth to one-sixth of a grain (0.003–0.01 Gm.).

Off. Prep.—Elixir Tongæ et Salicylatum, *N. F.*

PILULÆ.

PILLS

Pilules, *Fr.;* Pillen, *G.;* Pillole, *It.;* Pildoras, *Sp.*

These are globular masses of a size convenient for swallowing. They are well adapted for the administration of medicines which are unpleasant to the taste or smell, or insoluble in water, and which do not require to be given in large doses. Deliquescent substances should not be made into pills, and those which are efflorescent should be previously deprived of their water of crystallization. Care should be taken not to combine materials the mutual reaction of which may result in a change of physical conditions.

Some substances have a consistence which enables them to be made immediately into pills. Such are the softer extracts and certain gum-resins, and the addition of a little water to the former, and of a few drops of alcohol to the latter, will give them the requisite softness and plasticity, if previously wanting. Substances which are very soft, or in the liquid state, are formed into a pill mass by incorporation with dry and inert powders, such as althea, glycyrrhiza or starch. A mixture of syrup and mucilage of acacia is an excellent excipient for certain kinds of pills. Honey has also been highly recommended. Confection of rose and glucose are among the favored excipients when the pills are to be kept long. For the same purpose of keeping the pills soft, the addition of a small portion of some fixed oil or deliquescent salt has been recommended, but glycerin is still better. Glycerin incorporated with one-twenty-fifth of its weight of powdered tragacanth is said to cause pills to remain soluble for almost any length of time. Glycerite of tragacanth is an excellent excipient. It has been objected that pills made with glycerin could not be handsomely gilded or silvered, the luster of the metal disappearing. This is true, however, only of very recent pills, or of those in which an excess of glycerin has been used. Many substances require only water as an excipient to form a mass. Care should always be taken that the excipient or the absorbent is not incompatible with the therapeutic constituents of the pill. For a list of excipients for pills see J. Cohn (*Ph. Ztg.*, 1900, 221); also G. Grugge (*A. Ph. A. Year Book*, 1914, p. 81).

The materials should be accurately mixed together, and beaten in a mortar until formed into a perfectly uniform and plastic mass. This should be of such a consistence that the pills may preserve their form, without being so hard as to resist the solvent power of the gastric fluids. The mass is made into pills by rolling it with a spatula, or with a flat, smooth piece of hard wood, into a cylinder of precisely the same thickness throughout, and of a length corresponding to the number of pills required. It is then divided as equally as possible by the hand, or, more accurately, by a machine. (See Remington's *Practice of Pharmacy*, 5th edition, p. 1217.) The pills receive a spherical form by being rolled between the fingers or by the use of one of the pill rolling machines. In order to prevent the adhesion of pills to one another, or to the sides of the vessel in which they may be placed, it is customary to agitate them with some dry powder, called a consperging powder (pulvis) which gives them an external coating, that serves also to disguise their taste. For this purpose, rice flour, lycopodium, glycyrrhiza or starch may be used. It is the custom in some sections of the United States, particularly on the Pacific coast, to give the pill a coating of gold or silver leaf. This is done by agitating the pills, prepared without dusting powder, and with their surface still damp, or coated with a very small quantity of mucilage, with gold or silver leaf, in an ordinary round pill box or in a hollow spherical wooden box made by turning two hemispheres out of hard wood, fitting each other, and provided with a short handle.

The gelatin coating of pills, originally proposed by Garot, was formerly done on the small scale by forms of apparatus devised particularly for extemporaneous use. Gelatin coating of pills is now done on the large scale only. For forms of apparatus formerly used see *U. S. D.*, 20th ed., pp. 859 and 860.

Gelatin coating on the larger scale is accomplished by the use of the vacuum apparatus of J. B. Russell (see Remington's *Practice of Pharmacy*), or by simply rotating the pills in contact with a solution of gelatin in large spherical vessels, such as are used for sugar coating.

The sugar coating of pills is now conducted upon a large scale by manufacturers, who send immense quantities both of popular and of official pills into the market thus protected. The process employed is similar to that of the confectioners in coating almonds. After having been thoroughly dried, the pills are put into a hemispherical tinned copper basin, which is suspended from the ceiling and moved quickly backward and forward with an eccentric motion, so as to cause a constant attrition among the pills. First a little very thick syrup, or syrup of gum, is introduced in order to give a thin coating to their surface, and afterwards very finely powdered and very dry white sugar is sifted or thrown over them, the motion being constantly maintained. The sugar is fixed by the moist surface of the pills, and the coating made compact and smooth by the attrition. The process is aided by a gentle heat, but the heat must be guarded, lest the pills be much softened, and thus lose their shape and even discolor the coating. Dexterous manipulation is necessary in order that the process may succeed thoroughly.

Blanchard covers pills with a solution of Tolu balsam in ether, but H. C. Baildon objects to this, that it takes too long to dry, and suggests as a substitute a solution of a drachm of the balsam in three drachms of chloroform, which dries sufficiently in twenty minutes. If old and solid Tolu balsam be selected, it will be less liable to the objection of drying slowly. This balsam is officially employed in coating the U. S. pills of ferrous iodide. A solution of mastic in ether has also been used for coating pills, and the white of egg has been recommended for the same purpose.

Pills are sometimes coated with substances which do not dissolve in the stomach, with the object of permitting the passage of the undissolved pill into the intestines; for this purpose keratin coating has been largely used. (See *Keratin*, Part II, and Remington's *Practice of Pharmacy*, seventh edition.) Salol has also been employed, by melting it in an enamelled pan at a temperature of about 50° C. and dropping in the pills, rotating until covered, and then transferring to a dry pan, still rotating (to prevent adhesion) until cold. An improved method of salol coating for pills intended for enteric use has been contributed by J. C. and B. L. DeG. Peacock (*Proc. P. Ph. A.*, 1915, p. 258). The particular points to be observed are the amount of salol to be used and the shape and size of the vessel used in melting the salol. W. G. Toplis (*Proc. P. Ph. A.*, 1915, p. 262) proposes stearic acid as an enteric coating for pills and gives details of the method to be followed in producing a satisfactory article.

Maske (*J. A. Ph. A.*, 1917, vi, 1059) has investigated the rapidity of disintegration of pills made with various masses, in artificial gastric juice. He finds that a soft mass, composed of equal parts of glycyrrhiza and manna disintegrated in 15 minutes; and one of kaolin and petrolatum had not, even although the mixture was agitated mechanically, at the end of eight hours. Under the latter conditions no "enteric pill" was found that had not lost its coating at the end of one and a half hours.

Pills which are to be kept long should be well dried, and put into bottles with loosely fitting stoppers to prevent mouldiness. Though the U. S. Pharmacopœia, in almost every instance, orders the mass to be divided into pills, yet it should be understood rather as indicating the number of pills to be made from a certain quantity of the mass, when particular directions are not given by the physician, than as requiring the division to be made immediately after the materials have been mixed. It will be found convenient by the apothecary to retain a portion of the mass undivided, especially when it is desirable to keep the pills soft. The British Pharmacopœia furnishes formulas for pill masses, using the title of "Pilula" instead of "Massa," the title of the class adopted by the U. S. Pharmacopœia; there is, in our opinion, a decided advantage in selecting a name for the class which is not likely to be confused with that used for the divided pills.

Pills containing silver nitrate, potassium permanganate or other strongly oxidizing substances, should be made by diluting with kaolin or talc and massing with petrolatum or mixtures of petrolatum and paraffin. All organic matter should be excluded.

Compressed pills (*Pilulæ comprimatæ*) or *tablets* (*Tabellæ, Tablettæ*) as they are usually called are made directly from the medicinal substance without the aid of an excipient. The drug, if not already in granular powder, is made so, and then forced into pill shape by means of a powerful press. For certain substances which are crystalline in structure, such as quinine bisulphate, potassium bromide, and potassium iodide, and which have some cohesiveness and yet are of easy solubility, the process is a good one. An apparatus was contrived by J. P. Remington for compressing pills for extemporaneous prescription work (see 16th ed., *U. S. D.*, and *Practice of Pharmacy*). It is made of cast steel; the base has two countersunk depressions with a short post in the center of each, and a lenticular depression is made in the upper surface of each post. A steel cylinder having a central aperture of the diameter of the post is placed in the depression, the proper quantity of powder is introduced, and the plunger, which has a corresponding lenticular depression on its lower surface, is placed on the powder and is struck a quick blow with a mallet; the powder is compressed, and the pill adheres to the cylinder; by removing the cylinder and holding it over a box and tapping the plunger again lightly, the pill is forced out and falls into a box.

Compressed tablets are now used to an enormous extent, being made by various manufacturers with machinery of ingenious construction; the ease with which they can be tested, and their permanent character (in most cases being just as valuable years after they were made as when fresh) have caused their extensive employment.

For a description of some of the more important forms of pill compressing machines with illustrations, see Remington's *Practice of Pharmacy,* seventh edition.

PILULÆ ALOES. U. S. (Br.)

PILLS OF ALOE Pil. Aloes.

Pilula Aloes, *Br.;* Aloes Pill; Pill of Barbados Aloes, Pill of Socotrine Aloes; Pilules d'Aloés et de Savon, Pilules Aloétiques Savoneuses, *Fr.;* Alœpillen, *G.*

"Aloe, in very fine powder, 13 Gm.; Soap, in very fine powder, 13 Gm.; Water, a sufficient quantity, to make 100 pills. Mix the powders intimately, then incorporate sufficient water to form a mass, and divide it into 100 pills." *U. S.*

"Aloes, in powder, 58 *grammes;* Hard Soap, in powder, 29 *grammes;* Oil of Caraway, 3 *millilitres;* Syrup of Glucose, 10 *grammes* or *a sufficient quantity.* Mix to form a mass." *Br.*

In the Br. Pharm., 1898, confection of rose was used as the excipient. It is now replaced by syrup of glucose.

The former British process for *Pill of Socotrine Aloes* was the same except that Socotrine was substituted for Barbados Aloes, and the volatile oil of nutmeg for oil of caraway.

The soap, in this formula, not only serves to impart a proper consistence to the aloes, but is thought to qualify its operation and diminish its liability to irritate the rectum. They are employed as a laxative in *habitual costiveness.*

Dose, one, two or three pills at bedtime. The British pill mass is of very nearly the same strength as that of the U. S. Pharmacopœia.

PILULA ALOES ET ASAFETIDÆ. Br.

PILL OF ALOES AND ASAFETIDA

Pilules d'Aloés et d'Asefétide, *Fr.;* Aloe und Asafœtida-Pillen, *G.*

"Aloes, in powder, 30 *grammes;* Asafetida, 30 *grammes;* Hard Soap, in powder, 30 *grammes;* Syrup of Glucose, 10 *grammes,* or *a* *sufficient quantity.* Mix to form a mass." *Br.*

A similar pill is recognized by the N. F. (see Part III).

Pills made from this mass are peculiarly adapted, by the stimulant and carminative properties of the asafetida, to cases of *costiveness* attended with flatulence and debility of the digestive organs.

Dose, from four to eight grains (0.25–0.5 Gm.) of the mass.

PILULA ALOES ET FERRI. Br.

PILL OF ALOES AND IRON

Pilulæ Italicæ Nigræ; Pilules d'Aloés et de Fer, *Fr.;* Pilulæ Aloeticæ ferratæ, *P. G.;* Eisenhaltige Aloepillen, Aloe und Eisenpillen, Italienische Pillen, *G.*

"Exsiccated Ferrous Sulphate, 10 *grammes;* Aloes, in powder, 20 *grammes;* Compound Powder of Cinnamon, 35 *grammes;* Syrup of Glucose, 35 *grammes,* or *a sufficient quantity.* Mix to form a mass." *Br.*

The N. F. recognizes a very similar mixture (see Part III).

This pill is essentially an old preparation of the Edinburgh Pharmacopœia. The Br. Pharm., 1898, improved this mass by substituting exsiccated ferrous sulphate for the crystallized salt formerly employed, and by the use of syrup of glucose instead of confection of rose. It is said that the laxative power of aloes is increased, and its tendency to irritate the rectum diminished, by combination with ferrous sulphate. This pill is especially adapted to *amenorrhea* with debility of the stomach and constipation.

Dose, of the Br. mass, from three to eight grains (0.2–0.5 Gm.).

PILULA ALOES ET MYRRHÆ. Br.

PILL OF ALOES AND MYRRH

Rufus's Pills; Pilule d'Aloés et de Myrrhe, Pilules de Rufus, *Fr.;* Rufussche Pillen, *G.*

"Aloes, in powder, 44 *grammes;* Myrrh, in powder, 22 *grammes;* Syrup of Glucose, 34 *grammes,* or *a sufficient quantity.* Mix to form a mass." *Br.*

A very similar combination is recognized by the N. F. (see Part III).

This composition is employed, as a warm stimulant cathartic, in *general debility* attended with *constipation,* and in *retention* or *suppression of the menses.*

Dose, of the Br. mass, from four to eight grains (0.26–0.5 Gm.).

PILULÆ ASAFŒTIDÆ. U. S.

PILLS OF ASAFETIDA Pil. Asafœt.

Pilules d'Asefétide, *Fr.;* Asafœtida-Pillen, *G.*

"Asafetida, 20 Gm.; Soap, in very fine powder, 6 Gm.; Water, a sufficient quantity, to make 100 pills. Intimately incorporate the solids, using sufficient water to form a mass, and divide it into 100 pills." *U. S.*

Each of these pills contains three grains (0.20 Gm.) of asafetida. They are a convenient form for administering asafetida, the unpleasant odor and taste of which render it very offensive in the liquid state.

Dose, one to three pills.

PILULA COLOCYNTHIDIS COMPOSITA. Br.

COMPOUND PILL OF COLOCYNTH

Cochia Pills; Pilules de Coloquinte composées, *Fr. Cod.;* Pilules cochées mineures, *Fr.;* Zusammengesetzte Koloquinten Pillen, *G.*

"Colocynth Pulp, in powder, 20 *grammes;* Aloes, in powder, 35 *grammes;* Scammony Resin, in powder, 35 *grammes;* Potassium Sulphate, in powder, 5 *grammes;* Oil of Cloves, 5 *millilitres;* Distilled Water, *a sufficient quantity.* Triturate the Oil of Cloves with the Potassium Sulphate; add the Colocynth Pulp; mix; add the Aloes and Scammony Resin; mix; add Distilled Water, and mix to form a mass." *Br.*

This is not, like the old London pills of the same name, merely another form of the compound extract of colocynth, though containing essentially the same materials—one great difference being that colocynth and aloes are used in substance in the pill, instead of in the state of extract. Potassium sulphate is used to promote the more complete division of the aloes and scammony. The preparation is actively cathartic.

Dose, from five to eight grains (0.32–0.5 Gm.).

Off. Prep.—Pilula Colocynthidis et Hyoscyami, *Br.*

PILULA COLOCYNTHIDIS ET HYOSCYAMI. Br.

PILL OF COLOCYNTH AND HYOSCYAMUS

Pilules de Coloquinte et d'Extrait de Jusquiame *Fr.;* Koloquinten-Bilsenkrautpillenmasse, *G.*

"Compound Pill of Colocynth, 50 *grammes;* Extract of Hyoscyamus, 25 *grammes;* Distilled Water, *a sufficient quantity.* Mix to form a mass." *Br.*

This was an official pill of the Edinburgh College. It is asserted that the compound pill and compound extract of colocynth are almost entirely deprived of their griping tendency by combination, as above, with extract of hyoscyamus, without losing any of their purgative power.

Dose, from five to eight grains (0.32–0.5 Gm.).

PILULÆ FERRI CARBONATIS. U. S. (Br.)

PILLS OF FERROUS CARBONATE Pil. Ferr Carb [Ferruginous Pills, Chalybeate Pills, Blaud's Pills]

"Each Pill contains not less than 0.06 Gm. of $FeCO_3$." *U. S.*

Pilula Ferri, *Br.;* Iron Pill; Pilules Ferrugineuses de Blaud, *Fr. Cod.;* Pilules Chalybées de Blaud, *Fr.;* Pilulæ Ferri carbonici Blaudii, *P. G.;* Blaudsche Pillen, *G.;* Pillole di carbonato ferroso, *It.;* Pildoras de Blaud, *Sp*

"Granulated Ferrous Sulphate, 16 Gm.; Potassium Carbonate, 8 Gm.; Sucrose, 4 Gm.; Tragacanth, in very fine powder, 1 Gm.; Althea, in very fine powder, 1 Gm.; Glycerin, Water, each, a sufficient quantity, to make 100 pills. Triturate the potassium carbonate in a mortar with a sufficient quantity (about 5 drops each) of glycerin and water, then add the ferrous sulphate and sucrose, previously triturated together to a uniform, fine powder, and mix the mass thoroughly until it assumes a greenish color. When the reaction is complete, incorporate the tragacanth and althea, and add more water, if necessary, to obtain a mass of pilular consistence. Divide into 100 pills.

"Preserve in tightly-closed containers." *U. S.*

"Exsiccated Ferrous Sulphate, in powder, 33 *grammes;* Exsiccated Sodium Carbonate, in powder, 21 *grammes;* Tragacanth, in powder, 2 *grammes;* Gum Acacia, in powder, 8 *grammes;* Glucose, 31 *grammes;* Distilled Water, 2 *millilitres.* Mix the Glucose, Distilled Water, and Exsiccated Ferrous Sulphate; add the Exsiccated Sodium Carbonate; mix and set aside for ten minutes, or until the reaction is complete; add the Tragacanth and Gum Acacia, and mix to form a mass. This Pill contains about 22.5 per cent. of ferrous carbonate." *Br.*

Assay.—"Dissolve three Pills in 15 cc. of diluted sulphuric acid, and dilute the solution with distilled water to about 100 cc. Immediately titrate with tenth-normal potassium dichromate, potassium ferricyanide T.S. being used as indicator. Each cc. of tenth-normal potassium dichromate corresponds to 0.01159 Gm. of $FeCO_3$." *U. S.*

These pills afford one of the best forms of exhibiting iron, in the treatment of *anemia,* being nearly free from astringency. As their peculiar advantages depend upon the presence of ferrous carbonate, which speedily changes into the ferric salt on exposure, it is proper that only so much of the mass should be prepared as may be wanted for immediate use. They are sometimes called *Griffith's pills.* They closely resemble *Blaud's ferruginous pills,* made originally in 1831, and celebrated in France as a remedy in *chlorosis,* prepared from equal weights of ferrous sulphate and potassium carbonate, made into a pilular mass. (See *P. J.,* 1894, 131.) The pills contain, as the result of double decomposition, ferrous carbonate and potassium sulphate. Van de Velde and Van Melckebeke prefer the sodium bicarbonate to the potassium salt. For a brief historical account of these pills, see a paper by John Humphrey in *P. J.,* 1903, 643.

Blaud's pills may become very harl upon standing, but if properly made, they undergo very little alteration. For an assay of a very old specimen, see *N. J. Ph. A.,* 1912, p. 73.

Dose, from two to six pills, to be taken three times a day; of the Br. mass, five to twenty grains (0.32–1.3 Gm.).

PILULÆ HYDRARGYRI CHLORIDI MITIS COMPOSITÆ. U. S.

COMPOUND PILLS OF MILD MERCUROUS CHLORIDE Pil. Hydrarg. Chlor. Mit. Co. [Pilulæ Catharticæ Compositæ U. S. P. IX]

Compound Cathartic Pills; Compound Calomel Pills; Antibilious Pills; Pilules cathartiques composées, *Fr.;* Abführpillen, *G.*

The new name of these pills although rather cumbersome is to be preferred as descriptive of their chief ingredient rather than their therapeutic property.

"Compound Extract of Colocynth, 80 Gm.; Mild Mercurous Chloride, 60 Gm.; Resin of Jalap, in fine powder, 20 Gm.; Gamboge, in very fine powder, 15 Gm.; Diluted Alcohol, a sufficient quantity, to make 1000 pills. Mix the powders intimately, then incorporate a sufficient quantity of diluted alcohol to form a mass, and divide it into 1000 pills." *U. S.*

This cathartic compound was first made official in the second edition of the U. S. Pharmacopœia. It was intended to combine smallness of bulk with efficiency and comparative mildness of purgative action and a peculiar tendency to the biliary organs. The object of smallness of bulk is accomplished by employing extracts and the more energetic cathartics; that of a peculiar tendency to the liver, by the use of calomel, and that of efficiency with mildness of operation, by the union of several powerful purgatives. It is a fact, abundantly proved by experience, that drastic cathartics become milder by combination, without losing any of their purgative power. It is highly important that these pills be prepared in exact compliance with the directions, and that the compound extract of colocynth and the resin of jalap used be of good quality.

Each pill weighs about 3 grains (0.194 Gm.), and contains 2.70 grains (0.175 Gm.) of active ingredients. A single pill will generally be found to operate as a mild laxative. In a full dose, the preparation acts vigorously on the bowels, producing bilious stools, generally without much pain or disorder of the stomach. It may be employed in most instances where a brisk cathartic is required, but is particularly applicable to the early stages of *bilious fevers,* and to all those derangements which depend on congestion of the portal circle. It should not be used in habitual constipation.

Dose, one to three pills.

PILULA HYDRARGYRI SUBCHLORIDI COMPOSITA. Br.

COMPOUND PILL OF MERCUROUS CHLORIDE [Compound Calomel Pill, Plummer's Pill]

Compound Pills of Antimony; Pilula Calomelanos Composita, *Br.* 1864; Compound Pill of Mercurous Chloride; Pilules alterantes composées, Pilules antidartreuses, Pilules de Plummer, *Fr.;* Plummersche Pillen, Zusammengesetzte Calomelpillen, *G.*

"Mercurous Chloride, 20 *grammes;* Sulphurated Antimony, 20 *grammes;* Guaiacum Resin, in powder, 40 *grammes;* Gum Acacia, in powder, 1 *gramme;* Tragacanth, in powder, 1 *gramme;* Syrup of Glucose, 10 *grammes,* or *a sufficient quantity.* Mix to form a mass." *Br.*

Compound pills of antimony were dropped in the U. S. P. VIII, but the National Formulary IV has introduced the compound pill of antimony of the U. S. P., 1890, without alteration (see *Pilulæ Antimonii Compositæ,* Part III). This pill is official in the British Pharmacopœia, 1914, castor oil, which was used as an excipient, being replaced by syrup of glucose. "Compound Calomel Pill" of the British Pharmacopœia should not be confounded with the compound calomel pill of the U. S. as the two possess very different therapeutic virtues.

According to Vogel a reaction takes place between the calomel and the sulphurated antimony, resulting in the production of antimony chloride and mercury sulphide. The preparation was originally introduced to the notice of the profession by Dr. Plummer, who found it useful as an alterative, and upon whose authority it was at one time much employed under the name of *Plummer's Pills.* The combination is used in the treatment of *chronic rheumatism* and of scaly and other *eruptive diseases of the skin,* especially when accompanied with a syphilitic taint.

Dose, four to eight grains (0.26–0.5 Gm.) or more, morning and evening.

PILULA IPECACUANHÆ CUM SCILLA. Br.

PILL OF IPECACUANHA WITH SQUILL

Pilules d'Ipécacuanha et de Scille, *Fr.;* Brechwurzel-Meerzwiebelpillen, *G.*

"Compound Powder of Ipecacuanha, 30 *grammes;* Squill, in powder, 10 *grammes;* Ammoniacum, in powder, 10 *grammes;* Syrup of Glucose, *a sufficient quantity.* Mix to form a mass. This Pill contains about 5 per cent. of Opium." *Br.*

This is an old-fashioned combination of expectorants, intended for *chronic bronchitis,* but scarcely in keeping with modern practice.

Dose, from five to ten grains (0.32–0.65 Gm.).

PILULA IPECACUANHÆ CUM URGINEA. Br.

PILL OF IPECACUANHA WITH URGINEA

"Compound Powder of Ipecacuanha, 30 *grammes;* Urginea, in powder, 10 *grammes;* Ammoniacum, in powder, 10 *grammes;* Syrup of Glucose, *a sufficient quantity.* Mix to form a mass. This Pill contains about 5 per cent. of Opium." *Br.*

This is the same as Pill of Ipecacuanha with Squill, except that Indian Squill or Urginea is used in place of the Mediterranean variety.

PILULÆ PHOSPHORI. U. S. (Br.)

PILLS OF PHOSPHORUS Pil. Phosphor.

Pilula Phosphori, *Br.;* Phosphorus Pill; Pilules au Phosphore, Pilules Phosphorées, *Fr.;* Phosphorpillen, *G.*

"Phosphorus, 0.06 Gm.; Althea, in very fine powder, 6.00 Gm.; Acacia, in very fine powder, 3.00 Gm.; Chloroform, Glycerin, Water, Tolu, Ether, each, a sufficient quantity, to make 100 pills. Dissolve the phosphorus in a test tube in 5 cc. of chloroform, with the aid of a very gentle heat, replacing from time to time any of the chloroform which may be lost by evaporation. Mix the althea and acacia in a mortar, next add the solution of phosphorus, then immediately afterwards a sufficient quantity (about 4 cc.) of a mixture of 2 volumes of glycerin and 1 volume of water, and quickly form a mass. Divide it into 100 pills. Dissolve 10 Gm. of tolu in 15 cc. of ether, shake the pills with a sufficient quantity of this solution until they are uniformly coated and put them on a plate to dry, occasionally rolling them about until the drying is completed.

"Preserve in a well-stoppered bottle." *U. S.*

"Phosphorus, 1 *gramme;* Oil of Theobroma, 40 *grammes;* Wool Fat, 11 *grammes;* Kaolin, 16 *grammes;* Sodium Sulphate, dried at 100° C., 32 *grammes;* Carbon Disulphide, 20 *millilitres.* Dissolve the Phosphorus and 20 *grammes* of the Oil of Theobroma in the Carbon Disulphide. Allow the solution to evaporate in a mortar until a pasty mass is obtained. To this add the remainder of the Oil of Theobroma together with the other ingredients, and mix to form a mass. This Pill contains 1 per cent. of Phosphorus. It is of one-half the strength of the corresponding preparation of the British Pharmacopœia, 1898. It should be freshly prepared." *Br.*

The problem of preventing the oxidation of the phosphorus is believed to be solved by dissolving it in an excess of warm chloroform; this is accomplished in a stoppered test-tube, for it has been shown that no oxidation takes place in the presence of chloroform vapor. It is necessary to form the mass quickly, so that the chloroform may not all evaporate and leave the phosphorus exposed to the action of the air. Chloroform is preferable to carbon disulphide, as recommended in the Br., for, although the latter is a better solvent, it is difficult to rid the mass of the disgusting odor.

The formula for this pill in the British Pharmacopœia, 1914, has been improved and simplified by replacing white wax and lard with oil of theobroma and wool fat, and its strength has been reduced to one-half of that of the Br., 1898.

Each official U. S. pill contains about 1-100th of a grain (0.0006 Gm.) of phosphorus.

Dose, of the U. S. pills, one pill three times a day; of the Br. mass, one grain (0.065 Gm.).

PILULA PLUMBI CUM OPIO. Br.

PILL OF LEAD WITH OPIUM

Pilules d'Acétate de Plomb et d'Opium, *Fr.;* Bleiacetat-Opiumpillenmasse, *G.*

"Lead Acetate, in powder, 80 *grammes;* Opium, in powder, 12 *grammes;* Syrup of Glucose, 8 *grammes,* or *a sufficient quantity.* Mix to form a mass. This Pill contains about 12 per cent. of Opium." *Br.*

This pill would be better left to extemporaneous prescription, the requisite proportion of opium to the lead acetate varying in different cases. A similar preparation is also official in the N. F. (see *Pilulæ Opii et Plumbi,* Part III).

Dose, two or three grains (0.13–0.20 Gm.) to begin with.

PILULA QUININÆ SULPHATIS. Br.

PILL OF QUININE SULPHATE

Pilule de Quinine Sulfate, *Fr.;* Chininpillenmasse, *G.;* Pildoras de sulfato quinico, *Sp.*

"Quinine Sulphate, 82 *grammes;* Tartaric Acid, in powder, 3 *grammes;* Glycerin, 12 *grammes;* Tragacanth, in powder, 3 *grammes.* Triturate the Quinine Sulphate with the Tartaric Acid; add the product to the previously mixed Glycerin and Tragacanth; mix to form a mass." *Br.*

The reason for introducing a quinine pill mass in the British Pharm. is doubtless to serve the convenience of dispensers and to save time; tartaric acid aids in solubility and in making the pills smaller, while glycerin keeps the mass from undue hardening.

Dose, two to eight grains (0.13–0.5 Gm.).

PILULA RHEI COMPOSITÆ. Br.

COMPOUND PILL OF RHUBARB Pil. Rhei Co.

Pilules de Rhubarbe composées, *Fr.;* Rhabarber und Aloepillen, *G.*

"Rhubarb, in powder, 25 *grammes;* Aloes, in powder, 20 *grammes;* Myrrh, in powder, 14 *grammes;* Hard Soap, in powder, 14 *grammes;* Oil of Peppermint, 2 *millilitres;* Syrup of Glucose, 25 *grammes,* or *a sufficient quantity.* Mix to form a mass." *Br.*

A similar pill is recognized by the N. F. (see Part III).

This is a tonic laxative, useful in *costiveness.* If made in quantity the pills should be kept in loosely stoppered bottles. The use of glycerin favors the formation of mouldiness through the attraction of moisture, and it was replaced in the formula of the Br. Ph., 1898, by syrup of glucose.

Dose, from five to eight grains (0.32–0.5 Gm.) of the mass, twice a day.

PILULA SAPONIS COMPOSITA. Br.

COMPOUND PILL OF SOAP

Pilulæ Opii, *U. S. VIII,* Pill of Opium; Pilules de Savon composées, *Fr.;* Seifenpillenmasse, *G.*

"Opium, in powder, 20 *grammes;* Hard Soap, in powder, 60 *grammes;* Syrup of Glucose, 20 *grammes,* or *a sufficient quantity.* Mix to form a mass. This Pill contains about 20 per cent. of Opium." *Br.*

This pill is practically identical with the opium pill of the U. S. VIII. There is no evident need of such a pill; it might much more wisely be left to extemporaneous prescription. The name was probably intended to conceal the nature of the preparation, but, in our opinion, it is a mistake to omit the only important ingredient from the title. One grain (0.065 Gm.) of opium is contained in five grains (0.32 Gm.) of the mass.

Dose, from two to five grains (0.13–0.32 Gm.).

PILULA SCILLÆ COMPOSITA. Br.

COMPOUND SQUILL PILL

Pilules de Scille composées, *Fr.;* Meerzwiebelpillenmasse, *G.*

"Squill, in powder, 25 *grammes;* Ginger, in powder, 20 *grammes;* Ammoniacum, in powder, 20 *grammes;* Hard Soap, in powder, 15 *grammes;* Syrup of Glucose, 20 *grammes,* or *a sufficient quantity.* Mix to form a mass." *Br.*

This is a stimulating expectorant compound, depending for its virtues chiefly on the squill, and applicable to the treatment of *chronic bronchitis.* The mass should be freshly made when wanted, as the squill which it contains is liable to be injured by keeping.

Dose, from four to eight grains (0.25–0.5 Gm.).

PILULA URGINEÆ COMPOSITA. Br.

COMPOUND URGINEA PILL

"Urginea, in powder, 25 *grammes;* Ginger, in powder, 20 *grammes;* Ammoniacum, in powder, 20 *grammes;* Hard Soap, in powder, 15 grammes; Syrup of Glucose, 20 *grammes,* or *a sufficient quantity.* Mix to form a mass." *Br.*

This pill is the same as the Compound Squill pill, except that the Indian Squill, Urginea, replaces the ordinary variety.

Dose, from four to eight grains (0.25–0.5 Gm.).

PIMENTA. N. F.

PIMENTA Piment. [Allspice]

"Pimenta is the dried nearly ripe fruit of *Pimenta officinalis* Lindley (Fam. *Myrtaceæ*). Pimenta contains not more than 3 per cent. of foreign organic matter and not more than 0.4 per cent. of acid insoluble ash." *N. F.*

Allspice; Clove Pepper; Pimento; Semen Amomi; Piper Jamaicense; Pimento; Allspice; Jamaica Pepper; Piment de la Jamaïque, Touteépice; Poivre de la Jamaïque, *Fr.;* Englisches Gewürz; Neugewürz; Nelkenpfeffer, *G.;* Pimenti, *It.;* Pimienta de la Jamaica, *Sp.*

Pimenta Pimenta (L.) Karsten (*P. officinalis* Lindley; *Myrtus Pimenta* L.; *Eugenia Pimenta* DC.) is an evergreen tree, 25 to 40 feet in height, with an erect trunk and round-topped crown. The leaves are entire, ovate-oblong and glandular-dotted beneath. The flowers are small, white and borne in racemose cymes. Each consists of a sub-globose calyx tube with a four-divided limb, four petals, numerous stamens and a two-celled inferior ovary. The fruit is a two-celled and two-seeded inferior berry, each cell containing a single plano-convex, reddish-brown seed.

This tree is a native of the West Indies and the adjoining coast of continental America. The earlier Spanish adventurers mistook the berries for a species of pepper which mistake is commemorated in the botanical name of the genus, "pimenta" (from the Spanish word for a pepper) and is also perpetuated in one of the common English names, "Jamaica pepper." It is cultivated in Central America and the surrounding countries, but the supply to the United States and Great Britain comes from Jamaica, where the tree is so abundant as to form in the mountainous districts whole forests, and to require no further cultivation than the clearing out of the underbrush. The berries are gathered after having attained their full size, but while yet green, and are carefully dried in the sun. When sufficiently dry, they are put into bags and casks for exportation. The fruits of four other species of the genus *Pimenta*, found in Venezuela, Guiana, and the West Indies, are employed in their native countries as spices.

Description and Physical Properties.—"*Unground Pimenta.*—Sub-globular, from 4 to 7 mm. in diameter, apex with four calyx teeth forming a minute ring; externally dark brown, somewhat rough and glandular-punctate; pericarp brittle, about 1 mm. in thickness; two-celled and two-seeded; dissepiments thin; seeds plano-convex, slightly reniform, externally reddish brown, smooth, somewhat wrinkled and shiny. Odor and taste, particularly of the pericarp, aromatic and distinctive.

"*Powdered Pimenta.*—Reddish brown or dark brown, shows irregular fragments and numerous starch grains, the latter being either simple or compound, the individual grains spherical, plano-convex or polygonal, from 0.003 to 0.015 mm. in diameter, occasionally up to 0.020 mm. in diameter, and frequently with a central circular marking or cleft; stone cells numerous, of tabular, pyriform or variable shape and with thick, porous, and strongly lignified walls, the lumina frequently filled with a yellowish or reddish brown amorphous substance, fragments with oil secretion reservoirs containing globules of a yellowish brown oil; parenchyma cells with reddish brown tannin masses. Stem fragments very few, and characterized by more or less curved, thick-walled, non-glandular hairs, rosettes of calcium oxalate, from 0.006 to 0.020 mm. in diameter, tracheid-like tissues of the wood and long narrow bast fibers. The yield of crude fiber does not exceed 25 per cent." *N. F.*

The odor of Pimenta berries is thought to resemble that of a mixture of cinnamon, cloves, and nutmeg. Hence the name of *allspice*, by which they are best known in this country. They impart their flavor to water, and all their virtues to alcohol. The infusion is of a brown color, and reddens litmus paper.

Pimenta yields from 3 to 4.5 per cent. of a volatile oil. (See *Oleum Pimentæ.*) Besides the volatile oil, pimenta contains over 8 per cent. of tannic acid, a soft green resin with a burning aromatic taste and other unimportant vegetable matters. The ash, according to the standards of the Association of Food and Dairy Departments, should not be more than 6 per cent. and not more than 0.5 per cent. insoluble in hydrochloric acid. According to Bonastre, the shell contains 10 per cent. of the volatile and 8 of the fixed oil, the seeds only 5 per cent. of the former, and 2.5 of the latter. Dragendorff, in 1871, announced the existence of an alkaloid in allspice. It is present in exceedingly small quantity, and has somewhat the odor of coniine.

Pimenta is sometimes adulterated by the larger and less aromatic berries of the Mexican allspice (*Eugenia Tabasco* G. Don). Powdered pimenta has been also adulterated with all sorts of substances as ground cocoanut shells, cereal starches, etc.

Uses.—Pimenta is an aromatic spice, used in medicine chiefly as an adjuvant to tonics and purgatives. It is particularly useful in cases attended with much *flatulence*. It is, however, much more largely employed as a condiment than as a medicine.

Aqua Pimentæ Br., 1898, was formerly official—it was a distilled water.

Dose, ten to forty grains (0.65–2.6 Gm.).

Off. Prep.—Tinctura Guaiaci Composita, *N. F.*

PINUS ALBA. N. F.

WHITE PINE BARK Pin. Alb.

"White Pine Bark is the dried inner bark of *Pinus Strobus* Linné (Fam. *Pinaceæ*). White Pine Bark contains not more than 2 per cent. of outer bark and not more than 2 per cent. of foreign organic matter." *N. F.*

Deal Pine; Weymouth Pine; Northern Pine.

The *Pinus Strobus* or *white pine* is a large handsome evergreen tree reaching a height of 150 feet, found throughout the whole eastern portion of the U. S. and lower Canada as far south as Georgia, being most abundant in New England and Canada. Its leaves are soft, bluish-green, 2 to 5 inches long and occur in fascicles of five. Its carpellate cones are slender, cylindric and elongated with oblong-obovate scales bearing winged reddish-brown seeds. Its wood, because of its light color, ease of working and freedom from resin is one of the most highly esteemed sorts of lumber. The part used in medicine is the dried inner bark which is officially described as follows:

Description and Physical Properties.—"*Unground White Pine Bark.*—In flat pieces of variable size and from 1 to 3 mm. in thickness; outer surface varying from a pale pinkish white when fresh, to a light or rather deep yellowish brown on keeping, occasionally with small patches of the gray-brown periderm adhering; more or less cottony, and often showing small scattered pits; inner surface either lighter or darker than the outer, finely striate; fracture short, irregular, transverse section showing an outer yellowish and an inner whitish band. Odor slight, terebinthinate; taste slightly mucilaginous, bitter, sweet and astringent.

"*Powdered White Pine Bark.*—Numerous rounded or oval, simple starch grains, up to 0.030 mm. in diameter, a very few slightly larger, some having a cleft or fissure through the center; few monoclinic prisms of calcium oxalate up to 0.025 mm. in length; resin in reddish brown, angular masses; thin-walled parenchyma cells, isodiametric or elongated, many containing starch grains; tracheids very few or absent." *N. F.*

Of the medicinal constituents of the pine bark we have no satisfactory knowledge. It contains a glucoside *coniferin*, $C_{16}H_{22}O_8.2H_2O$. This, when decomposed, yields *coniferyl alcohol* which can be oxidized to vanillin. It is not probable that this principle is of any remedial value although it is a commercial source for synthetic vanillin. The bark also contains upwards of 10 per cent. of tannin. Presumably the therapeutic value of the bark resides in the resin, which, however, as far as we know, has not been carefully investigated.

Uses.—White pine bark is used as an ingredient in cough syrups. As it is always employed in conjunction with other remedial agents, it is difficult to determine whether it does possess any real virtues. We are strongly persuaded, however, that the syrup of white pine with morphine, although—or rather because of the fact—it is outside the limit of the Harrison Antinarcotic Act, has much more potency for evil as a habit-forming drug than for benefit as a therapeutic agent.

Dose, from fifteen to forty-five grains (1–3 Gm.).

Off. Prep.—Syrupus Pini Albæ Compositus, *N. F.;* Syrupus Pini Albæ Compositus cum Morphina, *N. F.*

PIPER. N. F.

PEPPER [Black Pepper]

"Pepper is the dried, unripe fruit of *Piper nigrum* Linné (Fam. *Piperaceæ*). Pepper contains not more than 2 per cent. of stems or other foreign matter." *N. F.*

Piper Nigrum, *Br.* 1898; Common Pepper; Fructus Piperis Nigri; Poivre noir, *Fr.;* Schwarzer Pfeffer, *G.;* Pepenero, *It.;* Pimienti negra, *Sp.;* Fifil uswud, *Arab.;* Lada, *Malay;* Maricha, *Jav.;* Sahan, *Palembang.*

The pepper vine (*Piper nigrum*) is a perennial plant, with a round, smooth, woody, articulated stem, swelling near the joints, branched, and from eight to twelve feet or more in length. The leaves are entire, broad-ovate, acuminate, five- to nine-nerved, coriaceous, very smooth, of a dark green color, and attached by strong sheath-like petioles to the joints of the branches. The flowers are small, whitish, sessile, covering thickly a cylindrical pendulous spike, and succeeded by globular sessile drupes which are red when ripe.

The plant is a native of southern India and grows wild in Cochin-China and various parts of India. It is cultivated on the coast of Malabar, in the peninsula of Malacca, in Siam, Sumatra, Singapore, Johore, Borneo, the Philippines, Japan and many other places in the East; also to some extent in the West Indies. The chief commercial supplies now come from Singapore. The plant is propagated by cuttings, and is supported by props, or trees planted for the purpose, upon which it is trained. In three or four years from the period of planting, it begins to bear fruit. The plant sometimes begins to bear as early as the first year after planting, increases in its yield to the fifth or sixth year, when it produces eight or ten pounds, and begins to lose its productiveness about the fifteenth year. The fruits are gathered while green and dried in the sun or above fires, when they become black and wrinkled. The fire-dried fruits possess a smoky odor and taste and are the most esteemed. The greatest production is in Sumatra, and the ports of export are principally Singapore and Penang, the Malabar pepper coming from Tellicherry. In England, at least, it is customary to mix peppers of different origin in grinding, taking Malabar for weight, Penang for strength, and Sumatra for color. Owing to the widespread cultivation of pepper a large number of varieties exist; these receive their names from the place of their production or their ports of shipment, as Singapore, Acheen, Penang, Siam, Tellicherry, Trang, Lampong, etc. For a description of the most important of these varieties with the percentage of active constituents contained in each, see J. W. Gladhill, *A. J. P.*, Feb., 1904; Kraemer and Sindall, *A. J. P.*, 1908, p. 1; also Blyth, *Foods: Their Composition and Analysis.*

White pepper is the nearly ripe drupe, deprived of the outer part of its pericarp by maceration in water and subsequent friction, and afterwards dried in the sun. It occurs as yellowish more or less broken grains with a smooth shiny surface from which the epicarp or outer layer of the fruit has been removed. It is sold in the market either as a whole white pepper or as broken white pepper; the whole peppers are very likely to have some of the epicarp or hull remaining. The removed hull is sold separately under the name of "pepper hulls"; it forms a light to dark brown powder, with a very pungent odor and taste and contains large amounts of the oleoresin of pepper, but according to Gladhill, no piperine. The hulls are sometimes sold mixed with broken white pepper. This mixture contains more oleoresin and less piperine than does the pure pepper; the percentage of the two active constituents varying according to the percentage of drugs in the mixture. White pepper is much less pungent but more aromatic than black pepper.

Long Pepper is obtained from *Piper officinarum* Casimir DC., and *P. longum* L., the former species yielding the principal commercial supplies and being grown in Java, India, and the Philippines. The plants are distinguished in having their flowers in dense, short terminal, and nearly cylindrical spikes and their fruits, consisting of very small one-seeded drupes, embedded in a pulpy matter. The fruit is green when immature, and becomes red as it ripens. It is gathered in the former state, as it is then hotter than when perfectly ripe. The whole spike is taken from the plant, and dried in the sun. The fruit of the *P. officinarum* is cylindrical, 2 to 6 cm. long and 4 to 7 mm. in diameter, indented on its surface, of a dark-gray color, a weak aromatic odor, and a pungent fiery taste. The fruits of *P. longum* are shorter and thicker. Dulong found its chemical composition to be closely analogous to that of black pepper. *West African* or *Ashantee Pepper* is the fruit of *P. Clussii,* C. DC., which grows abundantly in tropical Africa. It does not come into Western commerce, although much used in Africa. The berry is described as resembling cubeb, but less rugose, and with a more slender pedicel and having the odor and taste of black pepper. Stenhouse found piperine in this variety of pepper.

Kissi Pepper is a fruit yielded by the *Piper Famechoni,* Heckel, of Upper Guinea. The berries, which grow in cylindrical clusters, are small, blackish-brown, ovoidal, with a cubeb-like pedicel at their base. Their powder is very aromatic, with an especially pleasant taste. They have been found by A. Barille to contain 4.5 per cent. of volatile oil and 3.7 per cent. of piperine. (*J. P. C.,* 1903, 106.)

Description and Physical Properties.—"*Unground Pepper.*—Nearly globular, from 3.5 to 6 mm. in diameter, epicarp very thin, easily separable from the sarcocarp; externally blackish brown or grayish black, coarsely reticulate; unilocular, 1-seeded; seed nearly white, hollow, adhering to the pericarp. Odor aromatic, slightly empyreumatic; taste aromatic and very pungent.

"*Powdered Pepper.*—The powder is a mixture of blackish brown fragments of the pericarp and nearly white fragments of the perisperm and embryo; starch grains spherical or somewhat angular, from 0.001 to 0.003 mm. in diameter, mostly in the polygonal cells of the perisperm; stone cells of the epicarp varying from nearly isodiametric or palisade-like to long tapering or somewhat irregular in shape, with thick porous walls and large lumina frequently containing a reddish brown pigment; stone cells of the endocarp unevenly thickened, the outer walls being usually rather thin, and the lumina usually filled with a reddish brown substance; oil cells with suberized walls and containing a yellowish oil, from which monoclinic prisms of piperine occasionally separate. Pepper yields not less than 6 per cent. of non-volatile extract, soluble in ether. It contains not less than 25 per cent. of starch." *N. F.*

For information on the pharmacognosy of pepper, see Winton and Moeller in the "*Microscopy of Vegetable Foods;*" Spaeth, *Ztchr. f. Unters. d. Nahr. u. Genussm.,* 1908, xv, p. 472; Kraemer and Sindall, *A. J. P.,* 1908, lxxx, p. 1; Collin in *Ann. des. Falsifications,* 1910, iii, p. 272; Wallis, *Chem. News,* cxi, 143.

Constituents.—Pepper contains three important ingredients, a volatile oil, a resin and piperine. The volatile oil is composed of terpenes, chiefly lævo-phellandrene. It is colorless or slightly yellow lævo-rotatory with a specific gravity of 0.880 and 0.905. It is not pungent but represents the characteristic aromatic flavor of the pepper.

The resin, sometimes called *chavicin,* is a soft greenish substance, extremely pungent but without odor. Its pungency is by many attributed to the presence of piperine. A mixture of the volatile oil and resin which was made by extracting with ether, was formerly official under the name of *Oleoresina Piperis.* The process for this was as follows:

"Pepper, in No. 40 powder, *five hundred grammes;* Ether, *a sufficient quantity.* Place the pepper in a cylindrical glass percolator, provided with a stop-cock, and arranged with a cover and a receptacle for volatile liquids. Pack the powder firmly, and percolate slowly with ether, added in successive portions, until the drug is exhausted. Recover the greater part of the ether from the percolate by distillation on a water bath, and, having transferred the residue to a dish, set this aside in a warm place until the remaining ether has evaporated, and the deposition of piperine has ceased. Lastly, separate the Oleoresin from the piperine by straining through purified cotton. Keep the Oleoresin in a well-stoppered bottle." *U. S. IX.*

Piperine, $C_{17}O_{19}O_3N$, which may be regarded as the true active principle of black pepper was defined by the U. S. VIII as "a feebly basic substance [$CH_2O_2.C_6H_3.CH:CH.CH.:CH.CON.-C_5H_{10}$] obtained from Pepper and other plants of the *Piperaceæ.*" *U. S. VIII.*

Piperine is prepared by exhausting pepper with strong alcohol, recovering the solvent and treating the oleoresinous residue with sodium hydroxide solution to saponify the resins. The residue is taken up with boiling 95 per cent. alcohol, the solution filtered through animal charcoal and then allowed to crystallize.

The amount of piperine in the berries is from 4 to 10 per cent.

It was officially described as "colorless or pale yellowish, glistening, monoclinic crystals, odorless, permanent in the air, and containing no water of crystallization. When put into the mouth, it is at first tasteless, but on prolonged contact it develops a sharp, biting taste. It is optically inactive. Insoluble in water; soluble in 15 parts of alcohol, 36 parts of ether, and in 1.7 parts of chloroform at 25° C., soluble in 4.4 parts of alcohol at 60° C. It melts at 130° C. Upon ignition, it emits alkaline vapors, and is completely consumed. Its alcoholic solution is neutral to litmus paper. Sulphuric acid dissolves Piperine with the formation of a blood-red color, which disappears on dilution with water. On heating Piperine with alcoholic potassium hydroxide, it is converted into piperinic acid and piperidine, the latter recognizable by its alkaline, pepper-like odor, and the former by its melting point, 215° C. On adding a crystal of Piperine to sulphuric acid containing about half its volume of solution of formaldehyde, a permanently green liquid is formed. On adding a crystal of Piperine to sulphuric acid containing a fragment of potassium dichromate, it at once acquires a purple color, and, on stirring, dissolves, forming a reddish-brown solution, which becomes greenish on adding water to it. On adding a crystal of Piperine to sulphuric acid containing a trace of selenous acid, it turns brown, changing at once to violet, and dissolves, forming a brown solution changing to green. When heated with nitric acid, Piperine is colored at first orange, then red, and the acid acquires a yellow color, deepening to reddish as the crystals dissolve. On adding to this solution an excess of potassium hydroxide T.S., the color is at first yellow, but upon boiling, it becomes blood-red." *U. S. VIII.*

Piperine has such feebly basic properties that its salts are immediately decomposed by solution. By boiling with an alcoholic solution of potassium hydroxide, it is split up into a strongly basic substance, *piperidine,* and *piperic acid,* $C_{12}H_9O_3$. Piperidine, which probably occurs naturally in small quantities in pepper, is a volatile, liquid alkaloid with a boiling point of 106° C., soluble in either alcohol or water and forming crystalline salts. It is of great chemical interest as being a simple derivative of pyridine (See Part II), which seems to underlie the molecular structure of so many alkaloids. Piperidine is *hexahydropyridine,* $C_5H_{11}N$, and can be easily obtained from pyridine by the action of tin and hydrochloric acid, or when sodium acts upon the alcoholic solution. Conversely, piperidine can be changed into pyridine when sulphuric acid at 300° C. or gentle oxidizing agents act upon it. Coniine, it will be remembered (see *Conium*), has been shown synthetically to be a normal propyl-piperidine.

For a paper on commercial peppers, by J. W. Gladhill, see *A. J. P.*, 1904, 71.

Adulterations.—On account of its extensive use as a condiment pepper has been largely adulterated, especially when sold in the form of a powder. Chief of the adulterants are pepper-hulls, ground olive pits, wheat middlings, and roasted cereals. Among the other substances sometimes used have been ground beans or peas, corn starch, flaxseed, mustard hulls, and coffee hulls. The adulterated articles are usually fortified with the addition of Cayenne pepper. At the present time, by virtue of the National and State Food Laws, black pepper is seldom adulterated. Adulterations can be detected by the microscope with more or less ease (see *P. J.*, lxxi, 269; *P. J.*, June, 1890; *Bull. U. S. Dept. of Agriculture,* No. 13, Part II, pp. 183, 1887; *A. J. P.*, 1887, 146); but when pepper has been adulterated to the amount of 10 per cent. the discovery of the fraud is best made by determining the proportion of ash, of ether extract and of piperine present. The ash should never be above 6.5 per cent. for black and 3 per cent. for white pepper; the ether extract should be between 7.5 and 10 per cent. for black and 6 to 9 per cent. for white pepper, the U. S. standard being not less than 6 per cent. in which not less than 3.25 per cent. nitrogen shall be present. Piperine should be present in from 5.5 to 9 per cent. in good black pepper. The amount of oleoresin in any pepper can readily be determined by subtracting the weight of piperine from that of the mixture. Penang pepper is sometimes made to resemble the higher priced white peppers by coating the grains with an earthy matter (lime or clay). According to A. Mennechet, the fruits of *Myrsine africana* and of *Embelia Ribes* may sometimes be detected in the powder of pepper by extracting with ether and adding a little water, followed by a few drops of ammonia, when after shaking, a deep lilac-red color will appear in the aqueous layer. (*J. P. C.*, xiv, 587.)

Uses.—Black pepper is a warm carminative stimulant, capable of producing general arterial excitement, but acting with greater proportional energy on the part to which it is applied. From the time of Hippocrates it has been used as a condiment and in medicine. Its chief medicinal application is to excite the languid stomach and correct *flatulence.* In the early part of the 19th century piperine enjoyed a considerable popularity as a remedy for *malarial fever.* Although the evidence seems strong that it does really possess some antiperiodic powers, it is not comparable to the preparations of cinchona and has almost completely passed out of use except as an ingredient in Warburg's tincture and similar preparations. Some have attempted to explain its synergism with cinchona on the ground that its action on the stomach improves the absorption of quinine, but there is on the one hand no evidence that it does improve the absorption of quinine, and on the other hand considerable evidence that it possesses intrinsic anti-malarial powers (for evidence on this see Husemann, *Die Pflanzenstoffe,* 1882, p. 491).

The dose of the oleoresin of pepper is from one-fourth to one minim. Piperine as an antiperiodic was given in doses of five to eight grains (0.3–0.5 Gm.).

Dose, of pepper, five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Confectio Piperis, *Br.;* Pulvis Opii Compositus, *Br.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe. *N. F.*

PITUITARIUM. U. S.

PITUITARY Pituitar. [Hypophysis Sicca U. S. P. IX]

"Pituitary is the cleaned, dried, and powdered posterior lobe obtained from the pituitary body of domesticated animals which are used for food by man." *U. S.*

The *Hypophysis cerebri,* or *pituitary body,* is a small bean-shaped body found within the skull in the depression known as the *sella turcica* or pituitary fossa. Its longest diameter is in the transverse direction and it consists of two distinct portions enclosed together in a connective-tissue capsule. The smaller, or *posterior lobe,* is composed of nerve cells similar to the gray matter of the brain and continuous with the *infundibulum* which forms a portion of the floor of the third ventricle of the brain. The *anterior lobe,* which is much larger, is made up of glandular epithelium and contains here and there collections of colloid material homologous to that found in the thyroid body. In the human being the pituitary body measures about 12 mm. transversely, 7 mm. longitudinally and 5 mm. vertically, and weighs from five to twenty grains. In cattle the organ has a weight of two or three drachms (8–12 Gm.). When dried it loses approximately three-fourths of its weight.

Description and Physical Properties.—"A yellowish or grayish amorphous powder, having a characteristic odor. It is only partially soluble in water." *U. S.*

The anterior, or glandular, portion of the pituitary body has important relations with the metabolic processes. The condition known as gigantism or acromegaly, which is characterized by an increased growth of the bones, is generally attributed to overactivity of the pituitary gland; conversely, failure of this gland leads to retardation of growth. A lack of pituitary activity also leads to a peculiar form of corpulence, accompanied with loss of sexual characteristics, but it is not yet certain whether this form of hypopituitarism is due to disease of the anterior or posterior lobe. (See *Organotherapy,* Part II.)

When an extract of the posterior lobe is injected into the circulation of a normal animal it produces marked physiological effects which are more closely described below. This action is so analogous to other drug actions that it is impossible to escape the conviction that there is some principle or principles present in the posterior lobe which acts as a stimulant to unstriped muscle. What the nature of this principle is has not yet been determined. Abel demonstrated the presence of histamine in the hypophysis and at first was inclined to the opinion that this was the active principle, but in a later communication (*J. P. & Ex. T.,* 1920, xv, p. 347) expressed the conviction that the histamine was not the proper active principle but that it was a frequent contamination of commercial preparations. Dudley (*J. P. & Ex. T.,* 1919, xiv, 295) has separated, by means of a precipitation with colloidal ferric hydroxide, and subsequent extraction with butyl alcohol, crystalline residues which possessed all the physiological powers of the hypophysis extract, but not in a state of sufficient purity for analysis.

Because of our ignorance of the active principle of the hypophysis it is at present impossible to devise a process for chemical assay.

For description of the biological methods which have been suggested see under *Liquor Pituitarii.*

Uses.—In 1899 Schafer and Vincent (*J. P.,* 1899, xxv, 87) discovered that the injection of an aqueous extract of the hypophysis into the vein caused a rise of blood pressure rivalling, in height, that brought about by suprarenal extract and surpassing it in duration. The theory which was at one time advanced that the action of pituitary extract was similar to that of the suprarenal extract has been shown to be erroneous. The pressor principle is found only in the posterior lobe of the hypophysis and is not of the nature of an "internal secretion" as this is not a secreting structure.

The physiological effects of the posterior lobe of the pituitary body are stimulation of all the unstriped muscles, and increased secretion of the kidney and probably of the mammary glands. Among those muscles affected by the drug which are of importance from the standpoint of its clinical use, may be mentioned the circulatory, uterine, and intestinal muscles. The stimulant action upon the blood vessels is shown by the increase in arterial pressure which is apparently of purely vascular origin (Wiggers, *A. J. M. S.,* 1911, cxli, 142); the heart is not made up of unstriped muscle and does not appear to be stimulated by the drug. Repeated doses, even if intervals of an hour or two are allowed to elapse between their exhibition, do not produce the same degree of rise as the primary injection; indeed after a sufficient number of doses the drug exercises a depressor rather than a pressor influence. As was first shown by Ott and Scott (*Monthly Cylopedia and Med. Bull.,* August, 1909), the extract of hypophysis is one of the most powerful and certain stimulants for the uterine muscle that we possess. While it does increase the tonus of this muscle it seems to be especially efficient to increase the vigor of individual contractions. The effect of hypophysis on renal activity is very peculiar and not entirely understood. A considerable number of investigators have reported a definite diuretic effect. Hoskins and Means (*J. P. Ex. T.,* 1913, iv, 435) attribute this to a direct action upon the renal epithelium, but Knowlton and Silverman (*A. J. Phys.,* 1918, xlvii, p. 1) and Cushny and Lambie (*J. P.,* 1921, lv, p. 159) find that it is secondary to changes in the circulation of the kidney. On the other hand, in human beings at least, it usually caused a diminution in the urine. Abel and Geiling (*J. P. Ex. T.,* 1923, xxii, 289), although they report a diuretic action in rabbits, say "that the really characteristic and more important action on human beings is anti-diuretic." For review of literature on this subject see Mackersie (*J. P. Ex. T.,* 1924, xxiv, 83). Rees (*A. J. Phys.,* 1918, xlv, 471) believes that the diminution in the output of urine is due to delayed absorption of water from the intestines, but Brunn (*Cb. I. M.,* 1920, xli, 674) maintains that there is diminished ability of the kidney to excrete water. Certain it is that in cases of *diabetes insipidus* the injection of the present commercial pituitary extracts causes at least a temporary diminution in quantity and increased concentration of the urine.

The most common use of the hypophysis at present is as a uterine stimulant especially during *labor.* Although it is a very valuable drug in this condition when used circumspectly, there is no doubt that it is capable of doing great harm and has been greatly abused. While it seems less liable than ergot to cause tetanic spasm of the womb and there is therefore less danger of asphyxiation of the child (see Quigley, *J. A. M. A.,* 1915, lxiv, p. 1222), there have been reported several cases of rupture of the uterus from its injudicious use (Maxwell, *J. A. M. A.,* 1920, lxxiv, 1378). Before the head has passed the pelvic outlet its use in general should be avoided, although occasional circumstances may indicate its use at an earlier stage. For the treatment of *postpartum hemorrhage* it has the great disadvantage that its effects last only from one to two hours and there appears to be a tendency towards secondary relaxation. The promptness of its action, however, renders it in some cases superior to ergot; the two drugs may often be exhibited simultaneously, the pituitary for its primary, quick effect and the ergot to maintain the action. It has also been used to control *menorrhagia* and *metrorrhagia.* The effect of the extract of hypophysis on blood pressure suggests its use for the treatment of *surgical shock* and other forms of circulatory failure. Musser (*A. J. M. S.,* 1913, cxlvi, p. 208) has shown that even when exhibited by the mouth it causes a marked rise in blood pressure in human beings; Schmidt (*A. I. M.,* 1917, xix, 1059), however, failed to obtain any rise from solutions given orally although the same solutions were efficient when injected intramuscularly. Pohl (*D. M. W.,* 1921, xlvii, 1162) reports several cases of circulatory failure in which it was used with benefit. As an intestinal stimulant it has been highly lauded by many surgeons for the prevention or treatment of post-operative paralysis of the bowel (see Kirmisson, *B. A. M.,* 1918, lxxix, 82). The enormous increase in the secretion of milk which has followed its exhibition has naturally suggested its use as a lacteal stimulant both in human beings and also animals, but the present evidence seems to be that the primary stimulation is followed by a compensatory diminution of glandular activity (Rothlin, *Biochem. J.,* 1922, xvi, 3). Among other conditions for which it has been recommended may be mentioned *Graves's disease, hay fever, rickets, acromegaly,* and *tetany.* Its value in these conditions, if it has any, is probably dependent upon its influence over the nutritive processes and the whole gland is preferable. When, however, the effect upon the involuntary muscles is desired, whether of the uterus or arteries, we believe that the extract of the posterior lobe is to be preferred, since the anterior portion of the hypophysis has no effect upon these muscles and may exercise undesirable influences on the metabolism.

Dose, from one-half to two grains (0.032–0.12 Gm.).

Off. Prep.—Liquor Pituitarii, *U. S.*

PIX CARBONIS. N. F. (Br.)

COAL TAR Pix Carbon.

"The tar obtained as a by-product in the destructive distillation of coal in the manufacture of illuminating gas." *N. F.*

"Prepared Coal Tar is obtained by maintaining commercial coal tar at a temperature of 50° C. in a shallow vessel for one hour, stirring frequently." *Br.*

Pix Carbonis, *Br.;* Coal Tar; Gas Tar; Goudron Mineral, *Fr.;* Steinkohlenteer, *G.*

When bituminous coal is subjected to dry distillation, besides the incondensible gases which serve for lighting, and the charcoal left behind as coke, which is a valuable fuel, there are formed numerous other pyrogenic products, necessarily more or less varying in character and amount, not only according to the kind of coal used, but also with the varying circumstances of the decomposing process. Most of these newly formed bodies, all of which are volatilizable, are condensed into a dark thick liquid or semi-liquid substance called *coal tar.* Formerly this was considered as refuse matter, but from it are now prepared substances of great value in the arts and in medicine. We can give here only a brief review of the more important of these substances.

The composition of coal tar varies considerably with the temperature at which the distillation of the coal is effected, the yield of solid bodies and of gases being larger when the temperature is higher, while at a lower temperature the liquid portion of the tar is in increased amount.

When coal tar is submitted to fractional distillation it yields a number of valuable commercial products which are grouped as follows: *Light oils,* 2 to 8 per cent.; *middle* or *carbolic oils,* 8 to 10 per cent.; *heavy* or *creosote oils,* 8 to 10 per cent.; *anthracene oils,* 16 to 20 per cent. A residue of about 50 per cent. of pitch remains behind in the still. The light oils (sp. gr. 0.90 to 0.95) are redistilled and the higher boiling fractions added to the middle oils. The lighter fraction is purified by treatment with strong sulphuric acid in lead-lined vessels. The acid layer is recovered and worked up for *ammonium sulphate.* The oily layer is treated with caustic alkali to remove acid and is then fractionally distilled. The first runnings contain carbon disulphide, pentane, hexane and *acetonitrile,* the intermediate runnings consist mainly of *benzene* (*benzol*), the lower boiling portion being fractionated to produce pure benzene, the higher boiling fraction, containing toluene, xylene and cumene, being sold as solvent naphtha.

The middle oils contain principally *naphthalene, phenols* and *cresols.* The naphthalene is largely obtained by crystallization and is subsequently purified by sublimation. The mother liquors from the crystallization of the naphthaene contain 30 to 40 per cent. of phenolic bodies. This is purified by combining it with a weak solution of caustic soda and removing hydrocarbon impurities by blowing live steam through the solution. The phenols are then precipitated by the addition of acid and are fractionally distilled with zinc or silver condensing coils and the phenol (C_6H_5OH) separated from the *cresols* which occur as a liquid mixture of the three isomeric varieties.

The heavy creosote oils contain *naphthalene, dinaphthylene, methyl naphthalene, xylenol, naphthol* and *paraffins.* This fraction finds its principal uses in preserving timber which when impregnated with this complex liquid, sometimes under pressure is known as *creosoted timber.*

The anthracene oils contain some phenol, and a considerable amount of anthracene. This latter constituent is one of the most valuable fractions of coal tar. It is separated and purified from this fraction by cold crystallization and expression. There are also present in this fraction, small amounts of *methylanthracene, phenanthrene, diphenyl, naphthalene, pyrene, retene, carbazol, pyridine, quinoline, aniline,* etc.

The foregoing substances, all existing in coal tar, are properly known as coal-tar "fractions." The term "coal-tar products" is loosely applied to mean a "fraction," an "intermediate" or a "derivative." A coal-tar derivative does not exist in coal tar as such, but is prepared by chemical processes from some coal-tar fraction as the starting point. There are products of coal tar which are of importance as starting points in the manufacture of coal-tar derivatives. These are known as "intermediates."

Some of the coal-tar derivatives commonly used in medicine are also useful as intermediates and thus fulfil a double purpose.

Among the more important of these intermediates are the following: *Alphanaphthylamine,* $C_{10}H_7NH_2$; *alphanitronaphthalene,* $C_{10}H_7NO_2$; *aniline,* $C_6H_5NH_2$; *benzidine* (*p-p-diaminodiphenyl*), $NH_2C_6H_4\text{-}C_6H_4NH_2$. *Cleve's acids* (1 *naphthylamine-sulphonic acids*), $C_{10}H_6NH_2SO_3H$ 1:6 and 1:7; *cresotinic acid, cresotic, homosalicylic* or *toluic acid,* $C_6H_3CH_3OH.COOH$ 1:2:3; *dianisidine,* 4:3 $NH_2CH_3O.C_6H_3C_6H_3O.CH_3.NH_2$ 3:4; *dimethylaniline,* $C_6H_5N(CH_3)_2$; *dinitrobenzene,* $C_6H_4(NO_2)_2$ 1:3; *dinitrochlorobenzene,* $C_6H_3Cl(NO_2)_2$ 1:2:4; *dinitrophenol,* $C_6H_3OH(NO_2)_2$ 1:2:4; *dinitrotoluene,* $C_6H_3CH_3(NO_2)_2$ 1:2:4; *diphenylamine,* $(C_6H_5)_2NH$; *gamma acid* (2 *amino-8 naphthol-6-sulphonic acid*), $C_{10}H_5NH_2SO_3HOH.$ 2:6:8; *H acid* (1 *amino-8-naphthol-3-6 disulphonic acid*), $C_{10}H_{14}NH_2(SO_3H)_2OH$ 1:3:6:8; *Laurent's acid* (1 *naphthylamine-5-sulphonic acid*), $C_{10}H_6.NH_2SO_3H$ 1:5; *metanitroaniline,* $C_6H_4NH_2.NO_2$ 1:3; *metaphenylenediamine,* $C_6H_4(NH_2)_2$ 1:3; *metatoluenediamine,* $C_6H_3CH_3(NH_2)_2$ 1:2:4; *mononitrotoluenes,* $C_6H_4CH_3NO_2$ 1:2 and 1:4; *toluidines,* $C_6H_4CH_3NH_2$ 1:2 and 1:4; *monochlorobenzene,* C_6H_5Cl; *Nevile* and *Winter's acid* (1 *naphthol-4 sulphonic acid*), $C_{10}H_6OH.SO_3H$ 1:4; *nitrobenzene,* $C_6H_5NO_2$; *orthonitrotoluene,* $C_6H_4CH_3NO_2$ 1:2; *orthotoluidine,* $C_6H_4CH_3.NH_2$ 1:2; *para-aminophenol,* $C_6H_4OH.NH_2$ 1:4; *paranitroaniline,* $C_6H_4NH_2.NO_2$ 1:4; *paranitrochlorobenzene,* $C_6H_4Cl.NO_2$ 1:4; *paranitrotoluene,* $C_6H_4CH_3.NO_2$ 1:4; *paratoluidine,* $C_6H_4CH_3.NH_2$ 1:4; *picric acid,* $C_6H_2OH(NO_2)_3$ 1:2:4:6; *salicylic acid,* $C_6H_4OH.COOH$ 1:2; *sodium metanilate* (*sodium metaminobenzene sulphonate*), $C_6H_4NH_2SO_3Na$ 1:3; *sodium naphthionate* (*sodium 1 naphthylamine-4-sulphonate*), $C_{10}H_6NH_2SO_3Na$ 1:4; *sodium picramate,* $C_6H_2.ONa(NO_2)_2NH$ 1:2:4:6; *sulfanilic acid* (*para-aminobenzene sulphonic acid*), $C_6H_4NH_2SO_3H$ 1:4; *toluidine,* 4:3 $NH_2CH_3.C_6H_3\text{-}C_6H_3CH_3NH_2$ 3:4.

For description of some of the individual unofficial coal-tar colors and derivatives, see Part II.

Description and Physical Properties.—"A nearly black, thick liquid or semi-solid, heavier than water and possessing a characteristic, naphthalene-like odor and a sharp burning taste. It is only slightly soluble in water, to which it imparts its characteristic odor and taste and a faintly alkaline reaction. It is but partially dissolved by alcohol, acetone, methyl alcohol, or purified petroleum benzin; almost entirely dissolved by ether; entirely dissolved by benzene, carbon disulphide, or chloroform. On ignition it burns with a reddish, luminous and very sooty flame and upon strong heating is almost entirely consumed, leaving not more than 2 per cent. of ash." *N. F.*

Prepared coal tar is "a nearly black, viscous liquid, brown in very thin layers; heavier than *water.* Strongly empyreumatic characteristic odor. Almost entirely soluble in *benzene* and in *chloroform;* partially soluble in alcohol (90 per cent.), and in *ether;* very slightly soluble in *water.*" *Br.*

Uses.—Coal tar is occasionally used as a substitute for wood tar in external applications and according to Dind (*An. de Derm. et de Syph.,* 1909), has advantages over wood tar in that it is less irritant and less likely to produce nephritis or other toxic conditions after absorption. It is employed locally to relieve *itching* and to combat inflammation in such diseases as *lichen ruber, prurigo, eczema,* etc. It should not be used where the skin is infected with pyogenic cocci. It is most frequently applied in solution combined with saponin. (See *Liquor Picis Carbonis.*)

Off. Prep.—Liquor Picis Carbonis, *N. F., Br.*

PIX PINI. U. S. (Br.)

PINE TAR Pix Pin. [Pix Liquida U. S. P. IX]

"A product obtained by the destructive distillation of the wood of *Pinus palustris* Miller, or of other species of *Pinus* (Fam. *Pinaceæ*)." *U. S.* "Tar is a bituminous liquid, obtained by destructive distillation from the wood of Pinus sylvestris, *Linn.,* and other species of Pinus. Known in commerce as Stockholm tar." *Br.*

Pix Liquida, *Br.;* Pyroleum Pini; Resina Empyreumatica Liquida; Goudron végétal, Goudron, *Fr.;* Theer, *G.;* Pece liquida, *It.;* Brea de pino, Alquitran vegetal, *Sp.*

Pine tar is made by several processes. The most primitive method and one which is still used in the southern part of the United States is to pile pieces of stumps and of pine-wood waste, left over from lumbering operations, in a conical heap on a floor of hard-packed clay which slopes downward towards the center where is an opening connecting with a trench. The sides of the pile are covered with earth to prevent too much draft and the top of the pile ignited. During the slow combustion from above downwards, a certain amount of resins in the wood together with resin-like products of combustion, are melted by the heat and run down through the opening to the bottom of the floor and out into the trench where it is collected in barrels. It is obvious that in this method there will be a large loss of volatile substances. In Europe the burning of the wood is usually done in brick kilns with an opening at the side to admit fire and a two-way draining arrangement one of which leads upwards into a condenser to recover the more volatile substances and the other into a vessel to collect the liquid tar. A still more economical method is to heat the wood in large iron cylinders, in which case all the gases formed may be collected as well as the liquid distillate. The distillate yielded by any one of these methods, when allowed to stand, separates into two layers, a lower aqueous layer—containing chiefly acids of the methane series, like formic and acetic, and known as crude pyroligneous vinegar (see under *Acidum Aceticum*)—and an upper tarry layer which constitutes the substance recognized by the Pharmacopœias as pine tar. Any kind of wood may be carbonized in the manner above described, but when hard woods are used the tarry fractions are entirely different from official pine tar. (See *Creosote.*)

Pine wood when heated in retorts yields its products in the following proportions: Charcoal 24.2 per cent., tar 9.8 per cent., wood vinegar 42 per cent., gas 24.1 per cent. Cylindrical retorts are used, averaging in capacity one or two cords each.

Tar has an acid reaction, a peculiar empyreumatic odor, a bitterish, resinous, somewhat acrid taste, a color almost black, and a tenacious consistence intermediate between that of a liquid and that of a solid; by age it becomes granular and opaque.

Description and Physical Properties.—"A very viscid, blackish-brown, non-crystalline liquid. It is translucent in thin layers, becoming granular and opaque with age. It has an empyreumatic, terebinthinate odor and a sharp, empyreumatic taste. Pine Tar is heavier than water and is slightly soluble in it, the solution being pale yellowish to yellowish-brown and acid to litmus paper. Pine Tar is miscible with alcohol, ether, chloroform, glacial acetic acid, and fixed and volatile oils.

"Shake about 1 cc. of Pine Tar with 10 cc. of water for ten minutes, filter, and add 1 drop of ferric chloride T.S. to the filtrate. A green color is produced, rapidly changing to brown. Ash: not more than 0.25 per cent.

"Preserve in well-closed containers." *U. S.* "Dark brown or nearly black; semi-liquid; empyreumatic characteristic odor; heavier than *water. Water* shaken with it acquires a pale-brown color, sharp empyreumatic taste, and acid reaction; very dilute *T. Sol. of ferric chloride* colors the solution red. Tar is completely soluble in ten times its volume of *alcohol* (90 per cent.)." *Br.*

Tar yields a small proportion of its constituents to water, which is thus rendered medicinal, and is employed under the name of *tar water* (see below). Tar is dissolved by alcohol, ether, chloroform, and the volatile and fixed oils, and by a solution of potassium or sodium hydroxides. On spreading tar in a thin layer on a pane of glass it should present a homogeneous appearance. Those specimens which contain granular transparent masses should be rejected. These masses, which polarize brilliantly, are said to be *pyrocatechol.* Tar should have a specific gravity of 1.03 to 1.07; it should boil at from 250° to 400° C. Its reaction should be acid. *"Steam refined tar"* is tar which has been simply heated in steam caldrons and strained to remove foreign impurities.

Hirschsohn has suggested the following plan for the identification of different varieties of tar. (1) *Completely soluble in 95 per cent. acetic acid. Pine Tar.*—French turpentine dissolves it completely. The petroleum ether extract of the tar is colored greenish when shaken with a dilute solution of cupric acetate (1:1000). Chloroform and absolute ether dissolve it completely. *Beech Tar.*—Turpentine oil dissolves it only partially. The petroleum ether extract is not colored by copper acetate solution. Chloroform and absolute ether do not entirely dissolve it. (2) *Not completely soluble in 95 per cent. acetic acid. Juniper Tar.*—Turpentine oil dissolves it completely. Aniline dissolves it completely. The aqueous extract (1:20) yields a red coloration with dilute solution of ferric chloride (1:1000). *Birch Tar.*—Turpentine oil dissolves it completely. Aniline does not dissolve it completely. The aqueous extract is colored greenish by ferric chloride. *Aspen Tar.*—Benzene, chloroform, absolute ether, and olive oil dissolve it only partially. (*Ph. Ztg.*, 97, 396; *Ph. Z. R.*, 97.)

Composition.—When tar is distilled it yields a liquid portion (see *Oleum Picis Rectificatum* and *Acidum Aceticum*) and a black residue, *pitch* or *black pitch* (*pix nigra, resina nigra, pix navalis*). The latter has a faint tarry odor, is brittle at ordinary temperatures but softens by the warmth of the hand and melts in boiling water. It is soluble in alcohol or alkaline aqueous solutions. It consists chiefly of rosin and empyreumatic products of rosin.

Like all products of the destructive distillation of cellulose the composition of pine tar is largely phenolic. An extensive list of constituents that have been determined in pine tar are given in Hager's *Pharmaceutischen Praxis.* They are benzol, toluol, xylol, styrol, naphthalene, retene, paraffin, phenol, cresol, *phlorol* (ortho-ethyl-phenol), pyrocatechin, pyrogallic esters and *coerulignol* (methyl ether of 1:3:4 of prophyl-catechol). See also Williams, Lasselle and Reed (*J. I. E. C.*, 1925, 85).

Uses.—Tar owes its medicinal virtues chiefly to the phenol-like bodies which it contains; its effects resemble closely those of creosote, but it is less active and less liable to irritate the digestion. Its most important internal use is as a stimulating expectorant in subacute or chronic *bronchitis.* Externally it is widely employed as a stimulating and antiseptic application in various *skin diseases.* (See *Unguentum Picis Liquidæ.*)

In the middle of the 18th century tar water enjoyed a popular reputation, especially in England, as a panacea for nearly all the ills that afflict humanity—this reputation being due chiefly to the writings of the famous Bishop Berkeley—but because of the insolubility of tar no aqueous preparation can thoroughly represent the drug.

Pitch, the residue of tar after distilling off the oil was formerly employed as a local irritant in some sluggish skin diseases.

Dose, five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Unguentum Picis Pini, *U. S., Br.;* Glyceritum Picis Pini, *N. F.*

PLUMBI ACETAS. U. S., Br.

LEAD ACETATE Plumb. Acet. [Sugar of Lead]

"Lead Acetate contains not less than 85.31 per cent. and not more than 89.57 per cent. of $Pb(C_2H_3O_2)_2$, corresponding to not less than 99.5 per cent. of the crystallized salt [$Pb(C_2H_3O_2)_2.3H_2O$]." *U. S.* "Lead acetate may be obtained by dissolving lead oxide or lead carbonate in acetic acid. It contains not less than 99.5 per cent. of pure lead acetate, $Pb(C_2H_3O_2)_2$,-$3H_2O$." *Br.*

Acetas Plumbicus Neuter, Saccharum Saturni, Cerussa Acetata; Acétate neutre de Plomb, Sucre de Plomb, Sel de Saturne, *Fr.;* Plumbum Aceticum, *P. G.;* Bleiacetat Essigsaures Bleioxyd, Bleizucker, *G.;* Acetato neutro di piombo, Zucchero di Saturno, *It.;* Acetato plumbico neutro, Azucar de Saturno, *Sp.*

Preparation.—Lead acetate is obtained by two methods. By one method, thin plates of lead are placed in shallow vessels filled with distilled vinegar, in such a manner as to have a part of each plate rising above the vinegar, and these are turned from time to time, so as to bring different portions of the metallic surface in contact with the air. The metal, in the presence of the oxygen of the air, dissolves in the vinegar to saturation, and the solution is evaporated to the point of crystallization. This process is a slow one, but furnishes a salt which is perfectly neutral. The other method consists in dissolving, by the assistance of heat, litharge, in 60 per cent. acetic acid, in large wooden vats provided with mechanical stirrers. The acetic acid is heated to 60° C. and the litharge added by means of a distributing device. The oxide is quickly dissolved, and, when the acid has become saturated, the solution is permitted to clarify by subsidence in vessels provided with strips of lead which coming into contact with the solution remove small amounts of copper which may be present, and it is then transferred to other vessels to cool and crystallize. The crystals having formed, the mother waters are decanted, and, by evaporation, made to yield a new crop. These are generally yellow, but may be rendered white by repeated solutions and crystallizations.

Lead acetate is principally consumed in the arts of dyeing and calico printing, in which it is employed with alum, to form aluminum acetate, which acts as a mordant.

Description and Physical Properties.—"Colorless, shining, transparent, monoclinic prisms or plates, or heavy, white crystalline masses, or granular crystals. It has a faintly acetous odor, is efflorescent, and absorbs carbon dioxide on exposure to air. One Gm. of Lead Acetate is soluble in 1.4 cc. of water, and in 38 cc. of alcohol, at 25° C. One Gm. is soluble in about 0.5 cc. of boiling water. It is freely soluble in glycerin. When heated to 40° C., the salt loses its water of crystallization. When heated rapidly to 75° C., it liquefies in its water of crystallization, and at a temperature above 280° C. is decomposed, leaving a residue of finely divided metallic lead and lead oxide.

"An aqueous solution of Lead Acetate (1 in 10) is slightly alkaline to litmus paper, and responds to the reactions for lead, and for acetates.

"A solution of the salt (1 in 10) prepared with recently boiled, distilled water, is clear, or only slightly opalescent (*carbonate*) and yields with potassium ferrocyanide T.S. a precipitate which is neither blue nor red (*iron or copper*).

"Preserve in well-closed containers." *U. S.*

"Small, white, monoclinic prisms, or crystalline masses, slightly efflorescent. Acetous odor; taste sweet, astringent. Soluble in 2.5 parts of *water,* and in 30 parts of *alcohol* (90 per cent.). Aqueous solution slightly acid to *litmus,* clear, or with only a slight turbidity which disappears on the addition of *acetic acid.* Yields the *reactions* characteristic of lead and of acetates. Yields no characteristic *reactions* for silver, copper, arsenic, iron, zinc, calcium, chlorides, or nitrates. When 0.5 gramme is dissolved in *water* acidified with *acetic acid,* excess of *N/1 solution of oxalic acid* added, the precipitate collected, washed, transferred to a flask and decomposed with excess of *diluted sulphuric acid,* the mixture thus obtained, heated to 60° C., decolorises not less than 26.2 millilitres of *N/10 solution of potassium permanganate* (presence of not less than 99.5 per cent. of pure lead acetate, $Pb(C_2H_3O_2)_2,3H_2O$)." *Br.*

Exposed to the air, it effloresces slowly. In pure distilled water, free from carbon dioxide, it ought to dissolve entirely and form a clear solution. Commercial acetate is sometimes impure from the presence of lead sulphate and carbonate. In purchasing it large crystalline masses should be selected. Sulphuric acid, when added to a solution of lead acetate, produces instantly a precipitate of lead sulphate, and the disengaged acetic acid gives rise to vapors having the odor of vinegar. An important property of lead acetate is its power of dissolving a large quantity of lead monoxide. (See *Liquor Plumbi Subacetatis.*)

Assay.—"Dissolve about 5 Gm. of Lead Acetate, accurately weighed, in sufficient recently boiled distilled water to make exactly 100 cc. Mix 10 cc. of this solution with 50 cc. of tenth-normal oxalic acid in a 200 cc. measuring flask, agitate the mixture thoroughly for five minutes and fill the flask to the mark with distilled water. Filter, and titrate the residual oxalic acid in 100 cc. of the filtrate with tenth-normal potassium permanganate, the filtrate being previously acidulated with 10 cc. of sulphuric acid and warmed to 80° C. Each cc. of tenth-normal oxalic acid corresponds to 0.01626 Gm. of $Pb(C_2H_3O_2)_2$." *U. S.*

Incompatibles and Tests.—Lead acetate is decomposed by all acids, and by those soluble salts the acids of which produce with lead monoxide insoluble or sparingly soluble compounds. Acids of this character are sulphuric, hydrochloric, phosphoric, tannic, citric, and tartaric. It is also decomposed by lime water, and by ammonia, potassium and sodium hydroxide; the last two, if added in excess, dissolving the precipitate at first formed. It is decomposed by hard water, in consequence of the calcium sulphate, carbonates and sodium chloride which such water usually contains.

Uses.—Lead acetate is an active astringent with but slight irritant effect. It was formerly believed to exercise some peculiar local antiphlogistic action beyond its merely astringent powers and was very widely employed in all sorts of irritated conditions of the skin or mucous membranes. Internally it is also employed as an astringent in treatment of certain types of *diarrhea.* Its popularity as a remedial agent is rapidly on the wane, partly through loss of confidence in its virtues and partly because of the fear of lead poisoning.

As a local astringent over the unbroken skin it may be used in strengths of about 1 to 2 per cent. Over mucous membranes it should be more dilute, usually about 0.2 to 0.5 per cent.

In overdoses lead acetate may act as a local irritant to the stomach and cause severe, or occasionally, fatal intoxication. The usual symptoms are a metallic taste in the mouth followed by a burning sensation in the throat and, ordinarily within about half an hour, nausea and vomiting, the matters ejected being white and curdy from the presence of lead chloride. Later severe cramp-like pains in the abdomen may appear usually with constipation—although in some cases the bowels may be loose—the stools being black from the formation of lead sulphide. Afterwards there may be signs of involvement of the nervous system—as local paralysis—and in the fatal cases collapse develops after three or four days. The treatment consists in the immediate evacuation of the stomach, preferably by the stomach tube, or by the use of zinc sulphate or alum as emetics, followed by the administration of Epsom salts which acts both as a cathartic and chemical antidote. In the absence of a sulphate, sodium chloride may be used as a chemical antidote, although not quite as efficient.

Dose, one to three grains (0.065–0.20 Gm.).

Off. Prep.—Glycerinum Plumbi Subacetatis, *Br.;* Liquor Plumbi Subacetatis, *U. S.* (*Br.*); Pilula Plumbi cum Opio, *Br.;* Suppositoria Plumbi Composita, *Br.;* Unguentum Plumbi Subacetatis, *Br.;* Lotio Plumbi et Opii, *N. F.;* Pilulæ Opii et Plumbi, *N. F.;* Lotio Alba, *N. F.;* Mistura adstringens, *N. F.*

PLUMBI IODIDUM. N. F., Br.

LEAD IODIDE Plumb. Iod.

"Lead Iodide contains, when dried over sulphuric acid for 24 hours, not less than 99 per cent. of PbI_2(461.04)." *N. F.*

"Lead Iodide, PbI_2, may be obtained by the interaction of aqueous solutions of lead nitrate or acetate and potassium iodide." *Br.*

Ioduretum Plumbicum, Plumbum Iodatum, *Fr. Cod.;* Iodure de Plomb, *Fr. Cod.;* Jodblei, *G.;* Yoduro plumbico, *Sp*

Neither the present Br. nor N. F. give a process for lead iodide; that of the Br. 1885 was as follows:

"Take of Nitrate of Lead, Iodide of Potassium, each *four ounces* [avoirdupois]; Distilled Water *a sufficiency.* Dissolve the Nitrate of Lead, by the aid of heat, in a pint and a half, and the Iodide of Potassium in half a pint of the Water, and mix the solutions. Collect the precipitate on a filter, wash it with Distilled Water, and dry it in a warm place." *Br.*, 1885. The theoretical quantities of lead nitrate and potassium iodide are almost precisely equal quantities. The proportions should be as nearly as possible those of exact saturation. An excess of the potassium iodide, independently of the waste, has the disadvantage of holding a portion of the lead iodide in solution, while, according to Christison, an excess of lead over the iodine disposes to the formation of the lemon-yellow insoluble lead oxyiodide. As lead iodide is slightly soluble in cold water, it is desirable to use as little of the solvent as will answer, and hence the comparatively small proportion of water employed.

The Br. describes it as: "a heavy, bright-yellow powder. Soluble in about 2000 parts of cold *water*, and in about 200 parts of boiling *water*, from which it is deposited in golden-yellow crystalline scales as the solution cools; entirely soluble in *solution of ammonium chloride*. Yields the reactions characteristic of lead and of iodides. Yields no characteristic *reactions* for nitrates or acetates." *Br.*

Description and Physical Properties.—"Lead Iodide occurs as a heavy, bright yellow powder, without odor or taste; permanent in the air. One Gm. dissolves in about 1300 cc. of water at 25° C. and in about 200 cc. of boiling water, separating from the latter solution on cooling in brilliant, golden yellow crystalline laminæ; very slightly soluble in alcohol; soluble, without color, in solutions of the fixed alkalies, in concentrated solutions of the alkali acetates, of potassium iodide, and of sodium thiosulphate, and in a hot solution of ammonium chloride.

"When moderately heated, the salt fuses to a thick, reddish brown liquid, which congeals, on cooling, to a yellow, crystalline mass. At a higher temperature it is decomposed, with the evolution of violet vapors of iodine, leaving a lemon-yellow residue of lead oxyiodide.

"Triturate 1 Gm. of the salt with 2 Gm. of ammonium chloride and 2 cc. of distilled water; a nearly white mixture results. Transfer this to a test tube, and heat in a water bath for a few minutes; a clear, almost colorless solution is formed (*chromate and other insoluble foreign salts*). On cooling this solution, a solid mass of nearly colorless, fine, silky crystals is produced, and on adding water or diluted sulphuric acid to this mass, yellow Lead Iodide separates. Add 0.1 Gm. of the salt to 5 cc. of distilled water, and heat the mixture until it boils; cool the liquid and filter it into a test tube of about 40 cc. capacity, then add 5 cc. of sodium hydroxide T.S. and about 0.2 Gm. of aluminum wire; insert in the upper portion of the test tube a pledget of purified cotton, and over the mouth place a piece of moistened red litmus paper and then heat the tube on a water-bath during fifteen minutes; no blue coloration of the paper will be discernible (*nitrate*). Boil 1.5 Gm. of Lead Iodide for a few minutes with 15 cc. of distilled water, cool and filter. To 5 cc. of the filtrate add a slight excess of silver nitrate T.S., then a slight excess of hydrochloric acid and filter. Neutralize the filtrate with ammonia water and add a drop of ferric chloride T.S. No red color is produced (*acetate*). To another 5 cc. portion of the filtrate add an excess of hydrogen sulphide T.S., filter, evaporate to dryness and ignite; not more than 0.002 Gm. of residue remains.

"**Assay.**—Dry about 1 Gm. of Lead Iodide over sulphuric acid for 24 hours. Dissolve about 0.5 Gm. of the dried lead iodide, accurately weighed, in 30 cc. of sodium hydroxide T.S., heating on the water-bath if necessary, to facilitate solution. Cool the solution, add 40 cc. of tenth-normal silver nitrate and follow it with diluted nitric acid until the solution is slightly acid, and add 15 cc. more of the nitric acid. Now titrate the excess of silver nitrate with tenth-normal potassium thiocyanate, using 3 cc. of ferric ammonium sulphate T.S., as indicator, and deduct from the volume of tenth-normal silver nitrate consumed the volume required for the chloride present in the 30 cc. of sodium hydroxide T.S. Each cc. of tenth-normal silver nitrate corresponds to 0.023047 Gm. of PbI_2.

"Preserve it in well-closed containers, protected from light." *N. F.*

It is freely soluble in a concentrated solution of sodium acetate. It should be kept excluded from the light. It is stated by Engelhardt that iodine is separated from lead iodide by ferric and cupric chlorides, while the other metallic chlorides have no such effect, producing compounds of iodides of the metal employed with lead chlorides.

Uses.—This compound was supposed to have the resolvent properties of iodine, combined with the antiphlogistic powers formerly attributed to lead, and was employed in the treatment of *scrofulous tumors* and other indolent swellings. According to Cogswell, if given for some time in small doses, it produces the effects of lead, but not those of iodine, upon the system. It is more dangerous than useful. It is used only as an external remedy. The plaster of lead iodide was dropped from the British Pharm., 1914, but the ointment was retained.

Off. Prep.—Unguentum Plumbi Iodidi, *N. F.*, *Br.*

PLUMBI MONOXIDUM. U. S. (Br.)

LEAD MONOXIDE Plumb. Monoxid. [Plumbi Oxidum U. S. P. IX, Litharge]

"Lead Monoxide, when freshly ignited, contains not less than 97 per cent. of PbO." *U. S.* "Lead Oxide, PbO, may be obtained by the action of air on melted lead." *Br.*

Plumbi Oxidum, *Br.;* Oxide of Lead; Yellow Oxide of Lead; Plumbi Oxidum Semivitreum; Oxidum Plumbicum; Plumbum Oxydatum Fusum, *Fr. Cod.;* Oxide de Plomb Fondu, Protoxide de Plomb, *Fr.;* Lithargyrum, *P. G.;* Bleiglätte, Bleioxyd, *G.;* Litargirio, *It.*, *Sp.*

Lead monoxide occurs in two forms. First, an amorphous yellowish powder called *massicot* which is prepared by heating lead carbonate to a low redness. The second, litharge, is a semi-crystalline product prepared at a much higher temperature. Practically all of the litharge of commerce is obtained as a secondary product in the process for extracting silver from argentiferous galenas in the process known as "cupellation." In this the alloy of silver and lead is heated in a reverberatory furnace, the floor of which is covered with either bone-ash or a special clay and the wall provided with openings for an air-blast. When the metal is melted a current of air is blown over the surface which oxidizes the lead and the resulting oxide floats on the surface of the molten metal and is removed either by means of ladles or allowed to run off through lateral openings. When obtained in this manner it forms a semi-crystalline mass sometimes known as *vitrified lead oxide.*

The product of the latter process, which is known as litharge, varies in color from a pale yellow to a shade of orange; massicot usually has a redder tint, sometimes being almost scarlet, and is occasionally referred to as "red litharge." This red color was at one time taken to indicate the presence of minium but Leblanc has shown that the two varieties of litharge differ in color, structure, and density only, and not in chemical composition.

Description and Physical Properties.—"A heavy, yellowish or reddish-yellow powder, or minute scales, without odor or taste. On exposure to the air it slowly absorbs moisture and carbon dioxide. Lead Monoxide is almost insoluble in water, to which, however, it imparts a faintly alkaline reaction. It is insoluble in alcohol. The Monoxide is dissolved by acetic acid, by diluted nitric acid, and by warm solutions of the hydroxides of fixed alkalies.

"When heated, the Monoxide becomes darker in color, but assumes its original color on cooling. It fuses at a red heat. When heated in contact with charcoal, it is reduced to metallic lead. A solution of the Monoxide in diluted nitric acid (1 in 10) is colorless, and when nearly neutralized by ammonia T.S. responds to the reactions for lead.

"Shake 5 Gm. of the Monoxide in a small flask with 5 cc. of distilled water and add 20 cc. of acetic acid. Boil the mixture for a few minutes, filter, wash the insoluble residue thoroughly with diluted acetic acid, and dry at 110° C.: the residue weighs not more than 0.10 Gm. When strongly heated in a porcelain crucible, the Monoxide loses not more than 4 per cent. of its weight (*carbonate or moisture*).

"Preserve in well-closed containers." *U. S.*

"Heavy scales, or powder, of a pale yellowish-red color. Soluble in *diluted nitric acid* and in *acetic acid* with but slight effervescence, leaving not more than traces of insoluble residue. Yields the reactions characteristic of lead. Yields no characteristic *reactions* for copper, and not more than the slightest *reactions* for iron." *Br.*

It slowly attracts carbon dioxide from the air, and contains more of this acid the longer it has been exposed. It is on this account that it commonly effervesces slightly with the diluted acids. It has the property of decolorizing wines, when agitated with them. When heated with the fats and oils, in connection with water it saponifies them. (See *Emplastrum Plumbi Oxidum.*) As it occurs in commerce, it frequently contains iron, copper, and a little silver and silica. It may be purified from iron and copper by digestion in diluted sulphuric acid. In choosing litharge, samples should be selected which are free from copper and from mechanical impurities. Copper is detected if upon adding potassium ferrocyanide to a nitric acid solution of the litharge a brown instead of a white precipitate is produced. The carbon dioxide which it contains is variable, but its average amount is about 4 per cent. Lead peroxide and red lead in litharge may be detected by heating it in a test tube with sodium chloride and potassium bisulphate and introducing a slip of paper colored blue by indigo. If either of these oxides be present, the paper will be bleached by the chlorine evolved.

Assay.—"Dissolve about 0.4 Gm. of freshly ignited Lead Monoxide, accurately weighed, in 2 cc. of glacial acetic acid and 25 cc. of recently boiled, distilled water, in a 200 cc. volumetric flask, and mix the solution with 50 cc. of tenth-normal oxalic acid. Fill the flask to the 200 cc. mark with distilled water, mix well, filter through a dry filter into a dry flask, rejecting the first 20 cc. of filtrate, and titrate the residual oxalic acid in 100 cc. of the filtrate with tenth-normal potassium permanganate, the filtrate being previously acidulated with 20 cc. of diluted sulphuric acid, and warmed to 80° C. Each cc. of tenth-normal oxalic acid corresponds to 0.01116 Gm. of PbO." *U. S.*

Uses.—Litharge is never used internally, but is employed in several pharmaceutical operations, and forms an ingredient in various external applications, used for abating inflammation, and for other purposes. In the arts it is employed in the glazing of pottery, in painting to increase the drying property of oils, and as an ingredient in flint glass.

Off. Prep.—Emplastrum Plumbi Oleatis, *U. S.* (*Br.*)*;* Glycerinum Plumbi Subacetatis, *Br.;* Liquor Plumbi Subacetatis, *U. S.* (*Br.*).

PLUMBI OXIDUM RUBRUM. N. F.

RED LEAD OXIDE Plumb. Oxid. Rubr. [Red Lead]

"Lead orthoplumbate [Pb_2PbO_4 (685.6)] usually with some unconverted lead monoxide (PbO), corresponding to not less than 31 per cent. of lead dioxide (PbO_2)." *N. F.*

Lead Oxide, Red, Plumbum Hyperoxydatum Rubrum; Plumbas Plumbicus; Red Lead; Minium, Deutoxide de Plomb, Oxide Rouge de Plomb, Minium, *Fr.;* Mennige, *G.;* Minio, *It., Sp.*

As stated on page 867, lead may act as a base, or may unite with hydrogen and oxygen to form an acid radical. In the present salt the lead is considered to be in both conditions. That is, it is a plumbate. *Orthoplumbic acid* has the hypothetical constitution H_4PbO, but is unknown except in the form of its salts. When the hydrogen of this acid is replaced by two atoms of the bivalent lead, we have *lead orthoplumbate* or minium.

Minium is prepared by carefully heating lead monoxide to a temperature of 450° C. By some it is considered a mixture of lead monoxide and peroxide ($2PbO,PbO_2$). This view is rendered plausible by the fact that nitric acid dissolves out PbO and leaves a residue of PbO_2. It has a specific gravity of 8.6 to 9.0.

Red lead in the arts is used chiefly as a paint, for protecting metal surfaces, in the manufacture of flint glass, and in cements for metal joints.

Description and Physical Properties.—"Red Lead Oxide occurs as a heavy, orange-red powder without odor or taste. On exposure to the air it slowly absorbs moisture and carbon dioxide. Almost insoluble in water, insoluble in alcohol, but dissolved by an excess of glacial acetic acid; also dissolved by lactic acid with the evolution of carbon dioxide and the odor of acetaldehyde.

"When heated in a porcelain crucible, Red Lead Oxide at first changes color from red to a violet and then to a blackish tint, and regains its original color on cooling, but, when the heating is continued, it slowly decomposes, forming lead monoxide and oxygen. When heated in contact with charcoal, it is reduced to metallic lead.

"Treat 5 Gm. of Red Lead Oxide with 50 cc. of diluted nitric acid; little effervescence results (*carbonate*), and a brown, insoluble residue of lead dioxide (PbO_2) remains, which, upon the addition of solution of hydrogen dioxide, dissolves with the evolution of oxygen, forming a colorless solution. Boil this solution for fifteen minutes, cool, and filter; the undissolved residue weighs not more than 0.1 Gm. (*silicate or lead sulphate*). On completely precipitating a portion of the solution from the foregoing test, representing 1 Gm. of red lead oxide, with hydrogen sulphide, the filtrate on evaporation yields not more than 0.01 Gm. of residue. Separate portions of the solution obtained in the last test yield with hydrogen sulphide T.S. a black precipitate; with potassium iodide T.S., a yellow precipitate; and with diluted sulphuric acid, a white precipitate; the latter two precipitates being soluble in a solution of sodium hydroxide (1 in 4). From a solution of 0.5 Gm. of Red Lead Oxide in diluted nitric acid, obtained by the aid of solution of hydrogen dioxide, precipitate the lead with sulphuric acid and filter the mixture. After the addition of an excess of ammonia water this filtrate does not develop more than a slight, bluish tint (*copper*), or yield more than traces of a reddish brown precipitate (*iron*). Heat a mixture of 1 Gm. of Red Lead Oxide with 50 cc. of distilled water to boiling, cool, and filter. The filtrate is colorless, is not more than faintly alkaline to litmus, and, when evaporated to dryness, leaves not more than 0.01 Gm. of residue (*soluble impurities*).

"**Assay.**—Add about 1 Gm. of Red Lead Oxide accurately weighed, to a cool solution of 40 Gm. of crystallized sodium acetate and 2 Gm. of potassium iodide in 50 cc. of 50 per cent. acetic acid, agitate the mixture until all of the Red Lead Oxide has dissolved and then titrate the solution with tenth-normal sodium thiosulphate. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.01195 Gm. of lead dioxide (PbO_2). Each Gm. of Red Lead Oxide corresponds to not less than 25.9 cc. of tenth-normal sodium thiosulphate." *N. F.*

Minium is used externally, and almost solely in the form of the camphorated brown plaster.

Off. Prep.—Emplastrum Fuscum Camphoratum, *N. F.;* Unguentum Fuscum, *N. F.*

PLUMBUM

LEAD

Plomb, *Fr.;* Blei, *G.;* Lood, *Dutch;* Piombo, *It.;* Plomo, *Sp.*

Lead is not official in its metallic state, but enters into a number of important medicinal preparations. It occurs in nature in galena, PbS; in cerussite, $PbCO_3$; in *crocoite*, $PbCrO_4$; in *wulfenite,* $PbMoO_4$; and in *anglesite,* $PbSO_4$. The greater quantity is obtained from *galena* which is abundant in the United States, Spain, Germany and England; less important deposits are found in Venetia, Lombardy and Tuscany. The extraction is effected either by melting the ore in contact with charcoal, or, in the case of pure galenas, by what is termed the *air reduction* process. In this case the galena is first roasted, when it is part changed into oxide, PbO, and sulphate, $PbSO_4$. The doors of the furnace are then closed, and the unchanged sulphide reacts with both the oxide and the sulphate as follows:

$$2PbO + PbS = 3Pb + SO_2$$
$$PbSO_4 + PbS = 2Pb + 2SO_2$$

whereby all the lead is obtained in the metallic state. Lead is also successfully obtained by electrolysis directly from the galena. This is reduced at the cathode of an electrolytic cell, while hydrogen sulphide is formed at the same time and may be collected or burned to form sulphur dioxide, which is then utilized. This process is now in operation at Niagara Falls. The richest and most extensive mines of galena are found in this country. The non-argentiferous lead region of the United States extends in length from Wisconsin in the north to the Red River of Arkansas in the south, and in breadth about one hundred and fifty miles, being chiefly in the State of Missouri, while Utah, Idaho, Montana, and Colorado furnish argentiferous galena.

Properties.—Lead is a soft, bluish-gray, non-elastic and very malleable metal, presenting a bright surface when newly melted or cut. It has a perceptible taste, and a peculiar odor when rubbed. It undergoes but little change in the air, but is acted on by the combined influence of air and water, which produces the hydroxide, which is afterwards changed, in part, into carbonate, by absorbing carbon dioxide from the atmosphere. Waters containing much free CO_2 dissolve lead and acquire poisonous qualities. The chemical effect of water on the metal is greater in proportion as the water is purer. Aqueous vapor passed through leaden pipes has a similar corroding effect, which is greater as the lead is purer. Spring and river water act on lead differently according to the predominating constituents in the water. Hard water forms a protective coating of lead carbonate or lead sulphate on the inner surface of pipes through which it flows, but this protective condition disappears in waters which have been treated with chlorine or hypochlorites for the purpose of purification. Stalmann has satisfied himself, by experiment, that an extremely minute quantity of ammonia or of nitric acid will very much promote the action of water upon lead—a millionth of ammonia being sufficient for the purpose. (*J. P. C.*, iv, 467.) Metallic lead is liable to the attacks of certain insects, which bore into and sometimes through it, not using it as food, but apparently in search of secure places of retreat for future development. Its sp. gr. is 11.4, melting point 327° C., and atomic weight 207.20. Exposed to a stream of oxygen on ignited charcoal, it burns with a blue flame throwing off dense yellow fumes. The best solvent of lead is nitric acid, but the presence of sulphuric acid destroys, and that of hydrochloric acid lessens, its solvent power, on account of the insolubility of the lead sulphate and chloride. Lead forms a suboxide, Pb_2O, a monoxide, PbO, a sesquioxide, Pb_2O_3, a dioxide, PbO_2, and a compound of the monoxide and the dioxide, lead orthoplumbate, Pb_3O_4. The monoxide and the last named compound are official (see *Plumbi Monoxidum* and *Plumbi Oxidum Rubrum*).

The *sesquioxide*, discovered by Winckelblech, is unimportant. The *dioxide*, PbO_2, called also *puce* oxide from its flea-brown color, may be obtained by treating red lead with nitric acid. The acid takes up the monoxide and leaves the dioxide, which may be purified by washing with boiling water. A more productive process is to precipitate four parts of lead acetate by three of sodium carbonate, and then to pass into the thin pasty mass of lead carbonate a stream of chlorine, which converts the monoxide of the carbonate into the brown dioxide. (F. Wöhler.) Solution of chlorinated soda may be conveniently employed to furnish the necessary chlorine. Lead dioxide is a tasteless powder, of a dark brown color. When heated to redness it loses half its oxygen and becomes monoxide. It consists of one atom of lead and two atoms of oxygen. It is further described among the Pharmacopœial reagents. (See Part III.)

Lead forms two classes of compounds in one of which it acts as a base (as illustrated by the official salts of lead), and in the other of which it is contained in the acid group forming a class of compounds known as *plumbates* and *plumbites*. Lead combines with iodine, forming the official lead iodide. The acetate is also official.

The best tests for lead are hydrogen sulphide or a solution of potassium iodide. The former produces a black precipitate of lead sulphide, the latter a yellow one of lead iodide.

Poisoning.—In concentrated form and sufficient amount the soluble preparations of lead are violent irritant poisons. (See *Plumbi Acetas.*) The insoluble preparations of lead are incapable of acting as acute irritant poisons, but are the common causes of a chronic poisoning. The most common form of the poisoning, the so-called *colica pictonum*, is very common among painters, makers of white lead, and other artisans who work in the metal. It is, however, also frequently seen in other persons, into whom the lead finds entrance in almost innumerable ways, especially with drinking water and food. Colica pictonum usually begins with dyspeptic symptoms and obstinate constipation, associated with violent pain of a twisting character, which seems to center round the umbilicus; the abdominal walls are spasmodically retracted.

Accompanying these symptoms there is loss of appetite, pallor, lassitude, and failure of the general health. The stools are whitish and usually constipated, although occasionally there is diarrhea. A characteristic symptom is a blue line situated upon the margin of the gums where they join the teeth, due to the deposit of the lead sulphide. This blue line, if present, is pathognomonic, but may be absent even in the most severe cases. Basophilic degeneration of the red blood cells can be found in the majority of cases, and if present is a very suggestive symptom. The pulse is usually slow and hard.

Various symptoms of disorder of the nervous system or of nutrition may occur later. Occasionally these nervous disturbances are the sole evidence of the intoxication, although more frequently they are either accompanied with, or preceded by, the typical lead colic. The most characteristic of the nervous phenomena is the double wrist drop due to paralysis of the extensors of the fore arm, and associated with wasting and degenerative changes in the muscles involved. Rarer manifestations are: paraplegia simulating anterior poliomyelitis; cerebritis with wild delirium and sometimes convulsions; occasionally arthritis very much like that of typical gout may be seen. Chronic lead poisoning in rare cases may take on many other forms; indeed, it has been said that lead poisoning may simulate any known nervous disease. A peculiar form of lead poisoning occurred among the workers in the manufacture of *tetraethyl lead*, a compound used under the name of "ethyl gas" as an automobile fuel. These cases were characterized by a predominance of cerebral manifestations and an absence of the intestinal symptoms. (For description of these cases see Hamilton, *J. A. M. A.*, 1925, lxxxv, 1481, and Kehoe, *Ibid.*, lxxxvi, 108.) For further information on chronic lead poisoning, see *A. J. M. S.*, 1921, clxii, 833; *J. A. M. A.*, 1911, lvi, p. 1240; and 1921, lxxvi, 835.

The diagnosis of chronic lead poisoning is of the utmost importance, but sometimes of great difficulty. The blue line upon the gums, if present, is practically pathognomonic, but its absence is of no negative value. Extensive degeneration of the blood corpuscles is also a symptom of great diagnostic importance, but may be absent in even severe cases. In doubtful cases a chemical examination of the urine for the presence of lead should be made. It must be remembered, however, that the presence of the metal does not prove that the case is one of lead poisoning; lead has been found in the urine of many persons in apparently normal health. As the elimination of lead through the kidneys is hastened by the administration of potassium iodide it is generally advisable to give this salt two or three days before the collection of the sample for examination.

The treatment of chronic lead poisoning resolves itself into three divisions: to stop the ingestion of the poison, to hasten its elimination, and to relieve symptoms. The most important step in the first of these is to find the source. While in the majority of instances the disease is an occupational one, yet in some cases much ingenuity is required to trace its origin. It has been attributed in obscure cases to the use of various cosmetics containing lead, to lead-foil around chewing tobacco or confectionery, to biting of silk thread which has been weighted with lead, to the use of improperly glazed earthenware vessels, etc., but outside of workers in the metal it most commonly obtains entrance into the body with the drinking water. The daily use of magnesium sulphate serves the double purpose of keeping the bowels open and of precipitating any lead which may be eliminated into the intestinal tract. For the purpose of aiding in the excretion of the metal the most important single measure is the administration of potassium iodide which forms a soluble compound with the metal. The use of sweat baths containing sulphur has also been recommended.

Warm *sulphuretted baths* may be provided by dissolving four ounces of potassium sulphide in thirty gallons of water, in a wooden tub. These baths cause discoloration of the skin, from the formation of lead sulphide, and should be repeated every few days, until this effect ceases to be produced. After each bath the patient should be well washed with soap and water with the aid of a flesh brush, in order to remove the discoloration. By proceeding in this way, the lead on the skin, or in its pores, is rendered insoluble and inert, and at the same time removed.

The manifestations are so protean that it is impossible to consider here all the measures for relief of symptoms. For the colic the most generally useful drug is belladonna in full dose. If the pain is very severe morphine may be given which acts not only by its direct analgesic effect, but by relaxing the intestinal spasm.

We have seen life apparently saved in a violent attack of lead cerebritis by free venesection and the injection of physiological salt solution.

PODOPHYLLI INDICI RESINA. Br.

INDIAN PODOPHYLLUM RESIN [Podophyllum Emodi Resin]

"Indian Podophyllum Resin is a powdered resin prepared by the same process as that described under 'Podophylli Resina,' employing Indian Podophyllum Rhizome in place of Podophyllum Rhizome. It possesses the characters and responds to the tests described under 'Podophylli Resina.'" *Br.*

(See *Podophylli Indici Rhizoma.*)

The rhizome of the Indian Podophyllum has become a commercial article and appears to have been largely used in the making of podophyllin. The question as to the relative yield of the Indian and American plants is a matter of great importance to the manufacturer, it usually being stated that the Indian rhizome is twice as active. Some years since Dyrock and Hooper obtained 12 per cent. of resin from *P. Emodi;* Umney, working with large quantities (*P. J.*, Sept., 1902), got out 11.4 per cent.; since then John Barclay (*P. J.*, 1903, lxx) was not able to obtain a greater yield than 6.69 per cent. Umney, commenting on this, believes that of late years the Indian plant gives a much smaller product than formerly, probably on account of the time of year in which it is now dug. In regard to the therapeutic interchangeability of the two resins it has been demonstrated by the researches of Dunstan and Henry (*Proc. Chem. Soc.*, March, 1898) and J. C. Umney that the active substances, podophyllotoxin and podophyllo-resin, found in the American Podophyllum are also present in the Indian resin, but it is not assured that the proportion of these active principles is the same in the two resins. The proportion of podophyllotoxin in the Indian rhizome is generally considerably higher than in the American, ranging from 1 to 4 per cent. In the present state of our knowledge, the manufacturer is certainly not justified in putting upon the market a resin made from the Indian plant unless it is plainly marked as the Indian podophyllin. Distinguishing between the two resins has become a question of importance. The presence of a yellowish-green color does not, as has been affirmed, prove that a podophyllin is impure or of Indian origin. The test of solubility is also uncertain. The Indian podophyllin, properly prepared, is freely soluble in alcohol. It is commonly stated that the true podophyllin will dissolve in ammonia (1 to 100). The Indian species is seemingly much less soluble in ammonia than this, but a properly prepared official resin does not always come up to this standard. E. J. Millard (*P. J.*, lx) states that the Indian resin strikes with strong sulphuric acid an orange to red color, the official resin yellow coloration, tending to brown, but especially commends the following test:

To six grains (0.4 Gm.) of the resin in a test tube add one fluidrachm (3.75 cc.) of diluted alcohol sp. gr. 0.920, and eight or ten drops (0.4–0.5 cc.) of solution potash, B. P.; shake gently by rotating the test tube. In case of the Indian resin, the mixture becomes in a few seconds a semi-solid gelatinous mass, so that the test tube can be safely inverted. If this does not occur quickly, the mixture should be heated until it just begins to boil, and when cold it will be found to have gelatinized. The American resin similarly treated gives a dark fluid that shows no signs of gelatinizing even after standing for days. The Indian Podophyllum Resin is used for the same purposes as the American. (See *Resina Podophylli.*)

Dose, one-fourth to one grain (0.016 to 0.065 Gm.).

PODOPHYLLI INDICI RHIZOMA. Br.

INDIAN PODOPHYLLUM RHIZOME [Podophyllum Emodi Rhizome]

"Indian Podophyllum Rhizome is the dried rhizome and roots of Podophyllum Emodi, *Wall.*" *Br.*

Podophyllum Emodi (Fam. *Berberidaceæ*) is a perennial herb which is indigenous to Thibet and Afghanistan. It somewhat resembles our American Podophyllum. The stem rises to a height of six or twelve inches before the opening of the leaves which attain a diameter of six to ten inches when fully expanded. The latter are curiously reflexed, droop umbrella-like and are often spotted. The plant produces in May a large sub-sessile, pinkish-white, flower which arises from the axil of one of the leaves, maturing before the latter are fully expanded. The fruit is about the size of a small lemon, of a bright orange color, being fully ripe in about August or September.

The contorted rhizome of *Podophyllum Emodi* is from six to eight mm. in thickness, crowded above with numerous buds or short branches, marked by depressed oval or circular scars, and giving off numerous simple rootlets from the whole of the under surface. The terminal bud is enclosed in whitish papery sheaths. The color is earthy-brown. The fracture is white, short, and mealy, or yellow and horny, exhibiting a circular arrangement of yellow vascular bundles, and bounded on the outside by a thin brown cortical layer.

"Rhizome cylindrical or flattened, contorted, earthy-brown; usually about ten millimetres thick; below with numerous root-scars, or with stout roots and crowned with the short remains of aerial stems, bearing cup-shaped scars. In transverse section, pale-brown and starchy or horny, with a ring of radially elongated wood-bundles. Slight odor; taste bitter and acrid." *Br.*

It may be used for the same purposes as podophyllum, but is official only as a source of the resin.

Off. Prep.—Podophylli Indici Resina, *Br.;* Tinctura Podophylli Indici (from Resin), *Br.*

PODOPHYLLUM. U. S. (Br.)

PODOPHYLLUM Podoph. [Mandrake, May Apple]

"Podophyllum consists of the dried rhizome and roots of *Podophyllum peltatum* Linné (Fam. *Berberidaceæ*). Podophyllum yields not less than 3 per cent. of the resin of podophyllum." *U. S.* "Podophyllum Rhizome is the dried rhizome and roots of Podophyllum peltatum, *Linn.*" *Br.*

Podophylli Rhizoma, *Br.;* Podophyllum Root, Wild Mandrake, Devil's Apple, Umbrella Plant, Vegetable Calomel, *Mandrake,* American Mandrake, Wild Lemon, Ground Lemon, Hog Apple, Indian Apple, Raccoon Berry, Duck's Foot; Rhizome de Podophyllum, *Fr.;* Fussblattwurzel, *G.;* Podofillo, *It.;* Podofilo (Rizoma de), *Sp.*

Podophyllum peltatum is an indigenous perennial herb having a prolifically branching rhizome system. Each rhizome branch is horizontal, usually several feet in length, about one-quarter of an inch thick, brown externally, smooth, jointed, and furnished with roots at the joints. Two kinds of stems arise from separate joints of the rhizome and its branches, *viz.,* the flowerless and the flowering stems. The flowerless stem terminates in a peltate leaf having 7 to 9 wedge-shaped lobes. The flowering stem bifurcates at its summit to form two stalked, 5- to 7-lobed leaves from the fork of which a stalked, pendulous, white flower arises. The calyx is composed of six oval, obtuse concave, fugacious sepals. The corolla has from six to nine white, fragrant petals, which are obovate, obtuse, concave, with delicate transparent veins. The stamens are from thirteen to twenty, shorter than the petals, with oblong yellow anthers, of twice the length of the filaments. The stigma is sessile, fleshy and undulate. The fruit is a large oval berry, crowned with the persistent stigma, and containing a sweetish and slightly acrid fleshy pulp, in which about twelve ovate seeds are embedded, each inclosed in a fleshy aril. It is, when ripe, of a lemon-yellow color diversified by round brownish spots. Two species of the genus *Podophyllum* are known as growing in China while *Podophyllum Emodi,* which inhabits the interior ranges of the Himalayas and is very abundant in Cashmere is recognized in the Br.

The May apple is extensively diffused through the Eastern United States, growing luxuriantly in colonies, in moist open places of shady woods and in low marshy grounds from Canada to

Minnesota and southward to Florida and Texas. It is propagated by its creeping rhizome, and is often found in large patches. The flowers appear about the end of May and the beginning of June, and the fruit ripens in the latter part of July. The leaves are said to be poisonous. The fruit has a subacid, sweetish, peculiar taste, agreeable to some palates, and may be eaten freely with impunity. From its color and shape, it is sometimes called *wild lemon.* The rhizome is said to be most efficient when collected after the falling of the leaves. It shrinks considerably in drying.

The commercial supplies of podophyllum are obtained chiefly from Virginia, Kentucky, North Carolina, Tennessee and Indiana. The dried rhizome is much wrinkled lengthwise, is yellowish or reddish-brown externally, and furnished with roots of a similar but somewhat paler color. It was determined, by an experiment of Wm. Saunders, that these roots contain as much active matter as the rhizome itself.

Description and Physical Properties.—"*Unground Podophyllum.*—Rhizome nearly cylindrical, jointed, compressed on the upper and lower surfaces, sometimes branched; in pieces usually less than 20 cm. in length, the internodes from 2 to 9 mm. in diameter, some of the nodes thickened; dark brown; longitudinally wrinkled or nearly smooth, with irregular, somewhat V-shaped scars of scale leaves; some of the nodes annulate, the upper portion with large, circular, depressed stem-scars and with buds or stem-bases; on the lower portion numerous root-scars or roots from 2 to 7 cm. in length and about 2 mm. in thickness; fracture short; internally the cork light brown, the wood portion a circle of small yellowish vascular bundles and the pith large and white; odor slight; taste disagreeably bitter and acrid.

"*Structure.*—An outer portion consisting of one or two layers of reddish-brown suberized cells; parenchyma of cortex and pith containing numerous starch grains, or occasional rosette aggregates of calcium oxalate; vascular bundles from 24 to 34, separated by rather wide medullary rays and each containing a few lignified tracheæ, a more or less distinct cambium and a rather large phloem.

"*Powdered Podophyllum.*—Light brown; starch grains numerous, spherical or polygonal, from 0.003 to 0.020 mm. in diameter, single or 2- to 6-compound; calcium oxalate rosette aggregates few, from 0.03 to 0.08 mm. in diameter; tracheæ with simple pores or reticulate thickenings; fragments of starch-bearing parenchyma and reddish-brown cork cells." *U. S.*

Assay.—"Proceed as directed under *Jalapa,* using 10 Gm. of Podophyllum in fine powder." *U. S.*

"Rhizome nearly cylindrical, of very variable length, usually about five millimetres thick; dark reddish-brown, smooth or only slightly wrinkled; enlarged at intervals of about five centimetres, the upper surface of each enlargement being marked by a depressed circular scar, below which, on the under surface, are rather stout, brittle, brown roots, or the scars corresponding to them. In transverse section, either nearly white and starchy, or pale yellowish-brown and horny. Characteristic odor; taste slightly bitter and acrid." *Br.*

The root in its aggregate state is nearly inodorous, but in powder has a sweetish not unpleasant odor. The taste is at first sweetish, afterwards bitter, nauseous, and slightly acrid.

Constituents.—The active ingredient of podophyllum is a neutral substance called *podophyllotoxin* and first isolated, in an impure condition, by Podwyssotzki in 1882.

Podophyllotoxin occurs in the form of crystalline prisms, strongly lævo-rotatory, with a melting point of 117° C. (the melting point of 94° often given for this compound is that of Kursten (*A. Pharm.,* 1891), but it is generally believed today that the substance he called podophyllotoxin was not the pure principle). When heated with alkalies it takes on a molecule of water and is converted into an inert, gelatinous substance, *podophyllic acid,* $C_{15}H_{16}O_7$. This latter may be dehydrated to yield *picropodophyllin* which is isomeric with *podophyllotoxin.* Picropodophyllin is optically inert and has a melting point of 227° C. See Dunstan and Henry (*A. J. P.,* 1898, 246). Podophyllotoxin and picropodophyllin furnish identical decomposition products; when oxidized with nitric acid, oxalic acid is the principal product; when fused with alkalies, *orcinol* and acetic acid are produced. Both substances contain three methyl groups and no hydroxyl. It is likely that picropodophyllin is the lactone of podophyllic acid. Picropodophyllin is therapeutically inactive.

In addition to podophyllotoxin there appears to be present an amorphous resinous substance, *podophyllo-resin,* which is also active. Podwyssotzki also obtained *podophylloquercetin,* the coloring principle, which is the cause of the varying color of resin of podophyllum. According to Dunstan and Henry it is identical with quercetin obtained from black oak bark.

Podophyllotoxin, $C_{23}H_{24}O_9$, is obtained by extracting the coarsely powdered rhizome with cold, light petroleum, until freed from fat; after drying in the air, the extraction is continued with chloroform, until the liquid comes away almost free from yellow color. As it is not possible to work with alcohol-free chloroform, too prolonged extraction with chloroform would yield a more impure extract. The chloroform extract is distilled and the residue is dried over a not too warm water bath, partially dissolved in benzene, filtered, and the filtrate allowed to remain from three to eight days, when a brownish-yellow mass of well-formed, thick, strongly refractive prisms is produced. This is purified by washing with a 50 per cent. alcohol, then with ether, recrystallizing first from boiling benzene, and finally from solution in hot 45 per cent. alcohol; the compound is thus obtained in long, well-formed prisms which melt at 94° C.

A commercial variety of podophyllotoxin is prepared by concentrating the chloroformic extract to a thick syrup and treating with alcohol-free ether as long as a precipitate is produced. The clear liquid is decanted and again concentrated and poured into petroleum ether. The resulting precipitate is dried and sold as *commercial podophyllotoxin.*

B. F. Carter (*A. J. P.,* 1886, p. 449) also examined the leaves. He found tannin, uncrystallized sugar, coloring matter, and 6 per cent. of resin. This latter seems to be of two-fold character, ether dissolving the soft resin, while the hard resin remains behind. The resin has a bitter taste and a much milder action than that of the rhizome. Fused with potassium hydroxide a small amount of protocatechuic acid seems to be formed.

An extract of podophyllum, when subjected to Bornträger's test for emodin-containing drugs, gives a bright yellow color with ammonia. This coloration is probably produced by the *quercetin.*

A fatty oil has been separated from the rhizome of podophyllum by Dohme and Engelhardt. (See *Proc. A. Ph. A.,* 1904, 340.)

Assay.—"Proceed as directed under Jalapa, using 10 Gm. of Podophyllum in fine powder." *U. S.*

A method of assay for podophyllum has been proposed by W. M. Jenkins (*J. I. and E. C.,* 1914, p. 671) which is based upon a shaking out method using a mixture of chloroform and alcohol.

Gordin and Merrell (*Proc. A. Ph. A.,* 1902, 343) propose to judge of the quality of resin of podophyllum by an assay based on the percentage of crude picropodophyllin and the following requirements: 1. Pure podophyllin must be completely soluble in about twice its weight of cold alcohol. 2. It should contain about 64 per cent. ether-soluble and about 74 per cent. chloroform-soluble matter. 3. It should yield about 22 per cent. crude picropodophyllin when assayed by the method described by them.

Uses.—Podophyllum is a slow but active and certain cathartic producing copious liquid discharges often with much griping. It has been attributed with cholagogic properties and is used in various forms of *hepatic torpor* but its virtues in this direction are probably no greater than that of other active purgatives. In small doses it is frequently used in *chronic constipation,* especially in conjunction with aloes or cascara.

In overdoses podophyllum acts as an irritant poison; an amount estimated at five grains of the resin caused death in a woman sixty years old (*N. Y. M. R.,* April, 1890); the symptoms were vomiting and purging, followed some hours after their cessation by coma, full soft pulse, slight elevation of temperature, and hemoglobinuria.

Dose, five to ten grains (0.32–0.65 Gm.), but it is rarely exhibited in the crude form.

Off. Prep.—Resina Podophylli, *U. S.* (*Br.*)*;* Tinctura Podophylli (from Resin), *Br.;* Pilulæ Aloes et Podophylli Compositæ (from Resin), *N. F.;* Pilulæ Aloes, Hydrargyri et Podophylli (from Resin), *N. F.;* Pilulæ Aloini Compositæ (from Resin), *N. F.;* Pilulæ Catharticæ Vegetabiles (from Resin), *N. F.*

POPULI GEMMÆ. N. F.

BALSAM POPLAR BUDS Popul. Gem. [Balm of Gilead Bud]

"Balsam Poplar Buds consists of the air-dried, closed, winter leaf-buds of *Populus nigra* Linné, *Populus candicans* Aiton, or *Populus balsamifera* Linné (Fam. *Salicaceæ*). Balsam Poplar Buds contains not more than 10 per cent. of flower buds and yields not more than 1 per cent. of acid-insoluble ash." *N. F.*

Balsam Poplar Buds; Balm of Gilead Buds; Gemma Populi; Oculi Populi; Peuplier Noir, Bourgeons de Peuplier, *Fr.;* Pappelknospen, *G.;* Yema de Alama Negro, *Sp.*

In most trees of the genus *Populus,* the leaf-buds are covered with a resinous exudation, which has a peculiar, agreeable, balsamic odor, and a bitter, balsamic, somewhat pungent taste. It is abundant in the buds of *Populus nigra* L., or the *black poplar* of Europe, which are official in some parts of that continent. They contain resin and a peculiar volatile oil. The buds of *P. balsamifera* L., the *Balsam Poplar* or *Tacamahac,* growing in the northern parts of North America and Siberia, are also highly balsamic; and a resin is said to be furnished by the tree. The buds are also obtained from *P. Candicans* Ait. which is the true Balm of Gilead.

Description and Physical Properties.—"Conical, pointed, up to 2 cm. in length and from 2 to 5 mm. in thickness, consisting of closely imbricated scales, externally brown and glossy, glutinous with fragrant resin; internally with abundant oleo-resin and numerous crystals of salicin. Odor pleasant, balsamic; taste aromatic and bitter." *N. F.*

The bark of *P. tremuloides* Michx., or *American aspen,* and of *P. tremula* L., or *European aspen,* contain *salicin* and another crystallizable principle named *populin,* $C_{20}H_{22}O_8 + 2H_2O$. The leaves of *P. tremula* are also said to yield more populin than does the bark. It is probable that both principles exist in the bark of *P. tremuloides* and other species. Schaak (*A. J. P.,* 1892, 226) found a bitter principle in the bark of *P. alba* L., which was most likely populin. Populin is very light and white, of a bitter, sweetish taste, analogous to that of licorice. It is soluble in 1896 parts of cold and about 70 parts of boiling water, and is more soluble in boiling alcohol. It loses its two molecules of water of crystallization at 100° C., and at 180° C. it fuses to a colorless liquid, from which at a higher temperature benzoic acid may be sublimed. Acetic acid and the diluted mineral acids dissolve it, and, upon the addition of an alkali, let it fall unchanged. Piria first showed it to be *benzoyl salicin,* $C_{13}H_{17}(C_7H_5O)O_7 + 2H_2O$. He then decomposed it and prepared salicin from it. Populin has been prepared synthetically by Dobbin and White (*P. J.,* 1904, lxxiii, p. 233) by the direct combination of salicin and benzoyl chloride. The leaf buds of the poplar contain besides the glucosides salicin and populin, an oleo-resin which yields a terpene, probably dipentene, to which its therapeutic use is to be attributed. The flower-buds of *P. tremuloides* yielded a bitter resin to R. Glenk. It was of yellowish-brown color, strong, hop-like odor, and had a melting point of 51° C. (*A. J. P.,* 1889, 240.)

Poplar buds are capable of imparting a principle to ointments which lessens their tendency to rancidity. The *unguentum populeum, Pommade de Bourgeons de Peuplier,* is made, according to the directions of the French Codex, from 100 Gm. each of the dried contused leaves of white poppy, belladonna, henbane, and black nightshade, and 800 Gm. of dried poplar buds. The leaves are moistened with 400 Gm. of alcohol and allowed to stand twenty-four hours in a closed vessel; 4000 Gm. of lard is now added and the mixture heated gently during three hours, stirring frequently, the crushed poplar buds are then added and allowed to digest for ten hours at a gentle heat, and the whole strained and cooled slowly. This is an anodyne ointment, employed in Europe in painful affections.

Uses.—The therapeutic action of poplar bud is analogous to that of the turpentines. It has been used externally as a mild counter-irritant in *muscular rheumatism.* Internally it is of value chiefly as a stimulating expectorant in subacute or chronic *bronchitis.* It is comparatively little employed except in combination with other drugs.

Dose, one drachm (4 Gm.).

Off. Prep.—Syrupus Pini Albæ Compositus, *N. F.;* Syrupus Pini Albæ Compositus cum Morphinæ, *N. F.*

POTASSA SULPHURATA. U. S., Br.

SULPHURATED POTASSA Pot. Sulphurat.

" Sulphurated Potassa is a mixture composed chiefly of potassium polysulphides and potassium thiosulphate and contains not less than 12.8 per cent. of sulphur (S) in combination as sulphide." *U. S.* " Sulphurated Potash is a mixture of salts of potassium, chiefly sulphides." *Br.*

Sulphurated Potash, *Br.;* Hepar Sulphuris; Potassii Sulphuretum, *U. S.* 1870; Sulphuret of Potassium, Sulphurated Potash; Potassium Sulphide; Crude Potassium Sulphide; Liver of Sulphur; Polysulfure de Potassium solide, Sulfure de Potasse, Foie de Soufre, *Fr.;* Kalium Sulfuratum, *P. G.;* Schwefelleber, Kalischwefelleber, *G.;* Sulfuro (tri) potasico hiposulfitado, Higado de Azufre, *Sp.*

" Potassium Carbonate, in powder, 100 *grammes;* Sublimed Sulphur, 50 *grammes.* Mix the Potassium Carbonate, previously dried, with the Sulphur; heat in a covered crucible, at first gently, afterwards to dull redness, until effervescence ceases and the mass fuses; pour it on to a clean stone slab, and, after solidification, break it into fragments and transfer to a stoppered bottle." *Br.*

The U. S. P. X gives no process; that of the U. S. P., 1890, is as follows: " Sublimed Sulphur, *one hundred grammes,* Potassium Carbonate, dried, *two hundred grammes.* Mix the powdered and dried Potassium Carbonate thoroughly with the Sublimed Sulphur, and gradually heat the mixture, in a covered crucible, which should be only about half filled with it, until the mass ceases to foam and is in a state of perfect fusion. Then pour the fused mass on a cold marble slab, and, after it has cooled, break it into pieces, and keep it in a well-stoppered bottle." *U. S.* 1890.

These processes are essentially the same, except that a greater heat is used in the British process, which somewhat modifies the result. When potassium carbonate is melted with half its weight of sulphur, the sulphur unites with the base, carbon dioxide being expelled. The composition of the resulting compounds of potassium and sulphur will vary with the heat employed. If the heat does not exceed 185° C., the resulting preparation will contain potassium trisulphide and thiosulphate; if above 300° C., potassium pentasulphide and sulphate. The reaction for the preparation at the lower temperature is

$$3K_2CO_3 + 4S_2 = 2K_2S_3 + K_2S_2O_3 + 3CO_2$$

which at the higher temperature is changed as follows:

$$4K_2S_2O_3 = 3K_2SO_4 + K_2S_5$$

The potassium pentasulphide formed is decomposed at this high temperature into sulphur, which burns off, and K_2S_3. The U. S. preparation, therefore, which was made at the temperature of fusion, contains potassium thiosulphate, and may be represented by the formula $2K_2S_3 + K_2S_2O_3$, three molecules of CO_2 escaping, while the British, being prepared at a red heat, contains potassium sulphate, the reaction probably being

$$4K_2CO_3 + 5S_2 = K_2SO_4 + 3K_2S_3 + 4CO_2$$

The present commercial article is probably intermediate between these two products, and contains less than 50 per cent. of sulphides calculated from the sulphur requirement of the rubric.

Description and Physical Properties.—Sulphurated potassa, when properly prepared, is a hard, brittle substance having a nauseous, alkaline, and bitter taste. Its color is liver-brown, and hence its name of *hepar sulphuris,* or *liver of sulphur.* The color of the surface of a fresh fracture is brownish-yellow. It is inodorous when dry, but emits a slightly fetid odor when moist, owing to the extrication of a little hydrogen sulphide gas. It is soluble in water, forming an orange-yellow liquid, and exhaling the odor of hydrogen sulphide.

"Irregular pieces, liver-brown, when freshly made, changing to a greenish-yellow and finally to gray through absorption of moisture, oxygen, and carbon dioxide. It has an odor of hydrogen sulphide and a bitter, acrid, and alkaline taste. Sulphurated Potassa is very soluble in water, usually leaving a slight residue. Alcohol dissolves only the sulphides.

"An aqueous solution of Sulphurated Potassa (1 in 10) is light brown in color and is strongly alkaline to litmus paper. The addition of an excess of acetic acid to this solution causes a brisk evolution of hydrogen sulphide and a precipitation of sulphur. In the liquid thus treated, after filtration, an excess of sodium bitartrate T.S. produces within fifteen minutes an abundant, white, crystalline precipitate.

"Preserve in well-closed containers." *U. S.*

"Solid fragments, externally greenish-yellow, internally pale liver-brown, rapidly changing to greenish-yellow on exposure to the air. Odor that of hydrogen sulphide; taste alkaline and acrid. Readily soluble in *water.* Aqueous solution yellowish, opalescent; deposits only a trace of sediment on standing; evolves hydrogen sulphide freely on the addition of excess of *hydrochloric acid,* sulphur being deposited; this acid liquid, boiled and filtered, gives a yellow precipitate with *solution of platinic chloride.* Sulphurated Potash contains not less than 42 and not more than 45 per cent. of sulphur as determined by the following process:—Dissolve 0.2 gramme in 10 millilitres of *water* in a small flask, add 5 millilitres of *solution of sodium hydroxide,* heat the liquid to boiling, and add slowly, the flask being constantly rotated, *solution of bromine As T.* until a clear solution is obtained and bromine is present in excess. Acidify with *hydrochloric acid,* boil until the excess of bromine is driven off, add excess of *solution of barium chloride,* collect the precipitate formed, wash, dry, ignite, and weigh. It weighs not less than 0.611 or more than 0.655 grammes." *Br.*

By exposure to the air it attracts oxygen, and the potassium sulphide is gradually changed into potassium sulphate, when the preparation becomes inodorous, and white on the surface. When boiled with an excess of hydrochloric acid and filtered, it gives a yellow precipitate with platinic chloride, and a white one with barium chloride. The preparation of the Br. Pharmacopœia yields about one-half of its weight to alcohol (90 per cent.)—the portion dissolved being potassium sulphide, and the undissolved portion potassium sulphate.

Assay.—"Dissolve 1 Gm. of crystallized copper sulphate, accurately weighed, in 15 cc. of distilled water and 1 Gm. of Sulphurated Potassa, accurately weighed, in 10 cc. of distilled water, in a flask. Add the copper sulphate solution to the Sulphurated Potassa solution in a stoppered bottle, stopper, shake for a few minutes, and filter. Acidulate the filtrate with acetic acid, refilter if necessary, and add an equal volume of hydrogen sulphide T.S. No black precipitate is produced." *U. S.*

This compound has been used as an ingredient in the preparation known as *Lotio Sulphurata* (also called *Lotio alba* but not the same as the *Lotio alba Veterinaria* N. F.). The following formula for this is given by Raubenheimer (*J. A. Ph. A.,* 1914, 692): Zinc sulphate, 5 Gm.; sulphurated potassa, 5 Gm.; distilled water, q.s. to make 125 cc. Dissolve each chemical in 60 cc. of distilled water; filter the solutions separately and mix by slowly pouring the potassa solution into the zinc solution, then add sufficient distilled water to make 125 cc. Rose water may be used in place of distilled water. It is essential that the sulphurated potassa be fresh and free from iron compounds, as has been pointed out by J. C. and B. L. DeG. Peacock, *Proc. P. P. A.,* 1914, 256.

Uses.—Internally sulphurated potassa was formerly employed in *chronic rheumatism, skin diseases, asthma,* etc., but is to-day rarely used as an internal remedy. While if given in sufficient dose it may exercise the same effects upon the system as sulphur it is much more irritant to the stomach and has no advantages. It is, however, a valuable external agent in the treatment of various skin diseases. The alkaline sulphides exercise a solvent action upon the horny element of the skin and therefore sulphurated potassa is useful in *psoriasis* and other conditions in which there is excessive formation of scales. Because of the anti-parasitic action of the hydrogen sulphide which it liberates on contact with the skin, it is one of our most valuable remedies in the treatment of *scabies, ring-worm, tinea versicolor,* and other parasitic diseases. In *acne rosaceæ* and other skin diseases with sluggish circulation its local stimulating action tends to restore tone to the dilated blood vessel. It may be used either as a lotion, an ointment, or bath. As a lotion it is usually used in strengths of about 5 per cent. but in sluggish conditions may be employed up to 10 per cent. For an ointment one-half a drachm of sulphurated potassa (2 Gm.) may be rubbed up with one-half an ounce (15 Gm.) of lard. For a bath about one-half a drachm is employed for each gallon of water. The odor of sulphurated potassa is favorably modified whether in solution or ointment, by incorporating with it a little oil of anise.

The solution of sulphurated potassa is decomposed by the mineral acids, which liberate hydrogen sulphide and precipitate the excess of sulphur. It is also incompatible with solutions of most of the metals, which are precipitated as sulphides.

Dose, from two to ten grains (0.13–0.65 Gm.).

POTASSII ACETAS. U. S., Br.

POTASSIUM ACETATE Pot. Acet.

"Potassium Acetate, when dried to constant weight at 150° C., contains not less than 99 per cent. of $KC_2H_3O_2$." *U. S.* "Potassium Acetate may be obtained by fusing the product of the interaction of acetic acid and potassium carbonate. It contains not less than 90 per cent. of pure potassium acetate, $KC_2H_3O_2$." *Br.*

Kali Aceticum, Sal Diureticum, Acetas Potassicus, s. Kalicus, Terra Foliata Tartari; Acetate of Potassium; Diuretic Salt; Kalium Aceticum, *Fr. Cod.;* Acetate de Potasse sec, Terre Foliée de Tartre, *Fr.;* Essigsaures Kali, *G.;* Acetato di potassio, *It.;* Acetato potasico, *Sp.*

As this salt is practically never prepared on a small scale, no process is given in either of the Pharmacopœias. It may be prepared by the interaction between potassium carbonate and acetic acid. It is best to have the solution always slightly acid, for if the alkali predominate, it will react upon the acetic acid when the solution is concentrated, and give rise to discoloration. On account of the liability of discoloration, great care must be observed to avoid the contamination of iron. Some manufacturers use silver dishes.

Description and Physical Properties.—" A white powder, or crystalline flakes, or masses of satin-like luster. It is odorless or has a faint, acetous odor, and a warming saline taste. It is very deliquescent on exposure to the air. One Gm. of Potassium Acetate is soluble in 0.5 cc. of water and in 2.9 cc. of alcohol, at 25° C. One Gm. is soluble in about 0.2 cc. of boiling water.

" When slightly heated, the salt fuses. On strong ignition it is decomposed with the evolution of inflammable empyreumatic vapors and leaves a black residue of potassium carbonate and carbon. This residue imparts to a non-luminous flame a violet color, is alkaline to litmus paper, and effervesces with acids. An aqueous solution of Potassium Acetate (1 in 10) responds to the reactions for potassium, and for acetates.

" An aqueous solution of the salt (1 in 20) is alkaline to litmus paper but does not affect phenolphthalein T.S. An aqueous solution of the salt meets the requirements of the test for *heavy metals.* An aqueous solution of the salt meets the requirements of the test for *arsenic.*

" **Assay.**—Dry the salt to constant weight at 150° C. and proceed as directed under the assay for alkali salts of organic acids. Each cc. of half-normal sulphuric acid corresponds to 0.04907 Gm. of $KC_2H_3O_2$.

" Preserve in air-tight containers." *U. S.*

" White foliaceous satiny masses, or in granules. Taste sharp, saline. Very deliquescent. Soluble in 0.5 part of *water,* and in 2 parts of *alcohol* (90 per cent.). Aqueous solution alkaline to *litmus.* Yields the *reactions* characteristic of potassium and of acetates. Yields no characteristic *reactions* for copper, iron, aluminum, calcium, magnesium, carbonates, or sulphides, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million. Loses not more than 10 per cent. of its weight when dried at 100° C. One gramme, heated to redness until gases cease to be evolved, leaves an alkaline residue which, when treated with *water,* filtered, and well washed, yields a clear solution requiring for neutralisation not less than 18.3 millilitres of *N/2 solution of sulphuric acid." Br.*

Potassium acetate is incompatible with the mineral acids; with sodium and magnesium sulphates; with corrosive sublimate and silver nitrate, and with several other earthy and metallic salts.

Uses.—The effects of potassium acetate upon the system are very similar to those of the citrate (see *Potassii Citras*), except that it is less likely to act upon the bowels. Like the citrate it is oxidized in the system and appears in the urine as a carbonate and therefore tends to render this secretion alkaline. It is usually less acceptable to the palate than the citrate. It is especially employed in the treatment of *rheumatic fever* and the *uric acid diatheses.* It is also sometimes used for its diuretic effect in *dropsies* and *nephritis.* J. A. Easton, of Glasgow, has found it useful in several skin diseases, such as *psoriasis* and *eczema.*

Dose, fifteen to sixty grains (1–3.9 Gm.).

Off. Prep.—Elixir Buchu et Potasii Acetatis, *N. F.;* Elixir Buchu, Juniperi et Potassii Acetatis, *N. F.*

POTASSII BICARBONAS. U. S., Br.

POTASSIUM BICARBONATE Pot. Bicarb.

" Potassium Bicarbonate, when dried to constant weight over sulphuric acid, contains not less than 99 per cent. of $KHCO_3$." *U. S.* " Potassium Bicarbonate may be obtained by saturating a strong aqueous solution of potassium carbonate with carbon dioxide. It contains not less than 99 per cent. of pure potassium bicarbonate, $KHCO_3$." *Br.*

Bicarbonas Potassicus, s. Kalicus; Bicarbonas Monopotassicus; Potassium Hydrogen Carbonate; Acid Carbonate of Potassium; Bicarbonate of Potash; Potash Saleratus; Kalium Bicarbonicum, *Fr. Cod.;* Carbonate de Potasse Acide; Bicarbonate de Potasse, *Fr.;* Kalium Bicarbonicum, *P. G.;* Kalium-bicarbonat, Doppelt-Kohlensaures Kali, *G.;* Bicarbonato di potassio, *It.;* Bicarbonato potasico, *Sp.*

The process of the U. S. P. 1870, and also that of the British Pharmacopœia for this salt were abandoned at former revisions.

The reaction by which it is produced from potassium carbonate by the action of carbon dioxide is as follows:

$$K_2CO_3 + H_2O + CO_2 = 2KHCO_3$$

It was formerly made by numerous processes some of which being more or less empirical—such as one in which the waste CO_2 of breweries was allowed to act upon a concentrated solution of potassium carbonate—produced salts of indefinite composition. Much of the *potash saleratus* used, for leavening purposes in culinary operations, was in reality a sesquicarbonate, which is intermediate between a carbonate and a bicarbonate. The principle of the modern large scale process is the passing of carbon dioxide gas into a solution of potassium carbonate.

Description and Physical Properties.—"Colorless, transparent, monoclinic prisms or a white, granular powder. It is odorless, and has a saline and slightly alkaline taste. It is stable in the air. One Gm. of Potassium Bicarbonate is soluble in 2.8 cc. of water at 25° C. One Gm. is soluble also in 2 cc. of water at 50° C. It is almost insoluble in alcohol. When heated above 50° C., an aqueous solution of the salt loses carbon dioxide and water, and at boiling heat the salt is almost completely converted into normal carbonate. The dry salt begins to lose carbon dioxide and water at 100° C., this loss increasing at a higher temperature until at a red heat there remains a residue of carbonate, which imparts a violet color to a non-luminous flame.

"An aqueous solution of Potassium Bicarbonate (1 in 10) is slightly alkaline to litmus paper, but is neutral or very slightly alkaline to phenolphthalein T.S. An aqueous solution of Potassium Bicarbonate (1 in 10) responds to the reactions for potassium, and for carbonates.

"Add 2 cc. of tenth-normal hydrochloric acid and 2 drops of phenolphthalein T.S. to 1 Gm. of the salt, dissolved without agitation in 20 cc. of distilled water at a temperature not above 15° C.: a red tint does not appear immediately (*carbonate*). An aqueous solution of the salt (1 in 50), mixed with a slight excess of hydrochloric acid, meets the requirements of the test for *heavy metals*.

"Preserve in well-closed containers." *U. S.*

"Colorless, monoclinic, non-deliquescent prisms. Taste saline, feebly alkaline. Soluble in 4 parts of *water*, almost insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium and of bicarbonates. 1 gramme exposed to a low red heat leaves not less than 0.683 or more than 0.690 gramme of a white residue, which requires for neutralisation not less than 19.8 or more than 20 millilitres of *N/2 solution of sulphuric acid.* Yields no characteristic *reactions* for copper, sulphates, or sodium, and not more than the slightest *reactions* for iron or chlorides. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million. 20 grammes of Potassium Bicarbonate are neutralised by 14 grammes of Citric Acid, and by 15 grammes of Tartaric Acid." *Br.*

Assay.—"Dry about 4 Gm. of Potassium Bicarbonate to constant weight over sulphuric acid, weigh accurately, dissolve it in 25 cc. of distilled water, and titrate with normal sulphuric acid, methyl orange T.S. being used as indicator. Each cc. of normal sulphuric acid corresponds to 0.1001 Gm. of $KHCO_3$." *U. S.*

When heated to redness it loses carbon dioxide and returns to the state of carbonate, which, when thus obtained, is free from silica, and otherwise very pure. This method was adopted in the U. S. Pharmacopœia of 1870 for obtaining the pure carbonate. Potassium bicarbonate does not decompose calomel. When dissolved in 40 parts of water, it produces merely a white haze with a solution of corrosive sublimate; but if it contain so much as a hundredth part of carbonate, a brick-red precipitate is immediately produced. (Christison.)

Uses.—Potassium bicarbonate is comparatively little employed in medicine. It has approximately an equal neutralizing power weight for weight with bicarbonate of soda, and has the added advantage of being much more easily soluble in water. It should therefore be a valuable antacid in cases of *gastric hyperacidity,* but for some reason or other is comparatively rarely prescribed. As a systemic alkalizer it is inferior to the sodium salts because of the toxic effect of large doses of potassium.

Dose, ten to thirty grains (0.65–2 Gm.).

POTASSII BICHROMAS. Br.

POTASSIUM BICHROMATE

"Potassium Bichromate may be obtained by roasting chrome ironstone with lime in the presence of air, and treating the resulting chromate with a potassium salt, and subsequently with an acid. It contains not less than 99 per cent. of pure potassium bichromate, $K_2Cr_2O_7$." *Br.*

Potassii Dichromas, *U. S.* 1890; Potassium Dichromate, Red Chromate of Potash (Potassa), Bichromate of Potash; Kali Bichromicum, Kali Chromicum Rubrum; Dichromas Kalicus; Chromate Acide de Potasse, *Fr.;* Bichromate de Potasse, *Fr.;* Kalium dichromicum, *P. G.;* Kaliumdichromat, Zweifach Chromsaures Kali, Doppeltchromsaures Kali, *G.;* Bicromato di potassio, *It.;* Bicromato potasico, *Sp.*

Potassium dichromate was deleted from the U. S. P. IX list, but will be found among the reagents under *Potassium Dichromate, Purified.* (See Part III.)

This salt is most conveniently prepared from the neutral or yellow *potassium chromate,* by acidulating its solution with sulphuric acid and setting it aside for a day or two. In the action which follows we may suppose two reactions take place:

$$2K_2CrO_4 + H_2SO_4 = K_2SO_4 + 2KHCrO_4$$
$$2KHCrO_4 = K_2Cr_2O_7 + H_2O$$

As chromium is mainly found in nature as chrome iron ore, $FeO.Cr_2O_3$ or *chromite,* the salts of the element are usually made from this product. The yellow chromate is obtained from chrome iron ore by heating with potassium nitrate, and lixiviating the resulting mass with water, or it may be produced by heating the chrome iron ore in a reverberatory furnace with access of air in the presence of potassium carbonate and lime. This reaction is as follows:

$$2FeOCr_2O_3 + 4K_2CO_3 + 4CaO + 7O = Fe_2O_3 + 4CaCO_3 + 4K_2CrO_4$$

In another process the chrome iron ore is melted in a reverberatory furnace with soda and lime in the presence of air. The reaction is as follows:

$$2Cr_2O_4Fe + 4Na_2CO_3 + 4CaO + 7O = Fe_2O_3 + 4CaCO_3 + 4Na_2CrO_4$$

The manufacture of potassium dichromate is almost entirely an English monopoly at present, although some is manufactured in America from California ore. The solution, by evaporation, yields the yellow salt in crystals.

"In orange-red crystals. Soluble in 10 parts of *water.* Aqueous solution acid to *litmus;* gives a yellowish-white precipitate with *solution of barium chloride;* acquires an emerald-green color when warmed with *sulphuric acid* and *alcohol* (90 per cent.). When 0.1 gramme is dissolved in 20 millilitres of *water* acidified with 5 millilitres of *diluted sulphuric acid,* and then 2 grammes of *potassium iodide* added, the solution thus obtained, diluted with *water,* requires for decolorisation not less than 20.1 millilitres of *N/10 solution of sodium thiosulphate* (presence of not less than 99 per cent. of pure potassium bichromate, $K_2Cr_2O_7$)." *Br.*

The oxidizing action of potassium dichromate which is so especially marked in the presence of free sulphuric acid may be understood by the following reaction in which it will be seen that each molecule of the dichromate yields 3 atoms of nascent oxygen and a molecule of chrome alum.

$$K_2Cr_2O_7 + 4H_2SO_4 = 4H_2O + Cr_2(SO_4)_3.K_2SO_4 + 3O$$

Uses.—Potassium dichromate is an irritant caustic acting much like chromium trioxide (*q. v.*) It was used by Robin, in 1850, in the treatment of *syphilis,* but was entirely abandoned to be later revived by Helbig. (*Aerzt. Runds.,* 1910, p. 157.) He administers one-sixth of a grain (0.01 Gm.) well diluted three times a day. Fenwick (*B. M. J.,* 1909) recommends in *cancer* the injection of eight to fifteen minims (0.5–0.9 cc.) of a 10 per cent. solution into the tumor, and Gemmil (*B. M. J.,* 1909) has had good results from its local application in *rodent ulcer.*

In overdose it operates as a violent irritative and corrosive poison, producing severe vomiting, frequent dark hemorrhagic dejections, violent abdominal pains, pronounced disturbances of the circulation, coma, heart failure, collapse, etc. Less than an ounce has caused unconsciousness in five minutes, with death thirty-five minutes later. (*B. M. J.,* ii, 1888.) The antidote is a non-irritant alkali, such as sodium carbonate, soap or magnesia.

Potassium dichromate is used largely in calico printing and for other technical purposes. The workmen engaged in making it are liable to painful ulcerations of the hands, and, in consequence of the acrid vapors evolved, violent irritation of the nostrils is apt to be experienced, with severe pricking sensations and excessive sneezing, followed in time by destruction of the mucous membrane and even of the septum itself. It is asserted that this result may be avoided by breathing through the mouth exclusively, the profuse secretion of saliva produced carrying off the poisonous particles. (*B. F. M. R.,* Oct., 1863.)

Mueller's Fluid is used for preserving anatomical specimens. It consists of from 2 to 2.5 parts of potassium dichromate, 1 part of sodium sulphate, and 100 parts of water.

Dose, one-tenth to one-fifth of a grain (0.006–0.012 Gm.).

POTASSII BITARTRAS. U. S. (Br.)

POTASSIUM BITARTRATE Pot. Bitart. [Cream of Tartar, Potassium Acid Tartrate]

"Potassium Bitartrate, when dried to constant weight at 100° C., contains not less than 99.5 per cent of $KHC_4H_4O_6$." *U. S.* "Acid Potassium Tartrate may be obtained from the crude cream of tartar deposited during the fermentation of grape juice. It contains not less than 99 per cent. of pure potassium hydrogen tartrate, $KHC_4H_4O_6$." *Br.*

Potassii Tartras Acidus, *Br.;* Acid Potassium Tartrate Crystals of Tartar; Purified Cream of Tartar; Tartrate Acide de Potasse, Bitartrate de Potasse, Crème de Tartre, Pierre de Vin, *Fr.;* Kalium Bitartaricum, *Fr. Cod.;* Tartarus depuratus, *P. G.;* Weinstein, Kali Bitartaricum, Kalium Hydrotartaricum, Bitartras Potassicus, s. Kalicus, Cremor Tartari, *G.;* Tartrato acido di potassio, Cremor di tartaro, *It.;* Tartrato bi potasico, Cremor de tartaro, *Sp.*

During the fermentation of wines, especially those that are tart, a peculiar matter is deposited in the casks, forming a crystalline crust, called *crude tartar,* or *argol.* That deposited from red wines is of a reddish color, and called *red tartar,* while that derived from white wines is of a dirty-white color, and denominated *white tartar.* Both kinds consist of crude potassium bitartrate, or *cream of tartar* as it is commonly called. The deposition of the tartar is thus explained: The acid tartrate exists naturally in the juice of the grape, held in solution by saccharine matter. When the juice is submitted to fermentation in the process for converting it into wine, the sugar disappears, and is gradually replaced by alcohol, in which the salt is insoluble. It is from argol that acid potassium tartrate is obtained by a process of purification.

The process for purifying argol is very simple and is based upon the great difference in the solubility of the salt in hot and cold water. Simple solution, filtration, clarification if necessary, and crystallization yield an article which is of an exceedingly high degree of purity.

Description and Physical Properties.—"Colorless or slightly opaque, rhombic crystals, or a white, somewhat gritty powder. It is odorless, and has a pleasant acidulous taste. It is stable in the air. One Gm. of Potassium Bitartrate is soluble in 155 cc. of water and in 8820 cc. of alcohol, at 25° C. One Gm. is soluble in 16 cc. of boiling water.

"A saturated aqueous solution of the salt is acid to litmus paper. When Potassium Bitartrate is heated, it chars and emits inflammable vapors, having the odor of burning sugar. At a higher temperature and with free access of air, the carbon of the black residue is consumed, and a white, fused mass of potassium carbonate remains, which has an alkaline reaction, effervesces with acids, and colors a non-luminous flame violet. A saturated aqueous solution of

Potassium Bitartrate yields with sodium cobaltic nitrite T.S. a yellow precipitate.

"Neutralize a saturated aqueous solution of the salt with sodium hydroxide T.S. in a test tube, add silver nitrate T.S., then just sufficient ammonia T.S. to dissolve the white precipitate, and boil the solution; silver is deposited on the inner surface of the test tube, forming a mirror.

"When 0.5 Gm. of the salt is dissolved in 3 cc. of ammonia T.S., no insoluble residue remains (*starch, kaolin, calcium phosphate, or other insoluble matter*). A 10 cc. portion of an aqueous solution of the salt (1 in 50), made with the aid of just sufficient hydrochloric acid, meets the requirements of the test for *heavy metals.* Ammonia is not evolved on heating the salt with a slight excess of sodium hydroxide T.S. Mix 1 Gm. of Potassium Bitartrate in a platinum or silica crucible with 0.5 cc. of sulphuric acid and 1 cc. of nitric acid, and heat the mixture until fumes of sulphur trioxide begin to be liberated. Cool the resulting mass, treat it with 10 cc. of distilled water, and filter: the filtrate, made slightly alkaline with sodium hydroxide T.S., does not yield a gelatinous precipitate soluble in excess of the reagent (*alum*). Heat 10 Gm. of Potassium Bitartrate with 15 cc. of distilled water, add hydrochloric acid until the salt is dissolved, then add 2 cc. of sulphurous acid, and boil the mixture until the odor of sulphur dioxide is barely perceptible. Cool the solution, mix it with 1 cc. of sodium cyanide T.S., and follow this immediately with stronger ammonia water until the precipitate first formed is redissolved and the solution has a slight odor of ammonia. When cold, transfer the solution to a 50 cc. graduated, glass-stoppered cylinder, dilute it with sufficient distilled water to measure 50 cc., and add 3 drops of sodium sulphide T.S. After thorough mixing, the color produced in the solution, if any, when viewed downward against a white surface, is not greater than the color of a control solution prepared as follows: Dissolve 2 Gm. of reagent ammonium chloride in 20 cc. of distilled water, add 4 cc. of a solution containing 0.08 Gm. of lead nitrate in 1000 cc. of distilled water, and then 1 cc. of diluted hydrochloric acid. Treat this solution with the same quantities of hydrochloric acid, sulphurous acid, sodium cyanide T.S., and stronger ammonia water, as used above. Transfer it to another 50 cc. glass-stoppered cylinder, then dilute with sufficient distilled water to make 50 cc., and add 3 drops of sodium sulphide T.S. Before adding the sodium sulphide T.S. the liquid must possess a distinct odor of ammonia and the two cylinders used must be matched, be of practically colorless glass, and have the same internal diameter (*lead*).

"**Assay.**—Dry about 6 Gm. of Potassium Bitartrate to constant weight at 100° C., weigh accurately, dissolve in 100 cc. of boiling distilled water, and titrate with normal sodium hydroxide, using phenolphthalein T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.1882 Gm. of $KHC_4H_4O_6$.

"Preserve in well-closed containers." *U. S.*

"A gritty white powder, or fragments of crystalline cakes. Taste acid. Soluble in 220 parts of *water;* insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium and of tartrates. 1 gramme requires for neutralisation not less than 10.5 millilitres of *N/2 solution of sodium hydroxide.* Yields no characteristic *reactions* for copper, or iron, and not more than the slightest *reactions* for calcium, magnesium, sodium, chlorides, or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 2 parts per million." *Br.*

With salifiable bases which form soluble tartrates, it gives rise to double salts, consisting of neutral potassium tartrate, and the tartrate of the base added. Several of these are important medicines. Cream of tartar, though sparingly soluble in water, becomes abundantly so by the addition of borax or boric acid. *Soluble Cream of Tartar* (*Potassium Borotartrate, Tartarus boraxatus, Kali tartaricum boraxatum, Cremor tartari solubilis.*) Borax, 2 parts; distilled water, 20 parts. Dissolve, and add 5 parts purified cream of tartar. Agitate to dissolve, filter, evaporate to dryness, and powder. Soluble cream of tartar may be made by substituting boric acid for the borax. *Boric acid soluble cream of tartar* may be made by the following formula. Four hundred parts of cream of tartar and 100 of the acid are dissolved in a silver basin, at the boiling temperature, in 2400 parts of water. The solution is kept boiling until the greater part of the water is consumed. The fire is then moderated, and the solution continually stirred while the evaporation proceeds. When the matter has become very thick, it is removed by portions, which are flattened in the hand, completely dried by the heat of a stove, powdered, and kept in well-stoppered bottles. This form of soluble cream of tartar is more soluble than that made with borax. The product should not be powdered, but kept in large grains.

The cream of tartar of commerce is now nearly pure potassium bitartrate. It has been, however, found purposely mixed with various substances, such as sand, clay, gypsum, flour, chalk, alum, and potassium sulphate. These are excluded by the official tests except the last which may be recognized by its causing a precipitate with barium chloride, not entirely soluble in nitric acid. The action of the last-mentioned test is explained by the fact that the barium tartrate is soluble and the sulphate insoluble in nitric acid. The U. S. Pharmacopœia requires that it should contain 99.5 per cent. of pure potassium bitartrate, and there is no difficulty in obtaining it in commerce of this quality. Coupland gives in *P. J.*, 1901, 282, the results of an examination of commercial cream of tartar as follows: While in 1884 the assays of cream of tartar revealed from 8 to 14 per cent. of calcium tartrate, the quality has continuously improved and it contained, in 1901, 4.6 per cent. But cream of tartar of greater purity is by no means an exceptional article, potassium bitartrate of a quality of 98 and 99 per cent. being common, the latter coming from America. The competition among makers of "baking powders," into which it enters, explains in part the improvement in the quality of cream of tartar.

Uses.—The tartrates differ from the salts of most of the other vegetable acids in that they are not oxidized in the body but are eliminated unchanged through the kidney. It follows that they do not act as systemic alkalizers as do the citrates and acetates. The tartrates are also less readily absorbed from the intestines than the citrates, and therefore more prone to exercise a laxative effect. Potassium bitartrate when given in full dose has a mild saline cathartic action and is much used for this purpose, especially in combination with other laxatives. In smaller dose it may be absorbed from the alimentary canal and act as a diuretic. Some believe that its stimulating influence upon the kidney is more pronounced than that of the citrates, but it is probable that the only difference in their diuretic effect depends upon the antacid action of the citrate. Potassium bitartrate was formerly a favorite remedy in the treatment of *dropsies,* especially in conjunction with juniper, but we believe is less frequently employed at the present. Its solution in boiling water, sweetened with sugar and allowed to cool, forms an acid, not unpleasant, refrigerant drink, advantageously used in some *febrile affections,* and frequently employed as a domestic remedy. The beverage called *imperial* (*potus imperialis*) is a drink of this kind, made by dissolving half an ounce of the salt in three pints of boiling water, and adding to the solution four ounces of white sugar and half an ounce of fresh lemon peel.

As a diuretic, cream of tartar may be administered in the dose of a drachm and a half or two drachms (5.8–7.7 Gm.) several times a day. In pharmacy, cream of tartar is employed to obtain the neutral potassium tartrate (soluble tartar), potassium and sodium tartrate (Rochelle salt), antimony and potassium tartrate (tartar emetic), and iron and potassium tartrate (tartarized iron). Deflagrated with potassium nitrate, or incinerated alone, it is converted into a pure form of potassium carbonate, called salt of tartar.

Dose, as a diuretic, fifteen to forty-five grains (1–3 Gm.); as a cathartic, two to six drachms (8–23 Gm.).

Off. Prep.—Confectio Sulphuris, *Br.;* Pulvis Jalapæ Compositus, *U. S., Br.;* Trochiscus Sulphuris, *Br.;* Ferri et Potassii Tartras, *Br.;* Pulvis Kaladanæ Compositus, *Br.;* Species Laxativæ, *N. F.;* Tabellæ Sulphuris et Potassii Bitartratis, *N. F.*

POTASSII BROMIDUM. U. S., Br.

POTASSIUM BROMIDE Pot. Brom.

"Potassium Bromide, when dried to constant weight at 100° C., contains not less than 98.5 per cent. of KBr." *U. S.* "Potassium Bromide may be obtained by the interaction of ferrous bromide with potassium carbonate. When dried at 100° it contains not less than 98 per cent. of pure potassium bromide, KBr." *Br.*

Bromide of Potassium; Bromuretum Potassicum, s. Kalicum; Bromure de Potassium, *Fr.;* Kalium bromatum, *P. G.;* Bromkalium, Kaliumbromid, *G.;* Bromuro di potassio, *It.;* Bromuro potasico. *Sp.*

No process is given in recent Pharmacopœias but in the 1870 U. S. P. a solution of ferrous bromide was formed by the reaction between iron wire and bromine in boiling water and this, by the addition of the solution of potassium carbonate, was decomposed so as to produce ferrous carbonate, which precipitated, while potassium bromide remained in solution. By straining, the precipitated carbonate was separated, and from the strained liquor potassium bromide was obtained by evaporation and crystallization. In the process of the Br., 1885, by reaction between potassium hydroxide and bromine, the potassium bromide and bromate are produced in solution; these having been evaporated to dryness are mixed with charcoal and exposed to a red heat, whereby the potassium bromate is converted into potassium bromide. The solution of potassium bromide is then allowed to crystallize as in the preceding method. In either method the final crystallization takes place from a slightly alkaline solution in order to yield a more stable salt.

Description and Physical Properties.—"Colorless or white, odorless cubical crystals or a granular powder. It is stable in the air. One Gm. of Potassium Bromide is soluble in 1.5 cc. of water, in about 250 cc. of alcohol, and in 4.6 cc. of glycerin, at 25° C. One Gm. is soluble in 1 cc. of boiling water and in about 21 cc. of boiling alcohol. An aqueous solution of Potassium Bromide (1 in 20) is neutral or faintly alkaline to litmus paper. When the salt is heated upon platinum foil, it decrepitates; upon further heating (about 750° C.) it fuses without decomposition and at higher temperatures, it volatilizes, imparting a violet color to a non-luminous flame.

"An aqueous solution of the salt (1 in 5) responds to the reactions for potassium, and for bromides.

"Dissolve 1 Gm. of Potassium Bromide in 10 cc. of distilled water and add 0.1 cc. of tenth-normal sulphuric acid: no color is produced by the subsequent addition of a drop of phenolphthalein T.S. even after heating (*alkali*). Add a few drops of ferric chloride T.S. to 10 cc. of an aqueous solution of the salt (1 in 20), shake the mixture, and add 1 cc. of chloroform: the latter does not acquire a violet tint (*iodide*). Drop 1 cc. of diluted sulphuric acid upon about 1 Gm. of the powdered salt: no yellow color appears at once (*bromate*). A 10 cc. portion of an aqueous solution of the salt (1 in 20), when acidulated with hydrochloric acid, is not immediately rendered turbid by the addition of 1 cc. of potassium sulphate T.S. (*barium*). A solution of 2 Gm. of Potassium Bromide in 50 cc. of distilled water shows no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid. An aqueous solution of the salt meets the requirements of the test for *heavy metals*.

"**Assay.**—Dry the salt to constant weight at 100° C., and proceed as directed under the assay for bromides. Each cc. of tenth-normal silver nitrate corresponds to 0.01190 Gm. of KBr. Each Gm. of Potassium Bromide, previously dried, corresponds to not less than 82.8 cc. and not more than 84.8 cc. tenth-normal silver nitrate.

"Preserve in well-closed containers." *U. S.*

"Colorless cubical crystals. No odor; taste pungent and saline. Soluble in 2 parts of *water*, and in 200 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium and of bromides. Loses not more than 1 per cent. of its weight when dried at 100° C.; 0.5 gramme of this dried salt requires for complete precipitation not less than 41.2 or more than 42.5 millilitres of *N/10 solution of silver nitrate*. Yields no characteristic *reactions* for copper, iron, barium, calcium, magnesium, carbonates, bromates, or iodates, and not more than the slightest *reactions* for iodides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

According to Chas. D. Chase, the commercial salt often is too alkaline, and will precipitate the alkaloids from the solution of their salts; as some of the alkaloids are precipitated even by neutral bromides, pharmacists usually apply a "shake well" label to such prescriptions as contain combinations of the bromides and alkaloidal salts.

Uses.—The effects of potassium bromide on the system are due chiefly to the bromine ion, although under certain conditions they may be more or less modified by the potassium. The bromides in sufficient concentration are depressants apparently to all forms of nervous tissue but show a marked selective action for certain centers. In the frog the most susceptible part is the sensory side of the spinal cord and it is possible in these animals to produce a condition of almost complete anesthesia and loss of reflex activity, with the voluntary motion well preserved. In man, however, the first effect seems to be upon the motor area of the brain and while these centers are not completely paralyzed there is a great reduction in the irritability of the psychomotor tract from doses insufficient to cause any marked diminution of the reflexes or distinct loss of sensation. With sufficient doses, however, both of these evidences of depression of the sensory cells of the cord may be apparent even in human beings. While after toxic quantities or in certain specially susceptible individuals there may be marked disturbances of intellection, this psychical depression is usually a late phenomenon. As far as the circulatory apparatus and other vital functions are concerned the bromides are practically inert. The old belief that the bromides were depressant to the heart was based upon experiments made with the potassium salt and it has been shown by Greene and Kruse (*J. A. M. A.*, 1913, lxi, p. 271) that the depressant action of this salt is due to its potassium rather than to its bromine. When used continuously over long periods of time the bromides exert a profound influence upon the nutritive processes which, however, is not clearly understood. Schultz (*Z. B.*, 1883, xix, p. 301) has found an increase in the quantity of nitrogen eliminated but a diminution in the output of phosphorus.

As the drug is eliminated very slowly, when used continuously it tends to accumulate in the system and in sufficient dose may give rise to the phenomena known as *bromism*. The first symptom is usually an eruption on the skin of acne or furuncles, often associated with fetor of the breath. After more severe poisoning there may occur muscular weakness, general mental and bodily sluggishness, loss of memory, often marked sleepiness, depression of spirits deepening into complete apathy, lowering of temperature, and finally a universal depression of function, the patient lying in bed scarcely more than a feeble automaton. A remarkable thing about bromism is the rapidity and completeness with which the symptoms clear up on ceasing the use of the drug even without any treatment. Despite the fact that it leaves the system through practically all the excretory organs, having been found in the sweat, saliva, urine, and intestinal mucus, it is eliminated very slowly and has been found in the urine as much as a month after the last dose.

The bromides are used in medicine to check *convulsions*, alleviate *pain*, to promote sleep, and to allay general nervous excitation. In *epilepsy* the bromides are the most potent remedial agents that we possess. Their influence, however, is that of a suppressant and rarely, if ever, do they produce a true cure; while under their use the patient may remain free from seizures for months and even years, their withdrawal is generally followed by a return of symptoms. In *tetanus* the fact that they can be given in almost unlimited quantity without serious depression of the circulation renders them of peculiar value for the control of the convulsions. In *strychnine poisoning*, although theoretically important, their action is generally too slow to be of much practical utility. As analgesics the bromides when given by themselves are of only secondary power, but they greatly enhance the anodyne effects of other drugs such as morphine or acetanilid. In *insomnia* they have been greatly abused. They differ sharply from the true somnifacients, such as chloral, in the fact that in ordinary quantity they have almost no depressant action upon the intellectual centers. Their value in promoting sleep is due rather to the obtunding of the general sensibilities so that those distractions, such as noise and bodily discomforts, which may act as contributing causes to the wakefulness, are less potent. They have been used very freely in all forms of functional disorders of the nervous system for some of which they are very useful, but for others entirely unsuited. In *hysteria* they are almost habitually prescribed, but it is extremely doubtful whether they have any effect which cannot be ascribed to the mere effect of taking medicine, at least as far as the immediate relief of symptoms. In *neurasthenia* their analgesic properties often make them useful and there is reason to believe that at times they may exercise a favorable influence upon the metabolism of the nerve centers. In *vomiting* of reflex origin, as that of pregnancy, at times they are of service. Among other conditions in which they are frequently employed may be mentioned *alcoholism, delirium tremens,* various forms of *sexual excitement,* as *nymphomania, urethral fever,* etc.

The dose of potassium bromide varies much according to the purpose for which it is administered and the length of time over which it is employed. In conditions like epilepsy in which the use of the drug is continued, once the system has come under its influence relatively small doses are required to maintain the beneficial impression. Thus, while in the beginning of the treatment 1 or 2 drachms (3.9–7.7 Gm.) a day may be required, after the action of the bromide has once been well established their influence may often be continued by 8 or 10 grains (0.5–0.65 Gm.) three times a day. In tetanus it is essential that large quantities be exhibited; as much as from one-half to one ounce (15.5–31 Gm.) should be administered in the twenty-four hours. When only one dose is given very large quantities may be safely administered, thus for the relief of pain a drachm is generally required and in severe strychnine poisoning one-half ounce (15.5 Gm.), properly diluted, may be exhibited at once.

Dose, ten to forty-five grains (0.65–3.0 Gm.).

Off. Prep.—Elixir Potassii Bromidi, *N. F.;* Elixir Bromidorum Trium, *N. F.;* Elixir Bromidorum Quinque, *N. F.;* Mistura Chloralis et Potassii Bromidi Composita, *N. F.;* Sal Potassii Bromidi Effervescens Compositus, *N. F.;* Syrupus Bromidorum, *N. F.*

POTASSII CARBONAS. U. S., Br.

POTASSIUM CARBONATE Pot. Carb. [Salt of Tartar]

"Potassium Carbonate, when dried to constant weight at 180° C., contains not less than 99 per cent. of K_2CO_3. It contains not more than 15 per cent. of water." *U. S.* "Potassium Carbonate may be obtained by the interaction of potassium sulphate and calcium carbonate. It contains not less than 81.5 per cent. of pure potassium carbonate, K_2CO_3." *Br.*

Carbonate of Potassa from Pearlash; Salt of Wormwood; Potassii Carbonas Purus, Sal Tartari; Kali Carbonicum, Carbonas Potassicus, s. Kalicus; Subcarbonas Potassicus; Carbonate Neutre de Potasse, Carbonate de Potasse, Sel de Tartre, *Fr.;* Kalium Karbonicum, *P. G.;* Kohlensaures kali, Kaliumcarbonat, *G.;* Carbonato di potassio, *It.;* Carbonato potasico, *Sp.*

The present U. S. Pharmacopœia does not give a process for this salt. That formerly official was to purify the impure *potassium carbonate,* or pearlash. This generally contains certain insoluble impurities, as well as small portions of potassium sulphate, silicate, and chloride.

Impure Potassium Carbonate (Potassii Carbonas Impura) was official in 1870. It is commonly known as *Pearlash.*

Preparation.—Potash and pearlash of commerce were formerly procured exclusively from the ashes of wood by lixiviation, and the subsequent evaporation of the solution obtained. The alkali exists in the wood in combination with various organic acids, and is left behind after the incineration, principally in the form of carbonate according to the following reaction, taking the acetate as an example:

$$2KC_2H_3O_2 + O_4 = K_2CO_3 + CO_2 + 3H_2O$$

The wood is burned on the ground, in a place sheltered from the wind. The ashes consist of a soluble and an insoluble portion. The soluble part is made up of potassium carbonate, together with potassium sulphate, phosphate, and silicate, and potassium and sodium chlorides; the insoluble portion, of calcium and aluminum salts, oxidized iron and manganese carbonate and phosphate, and a little carbonaceous matter that has escaped combustion. The ashes are lixiviated in barrels with the addition of a portion of lime, and the soluble substances above mentioned are taken up. The lixivium is then evaporated in large iron kettles (or pots—hence the name *potash*), which for several days are kept constantly full. The evaporation is continued until the mass has become of a black color and of the consistence of brown sugar. It is now subjected to a powerful heat by means of which the remainder of organic matter is burnt up and the mass becomes of a bluish-white color. The extraction from wood ashes is no longer practised in the United States, but is still carried out, to some extent in Canada and the northern countries of Europe, especially Russia.

Within recent years the residues of beet root molasses, after fermentation of the sugar and distillation of the spirit, have served as a source of potash. The molasses contains 40 to 50 per cent. of sugar and 3 to 4 per cent. of potassium salts. The *suint* of sheep's wool constitutes another source of potash. The potassium in this case being combined with fatty substances.

Most of the potassium carbonate of to-day is produced from potassium sulphate, either the crude salt from Stassfurt deposits or that obtained from the crude potassium chloride of the same locality. This is converted into carbonate by a process analogous to Leblanc's soda process. The principle of the ammonia soda process can also be applied to the crude potassium chloride of Stassfurt, with this difference in the practical operation, that, because of the ready solubility of the acid potassium carbonate, trimethylamine is used instead of ammonia, as the chloride of this base is much more soluble than is ammonium chloride.

The most important of the German potassium beds consist either of *sylvite,* a native potassium chloride or of *carnallite,* a double magnesio-potassium chloride. These overlie a deposit of sodium chloride at Stassfurt, near Magdeburg, Prussia. Another extensive deposit is near Muhlhausen, Alsace.

Crude potash is prepared in large amount from German rock salt deposits, in a manner analogous to the preparation of sodium carbonate from sodium chloride. The natural mixture of magnesium and potassium chlorides may also be saturated with carbon dioxide, when an insoluble double salt separates out.

$$3MgCO_3 + 2KCl + CO_2 + 9H_2O = 2(MgCO_3.KHCO_3.4H_2O) + MgCl_2$$

By heating this with water under pressure it decomposes into insoluble magnesium carbonate and soluble potassium carbonate, which remains in solution and is obtained therefrom by evaporation.

$$2MgCO_3.KHCO_3.4H_2O = K_2CO_3 + 2MgCO_3 + 5H_2O + CO_2$$

Potassium carbonate may be produced from crude potassium sulphate by the following reaction:

$$K_2SO_4 + CaCO_3 = K_2CO_3 + CaSO_4$$

Feldspar, marl and other minerals, rich in potassium compounds, are occasionally utilized for the production of potassium carbonate and other salts of the element.

During the World War potash salts were very scarce and high in price in the United States for many months. A number of sources were utilized economically at that time which in times of peace are too expensive. Among these wartime processes was the commercial utilization of seaweed on the Pacific coast. A five million dollar plant was operated for a time near San Diego, Calif., utilizing various species of seaweed, the species *Macrocystis pyrifera* being the one principally used. Besides potassium salts, iodine, acetates and acetone were produced by the process employed. (See *A. J. P.,* 1918, xc, 591.) There are immense deposits of *alunite,* a basic potassium aluminum sulphate, in Utah which are worked for their potash content to a certain extent.

Crude potash occurs commercially in the form of fused masses, of a stony appearance and hardness, and a caustic burning taste. Its color varies from a pale greenish-gray to reddish and dark brown. When exposed to the air, it absorbs moisture and deliquesces, and, if sufficiently long exposed, finally becomes liquid. Pearlash is of a white color, with usually a tinge of blue.

Pearlash, from its impurity, is never used as a medicine. Inasmuch as potassium carbonate is now largely made electrolytically from the chloride, the presence of potassium chlorate as an impurity has been reported in the commercial carbonate.

Potassium carbonate crystallizes with half a molecule of water and theoretically should contain, therefore, about 88 per cent. of anhydrous salt. Practically, however, it usually contains also some adherent water and the Pharmacopœia of the U. S. allows 15 per cent. of moisture and the Br. 18.5 per cent. It will absorb upwards of 28 per cent. of moisture before deliquescing.

Description and Physical Properties.—"A white, granular powder, odorless, and having a strongly alkaline taste. It is very deliquescent. One Gm. of Potassium Carbonate is soluble in 0.9 cc. of water at 25° C. One Gm. is soluble in 0.7 cc. of boiling water. It is insoluble in alcohol. When heating to 180° C., the salt loses all the water which it may have retained or absorbed. At a bright red heat it melts, and at a white heat it is volatilized.

"An aqueous solution of Potassium Carbonate (1 in 20) is strongly alkaline to litmus paper and to phenolphthalein T.S., and effervesces with acids. An aqueous solution of the salt (1 in 10) responds to the reactions for potassium.

"No residue is left on dissolving 1 Gm. of Potassium Carbonate in 20 cc. of distilled water (*insoluble impurities*). An aqueous solution of Potassium Carbonate (1 in 50), mixed with a slight excess of hydrochloric acid, meets the requirements of the test for *heavy metals.* Dry about 3 Gm. of Potassium Carbonate, accurately weighed, to constant weight, at 180° C.: the loss does not exceed 15 per cent. (*water*).

"**Assay.**—Dry Potassium Carbonate to constant weight at 180° C., weigh accurately about 3 Gm. of the dried salt in a stoppered weighing bottle, dissolve the salt in 25 cc. of distilled water, and titrate with normal sulphuric acid, methyl orange T.S. being used as indicator. Each cc. of normal sulphuric acid corresponds to 0.06911 Gm. of K_2CO_3.

"Preserve in air-tight containers." *U. S.*

"A white crystalline powder, very deliquescent. Taste alkaline and caustic. Soluble in 1 part of *water;* insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium and of carbonates. 1 gramme requires for neutralisation not less than 11.8 millilitres of *H/1 solution of sulphuric acid.* Loses not more than 18.5 per cent. of its weight when exposed to a red heat. Yields no characteristic *reactions* for copper, aluminum, calcium, magnesium, sodium, cyanides, nitrates, sulphates, sulphides, or thiosulphates, not more than the slightest *reactions* for iron, and no strongly marked *reactions* for chlorides. *Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million." *Br.*

Potassium percarbonate, $K_2C_2O_6$, was made by Constans and von Hansen by electrolyzing a saturated solution of potassium carbonate, and gradually lowering the temperature. It is a bluish amorphous powder, hygroscopic and decomposing water at ordinary temperatures, bicarbonate being formed. (*Chem. News,* 1897, 170; 1898, 65.)

It is incompatible with acids and acidulous salts, ammonium chloride and acetate, lime water, calcium chloride, magnesium sulphate, alum, tartar emetic, silver nitrate, ammoniated copper and ammoniated iron, ferrous sulphate, tincture of ferric chloride, calomel and corrosive sublimate, lead acetate and subacetate, and zinc sulphate. It is not decomposed by iron and potassium tartrate.

Uses.—Potassium carbonate is too irritant to be valuable as a gastric antacid. It was at one time largely used as a systemic alkalizer and diuretic in the treatment of *rheumatic* and *gouty* conditions, but has been largely replaced by the less irritating citrate and acetate. Its greatest importance is for pharmaceutical and chemical manipulations.

In large quantities it acts as a corrosive poison, and is capable of producing death in a few hours. The symptoms and treatment are similar to those described under *Potassii Hydroxidum.*

Dose, five to twenty grains (0.3–1.3 Gm.).

Off. Prep.—Mistura Carminativa, *N. F.;* Unguentum Sulphuris Alkalinum, *N. F.;* Mistura Rhei Alkalina, *N. F.;* Syrupus Rhei, *U. S.;* Sal Vichyanum Factitium, *N. F.;* Tinctura Rhei Aquosa, *N. F.*

POTASSII CHLORAS. U. S., Br.

POTASSIUM CHLORATE Pot. Chloras

"Potassium Chlorate contains not less than 99 per cent. of $KClO_3$. *Great caution should be observed in handling it,* as dangerous explosions are liable to occur when it is heated or subjected to concussion or to trituration with organic substances such as cork, tannic acid, dust, sucrose, etc., or with charcoal, sulphur, sulphides, hypophosphites, or other easily oxidizable substances." *U. S.* "Potassium Chlorate, $KClO_3$, may be obtained by passing chlorine into water holding lime or magnesia in suspension, treating the clarified liquid with potassium chloride, and subsequently crystallising out the potassium chloride." *Br.*

Chlorate of Potash; Kali Oxymuriaticum, Kali Muriaticum Oxygenatum, Chloras Potassicus, s. Kalicus; Hyperoxymuriate of Potassa; Chlorate de Potassium, *Fr.;* Kalium Chloricum, *P. G.;* Kaliumchlorat, Chlorsaures Kali, *G.;* Clorato di potassio, *It.;* Clorato Potasico, Sal de Berthollet, *Sp.*

Preparation.—Neither the U. S. nor the Br. at present gives a process for the manufacture of potassium chlorate. It may be prepared on a small scale by passing chlorine into a hot concentrated solution of potassium hydroxide. It was formerly manufactured by the interaction between calcium chlorate and potassium chloride. In this process chlorine is passed into a solution of milk of lime having a specific gravity of 1.04 until the liquid is nearly saturated. The clear solution is evaporated until it has a specific gravity of 1.18, and then potassium chloride added, and the mixture boiled down until a specific gravity of 1.28 is attained. On cooling, crystals of potassium chlorate separate out. The reactions here are

$$6Ca(OH)_2 + 6Cl_2 = 5CaCl_2 + Ca(ClO_3)_2 + 6H_2O$$

$$Ca(ClO_3)_2 + 2KCl = CaCl_2 + 2KClO_3$$

Pechiney's improvement on this process is to separate the greater part of the calcium *chloride* from the calcium *chlorate* before adding the potassium chloride. For details, see *N. R.,* Feb., 1882.

The potassium chlorate of commerce has also been prepared by the reaction of solutions of potassium chloride and calcium hypochlorite, with the assistance of heat.

Potassium chlorate is now principally made commercially by the electrolysis of alkaline solutions at Niagara Falls, and elsewhere, in this country and in various places in Europe. The potassium chloride, on electrolysis in a lead-lined cell without diaphragm, yields first potassium hypochlorite, but as the temperature of the bath is kept above 50° C., it is changed to a mixture of chlorate and chloride, from which, on cooling, the former crystallizes out.

The anodes consist of an alloy of iridium 10 per cent., and platinum 90 per cent. in plates 1 mm. thick. The cathodes are formed of an iron-nickel alloy coated with asbestos. The cells are insulated by immersion in baths of oil. Working with pure potassium chloride the chlorate is easily obtained of 99 per cent. purity by this process.

Description and Physical Properties.—"Colorless, odorless, lustrous, monoclinic prisms or plates, or a white, granular powder. It is stable in the air. One Gm. of Potassium Chlorate is soluble in 16.5 cc. of water at 25° C. One Gm. is soluble in 1.8 cc. of boiling water. It is almost insoluble in alcohol but is soluble in glycerin.

"When heated to about 360° C., the salt gives off oxygen and finally leaves a residue of potassium chloride, which is readily soluble in water and which responds to the reactions for potassium, and for chlorides. Add about 0.2 Gm. of Potassium Chlorate to 1 cc. of hydrochloric acid: the liquid assumes a deep greenish-yellow color, and chlorine and oxides of chlorine are evolved.

"An aqueous solution of the salt (1 in 20) is neutral to litmus paper. An aqueous solution of the salt meets the requirements of the test for *heavy metals.*

"Preserve in well-closed containers." *U. S.*

"Colorless monoclinic crystals. Taste cool, saline. Soluble in 16 parts of *water*. Moistened with *hydrochloric acid* it evolves a yellow gas with an odor of chlorine. Yields no characteristic *reactions* for iron, calcium, magnesium, sodium, ammonium, or nitrates, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Potassium chlorate easily yields its excess of oxygen and when triturated with strongly reducing substances like sulphur, phosphorus, sugar, charcoal, etc., is liable to cause violent explosions. In solution it acts as an oxidizing agent only when heated. By sulphuric acid it is decomposed, liberating an explosive gas, *chlorine dioxide.* When decomposed with hydrochloric acid, there is formed a substance formerly called *euchlorine,* which, however, appears to be a mixture of chlorine and chlorine dioxide.

It is the chlorine dioxide that gives the bright-yellow color to a solution of potassium chlorate in concentrated hydrochloric acid. Chlorine dioxide decomposes in the presence of water to form a mixture of chlorous and chloric acids.

Assay.—"Dissolve about 0.1 Gm. of Potassium Chlorate, accurately weighed, in 10 cc. of distilled water. Transfer to a 250 cc. flask, and add 50 cc. of acid ferrous sulphate T.S. to the solution. Prepare a valve stopper by taking a piece of rubber tubing of convenient diameter and about 5 cm. in length, placing a piece of glass rod in one end and slipping the other end over a glass tube which passes through a perforated stopper of a size convenient to fit the flask used. Cut a longitudinal slit about 15 mm. long in one side of the rubber tube about half way up. Insert this stopper in the flask and boil the mixture for ten minutes. Cool the mixture, add 10 cc. of manganous sulphate T.S., and titrate the excess of ferrous sulphate with tenth-normal potassium permanganate. Conduct a blank experiment with another portion of 50 cc. of acid ferrous sulphate T.S. and subtract the result of the former titration from that of the latter. Each cc. of tenth-normal potassium permanganate corresponds to 0.002043 Gm. of $KClO_3$." *U. S.*

Frank X. Moerk (*J. A. P. A.*, 1913, p. 155) reviews various methods for the determination of chlorates and recommends the following: Place 0.1 Gm. of the salt in a glass-stoppered bottle and add 10 cc. of distilled water and 15 cc. 10 per cent. potassium bromide solution, and 20 cc. HCl (sp. gr. 1.20) and allow to stand 40 minutes tightly stoppered. Cool by immersing in water, add 20 cc. potassium iodide solution (10 per cent.), carefully rinsing the stopper and neck of the bottle, and titrate with tenth-normal sodium thiosulphate V.S. A blank test should be made with the reagents to prove that no iodine is liberated by them alone.

Potassium chlorate is *incompatible* in the dry state with all easily oxidizable substances, such as sulphur, cyanides and most of the organic compounds. With ammonium chloride it is said to also form an explosive compound. In solution it is decomposed by the mineral acids, ammonium chloride, etc.

Uses.—In the belief that potassium chlorate yielded oxygen in the system, it was formerly used in the treatment of various infectious diseases as well as a local disinfectant, but as decomposition of the salt takes place only in highly acid media this liberation in the body cannot occur. As a local antiseptic it is extremely feeble. According to the experiments of Sternberg a 4 per cent. solution—which is almost saturation at ordinary temperatures—is without germicidal power. It is used at present solely as a local remedy in *stomatitis, pharyngitis, vaginitis,* and other forms of *catarrh* as well as in *hemorrhoids* and *indolent ulcers.* Such slight beneficial influence as it may exert in these conditions is due to its stimulant saline properties combined with a mild astringent effect. On the theory that it would be eliminated through the salivary glands and keep the mouth constantly bathed with a solution, it has been recommended to administer the drug internally in mercurial *ptyalism* and other inflammatory conditions of the buccal cavity, but as the larger portion of the drug is excreted through the kidneys this use does not commend itself to the thinking physician.

In overdose potassium chlorate is an active poison, four drachms of it having caused death in the adult. The symptoms produced are violent vomiting, profuse diarrhea, excessive dyspnea, great failure of the heart's action, and marked cyanosis. The urine is lessened in quantity, albuminous, often of a dark reddish-brown or blackish color, and containing tube casts and the débris of blood corpuscles. In some cases there have been marked nervous symptoms, such as cramps, delirium, coma, etc. The lesions found after death are those of gastro-enteritis and acute nephritis, with alteration in the character of the blood due to the development in it of methemoglobin. On account of their irritant action on the kidneys, large doses are especially dangerous in *diphtheria.*

Dose, from five to fifteen grains (0.32–1.0 Gm.).

Off. Prep.—Trochiscus Potassii Chloratis, *Br.;* Gargarisma Guaiaci Compositum, *N. F.*

POTASSII CHLORIDUM. N. F.

POTASSIUM CHLORIDE Pot. Chloride.

"Potassium Chloride contains, when dried to constant weight at 100° C., not less than 99 per cent. of KCl (74.56)." *N. F.*

Kalium chloridum (chloratum); Sal digestivum Sylvii; Sel digestif, *Fr.*

This salt is found native in the free condition forming the basis of *sylvite* and in combination with magnesium chloride as *carnallite.*

Description and Physical Properties.—"Potassium Chloride occurs in colorless, elongated, prismatic, or cubical crystals, or as a white, granular powder; permanent in dry air. Odorless; taste saline. One Gm. dissolves in 2.8 cc. of water at 25° C., slightly more soluble in boiling water; insoluble in alcohol.

"An aqueous solution of the salt (1 in 10) is clear, and neutral to litmus. When heated, the dry salt decrepitates. To a non-luminous flame it imparts a violet color unmasked by yellow. An aqueous solution of the salt yields with silver nitrate T.S. a white, curdy precipitate, insoluble in nitric acid but soluble in an excess of ammonia water.

"Boil 5 cc. of an aqueous solution of the salt (1 in 10) in a test tube, then add an equal volume of barium hydroxide T.S. and stopper the tube; the solution is not rendered cloudy within fifteen minutes (*calcium or magnesium*). Dissolve 2 Gm. of the salt in 6 cc. of distilled water, add 1 cc. of chloroform, and then add, drop by drop, with constant agitation, 5 cc. of half-strength chlorine water; the chloroform does not acquire a transient violet or permanent orange color (*iodide or bromide*). An aqueous solution of the salt meets the requirements of the Test for arsenic. An aqueous solution of the salt does not respond to the Test for heavy metals.

"**Assay.**—Dissolve about 0.25 Gm. of Potassium Chloride, previously dried to constant weight at 100° C. and accurately weighed, in 25 cc. of distilled water in a 200 cc. measuring flask. Add 50 cc. of tenth-normal silver nitrate to the solution, then 5 cc. of nitric acid, afterward sufficient distilled water to make 200 cc. and mix thoroughly. Filter the mixture through a dry filter, reject the first 20 cc. of the filtrate, collect the following 100 cc. of filtrate, add to this 2 cc. of ferric ammonium sulphate T.S. and titrate with tenth-normal potassium thiocyanate, until the supernatant liquid remains reddish after it is well shaken. Each cc. of tenth-normal silver nitrate corresponds to 0.007456 Gm. of KCl. Each Gm. of Potassium Chloride, dried to constant weight, corresponds to not less than 132.8 cc. of tenth-normal silver nitrate." *N. F.*

Uses.—Potassium chloride is recognized by the N. F. because of its presence in certain mineral waters, imitations of which are official. There is no reason to believe that the small amount of potassium chloride present in these compound salts modifies materially their action.

Potassium chloride is recognized among the U. S. P. reagents because it is an ingredient in the Locke-Ringer solution. (See Part III; also under *Liquor Sodii Chloridi Physiologicus.*)

Dose, ten to twenty grains (0.6–1.2 Gm.).

Off. Prep.—Liquor Hydrastinæ Compositus, *N. F.;* Sal Kissengense Factitium, *N. F.;* Sal Kissengense Factitium Effervescens, *N. F.*

POTASSII CITRAS. U. S., Br.

POTASSIUM CITRATE Pot. Cit.

"Potassium Citrate, when dried to constant weight over sulphuric acid, contains not less than 99 per cent. of $K_3C_6H_5O_7.H_2O$." *U. S.*

"Potassium Citrate may be obtained by the interaction of citric acid and potassium carbonate. It contains not less than 99 per cent. of pure potassium citrate, $K_3C_6H_5O_7,H_2O$." *Br.*

Kalium Citricum, Citras Potassicus, s. Kalicus; Citrate of Potash; Salt of Riverius; Citrate de Potasse, *Fr.;* Kaliumcitrat, Citronsaures Kali, *G.*

No process for this salt is at present official. In the U. S. formula of 1870, it was made by the reaction between citric acid and potassium bicarbonate, the latter ingredient being preferred to the carbonate on account of its greater purity. The British 1885 process differed only in the use of the carbonate instead of the bicarbonate, and in providing more carefully for an exact neutralization.

Description and Physical Properties.—"Transparent, prismatic crystals, or a white, granular powder. It is odorless, and has a cooling, saline taste, and is deliquescent when exposed to moist air. One Gm. of Potassium Citrate is soluble in 0.6 cc. of water at 25° C. It is almost insoluble in alcohol and is freely soluble in glycerin.

"When heated above 100° C., the salt begins to lose water and at about 200° C., the water of crystallization is completely volatilized. At a higher temperature the salt begins to decompose, turns brown, and upon further heating carbonizes and emits inflammable gases which have a very pungent, acrid odor. After heating to redness, there remains a residue of carbon and potassium carbonate which has an alkaline reaction and effervesces with acids. An aqueous solution of Potassium Citrate (1 in 10) responds to the reactions for potassium, and for citrates.

"An aqueous solution of Potassium Citrate (1 in 20) is alkaline to litmus paper, but a 10 cc. portion of the solution is not reddened by one drop of phenolphthalein T.S. A solution of 1 Gm. of Potassium Citrate in 1 cc. of distilled water does not deposit a crystalline precipitate on the addition of 1 cc. of acetic acid (*tartrate*). An aqueous solution of the salt meets the requirements of the test for *heavy metals.* An aqueous solution of the salt meets the requirements of the test for *arsenic.*

"**Assay.**—Dry the salt to constant weight over sulphuric acid and proceed as directed under the assay for alkali salts or organic acids. Each cc. of half-normal sulphuric acid corresponds to 0.05407 Gm. of $K_3C_6H_5O_7.H_2O$.

"Preserve in well-closed containers." *U. S.*

The British Pharmacopœia gives the following tests of its character:

"A white, granular, or crystalline powder. Taste saline, feebly acid. Soluble in 1 part of *water.* Yields the *reactions* characteristic of potassium and of citrates. 1 gramme, heated to redness till gases cease to be evolved, leaves an alkaline residue which, when treated with *water,* filtered, and well washed, yields a clear solution requiring for neutralisation not less than 18.3 millilitres of *N/2 solution of sulphuric acid.*

Yields no characteristic *reactions* for iron, calcium, magnesium, sodium, carbonates, or tartrates, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million." *Br.*

Uses.—Potassium citrate is a type of those drugs which increase various secretions by what is known as their salt action. This group of drugs, which includes most of the non-toxic crystalloids, act by increasing the saline concentration of the blood, disturbing the osmotic balance between this fluid and the surrounding tissues thereby attracting water into the vessels and tending towards the production of a hydremic state. This tendency towards an increase in the volume of the blood is counteracted by greater activity on the part of the glandular structures. Not only is the secretion of urine greater, but there is also an increase in the bronchial, sweat, and other glands. The therapeutic uses of potassium citrate, however, are not due alone to this action. The citrates being oxidized in the body into carbonates, the salt tends to correct any systemic hyperacidity; and the potassium apparently increases the completeness of bodily combustion. This combination of actions makes the drug of peculiar value in those forms of metabolic disturbances accompanied with the over-production of uric acid, such as *acute* or *chronic rheumatism* and *gout.* It is, however, a valuable drug in a large variety of other conditions. Probably its most frequent use to-day is as an expectorant in the early stages of *acute bronchitis* or *tracheitis;* by increasing the secretion of the mucous glands it indirectly exercises a sedative action on the inflammatory mucous membrane. It is valuable as a sudorific in the early stage of the milder infections; it is sometimes of service as a diuretic although caution must be observed in its use when there is serious disease of the kidneys. In cases of *cystitis* when the urine is excessively acid it is especially valuable. It may be most pleasantly exhibited in conjunction with lemon juice which in no way lessens the alkalizing effect.

Dose, of the citrate, from fifteen to forty grains (1–2.6 Gm.). When a decided effect upon the system is desirable, as much as an ounce (31 Gm.) of it may be given in twenty-four hours.

Off. Prep.—Potassii Citras Effervescens, *U. S.*

POTASSII CITRAS EFFERVESCENS. U. S.

EFFERVESCENT POTASSIUM CITRATE Pot. Cit. Eff.

"Potassium Citrate, 200 Gm.; Sodium Bicarbonate, dried and powdered, 477 Gm.; Tartaric Acid, dried and powdered, 252 Gm.; Citric Acid, uneffloresced crystals, 162 Gm.; to make about 1000 Gm. Dry the potassium citrate on a water bath until it ceases to lose weight, and powder the dried salt. Mix intimately with the powdered citric acid and tartaric acid, and thoroughly incorporate the sodium bicarbonate. Place the mixed powders on a plate of glass or in a suitable dish in an oven heated between 93° and 104° C. Manipulate the mixture carefully with a wooden spatula until it becomes moist, rub it through a No. 6 tinned-iron sieve, and dry the granules at a temperature not exceeding 54° C. Immediately transfer the salt to suitable containers and seal them tightly. Care must be taken to prevent the product from coming in contact with air containing moisture." *U. S.*

This official effervescent salt affords an agreeable mode of administering potassium citrate. It is more prone to exert a laxative effect because of the sodium tartrate formed.

Dose, from one to two drachms (3.9–7.7 Gm.).

POTASSII ET SODII TARTRAS. U. S. (Br.)

POTASSIUM AND SODIUM TARTRATE Pot. et Sod. Tart. [Rochelle Salt]

"Potassium and Sodium Tartrate contains not less than 73.72 per cent. and not more than 77.39 per cent. of $KNaC_4H_4O_6$, corresponding to not less than 99 per cent. of the crystallized salt [$KNaC_4H_4O_6.4H_2O$]." *U. S.* "Sodium Potassium Tartrate may be obtained by neutralising Acid Potassium Tartrate with Sodium Carbonate. It contains not less than 98 per cent. of pure sodium potassium tartrate, $NaKC_4H_4O_6,4H_2O$." *Br.*

Sodii et Potassii Tartras, *Br.;* Sodium Potassium Tartrate; Tartrate of Potassium and Sodium; Soda Tartarata; Sodæ et Potassæ Tartras, *Br.* 1864, *U. S.* 1850; Sodæ Potassiotartras, Natro-kali Tartaricum; Tartarated Soda; Sal Polychrestum Seignetti, Tartras Potassico sodicus; Kalium Natrio Tartaricum, *Fr. Cod.;* Tartrate droit de Sodium et de Potassium, Sel de la Rochelle, Sel de Seignette, Soude Tartarisée, *Fr.;* Tartarus Natronatus, *P. G.;* Seignettesalz, Kaliumnatriumtartrat, *G.;* Tartrate sodico-potassico, *It.;* Tartrato sodico-potasico, *Sp.*

This salt cannot be made profitably on the small scale (for U. S. process, 1870, see the *U. S. Dispensatory,* 19th edition, page 1000); it is a double salt, consisting of a molecule of tartaric acid, $C_4H_4O_6.H_2$, in which one of the basic hydrogen atoms is replaced by potassium and the other by sodium; or it may be considered to be formed by the replacement of the hydrogen in the potassium bitartrate by sodium.

Description and Physical Properties.—"Colorless, transparent, rhombic prisms, or a white powder. It is odorless, and has a cooling, saline taste. The crystals effloresce slightly in dry air. One Gm. of Potassium and Sodium Tartrate is soluble in 0.9 cc. of water at 25° C. It is practically insoluble in alcohol.

"When heated to about 74° C., the salt fuses to a colorless liquid, which at a higher temperature froths, becomes brown, and is gradually carbonized, emitting inflammable vapors which have the odor of burning sugar. Finally a black residue is left, consisting of a mixture of potassium and sodium carbonates with carbon. To a non-luminous flame this residue imparts an intensely yellow color. An aqueous solution of the salt (1 in 20) yields a white, crystalline precipitate with an equal volume of acetic acid within fifteen minutes. An aqueous solution of the salt (1 in 10) responds to the reactions for tartrates.

"An aqueous solution of Potassium and Sodium Tartrate (1 in 20) is alkaline to litmus paper, but a 10 cc. portion of the solution is not reddened by a drop of phenolphthalein T.S. An aqueous solution of Potassium and Sodium Tartrate meets the requirements of the test for *heavy metals.* A 5 cc. portion of an aqueous solution of the salt (1 in 10) heated with sodium hydroxide T.S. does not evolve ammonia. Dissolve 10 Gm. of Potassium and Sodium Tartrate in 20 cc. of distilled water, add 2 cc. of sulphurous acid, and boil the mixture until the odor of sulphur dioxide is barely perceptible. Cool the solution, mix it with 1 cc. of sodium cyanide T.S., and follow this immediately with stronger ammonia T.S. until the solution has a slight odor of ammonia. When cold, transfer the solution to a 50 cc. graduated glass-stoppered cylinder, dilute it with sufficient distilled water to measure 50 cc., and add 3 drops of sodium sulphide T.S. After thoroughly mixing, the color produced in the solution, if any, when viewed downward against a white surface, is not greater than the color of a control solution prepared as follows: Dissolve 2 Gm. of reagent ammonium chloride in 20 cc. of distilled water, add 4 cc. of a solution containing 0.08 Gm. of lead nitrate in 1000 cc. of distilled water, and then 1 cc. of diluted hydrochloric acid. Treat this solution with the same quantities of sulphurous acid, sodium cyanide T.S. and stronger ammonia T.S., as used above, transfer it to another 50 cc. glass-stoppered cylinder, then dilute it with sufficient distilled water to make 50 cc., and add 3 drops of sodium sulphide T.S. Before adding the sodium sulphide T.S. the liquid must possess a distinct odor of ammonia, and the two cylinders used must be matched, be of practically colorless glass, and have the same internal diameter (*lead*).

"**Assay.**—Proceed as directed under the assay for alkali salts of organic acids. Each cc. of half-normal sulphuric acid corresponds to 0.05254 Gm. of $KNaC_4H_4O_6$.

"Preserve in well-closed containers." *U. S.*

"Trimetric prisms with hemihedral facets. Taste saline, cooling. Soluble in 1.5 parts of *water;* aqueous solution neutral to *litmus.* Yields the reactions characteristic of potassium, of sodium, and of tartrates. 1 gramme, heated to redness till gases cease to be evolved, leaves an alkaline residue which, when treated with *water,* filtered, and well washed, yields a clear solution requiring for neutralization not less than 13.9 millilitres of *N/2 solution of sulphuric acid.* Yields no characteristic *reactions* for copper, iron, calcium, ammonium, chlorides, or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 2 parts per million." *Br.*

When the salt is exposed to a very strong heat, it becomes blackened, and gives out inflammable gases with the odor of burnt sugar, the tartaric acid being destroyed, and a mixture of potassium and sodium carbonates left. It is incompatible with most acids, and with nearly all acid salts except potassium bitartrate. It is also decomposed by lead acetate and subacetate, silver nitrate, and by the soluble calcium and barium salts unless the solution of the tartrate be considerably diluted.

The way in which the acids act in decomposing potassium and sodium tartrate is by combining with the sodium, and throwing down potassium bitartrate as a crystalline precipitate. This double salt was discovered by Seignette, an apothecary of Rochelle, and hence is frequently called *Seignette's salt* or *Rochelle salt.*

Uses.—This salt is a mild, saline purgative, well suited to delicate and irritable stomachs, being among the mildest and least unpalatable of the neutral salts. It is an ingredient in the effervescing aperient called Seidlitz powders. (See *Pulvis Effervescens Compositus.*)

Potassium and magnesium tartrate, formed by saturating cream of tartar with magnesium carbonate, has been proposed by Maillier for use as a safe, pleasant purgative.

Dose, as a purge, from half an ounce to an ounce (15.5–31 Gm.).

Off. Prep.—Pulvis Effervescens Compositus, *U. S. (Br.).*

POTASSII HYDROXIDUM. U. S. (Br.)

POTASSIUM HYDROXIDE Pot. Hydrox.
[Caustic Potash]

"Potassium Hydroxide contains not less than 85 per cent. of KOH. *Great caution is necessary in handling it, as it rapidly destroys organic tissues." U. S.* "Potassium Hydroxide may be obtained by the interaction of potassium carbonate and calcium hydroxide. It contains not less than 85 per cent. of pure potassium hydroxide, KOH." *Br.*

Potassa Caustica, *Br.;* Kali Purum; Potassa, Hydrate of Potassa, Potassæ (Potassii) Hydras, Kali Hydricum Fusum, Lapis Causticus Chirurgorum Hydras Kalicus; Kalium Hydroxydatum Purum, *Fr. Cod.;* Hydroxide de Potassium, Potasse caustique, Potassee Fondue, Pierre à cautère, *Fr.;* Kali Causticum, *P. G.;* Kaliumhydroxyd, Kalium-Hydrat, Kaustisches Kali, Ætzkali, *G.;* Potassa caustica, *It.;* Hidrato potasico, *Sp.*

Formerly both of the Pharmacopœias recognized processes for the manufacture of potassium hydroxide which were based upon decomposition of a solution of potassium carbonate by means of calcium hydroxide and the evaporation of the resultant solution of potassium hydroxide. The evaporation must be performed in metallic vessels because of the injurious effect of the alkali upon glass. The method in principle is still employed to some extent on a commercial scale. Potassium hydroxide is now prepared at Niagara Falls, N. Y., by the electrolysis of strong potassium chloride solution. The metal at the cathode acts with water to form potassium hydroxide and free hydrogen, while chlorine is liberated at the anode. The ordinary white flint glass bottles are not suitable for preserving this solution, the bottles in which it is preserved should be of green glass or some other form of hard glass and the stoppers should be of rubber or of glass coated with petrolatum.

Description and Physical Properties.—"Dry, white, or nearly white, fused masses, or sticks, hard and brittle, showing a crystalline fracture. When exposed to the air, it rapidly absorbs carbon dioxide and moisture, and deliquesces. One Gm. of Potassium Hydroxide is soluble in 0.9 cc. of water, in about 3 cc. of alcohol, and in 2.5 cc. of glycerin, at 25° C. One Gm. is soluble in 0.6 cc. of boiling water. It is very soluble in boiling alcohol.

"An aqueous solution of Potassium Hydroxide, even when greatly diluted, is strongly alkaline to litmus paper. An aqueous solution of Potassium Hydroxide (1 in 25) responds to the reactions for potassium.

"An aqueous solution of Potassium Hydroxide (1 in 20) is clear and colorless (*organic matter or insoluble impurities*). An aqueous solution of Potassium Hydroxide (1 in 50) slightly acidulated with hydrochloric acid meets the requirements of the test for *heavy metals*.

"**Assay.**—Place about 10 Gm. of Potassium Hydroxide in a glass-stoppered weighing bottle, weigh accurately, transfer to a 500 cc. graduated flask, and dissolve it in 250 cc. of recently boiled distilled water. Add 30 cc. of barium chloride T.S., fill the flask to the mark with recently boiled distilled water, and thoroughly agitate the liquid. Filter the liquid in the flask through a dry filter into a dry flask, rejecting the first 20 cc., and titrate 200 cc. of the clear filtrate with normal hydrochloric acid, using phenolphthalein T.S. as indicator. Each cc. of normal hydrochloric acid corresponds to 0.05611 Gm. of KOH.

"Preserve in air-tight containers. If bottles are used, they must be made of hard glass, and cork stoppers should be paraffined." *U. S.*

"In hard white pencils or cakes, very deliquescent, very alkaline and corrosive. Soluble in 0.5 part of *water*, and in 3 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium. 1 gramme dissolved in *water* or in *alcohol* (90 per cent.) leaves only a slight sediment; the solution requires for neutralisation not less than 15.1 millilitres of *N/1 solution of sulphuric acid*. Yields no characteristic *reactions* for lead, copper, or arsenic." *Br.*

The *white stick caustic potassa* as found in commerce often contains from 15 to 28 per cent. of water. On account of its deliquescent property, and its strong attraction for carbon dioxide, potassium hydroxide requires to be kept in very closely stoppered bottles.

Official potassium hydroxide may be converted into a product of a much higher degree of purity by digestion in alcohol—which takes up only the hydroxide—evaporating the solution to dryness, and fusing the dry mass obtained. *Potassium hydroxide*, when thus procured, is called *potash by alcohol*. It is generally in flat white pieces, which are dry, hard and brittle. Its other properties are similar to those of the official hydroxide above described.

Uses.—Probably because of its powerful effect in dissolving the bodily tissues potassium hydroxide is a very potent escharotic. It is the old *causticum commune acerrimum* or *strongest common caustic*. Its action is not only very thorough, but it penetrates more deeply than either silver nitrate or nitric acid. It is also powerfully germicidal; although Sternberg found that it required a ten per cent. solution to destroy pus cocci in two hours, most authorities agree that one per cent. is sufficient to kill all vegetating bacteria. Because of difficulty of controlling its action it is not commonly employed for the destruction of benign growths as *warts*, but in *poisoned bites*, especially by *rabid animals*, the thoroughness of its action is an advantage.

In the application of potassium hydroxide as a caustic the surrounding skin should be protected by petrolatum. A stick of the caustic previously moistened is rubbed over the area to be cauterized. After the action is considered to have proceeded far enough, the part should be washed with diluted acetic acid and then cleansed with distilled water. In forming from it solutions of potassium hydroxide of definite strength, whether for medicinal or for pharmaceutical use, an allowance should be made for the percentage of water it always contains. (See *Liquor Potassii Hydroxidi.*)

Poisoning.—Because of their powerful caustic action, the hydroxides are dangerous poisons. Because of the frequent use of sodium hydroxide in the kitchen accidental poisoning, especially in children, is not uncommon. The symptoms are violent pains in the throat and epigastrium, vomiting—the matters rejected at first being the contents of the stomach, later of a brown color from the presence of decomposed blood—followed by collapse. The mucous membranes of the mouth have a slippery feel and are swollen and often brown in color. In those cases which do not immediately prove fatal there is caused so much destruction of the membranes of the esophagus that stricture develops and the patient is unable to swallow, and death from starvation may occur after some time has elapsed.

The treatment consists in the prompt neutralization of the alkali. For this probably the best agent is acetic acid which, in the form of vinegar, is usually at hand; one or two tablespoonfuls diluted with water may be given at a dose. Olive oil, or other bland fixed oil, is also very useful, forming with the hydroxide a comparatively non-irritating soap and also acting as a demulcent to the inflamed tissue. In the absence of vinegar, other acids, as lemon or orange-juice, or even the mineral acids—if well diluted—may be employed. Subsequent treatment involves the combating of the collapse and the relief of such symptoms as arise.

Off. Prep.—Liquor Potassii Hydroxidi, *U. S. (Br.)*; Liquor Picis Alkalinus, *N. F.*; Potassa cum Calce, *N. F.*

POTASSII HYPOPHOSPHIS. N. F.

POTASSIUM HYPOPHOSPHITE Pot. Hypophos.

"Potassium Hypophosphite contains, when dried to constant weight over sulphuric acid, not less than 98 per cent. of KPH_2O_2 (104.16). Caution should be observed in dispensing Potassium Hypophosphite, as an explosion is liable to occur if it is triturated or heated with nitrates, chlorates, or other oxidizing agents." *N. F.*

Kalium Hypophosphorosum, Hypophosphis Potassicus, s. Kalicus; Hypophosphite de Potasse, *Fr.*; Unterphosphorigsaures Kali, *G.*

This salt is prepared by mixing solutions of calcium hypophosphite and potassium carbonate. As a result of double decomposition between the two salts, calcium carbonate and *potassium hypophosphite* are formed. The calcium carbonate is removed by filtration, and the clear solution is evaporated until a pellicle forms, after which it is constantly stirred, with continuance of the heat, until the salt granulates. The heat employed in the evaporation should be kept considerably below 100° C., for fear of explosion. If the salt be required pure, it should be dissolved in the granulated state, in official alcohol, and the solution evaporated to a syrupy consistence and then set aside to crystallize. The calcium hypophosphite may be prepared by a formula given under the head of *Calcii Hypophosphis*.

Description and Physical Properties.—"Potassium Hypophosphite occurs as white, opaque, hexagonal plates, or crystalline masses, or as a granular powder; odorless, and having a pungent, saline taste; very deliquescent. One Gm. of Potassium Hypophosphite dissolves in 0.6 cc. of water and in 9 cc. of alcohol at 25° C.; also in 0.4 cc. of boiling water and in 5 cc. of boiling alcohol.

"An aqueous solution of the salt (1 in 20) is neutral or slightly alkaline to litmus and yields with sodium bitartrate T.S. a white, crystalline precipitate. When heated in a dry test tube spontaneously inflammable hydrogen phosphide is evolved which burns with a bright yellow flame. When an aqueous solution of the salt (1 in 20), acidulated with hydrochloric acid, is added drop by drop with agitation to an excess of mercuric chloride T.S., a white precipitate of mercurous chloride is formed. Upon the further addition of the solution of Potassium Hypophosphite, the precipitate becomes gray from reduction to metallic mercury.

"A solution of 1 Gm. of the salt in about 10 cc. of distilled water requires not more than 1.5 cc. of tenth-normal hydrochloric acid for neutralization, methyl orange T.S. being used as indicator. Heat 5 cc. of an aqueous solution of the salt (1 in 5) with 0.5 cc. of diluted hydrochloric acid in a test tube on a water bath for thirty minutes; no offensive odors are developed. Measure 5 cc. of an aqueous solution of Potassium Hypophosphite (1 in 25) into a beaker containing 3 cc. of nitric acid diluted with about 10 cc. of distilled water, and evaporate the mixture to dryness on a water bath; the residue meets the requirements of the Test for arsenic. Add magnesia mixture T.S. to 10 cc. of an aqueous solution of the salt (1 in 20) made alkaline with ammonia water; it is not affected within one minute (*phosphates*).

"**Assay.**—Dissolve about 1 Gm. of Potassium Hypophosphite, dried to constant weight over sulphuric acid and accurately weighed, in 10 cc. of distilled water, add 10 cc. of nitric acid and evaporate it to dryness on a water bath. Then add 5 cc. of nitric acid and again evaporate it to dryness on a water bath. Dissolve the residue in 20 cc. of distilled water, add a drop of phenolphthalein T.S. and sufficient special potassium hydroxide T.S. (free from chloride) to produce a pink color, and then dilute it to exactly 100 cc. with distilled water. Transfer 10 cc. of this solution to a 100 cc. graduate flask, add 50 cc. of tenth-normal silver nitrate and thoroughly agitate the mixture. Gradually add reagent zinc oxide, in small portions, until the liquid is neutral to litmus paper. Then add distilled water to make 100 cc., mix thoroughly, and filter through a filter paper not previously moistened, rejecting the first 25 cc. of filtrate. Collect 50 cc. of the subsequent filtrate, add 2 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate to the production of a permanent red color. Each cc. of tenth-normal silver nitrate corresponds to 0.003472 Gm. of KPH_2O_2. Each Gm. of Potassium Hypophosphite, previously dried, corresponds to not less than 282.3 cc. of tenth-normal silver nitrate.

"Preserve it in well-closed containers, in a dry place." *N. F.*

Uses.—This salt was introduced along with the other hypophosphites because of the claims made by Churchill of their curative value in *phthisis* (see *Acidum hypophosphorosum*), but has no therapeutic virtues justifying its continued recognition.

Dose, eight to twenty grains (0.5–1.2 Gm.).

Off. Prep.—Syrupus Hypophosphitum, *N. F.*; Emulsum Olei Morrhuæ cum Hypophosphitibus, *N. F.*; Liquor Hypophosphitum Compositus, *N. F.*; Syrupus Hypophosphitum Compositus, *N. F.*

POTASSII IODIDUM. U. S., Br.

POTASSIUM IODIDE Pot. Iod.

"Potassium Iodide, when dried to constant weight at 100° C., contains not less than 99 per cent. of KI." *U. S.* "Potassium Iodide may be obtained by adding a slight excess of iodine to a strong solution of potassium hydroxide, evaporating to dryness, fusing with charcoal, and purifying by crystallisation. When dried at 100° C. it contains not less than 99 per cent. of pure potassium iodide, KI." *Br.*

Iodide of Potassium; Potassii Hydriodas; Kali Hydriodicum, Ioduretum Potassicum, s. Kalicum; Joduretum Kalii, Iodure de Potassium, *Fr. Cod.;* **Kalium Jodatum,** *P. G.;* **Kaliumjodid, Jodkalium,** *G.;* Joduro di potassio, *It.;* **Yoduro potasico,** *Sp.*

No process is given in the U. S. or Br. Pharmacopœias. That of the U. S. P., 1870, did not differ essentially from the British, 1885. (See *U. S. Dispensatory,* 19th edition, page 1005.)

An aqueous solution of potassium hydroxide is treated with iodine in slight excess which causes the formation of potassium iodide and potassium iodate.

$$6KOH + 3I_2 = 5KI + KIO_3 + 3H_2O$$

By evaporating the solution to dryness the mixed salts are obtained, and, if the dry mass be exposed to a red heat, the iodate will be converted into iodide; charcoal facilitates the deoxidation of the iodate.

$$KIO_3 + 3C = KI + 3CO$$

This being accomplished by a dull red heat, the potassium iodide is dissolved out of the mass, and the solution is set aside to crystallize.

In the older processes the first step was to form ferrous iodide in solution, to decompose it by potassium carbonate, which gave rise to potassium iodide in solution, and a precipitate of ferrous carbonate. This method is analogous to that described under potassium bromide, which see. According to the method of E. Sonstadt, potassium iodide is prepared directly from the mother liquors of kelp by converting the alkaline iodides into iodates by means of chlorine or potassium permanganate, precipitating the iodic acid by a soluble barium salt, heating the precipitate with solution of potassium sulphate, evaporating the resulting potassium iodate solution to dryness, and crystallizing from its solution the potassium iodide thus obtained. (*Chem. News,* xxvi, 182.)

Large quantities are now manufactured from the cuprous iodide coming from the South American sodium nitrate works. The cuprous iodide is suspended in water acidified with hydrochloric acid, and a stream of hydrogen sulphide gas let in, whereby hydrogen iodide enters into solution. This solution is filtered, neutralized with potassium carbonate, and evaporated to crystallization.

$$CuI_2 + H_2S = CuS + 2HI$$
$$2HI + K_2CO_3 = 2KI + H_2O + CO_2$$

Description and Physical Properties.—"Cubical crystals, either transparent and colorless or more or less opaque and white, or a white, granular powder. It is stable in dry air, but slightly deliquescent in moist air. One Gm. of Potassium Iodide is soluble in 0.7 cc. of water, in 22 cc. of alcohol, and in 2 cc. of glycerin, at 25° C. One Gm. is soluble in 0.5 cc. of boiling water and in 8 cc. of boiling alcohol. An aqueous solution of the salt (1 in 20) is neutral or slightly alkaline to litmus paper. When heated, Potassium Iodide decrepitates. At a low red heat (about 684° C.) it fuses and at a bright red heat (about 720° C.) is volatilized without decomposition.

"An aqueous solution of Potassium Iodide responds to the reactions for potassium, and for iodides.

"Dissolve 1 Gm. of the salt in 10 cc. of distilled water and add 0.1 cc. of tenth-normal sulphuric acid: no color is produced by the subsequent addition of a drop phenolphthalein T.S. (*alkali*). Dissolve 0.5 Gm. of the salt in 10 cc. of distilled water, which has been previously boiled and cooled, and add two drops of diluted sulphuric acid: no distinct yellow color appears within half a minute (*iodate*), and no turbidity occurs (*thiosulphate*). Add 5 cc. of sodium hydroxide T.S. and about 0.2 Gm. of aluminum wire to a solution of 1 Gm. of Potassium Iodide in 5 cc. of distilled water contained in a test tube of about 40 cc. capacity. Insert a pledget of purified cotton in the upper portion of the test tube and place a piece of moistened red litmus paper over its mouth: on heating the tube and contents upon a water bath for fifteen minutes, no blue coloration of the paper is discernible (*nitrate or nitrite*). Acidulate slightly 10 cc. of an aqueous solution of the salt (1 in 20) with hydrochloric acid: it is not rendered turbid by the addition of 1 cc. of potassium sulphate T.S. (*barium*). A 2 Gm. portion of the salt shows no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid. Heat gently 5 cc. of an aqueous solution of the salt (1 in 10) with one drop of ferrous sulphate T.S. and 0.5 cc. of sodium hydroxide T.S.: no blue color appears after acidulating the mixture with hydrochloric acid (*cyanide*). An aqueous solution of the salt meets the requirements of the test for *heavy metals.*

"**Assay.**—Dry the salt to constant weight at 100° C. and proceed as directed under the assay for iodides. Each cc. of tenth-normal silver nitrate corresponds to 0.01660 Gm. of KI. Each Gm. of Potassium Iodide, previously dried, corresponds to not less than 59.6 cc. and not more than 61.0 cc. of tenth-normal silver nitrate.

"Preserve in well-closed containers." *U. S.*

"Colorless, generally opaque, cubic crystals. Taste saline, slightly bitter. Soluble in less than 1 part of *water,* and in 12 parts of *alcohol* (90 per cent.). Usually slightly alkaline to *litmus.* Yields the *reactions* characteristic of potassium and of iodides. Loses not more than 1 per cent. of its weight when dried at 100° C.; 0.5 gramme of this dried salt requires for complete precipitation not less than 29.8 nor more than 30.5 millilitres of *N/10 solution of silver nitrate.* Yields no characteristic *reactions* for copper, iron, aluminium, calcium, magnesium, bromates, cyanides, or nitrates, and not more than the slightest reactions for bromides, iodates, carbonates, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

R. Van Vorst has pointed out (*Ph. Ztg.*, 1914, p. 342) that the red spots seen sometimes upon crystals of potassium iodide are not always due to free iodine, as, in a case which he investigated, the salt dissolved to a colorless solution leaving an insoluble red precipitate, which upon closer investigation was found to be the cell structure of a microscopic form of mold.

Its solution is quickly decomposed by the addition of a few drops of sulphuric acid, hydriodic acid being generated, which speedily undergoes decomposition, with evolution of iodine, and, if starch be added after the lapse of a few minutes, a blue color will be produced. The starch test will not give the characteristic blue color immediately, if added simultaneously with the acid, unless the potassium iodide contains potassium iodate, which impurity causes an immediate liberation of iodine. The blue color being produced by the starch and acid, if simultaneously added, is, therefore, a sign of impurity. Hydrogen dioxide solution may be used in this test as it causes the liberation of free iodine from soluble iodides. A very delicate test for potassium iodide and other soluble iodides is that of Grange. It consists in pouring a little of the liquid to be examined into a test tube, adding a few drops of solution of starch, and passing through the mixture a few bubbles of fuming nitrous acid. The liquid immediately assumes a pale rose color, inclining to violet, if containing 1-200,000th of its weight of the iodide, and a bright blue color if 1-100,000th is present.

Years ago Payen noticed a curious effect produced by potassium iodide. In saturated solution, this salt causes in starch added to it an enlargement of its granules to twenty-five or thirty times their original volume, dissolving the interior substance of the granules, and enormously distending the exterior layer. Potassium bromide produces the same effect, but the alkaline chlorides cause neither the enlargement referred to, nor a solution of the amylaceous substance, and if the saturated solution of the iodide be diluted with three and a half volumes of water or more, it is inert in reference to starch in the cold.

It was first pointed out by Loew (*A. J. P.*, xlii, 80), and afterwards confirmed by various chemists that iodine is liberated from a solution of potassium iodide by direct sunlight; the more concentrated the solution the more energetic is the action. This effect appears to be due to the liberation of hydriodic acid, which is decomposed by light, and, it is stated, will not occur in alkaline solutions.

Melsens has noticed another very important fact in relation to the operation of potassium iodide. When this salt and potassium chlorate are mixed in solution, no change takes place at ordinary temperatures; but if a certain amount of a mineral acid be added to the solution of the mixed salts, a reaction occurs, attended with the escape of iodine, and evidences are presented of the existence of iodic acid in the solution. He ascertained by experiments on dogs that neither of these salts, if given separately and at different times, produces an evil effect, while if given together, so as to be in the system at the same time, they act as a poison, and may cause death in a few days. Melsens ascribed the result to the production of potassium iodate, which he has shown to be a poisonous salt. (*A. J. P.*, Nov., 1866, p. 521.) With certain alkaloids potassium iodide is incompatible, partly on account of the fact that it is permitted to contain a little alkaline carbonate to retard discoloration, and partly because with some alkaloids insoluble iodides are formed, and fatal results have been caused by the strychnine iodide crystallizing out of a prescription, so that the whole of it was taken at a single dose. It is customary for pharmacists to place a "shake-well" label upon the bottle containing such prescriptions in order to ensure uniform dosage of the active principle.

Potassium iodide is also *incompatible* with calomel, mercurous and mercuric salts, and metallic mercury. With nitrous ether potassium iodide reacts, yielding, among other products, ethyl iodide and a little ordinary ether. At ordinary temperatures potassium iodide is slowly decomposed, with evolution of iodine, by ammonium nitrate or boric acid, and at high temperatures, in a glass test tube, with escape of violet vapors, not only by the two substances just named, but also by ammonium sulphate, oxalate, carbonate, and chloride, sodium sulphate, phosphate, nitrate and borate, potassium and magnesium sulphates, and calcium nitrate.

Uses.—The general therapeutic properties of potassium iodide are the same as those of other iodides. (See *Iodum.*) It is useful especially in *syphilis, chronic fibrinous inflammations,* and certain *metallic poisons.* With corrosive sublimate it forms a soluble potassio-mercuric iodide which is the basis of the so-called "mixed treatment" for *syphilis.* When it is administered in large repeated doses it produces evidences of systemic affection, known as *iodism.* The most usual indication of its constitutional action is a pain over the brow, with coryza; in some cases a mild ptyalism, with fetor of the breath and slight swelling of the gums, is produced. In a number of cases it causes an eruption, sometimes simply of macula, but usually of acne and occasionally bullous or hemorrhagic. In unusual conditions of the system these skin affections may become very severe and ulcerations result. Knowles (*J. A. M. A.*, 1910, lv, p. 100) gives an extensive bibliography of the literature of this subject.

The dose of potassium iodide varies enormously, many persons will show symptoms of iodism from twenty grains (1.3 Gm.) a day, but other cases as much as one or two drachms (3.9–7.7 Gm.) have been given three times a day without toxic symptoms. Many clinicians believe that syphilitics are abnormally tolerant of the drug.

Potassium iodide is eliminated through the urine unchanged and may be detected by acidulating with nitric acid which causes the liberation of the free iodine, and by testing with starch.

Potassium iodide is employed as an external application in the form of ointment, either alone or mixed with iodine. (See *Unguentum Potassii Iodidi* and *Unguentum Iodi.*)

Dose, five to twenty grains (0.32–1.3 Gm.); in special cases much larger doses may be exhibited.

Off. Prep.—Linimentum Potassii Iodidi cum Sapone, *Br.;* Liquor Iodi Compositus, *U. S. (Br.);* Tinctura Iodi, *U. S., Br.;* Unguentum Iodi, *Br., N. F.;* Unguentum Potassii Iodidi, *U. S., Br.;* Liquor Hydrargyri et Potassii Iodidi, *N. F.;* Tinctura Iodi Fortior, *N. F.;* Tinctura Iodidorum, *N. F.;* Ampullæ Iodi, *N. F.;* Elixir Sodii Salicylatis Compositum, *N. F.;* Elixir Corydalis Compositum, *N. F.*

POTASSII NITRAS. U. S., Br.

POTASSIUM NITRATE Pot. Nit. [Saltpeter]

"Potassium Nitrate, when dried to constant weight at 100° C., contains not less than 99 per cent of KNO_3." *U. S.* "Potassium Nitrate, KNO_3, may be obtained by the interaction of sodium nitrate and potassium chloride." *Br.*

Potassæ Nitras; Nitrium Depuratum, Sal Petræ, s. Nitri, Nitras Potassicus, s. Kalicus; Nitrate of Potash, Nitre; Nitrate de Potasse, Azotate de Potasse, Saltpêtre, *Fr.;* Kalium Nitricum, *P. G.;* Kalium-nitrat, Saltpetersaures Kali, Kalisaltpeter, *G.;* Nitrato di potassio, Nitro, *It.;* Nitrato potasico, *Sp.*

Potassium nitrate, or *niter,* is both a natural and an artificial product. It occurs in many countries, existing in the soil, on which it forms a saline efflorescence, in the fissures of calcareous rocks, and in caves. It has been found in different parts of Europe, in South Africa, in Egypt, and in Chili, Peru and Bolivia, but the country in which it has been most largely produced is India, in the districts of Bengal and Bombay, and in the island of Ceylon. In the United States it has been found in caverns situated in limestone rock, called saltpeter caves, where it is associated with calcium nitrate. Considerable deposits also occur in San Bernadino County in California, but have not been developed as yet. At present it is chiefly obtained from deposits in India, or by acting on sodium nitrate with potassium chloride, $NaNO_3 + KCl = KNO_3 + NaCl$.

Potassium nitrate exists also in the vegetable kingdom, having been found in tobacco, borage, bugloss, sunflower, etc. The artificial sources are certain mixtures of animal and vegetable substances with wood ashes and calcareous matter, called niter-beds.

In India the saline earth, which sometimes contains over 25 per cent. of KNO_3 and usually above 3 per cent. is lixiviated in large mud filters lined with stiff clay, and furnished with false bottoms of bamboo, covered with grass mats, on which wood ashes are laid. The filters being then filled with the saline earth, water is added, and the solution filters through the wood ashes, with the effect of converting the calcium nitrate present into potassium nitrate. The solution obtained is evaporated in earthen pots, filtered, and set aside to crystallize. The impure potassium nitrate thus obtained contains from 45 to 70 per cent. of the pure salt. It is redissolved and crystallized, and thrown into commerce under the name of crude saltpeter. Besides the niter obtained in India by the filtration of the soil deposited during the overflow of the Ganges, much of the crude salt is procured, in the northwestern provinces of Hindostan, from the saline incrustations formed in and around the mud walls surrounding the dwellings of the natives. The scrapings from these sources are lixiviated, and the impure solution allowed to evaporate in shallow pans exposed to the sun. The impure niter extracted from the earthy matters crystallizes out, while from 1 to 9 per cent. of sodium chloride remains in the mother liquor, and is recovered by evaporation. The mother liquors from these crude extraction processes are used for lixiviating fresh portions of soil.

Within recent years potassium nitrate has been most largely manufactured from the native potassium chloride of Stassfurt and the native sodium nitrate of Chili, two cheap and abundant crude materials, which by their reaction yield potassium nitrate. (See reaction on previous page.) This so-called "conversion saltpeter" can be produced 99.9 per cent. pure nitrate.

Artificial niter beds are not as frequently employed as a source of this salt as formerly. They are formed of animal and vegetable remains, together with ashes and calcareous earth, which are mixed up with a portion of loose soil and placed under sheds, to shelter the mixture from the rain, while the sides are left open, to admit the free access of air. The mixture is disposed in little heaps, which are frequently turned over with a spade, and sprinkled with urine, as a substance containing a large quantity of nitrogen. At the end of two or three years the nitrogen is converted into nitric acid, and this, by reacting with the potassium compounds existing in the vegetable remains, forms niter. When the contents of the bed contain about four ounces of the salt for every cubic foot of the materials, they are deemed fit to be lixiviated. The extraction and purification is similar to that used in India for purifying the natural salt.

The continuous formation of niter in niter earths and in artificial niter beds results from the oxidation of the nitrogen of ammonia, thus generating nitric acid, the formation of which is facilitated by the presence of alkaline and earthy bases, with which the acid unites, but in reality depends upon the presence of nitrifying micro-organisms (*Bacillus nitrificans*); nitrification is, therefore, not a simple chemical oxidation process, as was at one time supposed. The ammonia is derived, for the most part, from the protein of the organic remains in the niter earths. There is first formed calcium nitrate which then reacts with the potassium carbonate of the wood ashes to form potassium nitrate, according to the following reaction:

$$Ca(NO_3)_2 + K_2CO_3 = 2KNO_3 + CaCO_3$$

According to Schoenbein, whose statement has been confirmed by Goppelsröder, the formation of the nitric acid is always preceded by that of nitrous acid.

Potassium nitrate, as first obtained, either from natural or from artificial sources, is called in commerce crude saltpeter, and requires to be purified before it can be used in medicine or in most of the arts. Like the process of purifying crude argol in making cream of tartar it consists only in dissolving, clarifying the hot solution and crystallizing. (For details, see *U. S. D.*, 20th ed., p. 907.)

Description and Physical Properties.—"Colorless, transparent, six-sided rhombic prisms, or a white, crystalline powder. It is odorless, has a saline taste, and produces a cooling sensation in the mouth. It is slightly hygroscopic in moist air. One Gm. of Potassium Nitrate is soluble in 2.8 cc. of water, and in 620 cc. of alcohol, at 25° C. One Gm. is soluble in 0.5 cc. of boiling water. It is soluble in glycerin. When strongly heated, the salt melts without decomposition. At higher temperatures it evolves oxygen and is partly reduced to nitrite. When Potassium Nitrate is heated with charcoal, the mixture deflagrates.

"An aqueous solution of the salt (1 in 10) responds to the reactions for potassium and for nitrates.

"An aqueous solution of Potassium Nitrate (1 in 10) is neutral to litmus paper. An aqueous solution of Potassium Nitrate meets the requirements of the test for *heavy metals.* No yellow color appears when 0.1 Gm. of the dry salt is sprinkled upon 1 cc. of concentrated sulphuric acid (*chlorate*).

"**Assay.**—Dry about 0.4 Gm. of Potassium Nitrate to constant weight at 100° C., weigh accurately, dissolve it in 10 cc. of hydrochloric acid in a small porcelain dish, and evaporate the solution to dryness on a water bath. Dissolve the residue in 10 cc. of hydrochloric acid, and again evaporate to dryness on a water bath, continuing the heat until the residue, when redissolved in distilled water, is neutral to litmus paper. Transfer the residue with the aid of 25 cc. of distilled water to a flask, and proceed as directed under the assay for chlorides, deducting from the amount of tenth-normal silver nitrate consumed the amount which would be consumed by the chlorides present in an equivalent weight of the salt originally taken, and previously determined by taking about 2 Gm. of the salt, accurately weighed, and proceeding as directed under the assay for chlorides. Each cc. of tenth-normal silver nitrate corresponds to 0.01011 Gm. of KNO_3.

"Preserve in well-closed containers." *U. S.*

"White crystalline masses, or colorless fragments of six-sided rhombic prisms. Taste cool, saline. Soluble in 4 parts of *water.* Yields the *reactions* characteristic of potassium and of nitrates. Yields no characteristic *reactions* for copper, iron, aluminium, zinc, calcium, magnesium, sodium, ammonium, chlorides, iodides, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

It is devoid of water of crystallization, but is apt to contain a portion of liquid mechanically lodged within the substance of the crystals. This is particularly the case with the large crystals, and, according to Berzelius, is a source of impurity, as the liquid in question is a portion of the mother water in which they were formed. It is on this account that Berzelius recommends that the solution of the purified salt should be stirred during crystallization, so as to cause it to shoot into small crystals. The fused mass, when cast in moulds, or formed into little circular cakes, constitutes that form of niter found in commerce under the name of *crystal mineral* or *sal prunelle.* If the heat is increased, the salt is decomposed, evolves pure oxygen, and is reduced to the state of nitrite, which, in powder emits orange-colored fumes of hyponitric acid, and nitrous oxide on the addition of sulphuric acid. Upon a further continuance of the heat, the nitrous acid itself is decomposed, and a large additional quantity of oxygen is evolved, contaminated, however, with more or less nitrogen. On account of the large proportion of oxygen which it affords, niter increases the combustion of many substances in a remarkable degree. When thrown on burning coal, it deflagrates with bright scintillations. In the reaction of niter with charcoal, carbon dioxide is produced, and never carbon monoxide, and the nitric acid is variously decomposed into nitrous oxide, nitrogen dioxide, or nitrogen, according to the proportion of the charcoal and to the heat employed.

Uses.—Potassium nitrate, when in sufficient concentration, acts upon a raw surface or a mucous membrane as a violent irritant, and taken internally in concentrated form produces violent burning pain, vomiting, purging, and other evidences of gastro-enteritis, which may end in collapse and death. Inflammation and ulceration of the mucous membrane are commonly found at the autopsies.

As a therapeutic agent potassium nitrate is of very little importance. Its former use as a diuretic and in *rheumatism* has passed into a well deserved desuetude. Locally, it has been used in the place of potassium chlorate in *stomatitis* and *angina* but is even less efficacious than that feeble remedy.

In *asthma,* nitrous fumigation is often useful, performed by inhaling the fumes from burning torch paper, prepared by dipping blotting paper in a saturated solution of niter and afterwards drying it. Such paper is official in the N. F. (See *Charta Potassii Nitratis,* Part III.) Vohl has examined the vapor resulting from the burning paper thus impregnated, and found it to consist of carbon dioxide and oxide, cyanogen, ammonia, nitrogen, aqueous vapor, and potassium carbonate and nitrite, and he ascribes the beneficial results of its inhalation to the ammonia and potassium nitrite. It is habitually added to stramonium leaves in the preparation of so-called asthmatic powders, but it is used under these circumstances more for its oxidizing effect in encouraging the combustion than for its own therapeutic action.

In pharmacy, potassium nitrate was formerly employed to form crocus of antimony, to procure nitric acid, and sometimes in the preparation of spirit of nitrous ether. In chemistry it is used as an oxidizing agent.

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Charta Potassii Nitratis, *N. F.*

POTASSII PERMANGANAS. U. S., Br.

POTASSIUM PERMANGANATE Pot. Permang.

"Potassium Permanganate, when dried to constant weight over sulphuric acid, contains not less than 99 per cent. of $KMnO_4$. *Great caution should be observed in handling it, as dangerous explosions are liable to occur when it is brought into contact with organic or other readily oxidizable substances, either in solution or in the dry condition.*" *U. S.* "Potassium Permanganate may be obtained by the interaction of potassium chlorate, potassium hydroxide, and manganese dioxide. It contains not less than 99 per cent. of pure potassium permanganate, $KMnO_4$." *Br.*

Potassæ Permanganas; Hypermanganas Potassicus, s. Kalicus; Permanganate of Potash; Permanganate de Potasse, Caméléon Violet, *Fr.;* Kalium Hypermanganicum, *Fr. Cod.;* Kalium Permanganicum, *P. G.;* Kaliumpermanganat Chamäleon, Uebermangansaures Kali, *G.;* Permanganato di potassio, *It.;* Permanganato pota, *Sp.*

The British Pharmacopœia 1885 furnished a detailed process for this salt. (See *U. S. D.,* 19th edition, page 1013.) This process resembles that of Woehler which is employed on the large scale as follows: a mixture of potassium chlorate and manganese dioxide is added to a solution of potassium hydroxide. The potassium chlorate yields oxygen to manganese dioxide, converting it into manganic acid, which unites with the potassium hydroxide to form the manganate, potassium chloride being formed at the same time; the reaction being

$$3MnO_2 + 6KOH + KClO_3 = 3K_2MnO_4 + KCl + 3H_2O$$

When this solution is boiled, while a current of chlorine or of ozone is passed through as an oxidizing agent the green potassium manganate which is sometimes called *chameleon mineral,* is oxidized and yields potassium permanganate, according to the reaction

$$3K_2MnO_4 + O_3 + H_2O = K_2Mn_2O_8 + O_2 + 2KOH$$

Potassium permanganate has also been made by the electrolysis of the manganate, the products being permanganate, potassium hydroxide, and hydrogen. A still more interesting result of electrolysis is the production of potassium permanganate by the electrolysis of potassium hydroxide, in which the negative electrode is of porous copper oxide and the positive electrode a piece of manganese or ferro-manganese held immersed by a loop of platinum wire. A process for the complete conversion of manganate into permanganate has been patented in Germany. The crude manganate obtained in the usual way by melting manganese dioxide and alkali under access of air, is exhausted with water and a current of *ozonized* air is passed into and through the alkaline solution. The conversion of the manganate into permanganate is complete and rapid, whereas when ordinary oxygen is thus introduced the formation is slow and incomplete. (*Ph. Ztg.,* 1901, 517.)

Description and Physical Properties.—"Odorless, slender, monoclinic prisms, of a dark purple color, almost opaque by transmitted light, and of a blue, metallic luster by reflected light. It is stable in the air. One Gm. of Potassium Permanganate is soluble in 13.5 cc. of water at 25° C. One Gm. is soluble in 3.5 cc. of boiling water. It is decomposed by alcohol.

"When heated, the Potassium Permanganate decrepitates, and at about 240° C. it is decomposed, yielding oxygen, potassium manganate and manganese dioxide. An aqueous solution of the salt is of a deep violet-red color when concentrated, and of a rose color when highly diluted and responds to the reactions for permanganates, page .

"**Assay.**—Dry about 0.10 Gm. of Potassium Permanganate to constant weight over sulphuric acid, weigh accurately, and dissolve it in 25 cc. of distilled water. Mix the solution with 1 cc. of sulphuric acid and 50 cc. of tenth-normal oxalic acid, warm the mixture to about 80° C., and titrate with tenth-normal potassium permanganate. Each cc. of tenth-normal oxalic acid corresponds to 0.003161 Gm. of $KMnO_4$.

"Preserve in glass-stoppered bottles." *U. S.*

"Dark purple, slender, prismatic, iridescent crystals. Taste sweet, astringent. Soluble in 20 parts of *water.* Aqueous solution neutral to *litmus.* The crystals heated to redness decrepitate, evolve oxygen, and leave a black residue from which *water* extracts potassium hydroxide, the resulting solution yielding the *reactions* characteristic of potassium. Yields no characteristic *reactions* for lead, arsenic, iron, sodium, ammonium, chlorides, nitrates, or sulphates. 1 gramme dissolved in *water,* acidified with 5 millilitres of *diluted sulphuric acid,* and heated to about 60° C., requires for complete decolorisation not less than 31.3 millilitres of *N/1 solution of oxalic acid.*" *Br.*

If the solution be evaporated to dryness, the salt has the form of an intensely black powder. If suddenly heated, the crystals detonate, evolving oxygen, and leaving a black residue, which yields potassium hydroxide to water.

Moderately heated, the crystals are partially volatilized, giving out violet vapors of a disagreeable metallic odor. The salt, in consequence of the facility with which it parts with oxygen, is one of the most powerful oxidizing agents known. It causes the combustion of certain inflammable bodies, imparts oxygen to almost all organic substances, and in chemistry is employed to bring various compounds to a higher degree of oxidation. The readiness with which it yields oxygen in the nascent state is sufficient to account for its oxidizing power. It may be kept indefinitely if pure, and carefully secured from contact with organic substances, or other decomposing agents.

H. B. Condy many years ago introduced a permanganate disinfectant, which is commonly called *Condy's Fluid.* This consists of a crude sodium permanganate in solution and containing also aluminum sulphate, which is said to increase the oxidizing effect of the permanganic acid.

Uses.—Potassium permanganate was brought to the notice of the profession by Condy in 1857, who recommended it as a powerful disinfectant. The findings of bacteriologists concerning the germicidal powers of this substance have varied most extraordinarily. These discrepancies have been due not solely to variations in the susceptibility of different species of bacteria but probably in greater degree, as pointed out by Sternberg, to the difference in conditions of test. In the absence of organic matter it is distinctly superior in power to phenol but it is so readily decomposed that in the presence of any considerable amount of pus or other albuminous matters it is almost inert. It appears to be especially poisonous towards *staphylococcus pyogenes,* Sternberg having shown that one part in 833 is sufficient to destroy these bacteria in the absence of organic matter. Because of its activity as an oxidizant it is useful as a cleanser of *wounds* and the more so because of its deodorizing properties. One great disadvantage is its strong powers of staining the skin, clothes, etc. The stain may be removed with oxalic acid in places where the use of this substance is permissible. It is used in the treatment of *fetid ulcers, hospital gangrene, abscesses, carbuncles,* and *wounds* of all kinds, of fetid discharges from the mucous membrane, as in *ozena, otorrhea, gonorrhea,* and *leucorrhea,* and of *diphtheritic affections;* and it has proved serviceable even in *cancerous ulcers.* As a local stimulant it has also been used in *chronic* and *indolent ulcers.* In all these cases it is applied to the diseased surface in solutions of various strengths, according to the effect desired. In concentrated solution it is capable of acting as a caustic and therefore requires caution. With the view to its caustic action, it may be sprinkled on the diseased surface by means of a pepper-box, or applied in saturated solution. It has been highly recommended as an external application, to prevent pitting and septic absorption, in *small-pox* by Balfour (*Tropical Med. and Hyg.,* 1921, xxiv, 37).

As an external disinfectant it is generally employed in strengths of from 1 to 5 per cent., but for application to mucous surfaces its strength must be greatly reduced and may be employed in strengths of from 1 part in 2000 and upwards.

Probably through its oxidizing influence potassium permanganate destroys many poisons and is a useful chemical antidote in *morphine* and *strychnine poisoning,* but especially in *snake bite.* The use of potassium permanganate as an antidote to snake poison was first suggested by Fayrer in 1869 and confirmed by Lauder Brunton in 1878. Today, potassium permanganate is generally considered as the most valuable single drug that we possess against snake bite. As its action is a chemical one—that is, destruction of the poison—it is purely local in nature and the antidote must, therefore, be brought in contact with the poison by introducing into the same area. Two methods of accomplishing this have been employed. Rogers (*Indian Med. Gaz.,* 1912, xlvii) recommended incision of the wound and rubbing in crystals of the permanganate. He devised a special lancet to be carried by those travelling in snake infested districts, the hollow handle of which contained the crystals of the permanganate. Bannerman (*Indian Journ. Med. Research,* 1913), however, concluded that the hypodermic injection, directly into the area bitten, of a 5 per cent. solution of potassium permanganate was more efficient; this solution, however, produces extensive sloughing. Widenmann (*Cb. B.,* 1915) found that a 1 per cent. solution, if injected immediately and rubbed into the perivascular lymph spaces, would save rabbits from double the ordinary lethal dose of venom. In human medicine it is generally injected hypodermically into the region of the bite in strengths of from 1 to 2 per cent.

It is evident that like any other chemical antidote potassium permanganate must come in direct contact with the poison—whether alkaloid or venom—and since it is immediately decomposed by the tissues of the body, contrary to the statements occasionally made, it is useless after the absorption of the drug.

It is also recommended as a local hemostatic. Voerner (*M. M. W.,* 1905) recommends a mixture of one part of infusorial earth and two parts of potassium permanganate made up into a paste with one-third their bulk of petrolatum. Internally it was at one time employed in various *infectious diseases,* but its use for this purpose has entirely ceased. It is occasionally administered in *atonic amenorrhea.*

In overdose potassium permanganate may give rise to serious poisoning. Rubin and Dorner (*D. A. K. M.,* 1910, xcviii, p. 267) report a fatal case in which an unknown quantity was taken with suicidal intent. The symptoms were violent vomiting, profuse salivation with brownish masses of mucus, rapid respiration, albuminuria, and death fifty hours later. At autopsy there was found a bronchial pneumonia and punctiform hemorrhages in the pericardium.

Dose, from one to two grains (0.065–0.13 Gm.).

Off. Prep.—Liquor Potassii Permanganatis, *Br.*

POTASSII SULPHAS. N. F., Br.

POTASSIUM SULPHATE Pot. Sulph.

"Potassium Sulphate contains, when dried to constant weight at 100° C., not less than 99 per cent. of K_2SO_4 (174.26)." *N. F.*

"Potassium Sulphate may be obtained by the interaction of sulphuric acid and potassium chloride or certain other potassium salts. It contains not less than 99 per cent. of pure potassium sulphate, K_2SO_4." *Br.*

Potassæ Sulphas; Sulfas Potassicus, s. Kalicus, Tartarum Vitriolatum, Arcanum Duplicatum, Sal Duobus, Sal Polychrestum Glaseri; Sulphate of Potash, Vitriolated Tartar; Sulfate de Potasse, Potasse vitriolée, *Fr.;* Kalium Sulphuricum, *P. G.;* Kaliumsulfat, Schwefelsaures Kali, *G.;* Solfato di Potassio, *It.;* Sulfato potasico, *Sp.*

Potassium sulphate is naturally present in sea water, in some mineral waters, and in some other naturally occurring sources.

Several chemical processes give rise to potassium sulphate as a secondary product. Thus, it is produced in the distillation of nitric acid from a mixture of potassium nitrate and sulphuric acid; in the decomposition of magnesium sulphate by potassium carbonate; in one of the processes for preparing magnesium carbonate; in the manufacture of sulphuric acid; in the manufacture of potassium dichromate; and in the decomposition of potassium tartrate by calcium sulphate. The *kainite* of the Stassfurt salt beds is a native double potassium and magnesium sulphate, combined with magnesium chloride, and the *schœnite,* a double potassium and magnesium sulphate, with 6 molecules of water. To obtain potassium sulphate, the former mineral is exposed to the air; it deliquesces, and as soon as the soluble magnesium chloride has been run off, the remaining salt is partially decomposed by boiling water, so that on cooling the difficultly soluble sulphate separates out.

Properties.—As officially described it is in "colorless, hard rhombic prisms terminated by six-sided pyramids. Taste saline, slightly bitter. Decrepitates strongly when heated. Soluble in 10 parts of *water;* insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium and of sulphates. 1 gramme dissolved in water acidified with *hydrochloric acid* gives, with *solution of barium chloride,* a white precipitate, which, when washed and dried, weighs not less than 1.326 grammes. Yields no characteristic *reactions* for copper, iron, calcium, magnesium, sodium, ammonium, or nitrates, and not more than the slightest *reactions* for chlorides. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million. Aqueous solution neutral to *litmus* (absence of acid potassium sulphate)." *Br.*

Description and Physical Properties.—"Potassium Sulphate occurs as hard, colorless, translucent, six-sided, rhombic prisms terminated by pyramids, or as a white powder; permanent in the air. Odorless; taste saline, somewhat bitter. One Gm. dissolves in 10 cc. of water at 25° C., and in 4 cc. of boiling water; insoluble in alcohol.

"When heated the crystals decrepitate. At a bright red heat the salt fuses, and at a white heat partial decomposition occurs. An aqueous solution of the salt (1 in 20) is neutral to litmus. A saturated aqueous solution of the salt yields a white, crystalline precipitate with an excess of sodium bitartrate T.S. An aqueous solution of the salt (1 in 20) yields with barium chloride T.S. a heavy white precipitate, insoluble in hydrochloric acid.

"Separate portions of 10 cc. of the aqueous solution of the salt (1 in 20) made slightly alkaline with ammonia, are not rendered turbid within one minute by the addition of ammonium oxalate T.S. or of sodium phosphate T.S. (*calcium or magnesium*). An aqueous solution of Potassium Sulphate does not respond to the Test for heavy metals. An aqueous solution of the salt meets the requirement of the Test for arsenic.

"**Assay.**—Dissolve about 0.6 Gm. of Potassium Sulphate, previously dried to constant weight at 100° C. and accurately weighed, in 200 cc. of distilled water, acidulate the solution with hydrochloric acid and heat it to boiling. Gradually add an excess of barium chloride T.S., and heat for thirty minutes on a water-bath; collect the precipitate of barium sulphate on a filter and wash it with distilled water until silver nitrate T.S. fails to produce an opalescence in 2 cc. of the filtrate, previously acidulated with nitric acid. Dry the precipitate, ignite and weigh the residue. Each Gm. of Potassium Sulphate corresponds to not less than 1.326 Gm. of $BaSO_4$." *N. F.*

For the mode of preparing and using *Sal Polychrestum, Potassii Sulphas cum Sulphure,* or *Sulphate of Potassa with Sulphur,* and for a discussion of *Plate Sulphate of Potassa,* see *U. S. D.,* 15th ed., p. 1187.

Uses.—Potassium sulphate is a mild purgative, operating usually without heat, pain, or other symptom of irritation. In small doses, of from twenty grains to half a drachm (1.3–2.0 Gm.), it operates as an aperient; in large doses, of four or five drachms (15.5–20 Gm.), it acts slowly as a purge, but because of its irritant action is not to be recommended. Potassium sulphate is a powerful irritant in excessive doses, and capable of producing fatal poisoning; an ounce and a half (46.5 Gm.) of it are said to have caused death. It is, like the nitrate and the chlorate, more dangerous when not given in sufficiently dilute solution. (See *Am. J. M. S.*, N. S., vii, 88.)

Dose, twenty grains to two drachms (1.3–7.7 Gm.).

Off. Prep.—Pilula Colocynthidis Composita, *Br.;* Pulvis Ipecacuanhæ Compositus, *Br.;* Sal Carolinum Factitium, *N. F.;* Sal Carolinum Factitium Effervescens, *N. F.*

POTASSII TARTRAS. Br.

POTASSIUM TARTRATE

"Potassium Tartrate may be obtained by neutralizing Acid Potassium Tartrate with potassium carbonate. It contains not less than 99 per cent. of pure potassium tartrate, $(K_2C_4H_4O_6)_2H_2O$." *Br.*

Potassæ Tartras; Tartras Potassicus, s. Kalicus; Tartarus Tartarisatus, Tartarus Solubilis; Tartrate of Potash; Soluble Tartar; Tartrate de Potasse neutre, *Fr. Cod.;* Tartre soluble, Sel végétal, *Fr.;* Kalium Tartaricum, *P. G.;* Kaliumtartrat, *G.;* Tartrato neutro di potassio, *It.;* Tartrato potasico neutro, *Sp.*

This salt was dropped at the 1890 revision of the U. S. Pharmacopœia; it is retained in the 1914 revision of the British authority.

In the U. S. 1870 process the excess of acid in the bitartrate is neutralized by potassium carbonate, the carbon dioxide is liberated with effervescence, and the neutral potassium tartrate is formed. Iron vessels should not be used in the process, as that metal is apt to discolor the salt.

Potassium tartrate is sometimes made in the process for preparing tartaric acid. When thus obtained, the excess of acid of the bitartrate is neutralized by means of calcium carbonate. This generates an insoluble calcium tartrate, and leaves the neutral tartrate in solution, from which it may be obtained by evaporation and crystallization. (See *Acidum Tartaricum.*)

Properties.—Potassium tartrate is officially described in the Br. Ph. 1914 as in "small, colorless, four or six-sided prisms. Taste saline, cooling. Soluble in 1 part of *water.* Yields the *reactions* characteristic of potassium and of tartrates. 1 gramme, heated to redness till gases cease to be evolved, leaves an alkaline residue which, when treated with *water,* filtered, and well washed, yields a clear solution requiring for neutralisation not less than 16.8 millilitres of *N/2 solution of sulphuric acid.* Yields no characteristic *reactions* for copper, or iron, and not more than the slightest *reactions* for calcium, magnesium, sodium, chlorides, or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 2 parts per million. Aqueous solution neutral to *litmus* (absence of acid potassium tartrate)." *Br.*

Uses.—Potassium tartrate is a mild, cooling purgative, operating, like most of the neutral salts, without much pain, and producing watery stools. It is applicable to *febrile diseases,* and is occasionally combined with senna, the griping effects of which it has a tendency to obviate.

Dose, from one to four drachms (4–15 Gm.).

POTASSIUM

POTASSIUM

Potassium, *Fr.;* Kalium, Kalimetall, *G.;* Potassio, *It.;* Potasico, *Sp.*

Potassium is a metal discovered in 1807 by H. Davy, who obtained it by decomposing fused potassium hydroxide by a voltaic current. It was afterwards procured in larger quantity by Gay-Lussac and Thénard, by bringing the fused alkali in contact with white-hot iron, which attracted the oxygen and set free the metal. The process of Brunner, as modified by Wöhler, consists in decomposing potassium carbonate, mixed with charcoal. The mixture of carbonate and charcoal is obtained by heating cream of tartar to redness in a covered crucible. Castner has also prepared it by the process invented by him for the manufacture of metallic sodium by electrolyzing potassium chloride. It has recently been prepared at low cost by heating a mixture of potassium fluoride or potassium fluosilicate with powdered metallic aluminum.

Metallic potassium may be purified by redistillation and pressing it through straining cloths while in the melted condition. (For commercial sources of potassium salts, see under *Potassii Carbonas.*)

Potassium is solid, softer and more ductile than wax, easily cut with a knife, and of a silver-white color. A newly-cut surface is brilliant, but the metal quickly tarnishes by combining with the oxygen of the air, and assumes the appearance of lead. It possesses a remarkably strong affinity for oxygen, and is capable of taking that element from almost every other substance. On account of this property it must be kept submerged in pure liquid hydrocarbons, such as the petroleum distillates. On the same account, when exposed with a freshly cut surface to the air, it becomes luminous through a slow combustion, like phosphorus, in the dark. Its sp. gr. is 0.865, melting point 58° C., atomic weight 38.86, and symbol K. It volatilizes at about 720° C. with the production of greenish vapors. When thrown upon water it floats, takes fire, and burns with a rose-colored flame, combining with oxygen, and generating potassium hydroxide which dissolves in the water. It forms numerous combinations, uniting with most of the non-metallic elements, and with several of the metals. It combines in three proportions with oxygen, forming a suboxide (K_4O) and a monoxide (K_2O) of a gray color, and a tetroxide (K_2O_4) of a yellowish-brown color.

Uses.—Although elemental potassium is not used in medicine it enters into so large a number of medicinal salts and so greatly modifies the action of some of them, that the effects of the potassium ion deserve a separate word of consideration. While the presence of a certain amount of potassium in the blood is essential for vital activity, a very slight increase in its percentage has a deleterious influence on many organs. The injection of a potassium salt into the circulation weakens the contractile power of all muscle fiber but affects especially the heart and blood vessels. It also exercises a marked depressant action upon the central nervous system, including the spinal cord, brain, and medulla. Although the depressant action of potassium is strong when it is injected directly into the blood stream, when taken by the mouth it exercises very little influence upon the circulation. This is due to the fact that it is excreted by the kidneys so rapidly that it cannot be absorbed in sufficient amounts through the alimentary tract to cause the accumulation of a poisonous dose in the blood. When the kidneys, however, are diseased it is probable that a poisonous dose of the ion could be absorbed from the intestines, and therefore while the potassium salts can be used with great liberality in healthy persons, when there is disease of the kidneys some caution is necessary in their employment. During the passage of the potassium through the system it appears to exercise a marked effect upon the metabolism. Not only is there an increase in the total solid matters of the urine, but apparently a disproportionate increase in the quantity of urea. This has led to the opinion that the increased elimination is not simply the result of its diuretic action, but betokens a more complete oxidation in the system. Because of this effect the potassium salts are generally preferred in cases of deficient combustion, especially that group of disorders known as *lithemia*.

PROCAINÆ HYDROCHLORIDUM. U. S.

PROCAINE HYDROCHLORIDE Procain. Hydrochl.

"Para-amino-benzoyl-diethylaminoethanol hydrochloride $[NH_2(C_6H_4CO)OC_2H_4N(C_2H_5)_2.HCl]$." *U. S.*

Ethocaine; Novocaine; Syncaine; Kerocaine.

Procaine may be prepared in several ways. All of the methods are difficult and involve the preparation of ethylene chlorhydrine, $ClCH_2\text{-}CH_2OH$; and diethylamine, $(CH_3CH_2)_2NH$. To make novocaine, ethylenechlorhydrine is heated with paranitrobenzoyl chloride and the resulting chlor-ethyl paranitrobenzoic ester is heated under pressure at 120° C. with diethylamine for twenty-four hours. This produces the diethylaminoethyl ester of paranitrobenzoic acid which is subsequently reduced with tin and hydrochloric acid to produce novocaine.

In another method ethylenechlorhydrine is condensed with diethylamine to form chlorethyldiethylamine which is then heated with sodium paraminobenzoate to form novocaine base. In still another process paraminobenzoic acid is condensed with ethylene chlorhydrine by heating to 100° C. in the presence of sulphuric acid. The resulting compound is then heated with diethylamine in a sealed tube to form novocaine.

Description and Physical Properties.—"Small, colorless crystals or a white, crystalline powder. It is odorless, and is stable in the air. One Gm. of Procaine Hydrochloride is soluble in 0.6 cc. of water and in 30 cc. of alcohol, at 25° C. It is slightly soluble in chloroform, and almost insoluble in ether.

"Procaine Hydrochloride melts between 153° and 156° C. An aqueous solution of Procaine Hydrochloride (1 in 10) yields precipitates with gold chloride T.S., iodine T.S., mercuric potassium iodide T.S., and picric acid T.S. An aqueous solution of Procaine Hydrochloride (1 in 10) remains unchanged upon the addition of a solution of sodium bicarbonate, but with sodium hydroxide T.S. or sodium carbonate T.S., a colorless, oily precipitate is produced, which becomes crystalline on standing. Silver nitrate T.S. produces in an aqueous solution of the salt (1 in 20) a white precipitate insoluble in nitric acid, but soluble in ammonia water. Dissolve 0.1 Gm. of Procaine Hydrochloride in 5 cc. of distilled water, add 2 drops each of hydrochloric acid and solution of sodium nitrite (1 in 10), and then a solution of 0.2 Gm. of betanaphthol in a mixture of 3 cc. of sodium hydroxide T.S. and 7 cc. of distilled water. A scarlet-red precipitate is produced (*difference from phenacaine* which yields a white precipitate). To a solution of 0.1 Gm. of Procaine Hydrochloride in 5 cc. of distilled water add 3 drops of diluted sulphuric acid, followed by 5 drops of potassium permanganate T.S.: the violet color of the latter is immediately discharged (*difference from cocaine hydrochloride*).

"Its aqueous solution (1 in 20) is neutral to litmus paper. The ash from 0.5 Gm. is negligible. A solution of 0.1 Gm. of Procaine Hydrochloride in 1 cc. of sulphuric acid is colorless or nearly colorless (*readily carbonizable substances*). An aqueous solution of Procaine Hydrochloride meets the requirements of the test for *heavy metals*." *U. S.*

Uses.—Procaine is used in medicine solely as a local anesthetic. Sollmann (*J. A. M. A.*, 1918, lxx, p. 216) has shown that in comparing the power of local anesthetics it is necessary to take into consideration the method of use; thus, procaine when applied directly to nerve trunks or when injected subcutaneously is approximately equal in power with cocaine, but when applied over mucous membranes is much inferior, being only about 1/16 as efficient as cocaine. It is, however, much less toxic than cocaine. Eggleston and Hatcher (*J. P. Ex. T.*, 1919, xiii, p. 433) found that when injected rapidly into the vein the lethal dose for the cat is about 40 milligrammes per kilo or nearly three times that of cocaine. When administered subcutaneously, because of the relatively rapid elimination of procaine, the difference is still more marked; Closson (*Jour. Mich. State Med. Soc.*, 1914, xiii, p. 587) finds that after subcutaneous injection the toxicity of procaine for the guinea pig is about 1/10 that of cocaine. Schmitz and Lowenhart (*J. P. Ex. T.*, 1924, xxiv, 167) find that the lethal dose for mice of procaine, subcutaneously, is six times that of cocaine and when tested on cats fifteen times as large. It differs from cocaine in that it does not affect the pupil nor cause local vasomotor spasm. It is practically non-irritant either to mucous membranes or to other tissues.

Clinical experience as to the value of procaine is in harmony with the scientific data. There is abundance of evidence to show that for intradermal, neural or spinal anesthesia it is a very valuable anesthetic; on the other hand, for surface anesthesia, of either the membranes of the nose or of the eye its action is generally not satisfactory. While in general its use is relatively safe, a committee of the Section Laryngology of the American Medical Association (*J. A. M. A.*, 1920, lxxv, p. 315) have collected six deaths following its use as a local anesthetic. Meeker and Frazer (*J. P. Ex. T.*, 1923, xxii, 375) are inclined to doubt whether these fatalities are properly attributed to the anesthetic. For subcutaneous anesthesia, taking into consideration both the relative safety and efficiency, it is probably unsurpassed by any anesthetic at present available. For this purpose it may be employed in strengths of from ½ to 1 per cent.

Off. Prep.—Liquor Procainæ Hydrochloridum, *N. F.*

PRUNUM. N. F.

PRUNE

"Prune is the partly dried, ripe fruit of *Prunus domestica* Linné (Fam. *Rosaceæ*). Prune should contain from 30 to 35 per cent. of its natural moisture when used for pharmaceutical purposes." *N. F.*

Prunes; Pruneau noir, *Fr. Cod.*; Pflaume, Zwetsche, *G.*

Prunus domestica L. (*P. communis* Huds.), the common *plum tree,* is a small tree with hairy twigs, large dull green ovate leaves, with coarsely serrate margins and pubescent lower surface, large white flowers and drupaceous fruits. The exact native home of the plum is unknown but is thought to be in the Caucasus or trans-Caucasus regions. It is now found in many varietal forms scattered throughout the world, some of which are extensively cultivated for their edible fruits which, when dried, are called *"prunes."* Chief among the varieties grown for their fruit are var. *insitia* Bailey which has forms known as *Damson* and *Bullace Plums;* the var. *Juliana* de Candolle, yielding the *Prune de Saint-Julien* of the French; the var. *Cereola* Linnæus, yielding the *Reine Claudes* or *Green Gages;* and the var. *maliformis* Linnæus or *Mirabelle Plum.*

The Damson Plum is a small leaved and small fruited form which often develops when plums are left to run wild. We are of the opinion that its characters are more nearly those of the primitive parent than those of any other form or variety extant.

The prunes in the American market come chiefly from California and southern France. Prunes from Bordeaux, France, were formerly considered the best, but with the recent advances and improved methods of dehydration carried on in California, this state now markets dehydrated prunes which excel alike in appearance and flavor all of the commercial varieties prepared by the ordinary methods of sun or oven drying.

Description and Physical Properties.—"Oblong, ellipsoidal, more or less compressed, from 3 to 4 cm. long; externally brownish black, shriveled; the sarcocarp sweet and acidulous; putamen hard, smooth or irregularly ridged; seed shaped like that of the almond but smaller, and of a bitter-almond taste.

"Preserve prune in air-tight containers in a cool place." *N. F.*

Prunes have a feeble odor, and a sweet mucilaginous taste, which is generally also somewhat acid.

They contain uncrystallizable sugar, malic and benzoic acids, and mucilaginous matter. The following is given as the average of nine analyses of dried prunes: Water 29.30 per cent., nitrogenous material 2.35 per cent., fat 0.53 per cent., free acid 2.72 per cent., sugar 44.35 per cent., other nitrogen-free material 17.89 per cent., woody fiber (not including the stone) 1.48 per cent., ash 1.38 per cent. (König, *Nahrungsmittel*, ii, 397, 1880.) In Hungary a kind of brandy (*Zwetschenbranntwein*), containing about 40 per cent. of alcohol, is obtained from them, which in some districts is largely consumed. Bonneberg, a German chemist, has extracted from prunes crystallizable sugar equal to that of the cane.

Uses.—Prunes are official in the N. F. because of their use in the confection of senna. There is a common belief that they possess laxative properties, but it is improbable that they have any virtues in this direction not common to other fruits. The popular superstition concerning their effects upon the intestines has probably arisen from the almost universal habit of associating them with senna. Their most valuable rôle in medicine is as a flavoring agent.

Off. Prep.—Confectio Sennæ, *N. F.*

PRUNUS VIRGINIANA. U. S. (Br.)

WILD CHERRY Prun. Virg. [Wild Black Cherry Bark]

"Wild Cherry is a stem bark of *Prunus serotina* Ehrhart (Fam. *Rosaceæ*), collected in autumn and carefully dried. Borke, if present,

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should be removed." *U. S.* "Wild Cherry Bark is the bark of Prunus serotina, *Ehrh.*, collected in autumn." *Br.*

Pruni Virginianæ Cortex, *Br.*; Wild Cherry Bark; Virginian Prune Bark; Rum, Whisky, or Cabinet Cherry, Wild Black Cherry; Ecorce de Cerisier de Virginie, *Fr.*; Wildkirschenrinde, Amerikanischer Zierstrauch, *G.*

The genus *Prunus* now includes the plums, almonds, peaches, apricots, and cherries, and comprises about one hundred and twenty species. They are generally distributed in the temperate regions of the northern hemisphere. In the United States there are about forty indigenous species.

Linnæus, in his *Species Plantarum,* describes under the name of *P. virginiana* a tree, the statements concerning which are equally applicable to the *black cherry* and *choke cherry.* The specimen now in the Linnæan herbarium is that of the choke cherry. For this reason the binomial, *P. virginiana* L., has been restricted by many botanists to the choke cherry. But since Linnæus did not consider his herbarium specimens as types and as there is no certainty that he used the specimen now in the Linnæan herbarium as a basis for the description which is equally applicable to both cherries, we are left only the old synonymy upon which to interpret the species and that is entirely that of the *black cherry.* We are inclined to the opinion that Linnæus, in recognizing only one American species of this group, regarded the *choke cherry* and *wild cherry* as conspecific. DuRoi and Miller both adopted the name *P. virginiana* for the black cherry or wild black cherry while Ehrhart coined the name *P. serotina* for the black cherry.

The *choke cherry* is distinguished from the *wild black cherry* by the following characteristics: The choke cherry has deciduous calyx lobes; oblong-obovate pointed endocarp (or stone); leaves broadly oval to oblong-obovate, and usually abruptly acuminate; inner bark with a rather disagreeable odor. The *wild black cherry* has persistent calyx lobes; the endocarp (or stone) oblong-obovate, usually gradually acuminate; leaves oblong or lanceolate-oblong, usually gradually acuminate; the inner bark and leaves possess an aromatic odor. The British synonym, "Virginian Prune Bark," for the bark is misleading; Virginian Peach Bark or Virginian Almond Bark would have been no more of a misnomer. Michaux observed specimens of these trees on the banks of the Ohio, from eighty to one hundred feet high, with trunks from twelve to fifteen feet in circumference, but usually met with in the Atlantic States the tree is much smaller. The trunk is regularly shaped, and covered with a rough blackish bark, which detaches itself semi-circularly in thick narrow plates. The leaves are alternate, oval-oblong, or lanceolate-oblong, acuminate, unequally serrate, smooth on both sides, of a beautiful brilliant green; the petioles are furnished with one or more reddish conspicuous glands. The flowers are small, white, and occur in long erect or spreading racemes. They appear in May, and are followed by globular drupes, about the size of a pea, and when ripe of a shining blackish-purple color. For a paper on the structure of species of *Prunus,* by E. S. Bastin, see *Proc. A. Ph. A.*, 1895, 211.

This tree is distributed from Ontario south to Florida, and westward to Dakota, Nebraska, Kansas, Indian Territory, and Eastern Texas. It extends along the mountain ranges of Western Texas, Mexico, and Pacific regions of Central America, Colombia, and Peru. In the United States it was once common throughout the Appalachian region. In the neighborhood of Philadelphia it affects open situations, growing solitarily in the fields and along fences, and seldom aggregated in woods or groves. It is highly valued by the cabinet-makers for its wood, which is compact, fine-grained, susceptible of polish, and of a light red tint which deepens with age.

Moser points out that collectors frequently mistake *P. virginiana* L. or choke cherry for *P. serotina* Ehrh. or black cherry, which is the official source of wild cherry bark. He presents a description of the two trees and of the characteristic features of their barks. (*A. J. P.*, 1909, lxxxi, p. 579.) Farwell reports that the bark of *P. demissa* (Nutt.) Walpers, a tree from west of the Rocky Mountains, has been found in commerce. It is much darker and the lenticels are much more prominent. The preparations made from it resemble the official wild cherry bark in color, odor and taste. Occasionally barks find their way into commerce as Prunus Virginiana which yield no odor of hydrocyanic acid when moistened and are probably obtained from other than the official wild cherry. (See Bastin, *A. J. P.*, 1895, and Finnemore, *P. J.*, 72.)

Wild cherry bark is collected in autumn and should be carefully dried and stored in closed containers. The commercial supplies consist of "rossed" and "unrossed" bark. *Rossed* bark is bark deprived of its borke. (The term "borke" is a word of German origin and is used to indicate that layer of the bark formed in some trees, as the sycamore and wild cherry, which scales off in patches; it is composed of cork and parenchymatous cells.)

Virginia, Indiana, North Carolina and Michigan furnish much of the bark of commerce. The chief substitute and adulterant for this drug is the bark of the *Prunus Virginiana* L. (*P. nana* DuRoi) commonly known as *choke cherry* bark. This differs from the bark of the wild black cherry by exhibiting no stone cells in the pericycle, by having medullary rays from 1 to 4 cells in width and by having more rosette aggregates of calcium oxalate in its phloem than monoclinic prisms. Ground wild cherry bark has frequently been adulterated with wood of the same species.

Description and Physical Properties.—"*Unground Wild Cherry.*—Usually in transverse curved pieces up to 8 cm. in width and from 0.5 to 8 mm. in thickness; outer surface of rossed bark light brown or greenish-brown, smooth, except for numerous lenticel-scars; outer surface of unrossed bark reddish-brown, glossy, smooth, with light colored, transversely elongated lenticels or roughened and flaky with gray lichens; inner surface light brown, with delicate, reticulate striations and numerous minute fissures; fracture short, granular; odor distinct, resembling bitter almond when macerated in water; taste astringent, aromatic, and agreeably bitter.

"*Structure.*—Outer layer, of several or many rows of very small cork cells; parenchyma, tangentially elongated, bearing chloroplasts, starch or calcium oxalate crystals; stone cells associated with small groups of bast fibers in a nearly continuous ring; medullary rays 1 to 8 cells wide, wavy or curved, starch-bearing and frequently separated from the phloem on one side by large intercellular spaces; between the medullary rays numerous small groups of stone cells, sometimes branched or modified into short bast fibers, and associated with crystal fibers.

"*Powdered Wild Cherry.*—Light brown, fragments of yellow brown cork, few; stone cells numerous, frequently elongated, with short branches or a wavy and irregular outline and with thick, lamellated, porous, strongly-lignified walls; bast fibers few, not greatly elongated, frequently accompanied by crystal-bearing fibers; calcium oxalate prisms or rosette aggregates numerous, from 0.010 to 0.075 mm. in diameter; starch grains single and compound, nearly spherical, from 0.002 to 0.015 mm. in diameter.

"Preserve Wild Cherry in tightly-closed containers, protected from light." *U. S.*

"In curved pieces or irregular fragments not more than three millimetres thick. Frequently covered with a smooth, thin, reddish-brown, papery cork, or, if this has been removed, exhibiting a greenish-brown cortex; marked with transversely elongated lenticels. Fracture short, granular; fractured surface reddish-gray. Inner surface reddish-brown, striated or reticulately fissured. In the bark numerous groups of sclerenchymatous cells of characteristic shape, but no typical bast fibres; in the parenchymatous cells minute starch grains and prismatic crystals of calcium oxalate. Slight odor; taste astringent, aromatic and bitter, recalling that of bitter almonds." *Br.*

The bark is obtained indiscriminately from all parts of the tree, though that of the roots is thought to be most active. The revisers of the Pharmacopœia believe with J. S. Perot that the bark is stronger when collected in autumn than in the spring.

Constituents.—All parts of the wild cherry, including the leaves, fruit, and the bark of the stem and of the root, yield on infusion hydrocyanic acid. This substance does not exist as such in the plant itself but is due to the action of an enzyme—identical with the *emulsin* or *synaptase* found in mustard, bitter almonds, etc.—upon a cyanogenetic glucoside which was, at one time, believed to be amygdalin; it is probably l-mandelonitrile, which is isomeric with prulaurasin found in the cherry laurel (see under *Amygdala amara*).

Besides the cyanogenetic principle, wild cherry bark contains tannic acid—according to Peacock (*J. A. Ph. A.*, 1923, xii, 774) about 3 per cent.—and a fluorescent bitter principle which is probably glucosidal. (See also Power and Weimer, *West. Drug.*, 1887, p. 331). Lemburger (*A. J. P.*, 1872) states that the tannic acid is most abundant in the bark in October and November, but, on the other hand, Cooley (*A. J. P.*, August, 1897) found more in the spring than in the fall. Free benzoic acid, probably from oxidation of benzaldehyde, is also present.

The amount of hydrocyanic acid yielded by the bark ranges from 0.05 to 0.35 per cent. According to Stevens and Judy (*A. J. P.*, 1895, 482, p. 534), the hydrocyanic content is higher in the bark of the root than of the stem, the bark of young trees gives a greater yield than of old trees, and thick bark than thin bark.

Its peculiar flavor and its medicinal virtues are injured by boiling, in consequence partly of the volatilization of the principles upon which they depend, partly upon a chemical change effected by the heat.

R. Rother (*A. J. P.*, 1887, p. 286), in searching for the fluorescent principle of wild cherry bark, obtained a reddish crystalline substance, soluble in water, chloroform, ether, and alcohol, the solution of which fluoresced strongly on addition of ammonia. Rother says that it does not agree in crystalline form with mandelic acid, but may be a derivative of it. (For elaborate analysis of this bark and of the leaves, see Power and Moore, *Tr. Chem. Soc.*, 1909, p. 243 and 1910, p. 1100, respectively.)

Uses.—Wild cherry bark has the stomachic effects of the simple bitters but is comparatively infrequently employed for this purpose. On the theory that hydrocyanic acid is a cough sedative, wild cherry bark has been popularly employed in the treatment of *bronchitis* of various types, but is of doubtful service. Its most frequent use is as a flavoring agent especially for cough-syrups.

Dose, from thirty to sixty grains (2.0–3.9 Gm.).

Off. Prep.—Syrupus Pruni Virginianæ, *U. S.*, *Br.;* Tinctura Pruni Virginianæ, *Br.;* Elixir Taraxaci Compositum (from Fluidextract), *N. F.;* Fluidextractum Pruni Virginianæ, *N. F.;* Syrupus Pini Albæ Compositus, *N. F.;* Syrupus Pini Albæ Compositus cum Morphinæ, *N. F.*

PULSATILLA. N. F.

PULSATILLA Pulsatil. [Pasque Flower]

"Pulsatilla is the dried herb of *Pulsatilla vulgaris* (Linné) Miller, *Pulsatilla pratensis* (Linné) or *Pulsatilla patens* (Linné) Miller

(Fam. *Ranunculaceæ*). Pulsatilla contains not more than 5 per cent. of foreign organic matter." *N. F.*

Wind Flower; Pasque Flower; Passe Flower; Meadow Anemone; Herba Pulsatillæ; Herba Venti,s. Nolæ Culinari; Pulsatille, Coquelourde, Herbe du Vent, *Fr.;* Kuchenschelle, *G.*

The genus *Anemone* of Linnæus (Fam. *Ranunculaceæ*) includes perennial herbs of temperate regions with acrid poisonous juices and radical and cauline leaves, the cauline leaves forming an involucre remote from a solitary or umbellate inflorescence. The sepals are numerous to few and petaloid. The petals are absent and the fruits represent flattened and pointed or tailed achenes. This genus contains two sub-genera or sections, viz., *Anemone* and *Pulsatilla.* The plants of the *Anemone* section possess flowers with short styles and no staminodes, whereas those of the *Pulsatilla* section have long plumose styles, and staminodes are present. The species yielding the drug Pulsatilla belong to the section which Persoon named *Pulsatilla.* This section has been given the full rank of a genus by Britton and other followers of the American code. *Pulsatilla vulgaris* (*Anemone pulsatilla* L.) and *P. pratensis* (*A. pratensis* L.) are native to Europe and Asia. The American Pasque Flower is known to botanists under a variety of names as: *Pulsatilla patens* (L.) Miller, *P. hirsutissima* (Pursh.) Britt., *Anemone Nuttaliana* DC., etc. It is indigenous to the United States and Canada, west of the Mississippi. It possesses ternately divided leaves whose lateral segments are 2-parted, the middle one being stalked and 1-parted, a sessile deeply and narrowly cleft involucre, and a purplish-blue to whitish calyx of 5 to 7 sepals.

The plant should be gathered at the time of flowering in spring and used in the fresh condition for preparing the best tincture. Most of the drug on the markets is dried. The chief present commercial source is Czecho-Slovakia, the supplies imported into the United States coming in bags or bales from Hamburg, Germany.

Description and Physical Properties.—"*Unground Pulsatilla.*—Leaves and flowering scapes matted, silky-villous, basal leaves with petioles up to 30 cm. in length, the latter hollow, often purplish in color, the blades twice or thrice deeply three- or four-parted or pinnately cleft, the lobes linear and acute, the base of the petiole more hairy than above and frequently attached to the short rootstock; flowering scapes up to 30 cm. in length, solid in the lower portion and hollow in the upper part, with sessile, involucral leaves near the flower, occasionally with remains of the dull purple hairy sepals and the dense-wooly, plumose-tailed achenes. Nearly odorless; taste very acrid.

"*Powdered Pulsatilla.*—Numerous simple, thick-walled hairs up to 2.5 mm. in length and up to 0.020 mm. in thickness; tracheæ up to 0.035 mm. in width and spiral markings or with simple or bordered pores; fragments of epidermal tissue with stomata, the latter being broadly elliptical and up to 0.055 mm. in length in leaf tissue and up to 0.065 mm. in length in stem tissue; some epidermal cells with wavy vertical walls; calcium oxalate crystals and starch grains few or absent." *N. F.*

The official species of anemone as well as a number of related plants yield a volatile oil from which can be separated a crystallizable intensely acrid substance known as *anemone camphor.* This is an unstable compound which splits up into *anemonin* and *iso-anemonic acid.* Anemonin is practically tasteless, but when melted or volatilized with vapors of boiling water it becomes quite irritant. The formula $C_{10}H_8O_4$ assigned by Beckurts has been confirmed by Meyer, who believes it is related to cantharidin (*Jahresb. Pharm.,* 1896). When treated with nascent hydrogen in an acid solution, anemonin yields *hydroanemonin,* $C_{10}H_{12}O_4$, which crystallizes from boiling petroleum in large colorless laminæ which contain 1 molecule of H_2O, melt at 78° C., and distil without decomposition at from 210° to 212° C. under a pressure of 10 mm. Hydroanemonin is much more stable than anemonin.

As the acrid principle is volatile, much of it is lost in the process of drying. Indeed some authorities state that the dried herb is inert.

Uses.—Pulsatilla is a powerful local irritant and when taken in sufficient amount produces gastro-enteritis with vomiting and purging and often accompanied with evidence of irritation of the kidneys, such as albuminuria and even hematuria. Bronevski (*Med. Press.,* 1886) and Noel and Lambert (*A. J. P.,* 1897) have studied the physiological action of anemonin. They agree that the drug is a powerful depressant to the central nervous system, and Bronevski says also to the heart, but Noel and Lambert could find no pronounced action upon the circulation.

Pulsatilla was extensively used by that group of physicians known as eclectics, in a large variety of conditions. There is no satisfactory evidence, however, that it possesses any therapeutic virtues not ascribable to its local irritating effect. It was supposed to act especially on the generative organs both in men and women, and to be useful in *dysmenorrhea* and *ovarian irritation;* also *epididymitis* and *orchitis.*

The *dose* of the powdered drug may be stated as two to ten grains (0.12–0.6 Gm.).

Off. Prep.—Tinctura Pulsatillæ, *N. F.*

PULVERES

POWDERS

Poudres, *Fr.;* Pulvern, *G.;* Polveri, *It.;* Polvos, *Sp.*

The form of *powder* is convenient for the exhibition of substances which are not given in very large doses, are not very disagreeable to the taste, have no corrosive property, and do not deliquesce rapidly nor undergo any chemical decomposition, on exposure.

Powders may be divided into the *simple,* consisting of a single substance, and the *compound,* of two or more mixed together. The latter only are embraced under the present head. In the preparation of the compound powders, the ingredients should be pulverized separately and then mixed. Deliquescent substances, and those containing fixed oil in large proportion, should not enter into the composition of powders intended to be kept,—the former because they render the preparation damp and liable to spoil, the latter because they are apt to become rancid and impart an unpleasant odor and taste. When deliquescent substances are extemporaneously prescribed, the apothecary should enclose them before delivery in parchment paper or other impervious covering; the same remark is applicable to volatile powders, as ammonium carbonate and camphor. The lighter powders may in general be administered in water or other thin liquid; the heavier, such as those of metallic substances, require a more consistent vehicle, as syrup, molasses, honey, or one of the confections. Resinous powders, if given in water, require the intervention of mucilage or sugar.

Powders whose dose is not too large may usually be most conveniently exhibited enclosed in gelatin capsules (see under *Gelatina*). These will hold generally up to about 10 grains of organic or 15 grains of inorganic drugs. Another useful container for powders is the *cachet de pain* or *konseal,* also called the *wafer capsule.* These are made of flour and water, usually circular in outline with a concavity in the center. They may be had in various sizes; the largest will hold up to 20 grains of most substances. In filling them, one wafer is placed upon a board, and the requisite amount of medicine is put in it; then a second wafer, whose interior margin has been wetted, is laid upon the first and pressed down upon it. When taken, they should be dipped in water, placed immediately upon a teaspoon containing a little water, and swallowed with a gulp of fluid.

In mixing powders the ingredients should not be added all together at once, but the more potent ingredient, or that present in the smallest amount should be mixed with an equal bulk of the diluent and thoroughly triturated until the mixture is uniform, after which another portion of the diluent or one of the other ingredients, if any are present, and the procedure repeated until all of the ingredients have been added and the mixture is of perfect homogeneity.

PULVIS AMYGDALÆ COMPOSITUS. Br.

COMPOUND POWDER OF ALMONDS

Confectio Amygdalæ; Conserva Amygdalarum, Confection of Almond; Conserve d'Amandes, *Fr.;* Mandeloonserve, *G.*

"Sweet Almonds, 60 *grammes;* Refined Sugar, in powder, 30 *grammes;* Gum Acacia, in powder, 10 *grammes.* Blanch and dry the Almonds; reduce them to a coarse powder; mix the Gum Acacia and Sugar; add to the powdered Almonds; mix." *Br.*

This is the old *Almond Confection* in powder form. It is intended to afford a speedy method of preparing the almond mixture, which, when made immediately from the almonds, requires much time, and which cannot be kept ready made. But from its liability to be injured by keeping, it is not to be commended.

Off. Prep.—Mistura Amygdalæ, *Br.*

PULVIS ANTIMONIALIS. Br.

ANTIMONIAL POWDER [James's Powder]

Pulvis Antimonii Compositus, Pulvis Jacobi; Poudre antimoniale de James, *Fr.;* Jamessches Antimonpulver, *G.*

"Antimonious Oxide, 25 *grammes;* Calcium Phosphate, 50 *grammes.* Mix." *Br.*

The *Pulvis Antimonialis* of the N. F. (see Part III) is a little stronger in antimony.

The only essential difference between the official and the Dublin powder is that the ingredients of the former are taken already prepared and mixed in fixed proportion, while those of the latter result simultaneously from one operation. The official powder is, of course, much more easily prepared, and less liable to uncertainty from any error in the process.

Michael Donovan believes that none of the official formulas fairly represent *James's powder,* and gives an elaborate history of this celebrated proprietary medicine, and a method for its preparation, in *P. J.,* 1869.

Uses.—This preparation is stated to be alterative, diaphoretic, purgative, or emetic, according to the dose in which it is given. It was formerly prescribed in febrile diseases, with a view to its diaphoretic effect.

As this preparation depends for its action on the presence in the alimentary canal of an acid which may form a salt with the antimonial oxide, it cannot always be relied on for a definite effect, being sometimes mild, and sometimes more active than might be desirable.

Dose, as a diaphoretic, from three to eight grains (0.2–0.5 Gm.) every third or fourth hour, given in the form of pill. In larger doses it is purgative and emetic.

PULVIS BUTEÆ SEMINUM. Br.

POWDER OF BUTEA SEEDS

"Soak Butea Seeds in Distilled Water; carefully remove the integuments; dry and powder the kernels." *Br.*

Uses.—(See *Butea Semina.*)

Dose, ten to twenty grains (0.6–1.2 Gm.).

PULVIS CATECHU COMPOSITUS. Br.

COMPOUND POWDER OF CATECHU

Poudre de Cashcuttie composée, *Fr.;* Zusammengesetztes Katechupulver, *G.*

"Catechu, in powder, 40 *grammes;* Kino, in powder, 20 *grammes;* Krameria Root, in powder, 20 *grammes;* Cinnamon Bark, in powder, 10 *grammes;* Nutmeg, in powder, 10 *grammes.* Mix." *Br.*

The *dose* of this agreeable, and active, astringent is from fifteen to sixty grains (1–4 Gm.).

PULVIS CINNAMOMI COMPOSITUS. Br.

COMPOUND POWDER OF CINNAMON

Poudre des Epices, P. des Aromates, Poudre aromatique, *Fr.;* Aromatisches Pulver, Gewürzpulver, *G.*

"Cinnamon Bark, in powder, 25 *grammes;* Cardamom Seeds, in powder, 25 *grammes;* Ginger, in powder, 25 *grammes.* Mix." *Br.*

The cardamom seeds should always be deprived of their pericarps before being weighed, and the powder, when prepared, should be kept in well-stoppered bottles.

The *aromatic powder* of the N. F. (see *Pulvis Aromaticus,* Part III) closely follows the formula of the U. S. IX and differs from the British preparation in containing nutmeg.

Uses.—The aromatic powder is stimulant and carminative, and the preparation may be given in the dose of from ten to thirty grains (0.65–2.0 Gm.), in cases of *enfeebled digestion with flatulence;* but it is chiefly used as a corrigent and adjuvant of other medicines. A mixture of aromatic powders in the form of a cataplasm is much used as a mild rubefacient, especially in nausea and vomiting, being applied over the epigastrium. Such a mixture is commonly called *spice plaster* and is official in the N. F. (see Part III), under the title *Pulvis Aromaticus Rubefaciens.* It contains clove, cinnamon, ginger, and capsicum, and the mixed powder may be distributed in a thin flannel bag, quilted in position, and the whole wet with bathing whisky when applied and covered with oiled silk.

Dose, fifteen to forty-five grains (1–3 Gm.).

PULVIS CRETÆ AROMATICUS. Br.

AROMATIC POWDER OF CHALK

Confectio Aromatica, *Lond.;* Poudre de Craie aromatique, *Fr.;* Gewürztes Kreidepulver, *G.*

"Cinnamon Bark, in powder, 10 *grammes;* Nutmeg, in powder, 8 *grammes;* Cloves, in powder, 4 *grammes;* Cardamom Seeds, in powder, 3 *grammes;* Refined Sugar, in powder, 50 *grammes;* Prepared Chalk, 25 *grammes.* Mix." *Br.*

This is the former "Aromatic Powder" of the Br. Pharmacopœia, with the addition of chalk and elision of saffron. It is also official in the N. F. V (see Part III). It is a warm stimulant and astringent, as well as antacid, and is well calculated for *diarrhea* connected with acidity and without inflammation. In such a combination, however, the due proportion and even the choice of the ingredients vary so much with the symptoms that they might well be left to extemporaneous prescription.

Dose, from fifteen to sixty grains (1.0–3.9 Gm.), in mucilage or sweetened water, frequently repeated.

Off. Prep.—Pulvis Cretæ Aromaticus cum Opio, *Br.*

PULVIS CRETÆ AROMATICUS CUM OPIO. Br.

AROMATIC POWDER OF CHALK WITH OPIUM

Pulvis Cretæ et Opii Aromaticus, *N. F.;* Aromatic Powder of Chalk and Opium; Poudre de Craie Opaciée, *Fr.;* Kreidepulver mit Opium, *G.*

"Aromatic Powder of Chalk, 97.5 *grammes;* Opium, in powder, 2.5 grammes. Mix. This Powder contains 2.5 per cent. of Opium." *Br.*

The N. F. powder is identical with the Br. (see Part III).

The addition of the opium greatly increases the efficacy of the compound powder of chalk in *diarrhea,* and its equal diffusion through the powder presents this advantage, that it may be conveniently given in minute doses applicable to infantile cases. Forty grains of the powder contain a grain of opium.

Dose, for adults, from fifteen to forty-five grains (1–3 Gm.).

PULVIS CRETÆ COMPOSITUS. U. S.

COMPOUND CHALK POWDER Pulv. Cret. Co.

Poudre de Craie composée, *Fr.;* Kreidepulver mit Gummi, *G.*

"Prepared chalk, 30 Gm.; Acacia, in very fine powder, 20 Gm.; Sucrose, in fine powder, 50 Gm.; to make 100 Gm. Mix the powders intimately by trituration and pass the product through a No. 60 sieve." *U. S.*

This official powder was introduced into the U. S. P., 1890, for the purpose of having on hand, in a convenient form, the dry powders necessary to make chalk mixture. (See *Mistura Cretæ.*)

This powder will be found, however, a very convenient basis for administering chalk in powder, and it will be easy to direct the addition of morphine, kino, pepsin, bismuth subnitrate, or any other indicated drug.

Dose, one-half to two drachms (2.0–7.7 Gm.).

Off. Prep.—Mistura Cretæ, *U. S.*

PULVIS EFFERVESCENS COMPOSITUS.
U. S. (Br.)

COMPOUND EFFERVESCING POWDER Pulv. Eff. Co. [Seidlitz Powder]

"The mixture in a blue paper weighs not less than 9.5 Gm. and not more than 10.5 Gm., and contains not less than 23 per cent. and not more than 27 per cent. of sodium bicarbonate [$NaHCO_3$], and not less than 73 per cent. and not more than 78 per cent. of potassium and sodium tartrate [$KNaC_4H_4O_6.4H_2O$]. The white paper contains not less than 2 Gm. and not more than 2.4 Gm. of Tartaric acid [$H_2C_4H_4O_6$]." *U. S.*

Pulvis Sodæ Tartaratæ Effervescens, *Br.;* Effervescent Tartarated Soda Powder; Pulveres Effervescentes Aperientes, *U S.* 1870; Seidlitz Powders; Poudre Gazogène laxative, Poudre de Seidlitz, *Fr.;* Pulvis aërophorus laxans, *P. G.;* Pulvis aërophorus Seidlitzensis, Abführendes Brausepulver Seidlitzpulver, *G.;* Polvo gasifero laxante, *Sp.*

"Sodium bicarbonate, dried and in fine powder, 30 Gm.; potassium and sodium tartrate, dried and in fine powder, 90 Gm.; tartaric acid, dried and in fine powder, 26 Gm. Mix the sodium bicarbonate intimately with the potassium and sodium tartrate, divide the mixture into 12 equal parts, and wrap each part in a blue paper. Then divide the tartaric acid into 12 equal parts, and wrap each part in a white paper. Preserve in well-closed containers in a dry place." *U. S.*

"No. 1 Sodium Potassium Tartrate, in dry powder, 7.5 *grammes;* Sodium Bicarbonate, in dry powder, 2.5 *grammes.* Mix. No. 2 Tartaric Acid, in dry powder, 2.5 *grammes.* Put No. 1 in blue paper, and put No. 2 in white paper." *Br.*

Test for Identity.—"To 5 cc. of an aqueous solution of the mixture in a blue paper (1 in 20) add 5 cc. of acetic acid, and when effervescence has ceased, shake the solution vigorously: a white, crystalline precipitate, soluble in ammonia T.S., separates." *U. S.*

Assay for Sodium Bicarbonate.—"Mix thoroughly the contents of a blue paper, then dissolve 2 Gm. of it in 80 cc. of distilled water, add 20 cc. of half-normal sulphuric acid, boil the solution until the volume is reduced to about 50 cc., and titrate the excess of acid with half-normal sodium hydroxide, phenolphthalein T.S. being used as indicator. Each cc. of half-normal sulphuric acid corresponds to 0.04201 Gm. of sodium bicarbonate.

"**Assay for Potassium and Sodium Tartrate.**—Proceed as directed under the assay for alkali salts of organic acids, using 2 Gm. of the mixture taken from the blue paper used in the preceding assay. The difference between the number of cc. of half-normal sulphuric acid consumed in this assay and in the assay for sodium bicarbonate, multiplied by 0.07056, represents the potassium and sodium tartrate. The sum of the percentage of sodium bicarbonate and of the potassium and sodium tartrate is not less than 99 per cent.

"**Assay for Tartaric Acid.**—The contents of the white paper should meet the requirements of the tests and assay under *Acidum Tartaricum.*" *U. S.*

Though named from the saline springs of Seidlitz, in Bohemia, Seidlitz powders do not correspond in composition with those famous waters. Of each pair of powders, one, much the smaller of the two, contains about thirty-five grains (2.25 Gm.) of tartaric acid, the other about forty grains (2.59 Gm.) of sodium bicarbonate mixed with about two drachms (7.7 Gm.) of Rochelle salt. The acid powder is usually put into a white paper, the alkaline into a blue paper, which latter should not be colored by aniline; a number of them are enclosed in a paper or tin box. They should not be kept in a damp place, as the tartaric acid is liable to deliquesce and be absorbed into the substance of the paper, thus altering the due proportion of the ingredients. The whole of the contents of the white paper has been known to disappear in the course of two or three years. The Rochelle salt is the ingredient upon which the aperient property mainly depends. In their administration, each powder is dissolved separately, the smaller in a fluidounce or more of water, the larger in twice or three times the quantity, and the two solutions are mixed gradually. A reaction takes place between the tartaric acid and the sodium bicarbonate, by which sodium tartrate is produced, adding somewhat to the laxative property of the draught, and carbon dioxide escapes, causing a brisk effervescence. The acid is in slight excess, and thus causes an agreeable acidity in the solution.

Uses.—These powders are refrigerant and aperient, and generally very acceptable to the stomach in consequence of the carbon dioxide eliminated. They are especially adapted to *febrile cases* with a somewhat irritable stomach. One pair of them will generally operate slightly, but, if required, two may be given at once, or the dose may be repeated every three or four hours until the desired effect is produced. The flavor may sometimes be advantageously improved by adding syrup of orange, or lemon to one of the solutions before admixture, and most persons prefer to dissolve the salts in very cold water, the saline taste being thereby greatly diminished. A lowering of the temperature always takes place, due to the solution of the salts.

Dose, one set of two powders.

PULVIS GLYCYRRHIZÆ COMPOSITUS.
U. S., Br.

COMPOUND POWDER OF GLYCYRRHIZA Pulv. Glycyrrh. Co. [Compound Licorice Powder]

Poudre de Réglisse composée, Poudre pectorale, *Fr.;* Pulvis Liquiritiæ Compositus, *P. G.;* Brustpulver, Pulvis Pectoralis Kurellæ, *G;*

"Senna, in very fine powder, 180 Gm.; Glycyrrhiza, in very fine powder, 236 Gm.; Washed Sulphur, 80 Gm.; Oil of Fennel, 4 Gm.; Sucrose, in fine powder, 500 Gm.; to make 1000 Gm. Mix the oil of fennel thoroughly with about one-half of the sucrose, then add the remainder of the sucrose and the other ingredients, and mix thoroughly. Finally, pass the powder through a No. 80 sieve, pulverize the residue if any should be left on the sieve, add it to the sifted powder, and mix thoroughly. Keep it in well-closed containers." *U. S.*

"Senna Leaves, in powder, 16 *grammes;* Liquorice Root, in powder, 16 *grammes;* Fennel fruit, in powder, 8 *grammes;* Sublimed Sulphur, 8 *grammes;* Refined Sugar, in powder, 52 *grammes.* Mix." *Br.*

Description and Physical Properties.—"Greenish-yellow to greenish-brown, with a fennel-like odor. The elements of identification are the tissues of glycyrrhiza and senna.

"Place 0.1 Gm. of Compound Powder of Glycyrrhiza in a test tube, moisten it with 2 cc. of alcohol, add 10 cc. of water, boil the mixture, cool, and filter. The filtrate is of a pale yellowish-brown color, which changes immediately to a yellowish-red on the addition of a drop of potassium hydroxide T.S.

"Compound Powder of Glycyrrhiza should be free from an odor of hydrogen sulphide." *U. S.*

The modification of this formula introduced by the U. S. in 1890, of using the oil instead of the fruit of fennel, is of advantage because of the greater uniformity of the product.

It would not seem *a priori* probable that the small amount of sulphur represented in an ordinary dose of this powder could perceptibly modify the laxative effect of the senna. Nevertheless the mixture is one of our most efficient and agreeable laxatives for the relief of habitual *constipation;* usually acting without much griping. It is a favorite laxative in *hemorrhoids* because of the softness of the movements usually produced. It may be conveniently taken by stirring up in a couple of ounces of water.

Dose, thirty to sixty grains (2.0–3.9 Gm.).

PULVIS IPECACUANHÆ ET OPII.
U. S. (Br.)

POWDER OF IPECAC AND OPIUM Pulv. Ipecac. et Opii [Compound Powder of Ipecac, Dover's Powder, Opii et Ipecacuanhæ pulvis compositus P. I.]

Pulvis Ipecacuanhæ Compositus, *Br., U. S.* 1870; Compound Powder of Ipecacuanha; Pulvis Doveri; Poudre d'Ipécacuanha Opiacée, *Fr. Cod.;* Poudre de Dover, *Fr.;* Pulvis Ipecacuanhæ Opiatus, *P. G.;* Doversches Pulver, *G.;* Polvere di oppio e di ipecacuana, Polvere del Dower, *It.;* Polvo de ipecacuana opiado, Polvo de Dower, *Sp.*

"Ipecac, in very fine powder, 10 Gm.; Powdered Opium, 10 Gm.; Lactose, in coarse powder, 80 Gm.; to make 100 Gm. Triturate the ingredients together thoroughly until the mixture is reduced to a very fine, uniform powder." *U. S.* "Ipecacuanha Root, in powder, 10 *grammes;* Opium, in powder, 10 *grammes;* Potassium Sulphate, in powder, 80 *grammes.* Mix. This Powder contains 10 per cent. of Opium." *Br.*

Description and Physical Properties.—"Grayish-white or very light brown; exhibiting coarse, angular, frequently more or less cone-shaped colorless fragments from 0.03 to 0.40 mm. in length, very slowly soluble in water and chloral hydrate T.S. and strongly polarizing light with a strong display of color (*fragments of lactose*); other elements of identification are the tissues of ipecac and the capsules of opium poppy." *U. S.*

The substitution of powdered sugar of milk for potassium sulphate in crystals as formerly used cannot be said to have improved this well-known powder, except in making it more agreeable to the taste. The U. S. process should have directed the powder to be sifted, in order to secure a thorough blending of the ingredients; the sifting should on no account be omitted by the operator. The potassium sulphate or the crystalline sugar of milk serves to promote that minute division and consequent thorough intermixture of the opium and ipecacuanha upon which the peculiar virtues of the compound depend, the potassium sulphate being preferable on account of the greater hardness of its particles. They also serve to dilute the active ingredients, and thus allow of their division into minute doses adapted to the complaints of children. This composition, though called Dover's Powder, does not precisely correspond with that originally recommended by Dover, which was prepared as follows: Four ounces of potassium nitrate and the same quantity of potassium sulphate were mixed in a red hot crucible, and afterwards very finely powdered; one ounce of opium, sliced, was then added, and ground to powder with the saline mixture; lastly, an ounce of ipecac with an ounce of licorice root, in powder, were mixed with the other ingredients. This process was adopted in a former French Codex, and has been retained with little change in the present. For a method of valuing Dover's Powder, by A. B. Prescott, see *A. J. P.,* Dec., 1878.

Uses.—This combination is widely employed under the name of Dover's Powder as a diaphoretic and sedative. It is especially prized in the early stages of the milder infections, such as *colds* and *influenza,* in which an effort is to be made to abort the disease by sweating. Because of its combination of sudorific and analgesic action it is also frequently employed in *muscular rheumatism.* Ordinarily as a sudorific about five grains should be administered either stirred up in water or as a bolus and preferably in connection with hot drinks and other measures for encouraging sweating. The dose may be repeated in four to six hours, when it is desirable to maintain a continued sudorific action.

Dose, three to ten grains (0.2–0.65 Gm.).

Off. Prep.—Pilula Ipecacuanhæ cum Scilla, *Br.*

PULVIS JALAPÆ COMPOSITUS.
U. S., Br.

COMPOUND POWDER OF JALAP Pulv. Jalap. Co.

Pulvis Purgans, Pulvis Jalapæ Tartratus, Pulvis Catharticus; Poudre de Jalap composée, *Fr.;* Jalapenpulver mit Weinstein, *G.*

"Jalap, in very fine powder, 35 Gm.; Potassium Bitartrate, in fine powder, 65 Gm.; to make 100 Gm. Mix the powders intimately by trituration and pass the product through a No. 60 sieve." *U. S.*

"Jalap, in powder, 30 *grammes;* Acid Potassium Tartrate, in powder, 60 *grammes;* Ginger, in powder, 10 grammes. Mix." *Br.*

Properties.—"Very light brown; when examined under a microscope it exhibits numerous, sharp-angular, colorless fragments mostly somewhat rectangular and with straight edges varying from 0.03 to 0.3 mm. in length, slowly soluble in water or hydrated chloral T.S. and polarizing light with a strong display of colors (fragments of crystals of *potassium bitartrate*); numerous starch grains of jalap, readily distinguished without the use of iodine T.S., usually single, occasionally 2- to 3-compound, and varying from 0.003 to 0.035 mm. in diameter; occasional fragments of laticiferous vessels and parenchyma with yellowish-brown walls, or tracheæ with bordered pores, and rosette aggregates of calcium oxalate from 0.01 to 0.035 mm. in diameter, that occur in jalap." *U. S.*

The rubbing of the bitartrate with the jalap is thought to favor its more minute division. Aside from this physical effect, the potassium bitartrate is calculated to increase the hydragogue action of the jalap and the powder is consequently employed chiefly in the treatment of *dropsies.* The proportion of bitartrate, however, is too small to exert any decided cathartic effect; a drachm of the powder would represent less than forty grains of the cream of tartar.

Dose, thirty to sixty grains (2.0–4 Gm.).

PULVIS KALADANÆ COMPOSITUS. Br.

COMPOUND POWDER OF KALADANA

"Kaladana, in powder, 30 *grammes;* Acid Potassium Tartrate, in powder, 60 *grammes;* Ginger, in powder, 10 *grammes.* Mix." *Br.*

This powder is used as a cathartic.

Dose, from ten to sixty grains (0.65–3.9 Gm.).

PULVIS KINO COMPOSITUS. Br.

COMPOUND POWDER OF KINO

Pulvis Kino et Opii Compositus, Compound Powder of Kino and Opium; Pulvis Kino cum Opio, *Br.* 1864; Powder of Kino and Opium; Poudre de Kino Opiacée, *Fr.;* Kinopulver mit Opium, *G.*

"Kino, in powder, 75 *grammes;* Opium, in powder, 5 *grammes;* Cinnamon Bark, in powder, 20 *grammes.* Mix. This Powder contains 5 per cent. of Opium." *Br.*

This is an anodyne astringent powder, useful in some forms of *diarrhea,* but of which the composition would be better left to extemporaneous prescription, as the proportion of the ingredients should vary with the circumstances. Twenty grains contain one grain of opium.

Dose, from five to twenty grains (0.32–1.3 Gm.).

PULVIS OPII COMPOSITUS. Br.

COMPOUND POWDER OF OPIUM

Poudre d'Opium composée, *Fr.;* Zusammengesetztes Opiumpulver, *G.*

"Opium, in powder, 10 *grammes;* Black pepper of commerce, in powder, 15 *grammes;* Ginger, in powder, 30 *grammes;* Caraway Fruit, in powder, 42 *grammes;* Tragacanth, in powder, 3 *grammes.* Mix. This Powder contains 10 per cent. of Opium." *Br.*

This seems to have been introduced in order to have at hand all the dry ingredients of the Confection of Opium. (See *Confectio Opii.*) Ten grains (0.65 Gm.) of the powder contain one grain (0.065 Gm.) of opium.

Dose, from five to fifteen grains (0.3–1 Gm.).

PULVIS RHEI COMPOSITUS. U. S., Br.

COMPOUND POWDER OF RHUBARB Pulv. Rhei Co. [Gregory's Powder]

Magnesia and Rhubarb, Gregory's Powder; Poudre de Rhubarbe composée, *Fr.;* Pulvis Magnesiæ cum Rheo, *P. G.;* Kinderpulver, Pulvis Infantum, s. P. Antacidus, *G.*

"Rhubarb, in very fine powder, 25 Gm.; Magnesium Oxide, 65 Gm.; Ginger, in very fine powder, 10 Gm.; to make 100 Gm. Triturate the rhubarb and ginger together, gradually add the magnesium oxide, continuing the trituration until the ingredients are thoroughly mixed, and finally pass the product through a No. 60 sieve." *U. S.*

"Rhubarb Root, in powder, 22 *grammes;* Light Magnesia, 66 *grammes;* Ginger, in powder, 12 *grammes.* Mix." *Br.*

Description and Physical Properties.—"A pinkish-white, mobile powder, becoming darker on exposure to moisture; it exhibits fine particles of magnesium oxide, numerous starch grains and characteristic fragments of tissues of ginger and rhubarb.

"Preserve in well-closed containers." *U. S.*

This is a good laxative antacid, well adapted to *bowel complaints,* especially in children.

Dose, for an adult, from one-half to one drachm (2.0–3.9 Gm.); for a child two or three years old, from five to ten grains (0.32–0.65 Gm.).

PULVIS SCAMMONIÆ COMPOSITUS. Br.

COMPOUND POWDER OF SCAMMONY

"Scammony Resin, in powder, 50 *grammes;* Jalap, in powder, 35 *grammes;* Ginger, in powder, 15 *grammes.* Mix." *Br.*

This does not appear to us a very eligible preparation.

Dose, from ten to twenty grains (0.65–1.3 Gm.).

PULVIS TRAGACANTHÆ COMPOSITUS. Br.

COMPOUND POWDER OF TRAGACANTH

"Tragacanth, in powder, 15 *grammes;* Gum Acacia, in powder, 20 *grammes;* Starch, in powder, 20 *grammes;* Refined Sugar, in powder, 45 *grammes.* Mix." *Br.*

This is applicable to the general purposes of the demulcents, but is chiefly employed in Great Britain as a vehicle for heavy insoluble powders.

Dose, one-half to one drachm (2.0–3.9 Gm.).

PUMEX. N. F.

PUMICE

"A substance of volcanic origin, consisting chiefly of complex silicates of aluminum, potassium, and sodium." *N. F.*

Pumice Stone; Ponce, Pierre Ponce, *Fr.;* Bimstein, *G.;* Pomice, *It.*

Pumice is a porous volcanic rock. Its spongy structure is believed to be due to the effects of aqueous vapor on the lava while still in a fluid state. While it is found in many volcanic sections, the bulk of the commercial supply comes from the Lipari Islands off the coast of Italy. Pumice also occurs in large areas in the western part of the United States and over 10,000 tons annually are produced in Nebraska. Because of its porous structure it is so light that it usually will float in water for some time, but eventually becomes waterlogged and sinks.

It is brittle and hard and relatively easily pulverized. Because of its hardness it is much used in the arts as an abrasive, either in the original form for removing the outer surfaces of bodies or "rubbing down" any inequalities, or in a powdered condition as the basis of metal polish.

Pumice is really a porous form of *obsidian*, which occurs usually in glassy form, and obsidian has been converted into pumice by heat. Volcanic lavas of various types may assume the porous form corresponding to pumice, but it is only those rich in silica that yield pumice of economic value. The sp. gr. of powdered pumice is about 2.3. The composition of pumice averages about as follows: Silica 70 to 75 per cent., iron and alumina oxides 15 to 20 per cent., calcium, magnesium, potassium and sodium compounds, traces.

Pumice was admitted to the National Formulary for use in several preparations to assist in distributing the particles of extracts, tar and resins to facilitate solution. It is described as follows:

Description and Physical Properties.—"Pumice occurs as very light, hard, rough porous gray mases, or as a gritty, gray-colored powder. It is permanent in the air, odorless and tasteless. The dry masses usually float on water.

"Boil 10 Gm. of Pumice with 50 cc. of distilled water for one-half hour, adding distilled water from time to time to maintain approximately the original volume and then filter; the filtrate is neutral to litmus, and one-half of this filtrate, when evaporated and the residue dried to constant weight at 110° C., yields not more than 0.01 Gm. of residue (*soluble substances*). The remaining half of the filtrate, after slightly acidulating with hydrochloric acid, does not yield a blue color with potassium ferrocyanide T.S. (*iron*). Boil 1 Gm. of Pumic with 25 cc. of diluted hydrochloric acid for one-half hour, adding distilled water from time to time to maintain approximately the original volume, and then filter the liquid; the filtrate yields upon evaporating to dryness, igniting and quickly weighing, not more than 0.05 Gm. of residue." *N. F.*

Pumice is official solely for pharmaceutical purposes.

PYRETHRI RADIX. Br.

PYRETHRUM ROOT

"Pyrethrum Root is the dried root of Anacyclus Pyrethrum *DC*." *Br.*

Pyrethrum, *U. S. IX;* Pellitory; Radix Pyrethri Romani; Spanish Chamomile, Longwort, Pellitory; Pyrèthre, P. vrai, Salivaire, *Fr.;* Bertramwurzel, Römische Bertramwurzel, *G.;* Pelitre (Raiz de), *Sp.*

Anacyclus Pyrethrum is a perennial, composite herb with a long fusiform root which sends up numerous stems, usually trailing at the base, erect in the upper portion, eight or ten inches high, and terminated by one large flower head. The leaves are doubly pinnate, with narrow, nearly linear segments of a pale-green color. The florets of the disk are yellow; the rays white on their upper surface, and reddish or purple beneath and at their edges. The fruit is an obovate achene with a short pappus.

The plant is a native of Northern Africa and is cultivated widely as an ornamental herb in gardens. The root is the part used under the name of pellitory, or *pellitory of Spain.* It is collected in autumn from plants growing in Algeria, and exported either direct or through France to Great Britain and the United States.

The German Pharmacopœia formerly recognized the root of *Anacyclus officinalis* Hayne (*A. Pyrethrum* Schrader), a plant cultivated in Magdeburg. The roots are smaller and thinner, attaining a length of 25 cm. and a thickness of 5 cm. They are externally grayish-brown; the bark is not radiating and does not contain many stone cells, such as are present in the official pyrethrum. The taste resembles that of the official drug but is even more pungent.

Properties.—Pyrethrum is officially described as "usually from five to ten centimetres long, and from ten to fifteen millimetres thick; unbranched, nearly cylindrical, or frequently tapering towards both extremities; the crown often bearing a tuft of nearly colorless hairs. Outer surface brown and longitudinally wrinkled. Fracture short. In transverse section, numerous, narrow, yellowish wood-bundles alternating with wider, brownish-grey medullary rays; in the cortex and medullary rays scattered, yellowish-brown oleo-resin ducts; in the parenchymatous tissue inulin, but no starch. Characteristic odor; taste pungent, salivant." *Br.*

The U. S. IX described the powder as "light to dark brown; when examined under the microscope it exhibits numerous spherical or irregular masses of inulin, the nature of which is especially seen with polarized light, and lignified fragments of the woody tissues and stone cells associated with cork; inulin in spherical granules or irregular masses, from 0.01 to 0.1 mm. in diameter, which is not affected by the addition of iodine T.S.; tracheæ with simple pores and reticulate or scalariform thickenings, usually associated with wood parenchyma and with few or no wood fibers; stone cells in groups, the cells more or less tabular in outline, and with thick, yellowish porous walls; cork in yellowish-brown or dark brown fragments. Pyrethrum yields not more than 5 per cent. of ash." *U. S. IX.*

Buchheim (*A. E. P. P.*, 1876, v) discovered an alkaloid, *pyrethrine,* to which the activity of the drug may be attributed. Pyrethrine when treated with alcoholic potassium hydroxide, splits up like piperine, and yields *piperidine* and *pyrethric acid.* Schneegans (*Proc. A. Ph. A.*, 1897, 736) has obtained pyrethrine in long branched needles united in tufts, melting at 46° C., with an extremely burning taste. It is soluble in absolute alcohol, acetone, ether, strong acetic acid, chloroform, and carbon disulphide, yields a yellow solution, which soon changes to red. *Pellitorin* of Dunstan and Garnett is probably identical with pyrethrine.

The chief adulterant of *pellitory* has been the root of *Corrigiola littoralis* L. (Fam. *Illecebraceæ*). It may be readily distinguished from the true pellitory root by exhibiting warty protuberances on its crown, by its cross section which exhibits 3 or 4 pale concentric circles, each alternating with a narrower translucent horny ring and by its absence of pungency.

Uses.—Pellitory is a powerful irritant, used almost exclusively as a masticatory in certain forms of *headache, rheumatic* and *neuralgic affections* of the face, *toothache,* etc., or as a local stimulant, in relaxation of the uvula. It is very rarely employed to-day. Its action upon the general system has not been studied to any extent, but 50 minims of a tincture of it very nearly killed a child three and a half years old. The symptoms were those of gastro-enteritis, followed by convulsions. (*London Practitioner,* Aug., 1876.)

Off. Prep.—Tinctura Pyrethri, *Br.*

PYROGALLOL. U. S.

PYROGALLOL Pyrogall. [Pyrogallic Acid]

"Trihydroxybenzene [$C_6H_3(OH)_3$ 1 : 2 : 3]." *U. S.*

Acidum Pyrogallicum; Trihydroxybenzene; Pyrogallol, *Fr. Cod.;* Acide Pyrogallique, *Fr.;* Pyrogallolum, *P. G.;* Pyrogallussäure, *G.;* Pirogallol, *It.*

This substance, although often called pyrogallic acid, is a triatomic phenol, $C_6H_3(OH)_3$, and not an acid at all; hence the change in the official title to "Pyrogallol." Of the three triatomic phenols indicated by theory, this is the best known, *phloroglucin* and *oxyhydroquinone* being the other two. It may be prepared synthetically, but is usually obtained as one of the results of the decomposition of gallic acid by heat, and may be obtained by submitting extract of galls to sublimation, the reaction produced by the heat being:

$$C_7H_6O_5 = C_6H_6O_3 + CO_2$$

The vapors of pyrogallol rise, and condense on the upper surface of the paper diaphragm. The chief difficulty in the process is to properly regulate the heat, as at a high temperature this acid passes rapidly into *metagallic acid,* and thus the product is diminished. When previously dried gallic acid is heated to 210° C. pure pyrogallol sublimes, but by this dry process much of the product is lost because of the rapidity with which pyrogallol decomposes at high temperatures; the yield is only about 25 per cent. when theoretically it should be nearly 75 per cent. De Luynes and Espandieu have succeeded in preventing this loss by decomposing gallic acid in water under pressure, instead of by dry sublimation. Gallic acid is introduced into a bronze boiler with twice or three times its weight of water; the temperature is raised to a point ranging from 200° C. to 210° C., and maintained at that point for half an hour, when the liquid is allowed to cool. The boiler now contains a slightly colored solution of pyrogallol. This is heated with a little pure animal charcoal, filtered, evaporated sufficiently, and set aside to crystallize. The crystalline mass obtained is somewhat colored. To obtain it entirely white, nothing more is necessary than to distil it in a vacuum. The carbon dioxide escapes through the joinings of the apparatus, while the aqueous vapor is retained. Another equally satisfactory procedure is that of Thorpe, for details of which see *A. J. P.*, 1881, p. 53, 236.

Description and Physical Properties.—"Light, white, or nearly white, odorless leaflets or fine needles. It acquires a grayish tint on exposure to air and light. One Gm. of Pyrogallol is soluble in 1.7 cc. of water, in 1.3 cc. of alcohol, and in 1.6 cc. of ether, at 25° C. It is very soluble in boiling water and in boiling alcohol.

"Pyrogallol melts between 130° and 133° C. An aqueous solution of Pyrogallol on exposure to air acquires a brown color and an acid reaction due to oxidation by the air. Absorption of oxygen and change of color take place very rapidly after the solution is rendered alkaline with an alkali hydroxide. An aqueous solution of Pyrogallol (1 in 10) reduces solutions of the salts of silver, gold, and mercury even in the cold. When freshly prepared 1 cc. of an aqueous solution of Pyrogallol (1 in 20) is colored brownish-red by a few drops of ferric chloride T.S. Freshly prepared ferrous sulphate T.S. produces a blue color in an aqueous solution of Pyrogallol (1 in 20).

"Ash: not more than 0.1 per cent. A freshly prepared solution of Pyrogallol (1 in 20) in recently boiled, distilled water is colorless or at most slightly yellow, and is neutral or only slightly acid to litmus paper.

"Preserve in well-closed containers, protected from light." *U. S.*

According to Rosing, of Christiana, it is always partially converted, when sublimed, into metagallic acid, to which probably it owes its acid reaction as generally found in commerce; for when quite pure it has no influence on litmus paper. One of its characteristic properties is its strong affinity for oxygen, in consequence of which it instantly undergoes change by contact with chlorine, iodine, bromine, and the acids which readily yield oxygen. Through the same property it rapidly reduces some of the metallic oxides, and its use in photography as a developing agent is based on this effect exercised on the salts of silver. Though unalterable in the air when quite dry, it is rapidly changed in alkaline solution by the absorption of oxygen, so that it may be used for ascertaining the proportion of this gas in a mixture of gases. Pyrogallol forms salts with bases but its acidic characters are not pronounced and the salts are quite unstable. In acid or neutral solutions it oxidizes to form *purpurogallol*, $C_{20}H_{16}O_9$, which crystallizes from alcoholic solution in brown needles, melting point 156°, insoluble in water and soluble in alkalies to form unstable blue compounds. In alkaline solutions the oxidation products are more difficult of identification. A dark brown water-soluble compound is produced, having the composition $C_{20}H_{20}O_{16}$, and a dark red crystallizable substance, soluble in ether, containing $C_{20}H_{20}O_{11}$, and related to purpurogallol. By the action of phthalic anhydride upon pyrogallol is formed *gallein*, a dye color much used in calico printing. By the action of glacial acetic acid upon pyrogallol in the presence of zinc chloride is formed gallacetophenone, $CH_3—CO—C_6H_2(OH)_3$, which has been used in medicine as a substitute for pyrogallol.

Uses.—Pyrogallol is an active irritant and in concentrated solution even caustic. It is somewhat germicidal, though distinctly inferior to phenol in power; according to Cooper (*B. M. J.*, 1912, i, 1235), its phenol coefficient is 0.8. When taken internally it is actively poisonous, its toxic effect being due in part to its local irritant action upon the alimentary tract, but also partly from a phenol-like action upon the central nervous system and a destructive effect upon the blood corpuscles. It causes a solution of the hemoglobin from the latter and a change of hemoglobin into methemoglobin, which, if death does not occur too soon, is manifested by the appearance of icterus and methemoglobinuria.

The toxic symptoms produced by it are vomiting and purging with collapse, pale or cyanosed lips, the skin often presenting a peculiar greenish hue or sometimes jaundiced; the urine is albuminous and may be brown or black from the presence of hemoglobin or methemoglobin. Fatty degenerations and enlargement of the liver, similar to those produced by phosphorus, have been noted by Personne. (*C. R. A. S.*, Oct., 1869.)

Even its external use is not devoid of danger, two deaths having been reported from its topical application, and Kuseh (*W. K. W.*, 1909) reports abortion in pregnant women from a 10 per cent. ointment.

Pyrogallol is used in medicine solely as an application in various skin diseases, especially *psoriasis*. In this condition it owes its therapeutic action probably to its reducing powers, although its local stimulating effect and antibacterial properties may also play a part in its usefulness. It is occasionally used in *lupus* for its caustic action. For medical purposes it is generally applied in the form of an ointment varying in strengths of from two to ten per cent.

PYROXYLINUM. U. S., Br.

PYROXYLIN Pyroxylin. [Soluble Gun Cotton]

"Pyroxylin is a product obtained by the action of a mixture of nitric and sulphuric acids on cotton, and consists chiefly of cellulose tetranitrate [$C_{12}H_{16}O_6(NO_3)_4$]." *U. S.*

Pyroxylon, *U. S.* 1870; Colloxylin, Gun Cotton, Collodion Cotton; Gossypium Igniarium; Fulmicoton soluble, *Fr.*; Schiessbaumwolle, Kollodiumwolle, *G.*; Piroxilina, *Sp.*

The U. S. X gives no process for this; that of the Br. is as follows:

"Cotton, 10 *grammes;* Sulphuric Acid, 50 *millilitres;* Nitric Acid, 50 *millilitres;* Distilled Water, *a sufficient quantity.* Mix the acids in a porcelain mortar; immerse the Cotton in the mixture, and after it is thoroughly wetted by the Acids stir it for three minutes with a glass rod; transfer it to Distilled Water, wash until free from acid, drain, and dry the Pyroxylin in a warm room." *Br.*

The present process of the Br. is better than that formerly recommended employing potassium nitrate and sulphuric acid. The method of the U. S. 1890 differed from the above chiefly in using a larger proportion of acids, and in directing that the maceration of the cotton be continued until the product was soluble in a mixture of one volume of alcohol and three of ether. For details of this and other methods see *U. S. D.*, 19th ed., p. 1030.

Gun cotton was discovered by Schönbein, of Basel, in Switzerland. The name is applied to several closely related, yet distinct, products. They are not, as was at first supposed, nitro-derivatives in which the group NO_2 merely replaces hydrogen, atom for atom, but compounds in which the nitric acid residue NO_3 is present, replacing OH groups of the cellulose formula. Thus, taking the doubled formula $C_{12}H_{20}O_{10}$ for cellulose, there is produced by the action of nitric acid under different circumstances $C_{12}H_{14}O_4(NO_3)_6$, and following this, successively, $C_{12}H_{15}O_5(NO_3)_5$, $C_{12}H_{16}O_6(NO_3)_4$, $C_{12}H_{17}O_7(NO_3)_3$, and $C_{12}H_{18}O_8(NO_3)_2$. The first of these, the hexanitrate, is insoluble in alcohol and ether, and constitutes the true explosive gun cotton. The soluble gun cotton used in the preparation of *collodium* is a varying mixture of the four lower nitrates, but is chiefly made up of the tri- and tetra-nitrates. The hexanitrate, when very thoroughly washed free from acid, is insoluble in water, alcohol, ether, and all mixtures of alcohol with ether. It constitutes the true explosive gun cotton, which when compressed in cakes and fired by a fulminate explodes with great violence. Other compounds intermediate between some of these have been described by different chemists, but Abel, the chemist of the Woolwich Arsenal in England, has shown that they were imperfectly purified preparations.

Description and Physical Properties.—"A yellowish-white, matted mass of filaments, resembling raw cotton in appearance, but harsh to the touch. It is exceedingly inflammable, burning, when unconfined, very rapidly and with a luminous flame. When kept in well-closed bottles and exposed to light, it is decomposed with the evolution of nitrous vapors, leaving a carbonaceous residue.

"Pyroxylin is slowly but completely soluble in 25 parts of a mixture of 3 volumes of ether and 1 volume of alcohol. It is soluble in acetone and in glacial acetic acid and is precipitated from these solutions on the addition of water.

"Saturate 0.5 Gm. of Pyroxylin with alcohol in a dish placed in cold water and ignite the Pyroxylin at the top. When combustion is complete and the dish heated to redness, no more than 0.3 per cent. of ash remains. Stir 1 Gm. of Pyroxylin with 20 cc. of distilled water for ten minutes and filter: the filtrate does not acquire an acid reaction. Evaporate 10 cc. of the filtrate from the preceding test to dryness on a water bath: not more than 0.0015 Gm. of residue remains (*soluble substances*).

"Preserve in cartons, packed loosely, and protected from light and moisture." *U. S.*

"Resembles cotton-wool, but is somewhat harsher to the touch. Highly inflammable. Readily soluble in a mixture of equal volumes of *alcohol* (90 per cent.) and *ether* (distinction from gun-cotton)." *Br.*

When kept for long periods, gun cotton is liable to spontaneous decomposition. The change is shown by the bottle in which the gun cotton is kept becoming full of nitrous acid vapor, and the substance is so far altered that it is no longer explosive or soluble in ether. The official direction to keep pyroxylin "in cartons, protected from the light" is a valuable precaution against decomposition. When kindled, gun cotton flashes off like gunpowder, burning without residue. Yet, according to Bleekrode, when wet with ether, or similar fluid, and touched with a light, the liquid will burn out of it without firing it. (*J. P. C.*, 4e sér., xviii.) Its inflaming point is at 187.7° C.

Prepared in various forms after acting upon it with solvents like amyl acetate, etc., to convert it into a plastic mass, the higher nitrates constitute the well known "smokeless powders" now so largely used in warfare. Pyroxylin, or soluble gun cotton, is now extensively used as the basis of transparent varnishes for lacquering metal and wood. When mixed with camphor it forms the combination known as *celluloid* which is plastic under certain conditions of temperature and pressure. The solvent employed is usually a mixture of methyl alcohol or acetone with petroleum benzin, the miscibility of which is affected by the addition of small quantities of compound ethers like amyl acetate. In medicine it is used as a protective covering, especially in the form of collodion.

Off. Prep.—Collodium, *U. S., Br.*

QUASSIA. U. S. (Br.)

QUASSIA Quass. [Bitter Wood]

"Quassia is the wood of *Picrasma excelsa* (Swartz) Planchon, known in commerce as Jamaica Quassia, or of *Quassia amara* Linné, known in commerce as Surinam Quassia (Fam. *Simarubaceæ*)." *U. S.* "Quassia Wood is the wood of the trunk and branches of Picræna excelsa, *Lindl.*" *Br.*

Quassiæ Lignum, *Br.;* Jamaica Quassia, Quassia Wood; Bitter Wood; Bitter Ash; Quassia Amara, *Fr. Cod.;* Quassie Amère, Bois amer de Surinam, Bois de Quassie, *Fr.;* Lignum Quassiæ, *P. G.;* Quassiaholz, Fliegenholz, *G.;* Quassia, Quassia della Giammaica, *It.;* Cuasia (Leno de), *Sp.*

The genus *Picrasma* is represented by eight species, which are found in the warmer regions of the Old and New World. They all possess a bitter wood and bark.

Picrasma excelsa (Swartz) Planchon (*Picræna excelsa* Lindley), as its name implies, is a lofty tree, sometimes attaining the height of not less than one hundred feet, with a straight, smooth tapering trunk, which is often three feet in diameter near its base, and is covered with a smooth, gray bark. The leaves are pinnate, the leaflets being petiolate and oblong pointed and arranged in opposite pairs, with a single leaflet at the end. The flowers are small, of a yellowish-green color, and disposed in panicles. They are polygamous and pentandrous. The fruit is a small black drupe. This species inhabits Jamaica and the Caribbean Islands, where it is called *bitter ash.* Most of the commercial quassia is obtained from this tree.

Quassia amara L. (*Picræna amara*), or bitter quassia, is a small tree or shrub, with alternate, imparipinnate leaves, consisting of two pairs of opposite leaflets, with an odd one at the end. The leaflets are elliptical, pointed, sessile, smooth, of a deep green color on their upper surface, and paler on the under. The common petiole is articulated and winged. The flowers, which are hermaphrodite and decandrous, are bright red, and terminate the branches in long racemes. The fruit is a two-celled capsule containing globular seeds. *Quassia amara* is a native of Surinam, and is found in Brazil, Guiana, Colombia, Panama, and the West Indies, as also in some tropical countries of the Old World. Its root and bark were formerly official. They are excessively bitter, as in fact are all parts of the plant. For the botanical description and history of *Quassia amara,* see J. U. Lloyd, *West. Drug.,* 1897, 7; also Gilling (*P. J.,* 1908, lxiii, p. 30).

About 225,000 pounds of quassia were imported into the United States in 1924 from Kingston and St. Ann's Bay, Jamaica, and from

Hamburg and London. The drug imported from Jamaica comes in the form of logs which are used in the manufacture of "quassia" or "tonic cups." The waste shavings and chips are then sold to the drug trade. The drug from Hamburg is milled into "cut quassia" and occurs in irregular cubes.

Quassia is at first whitish, but becomes yellow by exposure, and sometimes has blackish spots or markings, due to the presence of the mycelium of a fungus. The two varieties are thus officially described:

Description and Physical Properties.—"*Unground Jamaica Quassia.*—Usually in chips, raspings or shavings, occasionally in billets; yellowish-white or bright yellow, with a few light gray pieces; somewhat coarsely grained; fracture tough, fibrous; odor slight; taste very bitter.

"*Structure.*—Tracheæ large, occasionally with yellowish contents, usually in groups of 2 to 6 and surrounded by numerous wood fibers; medullary rays lignified, mostly 1 to 5 cells wide and from 10 to 20 rows deep; lignified parenchyma cells in interrupted tangential bands and containing calcium oxalate or starch grains.

"*Unground Surinam Quassia.*—Resembles Jamaica Quassia except that the billets are usually thinner, the tracheæ single or in pairs and smaller, the medullary rays usually 1 to 2 cells wide and from 10 to 30 rows deep, and the calcium oxalate crystals few or entirely absent.

"*Powdered Quassia.*—Pale yellow; containing fragments of tracheæ, the walls marked by numerous small, bordered pores; wood fibers with thin walls and oblique pores; medullary-ray and parenchyma cells with numerous pores; calcium oxalate in 4- to 6-sided prisms, from 0.006 to 0.030 mm. in length, sometimes in crystal fibers; starch grains few, spherical or ellipsoidal, and from 0.005 to 0.015 mm. in diameter." *U. S.*

The Br. recognizes only the Jamaica quassia which it describes as follows: "In logs of varying length, or in chips or raspings; yellowish white, tough and dense, but easily split. In longitudinal section, elongated cells containing single crystals of calcium oxalate; in transverse section, medullary rays mostly two or three cells wide. No odor; taste intensely bitter." *Br.*

Constituents.—The chemistry of quassia seems to merit further study. It is apparently well established that the active principles of the Jamaica quassia and of the Surinam variety are different. According to Massute (*A. J. P.*, 1890, p. 338), the Jamaica quassia (*Picrasma excelsa*) contains two related compounds—*alpha-picrasmine* and *beta-picrasmine*, which are neither alkaloids nor glucosides. The first named was in needles, melted at 204° C., and had the composition $C_{35}H_{46}O_{10}$, while the other was in prisms, melted at 209° to 212° C., and had the composition $C_{36}H_{48}O_{10}$. Both of these are homologues of a third crystalline principle, $C_{29}H_{34}O_{10}$, melting point 212° to 216° C., which occurs with them.

Alpha-picrasmine when heated with hydrochloric acid is changed into an acid substance, *picrasmic acid*, which has the formula $C_{33}H_{42}O_{10}$.

In addition to these bitter principles, there is present also a small amount of a yellow crystalline substance which imparts a blue fluorescence to acidulated alcohol.

The Surinam quassia contains, apparently, a homologous series of four bitter substances. The term *quassin* (*quassiin*) is sometimes applied to the mixture of these bitter principles, but more properly should be limited to the more abundant of these principles. This occurs in the form of colorless crystals freely soluble in alcohol or chloroform, sparingly soluble in water or ether. Its solutions are intensely bitter, rotate polarized light to the right, reduce Fehling's solution and tend to become yellowish on exposure to the air. The crystals melt at 210° to 211° C. Oliveri and Denaro (*A. J. P.*, 1885, p. 29) assert that when heated with hydrochloric acid it is demethylated, forming *quassic acid*. They assign to this compound the formula $C_{32}H_{44}O_{10}$, but Massute gives the formula as $C_{32}H_{40}O_{10}$. Of the other principles, according to Massute, one melted at 239° C. to 242° C.; this was in too small quantity to be further studied. A third principle melted at 215° to 217° C. and the fourth at 221° to 226°. Besides these four principles there is present also a yellow fluorescent principle mentioned under picrasmine. Oliveri and Denaro believe that quassin is a derivative of anthracene. Dymock and Warden believe that they have obtained quassin from the wood of *Picrasma quassioides* (Ham.) Benn. of India.

Uses.—Quassia was introduced into medicine about the middle of the 18th century by a negro of Surinam, named Quassi, who acquired considerable reputation in the treatment of the malignant fevers of that country by a secret remedy, which he was induced to disclose to Rolander, a Swede, for a valuable consideration. Specimens were taken to Stockholm by this gentleman in the year 1756, and the medicine soon became popular in Europe. The name of the negro has been perpetuated in the generic title of the plant. But the quassia of Surinam is now comparatively little used, it having been superseded by the product of *Picrasma excelsa* from the West Indies.

Quassia is among the most powerful of the simple bitters, useful in *failure of appetite* due to gastric debility, and in overdoses capable of sufficiently irritating the stomach to produce vomiting. Its active principle, *quassin*, has been studied by Comparden, who asserts that in moderate doses it acts as a stimulant to the salivary, hepatic and renal secretions, and in overdoses causes burning pain in the esophagus, with headache, nausea, vertigo, vomiting, diarrhea, and muscular cramps. It is also stated that if given in doses of six-tenths of a grain (0.04 Gm.) before meals it increases markedly the alvine discharges, and that it is especially useful in *constipation* from debility of the muscular and intestinal coats. On the other hand, Krogmann (*A. E. P. P.*, 1922, xciv, p. 97) finds that Simaruba bark is a depressant to involuntary muscle and recommends it in excessive intestinal peristalsis due to inflammatory states. The dose of pure quassin is from one-tenth to three-tenths of a grain (0.006–0.02 Gm.).

An infusion of quassia, two ounces in a pint of water, affords a valuable and safe injection for *seat-worms.*

Syrupus Quassiæ.—This syrup is used in the preparation of a harmless fly-poison. Macerate, during twenty-four hours, 1000 parts of quassia wood with 5000 parts of water, then boil for half an hour, set aside for twenty-four hours, and press; mix the liquid with 150 parts of molasses, and evaporate to 200 parts. A weaker decoction of quassia does not kill the flies. From this the *Fly Water* or *Fly Plate* is prepared as follows: Mix when needed, and dispense without filtering, 200 parts of syrup of quassia, 50 parts of alcohol, and 750 parts of water. It is used by moistening with the mixture a cloth or filtering paper on a plate.

Quassia is given in infusion, tincture, extract, or fluidextract. Some *dyspeptic* patients who have become habituated to its bitterness, chew the wood occasionally with benefit.

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Infusum Quassiæ, *Br.;* Tinctura Quassiæ, *Br.;* Fluidextractum Quassiæ, *N. F.*

QUERCUS. N. F.

QUERCUS Querc. [White Oak Bark]

"Quercus is the dried inner bark of the trunk and branches of *Quercus alba,* Linné (Fam. *Fagaceæ*). Quercus contains not more than 2 per cent. of its outer bark or wood or other foreign organic matter." *N. F.*

Oak; White Oak; Stone Oak; Ecorce de Chêne, *Fr.;* Cortex Quercus, *P. G.;* Eichenrinde, *G.;* Quercia, Corteccia de quercia, *It.*

There are more than fifty species of oak found in the U. S. Many of these are applied to important practical purposes. The official species known as the White Oak is a large handsome tree with leaves deeply pinnatifid-lobed. It is readily distinguished from other species by its light gray-colored, almost white bark which scales off in thin plates. The White Oak abounds from Maine to Ontario and southward to Florida and Texas. Its tough close-grained wood is the most highly valued of all the American oaks, except the live oak (*Q. virginiana* Mill.). The leaves are regular and obliquely divided into oblong, obtuse, entire lobes, which are often narrowed at their base. When full grown, they are smooth and light green on their upper surface, and glaucous beneath. Some of the dried leaves remain on the tree during the whole winter. The acorns are large oblong-ovoid or ellipsoidal, contained in rough, shallow, grayish cups, and supported singly or in pairs upon peduncles nearly 2.5 cm. in length.

The commercial supplies of oak bark used in the United States come largely from Michigan and Germany. The imported drug consists of cut and sifted bark and is shipped in bags. Other species of oak have been used in medicine, chiefly for their astringent properties. The *British oak* (*Quercus robur* L.) is widely distributed all over Europe and Northern Asia. There are two distinct varieties of it, one, *pedunculata,* with sessile or shortly stalked leaves and the acorns on long peduncles; the other, *sessiflora,* with the leafstalks more or less elongated and the acorns either sessile or provided with a very short peduncle. The dried bark of the smaller branches of the first variety (*Q. pedunculata* Willd.) were formerly recognized by the Br. Pharmacopœia (1885) under the name of *Quercus Cortex.*

The *Black Oak, Q. velutina* Lam. (*Q. tinctoria* Bartram), was official in the U. S. V. Like the white oak it contains much tannin, but is medicinally inferior because of its bitter taste and its staining properties. Its tinctorial powers are due to the presence of a peculiar coloring principle, *quercitrin.* The black oak has its trunk covered with a deeply furrowed bark, of a black or dark brown color. The leaves are ovate-oblong, pubescent, slightly sinuated with oblong, aculeate lobes. The fructification is biennial. The acorn is globose, flattened at top, and placed in a saucer-shaped cup. Moore (*Proc. Chem. Soc.,* 1910, xxvi, 183) assigned to quercitrin the formula $C_{21}H_{20}O_{11}.2H_2O$, and this is confirmed by Rudolph. (*Ph. Post,* 1893, 529.) The reaction for its decomposition is

$$C_{21}H_{20}O_{11} + H_2O = C_{15}H_{10}O_7 + C_6H_{12}O_5$$

the products being *quercetin* and rhamnose in equal molecules. Quercetin, also known as *meletin, quercitinic acid* and *flavin,* is a derivative of *flavone,* being a tetrahydroxyflavone. It is a brown crystalline powder, melting point 313° C. Soluble in alkaline solutions. Flavone is a phenyl derivative of *chromone.*

Quercitrin forms yellowish crystals, which, pulverized, yield a citron-yellow powder. It is neutral in reaction, is odorless, and in the dry condition tasteless, but in hot aqueous or alcoholic solution has a bitter taste. It fuses at 168° C. to a resinous mass. It is almost insoluble in cold water, sparingly soluble in hot water, and easily soluble in alcohol and alkaline or acid solution. Besides this principle, the bark contains much *quercitannic acid;* but it is less used in tanning than the other barks, in consequence of the color which it imparts to the leather. The bark of the black oak, deprived of its epidermis and reduced to a coarse powder, is largely used for dyeing woollen goods, under the name of *quercitron.*

Quercitrin has been found in various other plants, as in the leaves of *Ruta graveolens,* and the flower buds of *Capparis spinosa, Sophora japonica,* and *Æsculus Hippocastanum,* or horse chestnut. As this principle is capable of assuming various colors under various chemical influences, the idea has been advanced that it might be the coloring principle of flowers.

White oak bark, deprived of its epidermis, is of a light-brown color, of a coarse, fibrous texture, and not easily pulverized.

Description and Physical Properties.—"*Unground Quercus.*—In nearly flat pieces, from 2 to 10 mm. in thickness; externally light brown, becoming darker with age, rough-fibrous; fracture uneven, coarsely fibrous. Odor distinct; taste strongly astringent; not tingeing the saliva yellow when chewed.

"*Powdered Quercus.*—Light brown; fibers long, thick-walled, lignified from 0.015 to 0.033 mm. in width; numerous crystal fibers containing calcium oxalate in prisms from 0.010 to 0.050 mm. in diameter or in rosettes from 0.010 to 0.025 mm. in diameter; starch grains up to 0.010 mm. in diameter; stone cells with thick lamellated walls and simple pores up to 0.100 mm. in length; fragments composed of parenchyma with yellowish brown amorphous contents or of cork cells with a brownish amorphous content." *N. F.*

Constituents.—The medicinal value of oak bark depends on the presence of a peculiar tannin, known as *quercitannic acid,* of which it contains from 6 to 11 per cent. It belongs to the group of tannins that give brownish-green precipitates with ferric salts.

Lowe (*Zeit. An. Chem.,* xx, p. 208) says quercitannic acid occurs in two forms, one soluble in water and the other insoluble in that solvent. It is probable that all of the analyses of all of the earlier investigators were faulty because, as Trimble suggested, of the lack of authenticity of the extract used.

Etti (*M. Chem.,* x, 647) isolated from the wood of the Slavonian oak a tannin which proved to be a ketonic compound with the formula $C_{16}H_{14}O_9$. He was able to produce several anhydrides having the respective formulas $C_{32}H_{24}O_{16}$, $C_{32}H_{20}O_{14}$ and $C_{32}H_{18}O_{13}$. When boiled with dilute sulphuric acid a molecule of water is extracted from quercitannic acid with the formation of a coloring matter, *oak red.*

There is present also a small amount of a bitter principle, *quercin* $C_{15}H_{12}O_9$. The statement of Husemann that this is an impure quercite (a sugar found in acorns) seems improbable in view of the fact that quercite is sweet and quercin bitter. *Quercite* (*quercitol*), $C_6H_7(OH)_5$, is pentahydroxy-cyclohexane.

Acorns are highly nutritious containing besides starch, fat and protein, a peculiar unfermentable sugar known as *quercite.* Most of them are unfit for human food because of the presence of bitter principle, but some of the European species of oaks produce acorns free from bitterness, and it is stated that the American Indians employed even the native species, the bitter principle being removed by decoction.

Uses.—Oak bark is used in medicine solely as an astringent. It is not employed for internal use but affords a cheap astringent wash and is sometimes employed as an injection in *leucorrhea* or *hemorrhoids.*

Dose, fifteen grains (1 Gm.).

Off. Prep.—Fluidextractum Quercus, *N. F.*

QUILLAJÆ. N. F. (Br.)

QUILLAJA Quillaj. [Soap Tree Bark, Soap Bark]

"Quillaja is the dried inner bark of *Quillaja Saponaria* Molina (Fam. *Rosaceæ*). Quillaja contains not more than 5 per cent. of outer bark and not more than 1 per cent. of foreign organic matter." *N. F.*

"Quillaia Bark is dried inner part of the bark of Quillaja Saponaria *Molina.*" *Br.*

Quillæ Cortex, *Br.;* Quillaia Bark; Soaptree Bark; Soap Bark; Panama Bark; Bois de Panama; Ecorce de Quillaya, *Fr.* Cortex Quillayæ, *P. G.;* Seifenrinde, *G.*

The name of this genus is said to be derived from the popular name of the tree *Quillay,* which in turn comes from the Chilian word *quillean,* to wash.

Quillaja Saponaria Molina is a large polygamo-diœcious tree with alternate, short petiolate, ovate leaves with dentate margins, large white flowers and leathery follicular fruits occurring in clusters of 5. The bark is thick, the wood very hard. This tree was first described by the famous Abbé Giovanni Ignazio Molina in the *Saggio sulla Storia naturale del Chili,* published at Bologna, in 1782. The tree is a native of Chile, but is now cultivated in southern California and northern Hindostan.

Two spurious soap barks have appeared in commerce the botanical origins of which have not been definitely ascertained. One of these, thinner than the authentic article, with a reticulated outer surface, has been thought to be derived from *Quillaja Poeppigii* Walp. The second occurs in quills 7 to 15 cm. long, 1 to 2.5 cm. wide and about 3 mm. thick, is softer and not layered and is said to be derived from *Q. Smegmadermos* DC.

About 750,000 pounds of soap bark were imported into the United States during 1924. The chief bulk of the commercial supply comes from Valparaiso, Chile. The Chilean bark represents the crude inner bark and is shipped in burlap bags. Soap bark is also imported into the U. S. A. from Hamburg, Germany. This supply arrives here in two types. One type consists of square chips and is designated as "cut drug;" the other is designated as "siftings" and is usually high in ash (up to 20 per cent.). Some of the commercial supplies are utilized in the manufacture of metal polishes.

Description and Physical Properties.—"*Unground Quillaja.*—In flat pieces of variable length, from 3 to 8 mm. in thickness, or in small chips; outer surface brownish white, sometimes with a very few small patches of cork attached, otherwise nearly smooth; inner surface yellowish white, nearly smooth, with occasional circular depressions, conical projections or transverse channels; fracture uneven and strongly fibrous, the laminæ oblique to each other. Odor slight; taste acrid.

"*Powdered Quillaja.*—Pinkish white; very sternutatory; calcium oxalate in elongated prisms either isolated or in crystal fibers, the prisms from 0.035 to 0.200 mm. in length; numerous fragments composed of long, more or less irregular fibers with thick, strongly lignified walls, the fibers often associated with medullary rays the latter about 4 cells wide; stone cells with simple oblique pores; nearly spheroidal starch grains up to 0.010 mm. in diameter; occasional fragments composed of cork cells with brownish walls." *N. F.*

Soap bark is officially described in the Br. as "in flat pieces, from three to eight millimetres thick, but varying considerably in length and width. Outer surface brownish-white, or, where the outer bark has been incompletely removed, reddish or blackish-brown, and longitudinally striated. Inner surface white or yellowish-white and smooth. Fracture splintery and laminated, the tangential surfaces of the laminæ often exhibiting glistening prismatic crystals of calcium oxalate. In transverse section, chequered with delicate radial and tangential lines; medullary rays four cells wide; numerous irregular groups of bast fibres of varying size; scattered starch grains from four to six microns in diameter. Powdered Quillaja Bark is strongly sternutatory; *water* vigorously shaken with it forms copious persistent froth. Odor not marked; taste astringent and acrid. Ash not more than 15 per cent." *Br.*

The fracture exhibits, when slightly magnified, glistening prismatic crystals. Quillaja bark is histologically distinguished and its powder recognizable, by the large and numerous prismatic calcium oxalate crystals, which are from 0.035 to 0.200 mm. long.

When bruised and macerated in water quillaja bark imparts to that liquid the property of frothing like soap when agitated. The bark contains neither tannic acid nor any bitter principle. The detergent as well as medicinal properties of quillaja are due to the presence of at least two principles belonging to the group of saponins (see Part II). One of these is a neutral substance and seems to be identical with senegin (see *Senega*), the other known as *quillain* or *quillaic acid,* $C_{19}H_{30}O_{10}$, is an extraordinarily toxic substance. Both of these principles are glucosidal.

G. Melliers states that there is present in quillaja bark a carbohydrate which he has identified as *saccharose.* (*P. J.,* Feb., 1901, 161.)

Uses.—The effects of quillaja are those of the sapotoxins in general and are described under *Saponin* in Part II. Its use in medicine is based entirely on its local irritant action. Through its tendency to nauseate it is sometimes useful in the early stages of *acute bronchitis,* its action being very similar to that of senega, but it is comparatively little employed. Externally it is occasionally used for its detergent and stimulating effects. The quillaic acid is said to be extraordinarily poisonous, three-one-thousandths of a grain for each pound of body weight injected into the veins of a cat being sufficient to cause death, although thirty grains administered by the mouth are safely borne. Lohmann (*P. J.,* lxxiii, 477) affirms that chemically pure saponin is not injurious when taken by the stomach.

Both the active principles, quillaic acid and quillain, of quillaja bark are violent local irritants. In a case of poisoning by quillaic acid (*T. G.,* xi) the symptoms were violent vomiting, with epigastric pain, increased diuresis and cystic irritation, accompanied by cold sweats, feeble pulse, threatened syncope, and other evidences of collapse.

Quillaja is much used in the arts for washing silk, cloth, and other fabrics, for which soap would not be suitable. It is an emulsifying agent, but unless ordered by the physician should never be used by the pharmacist in the preparation of emulsions, on account of its active medicinal properties.

It has also been largely used in the production of foam on non-alcoholic carbonated beverages. This use has been criticized as harmful and it is now prohibited by law in many jurisdictions.

Off. Prep.—Liquor Picis Carbonis, *N. F., Br.;* Tinctura Quillajæ, *N. F.* (*Br.*).

QUINIDINA. N. F.

QUINIDINE Quinid.

"An alkaloid ($C_{22}H_{24}O_2N_2$ (324.31), isomeric with quinine, obtained from the bark of various species of *Cinchona* (Fam. *Rubiaceæ*)." *N. F.*

Conquinine; Beta-quinine; Chinotin; Pitayine; Chinidin, Conchinin, Beta-chinidin, *G.*

Quinidine is isomeric with quinine. It was discovered in 1833 by O. Henry and Delondre, but they afterwards concluded that it was quinine hydroxide, as it had the same composition as quinine. Winckler, in 1844, announced anew the existence of the same alkaloid, which he considered distinct, and named it "*chinidine*"; this substance was not pure, and Pasteur, in 1853, proved that it really consisted of two alkaloids, one of which he called *cinchonidine,* and the other *quinidine.* This view is now generally accepted, although Hesse insists on calling quinidine "*conchinine*"; but the latter name is used to only a limited extent in Germany, and scarcely at all elsewhere. It is found in several species of *Cinchona,* usually in small proportion, but in some, especially the *C. Calisaya* and *C. pitayensis,* in fairly large amount —as high as 3 per cent. has been reported.

It is prepared commercially from the "mother-liquors" from which quinine has been extracted. The solution left after the insoluble quinine sulphate has crystallized out is treated with ammonia which precipitates the cinchonine; after removal of the latter the addition of soda causes the separation of the quinidine. It may also be obtained from the mixture of alkaloids, called "quinoidine," that results from the addition of sodium hydroxide to the mother-liquor from which quinine sulphate has been removed. From this mixture the quinidine, together with cinchonine, is extracted with ether; this extract is dissolved in dilute sulphuric acid, then neutralized with ammonia, and the cinchonine precipitated with potassium tartrate.

Quinidine crystallizes with either one or two molecules of water, the crystals being strongly efflorescent. It is sublimable by heat without change, and is condensed in a crystalline form. It resembles quinine not only in composition, but also in its chemical relations with chlorine and ammonia, being rendered green by the successive action of those agents. According to Herapath, it resembles it also in causing a fluorescent appearance when dissolved in water, which is not the case with either cinchonine or cinchonidine, or at least, in a much less degree. It differs, however, in its greater facility of crystallization, in its much less solubility in ether, and in its influence on polarized light, it being dextro-rotatory. It may also be distinguished from quinine by the fact that its soluble salts are not precipitated by the neutral tartrates but are by potassium iodide; the latter test also differentiates it from all the other cinchona bases. The neutral sulphate is much more easily soluble than that of quinine. Vrevens (*C. D.*, 1898, p. 400) states that the crystals yielded by Marme's reagent (potassio-cadmium iodide) with quinidine are different from those obtained from any of the other cinchona alkaloids. They are seen under the microscope to consist of bundles of fine needle-like crystals quite different from those of quinine, cinchonine, and cinchonidine. Commercial quinidine is often contaminated with cinchonidine, indeed some samples may consist in chief part of the latter.

Description and Physical Properties.—"Quinidine occurs in acicular white crystals or as an amorphous white powder. When crystallized from alcohol it forms monoclinic prisms containing one molecule of alcohol which it slowly loses on exposure to air, and rapidly loses when heated to 100° C. When precipitated by ammonia water from an aqueous solution of a salt of Quinidine, washed and dried, it forms an amorphous powder. Odorless and having an intense and persistent bitter taste. When crystallized from an alcoholic solution, one gram dissolves at 25° C. in about 32 cc. of alcohol, 53 cc. of ether, and 1.5 cc. of chloroform; very slightly soluble in petroleum benzin; almost insoluble in water. One Gm. of dried amorphous Quinidine dissolves in about 36 cc. of alcohol at 25° C., 67 cc. of ether and 1.7 cc. of chloroform; very slightly soluble in petroleum benzin; almost insoluble in water.

"Quinidine melts at about 168° C. Incinerate 0.2 Gm. of Quinidine; no weighable residue remains. Its alcoholic solution is dextrorotatory, and its aqueous solution is alkaline to litmus. A solution of Quinidine in diluted sulphuric acid (1 in 1000) shows a strong blue fluorescence. Add a few drops of bromine T.S. to 10 cc. of an aqueous solution of Quinidine (1 to 1000), made with the aid of sufficient diluted sulphuric acid to produce complete solution, and then follow with ammonia water in slight excess; the liquid acquires an emerald-green color. A solution of about 0.1 Gm. of Quinidine in 5 cc. of sulphuric acid is not darker than pale yellow. Dissolve 0.5 Gm. of Quinidine in 10 cc. of distilled water at 80° C., with just enough sulphuric acid to form a solution neutral to litmus paper, and add a neutral solution of 0.5 Gm. of potassium iodide in 5 cc. of distilled water at 80° C. Agitate the mixture slightly, cool it to 15° C. and keep it at this temperature for one hour with occasional stirring. A white precipitate is formed (difference from *quinine*). Filter out the precipitate and add 2 drops of ammonia water to the filtrate; it does not cause more than a slight turbidity (*other cinchona bases*). Care must be taken to have the liquid perfectly neutral after the addition of the potassium iodide solution; if slightly acid, very dilute ammonia water must be added drop by drop, with constant stirring until exactly neutral to litmus paper.

"Preserve it in well-closed containers, protected from light." *N. F.*

The sulphate of this alkaloid is recognized by the U. S. P. and several other salts as the hydrochloride and tannate are commercially obtainable.

For description of the uses of this alkaloid see under *Quinidinæ Sulphas.*

Dose, two to five grains (0.12–0.30 Gm.).

Off. Prep.—Syrupus quinidinæ, *N. F.*

QUINIDINÆ SULPHAS. U. S.

QUINIDINE SULPHATE Quinidin. Sulph.

"The sulphate $[(C_{20}H_{24}O_2N_2)_2.H_2SO_4.2H_2O]$ of an alkaloid obtained from cinchona." *U. S.*

Chinidin Sulphate, Conquinine Sulphate; Sulphate de Quinidine, *Fr.;* Chinidin Sulfas; Schwefelsaures Chinidin, *G.*

For account of the sources and chemical properties of this base see preceding article.

Description and Physical Properties.—"Fine, needle-like, white crystals, frequently cohering in masses. It is odorless, has a very bitter taste, and darkens on exposure to light. One Gm. of Quinidine Sulphate is soluble in about 90 cc. of water, and in 10 cc. of alcohol, at 25° C. One Gm. is soluble in about 15 cc. of boiling water. It is soluble in chloroform but almost insoluble in ether.

"An aqueous solution of Quinidine Sulphate (1 in 100) is neutral or slightly alkaline to litmus paper, and is dextrorotatory. (Quinine sulphate is lævorotatory.) An aqueous solution of Quinidine Sulphate, when acidulated with diluted sulphuric acid, develops a vivid blue fluorescence. Add 1 or 2 drops of bromine T.S. to 5 cc. of an aqueous solution of the salt (1 in 1000) and follow with 1 cc. of ammonia T.S.: the liquid acquires an emerald-green color due to the formation of thalleioquin. To 5 cc. of an aqueous solution of Quinidine Sulphate (1 in 100) add 1 cc. of silver nitrate T.S. and stir the mixture with a glass rod: a white precipitate forms after a short interval (*difference from many other alkaloids*). Barium chloride produces in an aqueous solution of the salt a white precipitate which is insoluble in hydrochloric acid.

"Dried to constant weight at 100° C., Quinidine Sulphate loses not more than 5 per cent. (*water*). Ash: not more than 0.1 per cent. A solution of 0.1 Gm. of the salt in 2 cc. of sulphuric acid is not darker than light yellow (*readily carbonizable substances*). One Gm. of Quinidine Sulphate dissolves in 5 cc. of a warm mixture of 2 volumes of chloroform and 1 volume of dehydrated alcohol with not more than a slight turbidity (*ammonium or other inorganic salts*). Dissolve 0.5 Gm. of Quinidine Sulphate in 15 cc. of boiling water and add a solution of 0.5 Gm. of potassium iodide in 5 cc. of distilled water, which, if necessary, has previously been neutralized to litmus paper with tenth-normal sulphuric acid. A white precipitate is formed. Mix well, cool the mixture to 15° C., and keep it at this temperature for one hour with frequent agitation. Filter and add 2 drops of ammonia T.S. to the filtrate. No turbidity is produced within one minute (*other cinchona alkaloids*).

"Preserve in well-closed containers protected from light." *U. S.*

Uses.—Although quinidine possesses the antiperiodic and other properties of quinine and has been used as a substitute, it is so inferior that its employment for this purpose has almost completely ceased. In 1914 Wenkelbach reported remarkable effects in a patient suffering with auricular fibrillation, who had received quinidine for a malarial condition. This led Frey in 1918 to make some experiments with the use of quinidine in the treatment of this serious cardiac irregularity. Since then it has been used to a large extent not only in auricular fibrillation but in various other irregularities of the heart, especially paroxysmal tachycardia. Smith (*J. A. M. A.*, 1922, lxxviii, p. 877) collected the reports of 320 cases of auricular fibrillation treated with quinidine. It has been established beyond question that in a considerable proportion—between 50 and 60 per cent.—of these cases, normal heart rhythm is at least temporarily re-established. Where the disturbance of rhythm has been, as it usually is, dependent upon a valvular lesion, as the quinidine does not influence the latter the patient will probably sooner or later relapse; that is, the auricular fibrillation in the great majority of cases recurs sometimes after a few days and others after some weeks. In some cases, however, the normal rhythm has continued so long as to give promise of being practically permanent. The questions whether the patient is likely to be benefited by the re-establishment of normal heart rhythm and whether this likelihood is sufficient to outweigh the positive dangers of the drug is one which can be answered only by most careful study of all the surrounding conditions in each individual case.

The *modus operandi* of quinidine in these cases has been recently elucidated. Santessin (*A. E. P. P.*, 1893, xxxii, p. 327) showed that quinidine depresses the rhythmicity, contractility and irritability of the heart. Lewis (*Heart*, 1921, ix, p. 55) has shown that it also lowers conduction in the cardiac muscle, and Hofmann (*Z. B.*, 1920, lxxi, p. 47) that it lowers the excitability of the dog's heart to the electrical current (see also Hirschfelder and Cervenka, *J. P. Ex. T.*, 1925, xxvi, 19). The most plausible explanation of its effect is that it is due to a combined lessening of the irritability of the auricular muscle with a prolongation of its refractory period. It is of interest to note, in this latter connection, that Brody (*J. A. M. A.*, 1922, lxxix, p. 354) has shown a similar prolongation of the refractory period of the voluntary muscles after quinidine.

In considering the dangers from this drug, it should be noted in the first place that quinidine is to be regarded as a heart depressant, and if it fails to restore the normal rhythm of the heart, the patient's condition may be made perceptibly worse. The more serious dangers, however, are due to the dislodgment of an embolus from the heart, which may prove rapidly fatal if lodged in the brain or other vital organ, and the not infrequent idiosyncrasies towards the drug. The latter may be guarded against by the so-called test dose which is now practically always given. That is—the patient receives three grains (0.2 Gm.) of quinidine sulphate, and if no symptoms are produced, another three grains after two hours. Twenty-four hours later, if no unpleasant symptoms have occurred, is begun the therapeutic doses of the drug, which are usually from three to six grains, at such intervals that the patient receives from fifteen to thirty grains (1 to 2 Gm.) in the twenty-four hours. This is continued for about a week, unless the desired therapeutic effect occurs sooner or some toxic symptoms intervene. Against the dangers of embolism there is no way to guard, except to remember that they are much more likely to occur in cases of long standing than those in which the fibrillation is comparatively recent. There have been several sudden deaths following the use of the drug, some of which are not easily explained. In many other patients unpleasant symptoms such as headache, increased palpitation, precordial pain, nausea or vomiting, ringing in the ears, etc., have interrupted the treatment. It is generally recommended that no digitalis shall be administered during the quinidine treatment.

Dose, three to six grains (0.2–0.4 Gm.).

QUININA. U. S.

QUININE Quin.

"An alkaloid [$C_{20}H_{24}O_2N_2.3H_2O$] obtained from cinchona." *U. S.*

Chininum; Quinia; Quinine, *Fr.;* Chinin, *G.;* Chinina, *It.;* Quinina, *Sp.*

This alkaloid is prepared by adding to a solution of quinine sulphate a quantity of ammonia water or solution of sodium hydroxide just a sufficient quantity to cause a precipitation of the alkaloid.

Quinine is whitish, rather flocculent, and usually not crystalline; it may with care be crystallized from its alcoholic solution in silky needles, and Liebig obtained it from a somewhat ammoniacal aqueous solution in the same form. It is inodorous and very bitter. The crystals obtained from alcoholic solution have the composition $C_{20}H_{24}O_2N_2 + 3H_2O$, and fuse at 57° C. They may be deprived of water by warming or exposure over sulphuric acid, and they then fuse at 171.2° to 172° C. By carefully regulated heat, it may be sublimed unchanged, assuming a crystalline form. The alcoholic solution is intensely bitter. Quinine is unalterable in the air. It forms salts with the acids which readily crystallize. *Herapathite* was the name given by Professor Hardinger after the discovery in 1852, by Dr. W. B. Herapath, of a *periodide of quinine,* which has been used as an identifying test for this alkaloid. If an alcoholic solution of iodine is added to a solution of a quinine salt, a crystalline precipitate is formed which is golden-green by reflected light and pale olive-green by transmitted light. These crystals have been called *artificial tourmalines,* from their resemblance to that mineral.

Quinine and its salts may be distinguished from all other alkaloids and their salts, except a few others from cinchona, by the beautiful emerald-green color (*thalleioquin*) which results when their solution is treated first with solution of chlorine and then with ammonia, and which changes to a white or violet upon saturation with a dilute acid. (For further details of this test, seen under *Quininæ Sulphas.*)

Quinine, and to a less extent other cinchona alkaloids impart a fluorescence to their aqueous solution. This is more closely described under *Quininæ Sulphas.*

Description and Physical Properties.—"A white, microcrystalline, odorless powder. It has a bitter taste, which is intense and persistent. It is efflorescent in dry air. One Gm. of Quinine is soluble in 1560 cc. of water, 0.8 cc. of alcohol, 1.1 cc. of chloroform, 1.9 cc. of ether, and in 1890 cc. of ammonia water, at 25° C. One Gm. is soluble in 800 cc. of boiling water.

"An alcoholic solution of Quinine (1 in 10) is alkaline to litmus paper, and is lævorotatory. A solution of Quinine in diluted sulphuric acid shows a vivid blue fluorescence. Add 2 or 3 drops of bromine T.S. to 5 cc. of a saturated, aqueous solution of Quinine and add 1 cc. of ammonia T.S.: the liquid acquires an emerald-green color, due to the formation of thalleioquin.

"Dried to constant weight at 100° C., Quinine loses not more than 15 per cent (*water*). Ash: not more than 0.1 per cent. A solution of 0.1 Gm. of Quinine in 2 cc. of sulphuric acid is not darker than light yellow (*readily carbonizable substances*). Heat 0.2 Gm. of Quinine with 2 cc. of sodium hydroxide T.S. on a water bath: the odor of ammonia is not evolved (*ammonia salts*). Dry Quinine to constant weight at 100° C., dissolve 1.5 Gm. of the dried Quinine in 25 cc. of alcohol, dilute the solution with 50 cc. of hot water, add normal sulphuric acid (about 5 cc.) until the solution is acid, using 2 drops of methyl red T.S. as indicator, and neutralize the excess of acid with normal sodium hydroxide. Evaporate the liquid to dryness on a water bath, powder the residue, mix it in a test tube with 20 cc. of distilled water, and complete the test for *other cinchona alkaloids* as directed under *Quininæ Sulphas.*" *U. S.*

The chemical structure of quinine has been the subject of much recent study by chemists and the problem appears to have been practically solved although the alkaloid has not yet been made synthetically. In the first place it may be noted that quinine is, structurally, a methoxy-cinchonine. When oxidized by chromic acid quinine is broken up into *quininic acid* and a substance called *meroquinenine.* The former of these is the methoxy derivative of quinoline-4-carboxylic acid. Meroquinene, on further oxidation, yields *loiponic acid* which is an ethyl-methyl-pyridine. The structural formula of Rabe (*B. Chem. G.,* 1918, li, 466) is accepted by most chemists. For account of the investigation into the quinine molecule and attempts at its synthesis, with references to literature, see Henry, *Plant Alkaloids,* 1924, p. 148.

The most important salt of quinine is the *sulphate,* the process for procuring which, as well as its properties, will be hereafter described. Besides the salts which are official, a number of other compounds have been employed in medicine; the important ones are described in Part II.

Incompatibilities.—The soluble salts of quinine are precipitated from their aqueous solution by the ordinary alkaloidal reagents, such as tannic acid, the alkaline carbonates and hydroxides, the iodides, etc. In addition they are precipitated by certain organic acids, especially the benzoates, salicylates and tartrates. There is a widespread belief that a poisonous substance—quinotoxin—is formed by the interaction between quinine and acetyl salicylic acid, but Sollmann asserts that the compound form in this reaction is really quinicin and is of low toxicity although not possessed of the therapeutic properties of quinine. (See *Quinotoxin*, Part II.)

Uses.—In sufficient concentration quinine appears to be poisonous to all forms of protoplasm, as well of the unicellular micro-organisms as of the more highly organized tissue of man. While the general antiseptic value of quinine is comparatively low against certain bacteria it is peculiarly efficient. McDonald (*J. A. M. A.*, 1915, lxiv, p. 505) has shown that the sulphate inhibits the growth of typhoid bacillus in the strength of 1 to 30,000, and Schaeffer, that 1 to 10,000 will inhibit the growth of diphtheria bacillus. (*Bio. Chem. Zeit.*, 1917, lxxxiii, p. 269.) Among the unicellular organisms, in general the protozoa are more susceptible than the bacteria, but the drug is peculiarly poisonous to the plasmodia of malaria.

In the frog moderate doses of quinine cause a diminution in the reflex activity which is generally attributed to a stimulation of the spinal inhibitory center, commonly known as Setschenow's center. Larger quantities are directly depressant to the motor ganglia. In mammals it frequently gives rise to convulsions, which appear to be due to irritation of the motor area of the brain. Locally applied it is paralyzing to both the motor and sensory nerves, but especially to the latter. In moderate dose it has no demonstrable influence upon the circulation, but large quantities—equivalent to 75 or 80 grains for man—are depressant to the heart. It increases the vigor of the contractions of the voluntary muscles, but apparently lessens resistance to fatigue. According to Cushny, it is a direct stimulant to the uterine muscle, increasing the force of the contractions but not greatly affecting the tonus.

As was shown many years ago by Binz, when added to the blood outside the body in the proportions of about 1 part in 4000, it caused an immediate cessation of the ameboid movements of the white corpuscles. This effect is probably simply one of the manifestations of its general protoplasmic toxicity, and plays little part in its therapeutic action. According to Roth (*J. P. Ex. T.*, 1912, iii, p. 470), quinine causes a pronounced leukocytosis; at first there is an increase in the number of lymphocytes which he believes is due to contraction of the spleen and lymphatic tissues, but later there is an increase in the number of polymorphonuclear cells. According to De Sandro (*Rif. M.*, 1910), the continued use leads to an increase in the number of both red and white cells in the blood.

It has for many years been almost universally taught by pharmacologists that quinine has a marked power of lessening heat production in the body by retarding nitrogenous metabolism. This view has, however, been strongly combated by Hardikar (*J. P. Ex. T.*, 1925, xxv, 175) who maintains that it is founded on erroneous observations. Although he found that very large doses produce a definite fall in heat formation in the rabbit he failed to obtain such an effect in human beings with doses up to 2 Gm., and does not believe it is possible to influence katabolism through the oral administration of quinine. Senta (*A. I. P. T.*, xviii, p. 217) has found a diminution in the absorption of oxygen and gaseous exchange of isolated bits of muscles. Although in normal man ordinary doses do not cause a reduction of temperature, yet they prevent the natural rise of temperature which takes place after violent exercise and in febrile patients often gives rise to distinct lowering. The question of the influence of quinine on metabolism should, in our opinion, be regarded as still *sub judice*.

Quinine is used in medicine for a large variety of purposes. The oldest and most important of these is for the treatment of *malarial fevers*, for which disease it is by far the most reliable remedy that we possess. While the curative value of the drug is universally acknowledged there is some difference of opinion as to its usefulness as a prophylactic against this disease. On the one hand, Stitt (*J. A. M. A.*, 1908, li, p. 1682) concludes that it has no prophylactic action against malaria and Treadgold (*B. M. J.*, 1918, i, p. 525) that it is even harmful. On the other hand, Rodgers (*Indian Med. Gaz.*, 1918, liii, p. 249) says that failure with quinine as a prophylactic is due to the use of too small doses at too long intervals; he recommends ten grain doses given at intervals of not more than four days.

Quinine is useful for its antipyretic influence in certain febrile conditions, such as *typhoid fever*, but in some infections seems to have a direct curative action. The work of Cohen (*Pa. M. J.*, 1919, p. 506; *J. Inf. D.*, 1917, xx, p. 313) in collaboration with Kolmer and Heist, furnishes strong scientific, as well as clinical, evidence of its value in *pneumonia*. They have shown that various salts of this drug have a strong germicidal action on the pneumococcus and that the blood of patients taking large doses of quinine acquires pneumococcicidal properties. The evidence of its value in *influenza* is based on purely clinical data. Garin (*Prog. M.*, 1918, xxxiii, p. 365) sent a questionnaire to a large number of hospitals in southern Europe immediately after the epidemic of 1918; 61 per cent. of these hospitals reported that none of their malarial patients who were receiving large doses of quinine developed influenza and 20 per cent. more that the influenza was distinctly milder among the malarial patients than in the rest of the hospitals. Sterling (*Pa. M. J.*, Sept., 1920) has collected from the literature reports of more than 3000 cases of malaria in various European hospitals, with only 17 cases of influenza and these of a very mild type, during the epidemic when the great majority of the other inmates of the hospital were infected. In acute *coryza* it has long been a standard remedy and undoubtedly if used early will often abort the attack. In *septicemia* it was formerly highly esteemed but has not seemed to maintain its early popularity. Moon (*Journ. of Infectious Diseases,* 1913, xiii, p. 165) presented evidence of a curative effect in hydrophobia in dogs, but his results have been called in question by Cumming (*Journ. of Infectious Diseases,* 1914, xv) and by Frothingham and Halliday (*Jour. Med. Research,* 1914, xxx). It appears also to be of use in *whooping-cough.*

Because of its restraining effect upon destructive metabolism as well as its effect as a bitter upon the stomach, quinine is a valuable remedy in the treatment of various forms of *malnutrition.* In *Graves's disease* it appears to have an effect not merely in restraining the excessive catabolism which is characteristic of this disorder, but also to have a general sedative influence on the nervous system. Some years ago on the theory that *chorea* was due to a lack of spinal inhibition H. C. Wood suggested the use of quinine in the treatment of this disorder, and in many cases it has proven of marked benefit. Through a similar line of reasoning its use was extended to the treatment of *nocturnal enuresis.* It is also recommended as an internal remedy by a number of authors in the treatment of various forms of skin disease, especially *psoriasis* and *urticaria;* in *lupus erythematosus* it has been used both internally and locally. Quinine has for years been employed more or less frequently in the management of *cardiac arrythmias* and with the recent studies of quinidine has had a renewal of popularity.

Brooke (*J. A. M. A.,* 1914, lxii) experimentally determined that quinine sulphate would kill ameba in solutions of 1 to 20,000, and employed it in the form of enemata in the treatment of amebic *dysentery* with satisfactory results. It has also been used with good results in amebic dysentery (see Leiva, *J. P. Ex. T.,* 1924, xxii, 467).

Quinine possesses marked local anesthetic powers and was at one time considerably used as a substitute for cocaine. For this purpose the hydrochloride of quinine and urea is generally preferred.

Because of the insolubility of basic quinine it was formerly believed that the alkaloid was absorbed only from the stomach, but Grosser (*Biochem. Zeit.,* 1907, viii, p. 98) has shown that even the insoluble preparations are completely absorbed. Hartmann and Zila (*A. E. P. P.,* 1918, lxxxiii, p. 221) confirm the fact that the insoluble salts of quinine are as well absorbed as the soluble. They also found that if the quinine was given by the mouth the proportion of the alkaloid in the blood remained practically constant for twelve to twenty-four hours but that if the drug was injected intravenously 90 per cent. of it had disappeared from the blood within thirty minutes. Apparently much of the drug is destroyed in the body as various investigators have succeeded in recovering only from 40 to 60 per cent. of the ingested dose from the excreta. According to Kerner, a portion escapes in an amorphous uncrystallizable form, and a second portion as a substance free from bitter taste, though crystallizable and having the fluorescence of quinine; for this substance he has proposed the name of *dihydroxyl-quinine.*

Elimination seems to be freest between the sixth and twelfth hours, and about two-thirds of that which is recovered from the urine is excreted within twenty-four hours of its ingestion.

The dose of quinine varies greatly according to the purpose for which it is used, as well as the susceptibility of the patient. When used for its tonic effect from three to five grains (0.2–0.32 Gm.) may be given three or four times a day. The antipyretic dose is from fifteen to twenty grains (1.0–1.3 Gm.). S. Solis Cohen has administered, in *pneumonia* with asserted good effects, twenty-five to thirty grains hypodermically (1.7–2.0 Gm.). In the milder forms of *malaria,* such as the ordinary *tertian fever* of temperate climates, from five to ten grains may be given every hour until the patient has taken twenty or thirty grains, and so timed that the last dose comes about an hour before the expected chill. In the tropical varieties of malaria, however, very much larger quantities are required, and in malignant types many authorities recommend to give as high as seventy-five to one hundred grains (5.0–6.5 Gm.) immediately. Such doses cannot be administered by mouth because they are likely to provoke emesis, and moreover, absorption is so slow as to be dangerous in these pernicious fevers. Under such circumstances the quinine may be given hypodermically. The most soluble of the official salts is the dihydrochloride, and by many is the salt of choice for injection, but it is likely to prove irritant because of its acid reaction. The double hydrochloride of quinine and urea is neutral in reaction and is soluble in less than its own weight of water; the 50 per cent. solution may be employed. If injected immediately beneath the skin, solutions of quinine salts are liable to produce local necrosis and ulceration and therefore should always be injected into the muscle substance either in the lumbar or gluteal regions. Extreme care in asepsis is essential in making these injections. A number of cases of *tetanus* have followed the injections of quinine, but McCampbell (*J. A. M. A.,* March 16, 1907) from his experiments concludes that there is no peculiar relation between the quinine and the tetanus germs, except that the spores may be carried in mechanically with the injection and the local necrosis offers a favorable place for their growth.

While it has been used occasionally by intravenous injection McCarrison and Cornwall (*Indian Jour. of Med. Research,* 1920, vi, p. 248) conclude from their experiments that the method is so dangerous as to be justifiable only in cases of great urgency.

Toxicology.—Even in the quantities employed for therapeutic purposes quinine frequently produces unpleasant symptoms. The most common of these is ringing in the ears often accompanied with a sensation of fullness in the head, and perhaps some obtunding of the sense of hearing. With the use of larger doses these symptoms are intensified; the deafness is very marked, disturbed vision may exist, and the flushed face, with the sense of distension in the head, may point towards a cerebral congestion, which is in some cases relieved by spontaneous epistaxis. In decided cinchonism, giddiness and staggering in walking are very common. After toxic doses, severe headache, delirium, stupor, complete deafness and blindness, dilated pupils, embarrassment of respiration, great weakness, convulsions, paralysis, and finally collapse, either comatose or delirious, may result. The deafness produced by large doses of quinine usually passes off rapidly; very rarely is there a permanent impairment of hearing. Amaurosis, with a peculiar ischemia of the retinal vessel, has in a small number of cases been produced by very large therapeutic doses of the alkaloid. (For report of cases of quinine amblyopia, see Weens, *Archives of Ophthalm.*, 1917.) Besides its effects on the brain, quinine sulphate sometimes occasions great gastric and intestinal irritation, marked by oppression of stomach, nausea, abdominal pains, vomiting, and purging. In general, these effects of excessive doses gradually pass off, although partial deafness often continues for several days, and sometimes much longer, and permanent deafness has resulted. It is capable of taking life, although enormous amounts of it are requisite for this. Several cases of recovery are recorded after the taking of an ounce by the stomach. Probably only a portion of the drug was absorbed. Five ounces taken in ten days have caused death.

In certain individuals even very small doses may produce toxic symptoms. In these cases the poisoning usually differs very markedly from the ordinary type described above, in most instances being manifest by eruptions on the skin which frequently closely simulate scarlet fever. (See H. C. Wood, Jr., *T. G.*, January, 1902.)

Dose, two to twenty grains (0.13–1.3 Gm.).

Off. Prep.—Oleatum Quininæ, *N. F.;* Syrupus Ferri, Quininæ et Strychninæ Phosphatum, *N. F.;* Syrupus Hypophosphitum Compositus, *N. F.;* Liquor Hypophosphitum Compositum, *N. F.;* Oleatum Quininæ, *N. F.*

QUININÆ ÆTHYLCARBONAS. U. S.

QUININE ETHYLCARBONATE Quin. Æthylcarb.
[Euquinine]

" $C_{20}H_{23}O_2N_2.CO_2.C_2H_5$." *U. S.*

Chininum Æthylo-carbonicum; Euchinina; Æthylcarbonas Chininæ.

Euquinine is manufactured by passing carbonyl chloride (phosgene) into dehydrated alcohol, rectifying the resulting chlorocarbonic ester and then allowing it to act upon a solution of anhydrous quinine in ether. The resulting quinine ethylcarbonate is subsequently purified by washing and crystallizing. The final purification is very difficult as crystallization is hard to induce.

Description and Physical Properties.—"White, fine, soft needles, usually matted together in fleecy masses. Quinine Ethylcarbonate is odorless and practically tasteless, but when masticated it slowly develops a slightly bitter taste. It darkens on exposure to light. Quinine Ethylcarbonate is only slightly soluble in water. One Gm. is soluble in 2 cc. of alcohol, 1 cc. of chloroform, and in about 10 cc. of ether, at 25° C. It is readily soluble in dilute acids.

"Quinine Ethylcarbonate melts between 89° and 91° C. Its saturated aqueous solution is slightly alkaline to litmus paper. Its solution in diluted sulphuric acid exhibits a blue fluorescence. To 5 cc. of an aqueous solution of Quinine Ethylcarbonate (1 in 1000), made with the aid of a slight excess of diluted sulphuric acid, add 2 or 3 drops of bromine T.S., and follow with 1 cc. of ammonia water: the liquid acquires a green color, due to the formation of thalleioquin. To about 0.2 Gm. of Quinine Ethylcarbonate add 2 cc. of sodium hydroxide T.S. and 5 cc. of iodine T.S., and gently warm the mixture: the odor of iodoform is evolved. Digest about 1 Gm. of Quinine Ethylcarbonate with 10 cc. of a 5 per cent. solution of potassium hydroxide in dehydrated alcohol: a white precipitate is gradually formed which effervesces with acids.

"Ash: not more than 0.2 per cent. Dried over sulphuric acid for twenty-four hours, the loss in weight does not exceed 2 per cent. (*water*). Dissolve 0.3 Gm. of Quinine Ethylcarbonate in 10 cc. of diluted nitric acid and 20 cc. of distilled water: ten cc. portions of this solution are not rendered turbid at once by the addition of a few drops of silver nitrate T.S. (*chloride*) or of barium chloride T.S. (*sulphate*).

"Preserve protected from light." *U. S.*

Euquinine gives the thalleioquin, but not the herapathite, reaction.

Uses.—Despite its sparing solubility, euquinine seems to be rapidly absorbed, Panegrosso and Gammarelli (*G. Osp.*, Oct. 18, 1897) finding that it appears within the urine within a half an hour after its ingestion. On the other hand, Kleine could only recover 17 per cent. of the quinine administered in this form from the urine. It is probable, although as far as we know not definitely proven, that euquinine is absorbed unchanged and broken up by the blood with the liberation of its quinine radical. At any rate, there is considerable evidence that it exercises the characteristic therapeutic effects of quinine. Von Noorden (*Cb. I. M.*, 1896) and Oberlach (*D. M. Ztg.*, 1897) have used it with satisfactory results in *pneumonia* and other febrile affections, and Panegrosso and Celli and Mori (*Cb. B.*, xxix) have employed it successfully in *malaria*. Several writers have found it useful in chlorotic *anemias*. It is probably more frequently used in *whooping cough* than in any other disease.

The special value of euquinine lies in its comparative tastelessness which makes it suitable for giving to children. It may be conveniently prescribed suspended in a flavoring syrup. Although theoretically it represents about 83.8 per cent. of quinine, it is generally administered in considerably larger doses than the older salts of the alkaloid.

Dose, as a tonic, three to six grains (0.2–0.4 Gm.), as an antimalarial, thirty to forty grains (2 to 2.6 Gm.) may be given daily.

QUININÆ BISULPHAS. U. S.

QUININE BISULPHATE Quin. Bisulph. [Quinine Acid Sulphate]

"$C_{20}H_{24}O_2N_2.H_2SO_4.7H_2O$." *U. S.*

Chininum Bisulfuricum; Quininæ Sulphas Acidus; Acid Quinine Sulphate; Bisulphas Quinicus; Chininum Sulfuricum, *Fr. Cod.;* Sulfate de Quinine Neutre, *Fr.;* Saures Chininsulfat, Chininbisulfat, *G.;* Bisolfato di chinina, *It.;* Sulfato quinico neutro, *Sp.*

This salt, although commonly called the "acid sulphate," is strictly speaking the neutral sulphate (see discussion under *Quininæ Sulphas*). It is made by suspending 100 Gm. of quinine sulphate in 500 Gm. of warm distilled water, and adding 115 Gm. of diluted sulphuric acid (U. S. P.), filtering and crystallizing. It has been introduced because of the great advantages in solubility that it possesses over the ordinary sulphate. It requires but 9 parts of water to dissolve it, while the sulphate requires 720.

Description and Physical Properties.—"Colorless, transparent or whitish, orthorhombic crystals or small needles. It is odorless, and has a very bitter taste. It effloresces on exposure to air, and turns yellow on exposure to light. One Gm. of Quinine Bisulphate is soluble in 9 cc. of water, 23 cc. of alcohol, 15 cc. of glycerin, 625 cc. of chloroform, and in 2500 cc. of ether, at 25° C. One Gm. is soluble in 0.7 cc. of boiling water and in 0.7 cc. of alcohol at 60° C.

"An aqueous solution of Quinine Bisulphate (1 in 20) is strongly acid to litmus paper, and has a blue fluorescence. Add 2 or 3 drops of bromine T.S. to 5 cc. of an aqueous solution of Quinine Bisulphate (1 in 1000), and then add 1 cc. of ammonia T.S.: the liquid acquires an emerald-green color, due to the formation of thalleioquin. Barium chloride T.S. produces in an aqueous solution of the salt a white precipitate, insoluble in hydrochloric acid.

"Quinine Bisulphate loses not more than 24 per cent. when dried to constant weight at 100° C. (*water*). Ash: not more than 0.05 per cent. A solution of 0.1 Gm. of the salt in 2 cc. of sulphuric acid is not darker than light yellow (*readily carbonizable substances*). Heat 0.3 Gm. of the salt with 3 cc. of sodium hydroxide T.S. on a water bath: the odor of ammonia is not evolved (*ammonium salts*). Dissolve 2.52 Gm. of Quinine Bisulphate in a mixture of 20 cc. of alcohol and 50 cc. of hot distilled water, and neutralize the solution with normal sodium hydroxide, using 2 drops of methyl red T.S. as indicator. Evaporate the solution to dryness on a water bath, powder the residue, mix it in a test tube with 20 cc. of distilled water, and complete the test for other *cinchona alkaloids* as directed under *Quininæ Sulphas.*

"Preserve in well-closed containers, protected from light." *U. S.*

The acid sulphate of quinine is much more freely soluble than the neutral sulphate and is therefore by many preferred. It has, however, no very real advantage, being inferior for hypodermic injection to the dihydrochloride or the double hydrochloride of quinine and urea because of its lesser solubility, and when given by the mouth the slight increase in solubility over the neutral salt is a matter of small importance. It represents 59.12 per cent. of quinine.

Dose, two to fifteen grains (0.13–1.0 Gm.).

QUININÆ DIHYDROCHLORIDUM. U. S. (Br.)

QUININE DIHYDROCHLORIDE Quin. Dihydrochl.

"$C_{20}H_{24}O_2N_2.2HCl$." *U. S.* "Acid Quinine Hydrochloride, $C_{20}H_{24}N_2O_2,2HCl$, is the acid hydrochloride of an alkaloid, quinine, obtained from the bark of various species of Cinchona." *Br.*

Quininæ Hydrochloridum Acidum, *Br;;* Acid Quinine Hydrochloride; Chlorurum Quinicum; Chininum Bihydrochloricum, *Fr. Cod.;* Chlorhydrate de Quinine Neutre, *Fr.;* Saures Chininhydrochlorid, Saures Chlorwasserstoffsaures Chinin, *G.*

This has been introduced on account of its remarkable solubility in water—*i.e.*, less than its own weight. It may be made by passing hydrochloric acid gas over dry quinine, but more conveniently by decomposing quinine bisulphate with barium chloride or by mixing a solution of neutral hydrochloride with one molecular proportion of hydrochloric acid and evaporating the solution at a gentle heat. It contains 81.63 per cent. of quinine.

Description and Physical Properties.—"A white, odorless powder, having a very bitter taste. One Gm. of Quinine Dihydrochloride is soluble in about 0.6 cc. of water and in 12 cc. of alcohol, at 25° C. It is slightly soluble in chloroform and very slightly soluble in ether.

"An aqueous solution of Quinine Dihydrochloride is strongly acid to litmus paper. Add 2 or 3 drops of bromine T.S. to 5 cc. of an aqueous solution of the salt (1 in 1000), and then add 1 cc. of ammonia T.S.: an emerald-green color is produced, due to the formation of thalleioquin. Silver nitrate T.S. added to an aqueous solution of the salt (1 in 20) produces a white precipitate, insoluble in nitric acid but soluble in ammonia T.S.

"Quinine Dihydrochloride loses not more than 3 per cent. when dried to constant weight at 100° C. (*water*). Ash: not more than 0.05 per cent. A solution of 0.1 Gm. of Quinine Dihydrochloride in 2 cc. of sulphuric acid is not darker than light yellow (*readily carbonizable substances*). The addition of a few drops of diluted sulphuric acid to 10 cc. of an aqueous solution of the salt (1 in 20) produces no turbidity (*barium*). One Gm. of Quinine Dihydrochloride shows no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid. Dissolve 1.8 Gm. of Quinine Dihydrochloride in 10 cc. of distilled water, add a slight excess of ammonia T.S., shake out the mixture successively with 20, 10 and 10 cc. of chloroform, and evaporate the combined chloroform solutions to dryness on a water bath. Dissolve the residue in 25 cc. of alcohol, dilute the solution with 50 cc. of hot distilled water, add normal sulphuric acid (about 5 cc.) until the solution is acid, using 2 drops of methyl red T.S. as indicator, and neutralize the excess of acid with normal sodium hydroxide. Evaporate the liquid to dryness on a water bath, powder the residue, mix it in a test tube with 20 cc. of distilled water, and complete the test for *other cinchona alkaloids* as directed under *Quininæ Sulphas.*

"Preserve in well-closed containers, protected from light." *U. S.*

"A white amorphous powder. No odor; taste intensely bitter. Soluble in less than 1 part of *water*. Aqueous solution acid to *litmus*. Yields the *reactions* characteristic of chlorides. Yields not more than the slightest characteristic *reaction* for sulphates. 1 gramme dissolved in 20 millilitres of *water* requires for neutralisation not more than 5.0 millilitres of *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. Yields a green coloration when tested as described under 'Quininæ Hydrochloridum.' Loses not more than 3 per cent. of its weight when dried at 100° C. When 2 grammes are dissolved in 15 millilitres of *water*, the solution neutralised with *N/1 solution of sodium hydroxide*, mixed with 1 gramme of powdered non-effloresced *sodium sulphate*, and further treated as described under 'Quininæ Hydrochloridum,' the precipitate produced on the addition of *solution of ammonia* redissolves on rotating the tube (limit of other cinchona alkaloids). No appreciable ash." *Br.*

Uses.—The dihydrochloride is the most freely soluble of the official salts of quinine. For this reason it is frequently preferred for hypodermic injection. Because of its acid reaction, however, it is more likely to produce local irritation than the neutral salts.

Dose, two to ten grains (0.13–0.65 Gm.).

Off. Prep.—Ampullæ Quininæ Dihydrochloridum, *N. F.*

QUININÆ ET UREÆ HYDROCHLORIDUM. U. S.

QUININE AND UREA HYDROCHLORIDE Quin. et Urea. Hydrochl. [Quinine and Urea Chloride]

"Quinine and Urea Hydrochloride [$C_{20}H_{24}O_2N_2.HCl.CO(NH_2)_2.HCl.5H_2O$] contains not less than 58 per cent. of anhydrous quinine [$C_{20}H_{24}O_2N_2$]." *U. S.*

Quinine and Urea Muriate, Chininum Bimuriaticum Carbamidatum; Nikalgin; Quininæ Hydrochloro-carbamidum; Urea-quinine.

This salt, discovered by Kutais (1878), is best prepared by Rice's process. Seventy-nine parts of quinine hydrochloride are dissolved in 70 parts of hydrochloric acid (sp. gr. 1.050), the solution filtered, 12 parts of urea added, and the whole warmed until the liquid is clear. It is then set aside, that crystals may form. These are soluble in an equal weight of water, and also in strong alcohol, and are usually purified by recrystallization.

Description and Physical Properties.—"Colorless, translucent prisms, or a white, granular powder. It is odorless, and has a very bitter taste. One Gm. of Quinine and Urea Hydrochloride is soluble in 0.9 cc. of water and in 2.4 cc. of alcohol, at 25° C.

"An aqueous solution of Quinine and Urea Hydrochloride (1 in 20) is strongly acid to litmus paper. A solution of the salt in diluted sulphuric acid (1 in 1000) shows a blue fluorescence. Add 2 or 3 drops of bromide T.S. to 5 cc. of an aqueous solution of the salt (1 in 1000), and then add 1 cc. of ammonia T.S.: the liquid acquires an emerald-green color, due to the formation of thalleioquin. Add 2 cc. of colorless nitric acid to a cold solution of about 1 Gm. of the salt in 2 cc. of distilled water and cool the mixture at once to the temperature of melting ice: crystalline leaflets of urea nitrate are formed on standing. Collect the crystals in a funnel upon glass wool, wash them with about 5 cc. of a cold mixture of equal volumes of nitric acid and distilled water, and after draining, dissolve the crystals in a few cc. of distilled water: the addition of a few drops of mercuric nitrate T.S. to the urea nitrate solution, followed by sodium hydroxide T.S. to only a slightly acid reaction, produces a white precipitate. Silver nitrate T.S. produces in an aqueous solution of the salt (1 in 20) a white precipitate, insoluble in nitric acid but soluble in ammonia T.S.

"Ash: not more than 0.05 per cent. A solution of 0.1 Gm. of the salt in 2 cc. of sulphuric acid is not darker than light yellow (*readily carbonizable substances*). Warm 10 cc. of an aqueous solution of the salt (1 in 20) with 5 cc. of sodium hydroxide T.S. to 50° C.: the odor of ammonia is not evolved at once (*ammonium compounds*). Dissolve about 3 Gm. of Quinine and Urea Hydrochloride in 30 cc. of distilled water in a separator, add 10 cc. of ammonia water, shake out the mixture successively with 30 and 20 cc. of chloroform, and evaporate the combined chloroform solutions to dryness on a water bath. Dissolve 1.5 Gm. of this residue in 25 cc. of alcohol, dilute the solution with 50 cc. of hot distilled water, add normal sulphuric acid (about 5 cc.) until the solution is acid, using 2 drops of methyl red T.S. as indicator, and neutralize the excess of acid with normal sodium hydroxide. Evaporate the liquid to dryness on a water bath, powder the residue, mix it in a test tube with 20 cc. of distilled water, and complete the test for *other cinchona alkaloids* as directed under *Quininæ Sulphas.*

"Preserve in well-closed containers, protected from light." *U. S.*

Assay.—"Dissolve about 0.5 Gm. of Quinine and Urea Hydrochloride, accurately weighed, in 5 cc. of distilled water in a separator, add 3 cc. of ammonia T.S., and shake the mixture with successive portions of 10, 5 and 5 cc., respectively, of chloroform or sufficient to completely extract the quinine. Evaporate the combined chloroform solutions on a water bath, dissolve the residue in 10 cc. of ether, evaporate to dryness and dry to constant weight at 100° C. The residue of anhydrous quinine ($C_{20}H_{24}O_2N_2$) so obtained corresponds to not less than 58 per cent. of the weight of the Quinine and Urea Hydrochloride taken." *U. S.*

Uses.—Quinine urea hydrochloride is the most suitable of all the official salts of the alkaloid for hypodermic administration on account of its free solubility and of its neutral reaction. It is, therefore, widely employed in the treatment of the severer types of *malaria,* where the drug must be given subcutaneously, as well as in other conditions where large doses are required. In 1907 Thibault (*Journ. of the Arkansas Medical Soc.,* Sept., 1907), from observing the local effects following the hypodermic administration of this salt, was led to investigate the anesthetic properties of the quinine salts and found that all of the soluble ones produced local anesthesia, if in concentration of greater than 1.5 per cent. For some time quinine and urea hydrochloride was quite extensively used as a local anesthetic. It has, however, the disadvantages that it does not easily penetrate mucous membranes and is therefore of low efficiency when applied as a wash, and when injected is liable to produce extensive sloughing (see *J. A. M. A.,* 1920, lxxv, p. 316). In recent years it has largely passed out of vogue.

Dose, two to ten grains (0.13–0.65 Gm.).

Off. Prep.—Ampullæ Quininæ et Ureæ Hydrochloridum, *N. F.*

QUININÆ HYDROBROMIDUM. U. S.

QUININE HYDROBROMIDE Quin. Hydrobr.

"[$C_{20}H_{24}O_2N_2.HBr + H_2O$]." *U. S.*

Quininæ Hydrobromas; Quinine Bromide; Basic Quinine Hydrobromide; Bromhydras Quininæ Neutralis; Chininum Monobromhydricum, *Fr. Cod.;* Bromhydrate Basique de Quinine; Monobromhydrate de Quinine, *Fr.;* Chininum Hydrobromicum; Chininhydrobromid; Bromwasserstoffsaures Chinin, *G.;* Bromuro Quinico Neutro, *Sp.*

This salt may be made by suspending 10 parts of quinine sulphate in 80 parts of water, boiling, and adding 3.4 parts of barium bromide dissolved in 20 parts of water, filtering, evaporating, and crystallizing. It may also be prepared by combining quinine alkaloid with hydrobromic acid in proper proportions, evaporating and crystallizing.

Description and Physical Properties.—"White, light, small needles, or scale-like crystals. It is odorless, has a very bitter taste, and effloresces on exposure to the air. One Gm. of Quinine Hydrobromide is soluble in 40 cc. of water, 1 cc. of alcohol, 7 cc. of glycerin, 0.6 cc. of chloroform, and in 23 cc. of ether, at 25° C. One Gm. is soluble in 3.2 cc. of water at 80° C.

"Add 2 or 3 drops of bromine T.S. to 5 cc. of an aqueous solution of Quinine Hydrobromide (1 in 1000), and then add 1 cc. of ammonia T.S.: an emerald-green color is produced, due to the formation of thalleioquin. To 5 cc. of an aqueous solution of Quinine Hydrobromide (1 in 50) add 1 cc. of sodium hydroxide T.S., and warm the mixture for a few minutes. Cool well, filter, acidulate the filtrate with dilute hydrochloric acid, add 1 cc. of chloroform and a few drops of chlorine T.S., and shake gently; the chloroform acquires a reddish-brown color.

"An aqueous solution of Quinine Hydrobromide (1 in 50) is neutral or only slightly alkaline to litmus paper and is not fluorescent except when mixed with an excess of diluted sulphuric acid. Dried to constant weight at 100° C., Quinine Hydrobromide loses not more than 5 per cent. (*water*). Ash: not more than 0.05 per cent. A solution of about 0.1 Gm. of the salt in 2 cc. of sulphuric acid is not darker than light yellow (*readily carbonizable substances*). One Gm. of Quinine Hydrobromide shows no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid. The addition of a few drops of diluted sulphuric acid to 10 cc. of a hot aqueous solution of the salt (1 in 20) produces no turbidity (*barium*). One Gm. of Quinine Hydrobromide dissolves completely in 7 cc. of a mixture of 2 volumes of chloroform and 1 volume of dehydrated alcohol (*inorganic salts*). Dissolve about 3 Gm. of Quinine Hydrobromide in 80 cc. of warm distilled water in a separator, add 10 cc. of ammonia T.S., shake out the mixture successively with 30 and 20 cc. of chloroform, and evaporate the combined chloroform solutions to dryness on a water bath. Dissolve 1.5 Gm. of this residue in 25 cc. of alcohol, dilute the solution with 50 cc. of hot distilled water, add normal sulphuric acid (about 5 cc.) until the solution is acid, using 2 drops of methyl red T.S. as indicator, and neutralize the excess of acid with normal sodium hydroxide. Evaporate the liquid to dryness on a water bath, powder the residue, mix it in a test tube with 20 cc. of distilled water, and complete the test for *other cinchona alkaloids* as directed under *Quininæ Sulphas.*

"Preserve in well-closed containers, protected from light." *U. S.*

Uses.—There is a wide-spread belief that this salt acts somewhat differently from the other preparations of quinine. The proportion of hydrobromic acid is, however, too small to exert any influence upon the system; ten grains of quinine hydrobromide represents less than two grains of hydrobromic acid. The salt has achieved a high reputation in the treatment of *Graves's disease,* and certainly in many cases will cause at least a temporary amelioration of many of the nervous manifestations of this disorder. According to Cohen, the most powerfully pneumococcicidal salt of quinine is the di-hydrobromide and of the official salts, the neutral hydrobromide is the most efficient in *pneumonia.* He recommends a beginning dose of twenty grains (1.3 Gm.) followed by five grains (0.3 Gm.) every three or four hours.

Dose, from two to ten grains (0.13–0.65 Gm.).

QUININÆ HYDROCHLORIDUM.
U. S., Br.

QUININE HYDROCHLORIDE Quin. Hydroch.

"$C_{20}H_{24}O_2N_2.HCl.2H_2O$." *U. S.* "Quinine Hydrochloride, $C_{20}H_{24}N_2O_2,HCl,2H_2O$, is the hydrochloride of an alkaloid, quinine, obtained from the bark of various species of Cinchona." *Br.*

Muriate of Quinine; Quinine Chloride; Quininæ Hydrochloras; Quinine Monohydrochloride; Chininum Monochlorhydricum, *Fr. Cod.;* Chlorhydrate de Quinine, *Fr.;* Chininum hydrochloricum, *P. G.;* Chininhydrochlorid; Salzsaures Chinin, *G.;* Cloridrato di chinina, *It.;* Cloruro Quinico, *Sp.*

This quinine salt may be readily prepared by treating the alkaloid with diluted hydrochloric acid, or by double decomposition between barium chloride and quinine sulphate.

Description and Physical Properties.—"White, silky, glistening needles. It is odorless, and has a very bitter taste. The salt effloresces when exposed to warm air. One Gm. of Quinine Hydrochloride is soluble in 16 cc. of water, 0.8 cc. of alcohol, 7 cc. of glycerin, 0.7 cc. of chloroform, and in 340 cc. of ether, at 25° C. One Gm. is soluble in 0.5 cc. of water at 80° C.

"Add 2 or 3 drops of bromine T.S. to 5 cc. of an aqueous solution of Quinine Hydrochloride (1 in 1000), and then add 1 cc. of ammonia T.S.: an emerald-green color is produced, due to the formation of thalleioquin. Silver nitrate T.S. produces in an aqueous solution of the salt (1 in 20) a white precipitate, insoluble in nitric acid, but soluble in ammonia T.S.

"An aqueous solution of Quinine Hydrochloride (1 in 25) is neutral or not more than slightly alkaline to litmus paper, and is not fluorescent, except when highly diluted or when diluted sulphuric acid is added to it. Quinine Hydrochloride loses not more than 10 per cent. when dried to constant weight at 120° C. (*water*). Ash: not more than 0.05 per cent. A solution of 0.1 Gm. of the salt in 2 cc. of sulphuric acid is not darker than light yellow (*readily carbonizable substances*). One Gm. of the salt dissolves completely in 7 cc. of a mixture of 2 volumes of chloroform and 1 volume of dehydrated alcohol (*inorganic salts*). The addition of 5 drops of diluted sulphuric acid to 10 cc. of an aqueous solution of the salt (1 in 20) produces no turbidity (*barium*). One Gm. of Quinine Hydrochloride shows no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid. Dissolve about 2.5 Gm. of Quinine Hydrochloride in 60 cc. of distilled water in a separator, add 10 cc. of ammonia T.S., shake out the mixture successively with 30 and 20 cc. of chloroform, and evaporate the combined chloroform solutions to dryness on a water bath. Dissolve 1.5 Gm. of this residue in 25 cc. of alcohol, dilute the solution with 50 cc. of hot distilled water, add normal sulphuric acid (about 5 cc.) until the solution is acid, using 2 drops of methyl red T.S. as indicator, and neutralize the excess of acid with normal sodium hydroxide. Evaporate the liquid to dryness on a water bath, powder the residue, mix it in a test tube with 20 cc. of distilled water, and complete the test for *other cinchona alkaloids* as directed under *Quininæ Sulphas.*

"Preserve in well-closed containers, protected from light." *U. S.*

"White silky crystals, efflorescent in warm air. No odor; taste very bitter. Soluble in 36 parts of *water,* and in 2 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of chlorides. When to 10 millilitres of an aqueous solution (1 in 1000) 0.5 millilitre of *solution of bromine* and, after well shaking, 1 drop of *strong solution of ammonia* are added, a deep green coloration is produced. When 2 grammes are dissolved in a warm mortar in 20 *millilitres of water* at 60° C., 1 gramme of powdered non-effloresced *sodium sulphate* added, the mixture triturated, cooled, allowed to stand at exactly 15° C. for half an hour with occasional stirring, the crystals of quinine sulphate pressed, and the expressed liquid filtered, 5 millilitres of this filtrate, transferred to a dry test-tube and brought to a temperature of 15° C., yield, on the gradual addition of 6 millilitres of *solution of ammonia,* also at a temperature of 15° C., a precipitate which redissolves on rotating the tube (limit of other cinchona alkaloids). Dissolves in *sulphuric acid* and in *nitric acid* without coloration. 1 gramme dissolves in 7 millilitres of a mixture of 2 volumes of *chloroform* and 1 volume of *absolute alcohol.* Loses not more than 9.1 per cent. of its weight when dried at 100° C. Yields no characteristic *reactions* for barium or for sulphates. No appreciable ash." *Br.*

Only the compounds of quinine with the oxy-acids show the fluorescence in acid solution, none of the compounds of the haloid acids showing this reaction.

Quinine hydrochloride has a decided advantage over the sulphate in its greater solubility in water. It is, however, less soluble than the acid quinine hydrochloride. It represents 90.92 per cent. of anhydrous quinine.

Dose, two to ten grains (0.13–0.65 Gm.).

Off. Prep.—Tinctura Quininæ, *Br.;* Vinum Quininæ, *Br.;* Elixir Ferri, Quininæ et Strychninæ, *N. F.;* Syrupus Phosphatum cum Quinina et Strychnina, *N. F.;* Elixir Glycerophosphatum Compositum, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica Sine Aloe, *N. F.*

QUININÆ SULPHAS. U. S., Br.

QUININE SULPHATE Quin. Sulph.

"$(C_{20}H_{24}O_2N_2)_2.H_2SO_4$ (with 7 or $8H_2O$)" *U. S.* "Quinine Sulphate $(C_{20}H_{24}N_2O_2)_2,H_2SO_4,7\frac{1}{2}H_2O$, is the sulphate of an alkaloid, quinine, obtained from the bark of various species of Cinchona." *Br.*

Sulfas Quinicus; Basic Sulphate of Quinia; Chininum Subsulfuricum, *Fr. Cod.;* Sulfate Basique de Quinine, *Fr.;* Chininum Sulfuricum, *P. G.;* Chininsulfat; Schwefelsaures Chinin, *G.*; Solfato di chinina, *It.;* Sulfato quinico basico, *Sp.*

No process is given in the U. S. Pharm. for preparing quinine sulphate; that of the U. S. P., 1870, will be found in detail in the *U. S. D.*, 17th ed., p. 1141. The process, briefly stated, is to exhaust cinchona bark by boiling with water acidulated with hydrochloric acid and adding milk of lime in excess. The quinine is precipitated with lime, and the dried precipitate digested with boiling alcohol; the alcoholic solution of quinine is evaporated, and the mass dissolved in water acidulated with sulphuric acid. The hot solution is treated with animal charcoal to decolorize it, and then set aside to crystallize. Commercially the process is as follows:

The bark is powdered finely and then mixed with about ⅓ of its weight of finely sifted slaked lime and moistened thoroughly with a 5 per cent. sodium hydroxide solution. It is then extracted with hot high boiling kerosene in vessels provided with powerful stirrers and heated by steam; the selection of a kerosene of proper character is of great importance. Three successive extractions are made. The kerosene dissolves out all of the alkaloids, which are then converted into neutral sulphates in lead lined vessels by the careful addition of a weak sulphuric acid solution. Quinine sulphate crystallizes out first and is purified by decolorization with animal charcoal and recrystallization. The other alkaloids are precipitated by adding alkali to the mother liquor from the quininic and are separated by the use of specific solvents for each alkaloid.

In this country this is the substance usually intended by the term "quinine." Strictly speaking it is not the neutral sulphate although commonly so regarded. It contains two basic radicals to one acidic and is therefore a *diquinine sulphate* or a *quinine subsulphate;* in the Codex it is so denominated and the term "Chininum Sulfuricum" is applied to the salt usually known as the bisulphate. There are at least three quinine sulphates that have been obtained, of which two are now official. The first of these,

$$(C_{20}H_{24}N_2O_2)_2H_2SO_4 + 7H_2O$$

is a "*diquinic sulphate,*" but is the official salt known as quinine sulphate, or *Quininæ Sulphas,* U. S.; the second, formed by dissolving this first in dilute sulphuric acid, has the formula

$$C_{20}H_{24}N_2O_2,H_2SO_4 + 7H_2O$$

and is the official quinine bisulphate, or *Quininæ Bisulphas,* U. S.; while the third, a still more acid sulphate,

$$C_{20}H_{24}N_2O_2,2H_2SO_4 + 7H_2O$$

may be obtained from a solution of quinine in excess of diluted sulphuric acid. This salt is not official.

Description and Physical Properties.—"Hard, prismatic monoclinic needles or white, silky, light, flexible, glistening crystals, making a very light and easily compressible mass. It is odorless, and has a persistent, very bitter taste. It effloresces rapidly when exposed to dry air or when heated to 50° C., losing all but two molecules of its water of crystallization and becoming lusterless. When exposed to light, it acquires a brown tint. One Gm. of Quinine Sulphate is soluble in 725 cc. of water, 107 cc. of alcohol, and in 30 cc. of glycerin, at 25° C. One Gm. is soluble in 47 cc. of water at 80° C. and in about 12 cc. of alcohol at 60° C. It is slightly soluble in chloroform and in ether, but is freely soluble in a mixture of 7 volumes of chloroform and in 4 volumes of dehydrated alcohol.

"A saturated aqueous solution of Quinine Sulphate, when acidulated with diluted sulphuric acid, develops a vivid blue fluorescence. Add 1 or 2 drops of bromine T.S. to 5 cc. of an aqueous solution of the salt (1 in 1000) and then add 1 cc. of ammonia T.S.: the liquid acquires an emerald-green color, due to the formation of thalleioquin. Barium chloride T.S. produces in an aqueous solution of the salt a white precipitate, insoluble in hydrochloric acid.

"A saturated aqueous solution of Quinine Sulphate is neutral or not more than slightly alkaline to litmus paper. Quinine Sulphate loses not more than 16.2 per cent. when dried to constant weight at 100° C. (*water*). Ash: not more than 0.05 per cent. A solution of 0.1 Gm. of the salt in 2 cc. of sulphuric acid is not darker than light yellow (*readily carbonizable substances*). One Gm. of the salt dissolves completely when heated to 50° C. in 7 cc. of a mixture of 2 volumes of chloroform and 1 volume of dehydrated alcohol, and the solution remains clear on cooling (*inorganic salts*). Dry Quinine Sulphate (which must be neutral or slightly alkaline to litmus paper) at 50° C. for two hours, and then agitate 1.8 Gm. of the dried salt with 20 cc. of distilled water at 65° C. for half an hour. Allow the mixture to cool to 15° C., macerate it at this temperature for two hours with occasional shaking, and then filter it through a filter paper of a diameter from

8 to 10 cm. Transfer 5 cc. of this filtrate to a test tube and mix it gently (without shaking) with 6 cc. of ammonia T.S., which must contain not less than 10 per cent. and not more than 10.2 per cent. of NH_3, have a temperature of 15° C., and be added at once. A clear liquid is produced (*other cinchona alkaloids*).

"Preserve in well-closed containers, protected from light." *U. S.*

"Small, light, white, silky crystals. No odor; taste intensely bitter. Soluble in 800 parts of *water*, and in 65 parts of *alcohol* (90 per cent.). Aqueous solution exhibits a blue fluorescence. Entirely soluble in *water* acidified with a mineral acid. Yields the *reaction* characteristic of sulphates. When to 10 millilitres of an aqueous solution (1 in 1000) 0.5 millilitre of *solution of bromine* and, after well shaking, 1 drop of *strong solution of ammonia* are added, a deep green coloration is produced. Exposed to dry air the crystals effloresce until the water of crystallization is reduced from 7½ molecules to 2 molecules. Aqueous solution yields with *solution of ammonia* a precipitate soluble in *ether*. When 2 grammes, weighed after drying at 50° C., are digested at 60° to 65° C. in a stoppered test-tube with 20 millilitres of *water* for half an hour, repeatedly shaken, then allowed to cool to 15° C., kept at that temperature for half an hour, stirred from time to time, the crystals pressed, and the expressed liquid filtered, then 5 millilitres of this filtrate, transferred to a dry test-tube and brought to a temperature of 15° C., yield, on the gradual addition of 6 millilitres of *solution of ammonia*, also at a temperature of 15° C., a precipitate which redissolves on rotating the tube (limit of other cinchona alkaloids). 1 gramme dissolves in 7 millilitres of a mixture of 2 volumes of *chloroform* and 1 volume of *absolute alcohol*. No appreciable ash." *Br.*

The acid quinine salts possess fluorescent properties with the exception of those of the haloid acids. The fluorescence is recognizable in a solution containing only one part of quinine in 100,000 parts of water. It has also been discovered that the presence of acetphenetidin conceals the fluorescence of sulphuric acid solutions of quinine. The diluted acids, and tartaric and oxalic acids in excess, dissolve the sulphate easily. With an additional equivalent of sulphuric acid it forms another sulphate, which is more soluble in water than the official salt, and crystallizes from its solution with much greater difficulty.

Quinine sulphate, owing to the ease with which it parts with its water of crystallization, is apt to mislead those who seek to determine its quality. Forty samples examined by A. J. Cownley showed results varying from 8.1 to 15.95 per cent. of water of crystallization. He recommends for adoption in the Pharmacopœia the air-dried salt, which contains two molecules of water (4.6 per cent.), as being constant in composition. Farr and Wright confirm Cownley's views, and object to "anhydrous" quinine sulphate, which has been proposed by some chemists as the standard, because it has the opposite fault of absorbing moisture. (*P. J.*, 1896, 525; also *P. J.*, 1897, 203.)

The official test is probably the most reliable of all to establish a maximum limit of small quantities of other cinchona alkaloids. It is a modification of Kerner's (see *U. S. D.*, 19th edition, page 1045), and admits the presence of a trace of other alkaloids. This certainly is as pure as the quinine sulphate need be. To separate the remaining trace of alkaloids entirely would require too great an expense, in fact it would more than double the cost of the salt.

Quinine sulphate is decomposed by the alkalies, their carbonates, and the alkaline earths. In solution it affords white precipitates with potassium and sodium hydroxides, and ammonia, which are partly soluble in an excess of alkali. Quinine sulphate is also precipitated by astringent infusions, the tannic acid of which forms a white insoluble compound with quinine. The soluble salts of lead and of barium occasion precipitates; and that produced by the salts of barium is insoluble in the acids. The soluble salts of acetic, oxalic, tartaric, and gallic acids occasion more or less precipitation with solution of quinine sulphate without excess of acid. A solution of chlorine added to a solution of quinine sulphate and followed by the addition of ammonia water occasions an emerald-green color and, in certain proportions, the deposition of a green precipitate. The green compound has received the name of *thalleioquin*. The drop of ammonia should be put in without agitation. According to Flückiger, 1-5000th part of quinine can thus be found. With bromine instead of chlorine the test is more delicate. Flückiger states that 1-20,000th part of the alkaloid can be detected. (See a paper by C. F. Zeller, ***A. J. P.***, 1880, p. 385.) Some improvements in the thalleioquin test were suggested by LaWall (*A. J. P.*, 1912, p. 484), to obviate the difficulties frequently encountered, which were found to be principally due to oxyacids in the chlorine solution. This solution is frequently not freshly nor properly prepared. A much more delicate reaction is produced by the use of a reagent made by dissolving 0.5 Gm. of potassium bromate and 10 cc. of hydrochloric acid in enough water to make 100 cc. With this reagent it was found possible (when using volumes as large as 100 cc. of the solution being tested) to detect quinine in dilutions of 1-200,000. The procedure is as follows: Take 100 cc. of suspected solution, add 5 to 10 drops of the reagent, agitate well and immediately add 10 drops of stronger ammonia water and mix thoroughly.

F. S. Hyde (*Proc. A. Ph. A.*, 1897, 704) states that a solution of calcium hypochlorite gives more satisfactory results in the thalleioquin test than either chlorine or bromine water, the results being more certain and brilliant. If, previously to the use of ammonia in the chlorine test, a concentrated solution of potassium ferrocyanide be added, a dark red color is produced, which persists for several hours, but ultimately passes into green. This does not take place with cinchonine; and, though quinidine sulphate gives the same red color, this does not disappear as with the quinine salt, but is persistent. (Schwartzer, *J. P. C.*, 4e sér., iii, 475.) Quinine sulphate gives a reddish-brown precipitate with iodine dissolved in a solution of potassium iodide. (See *Herapathite* under *Quinina.*) A delicate reagent for quinine has been proposed by Giessa and Halberkann (*B. P. Ct.* through *Ph. Era*, 1919, lii, 100). It consists of potassium iodide 10 parts, mercuric chloride twenty-seven parts, glacial acetic acid 2.5 parts and water 200 parts. It is said to give a turbidity with 1 part of quinine in 200,000 parts of water. To detect quinine in urine with this reagent, the alkaloid should first be extracted with ether. Kolthoff (*D. C.*, 1919, lxiii, 381) has found that the well known *Kerner's test* for differentiating other cinchona alkaloids from quinine gives satisfactory results only when applied to quinine sulphate and that it is absolutely unreliable when applied to the bisulphate, hydrochloride or the alkaloid itself. No satisfactory method has yet been found for the quantitative separation of quinine and strychnine, for application to elixirs and similar preparations containing both alkaloids. For a discussion of the methods that have been proposed, see a paper by A. R. Bliss (*J. A. Ph. A.*, 1919, viii, 804). For valuable comments on quinine sulphate tests, see *Proc. A. Ph. A.*, 1897, 705.

Adulterations.—Quinine sulphate has often been adulterated. The effects of adulteration may be produced by the variable quantity of water which quinine sulphate may contain, without any observable alteration in its sensible properties. It is easy to detect and to obviate this natural sophistication by exposing a suspected specimen to a heat of 115° C. The loss of weight will indicate the quantity of water not essential to the salt. This is now covered by the official limiting test for the amount of moisture. Calcium sulphate, and other alkaline or earthy salts, gum, sugar, mannite, starch, stearin, caffeine, salicin, phlorizin, and the cinchonine sulphate, and sulphates of other cinchona alkaloids, are among the substances which are said to have been fraudulently added in former times, but such gross adulterants have disappeared from the market product. It is sometimes replaced by or mixed with other cinchona alkaloids. According to W. A. Puckner (*West. Drug.*, 1896, 393), nearly pure crystallized calcium sulphate in fine needle-shaped crystals has been exploited as tasteless quinine sulphate under the name of *flora china.*

Uses.—The fatuous persistence with which the American profession and public continue to prefer this salt is one of the peculiar problems of crowd psychology. It contains less quinine than the hydrochloride, representing 85.55 per cent. of anhydrous quinine, is practically insoluble and has no possible advantages. (See *Quinina.*)

Dose, two to ten grains (0.13–0.65 Gm.).

Off. Prep.—Ferri et Quininæ Citras, *Br.;* Pilula Quininæ Sulphatis, *Br.;* Syrupus Ferri Phosphatis cum Quinina et Strychnina, *Br.;* Tinctura Quininæ Ammoniata, *Br.;* Elixir Cinchonæ Alkaloidorum, *N. F.;* Elixir Ferri Pyrophosphatis, Quininæ et Strychninæ, *N. F.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Ferri, Quininæ, Aloes et Nucis Vomicæ, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arseni Fortiores, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arseni Mites, *N. F.;* Pilulæ Opii, Digitalis et Quininæ, *N. F.*

QUININÆ TANNAS. U. S.

QUININE TANNATE Quin. Tann

"Quinine Tannate is a compound of quinine with tannic acid, of somewhat varying composition, corresponding to not less than 30 per cent. and not more than 35 per cent. of anhydrous quinine [$C_{20}H_{24}O_2N_2$]." *U. S.*

Tannate of Quinine; Tannas Quinicus; Chininum Tannicum.

Quinine tannate may be prepared by precipitating one part of quinine sulphate, dissolved in thirty parts of water acidulated with a few drops of sulphuric acid, with a solution of three parts of tannic acid dissolved in thirty parts of cold water, and then washing and drying the precipitate. For other methods of preparing the tannate, see *West. Drug.*, 1893, 352; *Ph. Centralh.*, 1894, 155; *Proc. A. Ph. A.*, 1894, 675. It has the advantage of possessing little taste, but doubts have been repeatedly expressed about its efficiency.

Description and Physical Properties.—"A pale yellow or yellowish-white, amorphous powder. It is odorless and tasteless, or has not more than a slightly bitter, astringent taste. Quinine Tannate is only slightly soluble in water, chloroform, and ether. It is somewhat more soluble in alcohol.

"When heated it melts to a purplish, viscous mass. A saturated aqueous or alcoholic solution of Quinine Tannate is colored blue-black by ferric chloride T.S. The alkaloid obtained in the assay responds to the identity tests under *Quinina.*

"Quinine Tannate loses not more than 10 per cent. when dried to constant weight at 100° C. (*water*). Ash: not more than 0.3 per cent. Shake 0.5 Gm. of Quinine Tannate with 50 cc. of distilled water and 1 cc. of nitric acid for five minutes, and filter: a 10 cc. portion of the filtrate is not colored by 1 cc. of hydrogen sulphide T.S. (*heavy metals*). Other 10 cc. portions of the filtrate show no more *chloride* than corresponds to 0.5 cc. of fiftieth-normal hydrochloric acid and no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid. Shake 1 Gm. of Quinine Tannate with 25 cc. of dehydrated ether for five minutes, filter, and wash the filter with 10 cc. of dehydrated ether. Evaporate the combined filtrate and washings and dry at 100° C.: the residue does not exceed 1 per cent. (*uncombined quinine*).

"Preserve in well-closed containers, protected from light." *U. S.*

Assay.—"Transfer to a separator about 0.5 Gm. of Quinine Tannate, accurately weighed, add 10 cc. of distilled water and 10 cc. of ammonia T.S., and shake at first with 20 cc. of ether, then with three successive 10 cc. portions of ether. Evaporate the combined ethereal liquids and dry the residue to constant weight at 100° C. The weight of the anhydrous quinine ($C_{20}H_{24}O_2N_2$) so obtained corresponds to not less than 30 and not more than 35 per cent. of the weight of the Quinine Tannate taken." *U. S.*

Uses.—This is one of the least efficient of the quinine preparations; not only does it contain less than one-half the amount of alkaloid in the other salts but because of its slow hydrolysis and consequently delayed absorption has a still lower index of therapeutic activity. It is useful, however, as a means of administering quinine to young children, who are not able to swallow pills, because of its comparative tastelessness. It has to a considerable extent been replaced, even for this purpose, by some of the synthetic compounds such as the ethylcarbonate.

Dose, for adults, three to fifteen grains (0.2–1 Gm.).

RENNINUM. N. F.

RENNIN

"The partially purified milk-curdling enzyme obtained from the glandular layer of the stomach of the calf, *Bos taurus* Linné (Fam. *Bovidæ*), and capable of coagulating not less than 25,000 times its weight of fresh milk. Rennin of a higher coagulating power may be brought to the standard by admixture with sodium chloride and lactose. Rennin deteriorates rapidly and must be kept in well-stoppered, amber-colored bottles, and stored in a cool place." *N. F.*

Lab; Käselab, *G.;* Caillete, Présure, *Fr.*

Whether the milk-curdling enzyme of the gastric juice is distinct from pepsin is not certain although the majority of physiologists appear to so regard it. *Rennet* is an aqueous or vinous infusion of the dried stomach of the calf, though that of the sheep or other animal would probably answer the same purpose. It is much used, as every one knows, for curdling mild, a property which it owes to a portion of the gastric secretion, retained in the mucous tissue of the stomach. Such a solution was formerly recognized by the N. F. under the title *Liquor Seriparus.*

The N. F. recognizes a dried preparation containing the milk-curdling ferment. It is described as follows:

Description and Physical Properties.—"Rennin occurs as a grayish white or yellowish white powder, or as pale yellow grains or scales having a characteristic and slightly saline taste and a peculiar, not unpleasant odor. It is slightly hygroscopic. It is slowly soluble in water and in diluted alcohol, the solutions being more or less opalescent.

"When mounted in water or diluted alcohol and examined microscopically, it shows no cellular structure, and no blue coloration is produced on the addition of iodine T.S.

"**Assay.**—Mix 0.1 Gm. of Rennin with 50 cc. of distilled water by gentle stirring or trituration in a mortar (vigorous shaking or violent agitation must be avoided) and allow the liquid to stand for exactly 15 minutes. Place 50 cc. of cow's milk, having an acidity of not less than 0.14 per cent. nor more than 0.15 per cent., calculated as lactic acid (increasing the acidity of the milk, if low, by the addition of the required amount of lactic acid, or reducing it, if high, by the addition of the required quantity of sodium hydroxide) in a beaker about 12 centimeters high and 5 centimeters in diameter. Warm the milk rapidly on a water-bath to 43° C., add 1 cc. of the Rennin solution and stir the mixture slowly for 10 seconds. Maintain the temperature at 43° C. until the milk begins to thicken, as shown by a distinctly convex surface when the beaker is tipped to an angle of about 45°. This thickening must take place within 10 minutes from the time of the addition of the rennin solution. An additional 30 seconds on the water-bath produces a firm curd. The acidity of the milk used is ascertained by titrating 50 cc. of the undiluted milk with normal solution of sodium hydroxide, using phenolphthalein T.S. as indicator." *N. F.*

George Ellis prepared *rennet wine* as follows: Take the stomach of a calf immediately after the animal has been killed, cut off and reject about three inches of the upper or cardiac portion, slit the stomach longitudinally, wipe it gently with a dry napkin so as to remove as little of the clean mucous as possible, then cut it into small pieces, the smaller the better, put it into a common wine bottle, fill the bottle with good sherry, and let it stand corked for three weeks. It is known to be good if a teaspoonful will coagulate half a pint of milk in two minutes at 37.7° C.

Rennin was admitted to the National Formulary for the purpose of using it as an ingredient in making Compound Elixir of Pepsin and Rennin, which is chiefly used as a vehicle for nauseous medicines.

Off. Prep.—Elixir Pepsini et Rennini Compositum, *N. F.*

RESINA. U. S., Br.

ROSIN Resin. [Colophony]

"The residue left after distilling the volatile oil from the oleoresin obtained from *Pinus palustris* Miller and from other species of *Pinus*

(Fam. *Pinaceæ*)." *U. S.* "The residue left after the distillation of the oil of turpentine from the crude oleo-resin (crude turpentine) of various species of Pinus." *Br.*

Colophone, Arcanson, Brai sec, *Fr.;* Colophonium, *P. G.;* Kolophonium, Geigenharz, Fichtenharz, *G.;* Colofonia, Ragia, Pece greca, *It.;* Colofonia, Pez griega, *Sp.*

After the distillation of the volatile oil from turpentine (see *Terebinthina*), a resinous matter remains, which on the continent of Europe is called *colophony,* but with us is commonly, and now officially, known by the name of *rosin.* It is the *Resina* of the U. S. and British Pharmacopœias. It is sometimes called *resina flava,* or *yellow rosin.* When this, in a state of fusion, is strongly agitated with water it acquires a distinct appearance, and is denominated *resina alba,* or *white rosin.* The ports from which rosin is shipped are Wilmington, N. C., Charleston, S. C., and Savannah, Ga.

Common or *yellow rosin,* in its purest state, is beautifully clear and pellucid, but much less so as usually found in commerce. Its color is yellowish-brown with a tinge of olive, and more or less dark, according to its purity and the degree of heat to which it has been exposed in its preparation. Sometimes it is almost black. It is rather heavier than water. It is completely liquid at 152.5° C., begins to emit bubbles of gas at 157.5° C., and is decomposed at a red heat.

Description and Physical Properties.—"Sharply angular, translucent, amber-colored fragments, frequently covered with a yellow dust, fracture brittle at ordinary temperatures, shiny and shallow-conchoidal. The odor and taste are slightly terebinthinate. Rosin is freely soluble in alcohol, ether, benzene, glacial acetic acid, and in fixed or volatile oils. It is also soluble in dilute solutions of the fixed alkali hydroxides.

"Its alcoholic solution is acid to litmus paper. Specific gravity: 1.07 to 1.09 at 25° C. Rosin is easily fusible and burns with a dense yellowish smoke. Ash: not more than 0.05 per cent. Acid number: not less than 150." *U. S.*

"Translucent, of a light amber color, compact, brittle, pulverisable; fracture shining; odor and taste faintly terebinthinate. Soluble in *alcohol* (90 per cent.), in *ether, benzene,* and *carbon disulphide.* Readily fusible; burns with a dense yellow flame and much smoke, leaving no appreciable ash." *Br.*

Composition.—Rosin consists chiefly of several isomeric forms of the anhydride of *abietic acid* (*abietinic acid*), which has the formula $C_{19}H_{28}O_2$. Jean, however (*Chem. News,* xxvi, 207), has separated two other resinoid substances in addition to abietic acid. Lewkowitsch (*Chem. Analysis of Oils,* etc., 2d ed., 236) states that rosin also contains varying quantities of unsaponifiable hydrocarbons, due to the partial breaking up of the acid on distilling the pine rosin. This may vary from 5 to 9 per cent. in the American rosin. For a paper on abietic acid by Mead and Kremers, see *Proc. A. Ph. A.,* 1893, 198. By shaking coarsely powdered rosin with dilute alcohol and warming, it is converted into *abietic acid.* Cohn (*Ph. Wb.,* 1917, liv, 767) has done some research recently which indicates that rosin is simply impure abietic acid. Knecht and Hibbert (*J. P. C.,* 1919, xx, 324) have obtained from American rosin dextrorotatory *pimaric acid,* melting point 161°, and from French rosin a lævorotatory *pimaric acid* of the same melting point. Rosin, when it is boiled with alkaline solutions, forms greasy salts of abietic acid, the so-called rosin soaps which are used in admixtures with other soaps. As the acid is dibasic, these salts contain two atoms of alkali metal in combination. Rosin, distilled by itself, yields the so-called "rosin-oil," of which two fractions are taken separately—the first that distilling under 360° C., and the second that over 360° C.—and some 31 per cent. of fixed gases. The lighter fraction is known commercially as *rosin essence,* and is, according to Renard (*J. Chem. S.,* Aug., 1884, p. 843), composed of hydrocarbons, representing almost all series, from the paraffin series to the terpenes, including pentane and hexane, amylene and hexylene, toluene, xylene, and cumene, the tetra- and hexa-hydrides of all three of these, terebenthene and cymene. Several aldehydes and acids of the fatty series, such as isobutyric and valeric, were also recognized. The heavier fraction, or *rosin oil* in the stricter sense of the word, is composed of polymers of the hydrocarbons C_nH_{2n-2}, which readily resinify by the absorption of oxygen. This accounts for the use of rosin oil as an adulterant of linseed oil in the manufacture of printer's ink. When distilled with superheated steam, rosin yields benzene and toluene. *Sylvic acid,* formerly considered to be a constituent of rosin, is now regarded as abietic acid. Propionic acid has, according to Renard, been obtained in abundance from the tar produced by the destructive distillation of rosin. (*A. Pharm.,* 1886, p. 939.)

A. Tschirch and B. Studer determined the nature of the constituents of American rosin. The sample under examination (presumably from *P. palustris*) was completely soluble in the ordinary solvents for resin, including petroleum benzin, in which some other varieties of rosin are only partly soluble. Its alcoholic solution is strongly acid in reaction. Its sp. gr. at 15° C. was 1.090. Its composition was proved to be as follows:

1. Acids soluble in ammonium carbonate: *α-abietinic* (*abietic*) *acid,* $C_{19}H_{28}O_2$, forming an insoluble lead salt, 30 per cent.; *β-abietinic acid,* $C_{19}H_{28}O_2$, not forming a lead salt, 22 per cent. 2. Acid soluble in sodium carbonate: *γ-abietinic acid,* $C_{19}H_{28}O_2$, insoluble in ammonium carbonate, 31.06 per cent. 3. Volatile oil, 0.4 to 0.7 per cent. 4. Resene, 5 to 6 per cent.

The impurities amounted only to 0.1 per cent., the loss in operation, however, to 10 per cent.

Fahrion having proposed a method for the differentiation of different rosins, based upon their relative solubility in petroleum benzin, the authors determined the amount of solvent necessary to dissolve 1 Gm. of rosin, freshly powdered, and old powder; also abietinic acids and the resene in petroleum benzin, with the following results:

Rosin, old powder, 1 Gm. required	400 cc.
Rosin, fresh, 1 Gm. required	60 cc.
α-Abietinic acid, 1 Gm. required	500 cc.
β-Abietinic acid, 1 Gm. required	100 cc.
γ-Abietinic acid, 1 Gm. required	100 cc.
Resene	50 cc.

These results show that all the resin-acids, as well as the rosin, are more or less soluble in petroleum benzin, and that fresh rosin is more readily soluble than the isolated acids, a peculiarity which has also been noticed in the case of other bodies. On the other hand, old rosin is much less soluble in petroleum benzin than is fresh rosin. (*A. Pharm.*, Oct., 1903, 495–522.)

A new and very interesting class of derivatives from colophony or rosin has been prepared by Eugen Schaal, of Feuerbach, Germany, and introduced into commerce under the name of *ester gums*. These are the *glyceryl, methyl,* and *ethyl esters of abietic acid,* made by heating the resin acid and the alcohol under pressure until molecular condensation takes place. The product is then distilled off under reduced pressure. These "ester gums" are being used to advantage as substitutes for copal, damar, and kauri gum in varnish making.

Uses.—Rosin is important as an ingredient of ointments and plasters, but is rarely used internally. According to Olmstead, it has the property of preventing the oxidation of fatty substances, and thus contributes to the preservation of ointments. (*A. J. P.*, xxii, 325.)

Off. Prep.—Ceratum Resinæ, *U. S.* (*Br.*); Emplastrum Calefaciens, *Br.;* Emplastrum Resinæ, *Br.;* Emplastrum Saponis, *Br.;* Ceratum Resinæ Compositum, *N. F.;* Linimentum Terebinthinæ (from Rosin Cerate), *N. F.;* Solutio Resinæ Chloroformica, *N. F.*

RESINA IPOMŒÆ. U. S. (Br.)

RESIN OF IPOMEA Res. Ipom.

"Scammony Resin is a mixture of resins obtained from Scammony Root or from Orizaba Jalap Root." *Br.*

Scammoniæ Resina, *Br.;* Scammony Resin.

"Ipomea, in coarse powder, 1000 Gm.; Alcohol, Water, each, a sufficient quantity. Moisten the Ipomea with sufficient alcohol, pack it in a cylindrical percolator, and add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding alcohol until the percolate ceases to produce more than a slight turbidity when dropped into water. Distil off the alcohol until the percolate is reduced to the consistence of thin syrup, and pour this slowly, with constant stirring, into 1000 cc. of hot water. When the precipitate has subsided, decant the supernatant liquid, wash the precipitated resin twice by decantation with fresh portions of 1000 cc. each of hot water, drain off the water thoroughly, and dry the Resin on a water bath." *U. S.*

"Exhaust the coarsely powdered Root with Alcohol (90 per cent.). Recover most of the alcohol by distillation; pour the concentrated solution thus obtained into eight times its volume of Distilled Water; allow the resin that separates to subside, wash it with Distilled Water, and dry at a gentle heat." *Br.*

Because of the almost complete disappearance from the market of genuine scammony resin, the Br., 1914, permitted the substitution of the resin of the so-called "Mexican scammony." This, in our opinion, is an unfortunate procedure because there can be no doubt as to the difference in the composition of these two resins and there is no satisfactory evidence of their therapeutic interchangeability. The U. S. X faced with a similar problem has solved it, we believe, more satisfactorily by dropping altogether scammony and substituting the Ipomea resin.

Genuine scammony resin was originally prepared by incising the root and evaporating the milk juice which exuded. As thus collected it was really a gum-resin and formed spontaneous emulsions. This was known officially in the Pharmacopœia as *Scammonium,* and popularly called *Virgin Scammony.* Because of the adulteration practised by the natives in collecting and preparing this substance, both of the Pharmacopœias adopted the plan of importing whole root and preparing the resin by extracting with alcohol.

Description and Physical Properties.—"Translucent masses or fragments, of a brown color, breaking with a glossy, resinous fracture; odor characteristic. Resin of Ipomea is soluble in alcohol and in chloroform; from 80 to 90 per cent is soluble in ether, and less than 5 per cent. is soluble in petroleum benzin.

"Ash: not more than 0.5 per cent. Resin of Ipomea is slowly soluble in five times its weight of ammonia T.S. and in potassium hydroxide T.S., yielding a somewhat cloudy solution which does not become gelatinous on standing. When these solutions are acidified with hydrochloric acid, only a slight turbidity appears (*rosin, guaiac or other resins*). Resin of Ipomea, dried at 100° C., loses not more than 1 per cent. (*water*). Triturate Resin of Ipomea with distilled water: the latter does not become colored, none of the resin dissolves (*soluble impurities*), and the water does not have a bitter taste (*aloin*). Shake 0.02 Gm. of Resin of Ipomea with 5 cc. of ether, filter, and evaporate the filtrate on filter-paper: no greenish-blue color is produced by the addition of a drop of ferric chloride T.S. to the filter-paper (*guaiac*). Dissolve 0.02 Gm. of Resin of Ipomea in 2 cc. of glacial acetic acid and add a few drops of sulphuric acid: the mixture does not acquire a pink color (*rosin*). Acid number: not less than 25 and not more than 30. Ester number: not less than 170 and not more than 185. Saponification value: not less than 195 and not more than 215." *U. S.*

"Brownish, translucent, brittle fragments, breaking with a resinous fracture; readily reduced to a pale-brown powder. Characteristic, agreeable odor; taste acrid. Readily soluble in *alcohol* (90 per cent.). When 1 gramme of the powdered Resin is triturated with 20 millilitres of *water* and filtered, the filtrate is almost colorless. A solution of 0.1 gramme in 10 millilitres of *solution of sodium hydroxide,* boiled for a few moments and cooled, when acidified with *hydrochloric acid,* may become opalescent but not immediately turbid (absence of certain other resins). Not less than 75 per cent. soluble in *ether.*" *Br.*

The resin of Ipomea is liable to adulteration with rosin, guaiac or jalap resin. These are all excluded by the official tests.

Scoville (*J. I. E. C.,* 1919, xi, 335) has reported on a substance called *Resina drastica* which very closely resembles Ipomea resin. It is less soluble in ether and in chloroform than is true scammony resin or the Mexican scammony resin. It is more slowly soluble in alkalies than is the true or Mexican scammony resin. All three resins gave cloudy solutions in alkaline solution.

L. Lutz (*Pharm. Ztg.,* 1912, xxiii, p. 232) states that the behavior of the resin with iodine when examined microscopically affords a method of distinguishing the resin from a number of its substitutes and adulterants.

For chemistry of this resin see under *Ipomœa.*

Uses.—Ipomea resin is an energetic cathartic, likely to occasion griping, and sometimes operating with harshness. On account of its occasional violence, it is seldom administered, except in combination with other cathartics, the action of which it promotes, while its own harshness is mitigated. Its disposition to gripe may be counteracted by the addition of an aromatic.

Dose, from two to five grains (0.12–0.3 Gm.).

Off. Prep.—Extractum Colocynthidis Compositum, *U. S., Br.;* Pilula Colocynthidis Composita, *Br.;* Pilula Colocynthidis et Hyoscyami, *Br.;* Pilula Scammonii Composita, *Br.;* Pulvis Scammonii Compositus, *Br.;* Tinctura Jalapæ Composita, *N. F.*

RESINA JALAPÆ. U. S. (Br.)

RESIN OF JALAP Res. Jalap.

"Jalap Resin is a mixture of resins obtained from Jalap." *Br.*

Jalapæ Resina, *Br.;* Résine de Jalap, *Fr.;* Jalapenharz, *G.;* Resina di gialappa, *It.;* Resina de jalapa, *Sp.*

"Jalap, in fine powder, 1000 Gm.; Alcohol, Water, each, a sufficient quantity. Moisten the powder with 500 cc. of alcohol, pack it in a cylindrical percolator, and add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding alcohol, until the percolate ceases to produce more than a slight turbidity when dropped into water. Distil off the alcohol until the percolate is reduced in weight to 250 Gm., and add the latter slowly, with constant stirring, to 3000 cc. of water. When the precipitate has subsided, decant the supernatant liquid, and wash the precipitate twice by decantation with fresh portions of 1000 cc. each of hot water. After having drained off all of the liquid, transfer the Resin to a porcelain dish and heat it to dryness on a water bath." *U. S.*

"Exhaust coarsely powdered Jalap with Alcohol (90 per cent.). Recover most of the alcohol by distillation; pour the concentrated solution thus obtained into eight times its volume of Distilled Water; allow the resin that separates to subside, wash with Distilled Water, and dry at a gentle heat." *Br.*

Extract of Jalap was formerly official. It has been replaced in both the U. S. and British Pharmacopœias by the resin. (See *U. S. D.,* 19th edition, page 479.)

Description and Physical Properties.—"Yellow to brown masses or fragments, breaking with a resinous, glassy fracture and translucent at the edges, or a yellowish-gray to yellowish-brown powder. It has a slight, peculiar odor, a somewhat acrid taste, and is permanent in the air. Resin of Jalap is soluble in alcohol in all proportions; insoluble in carbon disulphide, benzene, and in fixed or volatile oils.

"Add 1 Gm. of the powdered Resin to 20 cc. of chloroform in a stoppered flask, shake the mixture occasionally during one hour, then filter, wash the flask and residue on the filter with three successive 5 cc. portions of chloroform, evaporate the combined filtrates in a tared dish, and dry the residue to constant weight at 100° C.: it weighs not more than 0.3 Gm. Add 1 Gm. of the powdered Resin to 20 cc. of ether in a stoppered flask, shake the mixture occasionally during one hour, then filter, wash the flask and residue on the filter with three successive 5 cc. portions of ether, evaporate the combined filtrates in a tared dish, and dry the residue to constant weight at 100° C.: it weighs not more than 0.12 Gm. (*rosin or other resins*). It is slowly but completely soluble in 5 times its weight of ammonia water, and the solution does not become gelatinous on standing. When this solution is acidified with hydrochloric acid, only a slight turbidity appears (*rosin, guaiac, or other resins*). When Resin of Jalap is dried at 100° C. the loss in weight should not exceed

1 per cent. (*water*). When Resin of Jalap is triturated with distilled water, the latter does not become colored, none of the Resin dissolves (*soluble impurities*), and the water does not have a bitter taste (*aloin*). Shake 0.02 Gm. of Resin of Jalap with 5 cc. of ether, filter, and evaporate the ethereal filtrate on filter paper: no greenish-blue color is produced by the application of a drop of ferric chloride T.S. to the filter paper (*guaiac*). One Gm. of Resin of Jalap when dissolved in 50 cc. of alcohol containing 1 cc. of phenolphthalein T.S., requires not more than 0.5 cc. of half-normal alcoholic potassium hydroxide to produce a red color (*acid resins*). Dissolve 0.02 Gm. of Resin of Jalap in 2 cc. of glacial acetic acid and add a few drops of sulphuric acid: the mixture does not acquire a pink color (*rosin*)." *U. S.*

"In dark-brown opaque fragments, translucent at the edges; brittle, breaking with a resinous fracture; readily reduced to a pale-brown powder. Characteristic odor; taste acrid. Readily soluble in *alcohol* (90 per cent.). When 1 gramme of the powdered Resin is triturated with 20 millilitres of *water* and filtered, the filtrate is almost colorless. A solution of 0.1 gramme in 10 millilitres of *solution of sodium hydroxide,* boiled for a few moments and cooled, when acidified with *hydrochloric acid* may become opalescent but not immediately turbid (absence of certain other resins). Not more than 15 per cent. of the powdered Resin is soluble in *ether* (absence of scammony resin)." *Br.*

The U. S. resin, although pure enough for practical purposes, is still colored. To obtain it colorless, the powdered jalap should be mixed, before percolation, with an equal quantity of finely powdered animal charcoal, and, previously to the introduction of this mixture into the percolator, half the quantity of animal charcoal, similarly powdered, should be packed in the bottom of the percolator. The coloring matter is thus left behind, and the resulting tincture, treated as directed in the process, yields the resin as white as starch.

For further information concerning this resin see under *Jalapa.*

Dose, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Pilulæ Hydrargyri Chloridi Mitis Compositæ, *U. S.;* Pilulæ Catharticæ Vegetabiles, *N. F.*

RESINA PODOPHYLLI. U. S. (Br.)

RESIN OF PODOPHYLLUM Res. Podoph. [Podophyllin]

Podophylli Resina, *Br.;* Podophyllum Resin; Resin of May-Apple; Résine de Podophylle, *Fr.;* Podophyllinum, *P. G.;* **Podophyllumharz,** *G.;* Podofillina, *It.;* Podofilino, *Sp.*

"Podophyllum, in fine powder, 1000 Gm.; Hydrochloric Acid, 10 cc.; Alcohol, Water, each, a sufficient quantity.

"Moisten the drug with 500 cc. of alcohol, pack it in a cylindrical percolator, and add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding alcohol, until the percolate ceases to produce more than a slight turbidity when dropped into water. Distil off the alcohol until the percolate is reduced to the consistence of a thin syrup, and pour this slowly, with constant stirring, into 1000 cc. of water, mixed with the hydrochloric acid and cooled to a temperature below 10° C. When the precipitate has subsided, decant the supernatant liquid, and wash the precipitate twice by decantation with fresh portions of 1000 cc. of cold water. Spread it in a thin layer upon a strainer and dry the product by exposure to the air, in a cool place, protected from light. Should it coalesce during the drying or aggregate into lumps having a glossy surface, break it into pieces, and powder it in a mortar." *U. S.*

"Podophyllum Rhizome, in No. 40 powder, 1000 *grammes;* Alcohol (90 per cent.), Distilled Water, Hydrochloric Acid, of each, a sufficient quantity. Exhaust the Podophyllum with the Alcohol by percolation; recover the greater part of the alcohol by distillation; pour the resulting liquid into eight times its volume of Distilled Water acidified with one twenty-fourth of its volume of Hydrochloric Acid, constantly stirring; after twenty-four hours collect the deposited resin, wash with Distilled Water, and dry at a temperature not exceeding 40° C." *Br.*

The British Pharmacopœia (1885) abandoned the use of hydrochloric acid, as it is not necessary if the tincture is evaporated to the consistence of *thick* honey. Hydrochloric acid was directed in the 1898 revision as it seems to aid the precipitation when the tincture is not so concentrated. The color and yield of resin of podophyllum may be made to vary by adding alum, acids, or other substances to the water. It darkens if dried with the aid of heat, and its color is indeed no indication whatever of its quality.

The proportion of resin contained in the root of the *P. peltatum* appears to vary very much, the variation possibly depending upon the season of the year at which the drug has been gathered. John Barclay (*P. J.,* 1903, Feb., 164) obtained a percentage of 1.6 to 3.86 per cent., stating that these figures were confirmed by the results of the manufacturers of podophyllin on a large scale, but J. C. Umney states that in five years' experience working with batches of 1000 pounds, the rhizome averaged a yield of 6.6 per cent. Both observers noticed that the Indian rhizome (*P. Emodi*) contains a much larger proportion of resin, the average according to Umney being 11.4 per cent. How far the proportion of podophyllotoxin varies in the different rhizomes does not seem to have been determined. (See B. D. Dott, *P. J.,* 1903, Mar., 460.) (*P. J.,* 1911, lxxxvii, p. 156.)

Lohmann (*Proc. N. J. Pharm. Assoc.,* 1896, 51) states that the fresh drug does not yield as large a percentage of resin as the same drug would if tested after being stored for several years; his experiments led him to the conclusion that in the order of value of resin of podophyllum obtained by various methods, that made by precipitation with water alone came first, that made by the U. S. P. process second, and that made by precipitation with solution of alum last. Dohme and Kelly (*D. C.*, 1903, 251), replying to statements of Lohmann (*Proc. A. Ph. A.*, 1903, 317) regarding the yield of resin from podophyllum, state that: 1, the yield from the method of pouring an alcoholic extract into water was 5 per cent.; 2, from pouring an alcoholic extract into acidulated water 5.5 per cent., and 3, from pouring an alcoholic extract into acidulated water containing 5 per cent. of alum, 4.9 per cent. (See also *Podophyllum.*) The color, by process 1, is grayish-white; 2, light brown; 3, greenish-yellow. The value of resin of podophyllum is accurately estimated by the percentage of podophyllotoxin that it yields. Nearly all of the resin of podophyllum in commerce is made by the alum process, has a deep yellow color and is not wholly soluble in alcohol.

Gordon and Merrell (*Proc. A. Ph. A.*, 1902, p. 343) have proposed a method of valuing resin of podophyllum, based upon the content of picropodophyllin and submit a method of assay.

Description and Physical Properties.—" An amorphous powder, varying in color from light brown to greenish-yellow, turning darker when subjected to a temperature exceeding 25° C. or when exposed to light. It has a slight, peculiar and a faintly bitter taste. *It is very irritating to the eye, and to mucous membranes in general.*

" Resin of Podophyllum is soluble in potassium or sodium hydroxide T.S., forming a deep yellow liquid, which gradually becomes darker on standing, and from which the resin is reprecipitated by acids. A hot aqueous solution of Resin of Podophyllum deposits most of its contents on cooling, and if the cooled liquid is filtered, the filtrate has a bitter taste, and turns brown upon the addition of a few drops of ferric chloride T.S.

" Ash: not more than 1.5 per cent. Resin of Podophyllum is soluble in alcohol with only a slight opalescence and the solution is faintly acid to litmus paper. Add 0.4 Gm. of Resin of Podophyllum to 3 cc. of 60 per cent. alcohol, follow with 0.5 cc. of potassium hydroxide T.S., and shake gently: the mixture does not gelatinize (*difference from resin obtained from Podophyllum Emodi*). Add 1 Gm. of the powdered Resin to 20 cc. of ether in a stoppered flask and shake the mixture occasionally during one hour. Filter, and wash the residue in the flask and on the filter with three successive 5 cc. portions of ether. Evaporate the combined ether solutions in a tared dish and dry the residue to constant weight at 100° C: it weighs not less than 0.75 Gm. Add 1 Gm. of the powdered Resin to 20 cc. of chloroform in a stoppered flask and shake the mixture occasionally during one hour. Filter, and wash the residue in the flask and on the filter with three successive 5 cc. portions of chloroform. Evaporate the combined filtrates in a tared dish and dry the residue to constant weight at 100° C.: it weighs not less than 0.65 Gm.

" Preserve in well-closed containers, protected from light." *U. S.*

" An amorphous powder, varying in color from pale yellow to deep orange-brown. Taste bitter. Entirely or almost entirely soluble in *alcohol* (90 per cent.) and in *solution of ammonia;* precipitated from the former solution by *water,* from the latter by acids. Partly soluble in *ether.* Ash not more than 1 per cent." *Br.*

The official resin is soluble in alkaline solutions, from which it is precipitated by acids, in this respect differing strikingly from the resins of jalap and scammony. It is insoluble in oil of turpentine. For discussion of the solubilities of the fresh resin, see G. M. Beringer (*A. J. P.*, 1894, 11). The name *podophyllin,* given to it by the eclectic practitioners, who have long been in the habit of using this resin, is inappropriate, and should be abandoned.

For description of the chemistry of this resin see under *Podophyllum.*

Uses.—Resin of podophyllum is an active cathartic. It forms the basis of several proprietary " liver pills." It is often used in combination with milder laxatives in chronic *constipation.* It was at one time supposed to be especially cholagogue, but this belief has been of late discredited. A small proportion of extract of belladonna or hyoscyamus mitigates its irritant action. Care must be taken in handling it in quantity, as it is a powerful irritant, frequently producing conjunctivitis.

Dose, one-eighth to one-fourth of a grain (0.008–0.016 Gm.).

Off. Prep.—Tinctura Podophylli, *Br.;* Pilulæ Aloes et Podophylli Compositæ, *N. F.;* Pilulæ Aloes, Hydrargyri et Podophylli, *N. F.;* Pilulæ Aloini Compositæ, *N. F.;* Pilulæ Catharticæ Vegetabiles, *N. F.*

RESINÆ

RESINS

The term " resin " is used in pharmacopœial parlance with a slightly different significance from that generally given to it by chemists. As employed by the latter, the word resin is applied to a group of hard, brittle vegetable products, which are soluble in alcohol and insoluble in water, soften when heated and melt to clear liquids; they are free from nitrogen and are generally supposed to be the products of the oxidation of volatile oils. They are not chemical identities but are mixtures of the following more or less closely related substances: *resinols* which are certain peculiar alcohols or their acid esters; *resino-tannols,* which are brownish alcohol derivatives that give reactions similar to the tannins; organic acids or their anhydrides; *resenes,* which are the oxidation products of terpenes and are neither esters, anhydrides nor acids. In pharmaceutical practice the term resin is applied to a group of preparations made by extracting the drug with either strong alcohol, or acetone, and adding water, the consequent precipitate being the resin. It is evident that this precipitate will contain all the alcohol soluble and water insoluble principles which may be present in the drug including not only the resins proper, but such substances as certain basic principles, substances of a fatty, waxy or caoutchouc-like nature, etc. It is obvious that the resins thus prepared are different substances from the alcoholic extracts, which contain all the ingredients of the medicine which alcohol is able to take from it.

RESORCINOL. U. S. (Br.)

RESORCINOL Resorcin. [Resorcin]

"Resorcinol, when dried to constant weight over sulphuric acid, contains not less than 99.5 per cent of $C_6H_4(OH)_2$ 1:3." *U. S.* "Resorcin, or meta-dihydroxy-benzene, $C_6H_6O_2$, may be obtained by the interaction of fused sodium hydroxide and sodium metabenzenedisulphonate." *Br.*

Resorcinum, *Br.;* Metadioxybenzene, Metadihydroxybenzene; Résorcine, *Fr.;* Resorcinum, *P. G.;* Resorcina, *It., Sp.*

Resorcinol is *metadihydroxybenzene,* while pyrocatechin is the *ortho* compound and hydroquinone the *para* compound. Hlasiwetz and Barth first obtained this organic body in 1864 by fusing galbanum resin with potassium hydroxide; it was subsequently obtained from sagapenum, asafetida, ammoniac, etc. At present it is made commercially by the following process: benzol-disulphonic acid is first made by the action of fuming sulphuric acid upon benzene. To the purified product milk of lime is added, and subsequently sodium carbonate; after the removal of all of the calcium as carbonate the filtrate is evaporated to dryness and fused with sodium hydroxide in an iron crucible. The melted mixture is dissolved in water, acidulated to liberate sulphur dioxide, filtered and extracted with ether or amyl alcohol. The crude resorcinol is purified by distillation and final recrystallization from benzol. It is important that the benzene used in the initial step be free from toluene.

Description and Physical Properties.—"Colorless, or nearly colorless, needle-shaped crystals, or powder. It has a faint, characteristic odor and a sweetish, followed by a bitter, taste. It acquires a pink tint on exposure to light and air. One Gm. of Resorcinol is soluble in 0.9 cc. of water and in 0.9 cc. of alcohol, at 25° C. One Gm. is soluble in about 0.2 cc. of water at 80° C. It is freely soluble in glycerin and in ether, and is slightly soluble in chloroform.

"Resorcinol melts between 109° and 111° C. The addition of 3 drops of ferric chloride T.S. to 10 cc. of an aqueous solution of Resorcinol (1 in 200) produces a bluish-violet color, changing to brownish-yellow on the addition of ammonia T.S. (*difference from catechol and quinol*). Dissolve 0.1 Gm. of Resorcinol in 2 cc. of sodium hydroxide T.S., add a drop of chloroform, and heat the mixture: an intense crimson color is produced, which changes to pale yellow on the addition of a slight excess of hydrochloric acid.

"Its aqueous solution (1 in 20) is neutral or only faintly acid to litmus paper. Ash: not more than 0.05 per cent. An aqueous solution of Resorcinol (1 in 20) does not emit the odor of phenol when gently warmed. Lead acetate T.S. produces no precipitate in an aqueous solution of Resorcinol (1 in 20) (*catechol*).

"Preserve in well-closed containers, protected from light." *U. S.*

"Colorless, shining, acicular or prismatic crystals. Faint odor; taste pungent and sweetish, followed by bitterness. Soluble in less than 1 part of *water,* or of *alcohol* (90 per cent.); very soluble in *ether,* and in *glycerin;* soluble in *olive oil;* slightly soluble in *chloroform.* Melting point 110° to 111° C.; at a higher temperature sublimes without residue and without evolving an odor of phenol. Alkaline solutions darken in color and exhibit a strong greenish fluorescence. A concentrated aqueous solution is colorless (absence of empyreumatic substances), and neutral or only slightly acid to *litmus;* it is unaffected by the addition of *solution of lead acetate* (absence of catechol). A weak aqueous solution is colored bluish-violet by *T. Sol. of ferric chloride,* the color changing to brownish-yellow on the addition of *solution of ammonia* (distinction from catechol and quinol). When 0.5 gramme is mixed with 2 millilitres of *solution of formaldehyde* and 2 millilitres of *solution of sodium hydroxide,* and the mixture heated to boiling, a deep red coloration is gradually developed." *Br.*

Assay.—"Dissolve about 1.5 Gm. of Resorcinol, previously dried to constant weight over sulphuric acid and accurately weighed, in sufficient distilled water to make 500 cc. Transfer 25 cc. of this solution, representing one-twentieth of the weight of Resorcinol taken, to a 500 cc. glass-stoppered flask having a long, narrow neck, add 50 cc. of tenth-normal bromine, dilute with 50 cc. of distilled water, add 5 cc. of hydrochloric acid, and at once stopper the flask. Shake, allow it to stand for one minute, dilute with 20 cc. of distilled water, add 5 cc. of potassium iodide T.S., allow to stand for five minutes, and titrate the liberated iodine with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal bromine corresponds to 0.001835 Gm. of $C_6H_4(OH)_2$." *U. S.*

Its official assay is based upon the following reaction:

$$C_6H_4(OH)_2 + 3Br_2 = C_6HBr_3(OH)_2 + 3HBr.$$

The excess of bromine is determined indirectly by titration with sodium thiosulphate V.S.

For method of differentiation of resorcinol from hydroquinone see Wolff, *J. P. C.*, 1917, xv, 94.

Dunlop (*P. J.*, 1909, lxxxii, p. 580) investigated the cause of coloration of resorcin. He found that moisture was the most important factor but that it apparently required light and heat to cause the change after it had once begun.

Uses.—Resorcinol appears in its physiological properties to be allied to phenol. It has marked antibacterial properties, and, according to Martin Cohn (*In. Dis.*, Berlin, 1882), a one per cent. solution of it is sufficient to arrest for a long time putrefactive changes; Cooper (*B. M. J.*, 1912, i, 1235) has shown that it is about one-third as actively germicidal as phenol. When given to the lower animals (Dujardin-Beaumetz, *B. G. T.*, ci, 113) it causes tremors, loss of consciousness, and epileptiform convulsions, which, when the dose has been sufficiently large, become more and more violent and associated with marked disturbances of respiration; this function is finally arrested and death ensues. During the spasms the temperature of the animal is distinctly elevated, but, when there is quiet narcosis, it may fall much below the normal. The urine becomes olive green, deepening into blackish. For two fatal cases of poisoning in children see Boeck, *Dermatol. Wochensch.*, 1915, lx, 449. The largest therapeutic doses produce flushing of the face, with giddiness and buzzing in the ears and some quickening of the breathing and pulse, followed after a time by violent perspiration. Sixty grains caused in man giddiness, violent perspiration with marked anxiety, followed by collapse and unconsciousness. Andeer (*Cb. M. W.*, 1881) took about one hundred and fifty grains of resorcinol dissolved in a pint of water during fifteen minutes. After disturbance of cerebration and of the special senses, he fell into a condition of collapse, with cold extremities, epileptiform convulsions, opisthotonos, loss of consciousness, and marked irregularity of the respiration. Consciousness did not return for five hours.

Resorcinol has been used in medicine as an intestinal antiseptic in *enteritis*, but is probably of no service. In *gastritis* it may exercise some effect but is usually inferior to phenol. Because of its lower toxicity it is frequently employed in gastric lavage or as a wash in *nasal catarrh, chronic colitis, leucorrhea*, and other inflammations of the mucous membranes. Schaffer (*B. K. W.*, 1910, p. 890) highly recommends as a surgical dressing, especially in *furuncles* and *cellulitis*, the use of 50 per cent. of alcohol with 2 or 3 per cent. of resorcinol added. He states that it has a remarkable effect in preventing suppuration. Elze (*Wochenschrift für Ther. and Hyg. des Auges*, 1909, xii, p. 202) asserts that a 1 or 2 per cent. resorcin ointment is useful in *cataract* and will often clear up opaque parts if not too far developed or too deeply located in the lens.

The most important use of resorcin, however, is in the treatment of skin diseases. Many dermatologists attribute it with peculiar alterative properties towards the skin. In dilute solution, 1 or 2 per cent., it is antipruritic as well as antiseptic, and may be used in *acute eczema, urticaria*, and other inflammatory disorders of the epiderm. In stronger solution, 3 to 4 per cent., it is actively stimulating and is employed in the more sluggish conditions as *chronic eczema, seborrhea, psoriasis*, etc. Andeer has used it for its caustic effect in the treatment of *chancres, papilloma*, and *epitheliomata* in the form of a dusting powder.

Dose, three to five grains (0.2–0.32 Gm.).

Off. Prep.—Pasta Resorcinolis Fortior, *N. F.;* Pasta Resorcinolis Mitis, *N. F.;* Unguentum Resorcinolis Compositum, *N. F.;* Curatio Paraffini, *N. F.*

RHAMNUS CATHARTICA. N. F.

RHAMNUS CATHARTICA Rham. Cathart. [Buckthorn Berries, Baccæ Spinæ Cervinæ]

"Rhamnus Cathartica is the dried, ripe fruit of *Rhamnus Cathartica*, Linné (Fam. *Rhamnaceæ*). Rhamnus Cathartica contains not more than 5 per cent. of unripe fruit or other foreign organic matter." *N. F.*

Rhamni Baccæ, Rhamni Catharticæ Fructus; Baccæ Spinæ Cervinæ; Buckthorn Berries; Hart's Horn Berries; Rhineberry, Waythorn Berries; Baccæ Domesticæ; Kreuzdornbeere, *G.;* Nerprun, Baies de Nerprun, *F.;* Spinamagna, *It.*

Rhamnus cathartica Linn. is a thorny shrub or small tree indigenous to Europe and Western Asia and naturalized in the Eastern United States. It possesses thin, ovate or elliptic leaves with acute or obtuse apex, rounded or cordate base and crenulate-serrate margins. Its flowers are imperfectly diœcious, tetramerous and thickly clustered in the axils of the opposite leaves. Its fruits ripen in September. Each of these is a black, globular drupe about the size of a pea and composed of three or (rarely) four indehiscent cocci, each enclosing a single albuminous seed.

Among other species of Rhamnus which have claimed attention are *R. Wightii* W. & A., a common shrub of Madras and Bombay (*P. J.*, Feb., 1888), and *R. californica* Eschsch. (*R. humboldtiana* Roem. and Schult.), of Mexico, which S. E. Sosa states sometimes produces paralysis in children (*El Estudio*, 1890). (See also *Cascara Sagrada.*)

Description and Physical Properties.—"*Unground Rhamnus Cathartica.*—Flattened, globoid or ovoid, from 4 to 8 mm. in diameter; externally purplish black, wrinkled from shrinking of the mesocarp in drying; three- to four-celled, each cell containing a brown, triangular-convex, seed-like nutlet; in the fully dried, ripe fruit the pedicel is usually lacking. Odor faint, unpleasant; taste at first sweetish, then nauseating and bitter; it colors the saliva purplish red. The unripe fruit, which is to be rejected, is green to greenish brown, firm, furrowed, pedicel usually attached; very bitter; it colors the saliva greenish yellow.

"*Powdered Rhamnus Cathartica.*—Dark brown; numerous fragments composed of epidermal cells and parenchyma some of the latter containing an amorphous substance which appears reddish violet in chloral hydrate T.S., others containing rosettes of calcium oxalate the latter from 0.005 to 0.025 mm. in diameter; fragments of sarcocarp composed of thin-walled cells among which are large secretion cells with a yellowish oily content; stone cells, thick-walled with simple or branching pores from 0.035 to 0.075 mm. in diameter containing a reddish brown amorphous content or prisms of calcium oxalate the latter from 0.005 to 0.025 mm. in length; fibers, long, thick-walled, associated with parenchyma containing prisms of calcium oxalate; fragments of endosperm tissue of cells containing fixed oil and ellipsoidal or nearly spherical aleurone grains.

"When macerated in water the drupe readily assumes its original globular shape, about 1 cm. in diameter. The expressed pulp is colored red by acids and greenish yellow by alkalies. Shake out an aqueous infusion of Rhamnus Cathartica with ether, separate the ethereal solution and shake it with 5 per cent. ammonia water; the ammonia solution assumes a cherry-red color." *N. F.*

The blackish, expressed juice of buckthorn berries was formerly recognized in the Br. Ph. under the name of *Rhamni Succus.* It has the color, odor, and taste of the parenchyma, is reddened by the acids, and from deep green is rendered light green by the alkalies. Upon standing it soon begins to ferment, and becomes red in consequence of the formation of acetic acid. Evaporated to dryness with the addition of lime or an alkali, it forms the color called by painters *sap-green.* The dried fruit of another species, *R. infectoria,* yields a yellow color, and is employed in the arts under the name of *French berries.* The same coloring principles appear to be found in both these species as well as the fruit of the *R. tinctoria.* According to N. Waljaschko and N. Krassowski (*Ph. Ztg.,* 1909, 159), the tinctorial powers are due to glucosides which yield quercetin and rhamnin, $C_{12}H_{12}O_5$.

Tschirch and Polacco (*Ph. Ztg.,* 1909, p. 159) found the fruits to contain about 2 per cent. of emodin-substances and as cleavage products of the glucosides obtained by the action of ferments from the emodin-substances: Emodin, *rhamnoxanthin,* which is isomeric but not identical with frangulin; *rhamnonigrin,* and a resin-like body containing emodin. Other constituents found in buckthorn berries are fixed oil, succinic acid, glucose, galactose, rhamnose, and a pentose, but of the four sugars only glucose was present in the free state, the others being derived from the glucosides. Tschirch and Bromberger (*Schw. Woch. f. Ch. u. Ph.,* 1912, p. 193) report the following constituents: *rhamno-sterin,* $C_{18}H_{28}O_2$; *rhamno-fluorin,* $C_{14}H_{12}O_6$; emodin, iso-emodin, chrysophanol (see under *Rheum*).

Uses.—Buckthorn berries exert an active cathartic effect, but are prone to cause nausea and severe griping. They have been used as hydragogues in *dropsy* and also in the treatment of *rheumatism* and *gout.*

The *dose* of the dried berries is from ten to twenty grains (0.65–1.2 Gm.).

Off. Prep.—Fluidextractum Rhamni Catharticæ, *N. F.;* Syrupus Rhamni Catharticæ, *N. F.*

RHEUM. U. S. (Br.)

RHUBARB

"Rhubarb consists of the dried rhizome and roots of *Rheum officinale* Baillon or of *Rheum palmatum* Linné (Fam. *Polygonaceæ*) or other species of *Rheum* grown in China and Thibet, deprived of periderm tissues. Rhubarb yields not less than 30 per cent. of diluted alcohol-soluble extractive." *U. S.* "Rhubarb is the rhizome of Rheum officinale, *Baill.,* and other species of Rheum, collected in China and Thibet., deprived of most of the cortex, and dried." *Br.*

Rhei Rhizoma, *Br.;* Rhubarb Root; Rhabarbarum; Rhubarbe, *Fr.;* Rhabarber, *G.;* Rhizoma Rhei, *P. G.;* Rabarbaro, *It.;* Ruibarbo, *Sp.;* Hainoung, *Chin.;* Schara-modo, *Thibet.*

The terms *rha* and *rheon*—from the former of which were derived the names *rhabarbarum* and *rhubarb,* and from the latter the botanical title *Rheum*—were applied by the ancients to a root which came from beyond the Bosphorus, and which is supposed, though upon somewhat uncertain grounds, to have been the product of *Rheum rhaponticum* L., growing on the banks of the Caspian Sea and the Volga. This species was also at one time believed to be the source of the medicine now in use; but the true rhubarb has long been known to be wholly distinct from the Rhapontic, and derived from a different source. It was not until the year 1732 that any authentic information was obtained as to its real origin. At that time plants were received from Russia by Jussieu in France, and Rand in England, which were said to be of the species affording the genuine rhubarb, and were named by Linnæus, under this impression, *Rheum rhabarbarum,* a title which has since given way to *Rheum undulatum.* Subsequently, Kaau-Boerhaave obtained from a merchant, who dealt in the rhubarb of Tartary, some seeds which he said were those of the plant producing the root sold by him. These, having been planted, yielded two species of *Rheum, R. undulatum,* and another which Linnæus named *R. palmatum.* Seeds transmitted by Mounsey from St. Petersburg to Hope, and planted in the botanical garden at Edinburgh, produced the latter species, and the same was also raised at Upsala from a root received by Linnæus from De Gorter, and was described in 1767 by the younger Linnæus, two years after the appearance of Hope's paper in the *Philosophical Transactions.* Thus far the evidence appears equally in favor of *R. palmatum* and *R. undulatum.* Colonel Przewalski concluded from personal observation that *R. palmatum* produces rhubarb; but the specimens of the root which he brought to St. Petersburg were stated by Dragendorff to be essentially different from true rhubarb. Claims have also been made from time to time for various other species of *Rheum* as sources of the drug. Pallas, upon exhibiting the leaves of *R. palmatum* to some Bucharian merchants, was told that the leaves of the rhubarb plant were entirely different in shape, and the description he received of them corresponded more closely with those of *R. compactum* than any other known species. Seeds of this plant were, moreover, sent to Miller from St. Petersburg as those of the true Tartarian rhubarb. Wallich, superintendent of the botanical garden at Calcutta, received seeds that were said to be those of the plant which yielded the Chinese rhubarb, growing on the Himalaya Mountains and the highlands of Tartary. These produced a species not previously described, which Wallich named *R. Emodi,* from the native title of the plant. It is the *R. australe* of Don and of Colebrooke, and has been ascertained to afford a root which, though purgative, is very unlike the official rhubarb. Holmstrom (*S. W. P.*, 1921, lix, 183) finds that its chemical constitution differs materially from the official variety. In 1867, French missionaries in Southeastern Thibet forwarded to Soubeiran of Paris, live specimens of a plant which they asserted to yield the true rhubarb, and Baillon subsequently described the flowering plant under the name of *R. officinale.* This species is now established as one of the important sources of the drug of commerce. It is now collected for the greater part, according to Greenish, in the mountains separating Thibet from the Chinese province of Szechuen and extending eastward to Huveh.

The old designations *Turkey Rhubarb* and *East Indian Rhubarb,* still occasionally heard, represent trade names and now indicate nothing more than the routes by which rhubarb was formerly carried into the European market. The official article is now collected entirely in China and Thibet and is most appropriately designated under the trade name of *Chinese Rhubarb.*

Tschirch in discussing the origin of Chinese rhubarb has come to the conclusion that that obtained from Szetschwan, "southern" rhubarb, is derived from *Rheum officinale,* while that obtained from Kukunoor, "northern" rhubarb, is the product of *Rheum palmatum tanguticum* (*A. Pharm.*, 1907, p. 680; and *S. W. P.*, 1910, xlviii, 292).

The genus *Rheum* comprises about twenty-five species of perennial herbs native to Asia. All of the species have large, mostly radical leaves, the blades of which are either entire, toothed and lobed or divided and the petioles thick. The stems arise to the height of 4 to 10 feet. The flowers are small, greenish to greenish-white and occur in panicles of racemes, elevated on scope-like stems which are provided with sheathing stipules (*ochreæ*). Each flower possesses a 6-parted perianth, 6 to 9 stamens and a 3-carpelled pistil with 3 styles which ripens into a triangular winged achene.

There is some difficulty in arranging the species, in consequence of the tendency of the cultivated plants to form hybrids, and it is frequently impossible to ascertain to which of the wild types the several garden varieties are to be referred. Lindley (*Flora Medica*) states that *R. rhaponticum, R. hybridum,* and *R. compactum,* and their hybrids, are the common garden rhubarbs.

R. officinale Baillon is indigenous to the high tablelands of Thibet and Western Asia. It is described in the *Pharmacographia* "as a perennial, noble plant, resembling the common garden rhubarb, but of larger size. It differs from the latter in several particulars: the leaves spring from a distinct crown rising some inches above the surface of the ground; they have a subcylindrical petiole, which, as well as the veins of the under side of the lamina, is covered with a pubescence of short erect hairs. The lamina, the outline of which is orbicular, cordate at base, is shortly 5- to 7-lobed, with the lobes coarsely and irregularly dentate; it attains 4 to 4½ feet in length, and rather more in breadth. The first leaves in spring display before expanding the peculiar metallic red hue of copper."

Rheum palmatum L. is indigenous to Northeastern Asia. Its leaf blades are broad, suborbicular and cordate, 3- to 5-ribbed and deeply palmately-lobed. Its panicle is leafy with pubescent branches, the pedicels of which are seldom longer than the flowers. The var. *tanguticum* of this species resembles the *R. palmatum* but its leaves differ in being more elongated and palmately-cleft. *Rheum palmatum* is known to occur in the province of Kansuh where considerable has been collected.

Besides the species already mentioned, *R. leucorrhizum,* growing in the Kirgheeze Desert in Tartary, *R. capsicum,* from the Altai Mountains, *R. webbianum, R. speciforme,* and *R. moorcraftianum,* natives of the Himalaya Mountains and *R. crassinervium* and *R. hybridum,* cultivated in Europe, but of unknown origin, yield roots which have either been employed as purgatives or possess properties more or less analogous to those of official rhubarb, though they have not entered into general commerce. In Java, the root of an indigenous species is used as a purgative. According to the analysis of J. H. Schmidt, it contains more chrysophan and emodin, and less chrysophanic and rheotannic acids, than does the official drug.

Rhubarb is produced abundantly over a large area of China. It is cultivated extensively in the northern provinces of Shensi, Shansi, Chihli and Honan, the Mongolian province of Tsinghai, in the northwest province of Kansuh and the western province of Szechuen. The rhizome and roots are not considered sufficiently mature for collection until the plant has attained the age of six years. It is dug up twice a year in Tartary, in the spring and autumn; in China not till the winter. After removal from the ground, it is cleaned, deprived of its cortical portion and the smaller branches, and then divided into pieces of a convenient size. Most of the drug is carried to Hankow whence it is shipped to Shanghai to be exported to Europe, and America. Smaller quantities are exported from Canton, Tientsin, Fuhchow and Ning-po. The commercial kinds of rhubarb imported into the United States from China are the " Shensi " and " Canton " varieties. The Shensi variety is considered the best. Both of these varieties occur on the market as *common rounds, flats,* and *high dried rhubarb. Common round rhubarb* represents segments of the dicorticated root and rhizome; *flats* are thick segments of the peeled rhizome split into halves lengthwise and *high dried rhubarb* represents rhubarb which has been first decorticated, then cut into segments which are bored with holes, and strung upon cords to dry either in a heated room or exposed to the sun.

Chinese Rhubarb.—The crude drug occurs in commerce in subcylindrical, conical or barrel-shaped pieces (" rounds "), in plano-convex pieces (" flats "), in cylindrical or barrel-shaped pieces which are perforated (" high dried ") or in square or rectangular pieces (" cut rhubarb "). The outer surface is dusted over with a bright yellow powder and shows evidences of having been peeled and scraped. The outer surface of the *Shensi* variety, when deprived of its yellowish powder, exhibits numerous minute dark reddish-brown lines and dots representing medullary rays imbedded in a whitish parenchyma. This variety is hard, compact and heavy and breaks with an uneven fracture. Its fractured surface varies from bright pink to dull grey and shows, under a hand lens, reddish-brown lines alternating with whitish ones, giving the surface a mottled appearance. It has a characteristic odor and a bitter, astringent taste. When chewed it is gritty between the teeth (due to abundant rosette crystals of calcium oxalate) and tinges the saliva yellow.

Canton Rhubarb differs from the *Shensi* variety in being lighter in weight and in color, less compact and more fibrous in texture, and in exhibiting a nearly uniformly granular instead of a marbled appearance, when fractured. With the pieces of good quality others often come mingled, defective from decay or improper preparation. These are usually lighter, and of a dark or russet color. Like all the other varieties of rhubarb, this is liable to be attacked by insects, and in almost every large parcel pieces may be found which have suffered from this cause. Occasionally pieces of the drug have been observed to possess dark-colored or hollow central areas. This is due to the decay of these portions during the preparation of the drug. Such specimens are known as " Black Hearted Rhubarb."

Chinese rhubarb is the only kind recognized by the U. S. or Br.

Description and Physical Properties.—" *Unground Rhubarb.*—In subcylindrical or flattened pieces, frequently showing a large perforation; from 5 to 17 cm. in length and from 4 to 10 cm. in diameter; outer surface yellowish-brown with lighter colored striations and occasional small patches of brown cork; more or less covered with yellowish-brown powder; hard; fracture uneven, showing stellate vascular bundles and a granular, yellowish or pinkish-brown mottled surface; odor aromatic, agreeable; taste bitter and astringent.

" *Structure.*—Occasional patches of thin-walled cork cells; medullary rays wavy, 2 to 4 cells in width, cells often with reddish-brown contents; vascular bundles with internal sieve and cambium; parenchyma cells containing either starch or large aggregate crystals of calcium oxalate.

" *Powdered Rhubarb.*—Yellowish-brown to reddish-brown; rosette aggregates of calcium oxalate up to 0.15 mm. in diameter; starch grains from 0.004 to 0.025 mm. in diameter, spheroidal, single and 2- to 3-compound, with central cleft hilum; tracheæ few, reticulate and spiral.

" Powdered Rhubarb becomes red upon the addition of alkalies. Boil 0.1 Gm. of powdered Rhubarb with 10 cc. of an aqueous solution of potassium hydroxide (1 in 100); allow it to cool, filter, acidulate the filtrate with hydrochloric acid and shake it with 10 cc. of ether: the ethereal layer is colored yellow on standing. Shake this ethereal solution with 5 cc. of ammonia T.S.: the latter is colored cherry-red (presence of *emodin*) and the ethereal layer remains yellow (presence of *chrysophanic acid*).

" Boil 10 Gm. of powdered Rhubarb for fifteen minutes with 50 cc. of diluted alcohol under a reflux condenser, filter, and concentrate to 10 cc. Cool, shake with 15 cc. of ether, and set aside for twenty-four hours: yellowish, prismatic crystals should not form (*rhapontic rhubarb*).

" **Assay.**—Proceed as under anhydrous diluted alcohol-soluble extractive, page 1552." *U.S.*

" In compact, firm, cylindrical, barrel-shaped, conical or plano-convex pieces, often perforated, the perforation sometimes containing a fragment of cord. Surface rounded or slightly angular, but not shrunken, marked with reddish-brown lines embedded in a whitish ground-substance;

usually covered with a bright brownish-yellow powder. Fracture granular and uneven, the pinkish-brown fractured surface exhibiting numerous reddish-brown points and lines on a white ground-substance. For a short distance within the cambium the structure is radiate; within this there is a more or less distinct ring of closely approximated vascular bundles with central bast and radiating, reddish-brown medullary rays; in the parenchymatous cells abundant starch grains, an amorphous yellow substance and very large cluster-crystals of calcium oxalate. In powdered Rhubarb large cluster-crystals of calcium oxalate, often more than 100 microns in diameter, simple or compound starch grains, the single grains seldom exceeding 20 microns in diameter, fragments of reticulated vessels and of parenchymatous tissue, and small yellowish masses and globules which assume a reddish-pink color with *solution of ammonia;* it is free from added starch and from sclerenchymatous cells and fibres. Characteristic, somewhat aromatic odor; taste bitter, slightly astringent. Ash not more than 15 per cent." *Br.*

European or English Rhubarb.—In various parts of Europe, especially in England, the *R. rhaponticum* and *R. officinale* are cultivated and are imported occasionally into the United States. The rhizomes are usually offered separately from the roots. English rhubarb (from *Rheum rhaponticum*) is lighter than the Asiatic, more spongy, and often somewhat pasty under the pestle. It is redder, and when broken exhibits a more compact and regular marbling, the pinkish lines being arranged like rays from the center towards the circumference. The "starlike spots" are either wanting or very few and scattered. The powder also has a brighter yellow tint. The odor is feeble and less aromatic than that of the Asiatic varieties; the taste is astringent and mucilaginous, with little bitterness, and the root, when chewed, scarcely feels gritty between the teeth, and but slightly colors the saliva. Few crystals of calcium oxalate are discoverable by means of the microscope. Much English rhubarb is obtained from *R. officinale,* and is put on the market in flat, concave, and convex pieces weighing from three to four ounces each. Externally the convex surface has deep longitudinal furrows and a longitudinal ramification of conspicuous veins, giving rise to an appearance of net-vein markings. In the center of the concave surface is a small hole similar to that formerly seen in Russian rhubarb. On the inner surface the stellate markings resemble very closely those found in Chinese rhubarb. The fracture of this form shows a parallel arrangement of whitish and reddish lines, representing parenchyma and medullary rays. When rapidly grown in rich soil, English rhubarb is lighter, more spongy, and less active than when slowly grown without high cultivation.

Rhapontic rhubarb is still found to some extent in European markets and occasionally has been detected in supplies offered for entry here. Tschirch has proposed a ready method for detecting the admixture. It depends on the insolubility in ether of the crystalline glucoside, rhaponticin or ponticin. This is not an anthraquinone derivative. (*A. Pharm.,* 1905, p. 443; and *S. W. P.,* xliii, p. 253.) Hesse has also made an elaborate study on the chemistry of rhapontic root grown in Austria. (*J. f. prakt. Chem.,* 1908, lxxvii, p. 320.)

The *rhapontic root* differs in transverse section from true rhubarb by its distinctly radiated structure, and by its stellate spots (compound bundles) being fewer, and more isolated and diffused.

Choice of Rhubarb.—In selecting good rhubarb, without reference to the commercial variety, those pieces should be preferred which are moderately heavy and compact, of a bright color, brittle, presenting when broken a fresh appearance, with reddish and yellowish veins intermingled with white, of an odor decidedly aromatic, of a bitter and astringent not mucilaginous taste, feeling gritty and staining the saliva yellow when chewed, and affording a powder either bright yellow, or yellow with but a slight reddish-brown tinge. When very light, rhubarb is usually partially decayed or worm-eaten; when very heavy and compact, it is of inferior species, culture, or preparation. Partially decayed, worm-eaten, or otherwise inferior rhubarb is often powdered, and colored yellow with turmeric. The shavings left when Chinese rhubarb is trimmed are used for powdering. The stellate markings observed in the cut or broken surface of the Chinese rhubarb has been believed by various pharmacologists to be of great practical value in determining the true character of the rhizome and especially in enabling a distinction between the Chinese and European rhubarb to be made. There has been a general concurrence with the statements of Tschirch that the star spots are never present in the root, occurring only in the rhizome. In an elaborate re-examination of this subject by Jakabhasy, however, the star spots were found in the root as well as in the root stock and also in the European as well as in the Asiatic rhubarb. Nevertheless, Jakabhasy states that it is possible to distinguish the two rhubarbs by the fact that in the European rhubarb the star spots occur in greater number on the longitudinal section while in the Chinese rhubarb they are present on the transverse section, where they form a circle. He believes also that the superabundance of starch and the lack of crystals in the star spots are diagnostic of the European drug. When the rhubarb is powdered these characteristics are not available, under which circumstances the percentage of ash seems to be valuable. The Chinese rhubarb, unless of very inferior quality, yields from 8 to 25 per cent.; the European 1.3 to 6 per cent. of ash. According to Jakabhasy, Shensi is the best, Shanghai the poorest, and Canton the intermediate variety of Chinese rhubarb. Of the European the English is the most, the French next, and the Austrian the least active.

Tschirch and Puzzkowski have reported that the rhubarb from the Altai Mountains meets all of the requirements for official rhubarb, *C. V. C. P. Al. J.*, 1916, xxiii, 12.

Constituents.—Rhubarb has been the subject of extensive and intensive chemical investigations, of which the most important in recent years have been those of Hesse (*Proc. A. Ph. A.*, 1896, p. 549), Tschirch and Heuberger (*A. Pharm.*, 1902, cciv, 596, and *Ph. Ztg.*, August 3, 1904, 651), Eyken (*Ph. Wb.*, 1904, xli, 177), and Tutin and Clewer (*Tr. Chem. Soc.*, 1911, xcix, 946). The result of these investigations may be briefly summed up as follows: There is present in rhubarb, besides various unimportant vegetable substances, a small amount of a volatile oil with a strong characteristic odor of rhubarb, and about 2 per cent. of gallic acid and smaller quantities of tannic acid. Its most important constituents, however, are certain derivatives of methylanthracene. In order to clear up some of the confusion which has arisen from reduplication of names, it will be necessary to briefly review the chemistry of this group of principles.

Anthraquinone Derivatives.—A number of the vegetable laxatives contain principles allied to methyl-anthraquinone—or glucosides which yield such substances on hydrolysis—to which it is generally believed they owe their cathartic powers. The names which have been applied to these are so numerous that it has given rise to much confusion. While our present state of knowledge does not permit of too dogmatic statements it has seemed worth while to briefly explain the probable relationship of these various compounds.

Chrysophanic acid—more properly *Chrysophanol,* as it is not an acid—is a dihydroxy-methyl-anthraquinone, $C_{14}H_5O_2(OH)_2CH_3$. It is found in rhubarb to the extent of 0.5 per cent., in aloes, cascara and other species of Rhamnus. *Emodin* (*Frangula-emodin, Rheum-emodin*) is a trihydroxy-methyl-anthraquinone, $C_{14}H_4O_2(OH)_3CH_3$. It exists—either free or combined with a sugar as a glucoside—in aloes, rhubarb, Rhamnus species, Rumex, etc. *Frangulin, avornic acid,* and *rhamnoxanthin* seem to be glucosides yielding emodin. *Aloe-emodin,* also called *iso-emodin,* is isomeric with emodin, its formula probably being $C_{14}H_5O_2(OH)_2CH_2OH$. *Rhabarberon,* of Hesse, found in rhubarb was probably an impure aloe-emodin. It occurs in aloes, and to the extent of about 0.2 per cent. in rhubarb. *Emodin monomethyl ether* has been found by Tutin and Clewer in rhubarb. Its formula is $C_{14}H_4O_2(OH)_2CH_3OCH_3$. *Rhein* is an acid found in rhubarb, which can be regarded as the acid of chrysophanol as it has the formula $C_{14}H_5O_2(OH)_2COOH$.

Rhubarb contains emodin, emodin monomethyl ether and rhein, which, however, according to Tutin and Clewer, are devoid of purgative powers, also aloe-emodin, chrysophanol and glucosides of these. According to Tutin and Clewer, however, the chief cathartic principle is a non-glucosidal resin which yielded on hydrolysis various anthraquinone compounds and which is present to the extent of about 10 per cent.

B. H. St. John of the laboratory of the A. M. A. has called attention to the fact that *Acer spicatum* gives reactions similar to the emodin test applied to rhubarb and other cathartic drugs. (*A. J. P.*, 1917, lxxxix, 10.)

There are other interesting principles in rhubarb. The calcium oxalate is interesting from its quantity, and from the circumstance that, existing in distinct crystals, it occasions the grittiness of the rhubarb between the teeth. The proportion seems to vary exceedingly in different specimens. According to Scheele and Henry, it constitutes nearly one-third, and Queckett found between 35 and 40 per cent., while Brandes obtained only 11, Schrader only 4.5 parts in the hundred, and Dragendorff, in five examples analyzed, from 1.2 to 5.6 per cent. Little or no difference of composition has been found between the Russian and the Chinese rhubarb. The European contains but a small proportion of calcium oxalate, and is therefore less gritty when chewed. It has, however, more tannin and starch than the Asiatic.

When powdered rhubarb is heated, odorous yellow fumes rise, which are probably in part the vapor of chrysophanic acid. Its infusion is reddened by the alkalies, in consequence of their union with this acid, and their reaction on the other coloring principles. It yields precipitates with gelatin, most of the acids, ferric salts, lead acetate, mercurous nitrate, silver nitrate, stannous chloride, lime water, and solutions of quinine. Nitric acid occasions at first a turbidity, and afterwards the deposition of a yellow precipitate. The substances producing precipitates may be considered as incompatible with the infusion.

For a method of detecting the presence of turmeric in powdered rhubarb by the influence of chloroform on the coloring principles of each of these substances, and of distinguishing through the same agency between the true Chinese rhubarb and that of European origin, see *P. J.*, 1898, 126, and *Chem. Abst.*, 1918, xii, 1337.

Uses.—Rhubarb differs from the other laxatives of the anthraquinone group—such as aloes, cascara, etc.—in that it has a larger percentage of tannic acid. On account of the considerable quantity of tannin its purgative action is often followed by constipation. This sequence of effects has led to its use in the treatment of *diarrheas,* especially of the inflammatory type, on the theory that the catharsis it caused would evacuate the irritant *materies morbi,* and that its subsequent astringency would check the excessive secretion. The logic is plausible, but erroneous. As the action of its cathartic principles is limited to the lower bowel it has very little influence in cleaning out the smaller bowel which is frequently involved in acute *diarrheas.* In inflammations of the colon, such as *dysentery,* its use might appear more reasonable, but even here it is greatly inferior to less irritant laxatives because it acts chiefly by virtue of its local irritant influence. Rhubarb is also widely prescribed in atonic *dyspepsia* attended with *constipation.* It is frequently combined with an alkali, either magnesia or soda.

It sometimes occasions griping. Its coloring principles is absorbed, and may be detected in the urine. By its long-continued use the perspiration, especially that of the axilla, is said to become yellow, and the milk of nurses cathartic. It gives a yellow color to the alvine discharges.

By the roasting of rhubarb its cathartic property is diminished, probably by the volatilization of the purgative principle, while its astringency remains unaffected. When so treated it is termed *torrefied rhubarb.* This mode of treatment has been sometimes resorted to in cases of *diarrhea.* By long boiling the same effect is said to be produced.

Few medicines are used in a greater variety of forms. It is most effectual in substance either as a pill or powder. It is frequently given in the shape of pill, combined with an equal proportion of soap when its laxative effect is desired. The infusion is much used in cases of delicate stomach, and is peculiarly adapted. The syrup, tincture, and fluidextract are also useful preparations; but the most popular forms are those in which it is combined with an antacid as in mixture of rhubarb and soda or the compound powder of rhubarb and magnesia.

Rhubarb Poisoning.—The stalks of certain species of rhubarb (sometimes called *pie-plant*) are widely used as a food-stuff. Several cases of severe, and even fatal, poisoning have been reported from them. While the acid taste of the stalks is in part due to malic acid it is well established that they contain also considerable quantities of oxalic acid, which is probably the toxic ingredient. The amount of oxalic acid is usually larger in the leaves than in the stems and the former are correspondingly more dangerous. Von Itallie and Lemkes (*Ph. Wb.,* 1917, v, 1234) found the oxalic acid, extractable with 5 per cent. of hydrochloric acid, in the stems of various species to range from 0.4 to 1.0 per cent., and in the leaves from 0.3 to 1.1 per cent. For report of cases of this poisoning, see *J. A. M. A.,* 1919, lxxiii, 926.

Dose, as a purgative, from twenty to thirty grains (1.3–2.0 Gm.); as a laxative and stomachic from five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Fluidextractum Rhei, *U. S.;* Extractum Rhei, *U. S., Br.;* Infusum Rhei, *Br.;* Liquor Rhei Concentratus, *Br.;* Pilulæ Rhei Compositæ, *N. F.* (*Br.*); Pulvis Rhei Compositus, *U. S., Br.;* Syrupus Rhei (from Fluidextract), *U. S., Br.;* Syrupus Rhei Aromaticus (from Aromatic Tincture), *U. S.;* Tinctura Rhei, *U. S.* (*Br.*); Tinctura Rhei Aromatica, *U. S.;* Tinctura Rhei Composita, *Br.;* Elixir Catharticum Compositum (from Fluidextract), *N. F.;* Fluidglyceratum Rhei, *N. F.;* Mistura Opii et Rhei Composita (from Tincture), *N. F.;* Mistura Rhei Alkalina (from Fluidextract), *N. F.;* Mistura Rhei Composita (from Fluidextract), *N. F.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloe, *N. F.;* Pilulæ Rhei, *N. F.;* Pulvis Rhei et Magnesiæ Anisatus, *N. F.;* Syrupus Sennæ Aromaticus, *N. F.;* Syrupus Sennæ Compositus (from Fluidextract), *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.;* Tinctura Rhei Aquosa, *N. F.;* Tinctura Rhei Dulcis, *N. F.;* Tinctura Rhei et Gentianæ, *N. F.*

RHŒADOS PETALA. Br.

RED POPPY PETALS

"Red-Poppy Petals are the fresh petals of Papaver Rhœas, *Linn.*" *Br.*

Corn Poppy, Corn Rose; Flores Rhœados; Poppy Flowers; Flos Papaveris; Coquelicot, Pavot rouge, *Fr.;* Wilder Mohn, Klapperrose, Llatschrosen, *G.;* Rosolaccio, *It.;* Amapola (Flor de), *Sp.*

The *red* or *corn poppy, Papaver Rhœas,* is distinguished by its hairy stem, which is branched, and rises about a foot in height, by its incised pinnatifid leaves, by its urn-shaped capsule, and by the full, bright, scarlet color of its petals. It is a native of Europe, where it grows wild in great abundance, adorning especially the fields of grain with its brilliant flower and often proving a troublesome weed to the farmer. It has been naturalized in this country.

Its capsules contain the same kind of milky juice as that found in *P. somniferum,* and an extract has been prepared from them having the properties of opium; but the quantity is too small to repay the trouble of its preparation. Filhol has shown that the extract contains morphine, but in a proportion exceedingly minute compared with that in which it exists in opium. The petals are the official portion. They have a characteristic odor, and a mucilaginous, slightly bitter taste. By drying, they lose their odor, and assume a violet-red color.

"Transversely elliptical, about five centimetres wide, bright scarlet, smooth and lustrous; margin entire. Characteristic, somewhat unpleasant odor; taste slightly bitter." *Br.*

Chevallier believed that he had detected a very minute proportion of morphine in an extract obtained from them; but Attfield seems to have determined satisfactorily the non-existence of morphine in the petals, having sought this alkaloid by three different processes, using a pound of the petals in each experiment, and failed to detect the least evidence of its presence. (*P. J.,* 1873.) Hesse, in 1867, found the alkaloid, *rhœadine* $C_{21}H_{21}O_6N$, in the expressed juice of the fresh petals but not in the dried drug. (See *A. J. P.,* 1890, p. 179). According to the same author there is also present a small amount of meconic acid.

Rhœadine is crystallizable, faintly alkaline to litmus, but does not readily form salts with the acids. It is sparingly soluble in water. It melts at 232° C. It is sparingly soluble in ether, alcohol, benzene, chloroform, water, and ammonia. Its solutions in dilute acids acquire an intense purple color on addition of strong hydrochloric or sulphuric acid, due to the formation of a coloring matter. This color is destroyed by alkalies and restored by acids, and is so intense that 1 part of rhœadine will color 10,000 parts of water purple-red, 200,000 deep rose-red, and 800,000 distinctly red, although only a portion of the base is converted into coloring matter. The solution then filtered through bone-black shows the presence of a base, *rhœagenine,* isomeric with rhœadine, but strongly basic. Rhœadine is found also in opium.

The physiological power of poppy petals on the system is exceedingly feeble, and they are valued more for their beautiful scarlet color, which they communicate to water, than for their medicinal virtues. The alkaloid rhœadine appears to be non-toxic. According to Leo Meier, the coloring principles of the flowers are two acids, which he denominates *rhœadic* and *papaveric acids.* (See *A. J. P.,* xviii, 211.) A syrup is prepared from them, which was formerly prescribed as an anodyne in catarrhal affections, but is now little esteemed except for its color.

Off. Prep.—Syrupus Rhœados, *Br.*

RHUS GLABRA. U. S.

RHUS GLABRA Rhus. Glab. [Sumac Berries]

"Rhus Glabra is the dried, ripe fruit of *Rhus glabra* Linné (Fam. *Anacardiaceæ*). Rhus Glabra contains not more than 5 per cent. of stems or other foreign organic matter." *U. S.*

Rhus Glabrum, *U. S.,* 1870; Sleek or Scarlet or White, Sumach; Shoe-make; Vinegar Tree; Sumac, *Fr.;* Sumach, *G.*

Rhus glabra called variously *smooth sumach, Pennsylvania sumach,* and *upland sumach,* is an indigenous shrub from four to twelve feet or more in height. The leaves are pinnately compound with smooth petioles, and blades consisting of numerous opposite leaflets, with an odd one at the extremity, all of which are lanceolate, acuminate, acutely serrate, glabrous, green on their upper surface, and whitish beneath. In the autumn their color changes to a beautiful red. The flowers are greenish red, and disposed in large, erect, terminal compound thyrses. The fruit is in clusters of small crimson drupes.

The shrub is found in Canada and almost all parts of the United States, growing in old neglected fields, along fences, and on the borders of woods. The flowers appear in July, and the fruit ripens in the early part of autumn. The bark and leaves are astringent, and are largely used, especially the leaves, in tanning leather and in dyeing. The sumach for the manufacture of extract for tanners' use is largely cultivated in Virginia, where the annual crop reaches from 7000 to 8000 tons, and is collected at any time between the first of July and the appearance of frost.

The drupes have a sour, astringent, not unpleasant taste, and are often eaten by the country people with impunity.

The fruits of *Rhus glabra* have been replaced by those of the *Stag Horn Sumac* (*Rhus typhina* L.) This shrub is very abundant in the Eastern United States. The fruits resemble those of *Rhus glabra* both in form and size but are distinguished by being covered with needle-like crimson hairs which are frequently over 2 mm. long. For detailed description of the fruits of these two plants see Kraemer. (*A. J. P.,* 1913, p. 398.)

Description and Physical Properties.—"*Unground Rhus Glabra.*—Flattened ovoid, nearly globular or somewhat reniform; from 3.5 to 5.5 mm. in length, nearly as broad, but usually somewhat less in thickness; a raised scar at the apex and the five-parted calyx occasionally with a short pedicel at the base; externally dark red, velvety with short hairs; endocarp smooth, shiny, crimson to yellowish-red; 1-locular, 1-seeded; seed brown, very hard; inodorous; taste acidulous and astringent.

"*Powdered Rhus Glabra.*—Brownish-red; non-glandular hairs numerous, elliptical, ovoid or spatulate, from 0.125 to 0.300 mm. in length and from 0.045 to 0.080 mm. in width, usually several-celled, uniseriate, the cells filled with pink or red dried sap in which occasionally occur rod-shaped crystals; also a few, slender, one-celled, colorless, non-glandular hairs; glandular hairs numerous, brownish or brownish-red with short, 1-celled stalks and multicellular heads, from 0.045 to 0.085 mm. in length; fragments of red-celled epicarp with adhering mesocarp having spiral tracheæ; stone cells of endocarp very small and with irregularly thickened walls; fragments of embryo with small angular cells containing aleurone and fixed oil." *U. S.*

For a paper on the relative proportion of the constituents found in the husk and seed portion of the fruit by Frankforter and Martin, see *A. J. P.,* 1904, 151.

Sumac berries contain malic acid as well as calcium malate, a small quantity of volatile oil, coloring matter, etc., but their therapeutic properties are due to the presence of a tannin, which is probably the same as gallo-tannic acid (see Peacock, *A. J. P.,* 1925, xcvii, 463). Gallic acid, according to Peacock, never occurs naturally but small amounts may be present, resulting from decomposition of the tannin. Much larger proportions of tannin are found in other parts of the plant, the leaves, for example, yielding from 16 to 25 per cent. and Trimble (*A. J. P.,* 1890, p. 564) collected some galls from the leaves that yielded from 61 to 71 per cent. An extract prepared from the sumac has been used in tanning leather.

Uses.—Sumac berries are used in medicine solely for their astringent effect. Because of their not unpleasant flavor they afford an excellent astringent gargle in various forms of *sore throat.* For this purpose the fluidextract may be diluted with from 1 to 3 parts of rose water. Internally the fluidextract is employed in *diarrhea.*

The *dose* of the fluidextract is fifteen to thirty minims (1–2 cc.).

Off. Prep.—Fluidextractum Rhois Glabræ, *U. S.*

ROSA. U. S. (Br.)

ROSE [Rosa Gallica U. S. P. IX]

"Rose is the dried petals of *Rosa gallica* Linné (Fam. *Rosaceæ*), collected just before the expansion of the flowers." *U. S.* "Red Rose petals are the fresh or dried unexpanded petals of Rosa gallica, *Linn.;* obtained from cultivated plants." *Br.*

Rosæ Gallicæ Petala, *Br.;* Red-Rose Petals; Flores Rosarum Rubrarum; Rose rouge, Rose de Provins, *Fr.;* Sammtrose, Zuckerrose, Französische Rose, Essigrosenblatter, *G.;* Rosa rossa, *It.;* Rosa roja (Flor de), *Sp.*

As one time pale rose or *Rosa centifolia* was official in addition to red rose or *Rosa gallica.* There is no uniformity on the subject in the several Pharmacopœias. The Pharmacopœia of the Netherlands and the French Codex still include both species. The German Pharmacopœia, on the other hand, specifies only the petals of *Rosa centifolia.* The British and Austrian Pharmacopœias are in unison with the U. S. Pharmacopœia in restricting the drug to *R. gallica.*

Rosa gallica is a shrub smaller than *R. centifolia* L., but resembling it in the character of its foliage. The stem is beset with short bristly prickles. The flowers are very large, with obcordate widely spreading petals, which are of a rich crimson color, and less numerous than in the *R. centifolia.* The stamens on thread-like filaments, and the villose styles bearing papillary stigmas, are numerous. The fruit is an oval, shining, orange red hip. The red rose is a native of the south of Europe, and is cultivated in gardens throughout the United States. The commercial supplies are obtained from France and Austria.

Description and Physical Properties.—"*Unground Red Rose.*—Petals either separate or imbricated in small cones, broadly ovate, summit rounded and deeply notched, margin entire and somewhat recurved, base obtuse; externally of a purplish-red color except the light brown claw; texture velvety; when dry brittle; odor agreeable; taste astringent and slightly bitter.

"Usually in little cone-like masses, or sometimes separate and more or less crumpled. Petals velvety, deep purplish-red passing into brownish-yellow towards the base. Fragrant odor; taste slightly astringent." *Br.*

The petals should be gathered before the flower has blown, separated from their claws, dried in a warm sun or by the fire, and kept in a dry place. Their odor, which is less fragrant than that of *R. centifolia,* is improved by drying. They have a velvety appearance, a purplish-red color, and a pleasantly astringent and bitterish taste.

An illustrated article, on the structural characteristics of rose petals, whole and powdered, has been published by Hans Kramer in *B. P. G.,* 1907, xvii, p. 354.

Various astringent principles have been suggested as occurring in rose petals. According to Peacock (*Proc. Penna. Pharm. Assn.,* 1920, xlv, 162), they contain no gallic nor gallotannic acids, their astringency is due chiefly to a new tannin for which the name of *rosatannic acid* is suggested. They also contain small amounts of quercitrin.

Their coloring matter is due to the decomposition of a glucoside, *anthocyanin,* a sap pigment which is found in many flowers, and other plant tissues.

The *anthocyanins* are glucosides of three parent bodies named *pelargonidin, cyanidin* and *delphinidin.* The *anthocyanins* are red in acid solution, violet in neutral and reddish brown to purple or blue in acid solution.

In the production of the color the glucosides are hydrolyzed by ferments of the emulsin type, the free chromogen is oxidized by atmospheric oxygen activated by oxydases. The chromogen in rose petals is *cyanin* which forms a chloride of the composition, $C_{27}H_{31}O_{16}Cl$. This hydrolyzes to form cyanidin, $C_{15}H_{11}O_6$ and glucose by the action of acids. Some rose petals contain as much as 10 per cent. of *cyanin.* Their infusion is of a pale reddish color, becoming bright red on the addition of sulphuric acid. As their color is impaired by exposure to light and air, they should be kept in opaque well-closed bottles or canisters.

Uses.—Red rose is at present chiefly employed as an elegant vehicle.

Off. Prep.—Confectio Rosæ Gallicæ, *Br.;* Fluidextractum Rosæ, *U. S.;* Infusum Rosæ Acidum, *Br.* (*N. F.*); Confectio Rosæ, *N. F.;* Syrupus Rosæ (from Fluidextract), *N. F., Br.*

RUBI IDÆI FRUCTUS. N. F.

RASPBERRY Rub. Id. Fruct.

"Raspberry is the fresh, ripe fruit of varieties of *Rubus Idaeus* Linné or of *Rubus Strigosus* Michaux (Fam. *Rosaceæ*)." *N. F.*

Framboise, *Fr.;* Himbeere, *G.;* Lampone, Mora di Rovo, *It.*

The genus *Rubus* is divided into a number of sections. The section *Idæobatus,* or raspberries, are shrubs with compound leaves having an edible fruit composed of pulpy one-seeded coherent little drupes which separate from the dry receptacle. In the blackberries, the receptacle is juicy and coheres with the fruit.

Of the official raspberries, the native species, R. *strigosus,* is a shrubby biennial about three to six feet in height, found in rocky hillsides throughout the North American Continent east of the Rocky Mountains. Its stems are shrubby and densely beset with weak glandular bristles. The European species, *R. Idaeus,* is taller and more erect and has a somewhat larger fruit It is widely cultivated in the United States and is the ordinary garden raspberry. The native purple wild raspberry, *R. neglectus* Peck, whose fruit is purple—or yellowish in cultivation—is also occasionally a commercial article.

Description and Physical Properties.—"An aggregate fruit, globular or hemispherical with a concave depression at the base where separated from the receptacle, composed of twenty or more small, rounded-polygonal, succulent drupelets; pericarps externally red, non-globular hairs numerous up to 0.640 mm. in length; mesocarps fleshy, juice red; parenchyma with rosettes of calcium oxalate up to 0.035 mm. in diameter; endocarps small stones with wrinkled surfaces. Odor characteristic, aromatic; taste pleasant, sweet, acidulous. For pharmaceutical purposes, Black Raspberries, the fresh ripe fruit of varieties of *Rubus occidentalis* Linné (Fam. *Rosaceæ*) may be substituted either in part or wholly for Red Raspberries." *N. F.*

The acids in raspberry juice have been found by Broeksmit to consist of citric acid with a small amount of acetic acid. No tartaric, malic or malonic acid is present (*Ph. Wb.*, 1918, lv, 1410).

The *Rubus occidentalis* L., *black raspberry* or *thimbleberry* of the Northern United States, which is also cultivated, is sometimes employed for the making of a raspberry syrup, but yields a very inferior product.

Rubus Chamœmorus L. (*Cloud Berry, Baked-Apple Berry*) inhabits the northern portions of both continents and is largely employed in northern Russia, in the form of an infusion of the berries or leaves, as a diuretic in *dropsy.* The fruits are about 2 cm. in diameter, of an amber color, and very juicy when ripe. Popoff found in it a crystallizable acid which is an essential diuretic, acting directly upon the renal secreting structures without affecting either cardiac action or arterial tension. (*Vrach.*, iv, 1886.)

Raspberries are used only for their flavor.

Off. Prep.—Syrupus Rubi Idæi, *N. F.*

RUBUS. N. F.

RUBUS [Blackberry Bark]

"Rubus consists of the dried bark of the rhizome and roots of the section *Eubatus* Focke of the genus *Rubus* Linné. Rubus contains not more than 10 per cent. of adhering wood and not more than 2 per cent. of other foreign organic matter." *N. F.*

Blackberry Bark; Bramble; Finger Berry; Ecorce de Ronce Noir, *Fr.;* Brambeeren, Brombeerrinde, *G.*

The N. F. IV recognized only, as the source of blackberry root, three species *Rubus villosus* Ait., *R. cuneifolius* Pursh. and *R. nigrobaccus* Bailey; the last named is not recognized by most botanists being considered identical with the *R. vollosus.* This group of plants is difficult to divide into species because of the occurrence of a great number of intermediate forms. The present edition of the N. F. has not attempted to differentiate between them and has admitted the whole section *Eubatus* of the genus *Rubus.* This section would include a very large number of plants most of which, however, do not grow in this country and probably never appear in American drug markets. The species which are of most importance as sources of the drug are described below.

Formerly the N. F. recognized both the root and the fruit, but only the first named is at present official.

Rubus villosus Ait. is the common blackberry of North America and is widespread in burned-over woodlands and along roadsides from New England to Florida. It is a shrub attaining a height of 4 to 6 feet and further characterized by possessing imparipinnate leaves with 3 to 5 ovate leaflets with serrate margin and hairy on the ribs of the lower surface. Its young, green branches and pedicels bear numerous glandular hairs while its older branches are straight-prickly, purplish and reclining.

The *R. Alleghaniensis* Porter, which is found in the mountainous portions of New England is generally regarded as a variety of this species. It differs from the type in having narrower leaflets and a longer, less succulent, fruit.

Rubus canadensis L. (*R. procumbens* Muhl.) is an upright or ascending shrub growing in sandy soil of many sections of the United States east of the Mississippi river. It attains a height of about 4 feet and differs from the preceding species chiefly by possessing recurved prickles and wedge-ovate leaflets which are serrate above middle and white-tomentose on lower surface.

Rubus villosus Ait. (*R. procumbens* Muhl.) or *dewberry* differs from the foregoing species in being low-growing or prostrate in habit. Its stems bear stout recurved prickles and its leaflets are rhombic-obovate with doubly serrate margins. It is a native of open fields of the northern United States, extending from Maine to Virginia and west to Kansas. The commercial supplies of the drug are obtained chiefly from North Carolina, Virginia, Michigan and Illinois.

Description and Physical Properties.—"*Unground Rubus.*—In elongated, tough, flexible quills or bands, from 3 to 6 mm. in diameter, the bark from 1 to 2 mm. in thickness; outer surface deep red-brown or dark gray-brown, occasionally blackish brown, somewhat scaly; inner surface yellow or pale brown, strongly and coarsely long straight-striate; fracture tough-fibrous; readily splitting. Inodorous; taste strongly astringent and bitter.

"*Powdered Rubus.*—Dark brown; fibers, long, irregular with thick, lignified walls from 0.010 to 0.045 mm. in width; numerous fragments composed of cortical parenchyma containing either rosettes of calcium oxalate the latter from 0.015 to 0.045 mm. in diameter or numerous simple to many-compound starch grains, the individual grains up to 0.015 mm. in diameter; fragments of cork tissue, the cells with light-brownish walls." *N. F.*

Its virtues depend chiefly upon tannin, which is an abundant constituent. The woody part of the roots is inert.

The fruit was described by the N. F. IV as "The fresh, ripe fruit of varieties of *Rubus nigrobaccus* Bailey or *Rubus villosus* Aiton (Fam. *Rosaceæ*). An aggregate fruit, ovate to oblong, rounded or slightly pointed, composed of numerous, shining black drupelets attached to an esculent receptacle; pericarp externally smooth or with only a few hairs (*R. villosus*), mesocarps fleshy, juice purple-red, endocarps hard, black, surfaces deeply wrinkled." *N. F. IV.*

Uses.—Dewberry and blackberry roots have long been a favorite domestic astringent remedy in *diarrheas*. Given in decoction, they are usually acceptacle to the stomach, without being offensive to the taste. The decoction may be prepared by boiling an ounce of the smaller roots, or of the bark of the larger, in a pint and a half of water down to a pint, of which from one to two fluidounces (30 to 60 cc.) may be given to an adult three or four times, or more frequently, during the twenty-four hours.

Dose, from fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Fluidextractum Rubi, *N. F.;* Syrupus Rubi, *N. F.*

RUMEX. N. F.

RUMEX [Yellow Dock, Curled Dock]

"Rumex is the dried root of *Rumex crispus* Linné, or of *Rumex obtusifolius* Linné (Fam. *Polygonaceæ*). Rumex contains not more than 5 per cent. of its stem bases or other foreign organic matter." *N. F.*

Yellow Dock; Curled Dock; Radix Lapathi; Rumex, *Fr.;* Ampferkraut, *G.;* Lapazio, *It.*

The docks are divided into two groups, one with hastate acid foliage and the other, much taller, with leaves which are neither acidulous in taste nor hastate in shape. The first group, sometimes known as the *sour dock,* or more frequently as *sorrel,* includes the *Rumex Acetosa* L. and the *R. Acetosella* L. which have been used as articles of diet in scurvy. They owe their acidity chiefly to acid potassium oxalate, although they also contain some tartaric acid. The amount of oxalic acid present is sometimes sufficient that when taken in large quantities they may produce poisonous effects. G. G. Flemyng (*L. L.,* i, 1896) reported the death of two sisters, aged respectively five and six and a half years, preceded by symptoms of oxalic acid poisoning as the result of the ingestion of sorrel leaves. Of the proper docks the roots of several species, besides those now official, have been employed. *R. Hydrolapathium* Hudson, which is the *R. aquaticus* of the old Dublin Pharmacopœia, is thought to be the *Herba Britannica* of the ancients, held in high esteem as a remedy for *scurvy. R. Britannica* L., *water dock,* was also formerly recognized by the U. S. Pharmacopœia (5th revision).

The official species, when full grown, are tall, (from two to four feet) perennial herbs with large leaves from six to twelve inches in length, the flowers being arranged in loose panicles. They may be readily distinguished from each other by their leaves which in *R. crispus* are lanceolate with strongly wavy-curled margins, whereas in *R. obtusifolius* they vary from ovate-cordate radical leaves to oblong-lanceolate cauline leaves with margins only slightly wavy-curled or frequently without curling. The commercial supplies of the drug used in the United States come chiefly from Virginia, North Carolina, Michigan and Indiana. They are both common in waste places throughout the United States—although they appear to have been naturalized from Europe—and often prove troublesome weeds.

Description and Physical Properties.—"*Unground Rumex.*—Nearly simple, slightly tapering, with few if any rootlets, somewhat twisted, up to 30 cm. in length and 7 cm. in diameter, externally reddish brown or grayish from adhering soil, finely annulate above, deeply wrinkled longitudinally, marked with small indented root scars which are often transversely elongated and with occasional stem scars or remains of stem, the latter being hollow and finely striated; leaf buds few, obconical; fracture short and dusty, somewhat fibrous; usually split longitudinally or cut into transverse pieces about 2 cm. in length. Odor, slight; taste, astringent and somewhat bitter.

"*Structure.*—A yellowish or brownish cortex and a whitish or yellowish wood which is finely radiate in the outer portion; cortex thick, with several layers of cork, beneath which is an interrupted row of lignified cells (*R. crispus*); a distinct cambium; and vascular bundles with few fibers.

"*Powdered Rumex.*—Calcium oxalate crystals in rosettes from 0.020 mm. to 0.065 mm. in diameter; numerous starch grains ellipsoidal or narrowly elongated, sometimes truncate, up to 0.028 mm. in length; lignified cells (in *R. crispus*) from 0.040 mm. to 0.200 mm. in diameter, with walls somewhat lamellated, from 0.008 mm. to 0.025 mm. in thickness and with few simple pores; fibers few, thin-walled with simple pores; tracheæ up to about 0.1 mm. in width with scalariform or reticulate thickenings of the wall; cork cells light brown." *N. F.*

Dock root has an astringent bitter taste with little or no odor.

Constituents.—Rumex contains tannin and a yellowish coloring matter, probably allied to anthocyanin. Beal and Okey (*J. Am. C. S.,* 1919, xli, 693) have found in it emodin (identical with that from cascara), monomethyl ether of emodin and chrysophanic acid; they surmise that these are, at least in part, in the form of glucosides. The total amount of emodin was about 0.17 per cent., of chrysophanic acid somewhat less. Tschirch and Weil (*A. Pharm.,* 1912, ccl, p. 20) find also *lapathinic acid,* $C_{20}H_{18}O_{14}$. According to Gilbert and Lereboulet, the *R. crispus* has the power of taking up iron present in the soil, and by watering plants with a solution of iron salts, roots may be obtained containing 1.5 per cent. of iron. In the sample examined by Tschirch and Weil there was present 0.379 per cent. of this element. From the root of *R. Nepalensis* Wall., which is largely used in Madras as an astringent for medicinal purposes and for dyeing, O. Hesse has separated three crystalline substances to which he gives the names of *rumicin, nepalin,* and *nepodin.* (*P. J.,* lvi; also *Proc. A. Ph. A.,* 1896, 551.) According to Tutin and Clewer (*Trans. Chem. Soc.,* 1910, xcvii), the *R. Eckolianus* Meissner, a South African herb, contains chrysophanic acid, emodin, and allied products, and is mildly purgative.

Dock root is mildly laxative and astringent and has been chiefly employed as an alterative in *syphilis* and chronic *skin diseases,* but its continued use is based on ancient tradition rather than any real therapeutic value. It is also employed locally in indolent skin diseases.

Dose, from thirty to sixty grains (2–4 Gm.).

Off. Prep.—Fluidextractum Rumicis, *N. F.*

SABAL. N. F.

SABAL [Saw Palmetto Berries]

"Sabal is the partially dried, ripe fruit of *Serenoa serrulata* (Michaux), Hooker filius (Fam. *Palmæ*). Sabal contains not more than 1 per cent. of foreign organic matter. Sabal should contain from 10 to 15 per cent. of its natural moisture when used for the manufacture of pharmaceutical preparations." *N. F.*

Saw Palmetto; Dwarf Palmetto.

The *saw palmetto* is a fan palm flourishing on the Atlantic coast from South Carolina to Jupiter Inlet, Florida, where it forms the so-called "palmetto scrub." According to Schneider, it is also found in the southern portions of California. The stem of saw palmetto is from 6 to 10 feet high, has a crown of large leaves, long petioled, with a circular fan-shaped leaf blade split at the edge into from 15 to 30 divisions, which are slightly cleft at their apices. The fruit is a one-sided, blackish-brown superior drupe, from half an inch to one inch long; ovoid-oblong in shape, with a somewhat wrinkled exterior, and a sweetish, not agreeable taste. It occurs in a large panicle which in some cases may weigh as much as nine pounds.

The fruits are gathered when fully mature, partially dried artificially and packed into barrels. To the contents of each barrel a small quantity of alcohol is added as a preservative. The commercial supplies are obtained largely from the Cape Canaveral district of Florida.

Description and Physical Properties.—"*Unground Sabal.*—Ellipsoidal or ovoid, occasionally compressed, from 1.5 to 3 cm. in length and from 1 to 1.5 cm. in diameter; externally brownish black to bluish black, smooth and somewhat oily, with a few large, more or less angular depressions due to the contraction of the sarcocarp, apex marked by the scar of the style, and the base either with a short stalk or stem-scar; epicarp and sarcocarp together forming a thin coriaceous shell enclosing a hard but thin endocarp, which is externally reddish brown and somewhat fibrous as is also the inner layer of the sarcocarp; inner layer of endocarp smooth, enclosing a hard, ellipsoidal or ovoid, somewhat flattened, reddish brown seed. Odor pronounced, aromatic; taste sweetish, aromatic, slightly acrid.

"*Powdered Sabal.*—Yellowish brown; parenchyma cells of sarcocarp containing a yellowish brown or brownish red, amorphous substance; whitish fragments of endosperm, the walls being considerably thickened and with large pores; stone cells occasional, nearly colorless, more or less tabular or irregular in shape, about 0.125 mm. in length, walls about 0.015 mm. in thickness, and with numerous simple or branching pores." *N. F.*

Kraemer gives an illustrated article on the pharmacognosy of the saw palmatto in the *Practical Druggist,* 1910, xxviii, p. 97.

By pressure they yield about 1.5 per cent. of a brownish-yellow to dark-red oil. Shermann and Briggs (*Ph. Archiv.,* 1899, 101, and *Ph. Rev.,* 1900, 217) found this to be composed of about 63 per cent. of free fatty acids and 37 per cent. of ethyl esters of these acids; there was no alkaloid present. Coblentz believed (*Proc. N. J. Ph. Assoc.,* 1895) that he found a volatile oil and an alkaloid, but Mann (*A. J. P.,* 1916, lxxxviii, p. 517) concluded that the so-called volatile oil was a mixture of the ethyl esters of the various fatty acids present due to the combination with the ethyl alcohol which is used as a preservative in shipping them. The fatty acids are caproic, caprylic, capric, lauric, palmitic and oleic.

Vanderkleed and E'we (*Proc. P. Ph. A.,* 1916, p. 284) contribute formulas for syrup of sabal and elixir of sabal with terpin hydrate. The latter is made as follows: Dissolve 1.75 Gm. of terpin hydrate in 40 cc. of fluidextract of sabal and 10 cc. of alcohol. Add 1 cc. of tincture of sweet orange peel, 0.2 cc. of solution of saccharin, 40 cc. of glycerin, and 100 cc. of syrup. This preparation will contain 8 grains of terpin hydrate and 184 grains of sabal in each fluidounce.

Uses.—Saw palmetto appears to exert a stimulant alterative action upon the mucous membrane of the genito-urinary tract, similar to but milder and less stimulant than is cubeb or copaiba, or the oil of sandal-wood. Like these drugs it also has the power of affecting the respiratory mucous membrane, so that it has been used not only in *chronic* and *sub-acute cystitis,* but also in *chronic bronchitis, laryngitis,* and the catarrhs which accompany *asthma, phthisis,* and other more serious diseases of the lungs. It has been affirmed that saw palmetto is capable of increasing the nutrition of the testicles and of the mammæ in functional atony of these organs, but this is very doubtful. It has been especially recommended in cases of *enlarged* *prostate* of old men; it is not probable that it has a direct influence upon the prostatic gland itself but there is much clinical testimony as to its value and it probably acts by reducing the catarrhal irritation and the relaxed condition of the mucous membrane of the bladder and urethra, which are almost universally present in prostatic hypertrophy.

Dose, ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Fluidextractum Sabal, *N. F.;* Tinctura Sabal et Santali, *N. F.;* Elixir Sabal et Santali Compositum, *N. F.*

SALICINUM. U. S., Br.

SALICIN Salicin.

" A glucoside [$C_{13}H_{18}O_7$] obtained from several species of *Salix* and *Populus* (Fam. *Salicaceæ*)." *U. S.* " Salicin, $C_{12}H_{18}O_7$, is a crystalline glucoside, which may be obtained from the bark of various species of Salix, and of Populus." *Br.*

Orthohydroxybenzylglucoside; Salicine, *Fr.;* Salicin, *G.;* Salicina, *It.*

The discovery of salicin is claimed by Buchner of Germany, and Fontana and Rigatelli of Italy; but Leroux of France deserves the credit of having first accurately investigated its properties. Salicin is a glucoside of ortho-hydroxybenzyl-alcohol, and is found in the bark of *Salix Helix, S. pentandra, S. præcox* and probably some other species of willow and of the *Populus tremuloides* and *P. tremula* (see *Populi Gemmæ*). *Salix nigra* yields a different principle (see below).

To prepare salicin the ground bark is extracted with boiling water, concentrated in a vacuum still and the extract purified by precipitation with lead acetate. The excess of lead is removed by hydrogen sulphide and the filtrate is neutralized with ammonia and carefully concentrated to the crystallizing point. The crude salicin is decolorized with animal charcoal and recrystallization from water and finally from alcohol. Merck obtained 251 grains from 16 ounces of the bark and young twigs of *Salix Helix,* and Erdmann 300 grains from the same quantity of the bark of *Salix pentandra.* It may probably be obtained from any of the willow barks having a bitter taste. T. Fawssett states that the best material for preparing salicin is undoubtedly the willow peelings, obtained as refuse from a basket factory, and known in Belgium as " rood schors." David Brown states that the peelings are produced from *Salix fragilis,* while Crispo considers the source to be *Salix purpurea.* These peelings should be used soon after they are stripped from the twigs. (*P. J.,* June 6, 1903, 784.) A new glucoside called *salinigrin,* $C_{13}H_{16}O_7$, has been isolated from black willow bark. It has been shown to be a glucoside of metahydroxybenzaldehyde. Its melting point is 195° C. For a paper by Jowett on the percentage of salicin obtained from various kinds of willow bark, see *Y. B. P.,* 1902, 483, and 1903, 474.

Description and Physical Properties.—" Colorless, silky, shining needles or prisms, or a white, crystalline powder. It is odorless and has a very bitter taste. One Gm. of Salicin is soluble in 23.5 cc. of water and in 88.5 cc. of alcohol, at 25° C. One Gm. is soluble in 3.3 cc. of water at 80° C., and in 30 cc. of alcohol at 60° C. It is insoluble in chloroform and in ether.

" Salicin melts between 199° and 202° C. Its aqueous solution (1 in 30) is neutral to litmus paper, and is lævorotatory. Heat a small portion of Salicin in a test tube until it turns brown, add a few cc. of distilled water, and a drop of ferric chloride T.S.: a violet color is produced. With sulphuric acid Salicin gives a red color which disappears on the addition of distilled water. Heat gently about 0.1 Gm. of Salicin with about 0.2 Gm. of potassium dichromate and 2 cc. of diluted sulphuric acid: the fragrant odor of salicylic aldehyde is developed.

" Ash: not more than 0.05 per cent. Ten cc. portions of an aqueous solution of Salicin (1 in 50) yield no precipitate on the addition of 1 cc. of tannic acid T.S., picric acid T.S., or mercuric potassium iodide T.S. (*alkaloids*), and another 10 cc. portion is not colored violet by a drop of ferric chloride T.S. (*salicylic acid*). An aqueous solution of Salicin meets the requirements of the test for *heavy metals.*

" Preserve in well-closed containers." *U. S.*

" Colorless, shining, trimetric, tabular crystals, or white, crystalline powder. Taste very bitter. Soluble in 28 parts of *water,* and in 80 parts of *alcohol* (90 per cent.); insoluble in *ether.* Melting point from 200° to 201° C. Colored red by *sulphuric acid.* When 0.1 gramme is gently heated with 0.2 gramme of *potassium bichromate* and 2 millilitres of *diluted sulphuric acid* an odor recalling meadowsweet is developed. No appreciable ash." *Br.*

Salicin gives with concentrated sulphuric acid a bright red color; this is known as the *rutilin reaction.*

It belongs to the class of glucosides, being resolved by boiling with diluted hydrochloric and sulphuric acids into grape sugar and *saligenin,* according to the reaction:

$$C_{13}H_{18}O_7 + H_2O = C_6H_{12}O_6 + C_7H_8O_2$$

Saligenin, which is ortho-oxybenzyl alcohol, $C_6H_4(OH)CH_2OH$, is converted by further boiling with dilute acids into a resinous body, *saliretin,* $C_{14}H_{14}O_3$; this is a polymerized aldehyde of saligenin. Nitric acid produces with salicin at first two principles called respectively *helicin,* $C_{13}H_{16}O_7$, and *helicoidin,* $C_{26}H_{34}O_{14}$, and afterwards picric and oxalic acids. (*J. P. C.,* xxx, 43.) Distilled with potassium dichromate and sulphuric acid, salicin yields, among other products, a volatile oleaginous liquid, identical with one of the components of oil of spiræa, and recognized as *salicyl aldehyde,* $C_7H_6O_2$ (incorrectly called *salicylous acid*), while *saligenin,* $C_7H_8O_2$, is the alcohol, and *salicylic acid,* $C_7H_6O_3$, the acid corresponding. The synthesis of salicin has been effected by Michael (*A. J. P.,* 1879), who obtained first helicin by the reaction of acetochlorhydrose and salicyl aldehyde, and, by the action of nascent hydrogen upon this, salicin.

Saligenin (*salicyl alcohol*) has recently become a commercial article, a proprietary form being known as *salicaine.* Saligenin occurs as a white crystalline powder permanent in the air, soluble in water, alcohol, ether or the oils, melting at 85° to 86° C. Its taste is at first pungent and followed by a sense of numbness.

Uses.—Salicin acts upon the stomach probably as a simple bitter, and after absorption as a feeble and uncertain form of salicylic acid, since it is rapidly, although not completely, decomposed in the system, the products of its change appearing in the urine fifteen to thirty minutes after the ingestion of a single dose. The elimination is partly as salicin, partly as salicylic acid, partly as a salicyluric acid, and partly as saligenin. It has been highly recommended as a substitute for salicylic acid in *rheumatism* by Maclagan and others, but since it owes its activity to its conversion in the blood into salicylic acid and since this conversion is uncertain, salicin is inferior in power to the salicylates. By some it is believed to be less liable to upset the stomach. Salicin has been used as an antiperiodic. One or two drachms may be given in the intermission. Hirschfelder (*J. A. M. A.,* 1920, lxxv, 1770) has shown that saligenin possesses marked local anesthetic powers and has used it with satisfaction as a clinical anesthetic in strengths of from 4 to 10 per cent. It has the great advantage of being practically non-toxic.

Dose, of salicin, from ten to thirty grains (0.65–2.0 Gm.).

SAMBUCUS. N. F.

SAMBUCUS Sambuc. [Elder Flowers]

" Sambucus is the air-dried flower of *Sambucus canadensis* Linné, or of *Sambucus nigra* Linné (Fam. *Caprifoliaceæ*). Sambucus contains not more than 2 per cent. of foreign organic matter." *N. F.*

Elder; Sambuci Flores, *Br.,* 1898; Sweet Elder; Black Elder; Sureau, Fleurs de Sureau, *Fr.;* Flores Sambuci, *P. G.;* Holunder, Fliederblumen, *G.;* Sambuco, *It.;* Sauco, *Sp.*

The indigenous *common elder, Sambucus canadensis,* is a shrub from six to twelve feet high, with a branching stem, covered with a rough gray bark, and containing a large spongy pith. The small branches and leaf-stalks are very smooth. The leaves are opposite, and pinnately-compound with usually seven leaflets The flowers are small, white, and disposed in loose cymes; the cream-colored corolla is wheel-shaped, with five stamens on the tube. The fruits are small, globular, black berry-like drupes which are edible when mature. The shrubs grow in low, moist grounds, along fences, and on the borders of small streams, throughout the United States, from Canada to the Carolinas, and westward as far as Arizona and Texas. It flowers from May to July, and ripens its fruit early in autumn.

The *Sambucus nigra,* of Europe, differs from the American most obviously in its size, approaching in height that of a small tree. The stem is much branched towards the top, and has a rough whitish bark. The leaves may show 3–7 leaflets but usually possess 5. The flowers are small, whitish and in five-parted cymes. The ovary consists of but three carpels, there being usually four cells in *S. canadensis* L. The berries are large in the European elder, globular, and blackish-purple when ripe. G. De Sanctis (*Gazz. Chim. Ital.,* 1895, xxv, 1, vol. xlix) obtained coniine from the leaves and stems of *Sambucus nigra.*

The flowers have an aromatic though rather heavy odor. The berries as well as other parts of the plant are employed in domestic practice.

Description and Physical Properties.—" Small, from 2 to 3 mm. in width, shriveled; calyx superior, five-lobed; corolla cream colored to brownish yellow, rotate, flat or slightly campanulate, regularly five-lobed; stamens five, inserted at the base of the corolla and alternating with its lobes, filaments lender, anthers oblong, yellow; pollen ellipsoidal or tetrahedral and rounded, covered with finely punctate markings, having three pores and up to 0.23 mm. in diameter, Odor faintly sweet and aromatic; taste slightly bitter." *N. F.*

The flowers yield their active properties to water by infusion, and when distilled give over a small proportion of volatile oil, which on cooling assumes a butyraceous consistence and contains an appreciable portion of ammonia. The *berries* are nearly inodorous, but have a sweetish, acidulous taste, dependent on the presence of saccharine matter and malic acid. Their expressed juice is susceptible of fermentation, and forms a vinous liquor used in northern Europe. It is colored violet by alkalies, and bright red by acids, and the coloring matter is precipitated blue by lead acetate. The *inner bark* is without odor. The *bark* of the elder contains tannin, valeric (*viburnic*) acid, resin, etc. (Traub, *A. J. P.,* 1881, p. 392). The resin, according to Simon (*Ann. Pharm.,* xxxi, p. 262), in doses of twenty grains is cathartic and emetic. Lloyd found in the flowers a white substance—*eldrin,* which turned a deep yellow on the addition of alkalies which he believed to be the coloring matter of white flowers (*A. J. P.,* 1921, xciii, p. 40). As far as we know, no substance has been found in the flowers suggesting any physiologically active principle. J. B. Metzgar made a partial examination of the fruit and found sugar, gum, tannin, fat, and a resinous body. (*A. J. P.,* 1881, p. 553.) It was also examined by F. F. Lyons (*A. J. P.,* 1892, p. 1), who found 0.5 per cent. of a volatile oil, an amorphous yellow compound of a glucosidal character, and a tannin. The volatile oil of elder flowers was examined by W. J. Bush & Co. (*C. D.,* 1897, 53.) It has the sp. gr. 0.827, and is solid at ordinary temperatures like oil of rose. The liquid portion possesses the fragrance of fresh elder blossoms.

Uses.—Elder flowers have been esteemed diaphoretic and diuretic and used in febrile complaints and also as an alterative in *syphilis* and *rheumatism.* There is, however, no reason to suspect that they possess any real curative properties. The berries, bark and root, however, appear to possess some laxative principles and especially the last named has been used as a hydragogue in *dropsy.*

Dose, from thirty to sixty grains (2–4 Gm.).

Off. Prep.—Fluidextractum Stillingiæ Compositum, *N. F.;* Species Laxativæ, *N. F.;* Syrupus Stillingiæ Compositus, *N. F.*

SANGUINARIA. N. F.

SANGUINARIA Sanguin. [Bloodroot]

"Sanguinaria consists of the dried rhizome and roots of *Sanguinaria canadensis* Linné (Fam. *Papaveraceæ*). Sanguinaria contains not more than 2 per cent. of foreign organic matter." *N. F.*

Blood-root, Red-root, Puccoon, Red Indian-plant, Puccoon-root, Coon-root, White puccoon, Pauson, Snakebite, Sweet-slumber, Red Puccoon, Tetterwort, Red Indian Paint; Sanguinaire, *Fr.;* Blutwurzel, *G.*

Sanguinaria canadensis, or, as it is sometimes called, *red puccoon,* is a perennial herb native to the rich open woods of North America. The rhizome is horizontal, abrupt, often contorted, about as thick as the finger, two or three inches long, fleshy, of a reddish-brown color on the outside, and emitting a reddish latex, when broken in the recent state. It is furnished with numerous slender roots, and makes offsets from the sides, which succeed the old plant. From the end of the rhizome arise the scape and leafstalks, surrounded by the large sheaths of the bud. These spring up together, the folded leaf enveloping the flower-bud, and rolling back as the latter expands. The leaf, which stands upon a long channelled petiole, is reniform, somewhat heart-shaped, palmately 7- to 9-lobed, smooth, yellowish green on the upper surface, paler or glaucous on the under, and strongly marked by orange-colored veins. The scape is erect, round, and smooth, rising from a few inches to a foot, and terminating in a single white flower. The calyx is two-leaved and deciduous. The petals, varying from seven to fourteen, but usually about eight in number, are spreading, ovate, obtuse, concave, mostly white, but sometimes slightly tinged with rose or purple. The stamens are numerous, with yellow filaments shorter than the corolla, and orange oblong anthers. The ovary is oblong and compressed, with a sessile, persistent stigma. The capsule is oblong, acute at both ends, one-celled, two-valved, and contains numerous oval, reddish-brown seeds. The whole plant is pervaded by an orange-colored sap, which flows from every part when broken, but is of the deepest color in the rhizome. The bloodroot is one of the earliest and most beautiful spring flowers of the northern United States, growing abundantly in loose, rich soils and shady situations. After the fall of the flower the leaves continue to grow, and by the middle of summer have become so large as to give the plant an entirely different aspect. Except the seeds, all parts of the plant are active.

The rhizome should be collected at the time of, or immediately subsequent to the flowering of the plant, for it is at this time that it possesses the largest amount of alkaloids.

Description and Physical Properties.—"*Unground Sanguinaria.*—Of horizontal growth, occasionally branching, more or less cylindrical, somewhat flattened, from 2 to 7 cm. in length and from 5 to 15 mm. in diameter; externally dark brown, slightly annulate, with a few stem-scars on the upper surface and numerous root-scars or more or less broken filiform roots on the lower surface; fracture short, most of the rhizomes showing a brownish red internal color, somewhat waxy and with numerous small circular, yellowish fibrovascular bundles within about 1 mm. of the epidermis and a very large pith. Odor slight; taste persistently acrid and bitter.

"*Structure.*—Rhizome; an outer layer of a single row of thin-walled epidermal cells; a cortex of from 10 to 15 rows of thin-walled parenchyma cells containing numerous starch grains, or a small amount of fixed oil; a zone of cambium, most of which is interfascicular; a narrow circular zone of small collateral fibrovascular bundles, bearing parenchyma cells; latex cells containing a red or orange colored secretion, either isolated or connected into irregular chains and distributed among the parenchymatous cells of the middle bark and pith; sections treated with glycerin for twenty-four hours show spheroidal aggregates of crystals in the secretion cells or latex tubes.

"*Powdered Sanguinaria.*—Brownish red, sternutatory; exhibits numerous starch grains, from 0.003 to 0.020 mm. in diameter, being mostly single, seldom 2- to 3-compound, the individual grains nearly spherical or ovoid, sometimes more or less plano-convex, somewhat resembling those of wheat starch in outline but polarizing light more strongly; numerous fragments of short latex cells with reddish brown resinous masses; tracheal fragments few, having numerous slit-like pores." *N. F.*

For an interesting microscopical description of the rhizome by E. S. Bastin, see *Pharm.,* 1885, p. 201. Sanguinaria has a faint odor, and a bitter, very acrid taste, the pungency of which remains long in the mouth and fauces. Lloyd states that sanguinaria is both a contamination and an adulterant of hydrastis. (*Pharm. Rev.,* 1905, xxiii, p. 332.) It yields its virtues to water and alcohol.

Constituents.—G. König (*A. J. P.*, 1891, p. 457) found *chelerythrine*, $C_{21}H_{17}O_4N$, which is present in greatest quantity, *sanguinarine*, $C_{21}H_{15}O_4N$, *β- and γ-homochelidonine*, $C_{21}H_{23}O_5N$, and *protopine*, $C_{20}H_{19}O_5N$. Chelerythrine crystallizes with a molecule of alcohol which is not separated at 150° C. It is identical with the alkaloid extracted from *Chelidonium majus* and *Stylophorum diphyllum.* (See Part II.) The salts are lemon-yellow. Sanguinarine is very similar to chelerythrine in its properties. It crystallizes with one molecule of H_2O, and melts at 211° C. It also crystallizes with one molecule of alcohol. Its salts are red. The base named γ-homochelidonine is probably identical with that separated by Selle from *Chelidonium majus.* The fourth alkaloid, protopine, has been prepared from *Chelidonium majus,* from *Sanguinaria canadensis,* and from opium, all three of the specimens being identical. It melts at 204° C. Beringer and Homerberg (*A. J. P.*, 1915, p. 97) found the alkaloidal content of the rhizome to range from 4.7 to 7.0 per cent. and of the rootlets to be about 1.8 per cent.; it was highest in the rhizome at the time of flowering. The virtues of the root are said to be rapidly deteriorated by time. *Sanguinarinic acid* L. C. Hopp has shown to be a solution of impure citric and malic acids.

Schlotterbeck (*Ph. Rev.*, 1900, 358) examined sanguinarine nitrate of commerce and found it to consist mainly of chelerythrine, with some sanguinarine and traces of protopine and homochelidonine; he believes that chelerythrine should be called sanguinarine. For methods of assay of sanguinaria, see *A. J. P.*, 1896, 305; *M. R.*, 1900, 451; *Proc. A. Ph. A.*, 1903, 284; *A. J. P.*, 1913, p. 395.

Uses.—Sanguinaria is an active local irritant, in large doses producing nausea and vomiting. When snuffed up the nostrils it excites much irritation and sneezing. According to the investigations of Meyer (*A. E. P. P.*, 1892, xxix, p. 397), sanguinarine is an active stimulant to the spinal cord producing in frogs strychnine-like convulsions followed, after very large doses, by complete paralysis. It also stimulates the respiratory center, increasing both the depth and rate of the breathing. By virtue of a stimulant action upon the vasomotor center it causes a rise in blood pressure which, with toxic doses, is followed by a fall in the blood pressure, due to weakening of the heart action. It also excites the flow of saliva and increases intestinal peristalsis. In toxic doses it acts as a poison to the voluntary muscles. When locally applied it causes at first pain, followed by a local anesthesia.

Chelerythrine, although present in larger amounts in sanguinaria, is a much less poisonous alkaloid than sanguinarine and it is probable that it plays a rôle of relatively small importance in the action of the whole drug. The physiological action of chelidonine has been studied by Meyer (*A. E. P. P.*, 1892, xxix, 397) and by Hanzlik (*J. A. M. A.*, 1920, lxxv, 1324 and *J. P. Ex. T.*, 1921, xviii, 63). It is feebly narcotic, according to Hanzlik having less narcotic power than papaverine. Its toxic action is comparatively low, the minimal lethal dose for the lower animals being between 0.3 and 0.4 Gm. per kilo. Its most important action is a depressant effect on the involuntary muscles; Hanzlik found that it not only produced a relaxation in normal involuntary muscles but antagonized the effect of such stimulants of these muscles as barium, pilocarpine, etc. Because of this action on muscle tissue it lowers blood pressure by relaxing the arteries and weakening the cardiac contractions. Beta-homochelidonine, the third most important alkaloid, has a feeble narcotic effect, produces cerebral convulsions, but does not increase reflex activity. It is an active local anesthetic without the irritant effect of sanguinarine.

Sanguinaria is used chiefly as an expectorant, especially in the treatment of subacute or *chronic bronchitis.* Whether it possesses any beneficial action for this purpose except that which may be attributed to its nauseating effect,—due largely to irritation of the gastric mucosa—seems doubtful. It has also been recommended by Graber (*J. A. M. A.*, 1907, xlix, p. 705) as a local application in chronic *eczema,* especially when secondary to *varicose ulcers.*

In toxic quantities sanguinaria produces burning in the epigastrium with vomiting, tormenting thirst, faintness, vertigo, dimness of vision, and alarming prostration. Twenty grains (1.3 Gm.) are said to usually act as a violent emetic. (For fatal cases see *Am. J. M. S.*, N.S., ii, p. 506.)

The alkaloid sanguinarine has been used in doses of from one-twelfth to one-sixth of a grain (0.005–0.01 Gm.). Sanguinaria is rarely given in substance.

Dose, two grains (0.13 Gm.).

Off. Prep.—Tinctura Sanguinariæ, *N. F.;* Fluidextractum Sanguinariæ, *N. F.;* Syrupus Pini Albæ Compositus, *N. F.;* Syrupus Pini Albæ Compositus cum Morphina, *N. F.*

SANTALUM ALBUM. N. F.

SANDAL WOOD Santal Alb. [White Sandalwood]

"Sandalwood is the heartwood of *Santalum album,* Linné (Fam. *Santalaceæ*). Sandalwood yields not less than 3.5 per cent. of volatile oil, and contains not more than 1 per cent. of foreign organic matter." *N. F.*

Lignum Santali Citrinum; Yellow Sandalwood; Santal Citrin, Bois de Santal blanc, *Fr.;* Gelbes Sandelholz, *G.;* Sandalo Cetrino (Leno de), *Sp.*

For description of this tree see under *Oleum Santali.*

Description and Physical Properties.—"In billets, pieces or chips of varying shapes and sizes, heavy, hard but splitting easily, color light yellow to light brown. Odor characteristic, aromatic, persistent; taste peculiar, strongly aromatic.

"*Structure.*—Transverse sections yellow to light reddish brown, with alternating light and dark concentric zones nearly equal in width, with numerous tracheæ and traversed by many very narrow medullary rays; the medullary rays from two to four cells wide, the cells thick-walled and radially marked; the wood wedges consisting largely of wood fibers with pointed ends and containing a few starch grains, large parenchyma and thick-walled oil secretion vessels and cells containing single crystals of calcium oxalate up to 0.030 mm. in length; the oil in globules adhering to the walls of the ducts and parenchyma cells and especially rich in the medullary ray cells." *N. F.*

Sandal wood owes its therapeutic virtues solely to its volatile oil (see *Oleum Santali*). It is not used in substance.

Dose, sixty grains (4 Gm.).

Off. Prep.—Fluidextractum Santali Albi, *N. F.;* Elixir Sabal et Santali Compositum, *N. F.;* Tinctura Sabal et Santali, *N. F.*

SANTALUM RUBRUM. U. S. (Br.)

RED SAUNDERS Santal. Rub.

"Red Saunders is the heart-wood of *Pterocarpus santalinus* Linné filius (Fam. *Leguminosæ*)." *U. S.* "Red Sanders Wood is the heart-wood of Pterocarpus santalinus, *Linn. f.*" *Br.*

Pterocarpi Lignum, *Br.;* Red Sanders Wood; Lignum Santali Rubri; Rasura Santalum Ligni; Red Sandal Wood; Red Santal Wood; Ruby Wood; Santal rouge, *Fr.;* Santelholz, Rothes Santelholz, *G.;* Sandalo rojo (Leno de), *Sp.*

Pterocarpus santalinus is a large tree, with alternate branches, and trifoliate leaves, each leaflet being ovate, somewhat notched at the apex, smooth on the upper surface, and hoary beneath. The flowers are yellow in axillary spikes, and have a papilionaceous corolla, of which the vexillum is obcordate, erect, somewhat reflexed at the sides, toothed and waved, the alæ spreading with their edges apparently toothed, and the carina oblong, short, and somewhat inflated. The fruit is a 2-seeded legume. The tree is a native of India, attaining the highest perfection in mountainous districts, and inhabiting especially the mountains of Coromandel and Ceylon. It is cultivated in Southern India and in the Philippine Islands.

The wood comes in heavy, irregular, roundish or angular billets of various size and thickness, externally brown from exposure, internally of a deep blood-red color, on transverse section variegated with zones of a lighter red. The structure is heavy, compact, and fibrous. In the pharmacies red saunders is usually kept in the shape of small chips, or raspings, or coarse powder, of a deep reddish-brown color, slightly astringent taste, and when rubbed of a faint peculiar odor. It has little odor or taste.

Description and Physical Properties.—"*Unground Red Saunders.*—Usually in the form of a coarse powder, of a purplish to brownish-red color and nearly odorless and tasteless.

"*Powdered Red Saunders.*—Wood-fibers numerous, mostly irregular in outline, with sharply pointed and occasionally forked ends, from 0.30 to 0.75 mm. in length, walls very thick, porous, yellowish, unevenly thickened and strongly lignified, and the lumina filled with a fine, granular, content; tracheæ few with simple or bordered pores and filled with light lemon-yellow, resinous masses; occasionally fragments showing medullary ray cells in narrow elliptical groups 1-cell wide and from 3- to 6-cells deep; crystal-fibers few with calcium oxalate in the form of monoclinic prisms, from 0.008 to 0.020 mm. in length. Mounts in chloral hydrate T.S. are of a deep, rich red color.

"Add 0.5 Gm. of Red Saunders to 10 cc. of alcohol: the solution becomes distinctly red. Add 0.5 Gm. of Red Saunders to 10 cc. of ether: the solution assumes an orange-yellow color and when held in a bright light shows a distinct greenish fluorescence.

"Add 0.5 Gm. of Red Saunders to 10 cc. of water: the solution remains clear and colorless." *U. S.*

"Imported in irregular logs or billets, freed from the pale sapwood; reddish-brown or blackish-brown externally, deep blood-red internally; hard, but easily split longitudinally. In transverse section, narrow, closely approximated, reddish medullary rays traversing a nearly black wood with scattered, large, isolated vessels. Coloring matter readily soluble in *alcohol* (90 per cent.), but almost insoluble in *water*. Odor of the warmed Wood faintly aromatic; taste very slightly astringent." *Br.*

It imparts a red color to alcohol, ether, and alkaline solutions, but not to water, and a test is thus afforded by which it may be distinguished from some other coloring woods. The alcoholic tincture produces a deep violet precipitate with ferrous sulphate, a scarlet with mercuric chloride, and a violet with the soluble salts of lead. The coloring principle, which was separated by Pelletier and called by him *santalin,* is of a resinous character, scarcely soluble in cold water, more so in boiling water, very soluble in alcohol, ether, acetic acid, and alkaline solutions, but slightly in the fixed and volatile oils, with the exception of those of lavender and rosemary, which readily dissolve it. It is precipitated when acids are added to the infusion of the wood, prepared with an alkaline solution. It is also called *santalic acid* and has the formula $C_{17}H_{16}O_6$. The formula $C_{23}H_{18}O_6(OCH_3)_2$ has also been given to it. (*Ann. Ch. Ph.,* lxxiv, p. 226.) Weidel (*Wien. Akad. Ber. Ph.,* lx, p. 388), by extracting the red saunders with potassium hydroxide, precipitating with hydrochloric acid, and again extracting from the purified precipitate with ether, obtained a colorless crystalline principle, which he calls *santal,* $C_8H_6O_3 + \frac{1}{2}H_2O$.

Cazeneuve and Hugonneng (*C. R. A. S.,* civ, 1725) have described two crystalline principles which they have extracted from red saunders, *pterocarpin*, $C_{20}H_{16}O_6$, and *homopterocarpin*, $C_{24}H_{24}O_6$, of which the former fuses at 152° C., and the latter at from 82° to 86° C.

The wood has no medicinal virtues, and is employed solely for the purpose of imparting color.

Off. Prep.—Tinctura Lavandulæ Composita, *U. S., Br.*

SANTONINUM. U. S., Br.

SANTONIN Santonin.

"The inner anhydride [$C_{15}H_{18}O_3$] of santoninic acid." *U. S.* "Santonin, $C_{15}H_{18}O_3$, is a crystalline principle which may be obtained from santonica, the dried unexpanded flowerheads of Artemisia maritima, *var.* Stechmanniana, *Besser.*" *Br.*

Santonine, Anhydride Santonique, *Fr. Cod.;* Santoninum, *P. G.;* Santonin, *G.;* Santonina, *It., Sp.*

The U. S. X no longer gives the botanical source of santonin. The U. S. IX gave it as *Artemisia pauciflora* (Ledebour) Weber (*A. Cina* Berger) but the Br. gives it from the *A. Maritima* var. *Stechmanniana* Besser. As a matter of fact santonin is found in several species of the genus *Artemisia;* Greenish and Pearson have found it in the *A. brevifolia* which grows in western Thibet (*P. J.*, 1921, cvi, p. 2) and Viehœver and Capen (*A. J. P.*, 1922, xciv, p. 446) in the *A. Mexicana* and *A. Neo Mexicana* which grow in Mexico and southwestern United States. It is probable even that several plants have served as a commercial source of the drug.

Formerly the flowers were largely exported from the Levant and were official in the U. S. VIII and also in the Br. 1867 under the name of *Santonica.* This was commonly called *wormseed,* or *Levant wormseed,* although it is not the seeds but the unexpanded flower heads from which the drug is derived. The *A. Cina* is a small semi-shrubby perennial, from whose oblique, knotted rootstalks arise numerous leafy shoots and flowering stems. The glabrous and woody stems bear on their many branches numerous small (one inch long) bi- to multi-pinnatifid leaves, while the leaves of the flowering stems are very minute, the upper ones simple. The flower heads are small, numerous, one-tenth of an inch long, with from twelve to eighteen involucral scales, and from three to five tubular flowers. The plant varies very greatly, and several species have been made out of its varieties. The plant grows in Persia and Turkestan and the flower-buds are collected in July and August. The Levant wormseed was officially described as "heads 2 to 4 mm. long, oblong-ovoid, slightly flattened, obtuse, consisting of an involucre of about 12 to 18 closely imbricated, glandular scales with broad midribs, enclosing 4 to 5 rudimentary florets. Santonica has the appearance of a granular, yellowish-green or greenish-brown, somewhat glossy powder; odor strong, peculiar, somewhat camphoraceous; taste aromatic and bitter." *U. S. VIII.* Astolfi (*Ph. Ztg.*, 1893, 333) gives the following test for recognizing adulteration of santonica. 1 Gm. of the suspected drug is finely pulverized and then agitated with 10 cc. of absolute alcohol; the whole is heated to boiling, filtered, a piece of potassium hydroxide is added to the filtrate, which is then heated. If the drug is pure, the liquid will acquire a pronounced red color; if falsified, the color will be yellow; and if no santonica be present, the liquid will be colored but faintly, if at all.

Attention was called by C. H. LaWall (*J. A. Ph. A.*, 1913, p. 596) to a variety of santonica that has appeared upon the market, which seems to be devoid of santonin or to contain not more than traces. He proposes a simple test which may be applied directly to the drug as a preliminary procedure and thus avoid the necessity of going through the long assay process if the sample is valueless: Place 5 Gm. of santonica (whole or ground) in a test tube, add 5 cc. of spirit of nitrous ether and boil gently. No color should be developed, or not more than a slight greenish yellow color due to the solvent action of the spirit on the resins of the drug. Now add 10 drops of alcoholic solution of potassium hydroxide. In an active drug a rose red color is developed in direct proportion to the amount of santonin present. A similar report has been made by van Itallie (*Ph. Wb.*, 1917, liv, 304). For a method of valuing santonica, by Dragendorff, see *Proc. A. Ph. A.*, xxvi, 229. For Ehling's process for valuing santonica, see *U. S. D.*, 19th ed., page 1085.

Wormseed contains, besides its chief principle santonin, a volatile oil—which consists chiefly of cineol with some dipentene—and, according to Merck (*P. J.*, 1896, 484), another crystalline principle, *artemisin,* $C_{15}H_{18}O_4$, which is apparently a *hydroxy-santonin.* The proportion of santonin reaches its maximum of from 2.5 to 3.5 per cent., just before the flower begins to open. After blooming the flowers rapidly lose this principle.

The present U. S. P. and the Br. Ph., 1898, very properly omit processes for the preparation of santonin. (See *U. S. D.*, 17th ed., 1191; also 19th ed., p. 1085.)

It has been intimated that the large manufacturers of santonin, abroad, first distil off from the santonica its volatile oil, which has some commercial value in Europe, and that the process for preparing santonin is probably facilitated thereby, the affinity of the oil for the santonin making the latter more difficult of purification.

Santonin was lowered in price after the erection of a factory in Tschimkent, Turkestan, where the Levant wormseed can be furnished cheaply; the process used there is to treat the wormseed with milk of lime; the calcium santoninate formed is next treated with sodium hydroxide and carbon dioxide; the sodium santonate is then decomposed by sulphuric acid.

The acid liquid, on refrigeration, deposits the santonin in crystals.

Crude santonin or calcium santoninate is usually shipped from the Levant to the countries where it is purified and marketed.

Description and Physical Properties.—"Colorless, shining, flattened rhombic prisms or a white, crystalline powder. It is colorless, and nearly tasteless at first, but afterwards develops a bitter taste. It is stable in the air, but rapidly becomes yellow on exposure to light. Santonin is almost insoluble in cold water, and only slightly soluble in boiling water. One Gm. of Santonin is soluble in 43 cc. of alcohol, 1.7 cc. of chloroform, and in 110 cc. of ether, at 25° C. One Gm. is soluble in 6.5 cc. of boiling alcohol.

"Santonin melts between 169° and 171° C. Its solution in alcohol (1 in 50) is neutral to litmus paper. Its solutions are lævorotatory. Heat about 0.2 Gm. of Santonin with 2 cc. of alcoholic potassium hydroxide T.S.: a red color is developed. Shake about 0.01 Gm. of Santonin with a cool mixture of 1 cc. each of sulphuric acid and distilled water, heat the solution to 100° C., and add a drop of dilute ferric chloride solution (1 volume of ferric chloride T.S. to 10 volumes of distilled water): a violet color results.

"Ash: not more than 0.1 per cent. The solution of 0.1 Gm. of Santonin in 2 cc. of sulphuric acid is not darker than pale yellow (*readily carbonizable substances*). Boil 0.5 Gm. of Santonin with 20 cc. of distilled water and 2 cc. of diluted sulphuric acid, cool, and filter: the addition of mercuric potassium iodide T.S. or of iodine T.S. to 10 cc. of the filtrate, mixed with 10 cc. of distilled water, produces no cloudiness even after standing for three hours (*alkaloids*).

"Preserve in well-closed containers protected from light." *U. S.*

"Colorless, flat, rhombic prisms. Taste slightly bitter. Almost insoluble in *water;* soluble in 2.5 parts of *chloroform,* and in 50 parts of *alcohol* (90 per cent.). Melting point 170° C. Sunlight renders it yellow. Added to warm *alcoholic solution of potassium hydroxide* it yields a violet-red color. Insoluble in diluted mineral acids. No appreciable ash." *Br.*

For a test for santonin, see *Ph. Era,* 1898, 210. The air has no effect upon it, but it becomes yellow on exposure to sunlight. According to Sestini, the santonin is changed, through the influence of light, into formic acid, and an uncrystallizable substance, much more soluble in alcohol and ether than santonin itself, which he calls *photosantonic acid,* $C_{15}H_{22}O_5$, and a red resinous substance. If the santonin be in alcoholic solution, after several months of exposure to sunlight it is changed into the ethyl ether of photosantonic acid. In its relations to polarized light it is very strongly lævogyrate, and retains this property with acids, though losing it entirely when combined with salifiable bases.

When warmed with alkalies, santonin is changed into monobasic *santoninic acid,* $C_{15}H_{20}O_4$, while concentrated baryta water changes it on prolonged boiling into the isomeric *santonic acid;* but Hesse (*B. Chem. G.,* vi, 1280) has shown santonin to be the anhydride of *santoninic acid,* and prepared this acid by adding an excess of diluted hydrochloric acid to an aqueous solution of the sodium salt, and adding ether, from which the acid may be recovered by evaporation. When santoninic acid is heated to 120° C., it is resolved into santonin and water. It has a strongly acid reaction, and decomposes sodium and calcium carbonate.

Sodium santoninate (*Sodii Santoninas*) was official in the *Pharmacopœia Germanica* of 1872, and was recognized in the U. S. P., 1880. It is a colorless crystalline substance freely soluble in water. It was very properly dropped at the U. S. P., 1890 revision, because it is more easily absorbed than santonin in crystals, and therefore much more dangerous to the patient and much less destructive to intestinal worms. For method of preparation and tests of purity, see *U. S. D.,* 19th ed., p. 1243.

For a history with a review of the chemical constituents and decomposition products of santonin see *Y. B. P.,* 1901, 487.

Cannizzaro and Carnelutti (*B. Chem. G.,* xvi, 2685) have shown that santoninic acid, an isomer, breaks up on high heating into *propionic acid,* $C_3H_6O_2$, and *dihydrodimethylnaphthol,* $C_{10}H_7(CH_3)_2.OH$, and distilled over zinc dust it gives a mixture of dimethylnaphthol, $C_{10}H_5(CH_3)_2.OH$, dimethylnaphthalene, $C_{10}H_6(CH_3)_2$, and propylene. *Santonone,* $(C_{15}H_{17}O_2)_2$, a decomposition product of santonin, is made by gradually adding zinc dust to a hot solution of santonin in acetic acid, preferably in the presence of a little platinum tetrachloride. It forms silky white needles, is very soluble in benzene, less so in hot alcohol, ether or diluted acetic acid, and insoluble in water.

Uses.—Santonin is used chiefly as a vermifuge. Against the *round worm* it is generally esteemed as one of the most efficient remedies we possess, its ease of administration as well as its certainty of action making it peculiarly valuable. The coarse crystals should be preferred to the powder as being less readily dissolved, and therefore less likely to be absorbed from the stomach. It may be well administered to children in the form of lozenges made with sugar and tragacanth (for formula, see *A. J. P.,* vi, 124), which if the unbroken crystals are used, can be rendered very pleasant to the taste, so that children will eat them as candy. The dose of santonin for a child two years old is from one-fourth to one-half grain (0.016–0.032 Gm.). To older patients it is best given by enclosing in gelatin capsules. It should always be followed by a cathartic, calomel being perhaps best; although castor oil is sometimes used it should be avoided as likely to increase the absorption. The santoninates, or any combination of santonin with alkali carbonates or hydroxides, should be sedulously avoided as vermifuges, because of the liability of their being absorbed.

Santonin has been recommended internally in a large variety of conditions, but has failed to establish itself in any of them. It was at one time used as a stimulant to the optic nerve in *amaurosis,* especially due to *nicotinism.* Drake (*S. M.,* 1907, p. 550) reports favorably on its use in *dysentery,* and Negro has used it as an analgesic in *tabes* and various forms of *neuralgia.* The statements of Sejournet that it would diminish the output of sugar in *diabetes* have been contradicted by the observations of Walterhoefer. (*B. K. W.,* 1911).

According to Walter G. Smith, the yellow color imparted to urine by santonin is distinguished from that produced by other substances by becoming purplish-red on the addition of ammonia or other alkali. (*P. J.,* Dec., 1870.) For researches upon the character of the urinary coloring matter, consult the same paper.

In overdose santonin produces a poisoning whose symptoms are giddiness, mental apathy or stupor, great paleness and coldness of the surface, vomiting, profuse sweating, trembling, mydriasis, and finally loss of consciousness, with convulsions, often violent and accompanied by opisthotonos and emprosthotonos and failure of respiration. Xanthopsia is an early and characteristic symptom. All objects appear discolored, generally yellow, but frequently green, and sometimes blue. At the same time the urine is tinged of a yellow or a green color. These effects were formerly thought to be due to the staining of the aqueous humor but are more probably to be attributed to a direct action on the retina. In regard to the minimum fatal dose, two grains are said to have killed a feeble child five years old, and a child of seven years is said to have suffered death from six grains after development of hematuria (*B. G. T.,* lxxiv, 362); four grains produced very serious symptoms in a child four years old. (*P. J.,* ix, 696.) The xanthopsia and discolored urine make the diagnosis of santonin poisoning easy. According to Crouzel the addition of alkalies to the urine will demonstrate the presence of santonin, before the coloration is pronounced, by the development of a characteristic carmine-red tint.

Dose, two to four grains (0.13–0.26 Gm.).

Off. Prep.—Tabellæ Santonini, *Br.;* Tabellæ Santonini Compositi, *N. F.*

SAPO. U. S. (Br.)

SOAP [Olive Oil Castile Soap]

"Soap prepared from olive oil and sodium hydroxide." *U. S.* "Hard Soap is soap made from sodium hydroxide and olive oil; it contains not more than 30 per cent. of water." *Br.*

Sapo Durus, *Br.;* Hard Soap, Castile Soap; Sapo Amygdalinus; Sapo Medicinalis, *Fr. Cod.;* Savon medicinal, Savon blanc, *Fr.;* Sapo medicatus, *P. G.;* Medizinische Seife, Oel-Sodaseife, Seife, Spanische Seife, *G.;* Sapone medicinale, S. amigdalino, Sapone duro, *It.;* Jabon de aceite de olivas, Jabon, *Sp.*

Soap is believed to have been discovered by the Gauls shortly after the beginning of the Christian Era. For a history of soap and of cleansing methods used by ancient races, see papers by Abraham (*J. A. Ph. A.,* 1916, v, 205) and by Cook (*A. J. P.,* 1925, xcvii, 398).

Soaps embrace all those compounds which result from the reaction of salifiable bases with fats and oils. Fats and oils, as has been explained under the titles *Adeps* and *Olea,* consist generally of three glyceryl esters, two solid, differing in fusibility, called stearin and palmitin, and one liquid, called olein. Stearin is found most abundantly in fats which are firm and solid, as suet and tallow, and palmitin and olein in the oils. When the fats and oils undergo saponification by reaction with a salifiable base, these three esters are decomposed into the fatty acids called stearic, palmitic, and oleic acids, which unite with the base to form the soap, and into glycerin (glycerol), which is set free. Hence, it is obvious that soaps are mixed stearates, palmitates, and oleates of certain bases.

Soaps are divided into the soluble and the insoluble. The soluble soaps are combinations of the fatty acids with sodium, potassium or ammonium hydroxides; the insoluble consist of the same acids united with other earths or metallic oxides. It is the soluble soaps only that are detergent, and to which the name *soap* is usually applied. Several of the insoluble soaps are employed in pharmacy, as, for example, the lead monoxide soap, or lead plaster, and the lime soap, or lime liniment. (See *Emplastrum Plumbi Oleatis* and *Linimentum Calcis.*) The two official soaps are of the soluble kind. One is a soda soap, made with olive oil (Castile soap), the other a potassium soap (soft soap). (See *Sapo Mollis.*)

The consistence of the fixed alkaline soaps depends partly on the nature of the oil or fat, and partly on the alkali present. Soaps are harder the more stearate and palmitate they contain, and softer when the oleate predominates, and, as regards the alkali present, they are harder when formed with sodium hydroxide, and softer when containing potassium hydroxide. Hence it is that of pure soaps, considered as salts, sodium stearate is the hardest and least soluble, and potassium oleate the softest and most soluble.

Liquid soaps are largely coming into use as economical and sanitary substitutes for soap in public lavatories. Several good formulas have been proposed by E. R. Jones (*J. A. Ph. A.,* 1914, 1537) for use with soft, medium and hard waters, respectively.

Preparation.—The following is an outline of the process for making soap. The oil or fat is boiled with a solution of caustic alkali, beginning with a weak solution, and as saponification proceeds using a stronger lye until the whole forms a thick mass, which can be drawn out into long clear threads. After the soap is completely formed, the next step is to separate it from the excess of alkali, the glycerin, and the redundant water. This is effected by adding common salt, or a very strong alkaline lye, in either of which the soap is insoluble. The same end may be attained by boiling down the solution until the excess of the alkali forms a strong alkaline solution, which acts the same part in separating the soap as the addition of a similar solution. As soon as the soap is completely separated, it rises to the surface, and, when it has ceased to froth in boiling, it is ladled out into wooden frames to congeal, after which it is cut into bars by means of a wire. The soap, as first separated, is called *grain soap.* It may be purified by dissolving it in an alkaline lye and separating it by common salt. During this process the impurities subside, and the soap combines with more water, and hence it becomes weaker, although purer and whiter. If the grain soap be not purified, it will form *marbled soap*—the colored streaks arising principally from an insoluble soap of oxidized iron. Sometimes the marbled appearance is produced by adding to the soap, as soon as it is completely separated, a fresh portion of lye, and immediately afterwards a solution of ferrous sulphate. The greenish-black ferrous hydroxide is precipitated, and gives rise to dark-colored streaks, which, by exposure to the air, become red in consequence of the conversion of the black hydroxide into the ferric hydroxide.

When commercial toilet soap is required, the *grained* soap, or, as it is sometimes called, *boiled* soap, is often remelted, perfumed, and worked over by the process of *milling, plotting,* and *moulding,* whereby the soap is brought into the desired shape for popular use. The *cold process* is also used, and is preferred by many because of its simplicity and economy. The following (from Sadtler's *Industrial Organic Chemistry,* 1906, 64) gives the outlines of the process. The so-called "cold process" requires the use of exact weights of well-refined fats and of caustic soda of a given specific gravity (from 32° to 36° B.), the quantities being such that only just enough soda is present to completely saponify the fat. The materials are allowed to stand together for a short time and then thoroughly mixed in a kettle provided with steam agitating paddles, and kept at a temperature of not over 48.9° C. The reaction proceeds rapidly, and after some fifteen minutes the materials have so far united that they will not separate on standing, although the complete saponification of the charge may require days. They are then run out into the cooling frames. It is obvious that soaps made in this way retain all the glycerin originally combined with the fatty acids disseminated through the particles of soap, and belong to the class of "filled" or "padded" soaps. When cocoanut oil alone is used, the temperature of working in this cold process need not be higher than 23.9° C. in summer and 32.2° C. in winter; if one-half tallow, from 40° to 42.2° C., and if two-thirds tallow, from 45° to 48.9° C. is necessary. A well-refined tallow can be saponified in this way, too, and rosin may be added. For a practical process for making soap in small quantities without boiling, see *U. S. D.,* 19th edition, page 1089.

The official *soap* (*Sapo,* U. S.; *Sapo Durus,* Br.) is an olive oil soda soap, made on the same general plan as that just explained.

Common soap is also a soda soap; but instead of olive oil it is made from various vegetable or animal fats. This soap corresponds with the white soap of northern European countries and of the United States.

Besides the official soaps of the U. S. and Br. Pharmacopœias, there are many other varieties, more or less used for medicinal or economical purposes. *Starkey's soap* is prepared by uniting, by trituration, equal parts of potassium carbonate, oil of turpentine, and Venice turpentine. *Beef marrow soap* is a fine animal oil soap, also included in the French standard. *Windsor soap* is a scented soda soap, made of one part of olive oil and nine parts of tallow. *Eau de luce* (*aqua luciæ*) is a kind of liquid soap, formed by mixing a tincture of oil of amber and balsam of Gilead with ammonia water. *Transparent soap* is prepared by several methods. In one process, glycerin is added which makes a clear transparent mass upon solidification; soap containing glycerin, however, is very hygroscopic. The German transparent soap always contains a large quantity of cocoanut-oil soap. Modern transparent soaps owe their transparency usually to their having been made into an alcoholic solution and then the alcohol carefully recovered, which leaves the mass transparent. Cheap grades of transparent soaps often owe this property to the presence of sugar which communicates the desired property when present to the extent of 5 or 10 per cent. *Marine soaps,* or *hard water soaps,* are soaps which possess the property of lathering freely with hard water. They are usually manufactured from cocoanut oil. *Palm soap* is prepared from sodium hydroxide and palm oil, to which tallow is added to increase its firmness. If it be wanted white, the palm oil may be bleached by heat, potassium dichromate with sulphuric acid, chlorine, or exposure to the sun. This soap has a yellowish color, and the agreeable odor of violets derived from the oil. *Soap balls* are prepared by dissolving soap in a little water and then forming it with starch into a mass of the proper consistence. *Common yellow soap* (*rosin soap*) derives its character from an admixture of rosin with the fats, rosin being saponifiable and yielding a detergent soap. Sodium silicate is largely used as a filler which adds to the detergent properties of the soap. It is too harshly alkaline for use in toilet soaps or soaps intended for anything but the crudest purposes.

Borax soap is soap containing borax as an added detergent ingredient.

Cereals such as cornmeal, oatmeal, etc., are sometimes added to soap for special purposes. Their mechanical presence is sometimes of value, though they are frequently added for cheapening purposes.

Soaps with fancy descriptive names are usually deceptive in their character. *Lemon juice, buttermilk, seaweed,* etc., are only of advertising value as soap constituents.

Floating soaps are those in which minute air bubbles have been incorporated in the soap mass before cooling. This makes the cakes buoyant.

All varieties of soap are now manufactured in the United States. Large amounts of olive oil soaps and very fine toilet soaps are, however, imported from France, Italy, and Spain.

SPECIFICATIONS FOR SOAPS.—The following standards and specifications have been adopted by the U. S. Bureau of Standards for various types of soaps, and have been published in Circular No. 62 of the Department of Commerce, June, 1919. In these specifications matter volatile at 105° C. is considered as moisture although volatile oils, when present as perfumes, are driven off at this temperature. *Milled Toilet Soap.*—Matter volatile at 105° C., not over 15 per cent.; free alkali as sodium hydroxide, not over 0.1 per cent.; alkaline salts as sodium carbonate, not over 0.3 per cent.; sodium sulphate, not over 0.1 per cent.; sodium chloride, not over 0.3 per cent.; material insoluble in water, not over 0.1 per cent.; unsaponifiable matter, not over 0.1 per cent.; rosin, sugar, and other foreign matter must be absent. *White Floating Soap* has the same standards as milled toilet soap, except that the matter volatile at 105° C. may reach 34 per cent. and the alkaline salts 0.5 per cent. *Liquid Soap* must contain not less than 20 per cent. of anhydrous soap, not more than 0.3 per cent. of alkaline salts, not more than 0.3 per cent. of potassium chloride, and no sulphates nor sugar. *Shaving Soap* must meet the following requirements: Matter volatile at 105° C., not over 15 per cent.; free alkali, not over 0.3 per cent.; potassium chloride, not over 0.3 per cent.; matter insoluble in water, not over 0.1 per cent.; unsaponifiable matter, not over 0.1 per cent.; rosin, sugar and other foreign matters must be absent, and at least 50 per cent. of the total alkali must be potash.

The following are the specifications for *salt water soap,* which is a cocoanut oil soap capable of lathering in brine: Matter volatile at 105° C., not over 55 per cent.; free alkali, not over 0.5 per cent.; alkaline salts, as sodium carbonate, not less than 2 per cent. nor more than 3 per cent.; chlorides, not less than 2.5 per cent. nor more than 3.5 per cent.; rosin, sugar, and other foreign matters must be absent. *Special Grade Laundry Soap.*—Matter volatile at 105° C., not over 34 per cent.; free alkali as sodium hydroxide, not over 0.2 per cent.; alkaline salts, not over 1 per cent.; sodium chloride and sulphate, not over 1 per cent.; matter insoluble in water, not over 0.1 per cent.; rosin, not over 15 per cent. *Ordinary Grade Laundry Soap.*—Matter volatile at 105° C., not over 34 per cent.; free alkali as sodium hydroxide, not over 0.5 per cent.; alkaline salts, not less than 2 per cent. nor more than 6 per cent.; sodium chloride, not over 1 per cent.; sodium sulphate, not over 1 per cent.; matter insoluble in water, not over 0.5 per cent.; rosin, not over 25 per cent. *Chip Soap.*—Matter volatile at 105° C., not over 15 per cent.; free alkali as sodium hydroxide, not over 0.5 per cent.; alkaline salts, not over 0.5 per cent.; sodium chloride, not over 0.5 per cent.; matter insoluble in water, not over 0.1 per cent. *Soap Powder.*—Anhydrous soap, not less than 30 per cent. nor more than 35 per cent.; sodium carbonate, not less than 40 per cent. *Hand Grit Soap.*—Matter volatile at 105° C., not over 15 per cent.; free alkali as sodium hydroxide, not over 0.1 per cent.; alkaline salts, not over 0.3 per cent.; insoluble siliceous material, not less than 30 per cent. nor more than 35 per cent.; 98 per cent. of the siliceous material must pass through a sieve having 200 meshes to the linear inch; rosin, sugar, and other foreign matters must be absent. *Scouring Soap A.*—Matter volatile at 105° C., not over 5 per cent.; free alkali as sodium hydroxide, not over 0.1 per cent.; alkaline salts, not over 1 per cent.; insoluble siliceous material, not less than 88 per cent. nor more than 93 per cent.; all of the siliceous material must pass through a sieve having 100 meshes to the linear inch, and at least 95 per cent. must pass through a sieve having 200 meshes to the linear inch, and it must not scratch glass. Rosin, sugar, and other foreign matters must be absent. *Scouring Soap B.*—Matter volatile at 105° C., not over 5 per cent.; free alkali as sodium hydroxide, not over 0.1 per cent.; alkaline salts, not over 3 per cent.; insoluble siliceous material, not less than 75 per cent. nor more than 85 per cent. The insoluble siliceous material should mainly consist of quartz, and it must all pass through a sieve having 100 meshes to the linear inch, and at least 75 per cent. must pass through a sieve having 200 meshes to the linear inch. Rosin, sugar, and other foreign matters must be absent. *Automobile Soap.*—Matter volatile at 105° C., not over 55 per cent.; free alkali as sodium hydroxide, not over 0.05 per cent.; free oleic acid, not over 0.1 per cent.; matter insoluble in water, not over 0.1 per cent.; alkaline salts, not over 0.5 per cent.

Properties.—Soap, whatever may be its variety, has the same general properties. Its aspect and consistence are familiar to every one. Its odor is peculiar, and its taste slightly alkaline. It is usually somewhat heavier than water, and therefore sinks in that liquid. Exposed to heat it quickly fuses, swells up, and is decomposed. It is soluble in water, and more readily in hot than in cold. Acids added to an aqueous solution of soap combine with the alkali, and set free the fatty acids, which, being diffused through the water give it a milky appearance. Its decomposition is also produced by metallic salts, which invariably give rise to insoluble soaps. Soap is soluble in cold and abundantly in boiling alcohol. This solution constitutes the *tincture of soap.* The efficacy of soap as a detergent depends probably in chief part on its power of emulsifying fats, although also in part upon its hydrolytic decomposition when in solution, whereby alkali is liberated which saponifies and emulsifies grease and fatty substances rendering them readily removable in the washing processes. The chief adulterations in soap are lime, silica, gypsum, heavy spar, steatite, pipe-clay, and sodium sulphate. Some of these constituents, however, are normal ingredients of soaps intended for special purposes as for scouring. When adulterated with these substances, it will not be entirely soluble in alcohol.

Description and Physical Properties.—"A white or whitish solid, in the form of bars, hard, yet easily cut when fresh, or a fine, yellowish-white powder. It has a faint, characteristic odor, free from rancidity and a disagreeable, alkaline taste. Soap is soluble in water and in alcohol, more readily, however, with the aid of heat. An aqueous solution of Soap is alkaline to indicators.

"Dissolve about 0.5 Gm. of Soap, accurately weighed, in 10 cc. of alcohol, evaporate the mixture to dryness in a tared beaker containing 1 Gm. of clean sand, which has been previously dried at 110° C., and dry the residue to constant weight at 110° C.: the loss does not exceed 36 per cent for unpowdered Soap or 10 per cent. for powdered Soap (*water*). A solution of a quantity of Soap corresponding to 0.64 Gm. of dried Soap in 25 cc. of hot alcohol does not gelatinize on cooling to 20° C. (*soap from animal fats*). Ten cc. of an aqueous solution of Soap (1 in 20) remains unchanged in color upon the addition of ammonium sulphide T.S., and upon acidulating another portion of 10 cc. of the solution with hydrochloric acid and filtering, the filtrate remains unchanged in color when an equal volume of hydrogen sulphide T.S. is added and the mixture allowed to stand well-stoppered, in a warm place, for half an hour (*heavy metals*). Dissolve about 10 Gm. of Soap, accurately weighed, in 100 cc. of neutralized alcohol, with the aid of heat. Transfer the undissolved residue, if any, to a tared filter which has been dried at 100° C., and wash it thoroughly with boiling neutralized alcohol. The weight of the residue after drying at 100° C. does not exceed 1 per cent. of the weight of dry Soap taken (*sodium chloride, carbonate, silica, or other alcohol-insoluble substances*). This residue, thoroughly washed with distilled water and dried at 100° C., does not yield a residue exceeding 0.15 per cent. of the weight of dry Soap taken (*silica or other water-insoluble substances*). The alcoholic filtrate and washings from the preceding test are not reddened by 3 drops of phenolphthalein T.S. (*sodium hydroxide*). Dissolve about 10 Gm. of Soap in 200 cc. of hot distilled water, add 2 drops of methyl orange T.S. and then diluted sulphuric acid with constant stirring until the aqueous layer becomes red. Boil the mixture until the supernatant layer of the fatty acids is clear and free from solid particles. Separate the aqueous layer with the aid of a siphon and wash the fatty acids by decantation with hot distilled water, until a 10 cc. portion of the washings, acidulated with a drop of hydrochloric acid, no longer gives a precipitate on the addition of barium chloride T.S. Place the dish containing the fatty acids on a water bath and heat until they are completely liquefied, filter the warm acids through a dry filter in a hot-water funnel into a flat dish, and dry over sulphuric acid. The iodine number of the acids thus obtained is not less than 84 and not more than 90.

"Preserve in well-closed containers." *U. S.*

"Greyish-white, yellowish-white, or greenish-white, becoming horny and pulverisable when dried. Nearly inodorous. Soluble in 20 parts of cold *water,* and in 1.5 parts of hot *water;* soluble in *alcohol* (90 per cent.), more readily when warmed. Responds to the tests for alkaline hydroxides and carbonates and for free fatty acids described under 'Sapo Animalis.' Does not impart a greasy stain to white unglazed paper (absence of free oil). Loses not more than 30 per cent. of its weight when dried at 110° C. Ash not deliquescent (absence of potassium soap). The absence of fatty acids derived from oils other than Olive Oil is determined by the following process:—Dissolve the Soap in hot *water,* add a slight excess of *hydrochloric acid* and heat on a water-bath until the liberated fatty acids form a transparent layer. Separate the fatty acids on a wet filter-paper, and wash with hot *water* until the washings are neutral to *solution of methyl orange.* Filter the oily layer through a dry filter-paper in a warm oven. The fatty acids thus separated possess the following characters:—*Iodine value,* 83 to 92; *acid value,* 195 to 205; melting point 21° to 28° C.; *refractive index* at 40° C., 1.4540 to 1.4580." *Br.*

Olive oil soda soap (*Sapo*), otherwise called *Castile* or *Spanish soap,* is a hard soap, and is presented under two principal varieties, the white and the marbled. *White Castile soap,* when good, is of a pale yellowish-white color, incapable of giving an oily stain to paper, devoid of rancid odor or strong alkaline qualities, and entirely soluble both in water and in alcohol. It should not feel greasy, nor grow moist, but, on the contrary, should become dry by exposure to the air, without exhibiting any saline efflorescence. This variety of soap contains about 21 per cent. of water. Sometimes it contains a larger proportion of water, with which the soap is made to combine by the manufacturer, with the fraudulent intention of increasing its weight. Soap thus adulterated is known by its unusual whiteness, and by its suffering a great loss of weight in a dry air. *Marbled Castile soap* is harder, more alkaline, and more constant in its composition than the other variety. It contains about 14 per cent. of water. Having less water than the white Castile, it is a stronger and more economical soap, but at the same time is less pure. The impurity arises from the veins of marbling, consisting of ferruginous matters, as already explained, and from various substances added as make-weights.

Soap bubbles have played an important part in the investigations of the subject of surface tension. Sir James Dewar has kept soap bubbles intact for more than a year in an atmosphere free from foreign particles or vibrations.

Soap is an emulsifying agent of peculiar value in certain cases. Scoville has prepared a stiff jelly-like emulsion of olive oil containing 97 per cent. of oil and only 0.15 Gm. of sodium oleate. (*Bull. Pharm.*, 1915, 141.)

The emulsifying action of soap, in connection with its detergent qualities, is due to the hydrolytic effect of water and the colloidal dispersion of the fatty acids.

A *soap substitute* for detergent purposes, which in some respects is superior to soap as a cleansing agent has been proposed by Schneider (*D. C.*, 1916, lx, 407). It is made as follows: One hundred grammes of soap bark are heated on a water-bath for a half hour with 300 grammes of water, the mixture strained, the liquid mixed with 400 grammes of kaolin and 400 grammes of powdered talcum, and the resulting paste perfumed with any suitable substance. The paste does not froth, but cleanses the hands, it is said, better than ordinary soap.

Incompatibles.—Soap is decomposed by all the acids, earths, and earthy and metallic salts. Acids combine with the alkali, and set free the fatty acids of the soap; the earths unite with the fatty acids, and separate the alkali, while the earthy and metallic salts give rise, by double decomposition, to an insoluble soap of their base and a saline combination between their acid and the alkali of the soap. Hard waters, in consequence of their containing salts of lime, decompose and curdle soap. They may be rendered soft, and fit for washing, by adding alkali carbonates, hydroxides or borates.

Uses.—Soap is laxative and antacid. It acts like an alkaline base and was formerly used to some extent internally, but has been entirely superseded by more elegant alkaline compounds, except in laxative preparations. In *constipation,* particularly when arising from hardened feces in the rectum, a strong solution of soap, especially of soft soap, forms a useful enema. When the latter is used, two tablespoonfuls may be dissolved in a pint of warm water. Externally soap is used in various *skin diseases,* not merely for its detergent effect, but also to soften the horny layer of the epiderm. Soap has a distinct if not very powerful antiseptic action. According to Hamilton (*J. I. E. C.,* 1911, iii, 582), it is practically impossible to get a strong enough solution of a hard neutral soap to exercise any distinct germicidal effect, but if free alkali be present it is much more active. Davis and Swartz (*J. A. M. A.,* December 11, 1921, lxxvii) find that sodium oleate has a definite value against the gonococcus. Attempts have been made to increase the germicidal value of soap by the addition of various disinfecting agents, especially cresol and mercuric iodide. The practical value of these soaps, however, is open to question; Wildman (*Ph. Era,* 1919, lii, p. 123) after bacteriological tests came to the conclusion that although the mercuric iodide soap had a distinct disinfectant action, for practical purposes the tincture of green soap had a greater sterilizing effect upon the hands.

In pharmacy, soap is frequently employed for the purpose of giving a proper consistence to pills; but care must be taken not to associate it with a substance which may be decomposed by it. It is an excellent emulsifying agent when the mixture is intended for external use. It is also an ingredient in some liniments and plasters. In toxicology it is used as a chemical antidote for the mineral acids and the caustic salts of iron, and should always be resorted to in poisoning by these agents, without a moment's delay, and its use continued until magnesia, chalk, or sodium or potassium bicarbonate can be obtained. The mode of administration, in these cases, is to give a teacupful of a strong solution of soap every three or four minutes, until the patient has taken as much as he can swallow.

Dose, five grains to half a drachm (0.32–2.0 Gm.), given in pill.

Off. Prep.—Emplastrum Saponis, *Br., N. F.;* Linimentum Saponis, *U. S., Br.;* Linimentum Chloroformi (from Soap Liniment), *U. S.;* Pilulæ Aloes, *U. S.;* Pilulæ Aloes et Asafetidæ, *N. F.;* Dentifricium, *N. F.;* Lavatio Ori, *N. F.*

SAPO ANIMALIS. Br.

CURD SOAP

"Curd Soap is soap made from sodium hydroxide and purified animal fats consisting principally of stearin; it contains not more than 30 per cent. of water." *Br.*

Sapo sebacinus; Sapo domesticus; Sapo Vulgaris; Animal Soap, Tallow Soap, Stearin Soap; Savon animal, *Fr.;* Hausseife, Talgseife, Stearinseife, *G.;* Sapone animale, *It.;* Jabon animal, *Sp.*

The British Pharmacopœia, 1914, has retained curd soap in its list, and thus describes it: "Yellowish-white or greyish-white; nearly inodorous; easily moulded when heated, becoming horny and pulverisable when dried. Sparingly soluble in cold *water;* completely soluble in hot *water;* soluble in *alcohol* (90 per cent.). When 5 grammes of the dried and powdered Soap are dissolved in 50 millilitres of boiling *alcohol* (90 per cent.), and the solution filtered while hot, the filter being thoroughly washed with more of the boiling *alcohol,* the filtrate is neutral to *solution of phenolphthalein* (absence of alkaline hydroxides and free fatty acids), and if the filter is then washed with hot *water,* the washings require for neutralisation not more than 5 millilitres of *N/10 solution of sulphuric acid, solution of methyl orange* being used as indicator (limit of alkaline carbonates). Does not impart a greasy stain to white unglazed paper (absence of free fats). Loses not more than 30 per cent. of its weight when dried at 110° C. Ash not deliquescent (absence of potassium soap)." *Br.*

Soap made from animal oils and fats is very largely used for all domestic purposes; it was long used for making *solid opodeldoc,* but is now replaced by sodium stearate. (See *Linimentum Saponato-Camphoratum,* N. F., Part III.)

Off. Prep.—Linimentum Potassii Iodidi cum Sapone, *Br.*

SAPO MOLLIS. U. S., Br.

SOFT SOAP Sapo Moll. [Green Soap]

"Soft Soap is soap made from potassium hydroxide and olive oil." *Br.*

Sapo Viridis, *U. S. P.* 1880; Savon Noir, Savon mou, *Fr.;* Sapo Kalinus, *P. G.;* Kaliseife, Schmierseife, *G.;* Sapone di potassa, *It.*

"Linseed Oil, 400 Gm.; Dekanormal Solution of Potassium Hydroxide, 29 cc.; Dekanormal Solution of Sodium Hydroxide, 110 cc.; Glycerin, 50 cc.; Water, a sufficient quantity, to make 1000 Gm. Mix the dekanormal solutions, pages and , with the oil and enough water to make the product weigh 925 Gm. Heat the mixture to boiling with frequent stirring, add the glycerin and continue the boiling until the mixture becomes transparent and a portion dissolves completely in hot water, producing a clear solution. Then add sufficient hot water to make the Soap weigh 1000 Gm. and allow to stand with little stirring until the water is absorbed.

"NOTE.—The 29 cc. of dekanormal solution of potassium hydroxide directed above may be replaced by 19.14 Gm. of 85 per cent. potassium hydroxide and the 110 cc. of dekanormal solution of sodium hydroxide may be replaced by 48.89 Gm. of 90 per cent. sodium hydroxide, dissolving the hydroxides in 100 cc. of water. If upon assay the potassium and the sodium hydroxides are found to be of any other strength, a proportionately larger or smaller quantity should be taken." *U. S.*

For more than one hundred years, under the name of *"green soap,"* there has been used in Europe a soap made by saponifying linseed, rape seed, or other vegetable oils with various refuse oils, usually including fish oils, an excess of potassium hydroxide, and a little sodium hydroxide. The green color of this soap was probably due to the presence of chlorophyll in the impure vegetable oils used. This green soap, or so-called "German soap," was formerly imported into America, but at present has been almost entirely superseded by soft soap made in this country, from which it does not differ in the nature of its active constituents or in its therapeutic properties.

Both the British and U. S. Pharmacopœias differ with the common practice and with each other in the formulas for soft soap. The Br. has for many years employed olive oil. The U. S., 1890 and VIII employed linseed oil, but in the 9th Revision experiment was made of using cottonseed oil. This, however, not proving satisfactory, the present U. S. has returned to linseed.

If a green soap be wanted, it may be made by the process given in the *U. S. D.,* 19th edition, p. 1093. The soft soap of France, formerly the *savon vert* of the French Codex, has a greenish color, and usually the consistence of a soft ointment. It is made of hemp seed oil, or sometimes of the dregs of olive oil, and potassium hydroxide. G. M. Beringer (*Proc. A. Ph. A.,* 1903, 420) prefers to use Malaga olive oil in making green soap, and M. I. Wilbert (*Proc. A. Ph. A.,* 1904, 228) extracts the green coloring matter from hemp seed by macerating 25 parts of ground hemp seed with alcohol and obtains 100 parts of a tincture; by substituting an equal measure of this tincture for the quantity of alcohol used in the official process, a green soap can be made, which will have the color which is regarded by some as a very important characteristic.

Description and Physical Properties.—"A soft, unctuous, yellowish-white to brownish-yellow mass, having a slight, characteristic odor and an alkaline taste. An aqueous solution of Soft Soap is alkaline to litmus paper and phenolphthalein T.S.

"Dissolve about 5 Gm. of Soft Soap, accurately weighed, in 100 cc. of hot neutralized alcohol, collect the residue, if any, on a filter, thoroughly wash it with hot neutralized alcohol, and dry it to constant weight at 100° C. The weight of the residue does not exceed 3 per cent. of the weight of Soap taken. The combined filtrate and washings, on the addition of 0.5 cc. of phenolphthalein T.S. and titration with tenth-normal sulphuric acid, shows not less than 0.1 per cent. and not more than 0.25 per cent of KOH. Each cc. of tenth-normal sulphuric acid corresponds to 0.00561 Gm. of KOH. A solution of Soft Soap in hot distilled water (1 in 20) is nearly clear. Soft Soap loses not more than 52 per cent. in weight when tested for water as directed under *Sapo.*" *U. S.*

"Yellowish-white to green; of an unctuous consistence. Nearly inodorous. Readily soluble in *alcohol* (90 per cent.), leaving not more than 3 per cent. of insoluble residue. Responds to the tests for alkaline hydroxides and carbonates and for free fatty acids described under 'Sapo Animalis.' Does not impart a greasy stain to white unglazed paper (absence of free oil). Ash very deliquescent, and yields no characteristic *reactions* for copper. The mixed fatty acids, liberated and treated as described under 'Sapo Durus,' possess the characters there specified." *Br.*

Uses.—Soft soap possesses not only the detergent properties of neutral soaps, but because of the excess of alkali has active medical virtues, especially as a topical remedy. In the first place it removes the fat more thoroughly from the skin and is therefore of service in those forms of *skin diseases* accompanied with disturbances of sebaceous secretion, such as *seborrhea* or *comedo.* It has also the property of softening the keratin elements of the epiderm, and is therefore useful in conditions accompanied with crusts and scales, such as *psoriasis* and *chronic eczema.* Because of its local irritating action it may also be used as a stimulant in *acne vulgaris* and *rosacea.* It is also asserted to be of adjuvant service in the treatment of various parasitic skin diseases.

Kappesser (*Fort. Med.,* 1912) has reported favorable results from the use of inunctions of one-half to one drachm (2–3.9 Gm.) of soft soap in *scrofulous lymphadenitis.* Kuelbes (*Th. M.,* 1914, xxviii) has found it of occasional benefit also in a large variety of other conditions, especially *cardiac neuroses* and *migraine.* In *chronic bronchitis* and *dyspepsia* he asserts the inunctions often improve the general condition of the patient, but in *asthma* they usually were without influence.

Off. Prep.—Linimentum Saponis Mollis, *U. S.* (*Br.*)*;* Linimentum Saponis Mollis Compositum, *N. F.;* Unguentum Sulphuris Compositum, *N. F.;* Pasta Betanaphtholis, *N. F.*

SAPPAN. Br.

SAPPAN

"Sappan is the heart-wood of Cæsalpinia Sappan, *Linn.*" *Br.*

Sappan wood, Sampfen wood, Bakam, Tairi, Patang, Teri, Verzino, *It.;* False Sandalwood, Indian Redwood, Samfen.

Cæsalpinia Sappan is a small thorny tree indigenous to the Eastern and Western Asiatic Peninsulas, Pegu and Tenasserim, and is also cultivated in Central India. The leaves are large and abruptly bi-pinnate; the flowers being yellow and in axillary racemes; and the pods are oblong, flattened, nearly smooth and dehiscent or indehiscent. The wood yields a valuable red dye which is also prepared from the pods and from the bark. The commercial samples vary considerably. There are two commercial varieties, viz., (1) Singapore or Dhansari, and (2) Ceylon sappan, the former being preferred. According to Dymock, the freshly cut wood is whitish, but becomes red on exposure to the air. He also states that the addition of alkalies increases the yield of coloring matter, turning it a reddish-violet.

According to the British Pharmacopœia, it occurs in "hard, heavy pieces of variable size, or in orange-red chips. In transverse section, well-marked concentric rings, numerous narrow medullary rays, and large vessels. No odor; taste slightly astringent. It communicates to *alcohol* (90 per cent.) and to *water* a red color, which becomes carmine-red, but not purple, upon the addition of *solution of sodium hydroxide* (distinction from Logwood)." *Br.*

According to the investigations of Bolley, sappan wood contains *brasilin,* $C_{16}H_{14}O_5$, identical with that of Brazil wood. (See Part II.)

Sappan, as it is sometimes called, has been an article of commerce for at least five hundred years. It is employed in the arts as a substitute for logwood in dyeing. Medicinally it is used as an astringent in the treatment of *diarrhea.* It may be given in the form of a decoction.

Dose, from fifteen to forty-five grains (1–3 Gm.).

Off. Prep.—Decoctum Sappan, *Br.*

SARSAPARILLA. U. S.

SARSAPARILLA Sarsap.

"Sarsaparilla is the dried root of *Smilax medica* Chamisso and Schlechtendal, known in commerce as Mexican Sarsaparilla; or of *Smilax officinalis* Kunth, or of an undetermined species of *Smilax* known in commerce as Honduras Sarsaparilla; or of *Smilax ornata* Hooker filius known in commerce as Central American or Jamaica Sarsaparilla (Fam. *Liliaceæ*). Sarsaparilla contains not more than 2 per cent. of foreign organic matter, excepting the rhizome and crown portion, which must be removed before the root is ground and powdered. Mexican Sarsaparilla yields not more than 4 per cent. of acid-insoluble ash. The other official varieties conform to the standards for acid-insoluble ash under Vegetable Drugs." *U. S.*

Sarsæ Radix, *Br.,* 1898; Jamaica Sarsaparilla; Salsepareille du Mexique, *Fr.;* Radix Sarsaparillæ, *P. G.;* Sarsaparille, Sarsaparilla, *G.;* Salsapariglia, *It.;* Zarzaparrilla (Raiz de), *Sp.*

The plants comprising the genus *Smilax* are climbing or trailing vines or shrubs, with a pair of tendrils arising as modified stipules from the bases of their petioles, 3- to 7-nerved and strongly reticulate leaf blades and prickly stems. The last mentioned character is expressed in the name of the drug, which is derived from two Spanish words (*zarza* and *parilla*), signifying a small, thorny vine.

The official sarsaparilla-yielding plants are all climbing evergreen shrubs with prickly stems, alternate, coriaceous leaves which vary from cordate, cordate-ovate, auriculo-hastate to ovate-oblong in outline, small flowers, arranged in axillary umbels, and berry fruits. They are indigenous to Mexico, Central America, and the warm latitudes of South America. The roots are very long and slender, and originate in great numbers from a common head or rhizome, from which the stems of the plant rise. The whole root with the rhizome is usually dug up, and as brought into market exhibits not unfrequently portions of the stems attached, sometimes several inches in length. The commercial sarsaparillas are conveniently divided into the mealy and non-mealy sarsaparillas. The first class comprises especially the Honduras, Guatemala, and Brazilian varieties; the second the Jamaica, Mexican and Guayaquil sarsaparillas. A very convenient key for distinguishing the commercial sarsaparillas by certain anatomical characters has been devised by Luerssen in his *Handbuch der Medicinpharm. Botanik*, ii, 404.

Smilax medica yields the variety known commercially as *Mexican, Vera Cruz, Tampico* or *Gray Sarsaparilla.* It occurs as clusters of long roots attached to a knotty crown (portion of the rhizome) or as rootlets deprived of the crown. These are packed, commonly, in large, rather loose bales weighing about 200 pounds. The roots are grayish-brown to dark brown, nearly devoid of fibrous rootlets and possess deep furrows to which a blackish earth frequently adheres. Histologically, they are characterized by their hypodermal and endodermal cells. The former show their outer and radial walls more thickened than the inner walls while the latter show the inner and radial walls more thickened than the outer walls. Mexican sarsaparilla is imported from Vera Cruz and Mexico City.

Smilax officinalis or an undetermined species of *Smilax* yields the commercial variety known as *Honduras* or *Brown Sarsaparilla.* It occurs in cylindrical bundles from 2 to 3 feet in length which are composed of long roots folded lengthwise. Each bundle is closely tied around with a long root usually of the same plant. The roots are externally of a reddish-brown or dark brown color and show occasional fibrous rootlets. Histologically they are characterized by their uniformly thickened hypodermal and endodermal cells. This variety is imported from Honduras in serons containing a number of bundles.

Smilax ornata yields the commercial variety known as Jamaica, Costa Rica or Red Sarsaparilla. It is collected in Central America, especially in Costa Rica, and it owes its name to the fact that it has been largely exported to London through the island of Jamaica. It is the most highly prized variety used in Great Britain. As found in commerce it is in rolls from twelve to eighteen inches long by four or five in thickness, composed exclusively of long slender many-radicled roots very loosely held together by a few turns. Sometimes it is pressed into large bales. It is further to be distinguished from Honduras sarsaparilla by its dark color, the greater abundance of coarse rootlets, the less quantity of starch, its relatively thick cortex, and its less sharp taste. Externally it is also redder than is commonly the case with Honduras sarsaparilla. Kobert (*P. J.*, 1912, lxxxviii, p. 779) has found that the *S. ornata* has only one-eighth of the hemolytic power of the Vera Cruz sarsaparilla, which he takes as a test of its saponin content. He believes the plant is unfit for medical use.

Cultivated Jamaica Sarsaparilla (*Roja Inglesa*) occurs in thick short rolls and is especially characterized by its yellow-brown or orange color. According to W. B. Hemsley, Hooker's I. P. pl. 2589, it is the product of *S. utilis* Hemsley, a species related to *S. ornata*, from which it differs by its long pediculated simple umbels.

Several other varieties of sarsaparilla occasionally occur on the world's markets, the most important of which are Guayaquil and Lima sarsaparillas.

Guayaquil Sarsaparilla, according to Spruce grows in valleys on the western slopes of the equatorial Andes. It is usually imported in rectangular shaped bales which contain a number of flattened bundles of rhizomes and roots, or roots only. The rhizome and a portion of the stem are often present, the latter being round and prickly. The root is mahogany brown, large, and coarse-looking, with a good deal of fiber. The bark is furrowed, rather thick, and not mealy in the slenderer portions of the root, which is near the rootstalk; but, as the root becomes stout, so its bark becomes smoother, thicker, and amylaceous, exhibiting when cut a fawn-colored or pale yellow interior. It is thought to be yielded by a variety of *S. papyracea.*

Lima or *Lima Jamaica Sarsaparilla* comes from Panama. It bears a close resemblance to Jamaica sarsaparilla but occurs in longer bundles and is packed in layer bales.

Carácas Sarsaparilla was formerly brought in large quantities from La Guayra but is now off the market.

Brazilian, Para or *Lisbon Sarsaparilla* which formerly came from Para, Brazil, has practically disappeared from North America and European commerce but is said to be still used in South American countries. It occurred in cylindrical bundles from three to five feet in length by about a foot in thickness, bound about by close circular turns of a very flexible stem, and consisting of unfolded roots, destitute of caudex (rhizome) and stems, and having a few radical fibers. It is distinguished by the thinness of its cortex, the large amount of starch that it contains and its large, radially elongated endodermal cells.

The rhizome of *Smilax China,* a native of China and Japan, has been employed under the name of *China Root* for similar purposes with the official sarsaparilla. As it occurs in commerce, it is in pieces from three to eight inches long and an inch or two thick, usually somewhat flattened, more or less knotty, often branched, of a brownish or grayish-brown color externally, whitish or of a light flesh-color internally, without odor, and of a taste flat at first, but afterwards very slightly bitterish and somewhat acrid, like that of sarsaparilla. The root of *Smilax aspera* is said to be employed in the south of Europe as a substitute for sarsaparilla; but it has little reputation. The East India sarsaparilla, which was at one time referred to this species of smilax, is the product of *Hemidesmus indicus*. (See *Hemidesmus.*)

The chief adulterants of Sarsaparilla roots have been aerial stems of similar plants, excessive rhizomes, roots of various species of *Philodendron* and rhizomes of *Pteris* species.

Description and Physical Properties.—"Sarsaparilla is nearly odorless; taste mucilaginous, somewhat sweetish and acrid.

"*Unground Mexican Sarsaparilla.*—Long roots from 3.5 to 6 mm. in diameter, frequently attached to a crown having one or more stout stems; usually shrunken, forming sharp longitudinal ridges and broad furrows; externally light grayish-brown to dark brown; the furrows may contain more or less blackish earth; finely hairy; nearly devoid of branches or fibrous rootlets; fracture of cortex brittle, of central cylinder tough and fibrous; cortex mealy and whitish or brownish and horny; woody zone yellow and porous; pith whitish and distinct.

"*Unground Honduras Sarsaparilla.*—Long roots from 2 to 5 mm., rarely 6 mm. in diameter and bound together by roots of the same plant into compact cylindrical bundles from 8 to 15 cm. in diameter; externally reddish-brown or dark brown, longitudinally wrinkled or finely furrowed with occasional fibrous rootlets; fracture short, sometimes tough and fibrous in the central cylinder; internally a reddish-brown, dark brown, or occasionally light gray cortex, a light yellow and porous woody zone and a whitish pith.

"*Unground Central American Sarsaparilla.*—Roots long, from 1 to 4, rarely 5 mm. in diameter; externally light brown or reddish-brown, longitudinally wrinkled, occasionally nearly smooth, rarely furrowed and bearing numerous coarse fibrous rootlets; fracture short or tough and fibrous in the central cylinder; internally a white or dark brown cortex, a yellow, porous woody zone and a yellow or white pith.

"*Structure.*—An epidermal layer with basal portions of root hairs; a hypodermis of several layers of strongly lignified cells, the walls being uniformly thickened, except in Mexican Sarsaparilla in which the inner walls are only slightly thickened; a cortex composed of parenchyma cells mostly containing starch, some containing resin or raphides of calcium oxalate, and an endodermis of a single layer of strongly lignified cells, the walls being uniformly thickened except in Mexican Sarsaparilla in which the outer walls are only slightly thickened; a central cylinder composed of a many-rayed vascular bundle and a pith of starch-bearing parenchyma cells; tracheæ large, oval in transverse section and the phloem in small groups near the periphery of the bundle.

"*Powdered Sarsaparilla.*—Light grayish-brown to dark grayish-brown; starch grains numerous, single or compound, the individual grains from 0.003 to 0.023 mm. in diameter, spherical, or biconvex or spherical-tetrahedral and frequently with a central elliptical cleft; calcium oxalate in raphides occurring singly or in groups up to 0.15 mm. in length; cells of the hypodermis and endodermis with lemon-yellow or reddish-yellow porous walls and in Mexican sarsaparilla showing an uneven or irregular thickening, the cells being from 0.08 to 0.50 mm. in length; fragments of tracheæ with simple and bordered pores or scalariform or reticulate thickenings, associated with fibers having rather thin, very slightly lignified and porous walls." *U. S.*

According to Tunmann (*Apoth. Zeit.*, xxv, p. 475), the consumption of sarsaparilla in Europe has decreased materially, and the chief market for this drug at the present time appears to be the United States. While the U. S. Pharmacopœia recognizes three commercial varieties, most of the drug which is used is the Mexican variety, a relatively small quantity of Honduras sarsaparilla being imported. The *Red Jamaica, Orange* or *Native Jamaica* varieties are used chiefly in England. Hartwich has pointed out that the varieties of sarsaparilla on the market are more numerous than are generally supposed. He also states that the greatest emphasis should be placed on the structural characteristics in order to distinguish the several varieties, rather than the form of packing and the supposed botanical origin. He has contributed numerous papers on the subject. (*S. W. P.*, 1897, 1898 and 1909; *A. Pharm.*, 1902; *B. P. G.*, 1907.) Rusby reports finding lots of Mexican sarsaparilla which consisted entirely of "butts" or rhizomes. (*Proc. A. Ph. A.*, 1908, lvi, p. 773.) Kraemer reports finding nineteen ounces of dirt in a bundle of Mexican sarsaparilla weighing four and a half pounds. (*Proc. A. Ph. A.*, 1906, liv, p. 345.) Rusby has reported the presence of a thick, blackish, woody and decidedly astringent root in several shipments of Vera Cruz sarsaparilla. (*J. A. Ph. A.*, 1913, p. 1104.)

Sarsaparilla is efficient in proportion as it is acrid to the taste, which is said by some authors to be confined to the cortical portion, while the ligneous fiber and medullary matter are insipid and inert. Hancock avers that all parts are equally acrid and efficacious. The truth is probably between the two extremes, and, as in most medicinal roots it must be admitted that the bark is more powerful than the interior portions, while these are not wholly inactive.

Constituents.—The most important principles in sarsaparilla are three glucosidal saponins: *smila-saponin*, $C_{20}H_{32}O_{10}$, *sarsa-saponin*, $C_{22}H_{36}O_{10}$, and *parillin*, $C_{26}H_{44}O_{10}$. These principles have been given various names by different chemists, thus smila-saponin has been known as *smilacin* and *sarsaparill-saponin*, and parillin has been known as *pariglin, parillinic acid* and *salseparin*. When the sugar radical is split off by hydrolysis, they yield products which are at least isomeric, and probably identical, and known as *sarsasapogenin* or *parigenin* ($C_{28}H_{46}O_4$). Because of the uncertainty of the botanical material with which many of the chemical investigations have been made, it is impossible to state definitely which of these glucosides occur in each of the plants known commercially as sarsaparilla, but it is probable that the varieties of this drug differ in their composition. Power and Salway (*Tr. Chem. Soc.*, 1914, cv, p. 201) found in the Jamaica sarsaparilla only one of these, sarsaponin, and are inclined to doubt the separateness of smilacin. They also found a new dicarboxylic acid, *sarsapic acid*, $C_6H_4O_6$.

For further details on chemistry, see Schulz (*P. J.*, 1892, p. 6), Kobert (*A. J. P.*, 1892, p. 465), and Apt (*B. P. G.*, 1921, xxxi, p. 155).

The sarsaparilla of commerce is apt to be nearly if not quite inert, either from age, or from having been obtained from inferior species of Smilax. This inequality of the medicine, with the improper modes of preparing it long in vogue, has probably contributed to its variable reputation. The only criterion of good sarsaparilla to be relied on is the taste. If it leave a decidedly acrid impression in the mouth after having been chewed for a short time, it may be considered efficient; if otherwise, it is probably inert. Various false sarsaparillas have been sent into commerce from South America. For description by C. Hartwich see *A. Pharm.*, July, 1902.

Uses.—The use of sarsaparilla in medicine is an interesting example of the power of superstition to survive the attacks of truth and reason. It was introduced into Europe about the middle of the 16th century as a remedy for *syphilis*, but soon fell into disrepute until revived by Fordyce in 1757. Subsequently it came to be used as an alterative in various other chronic diseases, especially *chronic rheumatism* and *scrofula*. There is, however, no reason to believe that it possesses any virtues except as a mild gastric irritant through its saponin content. Its most popular employment is in the form of its compound syrup which is used as a vehicle especially for mercury and potassium iodide.

Sarsaparilla may be administered in the form of infusion, compound decoction, compound syrup, or fluidextract. A beer made by fermenting an infusion of the drug with molasses is said to be a popular remedy in South America. The smoke of sarsaparilla has been recommended in *asthma*. (*J. P. C.*, xviii, 221.)

Dose, thirty to sixty grains (2–3.9 Gm.).

Off. Prep.—Fluidextractum Sarsaparillæ, *U. S.* (*Br.*); Fluidextractum Sarsaparillæ Compositum, *N. F.*; Syrupus Sarsaparillæ Compositus, *U. S.* (from Fluidextract); Decoctum Sarsaparillæ Compositum, *N. F.*

SASSAFRAS. N. F.

SASSAFRAS Sassaf.

"Sassafras is the dried bark of the root of *Sassafras variifolium* (Salisbury) O. Kuntz (Fam. *Lauraceæ*). Sassafras contains not more than 4 per cent. of adhering wood, outer corky tissues or other foreign organic matter and yields not more than 5 per cent. of acid-insoluble ash." *N. F.*

Sassafras Radix; *Br.*; Sassafras Bark, Sassafrax; Radix Sassafras; Cortex Sassafras; Lignum Sassafras, *P. G.*; Sassafras, Fenchelholz, *G.*; Sassafrasso, *It.*; Sasafras (Leño de), *Sp.*

Sassafras is an indigenous tree, of medium size, rising in favorable situations to a height of 35 feet. The bark of the stem and large branches is rough, deeply furrowed, and grayish; that of the extreme branches of twigs is smooth and beautifully green. The leaves, which are alternate, petiolate, and downy when young, vary much in their form and size even upon the same tree. Some are oval and entire, others have a lobe on one side, but the greater number are three-lobed. The flowers, which appear before the leaves, are small, of a pale greenish-yellow color, and disposed in racemes which arise from the branches below the leaves and have linear bracts at their base. The fruit is an oval drupe, about as large as a pea, of a deep blue color when ripe, and supported on a red pedicel, enlarged at the extremity into a cup for its reception. For the microscopical character of the root and bark, see E. S. Bastin, *A. J. P.*, June, 1895. See also *Ph. Rev.*, 1899, 450.

The sassafras is common throughout the eastern United States, extending west into Kansas and south into Mexico. The fresh flowers have a slightly fragrant odor, and almost all parts of the plant are more or less aromatic. The bark of the root is gathered in early spring and autumn, deprived of the outer cork and dried. The commercial supplies are obtained from Mississippi and North Carolina.

The living root-bark is nearly white, but becomes colored, on exposure, immediately after collection.

Description and Physical Properties.—"*Unground Sassafras.*—In irregular, transversely curved or quilled pieces, from 1 to 15 cm. in length and from 1 to 4 mm. in thickness; outer surface orange-brown, nearly smooth and marked with more or less irregular ridges; inner surface light to dark reddish brown, obscurely short-striate; fracture short with a thin reddish brown corky layer and a yellowish white inner bark. Odor aromatic; taste slightly mucilaginous, astringent, aromatic and somewhat pungent.

"*Powdered Sassafras.*—Light reddish brown; exhibits numerous starch grains either single or 2- to 4-compound, the individual grains being more or less spherical or polygonal and frequently with a distinct cleft, from 0.003 to 0.020 mm. in diameter, some of the swollen or altered grains attaining a diameter of 0.030 mm.; characteristic bast-fibers, spindle-shaped, occasionally very irregular in outline, with sharply pointed ends, from 0.150 to 0.400 mm. in length, about 0.025 mm. in diameter, and with very thick, strongly lignified walls, the lumina being frequently nearly obliterated; parenchyma cells containing either starch grains or irregular yellowish red masses of tannin and becoming bluish black upon the addition of ferric chloride T.S.; fragments of wood few, with large, thin-walled tracheæ marked by simple pores and associated with rather thin-walled wood-fibers." *N. F.*

According to Reinsch, the bark contains a heavy and light volatile oil, camphorous matter, fatty matter, resin, wax, a peculiar decomposition product of tannic acid called *sassafrid,* tannic acid, gum, albumen, starch, lignin, and salts. (See *Oleum Sassafras.*) The sassafrid bears some analogy to cinchonic red, and, like it, appears to be a derivative of the tannin, which exists in much larger proportion in the fresh bark than in that long kept. (Procter, *A. J. P.,* 1866, p. 490.)

Uses.—Sassafras owes whatever therapeutic virtue it possesses to its volatile oil. The hot infusion of the bark is a popular domestic remedy as a sudorific for *colds* and also attributed in the popular superstition with peculiar alterative virtues.

Off. Prep.—Fluidextractum Sarsaparillæ Compositum, *N. F.;* Syrupus Pini Albæ Compositus, *N. F.;* Syrupus Pini Albæ Compositus Cum Morphina, *N. F.*

SASSAFRAS MEDULLA. N. F.

SASSAFRAS PITH Sassaf. Med.

"Sassafras Pith is the dried pith of *Sassafras variifolium* (Salisbury), O. Kuntz (Fam. *Lauraceæ*). Sassafras Pith contains not more than 1 per cent. of foreign organic matter and yields not more than 0.5 per cent. of acid-insoluble ash." *N. F.*

Description and Physical Properties.—"In sub-cylindrical, often curved or coiled pieces, from 2 to 10 cm. in length and from 2 to 5 mm. in diameter; very light in weight, externally whitish, occasionally with small fragments of adhering wood; fracture short. Odor slight, sassafras-like; taste mucilaginous.

"*Structure.*—Sections mounted in phloroglucinol T.S. and hydrochloric acid, show nearly isodiametric cells with large intercellular spaces, the walls being more or less lignified and provided with numerous, simple pores; mounts made in water show the separation of a thin layer of mucilage from the inner walls of the cells characterized by the gradual disappearance of the pores.

"Macerate 0.5 Gm. of Sassafras Pith with 25 cc. of cold distilled water for several hours and filter it through purified cotton; a mucilaginous solution is obtained which does not give a precipitate upon the addition of an equal volume of alcohol; if an excess of alcohol is added precipitation takes place." *N. F.*

Sassafras pith should be collected after frost in autumn.

It abounds in a gummy matter, which it readily imparts to water, forming a limpid mucilage, which is not precipitated by alcohol, but has much less tenacity than that of gum arabic and will not answer as a substitute in the suspension of insoluble substances. J. C. and B. L. DeG. Peacock (*Proc. Penna. Ph. A.,* 1917, p. 171) report an investigation of several methods of preparing mucilage of sassafras pith in which the conclusion was reached that maceration of 3 Gm. of sassafras pith with 150 cc. of cold sterile water for ten minutes and subsequent filtration through a pledget of moistened cotton yielded a mucilage superior in characters and keeping quality to that made in any other manner.

Uses.—This mucilage is much employed as a soothing application in inflammation of the eyes, and forms an agreeable and useful drink in *dysenteric, catarrhal,* and *nephritic diseases.* It may be prepared by adding a drachm of the pith to a pint of boiling water.

Off. Prep.—Mucilago Sassafras, *N. F.*

SCAMMONIÆ RADIX. Br.

SCAMMONY ROOT Scam. Rad.

"Scammony Root is the dried root of Convolvulus Scammonia, *Linn.*" *Br.*

Radix Scammiæ; Levant Scammony; Aleppo Scammony; Scammonée d'Alep, *Fr.;* Scammonium, *Fr. Cod.;* Escaminœa, *Sp.*

Scammony root has been replaced in the U. S. by Ipomœa, but in the Br. is still official, although the substitution of Ipomœa is permitted in the preparation of the resin.

The true scammony is a twining perennial herb indigenous to the region around the eastern end of the Mediterranean, especially Syria.

Scammony root is officially described as: "Brownish-grey or yellowish-grey, tapering or nearly cylindrical, varying usually from two to eight centimetres, or more, in diameter. Frequently contorted and longitudinally furrowed; enlarged at the crown, and bearing the remains of slender aerial stems. Fracture very coarsely fibrous; internally light or dark grey. In transverse section, numerous rounded wood-bundles distributed throughout a paler ground-tissue in which dark resin cells can be distinguished with a lens; in the parenchymatous tissue abundant, characteristic starch grains. Characteristic odor; taste at first somewhat sweet, afterwards slightly acrid. Yields to *alcohol* (90 per cent.)

a resin which has the properties described under 'Scammoniæ Resina.'" *Br.*

The wood consists of compressed pale brown, coarsely porous, usually subdivided fibers in a parenchymatous tissue similar to the bark.

"Under the microscope, sections of Scammony Root show a corky layer consisting of from 2 to 10 rows of cells with thin, yellowish-brown lignified walls; an outer cortex with numerous stone cells occurring singly or in small groups, the walls being moderately thick, porous and not strongly lignified; parenchyma with numerous starch grains and monoclinic prisms of calcium oxalate; fibro-vascular bundles numerous, circular or elliptical with a well developed wood consisting of large tracheæ surrounded by slightly lignified wood-fibers; phloem or sieve prominent in which are included large resin ducts; the parenchyma, both in and surrounding the bundles more or less collapsed and containing either starch or calcium oxalate crystals. The powder is light grayish-brown; when examined under the microscope it exhibits starch grains from 0.003 to 0.018 mm. in diameter, mostly single, occasionally 2- to 4-compound, the grain showing occasionally a central cleft; calcium oxalate crystals numerous, in monoclinic prisms from 0.01 to 0.045 mm. in length; fragments of leptomes or sieve with accompanying yellowish-brown resin cells; tracheæ mostly with reticulate thickenings and simple or bordered pores and associated with short wood-fibers having prominent oblique pores; stone cells of variable shape and varying from 0.04 to 0.11 mm. in length, the walls being from 0.006 to 0.012 mm. in thickness, slightly lignified and traversed with prominent, often branching pores; lignified cork cells relatively few." *U. S. IX.*

The Levant or true scammony root, it is said, averages a little under 9 per cent. of resin, while the Mexican (Ipomœa) root usually yields over 15 per cent. For account of the chemistry and uses of Scammony root, see under *Ipomœa.*

Off. Prep.—Resina Scammoniæ, *Br.;* Tinctura Jalapæ Composita (from Resin), *Br.*

SCILLA. U. S., Br.

SQUILL. Scill.

"Squill is the cut and dried fleshy inner bulb scale of the white variety of *Urginea maritima* (Linné) Baker (Fam. *Liliaceæ*). Squill, in the form of the tincture, properly diluted and injected into the ventral lymph sac of a frog, has a minimum systolic dose (minimum dose producing in one hour a stoppage of the ventricle of the heart in systole) not exceeding 0.006 cc. of tincture, equivalent to 0.000,000,5 Gm. of ouabain, for each Gm. of body weight of frog." *U. S.* "Squill is the bulb of Urginea Scilla, *Steinh.*, divested of its dry membranous outer scales, cut into slices, and dried. When powdered should be kept quite dry over quicklime." *Br.*

Squills; Scille, *Fr.;* Bulbus Scillæ, *P. G.;* Meerzwiebel, *G.;* Scilla, *It.;* Escila (Bulbo de), Cebolla albarrana, *Sp.*

Urginea maritima (*Urginea Scilla* Steinh.) is a perennial herb, with fibrous roots proceeding from the base of a large bulb, which sends forth several long, lanceolate, pointed, somewhat undulated, shining, deep-green leaves. From the midst of the leaves a round, smooth, succulent flower-stem rises, from one to three feet high, terminating in a long, close spike of whitish flowers. The fruit is an oblong, 3-lobed capsule. The squill grows in sandy soil along the sea coast of Spain, France, Italy, Greece, and the other countries bordering on the Mediterranean. The bulbs are collected in August, deprived of their roots and dry membranous outer scales, cut into slices transversely dried in the sun and packed in casks for shipment. The drug is imported from Leghorn, Italy and Amsterdam, Holland.

Properties.—The fresh bulb is pear-shaped, from 15 to 30 cm. in diameter, weighing as much as 5 or 6 pounds, and consists of fleshy scales attenuated at their edges, closely applied over each other, and invested by exterior scales so thin and dry as to appear to constitute a membranous coat. There are two varieties, distinguished as the *red* and the *white squill.* In the former variety which is collected in Algeria and shipped to France, the exterior coating is of a deep reddish-brown color, and the inner scales have a whitish rosy or very light pink epidermis, with a yellowish-white parenchyma; in the latter the whole bulb is white. They do not differ in medicinal virtue. The bulb abounds in a viscid, very acrid juice, which causes it to inflame and even excoriate the skin when much handled. By drying, this acrimony is very much diminished, with little loss of medicinal power. The bulb loses about four-fifths of its weight in the process. The process is somewhat difficult, in consequence of the mucilaginous character of the juice. The bulb is cut into thin transverse slices, and the pieces dried separately by artificial or solar heat. The outer and central scales are rejected, the former being dry and destitute of activity, the latter too fleshy and mucilaginous.

Description and Physical Properties.—"*Unground Squill.*—Irregular, curved or flattened pieces, from 0.5 to 5 cm. in length; yellowish-white, somewhat translucent; brittle when dry, and tough and flexible when damp; odor slight; taste bitter, mucilaginous and acrid.

"*Structure.*—Upper and lower epidermal layers of thin-walled cells with few stomata; mesophyll of slightly elongated thin-walled cells, sometimes containing spheroidal aggregates of a sugar; occasional bundles of spiral and reticulate tracheæ; numerous, elongated mucilage cells containing raphides of calcium oxalate; few spheroidal starch grains in the parenchyma.

"*Powdered Squill.*—Light yellowish-brown; very hygroscopic, caking in moist atmosphere; raphides of calcium oxalate numerous, up to 1 mm. in length, isolated and in bundles imbedded in mucilage; fragments of thin-walled parenchyma with occasionally spiral and reticulate tracheæ; very few starch grains. Preserve in tightly closed containers in a cool place.

"**Assay.**—Prepare a tincture according to the official process and proceed as directed under *Tinctura Digitalis.*" *U. S.*

"In curved, yellowish-white, somewhat translucent strips, from about two and a half to five centimetres long, frequently tapering towards both ends; tough and slightly flexible while moist, but brittle and easily pulverisable when dry. Almost inodorous; taste disagreeably bitter. Ash not more than 5 per cent." *Br.*

Examined by the microscope, each bulb scale, representing a modified leaf, is seen to be pervaded by innumerable minute acicular crystals of calcium oxalate. Some of these attain a length of a millimeter. According to Hartwich, the mucilage occurs either in the form of large drops, filling the parenchymatous cells, or as masses enclosing the raphides. For an elaborate microscopic study, with plates, see *A. Pharm.*, July, 1889. When kept in a dry place, squill retains its virtues for a long time; but if exposed to moisture it soon becomes mouldy.

The virtues of squill are extracted by alcohol, but apparently only in part by water.

Constituents.—The chemistry of squill has been studied by Jarmersted (*A. E. P. P.*, 1879, xi, 22), Merck (*Ph. Ztg.*, 1879), Wanizewski (*A. J. P.*, 1893, 498), Buschmann (*A. Pharm.*, 1920) and Ewins (*J. P. Ex. T.*, 1911, iii, 155), but none of these investigators have isolated any active principles in a pure form. The substances described as *scillitoxin, scillipicrine,* and *scillin,* while more or less active, are apparently none of them even approximately pure. *Scillain* is apparently identical with scillitoxin. Although Wanizewski claimed to have separated three crystallizable substances—*scillinine, scillipicrine* and *scillimarine*—there is no sufficient experimental proof to substantiate this claim.

Ewins separated from the squill two active principles, although neither of them in crystallizable form. The first is water soluble glucoside, which is fatal to the frog in doses of 0.03 Gm. for a 25 gramme frog. The second is a resinous body, very slightly soluble in water, but readily so in alcohol. Fatal dose for a frog is 0.06. Besides these they found a trace of caffeine.

Schmiedeberg found a peculiar mucilage, analogous to dextrin, which he calls *sinistrin,* $(C_6H_{10}O_5)_n$. It is white, easily soluble in water, insoluble in alcohol, lævo-rotatory; on boiling with dilute sulphuric acid it yields levulose and an inactive sugar of reducing properties. The mucilage is not affected by saliva or diastase. This last statement, however, was contradicted by F. Kurtz (*A. J. P.*, 1894, 246), who says that diastase acts upon it, producing a reducing sugar. Kurtz also obtained a reducing sugar (probably dextrose) along with the gum direct by extracting the bulb with hot alcohol.

Uses.—Squill belongs to that series of drugs, commonly known as the digitalis group, which have for their characteristic properties the power of slowing and strengthening the pulse, of contracting the blood vessels, and in toxic doses causing systolic spasm of the frog's heart. (See *Digitalis.*) While it in many regards closely resembles digitalis in its physiological action, it is notable for the strong degree of vasomotor action and for its local irritant effect.

The medical reputation of squill was originally as a diuretic. The older authorities attributed its diuretic action to a direct stimulant effect upon the kidney, but White and Balboni (*J. A. M. A.*, 1920, lxxv, p. 971) who made careful studies on cardiac cases, were unable to perceive any diuretic action which could not be explained through the effects upon the circulation.

While squill is capable of exercising the characteristic effects of the digitalis group on the heart, and might therefore be useful in chronic *heart disease,* it is certainly a much less reliable drug for this purpose than digitalis. Physicians of the past generation, believing it had a direct diuretic action, favored it especially in cases which were associated with *dropsy.* When given in large dose, partly because of the central emetic effect which is characteristic of the digitalis group, but largely because of its local irritant influence upon the stomach, it produces severe nausea and even vomiting. In overdoses it has been known to cause hypercatharsis, strangury, bloody urine, and fatal inflammation of the stomach and bowels.

Like other emetic drugs, if given in sufficient doses to nauseate it tends to increase the bronchial secretions and is occasionally used as an expectorant in *bronchitis* and *spasmodic croup.* Because of its potent action upon the circulation its use for this purpose, however, is not to be encouraged.

Neither water nor dilute acetic acid entirely extract the activity of squill. The only liquid preparations, therefore, which thoroughly represent the drug are those made with alcohol, of which the tincture is probably the better.

When given in substance it is most conveniently administered in the form of pill.

Dose, of squill, from one to two grains (0.065–0.13 Gm.).

Off. Prep.—Acetum Scillæ, *U. S., Br.;* Fluidextractum Scillæ, *U. S.;* Oxymel Scillæ, *Br.;* Pilula Ipecacuanhæ cum Scilla, *Br.;* Pilula Scillæ Composita, *Br.;* Syrupus Scillæ, *U. S., Br.* (from Vinegar); Syrupus Scillæ Compositus, *U. S.* (from Fluidextract); Tinctura Scillæ, *U. S., Br.;* Mistura Pectoralis Stokes (from Fluidextract), *N. F.;* Oxymel Scillæ (from Vinegar), *N. F.;* Pilulæ Digitalis, Scillæ et Hydrargyri, *N. F.*

SCOPARII. N. F., Br.

SCOPARIUS Scopar. [Broom Tops]

"Scoparius consists of the dried tops of *Cytisus scoparius* (Linné) Link (Fam. *Leguminosæ*). Scoparius contains not more than 5 per cent. of stems over 3 mm. in diameter and not more than 2 per cent. of other foreign organic matter." *N. F.*

"Broom Tops are the fresh and the dried tops of Cytisus scoparius, *Link.*" *Br.*

Scoparius Cacumina, *Br.;* Herba Scoparii; Spartium; Irish or Scotch Broom; Besom; Genêt à balais, *Fr.;* Gemeine Besenginster, Besenginster, Besenkraut, Pfriemenkraut, *G.*

Cytisus scoparius is a common European shrub, cultivated as a sand-binder and locally naturalized on the Atlantic Coast at Nova Scotia and from northern Massachusetts to Virginia. It is a low, densely branched, glabrous shrub, from three to eight feet high, with numerous straight, pentangular, bright green, very flexible branches, and small, oblong leaves, usually trifoliate, but on the upper part of the plant sometimes simple. The flowers are numerous, papilionaceous, large, showy, of a golden-yellow color, and solitary or in pairs upon short axillary peduncles. The seeds are contained in a compressed legume, which is hairy at the sutures. It is essential that true broom be carefully distinguished from *Spanish broom* (*Spartium Junceum*), since a number of cases of poisoning have occurred from the substitution of the dried flowers of Spartium for those of broom. (See Part II.)

The whole plant has a bitter, nauseous taste, and, when bruised, a strong, peculiar odor. The tops of the branches are used in medicine.

Description and Physical Properties.—"*Unground Scoparius.*—Stems thin, flexible, with branched twigs, from 1 to 3 mm. in thickness, more or less angled and winged; externally dark green, nearly glabrous, with numerous reddish brown cork patches; internally yellowish, fracture short-fibrous, that of thicker pieces tough and splintery; leaves present in small amount or absent, upper leaves sessile, with often only one obovate leaflet. Odor slight, on bruising more distinct and peculiar; taste disagreeable, bitter.

"*Powdered Scoparius.*—Dark green; non-glandular, non-lignified hairs, unicellular, pointed, very long and more or less curved with thick walls over which are numerous small projections; fragments of leaf and stem tissue composed of chlorenchyma or epidermis, broadly elliptical stomata from 0.022 to 0.035 mm. in length; fibers with thin walls and simple pores, the fibers from 0.006 to 0.025 mm. in diameter and associated with pith and wood parenchyma and tracheæ with spiral thickenings; starch grains occasional, from 0.007 to 0.020 mm. in diameter; pollen grains few." *N. F.*

"Stem dark green, with long, straight, slender, alternate branches; the latter, like the upper part of the stem, winged, tough, flexible and glabrous. Leaves, when present, small, sessile, and simple above, stalked and trifoliate below. Odor of the fresh tops, especially when bruised, characteristic; the dry tops almost inodorous." *Br.*

The seeds are reported to be used sometimes, and to be as active as the tops. Farwell (*A. J. P.,* 1922, xciv, 429) says that the *Osyrius alba* is common in the market as a substitute for, or an adulterant of, Scoparius. There is considerable resemblance between the two but in the crude drug they can be distinguished by the fact that in the osyrius the stems are many striated, instead of five-angled as in the scoparius, and that the leaf buds are at the apex of the angles, instead of in the channels between them, and that the wood of the osyrius is white instead of yellowish. The powder of the osyrius is of much lighter color than that of the scoparius.

Constituents.—According to Cadet de Gassicourt, the flowers contain volatile oil, fatty matter, wax, chlorophyll, yellow coloring matter, tannin, a sweet substance, mucilage, albumen, and lignin. Stenhouse has separated from them two principles, *scoparin* and an alkaloid *sparteine.* Scoparin is a neutral substance. Stenhouse gives its composition as $C_{21}H_{22}O_{10}$, but Goldschmidt and Himmelmayer (*Ap. Ztg.,* 1893, 566) give the following formula: $C_{10}H_{16}O_8(OH)(OCH_3)$. It is in stellate crystals, only slightly soluble in cold water, more readily in hot water with greenish light yellow color, easily soluble in alkaline solutions or in alcohol. It is decomposed by heat. When fused with potassium hydroxide it yields, according to Hlasiwetz, phloroglucin and protocatechuic acid. *Sparteine,* $C_{15}H_{26}N_2$, was first obtained by distillation from the mother waters of the scoparin. Broom tops yield from 0.23 to 0.68 per cent. of sparteine, according to the time of collection, being richest in spring and poorest in summer at the flowering time of the plant. It is a colorless liquid having a peculiar bitter taste, and all the properties of a volatile alkaloid. Its sulphate occurs in colorless crystals, and is freely soluble in water. (See *Sparteine Sulphate,* Part II). For the commercial extraction of sparteine the ground drug is macerated for several days in a weak solution of sulphuric acid. This infusion is neutralized and evaporated to a syrupy consistency. It is then made alkaline and subjected to steam distillation. The volatilized sparteine is converted into the sulphate and purified by crystallization from water and finally from alcohol.

By the action of potassium dichromate and sulphuric acid, *oxysparteine,* $C_{15}H_{24}N_2O$, is formed, which has been used in medicine (see Part II). For further chemistry of sparteine and its derivatives see Schmidt, *Pharmaceutische Chemie,* 3te Auf., Bd. ii, 1276 and Henry, *Plant Alkaloids,* 2nd ed., 1924, p. 120. Yaleur (*C. R. A. S.,* 1918, clxvii, p. 163) has reported two other alkaloids, one volatile and one non-volatile; the former he calls *Genisteine* and gives it the formula $C_{16}H_{28}N_2$; the second he names *Sarothamnine,* $C_{15}H_{24}N_2$.

Uses.—Scoparius is diuretic and cathartic, and in large doses emetic, and has been employed with advantage in *dropsy.* Cullen prescribed it in the form of decoction, made by boiling half an ounce of the fresh tops in a pint of water down to half a pint, of which he gave a fluidounce (30 cc.) every hour until it operated by stool or urine. The seeds may be given in powder, in the dose of from ten to fifteen grains (0.65–1.0 Gm.).

Scoparin probably represents the diuretic and purgative influences of scoparius, although its physiological and therapeutic properties have not as yet been sufficiently investigated. For description of the effects of sparteine, see *Sparteine Sulphate.*

Dose, of scoparius, ten to fifteen grains (0.65–1.0 Gm.).

Off. Prep.—Fluidextractum Scoparii, *N. F.;* Infusum Scoparii, *Br.;* Succus Scoparii, *Br.*

SCOPOLAMINÆ HYDROBROMIDUM.
U. S. (Br.)

SCOPOLAMINE HYDROBROMIDE Scopolamin. Hydrobrom. [Hyoscine Hydrobromide]

"The hydrobromide [$C_{17}H_{21}O_4NHBr.3H_2O$] of lævorotatory scopolamine obtained from plants of the *Solanaceæ.*" *U. S.* "Hyoscine Hydrobromide, $C_{17}H_{21}NO_4$, HBr,$3H_2O$, is the hydrobromide of an alkaloid, hyoscine or scopolamine, obtained from various plants of the natural order Solanaceæ." *Br.*

Hyoscinæ Hydrobromidum, *Br., U. S. VIII;* Hyoscine Hydrobromide; Bromhydrate d'Hyoscine, *Fr.;* Scopolaminum Hydrobromicum, *P. G.;* Skopolaminhydrobromid, *G.;* Hyoscinum Hydrobromicum; Hydrobromate of Hyoscine.

Scopolamine, $C_{17}H_{21}O_4N$, is found in the leaves and seeds of *Hyoscyamus niger, Duboisia myoporoides, Scopola japonica, Atropa Belladonna* and other solanaceous plants. The term hyoscine, although originally applied to the substance now known as tropine, was used by Ladenburg for an alkaloid that he obtained from hyoscyamine which he believed to be isomeric with atropine. It is now generally held that he was mistaken in his statement concerning the composition of this alkaloid and that the substance with which he was dealing was in reality the alkaloid scopolamine, which however was not discovered until some years later by Schmidt (*A. Pharm.,* 1890, ccviii, 139, and 1892, ccxxx, 207). At present the terms hyoscine and scopolamine are used interchangeably, the Br. Pharmacopœia giving the preference to hyoscine by virtue of its priority, while the American and most of the European Pharmacopœias give a preference to scopolamine because of a greater accuracy. There is, however, in some parts a tendency to apply the word scopolamine to the optically inert alkaloid (analogous to atropine) which Hesse has called *atroscine,* and to save the word hyoscine to indicate lævo-scopolamine. When pure, it forms a syrupy liquid. The best salt for practical use is the hydrobromide.

Description and Physical Properties.—"Colorless, transparent, rhombic crystals, sometimes of large size. It is odorless, and slightly efflorescent. *Caution—Scopolamine Hydrobromide is extremely poisonous.* One Gm. of Scopolamine Hydrobromide is soluble in 1.5 cc. of water and in 20 cc. of alcohol, at 25° C. It is slightly soluble in chloroform, but insoluble in ether.

"When anhydrous, Scopolamine Hydrobromide melts between 190° and 192° C. The specific rotation $[\alpha]_D$ of the salt, determined at 25° C., in an aqueous solution containing the equivalent of 5 Gm. of anhydrous Scopolamine Hydrobromide in 100 cc. of solution, and using a 100 mm. tube, is not less than −22° and not more than −25.75°. Add 5 drops of nitric acid to about 0.01 Gm. of the salt, and evaporate the solution to dryness in a porcelain dish on a water bath: the residue yields a violet color upon the addition of alcoholic potassium hydroxide T.S. Add a few drops of chlorine T.S. to 1 cc. of an aqueous solution of the salt (1 in 20), and shake the mixture with 1 cc. of chloroform: the latter assumes a brownish color. Silver nitrate produces in an aqueous solution of the salt (1 in 20) a yellowish-white precipitate insoluble in nitric acid but soluble in ammonia T.S.

"Its aqueous solution (1 in 20) is neutral, or at most only slightly acid to litmus paper." *U. S.*

"Small, colorless, transparent, non-deliquescent rhombic crystals. Soluble in 4 parts of *water.* Loses about 12 per cent. of its weight when dried at 100° C. Yields the *reactions* characteristic of bromides. An aqueous solution (5 in 100) yields with *solution of sodium hydroxide* a white precipitate soluble in excess of the reagent, but no precipitate with *solution of ammonia.* The alkaloid removed from the ammoniacal solution by shaking with *chloroform,* separating and evaporating the chloroformic solution, when dissolved in *diluted hydrochloric acid,* yields with *solution of auric chloride* a yellow precipitate, which, recrystallised from *water* acidified with *hydrochloric acid* and dried, melts at 198° to 200° C. Treated with *nitric acid* as described under 'Atropina' a violet color is developed. No appreciable ash." *Br.*

Scopolamine when boiled in dilute alkali solution is hydrolyzed into tropic acid (see under *Atropina*) and a new base called *oscine* or *scopoline* $C_8H_{13}O_2N$. According to Cushny (*J. P. Ex. T.,* 1921, xvii, 41), both tropic acid and oscine contain asymmetric carbon atoms and are therefore optically active. It is, therefore, theoretically possible to have four combinations of these optical isomers, but only two have actually been prepared, namely—the l- and d-tropyl esters of dl-oscine; these are the products commonly referred to as lævo- and dextro-scopolamine.

Although the alkaloid scopolamine occurs like hyoscyamine in an optically inert and in a lævo-rotatory form, there is no such common distinction made in its nomenclature as is made in the case of hyoscyamine. While the Br. makes no distinction, except by melting point, the U. S. specifies an optical rotation of not less than 22.

Schmidt (*A. Pharm.*, 1915, pp. 497, 604) has stated that scopolamine is an alcohol $C_8H_{12}(NO)(OH)$ and that upon heating with hydrobromic acid it yields hydroscopolamine bromide $C_{18}H_{12}BrN(OH)_2$ and this upon reduction with zinc and sulphuric acid yields hydroscopolamine $C_{18}H_{13}N(OH)_2$. *Hydroscopolamine* when oxidized is converted into methyl-piperidine-dicarbonic acid. This is a derivative of *pimelenic* acid. For further information on the chemistry of solanaceous alkaloids, see *Belladonnæ Radix.*

Straub has stated that stable solutions of scopolamine may be made by using a 10 per cent. solution of mannitol and then sterilizing. (*Bull. Chim. Farm.* through *Chem. Abst.*, 1918, xii, 1103.)

Uses.—The older investigations into the effects of scopolamine upon the bodily functions are in many regards confusingly contradictory because of the failure to realize the difference in the physiological effects of *racemic* and *lævo-scopolamine.* While these two varieties of the alkaloid possess qualitatively the same physiological properties their actions are quantitatively so different that it is not to be wondered that different pharmacologists obtain such varying results. Lævo-scopolamine (the variety recognized by the U. S. P.) is paralyzant to the peripheral ends of the so-called autonomic, or parasympathetic, nerves acting in this regard precisely like atropine, although less powerful. By virtue of this action it dilates the pupil, causes dryness of the throat and of the skin, accelerates the heart's action, etc. It differs strikingly from atropine, however, in that it is not stimulant to the medullary centers and therefore does not increase the respiration nor elevate the blood pressure; and also in that it appears to act frequently as a cerebral depressant and tends to promote sleep. In some persons the sleep which it produces is interrupted by, or attended with, a kind of low muttering delirium, recalling the mental confusion of atropine poisoning. A striking feature of the effects of large doses of scopolamine is the loss of memory for events which happened while under its influence. It has slight analgesic properties, but according to the researches of Hauchold (*Z. E. P. T.*, 1910, vii, p. 743) greatly enhances the effect of other narcotics such as morphine or urethane. In large dose it is depressant to the respiratory center and apparently also in some degree to the motor ganglia of the spinal cord. The *racemic scopolamine*—sometimes known as atroscine—according to the studies of Cushny (*A. E. P. P.*, 1912, lxx, p. 433), differs from the optically active alkaloid only in being much less powerful in its effects upon the autonomic nerves. When locally applied it will cause dilatation of the pupil, but except in very large doses, it has no effect upon the pulse rate and scarcely any upon the secretions. Its action upon the central nervous system is about equal to that of the lævo-scopolamine.

The most important use of scopolamine is as a cerebral sedative. In ordinary *insomnias* it is usually much less efficient than the narcotics of the aliphatic group but is often useful as an adjuvant in the severer types of sleeplessness, such as seen in *delirium tremens.* In the *manias* it often acts most happily and in some cases even seems to exercise some curative influence. For the relief of *pain* it is rarely useful by itself, but may be advantageously combined with morphine. It is often of value as a symptomatic remedy in various forms of nervous excitement, such as is seen in *hysteria* or *neurasthenia.* It is probably its action upon the intellectual centers which make it so useful a drug in the treatment of *alcoholic* and other *drug habits.*

In a variety of other conditions of nervous excitement scopolamine has been found clinically useful, although its mode of action is not always clear; thus in *epilepsy,* while by itself of little avail, it greatly increases the effects of bromides; in *paralysis agitans* it is one of the most valuable drugs we possess; it is also useful to allay *sexual excitement* as *nymphomania* and *spermatorrhea,* and Hotz (*D. M. W.*, 1908) reports good results even in *tetanus.* As a mydriatic it is much quicker and less permanent in its effects than atropine and is therefore often used to paralyze accommodation in correcting errors of refraction.

In 1900 Schneiderlin, under the misapprehension that scopolamine was stimulating to the respiratory center and would therefore antagonize depressant effects of morphine, introduced the use of a combination of these alkaloids as a means of producing surgical anesthesia. Under the catchy name of "*Twilight Sleep*" this method of anesthesia has been used to a large extent not only for surgical operations, but in obstetrics, either by itself or as a preliminary to the use of chloroform or ether. As the sole means of producing unconsciousness for surgical operations the *scopolamine-morphine anesthesia* is certainly not to be recommended as a routine measure. Not only is the anesthesia unsatisfactory in a very large proportion of cases, but the method has given an extraordinarily high mortality. In 1906, H. C. Wood, Jr. (*Amer. Med.*, xii, p. 544), collected statistics of two thousand cases showing a mortality of 1 in 221 anesthesias, and Avarffi subsequently (*J. A. M. A.*, 1910, liv) in six thousand anesthesias found a mortality of 1 in 150. In obstetrical practice, however, it has been widely applauded and is apparently much less dangerous, at least to the mother, than in general surgery. Schwarz and Krebs (*J. A. M. A.*, 1923, lxxxi, 1083) report on 3000 cases of labor in which scopolamine-morphine anesthesia was successfully used, but conclude that the method to be safe for both child and mother requires such constant observation of the patient as is only possible in hospitals, and the treatment should therefore not be recommended for private practice. The question, however, of whether the use of scopolamine as a preliminary to ether anesthesia is advantageous or not is, as yet, a matter of great difference of opinion. While it is undoubted that the quantity of ether under such circumstances is less than that ordinarily required, it is not certain whether the danger is consequently diminished or not.

The ordinary dose of scopolamine ranges from 1/200 to 1/100 of a grain and occasionally even somewhat more. Many persons, however, are excessively susceptible to its influence and even these quantities may cause toxic symptoms. While scopolamine poisoning very rarely ends fatally the symptoms are often extremely alarming. There are marked disturbances of intellection, sometimes an active delirium resembling that of atropine poisoning and at others simply complete disorientation. Many cases present marked somnolence, but in others this may be lacking. At times the pupils are dilated, the pulse rate accelerated and there is dryness of the mouth with a peculiar husky character to the voice apparently due to laryngeal paralysis, but these symptoms are often absent or very mild, presumably dependent upon the variety of the alkaloid. The condition rarely requires active treatment but if there is serious embarrassment of the respiration strychnine may be used; it is usually better not to employ any drugs for the relief of the delirium, although if very active small doses of paraldehyde and bromides may be employed.

Dose, one two-hundredth to one-eightieth of a grain (0.0003–0.0008 Gm.).

SCUTELLARIA. N. F.

SCUTELLARIA Scutellar. [Skullcap]

"Scutellaria is the dried overground portion of *Scutellaria lateriflora* Linné (Fam. *Labiatæ*). Scutellaria contains not more than 3 per cent. of foreign organic matter." *N. F.*

Skullcap; Scullcap; Quaker Bonnet; Hoodwort; Madweed; Mad-dog or Sideflowering Scullcap; Blue Pimpernel; Hooded Willow-herb; Helmet Flower; Scutellaire, *Fr.;* Helmkraut, Schildkraut, *G.*

Several species of *Scutellaria* have attracted attention. *Scutellaria galericulata* L., which grows in wet places from Newfoundland to North Carolina and west to Nebraska, has a feeble, somewhat alliaceous odor, and a bitterish taste. It has been employed in intermittents, and externally in old *ulcers. S. integrifolia* L. is intensely bitter, and might probably be found useful as a tonic.

Scutellaria lateriflora is an indigenous, perennial herb, with a stem erect, much branched, quadrangular, smooth, and one or two feet high. The leaves are ovate, acute, dentate, subcordate upon the stem, opposite, and supported upon long petioles. The flowers are small, of a pale blue color, and disposed in long, lateral, 1-sided, leafy racemes. The fruit consists of four brown nutlets, enclosed by a persistent calyx having a shape quite similar to the head covering formerly worn by the women of the Quaker sect. The plant grows in wet shaded places in the United States and Canada. It is collected in summer when in flower and dried. The commercial supplies are largely obtained from the Southern and Western States.

Scutellaria has been one of the most substituted and adulterated drugs in the Materia Medica. While the *S. lateriflora* Linné is alone officially recognized as the source of the drug, various other native species of *Scutellaria* have more frequently represented the article of commerce than the officially specified herb. Chief among these have been *S. canescens* Nutt. or *Western Scullcap, S. cordifolia* Muehl. or *Southern Scullcap* and *S. galericulata* L.

Description and Physical Properties.—"*Unground Scutellaria.*—About 50 cm. in length or in shorter broken pieces, smooth; stem quadrangular, branched; leaves opposite, smooth, petiolate, about 5 cm. in length, ovate-lanceolate or ovate-oblong, serrate; flowers about 6 mm. in length, in axillary one sided racemes, with a pale blue corolla and bilabiate calyx, closed in fruit, the upper lip helmet-shaped. Odor slight; taste slightly bitter.

"*Powdered Scutellaria.*—Dark green; non-glandular hairs numerous, long, 1- to 3-celled with walls having numerous small centrifugal projections, the basal cell large, broadly cylindrical, the apical cell narrowly tapering, often recurved; glandular hairs with 1- to 2-celled stalks and 4-celled heads, the latter from 0.015 to 0.045 mm. in diameter; pollen grains smooth, nearly spheroidal from 0.015 to 0.025 mm. in diameter; fragments composed of chlorenchyma, epidermal cells and stomata, the latter broadly elliptical, about 0.020 mm. in length; long lignified fibers with simple pores and walls about 0.005 mm. in thickness; tracheæ narrow, mostly with scalariform or reticulate thickenings; occasional fragments composed of distinctly striated epidermal cells of corolla, the fragments often colored pink in chloral hydrate T.S." *N. F.*

H. Molisch and G. Goldschmidt (*Ph. Ztg.,* Dec. 4, 1901, 965) obtained from scutellaria and a number of other labiates an identical body, to which they gave the name *scutellarin.* It is present in all of the different scutellarias, being most abundant in the upper epidermis of the leaf, but found also in the roots, stems and flowers of the plant. It was further obtained from the leaves of *Galeopis Tetrahit* L., and of *Teucrium Chamaedrys* L. Scutellarin is obtained by boiling freshly gathered leaves for fifteen minutes in ten times their weight of water, filtering the decoction and adding from 1 to 2 per cent. of hydrochloric acid, which causes an abundant precipitate of scutellarin. If precipitation is effected from the hot solution, the scutellarin separates in the form of light yellow crystals. The formula $C_{10}H_8O_3$ has been assigned to scutellarin. Its alcoholic solution gives a red precipitate with lead acetate and an intense green color with ferric chloride, changing on heating to a red color if the reagent is not present in great excess; alcoholic potassium or sodium hydroxides, as also alkali acetates, produce reddish-yellow precipitates, which change to green on exposure to the air. Solution of barium hydroxide has the same effect. The green color is produced immediately if an oxidizing agent, such as chlorine or bromine water, is added.

Uses.—Scullcap is as destitute of medicinal properties as a plant may well be, not even being aromatic. When taken internally, it produces no very obvious effects, and probably is of no remedial value, although at one time it was esteemed as a remedy in *hydrophobia.* It has also been used in *neuralgia* and *epilepsy, chorea, delirium tremens,* and *nervous exhaustion* from fatigue or over-excitement. (See Bramwell, *B. M. J.*, 1916.) Dr. P. E. Hommell proposes formulas for various pharmaceutical preparations of scutellaria in an article in the *Druggists' Circular,* 1915, 797.

Dose, thirty to ninety grains (2.0–5.8 Gm.).

Off. Prep.—Fluidextractum Scutellariæ, *N. F.;* Tinctura Viburni Opuli Composita, *N. F.*

SENECIO. N. F.

SENECIO [Life Root Plant]

"Senecio is the dried plant of *Senecio aureus* Linné (Fam. *Compositæ*). Senecio contains not more than 10 per cent. of foreign organic matter." *N. F.*

Life-root, Golden Life-root, Ragwort, Golden Ragwort.

Several of the species of *Senecio* have been used in medicine. Among them are *S. vulgaris* L. (*Groundsel, Jacobskraut* G.) and the *S. Jacobœa* L. The official species, *S. aureus,* is a common indigenous perennial herb found in swamps and wet meadows, about 1 or 2 feet in height, bearing several floral heads, both the disk and ray flowers being of a golden yellow color. The commercial supplies of the drug are obtained chiefly from the central states.

Description and Physical Properties.—"*Unground Senecio.*—Stems from 3 to 6 dm. in length, if entire bearing a basal rosette of leaves; sparingly clothed with successively smaller leaves and bearing at the summit several yellow heads in a loose corymb, white floccose when young, but mostly glabrous when expanded, radical leaves on long, slender petioles, mostly of rounded form from 5 to 7 cm. in breadth, the base often cordate, the summit rounded, the margin crenate-dentate; stem-leaves gradually changing from the shape of the radical leaves to lyrately pinnate, then pinnatifid and sessile, and at length clasping, oblong and incised; heads slender peduncled from 12 to 25 mm. in width, the lance-linear involucral scales in about two series, closely appressed, rays about ten, bright-yellow, disk flowers very numerous, small, bearing a glabrous achene and a white pappus. Odor characteristically aromatic; taste bitter, slightly astringent and distinctly acrid and pungent.

"*Powdered Senecio.*—Dark green; numerous very long, much twisted or bent multicellular non-glandular hairs with thin walls and some with an oily content; fragments of leaf tissue composed of chlorenchyma, epidermal cells and elliptical stomata, the latter from 0.020 to 0.035 mm. in length; stem tissue composed of wood parenchyma and long thin-walled lignified fibers and tracheæ, the latter with spiral thickenings or simple pores; pollen grains few, or wanting, from 0.020 to 0.035 mm. in diameter." *N. F.*

Toxic alkaloids have been found in several species of Senecio, thus Watt (*Tr. Chem. Soc.*, 1909, xcv, 466) has found *senecifoline,* $C_{18}H_{27}O_8N$, and *senecifolidine,* $C_{18}H_{25}O_7N$, in the *S. latifolius.* We know of no chemical studies, however, of the official species.

In *S. vulgaris,* Grandval and Lajoux (*C. R. A. S.*, 1895, cxx, 1120) found two alkaloids, *senecionine,* $C_{18}H_{25}O_6N$, which is slightly, and *senecine,* which is readily, soluble in ether. According to Wiet, senecionine is a paralyzant of the peripheral motor and sensory nerves, while Bunch has found that the alcoholic extract of *Senecio Jacobœa* is capable of producing a rise of the arterial pressure due to contraction of the arterioles, followed, if the dose has been large enough, by arterial dilatation with fall of pressure. (*B. M. J.*, 1900, ii, 212.)

The rhizomes of the Mexican species, *Senecio grayanus* Hemsl. and *S. cervariæfolius* Sch., constitute *maturin,* the plants being known as *matarique, maturin,* or *guerena.* They produce rise of temperature, dilatation of the pupil, and violent tetanic spasms. Henckel states that they contain a glucoside resembling digitalin. (*A. J. P.*, Jan., 1891; also *Nouv. Rem.*, 1888, and *P. J.*, March, 1889.)

Uses.—Ragwort was formerly believed to exercise some peculiar influence upon the female generative organs and was used in such opposite conditions as *amenorrhea* and *menorrhagia,* as well as in various other uterine and in urinary diseases. It is, however, scarcely ever prescribed by regular physicians, and there is no reason to suspect it of therapeutic virtues.

The *S. vulgaris* and *S. Jacobœa* are of importance because of their toxic effects and have given rise to a peculiar type of poisoning in cattle and horses in South Africa. Cushny investigated the two alkaloids, *senecifoline* and *senecifolidine,* which are actively poisonous, causing symptoms similar to those which have occurred in animals after eating the compound. The most characteristic pathological lesion was cirrhosis of the liver.

Dose, of the fluidextract, one fluidrachm (4 cc.).

Off. Prep.—Fluidextractum Senecionis, *N. F.*

SENEGA. U. S. (Br.)

SENEGA Seneg. [Senega Snakeroot]

"Senega is the dried root of *Polygala Senega* Linné (Fam. *Polygalaceæ*). Senega contains not more than 5 per cent. of stems and other foreign organic matter." *U. S.* "Senega Root is the dried root of Polygala Senega *Linn.*" *Br.*

Senegæ Radix, *Br.;* Rattlesnake Root, Mountain Flax, Senega or Seneca Root, Radix Polygalæ Virginianæ; Polygala de Virginie, *Fr.;* Radix Senegæ, *P. G.;* Senegawurzel, Klapper-Schlangenwurzel, *G.;* Poligala Virginiana, *It.;* Poligala de virginia (Raiz de), *Sp.*

Polygala Senega is an indigenous herb with a perennial branching root, from which several erect, simple, smooth, round, leafy stems annually rise, from nine inches to a foot in height. The stems are occasionally tinged with red or purple below, but are green near the top. The leaves are alternate or scattered, lanceolate, pointed, smooth, bright green on the upper surface, paler beneath, and sessile or short petiolate. The flowers are small and white, and form a close spike at the summit of the stem. The calyx is their most conspicuous part. It consists of five sepals, two of which are wing-shaped, white, and larger than the others. The corolla is small and closed. The capsules are small, much compressed, obcordate, two-valved and two-locular, with two oblong-ovate, blackish, hairy seeds, slightly longer than the lobes of the caruncle.

This plant is found in woods and rocky soil of southern Canada and the eastern United States, south to Georgia and west to Wisconsin, Minnesota and Missouri. At one time it was largely collected in eastern Canada and the north-eastern Atlantic states; when this supply was exhausted, Kentucky and the States west and southwest of it were invaded; then Wisconsin and the northwestern states, from which with western Canada the commerce at present derives its chief supply. There are two varieties of the plant, the typical *P. Senega,* the form found in the Northern United States, and the variety *latifolia* (T. and G.) which extends from Maryland and Pennsylvania to the Dakotas and Tennessee. This variety is distinguished by its height (from ten to twenty inches) and its very large, ovate or ovate-lanceolate leaves, which taper towards each end and attain a length of four inches. The root of commerce is obtained from both varieties. It is brought into market in bales weighing from fifty to four hundred pounds. See True (*Ph. Era,* 1913, xlvi, p. 68).

Owing to the extensive use of senega considerable interest is manifested in the cultivation of the plant. Hood reports to have demonstrated that it can be successfully cultivated. (*Vermont Sta. Rept.,* 1907, p. 371.) It has also been grown by the Bureau of Plant Industry, U. S. Dept. of Agriculture.

Senega root varies somewhat in appearance according to the locality from which it is derived, and local varieties are recognized in commerce. Two varieties of senega occur in commerce, *viz.,* Northern and Southern Senega.

Northern or *Manitoba Senega* has the larger roots, being up to 15 cm. long and 12 mm. in thickness. Externally, it is dark brown and purplish near the crown. This variety is the more highly esteemed and is largely collected at present in Manitoba, Saskatchewan and Minnesota. *Southern* or *Small Senega* consists of roots up to 8 cm. long and 7 mm. in thickness, with a brownish-yellow color. A large percentage of rootlets are usually found in this variety. Most of it is shipped from South Carolina and Georgia.

Description and Physical Properties.—"*Unground Senega.*—Usually in pieces; when entire, slenderly conical, with an enlarged crown; from 3 to 15 cm. in length and from 2 to 10 mm. in thickness; tortuous, somewhat branched and bearing a few rootlets; crown knotty with numerous buds and short stem-bases; externally brownish-yellow, the crown darker and rose-tinted; longitudinally wrinkled, frequently with a distinct ridge or keel; fracture short, wood pale yellow; odor suggesting methyl salicylate; taste sweetish, afterwards strongly acrid.

"*Structure.*—A corky layer of several rows of tangentially elongated, light yellowish or yellowish-brown cells; outer bark of tangentially elongated parenchyma; inner bark of small groups of sieve tissue associated with parenchyma and alternating with medullary rays 1 to 3 cells wide; cortical cells somewhat collenchymatously thickened and with amorphous contents which form oily drops upon the addition of potassium hydroxide T.S. or of chloral hydrate T.S.; wood usually eccentrically developed, varying in outline, in transverse section, from circular or elliptical to reniform or irregularly fan-shaped or even separated by broad parenchyma rays into two or more masses; the inner bark adjacent to the radially longer wood-wedges thickened proportionally to their increased length and the outer bark opposite the radially shorter or absent wood-wedges also thickened proportionally to their shortness or absence.

"*Powdered Senega.*—Grayish-yellow to light yellowish-brown; somewhat sternutatory; consisting of scattered fragments of cork; fragments of parenchyma and sieve tissue developing oily globules; fragments of tracheæ and short, pointed tracheids with numerous, simple and bordered pores associated with short wood-fibers with oblique slit-like pores and lignified medullary ray cells with large simple pores." *U. S.*

"Greyish or brownish-yellow, slender, usually from five to ten centimetres long, with a knotty crown bearing the bases of numerous, slender, aerial stems; frequently curved or contorted, sparingly branched, keeled, sometimes transversely wrinkled. Fracture short. In transverse section, a horny translucent cortex free from starch grains and a white, often irregularly developed, wood. Characteristic odor; taste at first sweet, afterwards acrid." *Br.*

Holm describes the pharmacognosy of senega root and the morphology of the plant in *M. R.*, 1907, xvi, p. 155. Hartwich has made a very interesting observation in that he has found starch occasionally present in official senega. (*Apoth. Ztg.*, xxvi, p. 84.) Hartwich has also described two false senegas. (*S. W. P.*, xlvi, pp. 537 and 749.) The pharmacognosy of the drug has been well elaborated by Tunmann in *Ph. Zentralh.*, xlix, p. 61. Muller describes and figures senega and a number of the drugs that have been used as adulterants of this drug or as occasional contaminations. (*Pharm. Praxis.*, vii, p. 309.)

The roots of *Panax quinquefolium* L., or ginseng, were at one period frequently mixed with those of senega, but are easily distinguishable by their shape and taste. The roots of *Gillenia trifoliata* (L.) Moench., and *Asclepias Vincetoxicum* L. (*P. J.*, ix, 411), and of *Triosteum perfoliatum* L. (see Part II), have been noted as occurring in commercial senega; they are readily detected by the absence of the keel-like line.

For description of the roots of a number of species of Polygala see *Flora*, Jan., 1886, and *D. C.*, 1901, 26. The properties of senega as well as the medicinal virtues of the root, are extracted by boiling water and by alcohol. Diluted alcohol is an excellent solvent.

Constituents.—Senega owes its activity to two acrid principles called *senegin*, $C_{17}H_{28}O_{10}$, and *polygalic acid*, $C_{19}H_{30}O_{10}$. These substances belong to the group of saponins. *Polygalic acid* is a feebly acidic glucoside which on hydrolysis yields glucose and sapogenin. (For method of its preparation, see *U. S. D.*, 20th ed., p. 989.) It is a white odorless powder, whose taste is at first slight but becomes extremely pungent and acrid. It is soluble in water and in boiling alcohol, which precipitates it on cooling; it is insoluble in ether. It is precipitated from its aqueous solution by both neutral and basic lead acetate. *Senegin*, according to Atlass (*In. Dis.*, 1887), differs from polygalic acid in that it is not acid in reaction and is not precipitated from its aqueous solution by neutral lead acetate although it is by the basic.

Senega also contains, like most of the species of Polygala, small quantities of methyl salicylate which amounts to about 0.25 to 0.30 per cent. (see Reuter, *A. Pharm.*, 1889, 452; and Schroeder, *A. J. P.*, 1896, p. 178).

According to the researches of Trommsdorff and Schneider, saponin is contained solely in the bark, the woody tissues being inert. Kain (*Ph. Ztg.*, 1898, 562) states that he has discovered a lævo-rotatory glucoside distinguished from saponin by its mild taste, solubility in absolute alcohol, and in its not giving a precipitate with barium hydroxide.

Senega yields its virtues to water, cold or hot, but under the influence of heat a portion of the acrid principle unites with the coloring matter and coagulated albumen, and thus becomes insoluble in water. In forming an aqueous extract, the infusion should be prepared by percolation, as it is thus most concentrated, and consequently requires less heat in its evaporation. In preparing the infusion, the temperature of the water should not exceed 40° C. Experience has thoroughly proved the value of the use of an alkali in small proportion in making galenical preparations of senega, it prevents gelatinization and combines with the active principles. (See *Fluidextractum Senegæ.*)

Uses.—Senega owes what therapeutic virtues it possesses to its saponins. (See *Quillaia.*) These by their local irritant action upon the mucous membrane of the stomach tend to cause nausea, thereby increasing the secretions of the sweat glands and especially of the bronchial glands. For this reason the drug has been used as an expectorant in various forms of *bronchitis* and in *asthma.* In overdose it is capable of acting as an irritant poison producing violent vomiting and purging. Polygalic acid may be employed in doses of from one-fourth to one grain (0.016–0.65 Gm.), administered in the form of either pill or capsule.

Dose, of senega, from fifteen to twenty grains (1.0–1.3 Gm.).

Off. Prep.—Infusum Senegæ, *Br.;* Fluidextractum Senegæ, *U. S.;* Syrupus Senegæ (from Fluidextract), *U. S.;* Tinctura Senegæ, *Br.;* Syrupus Scillæ Compositus (from Fluidextract), *U. S.;* Mistura Pectoralis, Stokes (from Fluidextract), *N. F.*

SENNA. U. S. (Br.)

SENNA Senn.

"Senna consists of the dried leaflets of *Cassia Senna* Linné, known in commerce as Alexandria Senna, or of *Cassia angustifolia* Vahl, known in commerce as Tinnevelly Senna (Fam. *Leguminosæ*). Senna contains not more than 10 per cent. of its stems, and not more than 2 per cent. of its pods or other foreign organic matter, and yields not more than 3 per cent. of acid-insoluble ash." *U. S.* "Senna Leaves are the dried leaflets of Cassia acutifolia, *Delile*, and of Cassia angustifolia, *Vahl.* Known in commerce as Alexandrian senna, and Tinnevelly senna." *Br.*

Sennæ Folia, *Br.;* Senna Leaves; Séné; Feuilles de Séné, *Fr.;* Folia Sennæ, *P. G.;* Sennesblätter, *G.;* Sena, *It.;* Sen, *Sp.*

The plants which yield *senna* belong to the genus *Cassia*, several species of which have contributed commercial senna of the past. Only two of these, however, are now recognized in the United States and British Pharmacopœias, *viz.*, the *Cassia Senna* L. (*C. acutifolia* Delile) and the *C. angustifolia* Vahl. The leaves of a number of species of Cassia are utilized like senna leaves in the respective countries in which they grow, among which may be mentioned *C. marilandica* L.; *C. cathartica* Mart.; *C. rugosa* Don.; *C. splendida* Vog.; *C. lævigata* Willd.; *C. multijuja* Rich.; *C. Chamæcrista* L.; and *C. montana*

Hayne. Farwell asserts that *Cassia marilandica* and other American species of Cassia have been offered in large lots and sold as senna. (*M. R.*, xvii, p. 35.)

Cassia Senna, which furnishes the Alexandria Senna, is a shrub indigenous to the Anglo-Egyptian Soudan but found growing wild in other parts of Africa and in Hejaz. It has recently been introduced into India where it is now cultivated for the drug. It possesses a straight, branched whitish stem attaining a height of from two to ten feet, depending upon the locality of growth. The leaves are alternate and pinnate, with glandless petioles, and two small narrow pointed stipules at the base. The leaflets, of which from four to six pairs belong to each leaf, are almost sessile, ovate lanceolate, acute, oblique at their base, from half an inch to an inch long, and of a grayish-green color. The flowers are yellow, and in axillary racemes. The fruit is a flat, elliptical, obtuse, membranous, smooth, grayish-brown legume, about an inch long and half an inch broad, and divided into six or seven cells, each containing a hard, heart-shaped, ash-colored seed.

Cassia angustifolia is a low shrub having a habit somewhat similar to *C. Senna.* It is native to Arabia and probably Africa and is found growing in the wild condition in southern Arabia, northern India, Somaliland and the Anglo-Egyptian Soudan. It is cultivated extensively in southern India for medicinal use. It has an erect, smooth stem, and pinnate leaves, with from four to eight pairs of leaflets. These are nearly sessile, lanceolate, obscurely mucronate, oblique at the base, smooth above and somewhat downy beneath, with the veins turned inward so as to form a wavy line immediately within the edge of the leaflet. The most striking character of the leaflet is its length, which varies from 2 to 5 cm. The petioles are without glands; the stipules minute, spreading and semi-hastate. The flowers are bright yellow, and arranged in axillary and terminal racemes rather longer than the leaves. The legume is oblong, membranous, tapering abruptly at the base, rounded at the summit, and 4 to 5 cm. long by about 1.5 cm. broad.

Cassia obovata Colladon, the source of the formerly recognized *Dog Senna* or *Italian Senna*, possesses a rather shorter stem than that of *C. acutifolia*, rising to the height of only a foot and a half. The leaves have from five to seven pairs of leaflets, which are obovate, very obtuse, sometimes mucronate. The flowers are in axillary spikes, of which the peduncles are longer than the leaves of the plant. The legumes are very much compressed, curved almost into the kidney form, of a greenish-brown color, and covered with a very short down, which is perceptible only by the aid of a magnifying glass. They contain from eight to ten seeds. This species grows wild in Syria, the Anglo-Egyptian Soudan and Senegambia. It has been cultivated successfully in Italy, Spain, and the West Indies. It is said to be no longer gathered for senna, although its cut leaflets have been found in cut Alexandria Senna.

Description and Physical Properties.—"*Unground Alexandria Senna.*—Inequilaterally lanceolate or lance-ovate, frequently broken; from 2 to 3.5 cm. in length and from 6 to 10 mm. in width, unequal at the base, with very short, stout petiolules; acutely cuspidate, entire, brittle, subcoriaceous; hairs short and somewhat appressed, few on the upper surface, more numerous on the lower surface, where they occur spreading on the midrib, especially on the lower part; color light grayish-green; odor characteristic; taste mucilaginous, slightly bitter.

"*Unground Tinnevelly Senna.*—Usually unbroken, from 2 to 5 cm. in length, from 6 to 15 mm. in width; broadly acute at the apex, slightly hairy; light yellowish-green and otherwise resembling Alexandria Senna.

"*Structure.*—Epidermal cells polygonal, with straight walls and frequently containing mucilage; stomata numerous, broadly elliptical, mostly from 0.020 to 0.035 mm. in length, usually bordered by 2 neighbor-cells with their long axes parallel with that of the stoma, and rarely, though more frequently in Alexandria Senna, a third epidermal cell at the end of the stoma; hairs non-glandular, 1-celled, conical, often curved, with thick papillose walls, from 0.10 to 0.35 mm. in length; palisade cells in a single layer underlying both surfaces; calcium oxalate in rosettes, in the loose mesophyll parenchyma and in 6- to 8-sided prisms in crystal fibers, surrounding the conducting tissues of the veins.

"*Powdered Senna.*—Light green; displaying fragments of veins bearing lignified tracheæ and crystal fibers, isolated hairs, masses of palisade and mesophyll parenchyma, fragments of epidermis with stomata, free calcium oxalate rosettes and prisms from 0.01 to 0.02 mm. in length. In powdered Alexandria Senna the hairs are more numerous than in powdered Tinnevelly Senna.

"Mix 0.5 Gm. of powdered Senna with 10 cc. of an alcoholic solution of potassium hydroxide (1 in 10), boil the mixture for about two minutes, dilute it with 10 cc. of water, and filter. Acidify the filtrate with hydrochloric acid, shake it with ether, remove the ethereal layer, and shake it with 5 cc. of ammonia T.S.: the latter is colored pinkish-red or bluish-red." *U. S.*

"Pale grayish-green or yellowish-green, thin, brittle; usually from two to four centimetres long, the leaflets of Alexandrian senna being usually smaller than those of Tinnevelly senna; lanceolate, or oval-lanceolate, acute, entire, and unequal at the base. Surface finely pubescent or nearly glabrous; veins on the under surface distinct. Epidermis of both surfaces consisting of polygonal cells and bearing one-celled, thick-walled, warty hairs together with stomata, each stoma being enclosed between two cells with their long axes parallel to the ostiole. The powdered Leaves greenish-yellow, exhibiting, in addition to the characteristic epidermis, stomata, and hairs, elongated palisade cells and grouped sclerenchymatous fibres accompanied by prismatic crystals of calcium oxalate. Ash not more than 12 per cent." *Br.*

1. *Alexandria Senna.*—This variety is the product of *Cassia Senna* Linné. It is gathered from wild plants growing in El Hejaz, from wild and cultivated plants growing in the Soudan below Egypt and to a small extent from plants which have recently been cultivated in India. The Soudan Senna is claimed by Amin to be worthless, although used to adulterate the valuable supplies coming from the Hejaz. The leaflets are usually gathered during the winter months by the natives, dried in the sun and packed in hampers weighing about 225 pounds. Three of these are placed on the back of each camel and carried to Port Soudan and other convenient shipping points, whence the drug is shipped to Alexandria, Port Said or Cairo. Here it is claimed the worthless Soudan Senna has frequently been admixed with senna from Hejaz. About 75 per cent. of the Alexandria Senna imported into the United States comes from Cairo, Alexandria and Port Said, the remaining 25 per cent. comes indirectly through London. C. J. Zufall (*J. A. Ph. A.*, 1921, x, 185) reports that samples of a superior quality of Alexandria Senna which were imported by way of London were found to have been grown by a New York drug importer on his plantation in India. The leaves were hand picked, unbroken and free from stems and dirt, something not true of the senna coming from Soudan.

The chief adulterants of Alexandria Senna have been stems, midribs, dirt, the leaflets and fruits of *Tephrosia apollinea* DC., *Cassia obovata, C. angustifolia, C. auriculata,* worthless Soudan Senna and *Tephrosia apollinea.* The latter is a leguminous plant native to Egypt and Nubia. Its leaflets are averagely smaller than senna, of an obovate-oblong or obcordate outline, with an emarginate apex, downy lower surface and parallel, unbranched, lateral nerves. They are frequently folded longitudinally, which fact often aids their detection. The legumes of this species are 1 to 1½ inches long and up to ⅙ of an inch broad. Examination of recent senna importations at New York revealed considerable adulteration with *Tephrosia apollinea* (*C. D.*, 1917, lxxxix, 385). The leaflets of *C. obovata* are obovate, with obtuse to mucronate apex, 12 to 22 mm. long and about half as wide. The legumes are somewhat reniform, downy and contain 8 to 10 seeds.

A. Joenssen (*C. D.*, 1917, lxxxix, 47) finds that the broken leaflets of *"Arabian" Senna* (*Cassia angustifolia*) and *"dog" Senna* (*C. obovata*) have recently been used to adulterate commercial *"Alexandrian" Senna.* Casparis reports that *"Folia sennæ Palthe,"* a substitute appearing in Austria, is derived from *Cassia auriculata.* A similar substitute appearing in Switzerland and devoid of activity, is probably identical with it. (*Schweiz. Apoth. Ztg.* through *Chem. Abst.*, 1917, xi, 2020.) The leaflets of *Coriaria myrtifolia* L. (see Part II) have been detected occasionally as an admixture in commercial senna, especially the cut Alexandria variety. They are usually cut in several pieces for this purpose. In the entire condition they are ovate-lanceolate, grayish-green with a bluish tint, and are readily known, when not too much broken up, by their strongly-marked midrib and two lateral nerves running from the base nearly to the summit. They are free from hairs and do not contain crystals of calcium oxalate. Surface sections of their lower epidermis, when examined microscopically, show cells with rectilinear vertical walls, scattered among which are stomata, each with two parallel neighboring cells which are strikingly wrinkled.

Formerly *Argel leaves,* the leaves of *Solenostemma Argel* Hayne (Fam. *Asclepiadaceæ*), a native of Africa, were regularly mixed with Alexandria Senna but are now rarely seen in this variety. They somewhat resemble this senna but can readily be distinguished by their thicker texture, curved or curled margins, absence of conspicuous veins, outside of the midrib, and by their 3- to 4-celled, non-glandular hairs.

2. *Indian Senna.*—This variety is the product of *Cassia angustifolia* Vahl. which, while native to southern Arabia, is cultivated in the Anglo-Egyptian Soudan and to a larger extent in southern India, where, especially in the southeastern district of Tinnevelly, the plant produces larger leaves and leaflets than in its native home. The leaflets differ from those of the Alexandria Senna in being yellowish-green, in attaining a larger size, frequently up to 5 and occasionally 5.5 cm. in length, in having a less noticeable asymetrical outline, and in showing fewer hairs. They are collected for the market chiefly in southern India, dried in the sun and packed in bags or pressed into bales for shipment.

The finest grade of Indian Senna is that grown in the district of Tinnevelly and commercially known as *Tinnevelly Senna.* It is gathered from cultivated plants and usually represents leaflets of excellent appearance and free from pods, stems or other foreign matters. Before the World War the purity, high quality and low price of the Tinnevelly Senna placed it in the front rank on the purchasing markets. In 1914, however, its cultivation in Tinnevelly had been almost entirely discontinued due to the low price offered on the European market because of its indiscriminate adulteration. Since the war, it has been less manipulated and is now steadily regaining its lost repute. Tinnevelly Senna is shipped to the United States and Europe from Tuticorin, India, or indirectly to this country through London. Inferior grades of senna, containing discolored leaflets, stems, fruit, etc., have been sent from Aden, Mocha and other Red Sea ports to Bombay. Some of these have been exported from India as "Indian Senna." About 75 per cent. of Indian Senna used in the United States comes from India, the remaining 25 per cent. being imported from London.

Much study has been given to the question of distinguishing the powder of Alexandria and India Senna by means of the microscope. (See papers by Sayre, *A. J. P.,* 1896, 1897; Schneider, *Am. Drug.,* 1897; Denniston, *Ph. Rev.,* vol. xvi.) As a result of these studies it is asserted that it is possible to take advantage of the greater hairiness of the Alexandria Senna as a practical distinction, it being alleged that a fragment of the epidemis of Alexandria leaf contains twice as many hairs as does a similar sized shred of epidermis from the India Senna. It is especially proposed to count the number of epidermal cells between two hairs or their scars, the average distance of the hairs from one another being in the Alexandria Senna three epidermal cells, and in the India six cells. Advantage may also be taken of the difference in the neighboring cells of the stomata; in the majority of stomata, in each case, there are two of the neighbor-cells, but in India Senna the proportion is one having three neighbor-cells to seven having two, and in the Alexandria the proportion is one having three to two having two.

The so-called *Aden Senna,* which Holmes states to be active, is composed of small, broad, not very acute, hairy leaves, and is believed to be obtained from *C. holosericea* Fres. A false senna from Madras has been identified by E. M. Holmes as the product of *Cassia montana* Hayne. The leaflets are about the size of the Tinnevelly Senna, but are distinguishable by obtuse or rounded ends which are with distinctly mucronate (the tip is, however, often broken off and absent from individual leaves), by the obtuse angles of the lateral veins and by the presence of a well marked network of veins of the under surface. Further, the color of the upper surface is distinctly browner than of the Tinnevelly leaflet. The whole leaves of *Cassia montana* have from 10 to 15 pairs of leaflets, while the Tinnevelly Senna has only from 6 to 8 pairs. In the drug this character can usually be made out by noticing the number of scars on the rachis. For a microscopic description of powder, see H. G. Greenish, *P. J.,* lvi, 694. In detecting the adulteration of senna, the apothecary may avail himself not only of the general physical characteristics of the leaves, but also of the fact that while the senna leaf, containing no tannic acid, does not precipitate ferric chloride, most leaves used in adulteration do alter the ferric solution. The microscopic characteristics of the false leaves, though varying greatly, are almost always very different from those of senna. In the senna leaflets the epidermis from the upper and under surface is very similar. The stomata are numerous; the epidermal hairs are unicellular and deciduous, leaving, when detached, a base which has the appearance of an annular pad, around which the neighboring cells seem to radiate. The parenchyma of the cell has a thick epidermis, and is divided into three layers, the uppermost and lowest of which consist of palisade tissue, and are separated by a zone of very small, rounded, parenchymatous cells. Rosette aggregate crystals of calcium oxalate are scattered throughout the parenchyma, and prismatic crystals, one in each cell, occur clustered around the bast tissue of the principal veins.

3. *Arabian Senna.*—This commercial variety consists of the elongated lanceolate leaflets of wild plants of *C. angustifolia,* gathered in southern Arabia and exported from Hodeida to Port Soudan. Thence it is conveyed to Cairo where it is sometimes mixed with Alexandria Senna before packed for export.

4. *Mecca Senna.*—This article is also known commercially as *Bombay Senna* since it is largely shipped from Arabia to that seaport. It is collected both from wild and cultivated plants of *C. angustifolia.* The leaflets are oblong-lanceolate, on the average longer and narrower than those of *C. acutifolia,* and shorter than those of *C. elongata.* The variety in mass appears brownish-green but sometimes has a yellowish or tawny hue, more like that of India than like that of Alexandria Senna.

Constituents.—The cathartic principles of senna are insoluble in strong alcohol but may be extracted by either water or diluted alcohol. The odorous and coloring principles are soluble in either water or alcohol. It is stated that the activity of senna is destroyed by boiling, although there is some difference of opinion on the subject.

Dragendorff and Kubly in 1866 attributed the productive powers of senna to a substance which they called *cathartic acid* (*cathartin* seems to be a mixture containing this substance). Stockman (*P. J.,* 1885, p. 740) found cathartic acid to be glucosidal. It was further investigated by Gensz (*A. J. P.,* 1893, 334) who assigned it the formula of $C_{30}H_{36}NO_{15}$.

According to Groves (*P. J.,* Oct., 1868), both the ammonium and magnesium salts of cathartic acid are active. Tschirch and Hiepe (*A. Pharm.,* 1900, p. 448) besides cathartic acid obtained a mixture of glucosides, which they called *anthraglucosennin,* also *sennanigrin* from which they obtained emodin and chrysophanic acid. Tutin (*Tr. Chem. Soc.,* 1913, ciii, p. 2006) inclines to the opinion that cathartic acid is not a chemical individual. He finds that the only anthraquinone derivatives present are rhein and aloe-emodin with glucosides of the same. (For further account of these principles see under *Rheum.*)

Other peculiar substances which have been found in senna, but probably are not connected with its purgative property, are *sennacrol* and *sennapicrin* (Dragendorff), *sennarhamnetin* (Tschirch and Hiepe), *kaempferol,* $C_{15}H_6O_2(OH)_4$, and its glucoside *kempferin* (Tutin), and a small amount of essential oil.

Kaempferol is a trihydroxy-flavanol and may be extracted from acid aqueous extractions of senna with ether, which also extracts some emodin.

Some observations (published in the *J. P. C.,* Jan., 1874) upon the effect of certain solvents upon senna seem to be of sufficient interest to the pharmacist to deserve being noted. From this it would appear that the activity of senna is injured by heat, alkalies or mineral acids. Alcohol does not dissolve the active principles but extracts made with strong alcohol possess in a high degree the odor and taste of senna, and taken internally, imparts without purging a deep-yellow color to the urine, which the alkalies change to red. The leaves exhausted by alcohol have all their purgative effect, but lose the power of affecting the urine so that an alkaline solution shall color it red. The fact that alcohol removes the odor and taste of senna without affecting its purgative action may sometimes be advantageously applied in cases in which the taste of senna is extremely offensive. L. Siebold, after experimenting with senna leaves washed with alcohol, arrived at the following conclusions: (1) Strong spirit does not remove any of the active principle from senna leaves; (2) the therapeutic action of cathartic acid is assisted by one or more of the constituents yielded by senna to strong alcohol, though these constituents produce no purgative effect when taken alone; (3) senna exhausted by alcohol is a reliable and pleasant purgative, but somewhat weaker in its action than the unexhausted leaves. These conclusions have been confirmed by Maurin (*Rep. Pharm.,* 1921, xxxiii, 228).

When an extract of senna slightly acidified is shaken with ether, the ether solution will give the Bornträger reaction (a pink or red color with ammonia water). If the ether solution is agitated with a saturated solution of nickel acetate, the aqueous layer will develop a red color; on separating and adding potassium hydroxide solution a violet precipitate forms which Beal and Okey state is a characteristic test for senna.

Incompatibles.—Many substances produce precipitates with the infusion of senna, but it does not follow that they are all medicinally incompatible, as they may remove only inert ingredients. Cathartic acid is precipitated by infusion of galls and solution of lead subacetate. Lead acetate and tartar emetic which disturb the infusion, have no effect upon the solution of this substance.

Uses.—Senna was first used as a medicine by the Arabians. It was noticed in their writings as early as the ninth century, and the name itself is Arabic. Like the other cathartics of the anthraquinone series, its action is chiefly upon the lower bowel, and is therefore especially suitable in *habitual costiveness.* It increases the peristaltic movements of the colon by its local action upon the intestinal wall. The tendency to gripe may be obviated by combining it with aromatics or with a saline laxative. The coloring matter of senna is absorbable, and twenty or thirty minutes after the ingestion of the drug it appears in the urine and may be recognized by a red color on the addition of ammonia. It is asserted also that the milk of nursing women acquires purgative properties after the administration of senna.

Dose, one-half to two drachms (2.0–7.7 Gm.).

Off. Prep.—Confectio Sennæ, *Br., N. F.;* Fluidextractum Sennæ, *U. S.;* Infusum Sennæ, *Br.;* Infusum Sennæ Compositum, *N. F.;* Pulvis Glycyrrhizæ Compositus, *U. S., Br.;* Syrupus Sennæ (from Fluidextract), *U. S., Br.;* Tinctura Sennæ Composita, *Br.;* Mistura Sennæ Composita (from Infusion), *Br.;* Elixir Cascaræ Sagradæ Compositum (from Fluidextract), *N. F.;* Elixir Catharticum Compositum (from Fluidextract), *N. F.;* Species Laxativæ, *N. F.;* Syrupus Ficorum Compositus, *N. F.;* Syrupus Sennæ Aromaticus, *N. F.;* Syrupus Sennæ Compositus, *N. F.*

SENNÆ FRUCTUS. Br.

SENNA PODS

"Senna Pods are the dried ripe fruits of Cassia acutifolia, *Delile,* and of Cassia angustifolia, *Vahl.*" *Br.*

Senna pods, while regarded as an adulterant in the U. S. P. X in that the quantity is restricted, are official in the Br. Pharm. They are described as follows: "About five centimetres long, and from two to two and a half centimetres wide; broadly oblong or somewhat reniform; pale green; brownish in the centre above the seeds; very flat; rounded at the base, slightly mucronate at the apex. Pericarp papery. Seeds obovate-cuneate, flattened. Odor and taste slight." *Br.*

Experiments conducted by Ralph Stockman (*C. D.,* 1915, 156) with fluidextracts of whole senna pods, the pericarp freed from the seeds, and the whole seeds showed that the first gives the most violent purging, severe griping and sometimes sickness and faintness; the second is best, giving satisfactory purgation with least griping; and the last is the weakest purgative and causes considerable pain and griping.

Uses.—They were preferred by the Arabian and medieval physicians of Europe to the leaves, while Pereira states that they are much milder in their operation than the leaflets. This has been explained by the researches of E. F. Salmon, who has found that they contain about 25 per cent. more cathartic acid and emodin than the leaves, but no resinous principle or volatile oil. (*P. J.,* Oct., 1889.) The griping of senna being largely due to the resin, it is *a priori* to be expected that the pods would act more kindly than the leaves. A. W. Macfarlane has found this to be actually the case. From six to twelve pods for the adult, or from three to six for the young or very aged, infused in a claret-glass of cold water, in his experience, act very mildly but very thoroughly upon the whole intestine.

Dose, from one-half to one drachm (2.0–3.9 Gm.).

SERPENTARIA. U. S. (Br.)

SERPENTARIA Serpent.

" Serpentaria consists of the dried rhizome and roots of *Aristolochia Serpentaria* Linné, known in commerce as Virginia Snakeroot, or of *Aristolochia reticulata* Nuttall, known in commerce as Texas Snakeroot (Fam. *Aristolochiaceæ*). Serpentaria contains not more than 10 per cent. of its overground stems and not more than 2 per cent. of other foreign organic matter, and yields not more than 10 per cent. of acid-insoluble ash." *U. S.* " Serpentary Rhizome is the dried rhizome and roots of Aristolochia Serpentaria, *Linn.,* and of Aristolochia reticulata, *Nutt.*" *Br.*

Serpentariæ Rhizoma, *Br.;* Serpentary Rhizome; Virginia Serpentaria; Virginia Snakeroot; Texas Snakeroot; Snakeweed; Pelican-flower, Sangrel; Radix Colubrina; Radix Viperina; Serpentary, Sangree; Serpentaire de Virginie, Couleuvrée de Virginie, *Fr.;* Virginische Schlangenwurzel, *G.*

Many species of Aristolochia have been employed in medicine. Their supposed possession of emmenagogue properties has given origin to the name of the genus. Several of the non-official species are described in Part II.

Aristolochia Serpentaria is a perennial herb, with a short, slender, curved and oblique rhizome and numerous slender roots. Several stems often rise from the same rhizome. They are about eight or ten inches in height, slender, round, flexuose, jointed at irregular distances, and frequently reddish or purple at the base. The leaves are oblong-cordate, acuminate, entire, of a pale yellowish-green color, and supported on short petioles. The flowers proceed from the joints near the root, and stand singly on long, slender, round, jointed peduncles, which are sometimes furnished with one or two small scales, and bend downward so as nearly to bury the flower in the earth or decayed leaves. The tube of the calyx is curved like the letter S, enlarged at the base (ovary) and at its throat, the short limb being obtusely three-lobed. The anthers—six or twelve in number—are sessile, attached to the under part of the stigma, which is fleshy and from three to six-lobed. The fruit is an hexangular, six-celled capsule, containing several small flat seeds. The plant grows in rich shady woods from Connecticut west to Michigan and Missouri and south to Florida and Louisiana. On account of the rather large use of serpentaria the drug is becoming scarcer and attempts at cultivation have been made. (See *Proc. A. Ph. A.,* 1905, liii, p. 275, and *West. Drug.,* xxvii, 775.)

A. hastata (Nuttall.) Duchartre is now considered to be nothing more than a variety of *A. Serpentaria,* from which it differs in having hastate, acute, somewhat cordate leaves, and the lip of the corolla ovate. It flourishes on the banks of the Mississippi, in the Carolinas, and elsewhere. Its root scarcely differs from that of the official plant, and is frequently mixed with it.

A. reticulata Nuttall, known as *Texas Serpentaria* has a root similar to that of *A. Serpentaria* from which numerous short, slender, round, flexuose, jointed stems arise, usually simple, but sometimes branched near the root. The older stems are slightly villous, the young densely pubescent. The leaves, which stand on very short villous petioles, are round or oblong-cordate, obtuse, reticulate, very prominently veined, and villous on both sides, especially upon the veins. From the lower joints of the stem four or five hairy, jointed peduncles proceed, which bear small leafy villous bracts at the joints, and several flowers on short pedicels. The flowers are small, purplish, and densely pubescent, especially at the base and on the ovary. The hexangular capsule is deeply sulcate. This species grows in rich woods in Louisiana, Texas, Arkansas, and Oklahoma.

Description and Physical Properties.—" *Unground Serpentaria.*—Rhizome oblique, subcylindrical, more or less curved, from 10 to 30 mm. in length and from 1 to 2 mm. in diameter; externally dark brown, upper portion with short stem-bases and lower and lateral portions with numerous long, thin, nearly straight, yellowish-brown roots; fracture short; internally yellowish-white; wood with broad, eccentric wedges; odor camphoraceous, terebinthinate; taste bitter, aromatic.

" *Structure.*—Rhizome having an outer layer of epidermal cells; a cortex of from 10 to 15 rows of parenchyma; inner bark sometimes showing strongly lignified bast-fibers, either single or distributed in a more or less interrupted circle; a xylem of broad wood-wedges separated by medullary rays, the latter about 8 cells wide, and with walls strongly lignified and with numerous simple pores; pith eccentric, with polygonal cells with lignified and porous walls; starch in the cells of cortical parenchyma, medullary rays and pith. Stem with an interrupted circle of from 6 to 10 fibro-vascular bundles, a cortex with a prominent continuous ring of strongly lignified cells, and a few non-glandular hairs.

" *Powdered Serpentaria.* — Grayish - brown; starch grains numerous, single and 2- to 4-compound, the individual grains more or less spherical or plano-convex, frequently with a central cleft and from 0.003 to 0.018 mm. in diameter; lignified elements numerous, consisting of tracheæ, wood-fibers, medullary ray cells and pith cells; occasionally a few non-glandular hairs from the stem." *U. S.*

"Rhizome of Aristolochia Serpentaria tortuous and slender, about two centimetres long and three millimetres thick; on the upper surface the remains of slender, aerial stems, and on the under surface numerous wiry interlacing roots, often about seven centimetres long. Both rhizome and roots dull yellowish-brown. Characteristic odor; taste strong, camphoraceous, bitter. Ash not more than 10 per cent. Rhizome and roots of Aristolochia reticulata resemble the foregoing, but are longer and thicker, and the roots are straighter." *Br.*

Holm has published an illustrated article on the pharmacognosy of serpentaria, including the morphology of the stems and leaves. (*M. R.*, xvi, p. 276.)

Virginia Snakeroot is collected for the market in Virginia, North and South Carolina, Tennessee and Georgia. Texas Snakeroot is chiefly gathered in Texas.

Texas serpentaria contains a larger percentage of volatile oil than does the other variety of the drug. The color of serpentaria, which in the recent root is yellowish, becomes brown on keeping.

The roots of *Spigelia marilandica* are sometimes found associated with serpentaria. They may be distinguished by the absence of the terebinthinate odor, and, when the stem and foliage are attached, by the peculiar character of these parts. (See *Spigelia.*)

Constituents.—Serpentaria contains a volatile oil and a bitter principle. The volatile oil which has a camphor-like odor has been investigated by J. C. Peacock (*A. J. P.*, 1891, 257) who finds it consists of about 60 per cent. of a combined ester of borneol boiling at 211° C., sp. gr. 0.9849; the remainder being a terpene (probably pinene) boiling at 157° C., sp. gr. 0.865; a fraction, boiling at from 239° to 240° C., sp. gr. 0.9888 and a small quantity of a bluish-green fluorescent oil which decomposed when distilled even under reduced pressure.

In regard to the bitter principle, which was first described by Chevallier, we have no satisfactory information, although it has been suggested that it may contain some aristolochine.

Aristolochine is a poisonous alkaloid, first isolated by Pohl (*A. E. P. P.*, 1891, xxix, 282), from the seeds of *A. Clematitis* and *A. rotunda.* He obtained it as a yellow crystalline mass, soluble in chloroform, ether, acetone, acetic anhydride, and alcohol, insoluble in petroleum benzin, benzene, and carbon disulphide, almost insoluble in cold water, slightly soluble in hot water. An ultimate analysis gave for its composition $C_{32}H_{22}O_{13}N$. O. Hesse (*P. J.*, 1891, li, 551) found the same alkaloid in *A. argentina* but called it *aristolochic acid.* In the same plant he found four other alkaloids: *aristic acid, aristidinic acid, aristolic acid* and a substance he called *aristolochine* (but different from Pohl's aristolochine). *Aristinic acid* is a resinous substance which has been found in several species including the *A. serpentaria.*

Uses.—Serpentaria is to be classed among the aromatic bitters and in moderate dose acts as a gastric stimulant and is therefore of service in atonic types of *dyspepsia.* In overdose it acts as a local irritant, provoking nausea and griping pains in the bowels, sometimes vomiting and tenesmus. According to Pohl, aristolochine in sufficient dose produces in the higher animals violent irritation of the gastro-intestinal tract and of the kidneys, with death, in coma, from respiratory paralysis.

Dose, fifteen to thirty grains (1 to 2 Gm.).

Off. Prep.—Tinctura Cinchonæ Composita, *U. S., Br.;* Fluidextractum Serpentariæ, *N. F.;* Tinctura Serpentariæ, *N. F., Br.*

SEVUM BENZOATUM. Br.

BENZOATED SUET

"Prepared Suet, 1000 *grammes;* Benzoin, in coarse powder, 30 *grammes.* Melt the Suet, add the Benzoin, and maintain at a temperature of 60° C., for one hour, stirring frequently; strain, and stir until nearly cold. In India, Benzoated Suet should be employed in making the official preparations for which Benzoated Lard (Adeps Benzoatus) is directed to be used." *Br.*

It is also official in the N. F. V under the title *Sevum Benzoinatum* (see Part III).

SEVUM PRÆPARATUM. U. S., Br.

PREPARED SUET Sev. Præp. [Mutton Suet]

"The internal fat of the abdomen of the sheep *Ovis aries* Linné (Fam. *Bovidæ*), purified by melting and straining." *U. S.* "Prepared Suet is the purified internal fat of the abdomen of the sheep, Ovis aries, *Linn.*" *Br.*

Sevum, *U. S.* 1890; Sebum Ovillum; Mutton Suet; Prepared Mutton Tallow; Suif de Mouton Purifié, Graisse de Mouton, *Fr.;* Sebum ovile, *P. G.;* Hammeltalg, Talg, Schöpsentalg, Unschlitt, *G.;* Grasso di Moutone, Grasso duro, *It.;* Sebo de carnero, *Sp.*

Suet is the fat of the sheep, taken chiefly from about the kidneys. It is prepared by cutting the fat into pieces, melting it with a moderate heat, and straining it through linen or flannel. In order to avoid too great a heat, the crude suet is sometimes purified by boiling it in a little water. Mutton suet is of a finer consistence, and requires a higher temperature for its fusion, than any other animal fat. It is very white, sometimes brittle, inodorous, of a bland taste, insoluble in water, and nearly so in alcohol. Boiling alcohol, however, dissolves it, and deposits it upon cooling. It consists, according to Chevreul, of stearin, palmitin, and olein, containing approximately 70 per cent. of stearin and palmitin and 30 per cent. of olein. These principles are described under *Olea Fixa.*

Description and Physical Properties.—"A white, solid fat, having, when fresh, a slight characteristic odor and a bland taste. It becomes rancid on prolonged exposure to the air and must not then be used. Prepared Suet is insoluble in water and in cold alcohol. It is soluble in 45 parts of boiling alcohol, in about 60 parts of ether, and slowly dissolves in 2 parts of purified petroleum benzin. From its solution in the latter, when allowed to stand in a stoppered flask, it slowly separates in a crystalline form.

"Prepared Suet melts between 45° and 50° C. and congeals between 37° and 40° C. Saponification value, not less than 193 and not more than 200. Iodine value: not less than 33 and not more than 48. One Gm. of Prepared Suet, dissolved in 50 cc. of hot neutralized alcohol, with a few drops of phenolphthalein T.S. added, requires not more than 0.6 cc. of tenth-normal sodium hydroxide to produce a pink color (*free acid*).

"Preserve in well-closed containers impervious to fat." *U. S.*

"Firm, white, unctuous. Nearly inodorous; taste bland. *Saponification value* 192 to 195; *iodine value* 33 to 46; *acid value* not more than 2.0; melting point 45° to 50° C.; *refractive index* at 60° C., 1.4490 to 1.4510." *Br.*

E. Dieterich examined a large number of samples of mutton and beef suet, and found that they were without exception acid and that neutral suet does not exist. The melting point of mutton suet is between 48.5° and 50.5° C.; that of beef suet, between 47.5° and 48° C. The specific gravity of mutton suet lies between 0.937 and 0.952; that of beef suet, between 0.943 and 0.952. (*A. Pharm.*, 1887, 496.)

Off. Prep.—Sevum Benzoatum, *Br.;* Sevum Benzoinatum, *N. F.*

SINAPIS NIGRA. U. S.

BLACK MUSTARD Sinap. Nig. [Brown Mustard]

"Black Mustard is the dried ripe seed of *Brassica nigra* (Linné) Koch and *Brassica juncea* (Linné) Cosson and varieties related to these species (Fam. *Cruciferæ*). Black Mustard contains not more than 5 per cent. of other seeds or other foreign organic matter, and yields not less than 0.6 per cent. of volatile oil of mustard (calculated as allyl isothiocyanate)." *U. S.*

Sinapis Nigræ Semina, *Br.* 1898; Black Mustard Seeds; Semina Brassicæ; Moutarde noire, *Fr.;* Semen Sinapis, *P. G.;* Senfsamen, Schwarzer Senf.; Senape nera, *It.;* Mostaza (Semilla de), *Sp.*

The U. S. IX recognized two forms of mustard seed, the so-called black and white mustard, but the latter was dropped at the tenth revision, as it had largely passed out of use as a medicine because of its inferior strength. Linnæus divided the mustards into two genera, *Brassica* and *Sinapis,* and subsequent botanists have greatly disagreed as to whether they should be considered identical or not. The revisers of the U. S. P. have adopted the opinion of Engler and Prantl and of Britton and Brown, that the two genera are distinct. The genus *Sinapis* differs from *Brassica* in that the pods of the former are terminated by a long, flat, sword-like beak, whereas in *Brassica* the beak is cylindrical or conical.

Common black mustard (*Brassica nigra*) is an annual herb, with a stem three or four feet in height, divided and subdivided into numerous spreading branches. The leaves are petiolate and variously shaped. Those arising from the root are large, rough, lyrate-pinnate, and unequally toothed, those on the stem are smooth, and less lobed, and the uppermost are entire and narrow. The flowers are small, yellow, and stand closely together upon pedicels at the upper part of the branches. The pods (siliques) are smooth, erect, nearly parallel with the branches, quadrangular, and furnished with a slender beak; seeds numerous, dark brown.

Brassica nigra is a native of Europe and cultivated in our gardens, and has become naturalized in some parts of this country. Many forms of the plant have been described in horticultural literature. The flowers appear in June. The seeds are kept in the pharmacies, both whole and in the state of very fine powder as prepared by the manufacturers for the table. The latter is sometimes mixed with spices and ground into a smooth paste with water in a mill resembling a paint mill, and then is known as *French mustard* or *German mustard.* The seeds of *Sinapis alba* when treated in the same manner, but without added spices is known as *English mustard.*

Brassica juncea (L.) Coss. (*Sinapis juncea* L.) or *Chinese mustard* is a coarse annual herb indigenous to Asia and extensively grown in India and southern Russia. It possesses large ovate to obovate and lyrate radical leaves with angled or toothed blades and two kinds of stem leaves, the lower toothed and petiolate, the upper oblong to oblong-lanceolate and usually sessile. This species has numerous horticultural varieties.

Under the name of *Sinapis alba,* the U. S. formerly recognized "The ripe seeds of *Sinapis alba* Linné (Fam. *Cruciferæ*), without the presence or admixture of more than 5 per cent. of other seeds or other foreign matter." *U. S. IX.*

Yellow or *white mustard* is a native of Europe and is extensively cultivated, being occasionally spontaneous, in the United States. The commercial supplies are obtained from England, Holland, Germany and California. It is rather smaller than the preceding species. The lower leaves are deeply pinnatifid, the upper sublyrate, and all irregularly toothed, rugged, with stiff hairs on both sides, and pale green. The flowers are in racemes, with yellow petals, and linear, green calycine leaflets. The pods are spreading, bristly, rugged, roundish, swelling in the position of the seeds, ribbed, and provided with a very long ensiform beak.

The seeds of white mustard were officially described as follows: "Sub-globular, from 1.5 to 2.5 mm. in diameter; testa yellowish, nearly smooth; embryo yellowish, oily, with two large cotyledons; inodorous, taste mildly pungent, acrid. The powder is light yellowish or pale brownish-yellow, developing a slight odor when moistened; when examined under the microscope it exhibits numerous tissues of the embryo containing small aleurone grains and a fixed oil, the latter forming in large globules on the addition of hydrated chloral T.S.; fragments of seed-coat comparatively few, nearly colorless, with small, characteristic stone cells and large epidermal cells, the outer walls being mucilaginous. The powder contains few or no starch grains. White mustard does not yield allyl isothiocyanate upon distillation with steam (distinction from *Black Mustard*). White Mustard yields not more than 9 per cent of ash." *U. S. IX.*

For an illustrated monograph on the pharmacognosy of white mustard, see Winton and Moeller, "*Microscopy of Vegetable Foods.*" The only adulterant of white mustard are the seeds of the white Indian *colza,* obtained from *Brassica campestris* Sarson (L.) Prain. They are distinguished in having a more pronounced ridge over the radicle. Under the microscope the seeds have an indistinct epidermis, the collenchymatous subepidermal layer is wanting, and the palisade cells are quite large compared with white mustard.

The seeds of *Brassica ibertifolia* were formerly sold as true white mustard seed. O. Harz examined some obtained from Bavaria, which had been returned by customers to the dealers on account of their bitter and disagreeable taste. He furnishes characteristic microscopical tests for distinguishing the false from the true mustard seed. His statement, however, that powdered white mustard seed when mixed with water is odorless, and that the false gives off a strong odor of essential oil of mustard, would seem to be a good reason, if correct, for preferring the false seed. (*P. J.,* 1887, 478.)

The seeds of *Brassica juncea* afford a very fine mustard flour, and, according to Paul Birkenwald, yield 1.67 parts per hundred of volatile oils, against 1.89 parts per hundred by the true black mustard seed. (*S. W. P.,* 1888.)

Description and Physical Properties.—"*Unground Black Mustard.*—Spheroidal or irregularly spheroidal, from 1 to 1.6 mm. in diameter; testa dark reddish-brown, sometimes yellowish-brown and with a grayish tinge, minutely pitted or reticulate; embryo greenish-yellow or dark yellow, oily, with 2 large cotyledons; odor when dry, slight; on crushing and moistening, very irritating, strongly pungent, characteristic; taste strongly pungent, acrid.

"*Powdered Black Mustard.*—Light brown or greenish-brown; consisting mostly of tissues of the embryo, the cells containing small aleurone grains and a fixed oil, the latter forming in large globules on the addition of chloral hydrate T.S.; fragments of seed-coat conspicuous, with large polygonal, dark yellow areas, enclosing small yellowish stone cells, each of the latter with a dark lumen, few or no starch grains. In the preparation of powdered Black Mustard, a portion of its fixed oil may be removed to facilitate the powdering." *U. S.*

Both white and black mustard afford a powder, which has a somewhat unctuous appearance, and cakes when compressed. This is commonly called *flour of mustard,* or simply *mustard,* and is prepared by crushing and pounding the seeds and then sifting them, the purest flour being obtained by a second sifting. Both the black and the white seeds are used in its preparation. Formerly it was adulterated with wheat flour colored by turmeric, to which cayenne pepper was added to render the mixture sufficiently hot. Pure mustard powder contains very few starch granules, but was formerly adulterated with farinaceous powders; the U. S. P. VIII required that Mustard should conform to the following test: "If 1 Gm. of powdered White (or Black) Mustard be exhausted by slow percolation with alcohol, and the marc mixed with 200 cc. of water and heated to boiling, and if, after cooling, sufficient cold water be added to make the mixture measure 1000 cc., the addition of 4 cc. of tenth-normal iodine V.S. should not produce a dark blue color (limit of *starch*)." *U. S. VIII.* An excellent basic monograph on the pharmacognosy of black mustard is that given by Winton and Moeller in "*The Microscopy of Vegetable Foods.*" Tschirch and Oliva have made a comparative study of the seeds of the *Cruciferæ,* with special reference to the variations found in the seed-coat of the several species of mustard. (*S. W. P.,* xliii, p. 614.) Spaeth gives the results of chemical and microscopical study of the mustards and some of their adulterants in *Ph. Zentralh.,* xlix, p. 698. Carles has also contributed a valuable article on the pharmacognosy of the different mustard seeds and the commercial varieties of mustard flour in *J. P. C.,* 1913, pp. 438 and 535.

Assay.—Methods of assay for mustard seed have been proposed by several authorities (see Service and Regulatory Announcements of U. S. Dept. of Agriculture through *A. J. P.,* 1917, lxxxix, 550; see also *C. U. C. P. Al. J.,* 1916, xxiii, 169). The method of the U. S. P. is based on that of Wehrman, Wegener, Braunworth and Meyer (*A. Pharm.,* 1915, 306) which was awarded the prize of the German Apotheke Verein in 1913. It is as follows: "Place 5 Gm. of Black Mustard, in coarse powder, in a 200 cc. flask, add 100 cc. of water, stopper tightly, and macerate for two hours at about 37° C. Then add 20 cc. of alcohol, and distil about 70 cc. into a 100 cc. graduated flask containing 10 cc. of ammonia T.S. and 20 cc. of tenth-normal silver nitrate. Mix thoroughly, stopper, allow the distillate to stand over night, then heat on a bath of boiling water, cool, add water to make 100 cc., and filter, rejecting the first portions. Acidify 50 cc. of the filtrate, representing 2.5 Gm. of Black Mustard, with about 5 cc. of nitric acid and titrate with tenth-normal potassium thiocyanate, using 2 cc. of ferric ammonium sulphate T.S. as indicator. Each cc. of butyrorefractometer reading (15.5° C.), 74.5 to 0.004957 Gm. of allyl isothiocyanate." *U. S.*

Viehoever, Clevenger and Ewing report that some supplies recently imported from Europe as rape seed but offered for sale as mustard seed represented the seed of *Brassica campestris* *chinoleifera.* According to these authors the volatile oil obtained from this variety of seed is *crotonyl isothiocyanate* which is not a suitable substitute for mustard oil either for condimental, bactericidal or medicinal use. More than 40 per cent. of fixed oil was found which had the general composition of the rape oils. For further details including gross and microscopical features, see *J. Agr. Res.,* 1920, xx, 117, and *J. A. Ph. A.,* 1921, x, 16.

The most common adulteration of black mustard is *charlock,* which is the seeds of *Brassica arvensis* (L.) Ktze. This plant is especially abundant in the northwestern part of the United States and the Dakota mustard contains varying mixtures of brown mustard and charlock. The presence of charlock is very easily determined microscopically by the use of a solution of chloral hydrate which changes the color of the palisade cells to a crimson red.

Constituents.—Mustard seeds yield upon pressure a fixed oil, called *oil of mustard,* of a greenish-yellow color, little odor, and a mild not unpleasant taste; and the portion which remains is even more pungent than the unpressed seeds. The fixed oil of mustard consists of the glycerin compounds of stearic, oleic, and *erucic* or *brassic acid,* $C_{22}H_{42}O_2$, a homologue of oleic acid. Small quantities of *behenic acid,* $C_{22}H_{44}O_2$, also occur in oil of black mustard.

According to F. W. Widmayer (*D. C.,* 1904, 8) the fixed oil from yellow seed is of a greenish-yellow color, that of the brown seed a much darker shade. Both have but little odor and a mild, not unpleasant taste. Mustard seed oil is a semi-drying oil. The analytical data showing maximum and minimum results by M. L. Tolman and L. S. Munson on five samples are as follows: Specific gravity at 15.5° C., 0.9147 to 0.9193; butyrorefractometer reading (15.5° C.), 74.5 to 76.5; index of refraction at 15.5° C., 1.4750 to 1.4762; Maumené number 61.4 to 79.4; specific temperature reaction 130.9 to 190.3; Hübl number, 98.4 to 113.0; saponification value, 173 to 182.8; solidification from −8° to −18° C. Widmayer states that a remarkable feature of this oil is its penetrating or diffusing power; barrels that will hold olive, cotton seed, or petroleum oil, or even new oil or alcohol, invariably leak on being filled with it.

It has been long known that black mustard seeds yield by distillation with water a very pungent volatile oil, containing sulphur. This oil does not pre-exist in the seeds, but is produced by the action of water. Hence the very slight degree of odor in the seeds when bruised in a dry state, and their pungency when water is added. This oil is produced by the decomposition of a compound, *sinigrin* (*potassium myronate*), occurring there. This sinigrin, $C_{10}H_{18}KNS_2O_{10}$, is decomposed under the influence of *myrosin,* an albuminous ferment which is present, yielding C_3H_5CNS (*allyl isosulphocyanate*), $HKSO_4$ (acid potassium sulphate), and $C_6H_{12}O_6$ (glucose). "The aqueous solution of myrosin coagulates at 60° C., and then becomes inactive; hence mustard seed which has been heated to 100° C., or has been roasted, yields no volatile oil, nor does it yield any if powdered and introduced at once into boiling water."

An analogous but different reaction takes place in the case of white mustard; this contains a glucoside called *acrinyl sulphocyanate* (parahydroxy benzylisothiocyanate), C_7H_7OCNS, *sinapine bisulphate,* $C_{16}H_{25}NSO_9$, and sugar, $C_6H_{12}O_6$, an albuminoid substance being formed at the same time.

The analyses of mustard seeds and mustard flour, given in the table below, are by Piesse and Stansell. (*Analyst,* 1880, p. 161.)

Analysis of Brown Mustard.	Whole seeds.	Ground.	
	Cambridge.	Superfine.	Fine.
Moisture	8.52	4.35	4.52
Fatty oil	25.54	36.96	38.02
Cellulose	9.01	3.09	2.06
Sulphur	1.28	1.50	1.48
Nitrogen	4.38	4.94	5.01
Albuminoids	26.50	29.81	30.25
Myrosin and albumin	5.214	6.46	6.78
Soluble matter	24.22	31.14	32.78
Volatile oil	0.047	1.437	1.50
Potassium myronate	1.692	5.141	5.366
Ash	4.98	5.04	4.84

J. U. Lloyd (*A. J. P.,* 1898, p. 433) has proposed standards for black and white mustard seed, mainly directed towards limiting the proportion of starch; the latter is not a constituent of ripe mustard seed, but commercial mustard nearly always contains starch, due to starch-bearing seeds accidentally present in the mustard seed, or to fraudulent admixture.

Uses.—Mustard seeds were formerly sometimes employed in the whole state for their laxative effects. The powder, commonly called simply mustard, in the quantity of from one to two teaspoonfuls (4–8 Gm.), is an efficient and prompt—although unpleasant—stimulant emetic, especially valuable in *narcotic poisoning.* As a condiment mustard acts as a stimulant to the gastric mucous membrane, increasing according to Gottlieb (*A. E. P. P.,* 1894, xxxiii, 261), also the pancreatic secretion. By virtue of this stimulant action it will sometimes relieve obstinate *hiccough.*

But mustard is most valuable as a rubefacient. Mixed with water in the form of a cataplasm, and applied to the skin, it very soon produces redness with burning pain, which in less than an hour usually becomes insupportable. When a speedy impression is not desired, especially when the sinapism is applied to the extremities, the powder should be diluted with varying proportions of wheat flour. Care should be taken not to allow the application to continue too long, as vesication with obstinate ulceration, and even sphacelus, may result. This caution is particularly necessary when the patient is insensible and the degree of pain can afford no criterion of the sufficiency of the action. In making a mustard plaster the admixture of alcohol, vinegar, or other fluid than water, should be avoided as hindering the development of the volatile oil. The volatile oil is powerfully rubefacient, and capable of producing speedy vesication, but certainly is less controllable than is the mustard poultice. (See *Linimentum Sinapis Compositum,* N. F., Part III.) The volatile oil of mustard has been given internally in *colic.* In overdoses it is highly poisonous, producing gastro-enteric inflammation, and probably perverting the vital processes by pervading the whole system. Its odor is perceptible in the blood, and is said to impart the smell of horse-radish to the urine. A *spirit of mustard* may be prepared by macerating, for two hours, 250 parts of powdered black mustard with 500 parts of cold water, then adding 120 parts of alcohol of 86 per cent., and distilling over 120 parts of spirit.

Dose, of mustard seed, one to two drachms (4–8 Gm.).

SODII ACETAS. U. S.

SODIUM ACETATE Sod. Acet.

"Sodium Acetate contains not less than 59.97 per cent. and not more than 62.96 per cent. of $NaC_2H_3O_2$, corresponding to not less than 99.5 per cent. of the crystallized salt [$NaC_2H_3O_2 \cdot 3H_2O$]." *U. S.*

Acetate of Soda; Acetas Sodicus (Natricus), Terra Foliata Tartari Crystallisata, Terra Foliata Tartari; Acetate de Sodium (de Soude), *Fr. Cod.;* Natrium Aceticum, *P. G.;* Natriumacetat, Essigsaures Natron, *G.;* Acetato di Sodio, *It.*

Sodium acetate may be easily prepared by adding crystals of sodium carbonate to acetic acid until it is neutralized, filtering, concentrating the solution, and crystallizing. It is prepared in the large way in the manufacture of crude pyroligneous acid, for the purpose of being decomposed, so as to yield the official acetic acid, by the action of sulphuric acid. The steps of the process by which it is made from the crude acid have been given under *Acidum Aceticum.*

Description and Physical Properties.—"Colorless, transparent, monoclinic prisms, or a granular, crystalline powder. It is odorless, or has a faint, acetous odor. It is efflorescent in warm, dry air. One Gm. of Sodium Acetate is soluble in 0.8 cc. of water and in 19 cc. of alcohol, at 25° C.

"Heated to about 58° C., the salt begins to liquefy. At about 120° C., it becomes anhydrous; at a higher temperature it is decomposed, with the evolution of inflammable, empyreumatic vapors, leaving a residue of sodium carbonate and carbon. An aqueous solution of the salt responds to the reactions, for sodium, and for acetates.

"Dissolve 2 Gm. of Sodium Acetate in 20 cc. of distilled water, and add 2 drops of phenolphthalein T.S.: the pink color produced, if any, is discharged by the addition of 0.1 cc. of tenth-normal sulphuric acid (*alkalinity*). A saturated aqueous solution of Sodium Acetate is not rendered turbid by the addition of sodium bitartrate T.S. (*potassium*). An aqueous solution of the salt meets the requirements of the test for *heavy metals.* An aqueous solution of the salt meets the requirements of the test for *arsenic.*

"**Assay.**—Proceed as directed under the assay for alkali salts of organic acids. Each cc. of half-normal sulphuric acid corresponds to 0.04102 Gm. of $NaC_2H_3O_2$.

"Preserve in well-closed containers." *U. S.*

Sodium acetate, when crystallized, consists of one acetic acid molecule, one atom of sodium and 3 molecules of water.

Uses.—Sodium acetate is diuretic, acting much like potassium acetate, but is rarely used as a medicine. It is employed principally to yield acetic acid by the action of sulphuric acid. In prescribing this salt, the fact, first noticed by Violette, should not be forgotten, that the mixture of equal parts of it and potassium nitrate, if heated, explodes with great violence. (*N. R.,* April, 1873.)

Dose, twenty grains to two drachms (1.3–7.7 Gm.).

SODII ARSENAS. N. F.

SODIUM ARSENATE Sod. Arsen. [Natrii Arsenas, P. I.]

"Sodium Arsenate contains not less than 58.98 per cent. nor more than 61.92 per cent. of anhydrous sodium arsenate (di-sodium ortho-arsenate), corresponding to not less than 99 per cent. of the crystallized salt ($Na_2HAsO_4 \cdot 7H_2O = 312.08$)." *N. F.*

Arsenias Natricus (Sodicus); Sodium Arseniate; Arseniate of Soda; Natrium Arsenicum, *Fr. Cod.;* Arseniate de Sodium Officinal, Arséniate Disodique, *Fr.;* Natriumarsenat, Arsensaures Natron, *G.;* Arseniato bisodico, *It.;* Arseniato sodico, *Sp.*

The U. S. P., of the tenth revision, dismissed both the crystallized and anhydrous sodium arsenate, but they have been admitted to the N. F. Only the anhydrous salt is recognized in the Br. The exsiccated salt is to be preferred as the crystallized arsenate is apt to contain varying proportions of water of crystallization. The N. F. obviates the consequent uncertainty of dosage by inserting an assay provision.

No process for this salt is now official. In that formerly recommended (for details see *U. S. D.,* 19th ed., p. 1127) arsenic trioxide, sodium nitrate and sodium carbonate are heated together. The arsenic trioxide is converted into arsenic acid at the expense of the nitric acid of sodium nitrate, and then combines with the sodium of both salts, carbon dioxide and nitrous fumes being given off. The reaction seems to be as follows:

$$As_2O_3 + 2NaNO_3 + Na_2CO_3 + H_2O = 2Na_2HAsO_4 + N_2O_3 + CO_2$$

Description and Physical Properties.—"Sodium Arsenate occurs is colorless, transparent, monoclinic prisms; odorless. Efflorescent in dry air, and somewhat deliquescent in moist air. *Great caution must be used in tasting it and then only in very dilute solutions.* One Gm. of Sodium Arsenate dissolves in 1.5 cc. of water at 25° C.; also in about 1 cc. of boiling water; slightly soluble in alcohol at 25° C.; nearly insoluble in boiling alcohol.

"When gently heated, the salt loses five molecules of water, and is converted into a white powder. At a higher temperature it loses all of its water of crystallization; when strongly heated, the salt fuses, and at a red heat it is converted into pyroarsenate. Sodium Arsenate responds to the tests for identity and purity prescribed under Sodii Arsenas Exsiccatus when taken in proportionate amount.

"**Assay.**—Dissolve about 0.5 Gm. of Sodium Arsenate, accurately weighed, in 25 cc. of distilled water, heat the solution to 80° C. and add 10 cc. of hydrochloric acid and 3 Gm. of potassium iodide. Allow the mixture to stand for fifteen minutes at 80° C., then cool and titrate it with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.0092985 Gm. of Na_2HAsO_4. Each Gm. of Sodium Arsenate corresponds to not less than 63.44 cc. nor more than 66.59 cc. of tenth-normal sodium thiosulphate.

"Preserve it in well-closed containers." *N. F.*

Anhydrous sodium arsenate has the composition Na_2HAsO_4; in crystals it sometimes contains 12 molecules of water, equal to 53.73 per cent. of its weight. According to the official formula, this salt crystallizes with 7 molecules of water, or 40.39 per cent. "The latter salt loses 40.38 per cent. of its weight when dried at 300° F., becoming anhydrous. An aqueous solution of 12.4 grains of anhydrous arsenate of sodium, acidulated with acetic acid, requires not less than 34 grains of acetate of lead for complete precipitation." *Br.* 1885. If the temperature of a solution of the salt be kept at 30° C., crystals will be deposited which contain 4 molecules of water. J. Lefort examined 10 different samples of the salt, obtained from as many different sources, and found their water of crystallization to vary from 44.05 to 57.45 per cent. (*J. P. C.*, 1880, 487.)

Uses.—Sodium arsenate possesses the therapeutic properties of arsenic. (See *Arseni Trioxidum.*) It is usually exhibited in solution. According to H. N. Moyer it is less irritating to the stomach than the more frequently used potassium arsenite. It is also occasionally employed hypodermically.

Dose, of crystallized sodium arsenate, one-twentieth to one-eighth of a grain (0.003–0.008 Gm.).

Off. Prep.—Sodii Arsenas Exsiccatus, *N. F.*

SODII ARSENAS EXSICCATUS.
N. F. (Br.)

EXSICCATED SODIUM ARSENATE Sod. Arsen. Exsic.

"Exsiccated Sodium Arsenate contains, when dried to constant weight at 150° C., not less than 98 per cent. of Na_2HAsO_4 (185.97)." *N. F.*

Sodii Arsenas Anhydrosus, *Br.;* Anhydrous Sodium Arsenate; Natrium Arsenicum Exsiccatum; Dried Arsenate of Soda; Arséniate de Soude desséché, *Fr.;* Getrocknetes Natriumarsenate, *G.*

"Sodium Arsenate, in crystals, a sufficient quantity. Break the crystals into small fragments, and allow them to effloresce at a temperature between 40° and 50° C., until they are completely disintegrated; then gradually increase the temperature to 150° C., and continue the drying until the product ceases to lose weight. Reduce it to a fine powder, and transfer it to dry, well-closed containers." *N. F.*

"Anhydrous Sodium Arsenate is obtained by exposing to a temperature of 150° C. crystallised sodium arsenate, which may be prepared by treating with water the product of the fusion of arsenious anhydride with sodium nitrate and sodium carbonate. It contains not less than 98 per cent. of pure anhydrous di-sodium hydrogen arsenate, Na_2HAsO_4." *Br.*

For properties see also *Sodii Arsenas.*

Description and Physical Properties.—"Exsiccated Sodium Arsenate occurs as an odorless, amorphous, white powder. It is slightly hygroscopic. *Great caution must be used in tasting it and then only in very dilute solutions.* One Gm. of Exsiccated Sodium Arsenate dissolves in 3.1 cc. of water at 25° C.; also in 1.3 cc. of boiling water; slightly soluble in alcohol at 25° C.; nearly insoluble in boiling alcohol.

"Its aqueous solution (1 in 20) is alkaline to litmus. It imparts an intensely yellow color to a non-luminous flame. An aqueous solution of the salt (1 in 20) yields a white precipitate with barium chloride T.S., and a dark red precipitate with silver nitrate T.S.; both of these precipitates are soluble in nitric acid.

Dissolve 1 Gm. of Exsiccated Sodium Arsenate in 30 cc. of distilled water, render the solution slightly acid to litmus paper by the cautious addition of diluted sulphuric acid, add 20 cc. of a saturated solution of sodium bicarbonate and titrate the liquid with tenth-normal iodine, using starch T.S. as indicator. Not more than 1 cc. of tenth-normal iodine is required (limit of *arsenite*). Add 1 cc. of ammonium sulphide T.S. to 5 cc. of an aqueous solution of the salt (1 in 100); no dark coloration appears (*lead, copper, or iron*).

"**Assay.**—Dissolve about 0.3 Gm. of Exsiccated Sodium Arsenate, dried to constant weight at 150° C. and accurately weighed, in 25 cc. of distilled water, in a glass-stoppered bottle, heat the solution to 80° C. and add 10 cc. of hydrochloric acid and 3 Gm. of potassium iodide. Allow the mixture to stand in the stoppered bottle for fifteen minutes at 80° C., then cool and titrate it with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. It shows, in the dried salt, not less than 98 per cent. of Na_2HAsO_4. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.0092985 Gm. of Na_2HAsO_4. Each Gm. of Exsiccated Sodium Arsenate, previously dried, corresponds to not less than 105.4 cc. of tenth-normal sodium thiosulphate.

"Preserve it in well-closed containers." *N. F.*

"A white powder. Soluble in 6 parts of *water;* slightly soluble in *alcohol* (90 per cent.). Aqueous solution alkaline to *litmus.* Yields the *reactions* characteristic of sodium and of arsenates. When 0.25 gramme is dissolved in 25 millilitres of *water,* and to the solution 3 grammes of *potassium iodide* and 25 millilitres of *hydrochloric acid* are added, not less than 26.3 millilitres of *N/10 solution of sodium thiosulphate* are required to decolorise the iodine liberated. Yields no characteristic *reactions* for lead, copper, iron, aluminium, calcium, carbonates, chlorides, nitrates, or sulphates. Loses not more than 2 per cent. of its weight when dried at 150° C. (limit of moisture)." *Br.*

Uses.—Dried or exsiccated sodium arsenate is useful when it is desired to exhibit the salt in pill form, but differs in no way in its physiological action from sodium arsenate.

Dose, one-fortieth to one-fifteenth of a grain (0.0016–0.004 Gm.).

Off. Prep.—Liquor Sodii Arsenatis, *N. F., Br.;* Liquor Sodii Arsenatis Dilutus, *N. F.*

SODII BENZOAS. U. S., Br.

SODIUM BENZOATE Sod. Benz.

"Sodium Benzoate, when dried to constant weight at 110° C., contains not less than 99 per cent of $NaC_7H_5O_2$." *U. S.* "Sodium Benzoate may be obtained by neutralising benzoic acid with sodium carbonate. It contains not less than 96 per cent. of pure sodium benzoate, $NaC_7H_5O_2$." *Br.*

Benzoas Sodicus; Benzoate of Soda; Benzoate de Soude, *Fr.;* Natrium Benzoicum, *Fr. Cod.;* Natriumbenzoat, Benzoesaures Natron, *G.;* Benzoato di sodio, *It.;* Benzoato sodico, *Sp.*

Sodium benzoate is easily made by adding benzoic acid to a concentrated hot solution of sodium carbonate or bicarbonate until effervescence ceases, and allowing the solution to cool and crystallize. R. Rother, in order to avoid annoyances in the effervescence mixes four ounces of benzoic acid and two and three-fourths ounces of sodium bicarbonate in an evaporating dish with from two to four fluidounces of alcohol; when a uniform mixture is produced, from three to six fluidounces of water are added, heat applied gently, and the powder granulated.

Description and Physical Properties.—"A white, odorless, amorphous, granular or crystalline powder. It is stable in the air. One Gm. of Sodium Benzoate is soluble in 1.8 cc. of water and in 61 cc. of alcohol, at 25° C. One Gm. is soluble in 1.4 cc. of boiling water.

"When heated, Sodium Benzoate fuses, emitting vapors having the odor of benzoic acid, then chars, and finally leaves a residue of sodium carbonate and carbon. It responds to the reactions for sodium, and for benzoates.

"Diluted sulphuric acid added to 5 cc. of an aqueous solution of Sodium Benzoate (1 in 10) produces a voluminous white precipitate of benzoic acid. Dissolve about 1 Gm. of Sodium Benzoate in 10 cc. of distilled water in a separatory funnel, add 10 cc. of diluted sulphuric acid, and shake out the benzoic acid with 2 successive 20 cc. portions of ether. Evaporate the ether solution and test for chlorinated compounds as directed under *Acidum Benzoicum.* Dissolve 2 Gm. of Sodium Benzoate in 20 cc. of hot distilled water, and add 2 drops of phenolphthalein T.S.: the pink color produced, if any, is discharged by the addition of 0.2 cc. of tenth-normal sulphuric acid (*alkalinity*). Acidulate 10 cc. of an aqueous solution of the salt (1 in 50) with hydrochloric acid and filter: the filtrate does not respond to the test for *heavy metals.*

"**Assay.**—Dry Sodium Benzoate to constant weight at 110° C. and proceed as directed under the assay for alkali benzoates and salicylates. Each cc. of half-normal sulphuric acid corresponds to 0.07204 Gm. of $NaC_7H_5O_2$.

"Preserve in well-closed containers." *U. S.*

"A white subcrystalline, or amorphous powder. Inodorous, or with a faint odor of benzoin; taste unpleasant, sweetish, saline. Soluble in 2 parts of *water,* and in 24 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of sodium. An aqueous solution (1 in 10) is slightly alkaline to *litmus,* gives a pale reddish precipitate with *T. Sol. of ferric chloride,* and yields with *diluted hydrochloric acid* a crystalline precipitate of benzoic acid. Loses not more than 4 per cent. of its weight when dried at 110° C. 1 gramme of this dried salt heated to redness till gases cease to be evolved leaves an alkaline residue which, treated with *water,* filtered, and well washed, yields a clear solution requiring for neutralisation not less than 13.7 or more than 13.9 millilitres of *N/2 solution of sulphuric acid.* Yields no characteristic *reactions* for copper, iron, potassium, or carbonates, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million." *Br.*

C. E. Smith (*A. J. P.,* 1917, lxxxix, 576) points out some difficulties likely to be encountered in passing on samples of sodium benzoate for purity and strength.

Uses.—Sodium benzoate is used in the treatment of *rheumatism,* either of the acute or chronic type. Its mode of action in these conditions is apparently similar to that of the salicylates, although it is usually a less efficacious remedy. It has also been used in the treatment of *lithemia* and *gouty conditions* but with less convincing benefit. It is of service also as a urinary antiseptic, but the ammonium salt is generally preferred. Although benzoic acid is a powerful germicide the neutral salts are only feebly so. According to Doepner a 1 per cent. solution of sodium benzoate has only a slight retarding influence upon the growth of the bacteria; on the other hand, Herter (*J. A. M. A.*, 1910, liv) states that one-fifth of one per cent. has a perceptible inhibiting action. It is probable that the strong effects of sodium benzoate as a food preservative are due to a partial liberation of benzoic acid by the acidulous matters of the food stuff to which it is added. It is quite certain that an acid condition of the urine very greatly increases its efficacy as a urinary antiseptic.

Dose, from fifteen to thirty grains (1.0–2.0 Gm.).

SODII BICARBONAS. U. S., Br.

SODIUM BICARBONATE Sod. Bicarb

" Sodium Bicarbonate, when dried to constant weight over sulphuric acid, contains not less than 99 per cent. of $NaHCO_3$." *U. S.* " Sodium Bicarbonate may be obtained by exposing crystals of sodium carbonate to carbon dioxide, or by the interaction of sodium chloride and ammonium bicarbonate. It contains not less than 98.5 per cent. of pure sodium hydrogen carbonate, $NaHCO_3$." *Br.*

Natrium Carbonicum Acidulum; Natrium Hydrocarbonicum; Bicarbonas Sodicus; Bicarbonate of Soda, Saleratus; Soda Saleratus, Acid Sodium Carbonate; Sodium Hydrogen Carbonate; Carbonate Acide de Sodium, Sel de Vichy, *Fr.;* Natrium Bicarbonicum, *P. G.;* Natriumbicarbonat, Doppeltkohlensaures Natron, *G.;* Bicarbonato di sodio, *It.;* Bicarbonato sodico, *Sp.*

Two kinds of sodium bicarbonate were formerly official—one, which is known by the title of this article, and which, to comply with the tests, must not have more than one per cent. of impurity, and the other, " commercial bicarbonate," which must contain at least 95 per cent. of pure bicarbonate. Formerly to obtain a salt which would comply with the official test it was necessary to purify the commercial salt. The U. S. Pharm. 1890 recognized only the purer salt, having dismissed *Sodii Bicarbonas Venalis.* Sodium bicarbonate must now contain 99 per cent. of the pure salt, and it is rarely found below this standard even when sold in grocery stores.

Immense quantities of sodium bicarbonate were formerly imported from Great Britain, but the importation has ceased because of the development of the industry in this country. It is now made of excellent quality by the Pennsylvania Salt Manufacturing Co., at Natrona, Pa., using cryolite as raw material; and by the Solvay Process Co., of Geddes, near Syracuse, N. Y., using the ammonia-soda process; and the Michigan Alkali Co., of Wyandotte, Mich., and the Mathison Alkali Co., of Saltville, Va., from brine.

Description and Physical Properties.—" A white, opaque, odorless powder. It is stable in dry air, but slowly decomposes in moist air. One Gm. of Sodium Bicarbonate is soluble in 10 cc. of water at 25° C. It is insoluble in alcohol.

" An aqueous solution of Sodium Bicarbonate (1 in 20), when freshly prepared with cold distilled water, without shaking, is slightly alkaline to litmus paper. The alkalinity increases upon standing, agitation, or increase in temperature. When heated above 15° C., an aqueous solution of the salt gradually loses carbon dioxide, and at boiling temperature the salt is almost completely converted into normal sodium carbonate. When heated, the salt is decomposed into sodium carbonate, water, and carbon dioxide, and at 100° C., loses about 36.5 per cent. of its original weight. An aqueous solution of the salt responds to the reactions for sodium, and for bicarbonates.

" Dissolve 1 Gm. of Sodium Bicarbonate in 20 cc. of distilled water at 25° C.: it yields a clear and colorless solution, leaving no residue. Heat Sodium Bicarbonate in a test tube: no odor of ammonia is evolved and moist red litmus paper is not colored blue. Dissolve 1 Gm. of the salt without agitation in 20 cc. of distilled water at a temperature not exceeding 15° C., and add 0.2 cc. of normal hydrochloric acid and 2 drops of phenolphthalein T.S.: a red tint does not appear immediately (*carbonate*). An aqueous solution of the salt (1 in 50), mixed with a slight excess of hydrochloric acid, meets the requirements of the test for *heavy metals.*

" Preserve in well-closed containers, in a cool place." *U. S.*

" A white powder, or small, opaque, monoclinic crystals. Taste saline. Soluble in 11 parts of *water.* Yields the *reactions* characteristic of sodium and of bicarbonates. 1 gramme requires for neutralisation not less than 11.7 or more than 11.9 millilitres of *N/1 solution of sulphuric acid.* Yields no characteristic *reactions* for copper, iron, aluminium, calcium, sulphites, or thiosulphates, and not more than the slightest *reactions* for chlorides, sulphates, or ammonium. *Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million. When 1 gramme of Sodium Bicarbonate is dissolved in 20 millilitres of cold *water,* without shaking, and 0.2 millilitre of *N/1 solution of sulphuric acid* and 2 drops of *solution of phenolphthalein* are added, no red color is immediately developed (limit of carbonate). The addition of *T. Sol. of ferric chloride* to the aqueous solution acidified with *hydrochloric acid* causes no red coloration (absence of thiocyanates)." *Br.*

Assay.—" Dry about 3 Gm. of Sodium Bicarbonate over sulphuric acid to constant weight, weigh accurately, mix it with 25 cc. of distilled water, and titrate with normal sulphuric acid, methyl orange T.S. being used as indicator. Each cc. of normal sulphuric acid corresponds to 0.08401 Gm. of $NaHCO_3$." *U. S.*

" 20 grammes of Sodium Bicarbonate are neutralised by 16.7 grammes of Citric Acid, and by 17.8 grammes of Tartaric Acid." *Br.*

The salt furnished by the manufacturers almost always comes up to the requirements of the Pharmacopœias. The presence of carbonate may be known by a decided alkaline taste and reaction, by a cold solution of the salt yielding a precipitate with magnesium sulphate, and by a solution in 40 parts of water affording, without agitation, an orange-colored or reddish-brown precipitate with corrosive sublimate. E. Kuhlmann recommends rosolic acid as the best test for detecting monocarbonate; if a small fragment be placed in a solution of sodium bicarbonate, the liquid remains perfectly colorless even after a quarter of an hour if the salt be pure; but if it contain from one to four per cent. of monocarbonate a rose-red color will be produced after a few moments, and *immediately* in the presence of larger quantities, rapidly changing it to purple-red. (*A. Pharm.,* 1887, p. 72.)

When the solution is exposed to heat, the salt gradually parts with carbon dioxide, and, at the temperature of 100° C., is converted into sesquicarbonate, $Na_2CO_3.NaHCO_3.2H_2O$. At red heat the second equivalent of carbon dioxide is expelled, and the anhydrous carbonate is left.

Sodium bicarbonate of course is incompatible with acids which decompose it with effervescence, and with all salts of metals which produce insoluble carbonates or which possess an acid reaction. Many salts of bismuth magnesium, lithium, lead and zinc liberate CO_2 when brought into contact with sodium bicarbonate. Acetylsalicylic acid, heroin and diacetyl tannin also decompose it, probably on account of the instability of their molecular structure.

Uses.—Sodium bicarbonate is used in medicine solely for the purpose of overcoming hyperacidity either of the stomach, blood, or urine.

As a local remedy it has the great advantage over the basic carbonate of being less irritant to the mucous membrane and for systemic use that it can be given intravenously in large quantities with less danger of hemolysis.

In various types of *dyspepsia* the bicarbonate of soda is probably the most frequently used and one of our most valuable agents. In *hyperchlorhydria* it is useful for its antacid action, although it requires large doses compared to either calcium or magnesium salts. In *gastric ulcer* and other painful conditions, as pointed out by Bastedo (*Am. Med.,* Aug., 1920) its pain relieving effect cannot be attributed entirely to its antacid action.

The second great use for soda is for the correction of the condition commonly known as *acidosis* or *acidemia.* Attention may be called to the incorrectness of this name as the blood never becomes acid in reaction during life; the condition involves a diminution of the alkali reserve, not an actual alteration of the reaction of the blood. The most severe type of acidosis is that which gives rise to the *diabetic coma.* Milder types are seen in the post-anesthetic *nausea,* in certain types of *nephritis* such as that seen after poisoning by mercury bichloride. In these cases large doses are employed. Thus Cary (*J. A. M. A.,* 1921, lxxvi, p. 1393) recommends in diabetic coma the administration of from 25 to 50 Gm. (6 to 13 drachms) in the first two hours, of which part may be given by mouth and the remainder either by rectum or by intravenous injection. As has been shown by Goto (*J. Ex. M.,* 1917, xxv, p. 693), McNider and others soda has the power of protecting the kidney against the irritating effects of certain poisons and is therefore useful in some types of *nephritis* and in the treatment of poisonings by mercury, uranium, etc. It is also employed to alkalize urine in various types of *rheumatic* and *gouty* disorders, but for this purpose usually has no superiority over the citrates which are more agreeable to take. Castellani (*B. M. J.,* 1921, i, p. 338) recommends the use of large doses of sodium bicarbonate in the treatment of *sprue.*

When used for its systemic effect, sodium bicarbonate is least objectionable if administered dissolved in carbonated water which may be flavored to taste.

In pharmacy it is widely employed for making effervescent powders.

Dose, for an adult, from ten grains to a drachm (0.65–3.9 Gm.), taken most conveniently in a glass of carbonic acid water.

Off. Prep.—Tabellæ Sodii Bicarbonatis, *N. F.;* Liquor Sodæ et Menthæ, *N. F.;* Mistura Rhei Composita, *N. F.;* Liquor Sodii Boratis Compositus, *N. F.;* Pulvis Pancreatini, *N. F.*

SODII BIPHOSPHAS. U. S. (Br.)

SODIUM BIPHOSPHATE Sod. Biphos. [Sodium Dihydrogen Phosphate, Monosodium Orthophosphate]

"Sodium Biphosphate, when dried to constant weight at 100° C., contains not less than 98 per cent. of NaH_2PO_4. It contains not more than 15 per cent. of water." *U. S.* "Acid Sodium Phosphate may be obtained by the combination of di-sodium hydrogen phosphate with phosphoric acid. It contains not less than 70 per cent. of pure sodium di-hydrogen phosphate, NaH_2PO_4." *Br.*

Sodii Phosphas Acidus, *Br.;* Acid Sodium Phosphate; Sodium Di-hydrogen Phosphate; Sodium Biphosphate, Monosodium Hydrogen Phosphate.

This salt, which has been introduced into medicine and is found as a commercial article, is sometimes known as *primary sodium phosphate* or *monosodium orthophosphate.* It is prepared by adding the proper molecular proportions of the ordinary disodium orthophosphate and phosphoric acid according to the following reaction:

$$Na_2HPO_4 + H_3PO_4 = 2NaH_2PO_4.$$

This salt is not only used in medicine, but is employed in the manufacture of baking powders in which it plays the part of the acidic element in liberating CO_2 from $NaHCO_3$.

Description and Physical Properties.—"Colorless, transparent crystals or a white, granular, crystalline powder. It is odorless and slightly deliquescent. It is freely soluble in water and practically insoluble in alcohol, chloroform, and ether.

"At 100° C. Sodium Biphosphate loses its water of crystallization (13.04 per cent.); at 210° C., it is converted into disodium dihydrogen pyrophosphate ($Na_2H_2P_2O_7$). At still higher temperatures it is changed into a mixture of sodium metaphosphate ($NaPO_3$) and modifications of sodium metaphosphate. An aqueous solution of Sodium Biphosphate is acid to litmus paper and produces effervescence with sodium carbonate. An aqueous solution of the salt (1 in 20) responds to the reactions for sodium, and for phosphates.

"Dissolve 2 Gm. of Sodium Biphosphate in 40 cc. of distilled water, and add 1 drop of methyl orange T.S. If the solution is pink, it requires not more than 0.3 cc. of normal sodium hydroxide to discharge the pink color (*free acid*). If the solution is yellow, it requires not more than 0.3 cc. of normal sulphuric acid to render it pink (*disodium phosphate*). An aqueous solution of the salt (1 in 10) does not become turbid when rendered slightly alkaline to litmus paper with ammonia T.S. (*aluminum, calcium,* etc.). Dissolve 1 Gm. of the salt in 100 cc. of 1 per cent. hydrochloric acid: a 10 cc. portion of this solution meets the requirements of the test for *heavy metals.* Dissolve 0.1 Gm. of the salt in 10 cc. of diluted sulphuric acid: the solution meets the requirements of the test for *arsenic.* One Gm. of Sodium Biphosphate shows no more *chloride* than corresponds to 0.2 cc. of fiftieth-normal hydrochloric acid, and 0.2 Gm. shows no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid. Dry about 2 Gm. of the salt, accurately weighed, for one hour at 60° C. Raise the temperature to 100° C., and maintain that temperature until it ceases to lose weight: the loss in weight should not exceed 15 per cent. (*water*).

"Preserve in tightly-closed containers." *U. S.*

It is described in the British Pharmacopœia, as "transparent, colorless, rhombic crystals, or in crystalline powder. Taste saline, acid. Readily soluble in *water,* the solution being acid to *litmus.* Yields the *reactions* characteristic of sodium and of phosphates. 1 gramme dissolved in a mixture of 10 millilitres of *water* and 10 millilitres of *glycerin* requires for neutralisation not less than 5.8 millilitres of *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. Yields no characteristic *reactions* for potassium and ammonium, and not more than the slightest *reactions* for sulphates or chlorides. *Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million." *Br.*

Assay.—"Dry about 2 Gm. of Sodium Biphosphate to constant weight at 100° C., weigh accurately, and dissolve in 10 cc. of distilled water, add 10 cc. of a cold saturated solution of sodium chloride, and titrate the solution with normal sodium hydroxide, using phenolphthalein T.S. as indicator. Each cc. of normal sodium hydroxide corresponds to 0.1201 Gm. of NaH_2PO_4. Dry about 0.15 Gm. of the salt to constant weight at 100° C., weigh accurately, dissolve in 10 cc. of distilled water, and neutralize the solution with normal sodium hydroxide (free from chloride), using phenolphthalein T.S. as indicator. Then add 50 cc. of tenth-normal silver nitrate, and thoroughly agitate the mixture. Gradually add reagent zinc oxide in small portions until the mixture is neutral to litmus paper, then dilute the mixture to 100 cc. with distilled water, and filter through a filter which has not been previously moistened. Reject the first 20 cc. of filtrate, collect 50 cc. of the subsequent filtrate, add 2 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate to the production of a permanent red tint. Each cc. of tenth-normal silver nitrate corresponds to 0.004002 Gm. of NaH_2PO_4." *U. S.*

Uses.—The acid sodium phosphate is used in medicine for the purpose of increasing the acidity of the urine, especially in certain types of *cystitis.* It may be prepared extemporaneously by treating the neutral phosphate with phosphoric acid; to prepare it extemporaneously about 32 parts of the official phosphoric acid is required for each 100 parts of the neutral sodium phosphate in solution.

Dose, from ten to thirty grains (0.6–2 Gm.).

SODII BORAS. U. S. (Br.)

SODIUM BORATE Sod. Bor. [Borax, Sodium Tetraborate, Sodium Pyroborate]

"Sodium Borate contains not less than 52.32 per cent. and not more than 54.92 per cent. of $Na_2B_4O_7$, corresponding to not less than 99 per cent. of the crystallized salt [$Na_2B_4O_7.10H_2O$]." *U. S.* "Purified Borax may be obtained from native borax; it may also be obtained by boiling native calcium borate with solution of sodium carbonate, and contains not less than 98.9 per cent. of sodium pyroborate, $Na_2B_4O_7,10H_2O$." *Br.*

Borax Purificatus, *Br., P. G.;* Purified Borax; Sodæ Biboras, Biborate of Sodium; Sodium Biborate; Natrium Biboracicum, Boras Sodicus; Natrium Boracicum, *Fr. Cod.;* Borate de Sodium Officinal, Borax Prismatique, Borate de Soude, Bauracon, Sel de Perse, *Fr.;* Borsaures Natron, *G.;* Borato di sodio, Borace, *It.;* Borato sodico, Borax, *Sp.*

Borax was known to the ancients; but its chemical character was first ascertained by Geoffroy in 1732. It exists in nature, and may be obtained by artificial means. It occurs in several localities in Europe, in Peru, and in beds, associated with calcium borate, in the district of Iquique, in the republic of Ecuador. This mineral (*boronatrocalcite*), which has become an article of commerce, and is considerably used as a substitute for borax, contains, according to T. L. Phipson, 34 per cent. of water, 11.95 of soda, 14.45 of lime, 34.71 of boric acid, 1.34 of chlorine, 1.10 of sulphuric acid, 0.60 of silica, and 2 of sand, and may be considered as a compound essentially of one molecule of crystallized sodium borate and two molecules of calcium borate, with two molecules of water. It is said also to contain usually some iodine and bromine. (G. Sims.) Borax has long been known to occur in certain lakes of Thibet and Persia, from which it was obtained by spontaneous evaporation; this impure borax was called in commerce *tincal.*

Several sources of borax have been developed within the limits of the United States. The existence of a borax lake in California was first made known by J. A. Veatch in September, 1856, about 100 miles north of San Francisco. This lake supplied large quantities of borax to commerce up to 1868. More recently attention has been attracted to Searles Lake, in San Bernardino County, where potash salts occur with the borax and soda salts. This is now being worked for both potash and borax by concentration and fractional crystallization.

At present the chief supply of American borax comes from the more easily worked deposits in the sandy deserts, southeast of Pyramid Lake, in Nevada, in the Slate Range district, San Bernardino Co., and Death Valley and Saline Valley, Inyo Co., California. In order to reduce as much as possible the cost of transportation before the present railway facilities, the boraxes of the Pacific coast were made usually of high quality, and the so-called *"boracic acid glass,"* one pound of which is equal to three pounds of ordinary borax, was prepared. For an interesting description of the Slate Range district, see *Chem. News,* 1886, 245. Another important source in California are the *colemanite* (*calcium borate*) deposits twelve miles northeast of Daggett, in the Mojave Desert. This formation (one hundred feet or more in width) has been traced for fully ten miles. The colemanite is readily dissolved by sodium carbonate solution, when the borax crystallizes out.

Borax is also prepared from the boric acid deposits which are found in various volcanic regions of Italy (see *Acidum Boricum*). This acid is neutralized either by adding sodium carbonate to a hot saturated solution or the manufacturer mixes the acid in a solid state with a proper proportion of soda ash, and exposes the mixture to the heat of a reverberatory furnace, provision being made for the collection of a large quantity of ammonia, which is always present in the crude acid and escapes during the process.

Description and Physical Properties.—"Colorless, odorless, transparent, monoclinic prisms, or a white powder. It is efflorescent in warm, dry air. One Gm. of Sodium Borate is soluble in 15 cc. of water and in about 1 cc. of glycerin, at 25° C. One Gm. is soluble in 0.6 cc. of boiling water. It is insoluble in alcohol. When heated, the salt at first loses part of its water of crystallization, then melts, and, when further heated, swells and forms a white, porous mass. At red heat, Sodium Borate loses all of its water of crystallization and fuses to a colorless glassy mass or bead.

"An aqueous solution of Sodium Borate (1 in 20) is alkaline to litmus paper. An aqueous solution of the salt (1 in 20) responds to the reactions for sodium, and for borates.

"An aqueous solution of Sodium Borate (1 in 20) does not effervesce with acids (*carbonate or bicarbonate*). An aqueous solution of the salt (1 in 20) meets the requirements of the test for *heavy metals.* An aqueous solution of the salt meets the requirements of the test for *arsenic.*

"**Assay.**—Dissolve about 5 Gm. of Sodium Borate, accurately weighed, in 100 cc. of distilled water, and titrate the solution with normal hydrochloric acid, methyl orange T.S. being used as indicator. Each cc. of normal hydrochloric acid corresponds to 0.1008 Gm. of $Na_2B_4O_7$.

"Preserve in well-closed containers." *U. S.*

"Transparent colorless crystals, sometimes slightly effloresced, with a weak alkaline reaction. Taste saline, alkaline. Soluble in 25 parts of *water,* and in 1 part of *glycerin;* insoluble in *alcohol* (90 per cent.). Colors flame intensely yellow. Its aqueous solution, acidified with *hydrochloric acid,* turns *turmeric paper* brown. A hot saturated solution, acidified with a mineral acid, deposits, as it cools, crystals of boric acid, the solution of which in *alcohol* (90 per cent.) burns with a green flame. 2 grammes dissolved in *water* require for neutralisation 10.4 millilitres of *N/1 solution of sulphuric acid, solution of methyl-orange* being used as indicator; and if to this neutralised solution an equal volume of *glycerin* is added, 20.8 millilitres of *N/1 solution of sodium hydroxide* are required for neutralisation, *solution of phenolphthalein* being used as indicator. Yields no characteristic *reactions* for copper, iron, or calcium, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Above a red heat it melts into a limpid liquid, which, after cooling, concretes into a transparent solid, called *glass of borax,* much used as a flux in assays with the blowpipe. Commercial borax is used as a flux in metallurgical operations; as the basis of the enamel so much applied to iron utensils, glazed brick, and much china, earthenware, and tiling; in the laundry with starch to impart a gloss to linen; by the meat packers of the United States (1000 tons yearly) as an antiseptic for meat intended for export to countries whose laws permit its presence, and very largely in soaps and toilet preparations and in detergent powders.

Borax has the property of rendering cream of tartar very soluble in water, and forms a combination with it called *soluble cream of tartar.* (See under *Potassii Bitartras.*) R. F. Fairthorne states that borax is more soluble in water if sugar has been added to it. (*A. J. P.,* March, 1881.)

Composition.—Borax has the formula Na_2B_4-

$O_7 + 10H_2O$. It ordinarily crystallizes in monoclinic prisms, and contains ten molecules of water (*prismatic borax*); but a variety of the salt exists which crystallizes in octahedrons, and contains only five molecules of water (*octahedral borax*). The latter is obtained in the artificial production of borax by crystallizing from a concentrated solution at a temperature between 60° and 80° C. When a solution of borax is evaporated at 100° C., the salt is left as a transparent, amorphous, brittle mass, containing four molecules of water. (Schweitzer.) Borax is looked upon as having the following probable composition, $2NaBO_2.B_2O_3.10H_2O$.

Sodium borate (neutral).—A soluble borate may be made by adding boric acid to a hot concentrated aqueous solution of sodium biborate or borax until it has a neutral reaction; crystals separate which have been erroneously described under the name sodium tetraborate. They are transparent, fragile, and glassy; it is found in commerce in glass-like masses. It is soluble in cold water, but more soluble (70 per cent.) in hot water. It is probably a mixture and not a true compound. Sodium metaborate, $NaBO_2H_2O$, is also known as neutral sodium borate and several compounds of this salt with free metaboric acid, HBO_2, are also known but are little used.

Boron is a non-metallic element which was first produced in the elemental condition by Moissau by the use of the electric furnace. It is an amorphous brown powder, sp. gr. 2.45. The so-called *"crystalline boron"* of the older text books was really *aluminum boride*, AlB_2, which separated out during the electric furnace process of purification.

Uses.—The effects of borax upon the animal system are very feeble, Cyon having found that in daily doses of three drachms borax exerts no preceptible influence upon the dog. Nevertheless, in sufficient amount it exerts a depressing influence upon the heart as well as upon the spinal centers, and a number of instances of poisoning from it have been reported. (For fatal case, see Potter, *J. A. M. A.*, 1921, lxxvi, 378.) The symptoms have varied somewhat, but in most if not all the cases there have been great depression of spirits, fall of bodily temperature, a very feeble pulse—rapid or slow—and an erythematous eruption accompanied with much swelling of the parts, and especially affecting the lower extremities, and followed by exfoliation; nausea, violent vomiting, and hiccough have been present in some cases; ecchymoses have been noted; the mind usually remains clear until late in the poisoning, but death has been preceded by coma, with disturbances of the respiration, and involuntary discharges. The continued use of borax has produced *"borism,"* which is characterized by gastric irritation, a peculiar absence of fatty matter and of moisture from the skin, and various skin eruptions, especially eczema, reddish papules with squamous desquamating borders, seborrheic acne, and scarlatiniform plaques.

The only systemic purpose for which borax is at present employed is in the treatment of *epilepsy*, but in a careful test made on a large scale in the epileptic ward of the Philadelphia Hospital, by H. C. Wood many years ago, it was found to have little or no influence upon that disorder, and these unfavorable conclusions have been confirmed by Yoedicke (*Med. Klin.*, 1912, p. 2020), who found that only a small percentage of cases seemed to be benefited by it. McCartney (*T. G.*, Oct., 1920), however, has reported a number of favorable results.

Borax even in saturated solution is not at all germicidal, but it does possess slight antiseptic properties. According to Miquel the antiseptic strength is 1 in 14, which would be approximately a saturated solution at ordinary temperatures. It is widely employed as a wash for *ulcers* and *abscesses*, but especially for inflammatory conditions of the mucous membranes, such as *conjunctivitis, stomatitis, cystitis, vaginitis*, and the like. It is probable that its beneficial action in these conditions is due more to its innocuousness than to its antibacterial powers. Because of its alkalinity it is a valuable detergent, especially for cleansing mucous membranes. It is sometimes of service as a urinary antiseptic for administration by the mouth, especially when the urine is too highly acid; being eliminated unchanged it tends to alkalinize the urine.

Dose, ten to twenty gains (0.65–1.3 Gm.).

Off. Prep.—Glycerinum Boracis, *Br.;* Mel Boracis, *Br.;* Liquor Aromaticus Alkalinus, *N. F.;* Liquor Sodii Boratis Compositus, *N. F.;* Mel Rosæ et Sodii Boratis, *N. F.;* Mel Sodii Boratis, *N. F.*

SODII BROMIDUM. U. S., Br.

SODIUM BROMIDE Sod. Brom.

"Sodium Bromide, when dried to constant weight at 100° C., contains not less than 98.5 per cent. of NaBr." *U. S.* "Sodium Bromide may be obtained in the same manner as Potassium Bromide, sodium carbonate being used in place of potassium carbonate. When dried at 110° C. it contains not less than 99 per cent. of pure sodium bromide, NaBr." *Br.*

Bromuretum Natricum; Bromure de Sodium, *Fr.;* Natrium bromatum, *P. G.;* Natriumbromid, Bromnatrium, *G.;* Bromuro di sodio, *It.;* Bromuro sodico, *Sp.*

This salt contains a larger proportion of bromine than does potassium bromide, on account of the lower atomic weight of sodium, sodium bromide containing about 77 per cent. of bromine, while potassium bromide contains about 10 per cent. less. It is a trifle more soluble in water and alcohol. It may be made by the same process that is employed for potassium bromide, substituting sodium carbonate for potassium carbonate.

Description and Physical Properties.—"Colorless or white, odorless, cubical crystals, or a white, granular powder. The salt absorbs moisture from the air without deliquescing. One Gm. of Sodium Bromide is soluble in 1.1 cc. of water and in 16 cc. of alcohol, at 25° C.

"When heated to about 760° C., the salt fuses without decomposition, and at a somewhat higher temperature it volatilizes. An aqueous solution of the salt (1 in 10) responds to the reactions for sodium, and for bromides.

"Dissolve 1 Gm. of Sodium Bromide in 10 cc. of distilled water, and add 0.1 cc. of tenth-normal sulphuric acid: no color is produced upon the subsequent addition of a drop of phenolphthalein T.S. even after boiling (*alkali*). Add a few drops of ferric chloride T.S. and 1 cc. of chloroform to 10 cc. of an aqueous solution of the salt (1 in 20), and shake the mixture: the chloroform does not acquire a violet tint (*iodide*). Drop 1 cc. of diluted sulphuric acid on about 1 Gm. of the powdered salt: no yellow color appears at once (*bromate*). A 10 cc. portion of an aqueous solution of the salt (1 in 20), when acidulated with hydrochloric acid, is not rendered turbid by the addition of 1 cc. of potassium sulphate T.S. (*barium*). A 2 Gm. portion of Sodium Bromide shows no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid. An aqueous solution of the salt meets the requirements of the test for *heavy metals*.

"**Assay.**—Proceed as directed under the assay for bromides, using about 0.4 Gm. of Sodium Bromide, dried to constant weight at 100° C. and accurately weighed. Each cc. of tenth-normal silver nitrate corresponds to 0.01029 Gm. of NaBr. Each Gm. of Sodium Bromide, previously dried, corresponds to not less than 95.7 cc. and not more than 98.3 cc. of tenth-normal silver nitrate.

"Preserve in well-closed containers." *U. S.*

"Small, white, cubic crystals, or a white granular powder, somewhat deliquescent. Taste saline, somewhat bitter. Soluble in 1.5 parts of *water*, and in 16 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of sodium and of bromides. Loses not more than 5 per cent. of its weight when dried at 110° C. 0.5 gramme of this dried salt, dissolved in *water*, requires for complete precipitation not less than 48.1 or more than 48.9 millilitres of *N/10 solution of silver nitrate*. Yields no characteristic *reactions* for copper, iron, aluminium, zinc, calcium, magnesium, potassium, ammonium, carbonates, cyanides, bromates, or iodates, and not more than the slightest *reactions* for chlorides, iodides, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Uses.—The physiological and therapeutic properties of sodium bromide are precisely similar to those of potassium bromide, which see. Because of the depressant effects of potassium on the heart when injected into the blood stream some believe that sodium bromide is preferable in cases of circulatory weakness. It appears to be somewhat less prone to disturb the stomach than the potassium salt and is usually to be preferred.

Dose, ten to sixty grains (0.65–3.9 Gm.).

Off. Prep.—Elixir Sodii Bromidi, *N. F.;* Elixir Bromidorum Trium, *N. F.;* Elixir Bromidorum Quinque, *N. F.;* Elixir Sodii Bromidi, *N. F.;* Elixir Euphorbia Compositum, *N. F.;* Syrupus Bromidorum, *N. F.*

SODII CACODYLAS. U. S.

SODIUM CACODYLATE Sod. Cacodyl.

"Sodium Cacodylate contains not less than 72 and not more than 75 per cent. of $Na(CH_3)_2AsO_2$ with variable amounts of H_2O." *U.S.*

Dimethylarsenas Monosodicus; Natrium Cacodylicum, *Fr. Cod.;* Cacodylate de Sodium, *Fr.;* Kakodylsaüres Natrium, *G.*

This compound is prepared by heating together potassium acetate and arsenic trioxide which yields a distillate containing *cacodyl,* $As_2(CH_3)_4$, and *cacodyl oxide,* $As_2(CH_3)_4O$. This mixture is treated with an oxidizing agent which produces cacodylic acid, $(CH_3)_2AsO.OH$, which is then neutralized with sodium hydroxide, concentrated and crystallized.

For description of cacodylic acid and other cacodylates, see Part II.

Description and Physical Properties.—"White prisms, or a white, granular powder. It is odorless and deliquescent. One Gm. of Sodium Cacodylate is soluble in about 0.5 cc. of water and in about 2.5 cc. of alcohol, at 25° C.

"An aqueous solution of Sodium Cacodylate (1 in 20) is alkaline to litmus paper. Sodium Cacodylate melts in its water of crystallization at about 60° C. and becomes anhydrous at 120° C. It burns with a bluish flame, emitting a garlic-like odor, and to a non-luminous flame it imparts an intensely yellow color. A mixture of a few drops of an aqueous solution of the salt (1 in 100) with 2 cc. of hypophosphorous acid T.S., allowed to stand in a stoppered tube, develops the odor of cacodyl within one hour.

"A solution of 2 Gm. of Sodium Cacodylate in 50 cc. of distilled water requires not more than 0.5 cc. of tenth-normal acid or 1 cc. of tenth-normal alkali to render it neutral, using 2 drops of phenolphthalein T.S. as indicator. No turbidity is produced in 10 cc. of an aqueous solution of the salt (1 in 20) by 1 cc. of calcium chloride T.S., either in the cold or on heating (*mono-methylarsenate*), or in 5 cc. of the solution by 2 cc. of magnesia mixture T.S. within one hour (*arsenate or phosphate*). An aqueous solution of the salt meets the requirements of the test for *heavy metals*. One Gm. of Sodium Cacodylate shows no more *chloride* than corresponds to 0.3 cc. of fiftieth-normal hydrochloric acid. The addition of 5 drops of barium chloride T.S. to 10 cc. of an aqueous solution of the salt (1 in 50), acidulated with 2 drops of hydrochloric acid, produces no turbidity within one-half minute (*sulphate*).

"**Assay.**—Dissolve about 2.5 Gm. of Sodium Cacodylate, accurately weighed, in 30 cc. of distilled water, render the solution neutral to phenolphthalein T.S. if necessary, and then titrate with normal hydrochloric acid, using methyl orange T.S. as indicator. Each cc. of normal hydrochloric acid corresponds to 0.16002 Gm. of $Na(CH_3)_2AsO_2$.

"Preserve in well-closed containers." *U. S.*

Uses.—Although cacodylic acid was employed as a therapeutic remedy by Jochheim in 1864, its popularity as a remedy may be dated from the writings of Gautier (*B. A. M.*, 1899, p. 604), since which time the salts of this acid have been used to a large extent in a number of conditions, chiefly those in which arsenic has been found to be of value.

The physiological and therapeutic effects of arsenic are the properties of arsenous oxide ion, not of the element arsenium: One should not therefore expect an arsenical action from the cacodylates, and as a matter of experimental fact the toxicity of these salts is in no ways comparable to the proportion of arsenium they contain. On the other hand, cacodylic acid is in part slowly demethylized in the system and yields more or less arsenous acid. For this reason the cacodylates are capable of exercising the therapeutic effects of the inorganic forms of arsenic. Heffter (*A. E. P. P.*, xlvi, p. 230) has shown that a small, and not always constant proportion, ranging between two and three per cent. of the ingested dose of the arsenic is split off in the system, and eliminated in an inorganic form. This view is also sustained by the clinical study of Dawes and Jackson. (*J. A. M. A.*, 1907, xlviii, p. 2090.)

The range of demonstrated therapeutic usefulness of cacodylic acid is similar to that of arsenic. Its early popularity was achieved chiefly in the treatment of skin diseases, especially *psoriasis*, and in *tuberculosis*. (See Cleuet, *Gaz. des Hôp.*, 1921, xciv, 1538.) In the latter condition it seems to act precisely as does arsenic, simply by improving the general nutritive state of the patient. There is also much clinical evidence of its value in various forms of *anemia, leukemia, asthma, chronic bronchitis, malaria,* and various other conditions in which arsenic is useful. It is especially employed in those conditions, such as pernicious *anemia,* in which it is desired to give very large doses of arsenic; Dawes (*J. A. M. A.*, 1911) reports a number of cases of this intractable infection which have been apparently cured, one having shown no symptoms for over three years. It has also been employed in *syphilis,* but the experimental investigations of Nichols (*J. A. M. A.*, 1911, lvi, p. 492) seem to demonstrate that it has no direct action upon the spirochetes. It has also been employed in experimental *trypanosomiasis* (see Pflugholt, *M. M. W.*, 1910) with hopeful results. Besides the above conditions, it has been tried in the treatment of *carcinoma, leprosy,* and *pellagra,* but not to sufficient extent to allow of a positive conclusion as to its value. Although, as stated above, it is probable that cacodylic acid possesses no virtues which are not inherent in arsenic, it deserves recognition as a useful remedial agent. Its advantages over arsenous acid lie not merely in the fact of its lower toxicity, but especially in that it can be given hypodermically. If it be reduced in the system and arsenic eventually liberated, this change will not begin until after the remedy has passed the stomach, and probably does not occur to any large extent until after absorption, so that a comparatively large amount of arsenic can be introduced through the alimentary canal with little danger of deranging digestion. When given by the mouth, however, it generally imparts such a strong garlicky odor to the breath that this method of exhibiting the drug is rarely available.

Dose, one-fourth of a grain to two grains (0.016–0.13 Gm.).

Off. Prep.—Ampullæ Sodii Cacodylas, *N. F.*

SODII CARBONAS. Br.

SODIUM CARBONATE

"Sodium Carbonate may be obtained from sodium chloride by interaction with ammonium bicarbonate, ignition, and subsequent crystallisation. It contains not less than 99 per cent. of pure sodium carbonate, $Na_2CO_3,10H_2O$." *Br.*

Carbonate of Soda, Sal Soda, Washing Soda; Natrium Carbonicum, *P. G.;* Carbonas Sodicus, Sal Sodæ; Carbonate Neutre de Sodium Cristallisé Officinal, *Fr. Cod.;* Einfach Kohlensaures Natron, Kohlensaures Natron, *G.;* Carbonate di sodio, *It.;* Carbonato sodico cristalizado, Cristales do Sosa, *Sp.*

There are three forms of sodium carbonate employed in medicine containing various amounts of water of crystallization. The dried sodium carbonate of the Br. represents 95 per cent. of absolute Na_2CO_3, the monohydrated of the U. S. represents about 86 per cent., while the crystalline salt of the Br. represents approximately 37 per cent. The latter compound is a dekahydrate and is the kind usually sold in grocery stores as a water softener, whence the name, *washing soda.*

Sodium carbonate is official in the U. S. P. only as *Sodii Carbonas Monohydratus.*

Native soda, sometimes called *natron,* is found in various parts of the world and exists either in the surface earth, which often exhibits a saline efflorescence, or in solution in small lakes, from which it is extracted by taking advantage of the drying up of the water during the heats of summer. (See *U. S. D.*, 19th ed., p. 1136.)

Sodium carbonate is made from common salt by the older or Leblanc process in two steps; first, converting the salt by sulphuric acid into sodium sulphate, and, then, decomposing the sulphate by calcium carbonate and charcoal at a high temperature, so as to yield sodium carbonate. The chemical reactions may be summarized as follows:

$$2NaCl + H_2SO_4 = Na_2SO_4 + 2HCl$$

$$Na_2SO_4 + CaCO_3 + C_4 = Na_2CO_3 + CaS + 4CO$$

Later a process was put in practice which has given so much satisfaction in its results that it has superseded the process of Leblanc. It is designated the *ammonia-soda* or *Solvay* process, and is based on the fact that when carbon dioxide is passed into a solution of common salt in aqueous ammonia a double decomposition occurs, and the slightly soluble sodium bicarbonate is precipitated:

$$NH_3 + CO_2 + NaCl + H_2O = HNaCO_3 + NH_4Cl$$

From the mother liquor containing the sal-ammoniac, if deemed advisable, the ammonia may by withdrawn by the action of lime, and serve in the renewal of the operation. The sodium bicarbonate is reduced by heat to the carbonate, and the carbon dioxide thus obtained serves to convert the ammonia into the ammonium bicarbonate necessary in the proceeding. The waste product here is calcium chloride, which takes with it all the chlorine of the salt originally used. Therefore if the ammonia-soda process were to replace the Leblanc process, hydrochloric acid and chlorine would have to be made independently, and would become much dearer than at present. To obviate this objection to the ammonia-soda process and to produce hydrochloric acid as one product of the same process, the late Walter Weldon proposed to use magnesia instead of lime in the decomposing of the sal-ammoniac. This would leave magnesium chloride instead of calcium chloride. Steam will liberate hydrochloric acid from the magnesium chloride. This process is carried out practically at Salindres in France, although its economy is not definitely established. Ludwig Mond proposed to freeze out the ammonium chloride from the mother liquors by artificial refrigeration, sublime it, and pass the vapor over magnesia, whereby the hydrochloric acid is retained in combination with the magnesia as magnesium chloride, while the ammonia passes on. The magnesium chloride is then heated in a current of air, when it is split up into chlorine and magnesia.

The reaction between ammonium bicarbonate and sodium chloride, upon which the ammonia process was founded, was first discovered by Dyar and Hemming about 1838, but it was only in 1863 that Ernest Solvay, a Belgian chemist, made it a practical success. The advantages of this method are that the sodium chloride is directly transformed into sodium carbonate, that in the precipitation sodium is the only metal thrown down, and that the preparation is therefore remarkably pure, that the apparatus used is very simple, that the process is inexpensive, great saving of fuel and of labor, and, finally, that no unwholesome gases are diffused in the atmosphere. In this double decomposition between ammonium bicarbonate and sodium chloride only about two-thirds of the chloride undergoes the change. The reaction is limited by another in an inverse direction. Thus, if ammonium bicarbonate and sodium chloride yield sodium bicarbonate and ammonium chloride, these, put together, inversely yield ammonium bicarbonate and sodium chloride. An equilibrium is thus established, and the mixture preserves a constant composition, at the point where the two reactions take place at the same time.

Another source of sodium carbonate was discovered in *cryolite,* a mineral existing in great abundance on the coast of Greenland, and largely imported into America for the manufacture of soda. Cryolite consists mainly of a double aluminum and sodium fluoride, containing in 100 parts 13 of aluminum, 34 of sodium, and 53 of fluorine. Sodium carbonate is obtained by heating cryolite with lime, whereby calcium fluoride is formed, while the sodium and aluminum combine to form a sodium aluminate, a weak salt, which is dissolved out by lixiviation. The soda is converted into carbonate by passing carbon dioxide under pressure through the solution, and the alumina, separated from the soda, becomes insoluble, and is deposited.

Besides the preparation of sodium carbonate, cryolite is employed for other important purposes. Within recent years it has become quite important as a flux for the electrolytic production of aluminum by the Hall and similar processes. (See *Alumen.*) Its only known locality, at least in large amount, is Greenland, where it is found on the southwest coast, near Cape Farewell, existing in beds, of which one is said to be eighty feet thick and three hundred long. It is a handsome mineral, hard, brittle, and translucent, sometimes almost transparent, but generally of a frosty whiteness, which probably suggested its name of *cryolite* or *kryolite,* from the Greek *κρύος, frost.* Though homogeneous in great degree, it exhibits here and there in its substance dark spots, sometimes mere specks, sometimes of considerable size, which appear to be crystalline centers of substances mixed with it at the time of solidification, such as galena, ferrous carbonate, copper and iron pyrites, etc.

Soda-ash is a name given to crude sodium carbonate. It was formerly found in commerce in white or gray masses, and contains about half its weight of foreign salts, consisting of sodium chloride and sodium sulphate. The soda-ash of the modern soda industry is almost pure anhydrous sodium carbonate. Soda-ash is used in soap making, in the glass industry, and in many industries where an alkali is needed as in dyeing and bleaching.

Properties.—" Transparent, colorless, rhombic crystals, efflorescent. Taste strongly alkaline. Soluble in 2 parts of *water.* Aqueous solution strongly alkaline to *litmus.* Free from the impurities enumerated under 'Sodii Bicarbonas.' When heated it liquefies and then dries, losing 62.9 per cent. of its weight. 1 gramme requires for neutralisation not less than 13.8 millilitres of *N/2 solution of sulphuric acid. Lead limit* 10 parts per million. *Arsenic limit*

2 parts per million. 20 grammes of Sodium Carbonate are neutralised by 9.8 grammes Citric Acid, and by 10.5 grammes of Tartaric Acid." *Br.*

Sodium carbonate is incompatible with acids, which decompose it with effervescence, acidulous salts, lime water, ammonium chloride, and earthy and metallic salts.

Uses.—Sodium carbonate may be used to correct excessive acidity either of the alimentary tract or of the general system. For reasons pointed out under sodium bicarbonate, the latter is usually to be preferred to the basic salt. On the basis of some old experiments by Lewaschen many years ago, who asserted that soda markedly increased the liquidity of the bile and diminished the percentage of solids in it, the drug has been largely used in the treatment of *gallstones* and other affections of the biliary passages. While there is considerable clinical evidence as to the value of alkalies in these conditions, their beneficial effect must be attributed to other factors, as it seems to be pretty well established that the alkalies increase neither the quantity nor the alkalinity of the bile (see Glass, *A. E. P. P.*, 1892, xxx).

Fischer's solution, which is largely employed as an intravenous or rectal injection to alkalize the system, is composed of sodium carbonate, crystallized (not the U. S. P. monohydrated which is much stronger) 10 Gm., Sodium Chloride 14 Gm., Water 500 cc. It should not be used hypodermically as it is liable to cause serious sloughing.

Alkaline sodium salts are also employed with advantage, internally and externally, in *skin diseases,* especially those of a papulous and scaly character. A lotion suitable for these cases may be formed by dissolving from two to three drachms of the carbonate in a pint of water. For a bath, from eight to sixteen ounces of the salt may be dissolved in the necessary quantity of water. In recent *burns* without much destruction of the skin, the free application of a saturated solution will usually give immediate relief. When swallowed in an over-dose, it acts as an irritant poison. The best antidotes are the fixed oils, acetic acid, and lemon juice.

Dose, from five to thirty grains (0.32–2.0 Gm.).

SODII CARBONAS EXSICCATUS. Br.

EXSICCATED SODIUM CARBONATE

"Exsiccated Sodium Carbonate is obtained by heating Sodium Carbonate until it loses nearly 63 per cent. of its weight. It contains not less than 95 per cent. of pure anhydrous sodium carbonate, Na_2CO_3." *Br.*

Dried Carbonate of Soda; Exsiccated Sodium Carbonate; Carbonate Neutre de Sodium sec, *Fr. Cod.;* Natrium carbonicum siccum, *P. G.;* Getrocknetes Natriumcarbonat, Entwässerte Soda, *G.;* Carbonato sodico seco, *Sp.*

The dried sodium carbonate (*Natrium Carbonicum Siccum*) of the *P. G. V* contains about 75 per cent. of anhydrous sodium carbonate and corresponds to the formula $Na_2CO_3 + 2H_2O$. This is not as stable a form as the U. S. P. monohydrated salt.

The crystallized sodium carbonate of commerce, known commonly as *washing soda,* contains ten molecules of water of crystallization, and, when heated, readily undergoes aqueous fusion. This "*dekahydrate*" as it is called in the chemical industries is a very unstable compound, losing water spontaneously during its efflorescence, and gaining in actual strength in terms of its alkalinity. The uncertainty of its strength is what led to the adoption of the stable monohydrate in the U. S. P. Upon continuing the heat, the water is driven off, and a white porous mass remains, which is easily reduced to powder. Dried sodium carbonate is in the form of a white powder, and differs in nothing from the crystallized, except in being devoid of water of crystallization. (See *Sodii Carbonas.*) It is officially described as "a whitish powder. Taste strongly alkaline. Yields the *reactions* characteristic of sodium and of carbonates. 1 gramme requires for neutralisation not less than 17.9 millilitres of *N/1 solution of sulphuric acid. Lead limit* 25 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Uses.—This preparation is not used for medicinal purposes. For certain pharmaceutical manipulations it has the advantage not merely of greater concentration but of greater accuracy because of the variable amount of water in the crystalline variety. Exsiccated sodium carbonate is very hygroscopic and must be kept in well closed containers to prevent absorption of moisture and consequent loss of strength. (See *Sodii Carbonas Monohydras.*)

Dose, two to ten grains (0.13–0.65 Gm.) may be given three times a day, in the form of pill prepared with soap and aromatics.

SODII CARBONAS MONOHYDRATUS. U. S.

MONOHYDRATED SODIUM CARBONATE

Sod. Carb. Monohyd.

"Monohydrated Sodium Carbonate, when rendered anhydrous by gentle ignition, contains not less than 99.5 per cent. of Na_2CO_3." *U. S.*

Preparation.—This salt was introduced into the U. S. P., upon the recommendation of Coblentz and Frerichs, on account of its much greater stability when compared with sodium carbonate; it contains but one molecule of water of crystallization, while the ordinary carbonate contains ten; as it is almost impossible to keep the carbonate without efflorescing, it became difficult to use it for chemical or pharmaceutical purposes without previously determining the quantity of water present. Coblentz ascertained by experiment that by exposure in an open vessel, monohydrated sodium carbonate gained the first week but 0.14 per cent. of moisture, this increased to only 0.16 per cent. by the second week. It is prepared by heating and crystallizing sodium carbonate at a temperature above 35° C. As it can be prepared commercially at a low price of excellent quality and is in the form of granular crystals its introduction into the Pharmacopœia has proved a great convenience. It may be used in the place of sodium carbonate.

Description and Physical Properties.—"A white, odorless, crystalline, granular powder. When exposed to the air, under ordinary conditions, it absorbs only a slight percentage of moisture. When exposed to warm, dry air at or above 50° C., the salt effloresces, and at 100° C. becomes anhydrous. One Gm. of Monohydrated Sodium Carbonate is soluble in 3 cc. of water, and in 7 cc. of glycerin, at 25° C. One Gm. is soluble in 1.8 cc. of boiling water. It is insoluble in alcohol.

"An aqueous solution of Monohydrated Sodium Carbonate (1 in 10) is strongly alkaline to litmus paper and to phenolphthalein T.S., and responds to the reactions for sodium, and for carbonates.

"An aqueous solution of Monohydrated Sodium Carbonate (1 in 50), mixed with a slight excess of hydrochloric acid, meets the requirements of the test for *heavy metals.* Weigh accurately about 2 Gm. of Monohydrated Sodium Carbonate and heat it in a crucible at 110° to constant weight: the loss is not less than 10 per cent. and not more than 15 per cent. (*water*).

"**Assay.**—Transfer the anhydrous sodium carbonate obtained in the foregoing test to a flask with the air of 50 cc. of distilled water and titrate with normal sulphuric acid, methyl orange T.S. being used as indicator. Each cc. of normal sulphuric acid corresponds to 0.05301 Gm. of Na_2CO_3.

"Preserve in well-closed containers." *U. S.*

Uses.—Monohydrated sodium carbonate can be used for the same purposes that sodium carbonate can, in the proportion of 1 of the former to 2.3 of the latter. (See *Sodii Carbonas.*) It contains approximately 86 per cent. of Na_2CO_3 against the 95 per cent. of the dried salt of the Br.

Dose, two to ten grains (0.13–0.65 Gm.).

SODII CHLORIDUM. U. S., Br.

SODIUM CHLORIDE Sod. Chlorid.

"Sodium Chloride, when dried to constant weight at 110° C., contains not less than 99 per cent. of NaCl." *U. S.* "Sodium Chloride, NaCl, may be obtained by purifying common salt." *Br.*

Chloruretum Sodicum, Sal Commune, s. Culinare; Table Salt; Muriate of Soda, Sea Salt, Salt; Chlorure de Sodium Officinal, Sel Commun, Sel marin, *Fr.;* Natrium Chloratum, *P. G.;* Natriumchlorid, Chlornatrium, Kochsalz, *G.;* Chloruro di sodio, Sal commune, *It.;* Cloruro sodico, Sal comun, *Sp.*

This mineral production, so necessary to mankind, is universally distributed over the globe, and is the most abundant of the native soluble salts. Most animals have an instinctive relish for it, and from its frequent presence in the solids and fluids of the animal economy, it may be supposed to perform an important part in assimilation and nutrition.

Common salt exists in nature either in the solid state or in solution. In the solid state, called *halite, rock salt, fossil salt,* or *sal gemmæ,* it is often found forming extensive beds, and even entire mountains, from which it is extracted in blocks or masses by mining operations. Its geological position is very constant, it occurring almost invariably in secondary formations, associated with clay and gypsum. In solution it exists in certain springs and lakes, and in the waters of the ocean. The principal salt mines are found in Poland, Hungary, and Russia; in various parts of Germany and Austria, particularly the Tyrol; in Cheshire, England; in Spain; in various parts of Asia and Africa; in Turk's island near St. Domingo; and in Peru and other countries of South America. There are but few mines in the United States where rock salt has been produced—in Louisiana, in Kansas, and in the western part of the State of New York; but there are numerous salt springs, which either flow naturally or are produced artificially by sinking wells to various depths in places where salt is known to exist. These are found principally in Missouri, Kentucky, Illinois, Ohio, Michigan, Pennsylvania, Virginia, West Virginia, and New York. Much commercial salt is obtained from the water of the Great Salt Lake in Utah, which contains nearly 25 per cent. of sodium chloride. California is the only one of the United States in which sea water is utilized for salt production by solar evaporation; this is done extensively at San Diego Bay.

The salt is obtained from these various sources by evaporation. Sometimes solar heat is used and sometimes artificial heat is employed.

The size of the crystals, known as the grain of the salt, is influenced by the temperature of the evaporation and by the presence of foreign materials, some of which are purposely added to produce fine crystals.

Rock salt is always transparent or translucent; but it often exhibits various colors, such as red, yellow, brown, violet, blue, etc., which are supposed to be derived from iron and manganese.

Extraction.—Mines of salt are worked in two ways. When the salt is pure, it is merely dug out in blocks and thrown into commerce. When impure, it is dissolved in water, and extracted afterwards from the solution by evaporation. When the salt is naturally in solution, the mode of extraction depends upon the strength of the brine and the temperature of the place where it is found. When the water contains from 14 to 15 per cent. of the salt, it is extracted by evaporation in open pans or vacuum pans provided with crystallizing boxes. From weaker solutions, however, the salt is obtained in a different manner. If the climate be warm, it may be procured by spontaneous evaporation, effected by the heat of the sun; if temperate, by a peculiar mode of evaporation, to be mentioned presently, and the subsequent application of artificial heat.

Sea water is a weak saline solution, containing approximately 2.7 per cent. of common salt, (see under *Aqua*), which is extracted by the agency of solar heat in warm countries. Salt thus obtained is called *bay salt.* The extraction is conducted in Europe principally on the shores of the Mediterranean, the waters of which are saltier than those of the open ocean. The mode in which it is performed is by letting the sea water into shallow dikes, lined with clay, and capable, after having been filled, of being shut off from the sea. In this situation the heat of the sun gradually concentrates the water, and the salt is deposited. In temperate climates, weak brines are first concentrated in buildings called *graduation houses.* These are rough wooden structures open on the sides, ten or eleven yards high, five or six wide, and three or four hundred long, and containing an oblong pile of brushwood somewhat smaller than the building itself. The brine is pumped up into troughs full of holes, placed above the brushwood, upon which it is allowed to fall, and in its descent, it becomes minutely divided. This operation, by greatly increasing the surface of the brine, promotes its evaporation; and, being repeated several times, the solution is at last brought to the requisite degree of strength to permit of its final concentration in iron boilers by artificial heat.

A very interesting and valuable article describing the American salt industry, well illustrated with photographs, will be found in the *American Food Journal* for December, 1916.

It usually crystallizes in cubes; but by quiet evaporation it often assumes the form of hollow quadrangular pyramids, or hopper-shaped crystals, consisting of an aggregation of cubes. When perfectly pure sodium chloride is permanent in the air but most of the commercial salt is more or less hygroscopic because of the presence of magnesium chloride.

The common salt of commerce, besides pure sodium chloride, usually contains traces of insoluble matter, and usually small amounts of calcium and magnesium sulphates and calcium and magnesium chlorides. This kind of salt, which is used for culinary and for industrial purposes, is usually damp from the hygroscopic character of the calcium and magnesium chlorides present. To overcome this tendency and produce what is called "free running" salt, for use in table salt shakers, several forms of special table salt have appeared upon the market. In some of these a small amount of foreign matter, as a moisture absorbent, is present. For this purpose calcium phosphate, magnesium carbonate and starch have all been used. In some varieties the same end is attained by the purification of the salt to eliminate these hygroscopic constituents. It follows, therefore, that neither culinary salt nor table salt may be used for U. S. P. sodium chloride because of the uncertainty of their composition and the likelihood of some substances being present which would interfere with the official or medicinal uses for which the pharmacopœial article is intended.

Description and Physical Properties.—"Colorless, odorless, transparent, cubical crystals, or a white, crystalline powder. It is usually slightly hygroscopic. One Gm. of Sodium Chloride is soluble in 2.8 cc. of water, and in 10 cc. of glycerin, at 25° C. One Gm. is soluble in 2.7 cc. of boiling water. It is slightly soluble in alcohol.

"When heated somewhat above 100° C. the salt decrepitates. At higher temperatures it fuses, and is slowly volatilized and partly decomposed. An aqueous solution of the salt (1 in 20) responds to the reactions for sodium, and for chlorides.

"An aqueous solution of Sodium Chloride (1 in 10) is neutral to litmus paper. An aqueous solution of Sodium Chloride meets the requirements of the test for *heavy metals.* Separate portions of 10 cc. each of an aqueous solution of Sodium Chloride (1 in 100) after the addition of 1 cc. of ammonia T.S. show no immediate turbidity upon the addition of ammonium oxalate T.S. (*calcium*), or of sodium phosphate T.S. (*magnesium*). Digest 2 Gm. of the finely powdered salt for three hours with 25 cc. of warm alcohol, cool the mixture, and remove the undissolved salt by filtration. Evaporate the filtrate to dryness, dissolve the residue in 5 cc. of distilled water, add 1 cc. of chloroform, and cautiously introduce, drop by drop, with constant agitation, chlorine T.S. which has been diluted with twice its volume of distilled water: the chloroform does not acquire a violet, yellow, or orange color (*iodide or bromide*).

"**Assay.**—Proceed as directed under the assay for chlorides, using about 0.25 Gm. of Sodium Chloride, dried to constant weight at 110° C. and accurately weighed. Each cc. of tenth-normal silver nitrate corresponds to 0.005846 Gm. of NaCl.

"Preserve in well-closed containers." *U. S.*

"Small, white, crystalline grains, or transparent, cubic crystals, free from moisture. Taste saline. Soluble in 3 parts of *water.* Yields the *reactions* characteristic of sodium and of chlorides. Yields no characteristic *reactions* for potassium, bromides, or iodides, and not more than slight *reactions* for calcium, magnesium, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million. 20 millilitres of an aqueous solution (1 in 20) are not immediately colored blue by 0.5 millilitre of *solution of potassium ferrocyanide* (limit of iron)." *Br.*

S. Hill (*Ph. Post.*, 1912, p. 37) states that the flame test for potassium in sodium chloride is unreliable, especially as a great deal of the blue glass gives fallacious results owing to its unsuitability. He recommends the use of *Koevenagel's reagent of cobalt sodium hexanitrite,* which produces a yellow precipitate in potassium solutions as dilute as 1-2000.

Sodium Chloride is decomposed by several of the acids, particularly sulphur and nitric, which disengage vapors of hydrochloric acid; by potassium carbonate with the assistance of heat; and by silver nitrate and mercurous nitrate. In contact with iron, in the presence of air and moisture, it undergoes decomposition. It is decomposed by steam excessively heated, with the escape of hydrochloric acid and an alkaline residue. Several varieties of common salt are distinguished in commerce, as *stored salt, fishery salt, bay salt,* etc.; but they are characterized by the size and compactness of the grains, and not by any difference in composition.

Sodium chloride is incompatible with mercurous, lead, and silver salts with the formation of the corresponding insoluble metallic chloride.

Uses.—Although sodium chloride, like other salines, is capable of exercising a diuretic and cathartic action, because of its rapid diffusibility it is much inferior to many other substances. Common salt has for many years been a household remedy in the treatment of *hemoptysis* in doses of one teaspoonful (3.9 Gm.) taken dry. The observations of Belden (*Z. E. P. T.,* 1909, vii, p. 290) lend support to this employment; he found that although when mixed with the blood outside of the body it had no effect, when administered either by the stomach or by injection it increased the coagulability of the blood. He believed the effect to be due to alteration in the concentration of the blood. Externally applied in solution it is stimulant and may be used either locally or generally. Locally it has been employed in the form of fomentations in *sprains* and *bruises.* Salt baths are used for their tonic and exciting effect in various diseases, especially when attended with weakness of the circulation. A pound of salt to four gallons of water forms a solution of about the strength of sea water and suitable for a bath. (See also under *Aqua.*) Because of its physiological inertness sodium chloride is the substance generally preferred to increase the density of water when for any reason it is desired to inject that fluid directly into the vein (see *Liquor Sodii Chloridi Physiologicus*).

The uses of common salt in domestic economy as a condiment and an antiseptic are well known.

Off. Prep.—Liquor Sodii Chloridi Physiologicus, *U. S.;* Sal Carolinum Factitium, *N. F.;* Sal Carolinum Factitium Effervescens, *N. F.;* Sal Kissingense Factitium, *N. F.;* Sal Kissingense Factitium Effervescens, *N. F.;* Sal Vichyanum Factitium, *N. F.;* Sal Vichyanum Factitium Effervescens. *N. F.*

SODII CITRAS. U. S.

SODIUM CITRATE Sod. Cit.

"Sodium Citrate contains not less than 98 per cent. of $Na_3C_6H_5O_7.2H_2O$." *U. S.*

Citrate of Soda; Citras Sodicus; Citrate de Soude, *Fr.;* Natrium Citricum; Natriumcitrat, Citronsaures Natron, *G.*

The official salt is the normal salt of citric acid and sodium, there being three possible combinations owing to the tri-fold basicity of citric acid. It may be made by adding to a hot aqueous solution of 59 parts of citric acid an aqueous solution of 53 parts of monohydrated sodium carbonate, neutralizing, evaporating, and crystallizing.

Description and Physical Properties.—"Small crystals or a white, granular powder. It is odorless, and has a cooling, saline taste. One Gm. of Sodium Citrate is soluble in 1.3 cc. of water at 25° C. and in 0.6 cc. of boiling water. It is insoluble in alcohol.

"When heated to about 150° C., the salt loses all of its water of crystallization; on ignition at a red heat, it carbonizes and emits inflammable gases which have a very pungent, acrid odor, and a residue remains which is alkaline to litmus paper and strongly effervesces with acids. An aqueous solution of the salt (1 in 20) responds to the reactions for sodium, and for citrates.

"An aqueous solution of Sodium Citrate (1 in 20) is slightly alkaline to litmus paper, but is not reddened by 1 drop of phenolphthalein T.S. To a solution of 1 Gm. of Sodium Citrate in 2 cc. of distilled water, add 1 cc. of potassium acetate T.S. and 1 cc. of acetic acid: no crystalline precipitate forms (*tartrate*). An aqueous solution of Sodium Citrate meets the requirements of the test for *heavy metals.* An aqueous solution of the salt meets the requirements of the test for *arsenic.*

"**Assay.**—Proceed as directed under the assay for alkali salts of organic acids. Each cc. of half-normal sulphuric acid corresponds to 0.04902 Gm. of $Na_3C_6H_5O_7.2H_2O$.

"Preserve in well-closed containers." *U. S.*

Uses.—Sodium citrate, like the potassium salt, is oxidized in the system and appears in the urine in the form of a carbonate, and may therefore be used to overcome excessive acidity of the urine. Lichtwitz (*Th. M.,* 1911, xxv, p. 81) recommends it especially in the treatment of *diabetic acidosis* instead of the carbonates. When added to the blood outside of the body it prevents coagulation, presumably by the formation of non-ionizing calcium citrate. In the same way it prevents the curdling of milk by rennin, the sodium caseinate which is formed by this ferment after the addition of the citrate being soluble. According to Robertson and Burnett (*J. P. Ex. T.,* 1912, lix), when administered in large doses to mammals it causes severe symptoms by depriving the tissues of ionizable calcium. While it has been experimentally shown that the administration of sodium citrate by the mouth may delay the coagulability of the blood, it is improbable that any severely toxic symptoms can be caused by its oral administration. Leone (*Rif. M.*, 1922, xxxviii, p. 312) denies the commonly accepted view that the drug is capable of retarding coagulation when given by the mouth, although he finds that the intravenous injection greatly delays, or in sufficient quantity entirely prevents, coagulation of the blood.

As an anti-coagulant sodium citrate is used very largely in transfusion of blood from one individual to another. For the same reason Steel (*J. A. M. A.*, 1921, lxxvi, p. 429) has recommended it in *thrombo-angiitis obliterans* or Burger's disease; he gives intravenously 250 cc. (8½ fluidounces) of a 2 per cent. solution every other day.

Sodium citrate may be used for the various purposes to which potassium citrate is put (see *Potassium Citrate*), but is probably somewhat less efficient as a diuretic or diaphoretic. It is widely employed in the modification of cow's milk for infant feeding for the purpose of preventing the formation of large hard curds. For this purpose from one to two grains of the salt may be added to each ounce of milk used in the mixture. It has also been highly lauded by Weaver (*New Orleans Med. and Surg. Journ.*, lxxi, 181) in the treatment of *pneumonia.* Wright reported remarkable results from its use as a local application for *furunculosis. Wright's solution* consists of sodium citrate, 2 grains, sodium chloride, 20 grains, water, 1 ounce; cotton saturated with this solution is placed over the boil and covered with waxed paper to prevent evaporation.

Dose, fifteen to sixty grains (1.0–3.9 Gm.).

SODII CITRO-TARTRAS EFFERVESCENS. Br.

EFFERVESCENT SODIUM CITRO-TARTRATE

"Sodium Bicarbonate, in powder, 510 *grammes;* Tartaric Acid, in powder, 270 *grammes;* Citric Acid, in powder, 180 *grammes;* Refined Sugar, in powder, 150 *grammes.* Mix the powders thoroughly; place the mixture in a dish or pan of suitable form heated to between 90° and 105° C. When the mixture, by aid of careful manipulation, has assumed a granular character, separate it into granules of uniform and convenient size by means of suitable sieves. Dry the granules at a temperature not exceeding 55° C. The product weighs about one thousand grammes." *Br.*

The object of this combination is to furnish an effervescing powder, for making extemporaneous saline mixtures, in a convenient and portable form. As the water has been driven off by heat, no reaction takes place until dissolved in water, when the two acids combine with the soda of the bicarbonate to produce sodium tartrate and citrate, and the carbon dioxide escapes with brisk effervescence. It is in this form that the preparation is intended to be used.

It may be mixed with unpleasant salines whose taste it hides by effervescence. In full dose it has a laxative action similar to that of Seidlitz powders.

Dose, one to two drachms (3.9–7.7 Gm.), which may be taken in a small wineglassful or more of water, and repeated occasionally as required.

SODII GLYCEROPHOSPHAS. N. F.

SODIUM GLYCEROPHOSPHATE Sod. Glycerophos. [Sodium Glycerinophosphate]

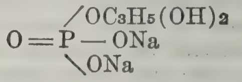
"Hydrated Sodium Glycerophosphate containing not less than 68 per cent. of the anhydrous salt ($Na_2C_3H_7PO_6$ or $C_3H_5(OH)_2PO_4\text{-}Na_2 = 216.11$)." *N. F.*

Natrium Glycerophosphoricum; Glycerophosphate de Soude, *Fr.;* Glycerinphosphorsaüres Natrium, *G.*

Sodium glycerophosphate which formerly existed as a pasty mass can now be found in commerce in solid plates or scales which renders it more convenient for pharmaceutical use. Sodium glycerophosphate has been made by two methods. One is by treating glycerophosphoric acid with sodium hydroxide in a manner similar to the process for calcium glycerophosphate. This method affords a salt of alpha-glycerophosphoric acid. The other method is by heating monosodium phosphate with two molecular proportions of glycerol and hydrolyzing the resulting diglyceryl ester with sodium hydroxide. The first reaction is as follows:

$$NaO.PO.(OH)_2 + 2C_3H_8O_3 = NaO.PO(OC_3H_7O_2)_2$$

A considerable amount of *sodium betaglycerophosphate* crystallizes out at first. This constitutes the official salt. The liquor from which no further amount of salt will crystallize constitutes the *liquid sodium glycerophosphate* of commerce. The official sodium glycerophosphate is the normal salt having the following structural composition, exclusive of water of hydration:



$$O = P \begin{cases} OC_3H_5(OH)_2 \\ ONa \\ ONa \end{cases}$$

Description and Physical Properties.—"Sodium Glycerophosphate occurs as white monoclinic plates or scales, or as a white powder, having a saline taste; odorless. It is very soluble in cold or hot water; nearly insoluble in alcohol.

"An aqueous solution of the salt (1 in 20) is alkaline to litmus and to phenolphthalein T.S. When strongly heated the salt is decomposed, evolving inflammable vapors, and at a red heat is converted into sodium pyrophosphate.

"Dissolve 1 Gm. of Sodium Glycerophosphate in 10 cc. of distilled water and add 3 drops of phenolphthalein T.S.; the red color produced is discharged by the addition of 1.5 cc. of tenth-normal sulphuric acid (*free alkali*). An aqueous solution of the salt does not respond to the Test for heavy metals. Add an equal volume of cold ammonium molybdate T.S. to 10 cc. of an aqueous solution of the salt (1 in 20); no precipitate is formed within one hour (*phosphates*). On heating this mixture a yellow precipitate is formed. Triturate 1 Gm. of the salt with 20 cc. of dehydrated alcohol, filter the mixture, evaporate the filtrate on a water-bath and dry the residue for one hour at a temperature not exceeding 70° C.: the weight of this residue does not exceed 0.01 Gm. (*alcohol-soluble impurities*).

"**Assay.**—Dissolve about 3 Gm. of the salt, accurately weighed, in 30 cc. of distilled water and titrate with half-normal hydrochloric acid, using methyl orange T.S. as indicator. Each cc. of half-normal hydrochloric acid used corresponds to 0.10805 Gm. of $Na_2C_3H_7PO_6$. Each Gm. of Sodium Glycerophosphate corresponds to not less than 6.29 cc. of half-normal hydrochloric acid." *N. F.*

Uses.—The glycerophosphates have been used in medicine on the supposition that being more nearly allied chemically to the form in which phosphorus is found in the body, they would be more easily utilized in conditions of depraved phosphorus nutrition and thereby aid in the upbuilding of nerve strength. It seems well established that when taken by the mouth they are absorbed unchanged but, according to Marfori (*A. E. P. P.*, Schmiedeberg Festsch., 1908, p. 378), when injected subcutaneously they are rapidly excreted by the kidneys. The glycerophosphoric acid absorbed from the alimentary tract is retained for some days but is slowly decomposed in the body, being eliminated through the urine as inorganic phosphate. It is probable that the system is capable of utilizing a portion of the glycerophosphoric acid, synthesizing from it the complex organic bodies in which phosphorus exists in the tissues. But the same thing is true of sodium phosphate. Whether glycerophosphate has any higher nutritive value than inorganic phosphates is extremely doubtful. Forbes (*Ohio Technical Bull.* No. 6, 1914), in an elaborate research upon swine, reaches the conclusion that there is no fundamental differences in the nutritive values of the glycerophosphates and phosphates, except that the former are less likely to disturb the digestive tract. In a review of the literature on this subject for the Council on Pharmacy and Chemistry, Marshall (*J. A. M. A.*, 1915, lxiv, p. 573) concluded "that organic phosphorus is of no more value as a food than inorganic." Granting this be true, however, does not necessarily disprove their therapeutic utility. It is possible to conceive that the unbroken molecule of glycerophosphoric acid, circulating in the blood, may in some way exercise a stimulating action on the metabolism of the central nervous system. While there is considerable clinical evidence of the usefulness of the glycerophosphates in various conditions of depraved metabolism, such as *neuralgia, neurasthenia, senility, Graves's disease, etc.*, the testimony is not unanimous. We must regard, therefore, the question of value of sodium glycerophosphate as a remedy in conditions of general debility, as still *sub judice*. It has the advantage over the calcium salt that being soluble it may be administered in liquid form.

Dose, ordinarily five to fifteen grains (0.3–1 Gm.), although much larger quantities may be given safely.

Off. Prep.—Elixir Calcii et Sodii Glycerophosphatum, *N. F.*; Elixir Glycerophosphatum Compositum, *N. F.*; Elixir Terpini Hydratis et Creosoti Compositum, *N. F.*

SODII HYDROXIDUM. U. S.

SODIUM HYDROXIDE Sod. Hydrox. [Caustic Soda]

"Sodium Hydroxide contains not less than 90 per cent. of NaOH. *Caution—Great care is necessary in handling it, as it rapidly destroys organic tissue.*" *U. S.* "Sodium Hydroxide of commerce purified by means of alcohol." *Br.*, 1914 Appendix.

Soda Caustica; Sodium Hydrate; Hydrate of Soda; Natrium Causticum; Natrium Hydroxydatum; Soude caustique, *Fr.*; Natron, Aetznatron, *G.*; Soda caustica, *It.*; Hidrato sodico, *Sp.*

In the U. S. P. V and previous editions, this salt was prepared by acting upon a solution of sodium carbonate with a suspension of calcium hydroxide and after filtering off the precipitated calcium carbonate, evaporating the solution. At present there is no official recognized method.

Sodium hydroxide has been made on a large scale by simply modifying the Leblanc process (see *Sodii Carbonas*), so that more coal is added in the black-ash fusion, when carbonate is reduced to hydroxide with the liberation of carbon monoxide by the action of the quick-lime, the reactions being:

$$CaCO_3 + C = CaO + 2CO$$

$$Na_2CO_3 + CaO + H_2O = 2NaOH + CaCO_3$$

It is also made like the corresponding compound, caustic potash, by the decomposition of sodium carbonate in solution by quick-lime.

The manufacture of caustic soda by electrolytic means from brine in the United States has developed very greatly. In this sodium chloride is decomposed, the sodium uniting with the elements of water to form the hydroxide and the chlorine which is liberated, being absorbed by slaked lime furnishes the bleaching powder of commerce (see *Calx Chlorinata*).

There are three separate methods in use.

1. The electrolysis of solution of sodium chloride without diaphragms. 2. The electrolysis of sodium chloride with diaphragms. 3. The electrolysis of fused sodium chloride. The composition of the electrodes is of great importance. The materials used are retort graphite, platinum, and artificial graphite. The latter form is usually preferred. In the diaphragm

process, partitions of porous earthenware serve to keep the products of electrolytic decomposition separate to a certain extent, thus minimising the production of interfering compounds. The Acker process of electrolyzing fused sodium chloride is used at Niagara Falls.

Sodium hydroxide, or "caustic soda," of commerce, occurs in hard grayish-white rods or cakes, deliquescent, very alkaline and corrosive. It usually contains as impurities alumina, carbonates, chlorides, phosphates, and sulphates.

Purified Sodium Hydroxide may be obtained by dissolving caustic soda in ethylic alcohol, filtering the solution, evaporating it to dryness in a silver dish, occasionally adding distilled water during the evaporation. The residue is *Purified Sodium Hydroxide.* It should yield no characteristic reaction with the tests for phosphates or sulphates, and not more than the slightest reactions with the tests for carbonates. It is not quite free from alumina.

Description and Physical Properties.—"Dry, white, or nearly white, fused masses, or sticks, hard and brittle, showing a crystalline fracture. Exposed to the air, it deliquesces, absorbs carbon dioxide, and becomes covered with a coating of carbonate. One Gm. of Sodium Hydroxide is soluble in 0.9 cc. of water at 25° C. One Gm. is soluble in about 0.3 cc. of boiling water. It is very soluble in alcohol.

"A solution of Sodium Hydroxide even when greatly diluted is strongly alkaline to litmus paper. An aqueous solution of Sodium Hydroxide (1 in 25) responds to the reactions for sodium.

"An aqueous solution of Sodium Hydroxide (1 in 20) is clear and colorless (*organic matter or insoluble impurities*), and, after being acidulated with acetic acid, it yields no precipitate on the addition of an excess of tartaric acid T.S. or upon the addition of a few drops of sodium cobaltic nitrite T.S. (*potassium*). An aqueous solution of Sodium Hydroxide (1 in 50), slightly acidulated with hydrochloric acid, meets the requirements of the test for *heavy metals.*

"**Assay.**—Place about 10 Gm. of Sodium Hydroxide in a glass-stoppered weighing bottle, and weigh accurately. Transfer it to a 500 cc. graduated flask, dissolve it in 250 cc. of recently boiled distilled water, and add 30 cc. of barium chloride T.S. Fill the flask to the mark with recently boiled distilled water, and thoroughly agitate the liquid. Filter it through a filter, which has not been previously moistened, into a dry flask, rejecting the first 20 cc., and titrate 100 cc. of the subsequent clear filtrate with normal hydrochloric acid, using phenolphthalein T.S. as indicator. Each cc. of normal hydrochloric acid corresponds to 0.04001 Gm. of $NaOH$.

"Preserve in well-closed containers. If bottles are used as containers, they must be made of hard glass and cork stoppers, if used, should be paraffined." *U. S.*

When heated it melts, and at an intense heat evaporates. Though deliquescent, like potassium hydroxide, it does not, like that alkali, become permanently liquid, but forms a paste, which after a time effloresces. The difference in this respect between the two alkalies is owing to the circumstance that, while both are converted into carbonates by uniting with the carbon dioxide of the air, potassium hydroxide forms a deliquescent and sodium hydroxide an efflorescent salt. It is apt to contain 20 or 25 per cent. of water and impurities originating from the sodium carbonate used in preparing the solution from which it is made. The official volumetric assay permits the presence of 10 per cent. of water and impurities, but limits the fixed impurities to 2 per cent.

If the solution be colored brown by hydrogen or ammonium sulphide, the presence of lead may be suspected, derived probably from the glass vessels in which it has been kept.

Uses.—Sodium hydroxide is rarely employed as an internal remedy. Its most important medical use is as a caustic for the same class of cases in which potassium hydroxide is employed. (See under *Potassii Hydroxidum.*) It has the advantage over the latter of being less deliquescent and is probably milder. Its chief use is in various chemical and pharmaceutical manipulations.

Sodium hydroxide when taken in overdose acts as a caustic poison, although not quite so severe as the potassium hydroxide. Accidental poisoning is not uncommon, especially in children, because of its domestic use as lye. The symptoms are pain in the throat, vomiting—which may become bloody—abdominal cramps with purging, swelling and discoloration of the visible mucous membranes, and collapse. The most important factor in the treatment is the immediate neutralization of the poison. For this purpose vinegar or lemon juice (in tablespoonful doses, diluted) are efficient; olive oil, or other bland oil, is also of service. If the patient survive the immediate danger there is very likely to be such serious sequelæ from the destruction of the mucous membranes of the alimentary tract that death may follow later from starvation. For further details see under *Potassii Hydroxidum.*

Off. Prep.—Liquor Sodii Hydroxidi, *U. S.*

SODII HYPOPHOSPHIS. N. F., Br.

SODIUM HYPOPHOSPHITE Sod. Hypophos.

"Sodium Hypophosphite contains not less than 98 per cent. of $NaPH_2O_2.H_2O$ (106.07). Caution should be observed in dispensing Sodium Hypophosphite, as an explosion is liable to occur if it is triturated or heated with nitrates, chlorates or other oxidizing agents." *N. F.*

"Sodium Hypophosphite may be obtained by the interaction of sodium carbonate and calcium hypophosphite. When dried at 110° C. it contains not less than 97 per cent. of pure sodium hypophosphite, $NaPH_2O_2$." *Br.*

Natrium Hypophosphorosum, Hypophosphis Sodicus; Hypophosphite of Soda; Natrium Hypophosphorosum, *Fr. Cod.;* Hypophosphite de Sodium, *Fr.;* Unterphosphorigsaures Natron, *G.;* Hipofosfito sodico, *Sp.*

Preparation.—*Sodium hypophosphite* is prepared by mixing solutions of calcium hypophosphite and monohydrated sodium carbonate, in the proportion of eight ounces of the former, dissolved in five pints of water, to six of the latter in two pints of water. Double decomposition takes place, with the formation of calcium carbonate and sodium hypophosphite, of which the latter is held in solution and the former is precipitated.

$$Ca(H_2PO_2)_2 + Na_2CO_3 = 2NaH_2PO_2 + CaCO_3$$

After filtration to separate the calcium carbonate, the solution is evaporated to a pellicle, and then stirred constantly until the salt granulates, the heat being continued. If required quite pure, the granulated salt is dissolved in official alcohol, and the liquid, having been evaporated to a syrupy consistence, is set aside to crystallize.

Sometimes sodium hypophosphite explodes with violence during the evaporation of its solution. This was ascribed to the use of too high a temperature; but the same accident has occurred when the heat was applied by means of a water bath. In the *Chemical News* (No. 31, p. 46), Tuson stated that, though he had superintended the manufacture of large quantities of calcium and sodium hypophosphites, he had never witnessed anything like an explosion; but the heat employed in evaporation had never approached 100° C., and this is probably the true explanation. Caution, therefore, should be observed to evaporate at a low temperature.

Description and Physical Properties.—"Sodium Hypophosphite occurs as small, colorless, transparent, rectangular plates of a pearly luster, or as a white, granular powder; odorless, and having a saline taste. It is deliquescent on exposure to moist air. One Gm. of Sodium Hypophosphite dissolves in 1 cc. of water at 25° C.; also in about 0.15 cc. of boiling water; soluble in alcohol, slightly soluble in dehydrated alcohol, and freely soluble in glycerin at 25° C.; freely soluble in boiling alcohol.

"An aqueous solution of Sodium Hypophosphite (1 in 20) is neutral or slightly alkaline to litmus. When heated in a test tube, the salt at first loses its water of crystallization, and upon further heating is decomposed, evolving spontaneously inflammable hydrogen phosphide, which burns with a bright yellow flame. To a non-luminous flame the salt imparts an intensely yellow color. When an aqueous solution of the salt (1 in 20), acidulated with hydrochloric acid, is added drop by drop with agitation to an excess of mercuric chloride T.S., a white precipitate of mercurous chloride is formed. Upon the further addition of the solution of Sodium Hypophosphite, the precipitate becomes gray from reduction to metallic mercury.

"A solution of 1 Gm. of the salt in about 10 cc. of distilled water requires not more than 1.5 cc. of tenth-normal hydrochloric acid for neutralization, methyl orange T.S. being used as indicator. Heat 5 cc. of an aqueous solution of the salt (1 in 5) in a test tube with 0.5 cc. of diluted hydrochloric acid on a water bath for thirty minutes; no offensive odor is developed. Measure 5 cc. of an aqueous solution of the salt (1 in 25) into a beaker containing 3 cc. of nitric acid, diluted with about 10 cc. of distilled water, and evaporate the mixture to dryness on a water-bath; the residue meets the requirements of the Test for arsenic. An aqueous solution of the salt does not respond to the Test for heavy metals. Add magnesia mixture T.S. to 10 cc. of an aqueous solution of the salt (1 in 20), made alkaline with ammonia water; it is not affected within one minute (*phosphate*).

"**Assay.**—Dissolve about 1 Gm. of Sodium Hypophosphite, previously dried for twenty-four hours over sulphuric acid and accurately weighed, in 10 cc. of distilled water, add 10 cc. of nitric acid and evaporate the solution to dryness on a water bath. Dissolve the residue in 20 cc. of distilled water, add a drop of phenolphthalein T.S. and sufficient special potassium hydroxide T.S. (see Reagents U. S. P.) to produce a pink color, and then dilute to exactly 100 cc. with distilled water. Transfer 10 cc. of this solution to a 100 cc. graduated flask, add 50 cc. of tenth-normal silver nitrate and proceed from this point as directed in the assay under Potassii Hypophosphis. Each cc. of tenth-normal silver nitrate used corresponds to 0.0035357 Gm. of $NaPH_2O_2.H_2O$. Each Gm. of Sodium Hypophosphite corresponds to not less than 277.2 cc. of tenth-normal silver nitrate.

"Preserve in well-closed containers." *N. F.*

"White granules, deliquescent. Taste bitter, nauseous. Soluble in 1 part of *water* and in 30 parts of *alcohol* (90 per cent.); insoluble in *ether.* Yields, when heated, spontaneously inflammable hydrogen phosphide and hydrogen. Yields the *reactions characteristic* of sodium. Rapidly attacked by oxidising agents. Its solution yields with a warm aqueous solution of *copper sulphate* a red precipitate of cuprous hydride, which on boiling evolves hydrogen. Yields no characteristic *reactions* for copper, iron, aluminium, zinc, calcium, magnesium, potassium, or ammonium, and not more than the slightest *reactions* for carbonates, chlorides, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million. Loses not more than 2 per cent. of its weight when dried at 110° C. When the salt thus dried is assayed by the process described under 'Calcii Hypophosphis' not more than 28 millilitres of *N/10 solution of sodium thiosulphate* are required to decolorise the iodine liberated, corresponding to not less than 97 per cent. of pure sodium hypophosphite, $NaPH_2O_2$." *Br.*

The solubility of sodium hypophosphite is increased by the addition of hypophosphorus acid. As the soluble salts of mercury and silver are reduced by the hypophosphites, they are, of course, incompatible with sodium hypophosphite in prescriptions.

Uses.—This preparation is as useless as the other hypophosphites (See *Acidum Hypophosphorosum*).

Dose, ten to twenty grains (0.65–1.3 Gm.), three times a day.

Off. Prep.—Emulsum Olei Morrhuæ cum Hypophosphitibus, *N. F.;* Liquor hypophosphitum Compositus, *N. F.;* Syrupus Calcii et Sodii Hypophosphitum, *N. F.;* Syrupus Hypophosphitum Compositus, *N. F.*

SODII INDIGOTINDISULPHONAS. U. S.

SODIUM INDIGOTINDISULPHONATE Sod. Indigotin. [Indigo Carmine]

"Chiefly the sodium salt [$C_{16}H_8O_2N_2(SO_3Na)_2$] of indigotindisulphonic acid." *U. S.*

Sodium Indigodisulphonate; Soluble Indigo; Sodium Coerulein-sulphonate; Coeruline; Ceruleinum; Indigo Soluble, *Fr. Cod.*

Indigotin, commonly called *indigo blue,* $C_{16}H_{10}O_2N_2$, is a neutral, tasteless, dark blue powder, insoluble in water. When this is acted upon by sulphuric acid it forms disulphindigotic (sulpho-coerulic) acid, $C_{16}H_8N_2O_2(HSO_3)_2$. This acid is neutralized by sodium and the official salt is produced.

Description and Physical Properties.—"A blue powder or a dark purple paste. When compressed, it acquires a coppery luster. Sodium Indigotindisulphonate is sparingly soluble in water, yielding a dark blue solution. It is almost insoluble in alcohol.

"If in the form of paste, Sodium Indigotindisulphonate should be deprived of water by drying to constant weight at 100° C. before applying the following tests: The addition of nitric acid, bromine T.S., or chlorine T.S. to an aqueous solution of the salt (1 in 200) discharges the blue color. The blue color is also discharged by warming the solution with sodium hydroxide and zinc dust or with stannous chloride T.S.

"Dissolve 1 Gm. of Sodium Indigotindisulphonate, previously dried to constant weight at 100° C., in 200 cc. of distilled water, filter the solution through counterbalanced filters or a Gooch crucible, wash the residue and the filters with distilled water until the washings cease to be colored blue, and dry at 100° C.: the residue remaining on the filter does not exceed 2 per cent. Boil 0.2 Gm. of Sodium Indigotindisulphonate for two minutes with 10 cc. of distilled water, cool, and then agitate the solution with small portions of bromine T.S. until the blue color disappears. On now adding a few drops of potassium iodide T.S. to the liquid, no blue color is produced (*starch or starch iodide*). Add 15 cc. of hydrogen dioxide T.S. and 10 cc. of sodium hydroxide T.S. to 0.2 Gm. of the salt, shake the mixture until the blue color disappears, evaporate the liquid to about 10 cc., cool, acidulate with hydrochloric acid, and add a few drops of ferrous sulphate T.S.: no blue color is produced (*iron ferricyanide or ferrocyanide*)." *U. S.*

Uses.—This salt is used as a dye and also as a microscopic stain and in certain chemical reagents both for qualitative and quantitative tests. It is official for the purpose of coloring the tablets of corrosive sublimate (see *Toxitabellæ Hydrargyri Chloridi Corrosivi,* U. S.).

Indigo carmine has also been used as a test of kidney function. For this purpose 0.08 Gm. (one and one-third grains) is injected intramuscularly and the urine collected at the end of ten minutes and each hour thereafter for three hours. The proportion of dye eliminated is determined by comparing the depth of color in the urine with a standard solution. Normally the dye should appear within less than ten minutes and about 10 per cent. should be eliminated within the first hour. For further information on this test, see Thomas and Birdsall (*J. A. M. A.,* 1917, lxix, 1747).

SODII IODIDUM. U. S., Br.

SODIUM IODIDE Sod. Iod.

"Sodium Iodide, when dried to constant weight at 120° C., contains not less than 99 per cent. of NaI. It contains not more than 7 per cent. of water." *U. S.* "Sodium Iodide may be obtained from iodine and sodium hydroxide by a process similar to that employed in making Potassium Iodide, the salt being crystallised at a temperature not lower than 20° C. When dried at 110° C. it contains not less than 99 per cent. of pure sodium iodide, NaI." *Br.*

Iodurum Sodicum; Natrium Iodatum, *Fr. Cod.;* Iodure de Sodium, *Fr.;* Natrium Jodatum, *P. G.;* Natriumjodid, Jodnatrium, *G.;* Yoduro sodico, *Sp.*

This iodide may be prepared either by treating a solution of sodium hydroxide with iodine, or by double decomposition between ferrous iodide and sodium carbonate, precisely as potassium iodide is obtained by the corresponding processes for that salt.

It crystallizes in anhydrous cubes from a hot solution, and in oblique rhombic prisms, with two molecules of water, by spontaneous evaporation.

Description and Physical Properties.—"Colorless, odorless, cubical crystals, or a white, crystalline powder. In moist air Sodium Iodide deliquesces, or at first cakes and then deliquesces, and frequently undergoes decomposition, assuming a brown tint. One Gm. of Sodium Iodide is soluble in 0.55 cc. of water, in about 2 cc. of alcohol, and in 1 cc. of glycerin, at 25° C. One Gm. is soluble in 0.4 cc. of boiling water. When heated to about 660° C., Sodium Iodide melts, and at higher temperatures it is slowly volatilized and partly decomposed.

"An aqueous solution of the salt (1 in 20) responds to the reactions for sodium, and for iodides.

"Dissolve 1 Gm of Sodium Iodide in 10 cc. of distilled water, and add 0.15 cc. of tenth-normal sulphuric acid: no red color is produced by the addition of a drop of phenolphthalein T.S. (*alkali*). A solution of 1 Gm. of the salt in 2 cc. of distilled water yields no precipitate with 1 cc. of sodium bitartrate T.S. (*potassium*). Dissolve 0.5 Gm. of the salt in 10 cc. of distilled water which has been previously boiled and cooled, and add 2 drops of diluted sulphuric acid: no distinct, yellow color appears within half a minute (*iodate*), and no turbidity occurs (*thiosulphate*). Add 5 cc. of sodium hydroxide T.S. and about 0.2 Gm. of aluminum wire to a solution of 1 Gm. of Sodium Iodide in 5 cc. of distilled water contained in a test tube of about 40 cc. capacity. Insert a pledget of purified cotton in the upper portion of the test tube, and place a piece of moistened red litmus paper over its mouth. On heating the tube and contents on a water bath for fifteen minutes, no blue coloration of the paper is discernible (*nitrate or nitrite*). A 10 cc. portion of an aqueous solution of the salt (1 in 20), acidulated with hydrochloric acid, is not rendered turbid by the addition of 1 cc. of potassium sulphate T.S. (*barium*). A 2 Gm. portion of Sodium Iodide shows no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid. Heat gently 5 cc. of an aqueous solution of the salt (1 in 10) with 1 drop of ferrous sulphate T.S., 1 drop of ferric chloride T.S., and 0.5 cc. of sodium hydroxide T.S.: no blue color appears after acidulating the mixture with hydrochloric acid (*cyanide*). An aqueous solution of the salt meets the requirements of the test for *heavy metals*. Dry the salt to constant weight at 120° C.: the loss in weight does not exceed 7 per cent. (*water*).

"**Assay.**—Proceed as directed under the assay for iodides, using about 0.5 Gm. of Sodium Iodide, previously dried to constant weight at 120° C. and accurately weighed. Each cc. of tenth-normal silver nitrate corresponds to 0.01499 Gm. of NaI. Each Gm. of Sodium Iodide, previously dried, corresponds to not less than 66 cc. and not more than 67.7 cc. of tenth-normal silver nitrate.

"Preserve in well-closed containers." *U. S.*

"A white crystalline powder, deliquescent. Taste saline and somewhat bitter. Soluble in less than 1 part of *water* and in 3 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of sodium and of iodides. Loses not more than 5 per cent. of its weight when dried at 110° C.; 0.5 gramme of this dried salt requires for complete precipitation not less than 33.0 or more than 33.9 millilitres of *N/10 solution of silver nitrate*. Yields no characteristic *reactions* for copper, iron, aluminium, calcium, magnesium, potassium, ammonium, bromates, cyanides, carbonates, or iodates, and not more than the slightest *reactions* for bromides, chlorides, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Sodium iodide possesses the same incompatibilities as the other soluble iodides. It produces insoluble precipitates with mercurous, lead and silver salts and even weak oxidizing agents liberate iodine from it when the solution.

Uses.—Sodium iodide has the same therapeutic effects as the other iodides. (See *Iodum.*) It is said to be better borne by the stomach than potassium iodide, although it contains 8 per cent. more iodine. Pfannenstill (*D. M. W.*, 1911, p. 2420) asserts that by the conjoint internal administration of large doses of sodium iodide and hydrogen peroxide externally, a local liberation of free iodine may be obtained at the point of application of hydrogen dioxide. He recommends this method of treatment, especially in *tuberculous ulcers* of the mucous membrane and in *lupus*. His method has received some confirmation, and Reuterskiold (*Cb. Chir.*, 1911, p. 985) has found it of service in various surgical conditions, such as *osteomyelitis, cellulitis, infected leg ulcers*, etc. Cameron and Grundy (*J. A. M. A.*, 1918, lxxi, 1516) recommend the use of a 25 per cent. solution for roentgenography of the urinary tract, the salt being opaque to the X-ray.

Dose, five to thirty grains (0.32–2.0 Gm.).

Off. Prep.—Syrupus Ferri et Mangani Iodidi, *N. F.*; Elixir Euphorbiæ Compositum, *N. F.*

SODII NITRIS. U. S., Br.

SODIUM NITRITE Sod. Nitris.

"Sodium Nitrite, when dried to constant weight over sulphuric acid, contains not less than 95 per cent. of $NaNO_2$." *U. S.* "Sodium Nitrite may be obtained by fusing sodium nitrate with metallic lead. It contains not less than 95 per cent. of pure sodium nitrite, $NaNO_2$." *Br.*

Nitrite of Sodium; Nitrite de Soude, *Fr.*; Natrium Nitrosum, *P. G.*; Salpetrigsaures Natron, *G.*

Preparation.—According to M. A. Darbon, it is made on a large scale as follows: Sodium nitrate is melted in large cast iron vessels, whereby hygroscopic water is removed and a part of the iodides and iodates, still present, are decomposed. At 310° C. the nitrate begins to fuse. It is heated to 400° to 420° C., and pure metallic lead in thin sheets is gradually added, the mass being constantly stirred, about 280 parts of lead being necessary for 100 parts of sodium nitrate used. The lead must be as free as possible from other metals and antimony particularly must be absent. When all the lead has been added, care having been exercised to prevent overheating, the stirring must be kept up for some time, and the melted mass is then, by means of a cast iron ladle, run in the form of thin threads into water with constant stirring.

In this process, besides the nitrite, about 1 per cent. of sodium hydroxide is produced, which in its turn dissolves a portion of lead, and has to be removed during the subsequent purification, either by nitric acid or by lead nitrate or sulphuric acid. The crude products are a solution containing the nitrite, undecomposed saltpeter, sodium hydroxide holding lead in solution, the soluble impurities of the sodium nitrate, such as sodium chloride, etc., and a residue consisting of lead oxide, a little metallic lead, and a certain proportion of lead peroxide. The solution strained from the residue, with the washings, is diluted to about 6° to 8° B., neutralized with nitric acid as long as a precipitate is formed, separated from this precipitate, concentrated to 42° to 45° B. while warm, and then left to crystallize—the crystals requiring possibly recrystallization. The pure crystals are separated by a centrifugal machine, washed, dried and packed in cylinders of double thickness of parchment paper. (*Chem. News,* Sept. 22, 1899, 146.)

Another process is by heating sodium nitrate with quick-lime and passing in a current of SO_2.

$$NaNO_3 + CaO + SO_2 = NaNO_2 + CaSO_4$$

Still another source of sodium nitrite is as a by-product from the synthetic process of making nitric acid from atmospheric nitrogen by the use of the electric current. Most of the European nitrite now comes from Norway as a result of this process.

Description and Physical Properties.—"White, or nearly white, opaque, fused masses or sticks; or colorless, transparent crystals; or a white or slightly yellow granular powder. It is odorless and has a mild saline taste. When exposed to the air, Sodium Nitrite deliquesces and is gradually oxidized to sodium nitrate, making it unfit for use. One Gm. of Sodium Nitrite is soluble in 1.5 cc. of water at 25° C. It is sparingly soluble in alcohol, and is very soluble in boiling water. When heated to about 270° C. the salt melts, and at a red heat it decomposes yielding oxygen, nitrogen, nitrous oxides, and sodium oxide.

"An aqueous solution of the salt responds to the reactions for sodium, and for nitrites. An aqueous solution of the salt (1 in 20) is slightly alkaline to litmus paper.

"Dissolve 0.5 Gm. of Sodium Nitrite in 25 cc. of diluted hydrochloric acid, evaporate the solution to dryness, and dissolve the residue in 25 cc. of distilled water, adding a few drops of diluted hydrochloric acid: a 10 cc. portion of the resulting solution meets the requirements of the test for *heavy metals.*

"**Assay.**—Dry about 1 Gm. of Sodium Nitrite to constant weight over sulphuric acid, weigh accurately in a stoppered weighing-bottle, dissolve the salt in a measuring flask with sufficient distilled water to make 100 cc., and add 10 cc. of this solution, from a pipette, to a mixture of 50 cc. of tenth-normal potassium permanganate, 100 cc. of distilled water, and 5 cc. of sulphuric acid. In adding the sodium nitrite solution, immerse the tip of the pipette beneath the surface of the permanganate mixture. Warm the liquid to 40° C., allow it to stand for five minutes, and then titrate with tenth-normal oxalic acid. Each cc. of tenth-normal potassium permanganate corresponds to 0.003451 Gm. of $NaNO_2$.

"Preserve in well-closed containers." *U. S.*

Another method of assay has been proposed by Kalmann which is based upon the following reaction:

$$NaNO_2 + 2HI = NaI + I + NO + H_2O$$

When carried out under specified conditions it is stated to be very satisfactory. (*J. P. C.,* 1918, xviii, 217.)

"A white crystalline powder, deliquescent. Taste saline. Soluble in 1.5 parts of *water.* Yields the *reactions* characteristic of sodium and nitrites. 0.1 gramme dissolved in *water* decolorises not less than 27.5 millilitres of *N/10 solution of potassium permanganate,* the solution being maintained slightly acid. Aqueous solution neutral or only slightly alkaline to *litmus;* gives no precipitate on the addition of *diluted sulphuric acid* (absence of lead). *Arsenic limit* 5 parts per million." *Br.*

Uses.—The injection of a nitrite into the circulation produces an increase in the rate of the pulse with a marked fall of blood pressure. At the same time if the dose has been sufficient there develops motor weakness and diminution of reflex activity. After toxic doses the breathing becomes rapid and often of dyspneic character, the mucous membranes of a peculiar slate color, and convulsions may occur. The acceleration of the heart rate is due to a depressant action upon the cardio-inhibitory center in the medulla. The fall of blood pressure is due to a dilatation of the arteries through a direct action upon the muscular coat of their walls. (See Pilcher and Sollmann, *J. P. Ex. T.,* 1915, vi, 323.) The vessels of the lungs do not share in this action, for H. C. Wood, Jr. (*J. Ex. M.,* 1911, xiv), has shown that the pulmonary artery is contracted rather than dilated. Lieb and McWhorter (*J. P. Ex. T.,* 1915, vii, 93) have found that the nitrites relax the tonus of the gall-bladder muscles; and it is to be presumed that they have the same effect on all unstriped muscle. As was first shown by H. C. Wood (*Am. J. M. S.,* July, 1871), the motor weakness and diminished reflexes are the result of an action upon the spinal cord. The increased breathing is not due to any action upon the respiratory center, but is a response to the deprivation of the system for oxygen which is brought about through chemical alteration of the coloring matter of the blood. Whether or not the new compound formed is identical with methemoglobin, which results from the action of a number of poisons, is at present uncertain, but it is a so much more stable compound than oxyhemoglobin that the system is unable to obtain sufficient oxygen to maintain normal functions.

Of the various compounds which liberate the nitrite ion in the system and produce the physiological results described above, those official are amyl nitrite, glyceryl nitrate, ethyl nitrite, and sodium nitrite. The difference between the effects of these drugs is chiefly in their rapidity and duration. The influence of amyl nitrite may be perceived usually within 30 seconds after its administration, and lasts for from 5 to 10 minutes, that of nitroglycerin begins within 1 or 2 minutes, and rarely endures more than one-half hour, sodium nitrite manifests its action in from 5 to 10 minutes and lasts for about 2 hours. (See Wallace and Ringer, *J. A. M. A.*, 1909, liii, 1629.)

The most important use of sodium nitrite is for the purpose of reducing arterial pressure in threatened *apoplexy,* certain types of *chronic nephritis,* the early stages of *arterial degenerations,* and other conditions of too *high blood-pressure.* In arterio-sclerosis, after actual degenerative changes have taken place in the walls of the blood vessels, although widely employed it is incapable of much benefit because when the muscular tissue is replaced by connective tissue the drug can no longer cause dilatation of the arteries. On the other hand, in those forms of too high blood pressure in which there is no degenerative change in the walls of the vessels it is one of the most valuable drugs we possess to cause a temporary reduction. It has the great advantage over nitroglycerin in the longer duration of its effects. In convulsive disorders the nitrites are useful only for immediate effects and for this purpose the other preparations are superior to the sodium salt.

Because of its deliquescence sodium nitrite should be prescribed only in solution and should always be given well diluted, but even with the greatest care it will very often cause such marked gastric disturbance as to interdict its use.

Dose, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Spiritus Ætheris Nitrosi, *U. S.*

SODII PERBORAS. N. F.

SODIUM PERBORATE Sod. Perbor.

" Sodium Perborate contains not less than 9 per cent. of available oxygen, corresponding to about 86.5 per cent. of $NaBO_3.4H_2O$ (154.06)." *N. F.*

Sodium perborate is made by decomposing sodium peroxide with acid under a patented process.

In the presence of water, this salt undergoes decomposition with the formation of hydrogen dioxide and sodium metaborate, the resulting solution being slightly alkaline in reaction.

$$NaBO_3 + H_2O = H_2O_2 + NaBO_2$$

In the dried state, sodium perborate, if pure, is permanent in the air. Commercial varieties of sodium perborate yield from 5 per cent. to 10 per cent. of free oxygen.

Description and Physical Properties.—" Sodium Perborate occurs as white, crystalline granules or as a powder; odorless, and having a saline taste. It is stable in cool and dry air, but is decomposed with the evolution of oxygen in warm or moist air. Sodium Perborate is soluble in water.

"A saturated aqueous solution of the salt is alkaline to litmus or phenolphthalein T.S. In aqueous solution the salt is decomposed into sodium metaborate and hydrogen dioxide, the solution gradually evolving oxygen. Oxygen is evolved more rapidly if the solution is warmed. The salt imparts an intensely yellow color to a non-luminous flame. Turmeric paper, if moistened with an aqueous solution of the salt which has been acidulated with hydrochloric acid, becomes brown in color, particularly on drying; on moistening the dried test paper with ammonia water, the color is changed to greenish black. Agitate a mixture of 1 cc. of an aqueous solution of the salt (1 in 50), 1 cc. of diluted sulphuric acid, a few drops of potassium dichromate T.S., and 2 cc. of ether; the ether acquires a blue color.

" Strongly heat 0.5 Gm. of the salt in a platinum crucible, and dissolve the residue in 25 cc. of distilled water with the aid of a few drops of hydrochloric acid; 10 cc. of the resulting solution does not respond to the Test for heavy metals.

"**Assay.**—Dissolve about 0.25 Gm. of the salt, accurately weighed, in a mixture of 50 cc. of distilled water and 10 cc. of diluted sulphuric acid and titrate the solution with tenth-normal potassium permanganate. Each cc. of tenth-normal potassium permanganate corresponds to 0.0008 Gm. of available oxygen. Each Gm. of Sodium Perborate corresponds to not less than 112.5 cc. of tenth-normal potassium permanganate.

" Preserve it in well-closed containers, in a cool place." *N. F.*

Under the trade name of *Pergenol* has also been introduced a mixture of sodium perborate and sodium bitartrate. This is asserted to correspond to 12 per cent. of hydrogen dioxide, so that the preparation of a solution corresponding to the official solution of hydrogen dioxide requires one part of pergonal and three of water. *Perboral* is a mixture of the perboric acid and para-iodo-sulfonic acid. According to Jaubert (*B. M. J.*, 1905), *perborax* has the formula $Na_2B_4O_8 + 10H_2O$.

Uses.—Sodium perborate is used as a means of obtaining the therapeutic effects of hydrogen dioxide. According to Herbol (*D. M. W.*, 1908, p. 1092), a 2 per cent. solution of sodium perborate is equivalent in germicidal activity to an 0.4 per cent. solution of hydrogen dioxide. In *wounds* or *ulcers* it may be used in solution or as a dusting powder. For the preparation of antiseptic mouth wash it has the advantage over the solution of the dioxide of hydrogen of being alkaline instead of acid. It has also been employed in various skin diseases, especially in acne vulgaris. Herzfeld (*J. A. M. A.*, 1911, lvii, p. 6113) has used it not only as an antiseptic dressing in infected wounds, chronic ulcers, or diabetic gangrene, but as a hemostatic in epistaxis and other local bleedings. It may be employed either as a dusting powder or as a solution in strengths of from 2 per cent. upwards. It is rarely used internally.

Dose, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Dentifricium, *N. F.*

SODII PHOSPHAS. U. S., Br.

SODIUM PHOSPHATE Sod. Phos.

"Sodium Phosphate contains not less than 39.25 per cent. and not more than 44.00 per cent. of Na_2HPO_4, corresponding to not less than 99 per cent. of the crystallized salt [$Na_2HPO_4.12H_2O$]." *U. S.* "Sodium Phosphate may be obtained by the interaction of sodium carbonate and the solution of acid calcium phosphate produced on mixing bone-ash and sulphuric acid. It contains not less than 99.5 per cent. of pure di-sodium hydrogen phosphate, $Na_2HPO_4,12H_2O$." *Br.*

Tribasic Sodium Phosphate; Sodium Orthophosphate; Phosphate of Soda; Disodium Hydrogen Phosphate; Phosphas Sodicus (Natricus); Phosphas Bisodicus; Sal Mirabile Perlatum; Phosphate Monoacide de Sodium, Phosphate Disodique, *Fr.;* Natrium Phosphoricum, *P. G.;* Natriumphosphat, Phosphorsaures Natron, *G.;* Fosfato bisodico, *It.;* Fosfato sodico, *Sp.*

A process for this salt is no longer official; for that of the U. S. P., 1870, see *U. S. Disp.*, 19th edition, page 1151.

The incombustible part of bones is obtained by burning them to whiteness, and consists of neutral calcium phosphate, called bone phosphate, associated with some calcium carbonate, etc. When this is mixed with sulphuric acid, the calcium carbonate is entirely decomposed, giving rise to effervescence. The calcium phosphate undergoes partial decomposition; the greater part of the lime, being detached, precipitates as calcium sulphate, while the phosphoric acid, set free, combines with the undecomposed portion of the phosphate, and remains in solution as an acid calcium phosphate, holding dissolved a small portion of the calcium sulphate. In order to separate the acid phosphate from the precipitated mass of calcium sulphate, boiling water is added to the mixture, the whole is strained, and the sulphate washed as long as acid phosphate is removed, which is known by the water passing through in an acid state. The different liquids which have passed the strainer, consisting of the solution of acid calcium phosphate, are mixed and allowed to stand, and by cooling a portion of calcium sulphate is deposited, which is removed by decantation. The bulk of the liquid is now reduced by evaporation, and, in consequence of the diminution of the water, a fresh portion of calcium sulphate is deposited, which is separated by subsidence and decantation as before. The acid calcium phosphate solution, being heated, is now saturated by means of a hot solution of sodium carbonate. The calcium carbonate is separated by a new filtration, and the filtered liquor, which is a solution of sodium phosphate, is evaporated so as to crystallize.

The reactions are as follows:

$$Ca_3(PO_4)_2 + 2H_2SO_4 = 2CaSO_4 + Ca(H_2PO_4)_2$$

$$Ca(H_2PO_4)_2 + 2Na_2CO_3 = 2Na_2HPO_4 + CaCO_3 + CO_2 + H_2O$$

Funcke, a German chemist, has given the following cheap and expeditious method for obtaining sodium phosphate. To the powdered calcined bone, diffused in water, sufficient diluted sulphuric acid is added to decompose all the calcium carbonate which it contains. When the effervescence ceases, the matter is treated with nitric acid, which dissolves the calcium phosphate and leaves the sulphate. The nitric solution of the phosphate is then treated with sodium sulphate, equal in quantity to the bone employed, and after the reaction is completed, the nitric acid is recovered by distillation. In consequence of a double decomposition, calcium sulphate and sodium phosphate are formed, the latter of which is separated by water, and crystallized in the usual manner.

Description and Physical Properties.—"Large, colorless, odorless, monoclinic prisms, or a granular, crystalline salt. The crystals effloresce in the air. One Gm. of Sodium Phosphate is soluble in 2.7 cc. of water at 25° C. It is very slightly soluble in alcohol. When heated to about 40° C., the salt fuses, yielding a colorless liquid. At 100° C. it loses all of its water of crystallization, and at about 300° C. is converted into sodium pyrophosphate.

"An aqueous solution of Sodium Phosphate (1 in 10) is alkaline to litmus paper and phenolphthalein T.S. An aqueous solution of the salt (1 in 20) responds to the reactions for sodium, and for phosphates.

"Dissolve 10 Gm. of Sodium Phosphate in 100 cc. of distilled water: not more than 0.02 Gm. of residue remains (*calcium or aluminum*). No effervescence occurs on the addition of hydrochloric acid to a solution of the salt (*carbonate*). One Gm. of Sodium Phosphate shows no more *chloride* than corresponds to 0.2 cc. of fiftieth-normal hydrochloric acid, and 0.2 Gm. shows no more *sulphate* than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid. An aqueous solution of the salt meets the requirements of the test for *heavy metals*. An aqueous solution of the salt meets the requirements of the test for *arsenic*.

"**Assay.**—Place about 0.4 Gm. of Sodium Phosphate, accurately weighed, in a 100 cc. graduated flask, dissolve it in 10 cc. of distilled water, add 50 cc. of tenth-normal silver nitrate, and thoroughly agitate the mixture. Gradually add reagent zinc oxide in small portions until the liquid is neutral to litmus paper. Then add distilled water to make 100 cc., agitate the mixture thoroughly, and filter through a filter which has not been previously moistened, rejecting the first 20 cc. of filtrate. Collect 50 cc. of the subsequent clear filtrate, add 2 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate to the production of a permanent red color. Each cc. of tenth-normal silver nitrate corresponds to 0.004735 Gm. of Na_2HPO_4.

"Preserve in well-closed containers." *U. S.*

"Transparent, colorless, rhombic prisms, efflorescent. Taste saline. Soluble in 7 parts of *water,* the solution being slightly alkaline to *litmus.* Yields the *reactions* characteristic of sodium and of phosphates. 5 grammes dissolved in 50 millilitres of *water* require for neutralisation not less than 13.9 millilitres of *N/1 solution of sulphuric acid, solution of methyl orange* being used as indicator. Yields no characteristic *reactions* for potassium, ammonium, carbonates, or chlorides, and not more than the slightest *reaction* for sulphates. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Samples of sodium phosphate have been found in commerce contaminated with arsenic in dangerous quantities. The official test to detect arsenic should always be applied to sodium phosphate. (*C. D.,* June 30, 1900, 1073; *Am. Drug.,* Aug. 27, 1900, 103.)

The medicinal sodium phosphate is one of the three sodium salts of tribasic phosphoric acid, H_3PO_4. In this salt two of the three replaceable hydrogen atoms have been replaced by sodium, so that its formula is HNa_2PO_4, which then crystallizes out with 12 molecules of water. Its complete formula is then $HNa_2PO_4 + 12H_2O$. When gently heated, it loses its water of crystallization (see *Sodii Phosphas Exsiccatus*) and at a red heat the salt is converted into *sodium pyrophosphate,* $Na_4P_2O_7$. (See *Sodii Pyrophosphas.*)

Sodium phosphate precipitates some of the alkaloidal salts, notably those of strychnine. It is also incompatible with the salts of calcium, magnesium and most of the heavy metals.

Uses.—Sodium phosphate was introduced into practice about the year 1800 by Pearson of London. In doses of from one to two ounces (31 to 62 Gm.) it is a mild purgative, and, from its pure saline taste, is well adapted to the cases of children, and of persons of delicate stomach. In smaller doses it has been considerably used, generally in connection with other phosphates, to meet any real or supposed deficiency of phosphates in the system, and for this purpose it is well adapted by its ready solubility. It is widely believed that it exerts, especially in children, an extraordinary influence upon the hepatic secretion. It is therefore employed in *constipation* where the stools are light in color, in infantile *diarrhea,* with *white* or *green stools,* and sometimes with *jaundice,* these evidences of deficient or disordered bile are said to quickly yield to small doses of sodium phosphate, the passages assuming their healthy yellow color, and the attendant disease generally disappearing. It probably, however, possesses only the virtues of the other saline laxatives.

Dose, as a laxative, from one to four drachms (3.9–15.5 Gm.); as a hepatic stimulant, from twenty to forty grains (1.3–2.6 Gm.) may be given, dissolved in water, after meals.

Off. Prep.—Sodii Phosphas Effervescens (from Dried Salt), *U. S., Br.;* Sodii Phosphas Exsiccatus, *U. S.;* Liquor Sodii Phosphatis Compositus, *N. F.*

SODII PHOSPHAS EFFERVESCENS. U. S., Br.

EFFERVESCENT SODIUM PHOSPHATE

Sod. Phos. Eff.

Sodæ Phosphas Effervescens; Effervescent Phosphate of Soda; Natrium Phosphoricum Effervescens; Phosphate de Soude effervescent, *Fr.;* Brausendes Natriumphosphat, *G.*

"Exsiccated Sodium Phosphate, in fine powder, 200 Gm.; Sodium Bicarbonate, dried and powdered, 477 Gm.; Tartaric Acid, dried and powdered, 252 Gm.; Citric Acid, uneffloresced crystals, 162 Gm.; to make about 1000 Gm. Powder the citric acid, and mix it intimately with the exsiccated sodium phosphate and tartaric acid, and then thoroughly incorporate the sodium bicarbonate. Place the mixed powders on a plate of glass or in a suitable dish in an oven heated to between 93° and 104° C. Manipulate the mixture carefully with a wooden spatula, and, when it has become moist, rub it through a No. 6 tinned-iron sieve, and dry the granules at a temperature not exceeding 54° C. Immediately transfer the salt to suitable containers and seal them tightly. Care must be taken to prevent the product from coming in contact with air which contains moisture." *U. S.*

"Sodium Phosphate, in crystals, 500 *grammes;* Sodium Bicarbonate, in powder, 500 *grammes;* Tartaric Acid, in powder, 270 *grammes;* Citric Acid, in powder, 180 *grammes.* Dry the Sodium Phosphate until it has lost about 60 per cent. of its weight; powder the dried salt and mix it with the other ingredients. Place the whole in a dish or pan of suitable form heated to between 90° and 105° C. When the mixture, by aid of careful manipulation, has assumed a granular character, separate into granules of uniform and convenient size by means of suitable sieves. Dry the granules at a temperature not exceeding 55° C. The product weighs about one thousand grammes." *Br.*

This salt affords a pleasant means of giving sodium phosphate.

Dose, one-fourth to one-half ounce (7.7–15.5 Gm.).

SODII PHOSPHAS EXSICCATUS. U. S.

EXSICCATED SODIUM PHOSPHATE

Sod. Phos. Exsic.

"Exsiccated Sodium Phosphate, when dried to constant weight at 110° C., contains not less than 98 per cent. of Na_2HPO_4." *U. S.*

"*Sodium Phosphate,* a convenient quantity. Allow the crystals to effloresce for several days in warm air at a temperature of from 25° to 30° C., then continue the drying in an oven, raising the temperature very gradually until 110° C. has been reached. Maintain this temperature until the salt ceases to lose weight, powder and sift the residue, and transfer to well-closed containers." *U. S.*

Description and Physical Properties.—"A white powder which readily absorbs moisture. One Gm. of Exsiccated Sodium Phosphate is soluble in 8.1 cc. of water at 25° C. and in 1.1 cc. of boiling water. It is insoluble in alcohol.

"Exsiccated Sodium Phosphate meets the requirements of the tests for identity, and, after allowance is made for the loss of water of crystallization, meets the requirements of the tests for purity under *Sodii Phosphas.*

"**Assay.**—Proceed as directed under *Sodii Phosphas* using about 0.15 Gm. of the salt, previously dried to constant weight at 110° C. and accurately weighed. Each cc. of tenth-normal silver nitrate corresponds to 0.004735 Gm. of Na_2HPO_4.

"Preserve in well-closed containers." *U. S.*

Uses.—This salt was introduced in this form for use in making effervescent sodium phosphate. Forty parts of exsiccated sodium phosphate represent about 100 parts of crystallized sodium phosphate (see *Sodii Phosphas*), although in damp atmosphere it absorbs water readily and may contain from 10 to 25 per cent. The water content should always be determined before it is used in any important preparation. It is not used medicinally unless in combination.

Off. Prep.—Sodii Phosphas Effervescens, *U. S.*

SODII SALICYLAS. U. S., Br.

SODIUM SALICYLATE Sod. Salicyl.

"Sodium Salicylate, when dried to constant weight at 100° C., contains not less than 99.5 per cent. of $NaC_7H_5O_3$." *U. S.* "Sodium Salicylate may be obtained by the interaction of salicylic acid and sodium carbonate. It contains not less than 99.5 per cent. of pure sodium salicylate, $NaC_7H_5O_3$." *Br.*

Salicylus; Sodicus; Salicylate of Soda; Salicylate Neutre de Sodium, *Fr.;* Natrium salicylicum, *P. G.;* Natriumsalicylat, *G.;* Salicilato di sodio, *It.;* Salicilato sodico, *Sp.*

This salt is prepared by mixing 100 parts of pure salicylic acid with sufficient water to form a paste, and then with 104 parts of pure crystallized sodium carbonate (U. S. P. 1890, uneffloresced) in a glass or porcelain vessel; carbon dioxide will be evolved, and sodium salicylate will remain in solution. The liquid may be strained through thoroughly washed muslin, if necessary, and heated in an evaporating dish until the carbon dioxide is expelled. If alkaline to litmus paper, enough salicylic acid must be added to be slightly in excess, and the solution is then evaporated at a low heat to dryness. If the acid be not in excess, the salt will not be white, but gray or lead-colored.

Description and Physical Properties.—"White, microcrystalline powder, or scales, or an amorphous powder. It is colorless or has not more than a faint pink tinge. It is odorless, or has a faint, characteristic odor, and possesses a sweet, saline taste. One Gm. of Sodium Salicylate is soluble in 0.9 cc. of water and in 9.2 cc. of alcohol, at 25° C. It is very soluble in boiling water and in boiling alcohol, and is soluble in 4 parts of glycerin.

"When heated, the salt is decomposed, giving off inflammable vapors and an odor of phenol, and finally leaving a residue of sodium carbonate and carbon. An aqueous solution of Sodium Salicylate (1 in 4) responds to the reactions for sodium, and for salicylates.

"An aqueous solution of Sodium Salicylate (1 in 10) when freshly made is colorless or nearly colorless, and is neutral or slightly acid to litmus paper. Add 1 cc. of hydrochloric acid to a solution of 1 Gm. of Sodium Salicylate in 20 cc. of distilled water, and filter the liquid: the filtrate does not decolorize 2 drops of tenth-normal iodine (*sulphite or thiosulphate*). Add a slight excess of hydrochloric acid to an aqueous solution of the salt (1 in 50), and filter: the filtrate meets the requirements of the test for *heavy metals.*

"**Assay.**—Proceed as directed under the assay for alkali benzoates and salicylates, using about 2 Gm. of Sodium Salicylate, previously dried to constant weight at 100° C. and accurately weighed. Each cc. of half-normal sulphuric acid corresponds to 0.08004 Gm. of $NaC_7H_5O_3$.

"Preserve in well-closed containers, protected from heat and light." *U. S.*

"Small colorless scales, or tabular crystals with a pearly lustre. No odor; taste sweetish, unpleasant, saline. Soluble in 1 part of *water,* but this solution, when allowed to stand, is liable to deposit crystals of the salt containing 6 molecules of water of crystallisation; soluble in 6 parts of *alcohol* (90 per cent.). Solutions neutral or faintly acid to *litmus.* Carbonises when heated, leaving finally a white ash which effervesces with acids and imparts an intense yellow color to flame. *T. Sol. of ferric chloride* colors a dilute solution violet. 2 grammes, heated to redness till gases cease to be evolved, leave an alkaline residue which, when treated with *water,* filtered, and well washed, yields a clear solution requiring for neutralisation not less than 24.8 millilitres of *N/2 solution of sulphuric acid.* When to a concentrated aqueous solution excess of *diluted nitric acid* is added, a precipitate is produced which, collected, washed, and dried, responds to the tests described under 'Acidum Salicylicum,' and the filtrate yields not more than the slightest *reactions* for sulphates or chlorides. *Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million. 50 to 100 grammes kept in a closed vessel for several days do not evolve the slightest odor of phenol. Dissolves without coloration or effervescence in *sulphuric acid* (absence of certain organic impurities and of carbonates)." *Br.*

Sodium salicylate is incompatible with antipyrine, forming, when mixed in powder, a liquid mixture. It is also incompatible with ferric salts. Acids decompose it when in solution, precipitating salicylic acid. The discoloration of sodium salicylate solutions which is often noticed after they have been dispensed is said to be due to the absorption of small amounts of ammonia from the air. (*P. J.*, 1915, 355.)

Uses.—The action of sodium salicylate upon the economy, and its therapeutic use, are precisely those of salicylic acid, except that the salt is not locally irritating, and, being soluble, is more rapidly absorbed. When salicylic acid is administered, it is mostly converted into sodium salicylate before it is absorbed into the blood. One drachm of the salt contains about fifty grains of the acid.

Dose, from ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Caffeinæ Sodio-Salicylas, *N. F.;* Elixir Sodii Salicylatis, *N. F.;* Elixir Sodii Salicylatis Compositum, *N. F.;* Elixir Manacæ Compositum, *N. F.;* Elixir Tongæ et Salicylatum, *N. F.;* Liquor Ferri Salicylatis, *N. F.*

SODII SULPHAS. U. S., Br.

SODIUM SULPHATE Sod. Sulph. [Glauber's Salt]

"Sodium Sulphate contains not less than 43.64 per cent. and not more than 48 per cent. of Na_2SO_4, corresponding to not less than 99 per cent. of the crystallized salt [$Na_2SO_4.10H_2O$]." *U. S.* "Sodium Sulphate, $Na_2SO_4,10H_2O$, may be obtained by the interaction of sodium chloride with sulphuric acid." *Br.*

Sulphate of Soda; Sulfas Sodicus (Natricus), Sal mirabile Glauberi; Vitriolated Soda, Glauber's Salt, Sulfate de Sodium Officinal, Sel de Glauber, *Fr.;* Natrium Sulfuricum, *P. G.;* Natriumsulfat, Schwefelsaures Natron, Glaubersalz, *G.;* Solfato di Sodio, *It.;* Sulfato Sodico, Sal admirabile de Glaubero, *Sp.*

Sodium sulphate, in small quantities, is extensively diffused in nature, and is obtained artificially in several chemical operations. It exists in solution in many mineral springs, among which may be mentioned those of Cheltenham and Carlsbad, and it is found combined with calcium sulphate constituting a distinct mineral. It was the *sal mirabile* to which Glauber, the 18th century chemist, attributed such wonderful therapeutic properties, and in consequence of which it is still called *Glauber's salt.*

Immense quantities of sodium sulphate are made by decomposing common salt by sulphuric acid, in the manufacture of soda-ash and sodium carbonate (see *Sodii Carbonas*), in both the Leblanc and the Hargreave's processes. So far from the generated hydrochloric acid being a product of much value, its absorption in a convenient way, so as to avoid the nuisance of its escape into the atmosphere in a gaseous state, is an object of importance to the manufacturer. (See *Acidum Hydrochloricum.*) At Strassfurt sodium sulphate is produced extensively by utilizing the mother liquors from the treatment of carnallite or kilderite, which still contains about 25 per cent. of magnesium sulphate and 50 per cent. of sodium chloride.

The residue of the process for obtaining chlorine by the action of sulphuric acid and manganese dioxide on common salt is a mixture of sodium sulphate and manganous sulphate. Large quantities of this residue are formed in manufacturing chlorinated lime (bleaching powder), and the sodium sulphate in it, roughly purified, supplies a part of the salt consumed in making soda-ash and sodium carbonate.

The process for obtaining ammonium chloride from ammonium sulphate and common salt forms another source of sodium sulphate. By double decomposition, sodium sulphate and ammonium chloride are formed, and by exposing the mixed salts to heat, the ammonium chloride sublimes, and the sodium sulphate remains behind. (See *Ammonii Chloridum.*)

Description and Physical Properties.—"Large, colorless, odorless, transparent, monoclinic prisms, or granular crystals. The salt effloresces rapidly in the air. One Gm. of Sodium Sulphate is soluble in about 1 cc. of water at 25° C. It is insoluble in alcohol but soluble in glycerin. When heated to about 33° C., Sodium Sulphate melts in its water of crystallization and on continuing the heat, maintaining it at 100° C., it loses all of its water of crystallization (about 56 per cent.). At a red heat, the anhydrous salt fuses without decomposition.

"An aqueous solution of Sodium Sulphate (1 in 20) responds to the reactions for sodium, and for sulphates.

"An aqueous solution of the salt (1 in 10) is neutral to litmus paper. An aqueous solution of the salt meets the requirements of the test for *heavy metals.* An aqueous solution of the salt meets the requirements of the test for *arsenic.*

"**Assay.**—Dissolve about 1 Gm. of Sodium sulphate, accurately weighed, in 250 cc. of distilled water, acidulate the solution with 1 cc. of hydrochloric acid, and heat it to boiling. Gradually add an excess of hot barium chloride T.S., heat for thirty minutes on a water bath, collect the precipitate of barium sulphate on a filter, wash it until it is free from chlorides, then dry, ignite, and weigh. The weight of the barium sulphate thus obtained, multiplied by 0.6086, indicates its equivalent in Na_2SO_4. Each Gm. of Sodium Sulphate corresponds to not less than 0.717 Gm. and not more than 0.789 Gm. of $BaSO_4$.

"Preserve in well-closed containers, in a cool place." *U. S.*

"In transparent monoclinic prisms; efflorescent. Taste bitter, saline. Soluble in 3 parts of *water;* insoluble in *alcohol* (90 per cent.). Loses about 55.9 per cent. of its weight when dried at 100° C. Yields the *reactions* characteristic of sodium and of sulphates. 1 gramme dissolved in *water* acidified with *hydrochloric acid* yields, on the addition of excess of *solution of barium chloride,* a white precipitate which, washed and dried, weighs about 0.724 gramme. Yields no characteristic *reactions* for iron, magnesium, potassium, ammonium, or carbonates, and not more than the slightest *reactions* for chlorides. *Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million." *Br.*

When recently prepared it is beautifully transparent; but on exposure to the air it effloresces, and the crystals become covered with an opaque white powder. After long exposure it undergoes complete efflorescence, and falls into powder with loss of more than half its weight. A supersaturated solution of sodium sulphate will remain without crystallizing at ordinary temperatures, even though containing several times the weight of the salt that will be dissolved at the same degree of heat. But the solution instantly forms into a crystalline mass upon adding to it a fragment of the same salt crystallized, or other substances that have been exposed to the air, or upon abruptly placing it in contact with the air.

When crystallized sodium sulphate is subjected to heat it dissolves in its water of crystallization, then dries, and afterwards by the application of a red heat melts with the loss of 55½ per cent. of its weight. It is incompatible with potassium carbonate, calcium chloride, the salts of barium, lead acetate and subacetate, and with silver nitrate if the solutions are strong.

Uses.—Sodium sulphate in doses of from half an ounce to an ounce (15.5–31 Gm.) is an efficient hydragogue cathartic; in smaller doses, an aperient and diuretic. When in an effloresced state, the dose must be reduced one-half, on account of its having lost about one-half of its weight of water. Sodium sulphate is much less used than formerly, having been almost entirely superseded by magnesium sulphate, which is less disagreeable to take and milder in its action. Its nauseous taste, however, may be disguised by the admixture of a little lemon juice or cream of tartar, or by the addition of a few drops of sulphuric acid. D. de Luca has found sodium sulphate remarkably efficient in removing *stains* or *opacity* of the *cornea,* if applied in the form of powdered crystals directly to the eyeball twice daily. (*J. P. C.,* Sept., 1867.) The only uses of sodium sulphate in the arts are to make sodium carbonate and some kinds of glass.

Dose, two drachms to an ounce (7.7–31 Gm.).

Off. Prep.—Sodii Sulphas Effervescens, *Br.;* Sal Carolinum Factitium, *N. F.;* Sal Carolinum Factitium Effervescens, *N. F.*

SODII SULPHAS EFFERVESCENS. Br.

EFFERVESCENT SODIUM SULPHATE

Sodæ Sulphas Effervescens; Effervescent Sulphate of Soda; Natrium Sulfuricum Effervescens; Brausendes Natriumsulfat, *G.*

"Sodium Sulphate, in crystals, 500 *grammes;* Sodium Bicarbonate, in powder, 500 *grammes;* Tartaric Acid, in powder, 270 *grammes;* Citric Acid, in powder, 180 *grammes.* Dry the Sodium Sulphate until it has lost about 55 per cent. of its weight; powder the dried salt, and mix it with the other ingredients. Place the whole in a dish or pan of suitable form, heated to between 90° and 105° C. When the mixture, by aid of careful manipulation, has assumed a granular character, separate it into granules of uniform and convenient size by means of suitable sieves. Dry the granules at a temperature not exceeding 55° C. The product weighs about one thousand grammes." *Br.*

It is used as an effervescent laxative, in the *dose* of from one-fourth to one-half ounce (7.7–15.5 Gm.) dissolved in cold water and taken while effervescing.

SODII SULPHIS. Br.

SODIUM SULPHITE

"Sodium Sulphite may be obtained by the interaction of sulphurous acid and sodium carbonate. It contains not less than 94 per cent. of pure sodium sulphite, $Na_2SO_3,7H_2O$." *Br.*

Natrium Sulfurosum, Sulfis Sodicus (Natricus), Sulfite de Soude, *Fr.;* Natriumsulfit, Schwefligsaures Natron, *G.*

This salt may be prepared by passing sulphurous acid gas into a solution of sodium carbonate, and evaporating out of contact of the air. The sulphurous acid unites with the soda of the carbonate to form sodium sulphite, and the carbon dioxide escapes. After sufficient concentration, the solution is allowed to cool, and the salt crystallizes. A better way, however, is to dissolve a convenient weight of sodium carbonate in a small quantity of water, then pass the sulphurous acid gas through the solution until it is completely saturated, and acid sodium sulphite is formed. The addition of an equal weight of sodium carbonate forms a solution of the neutral sulphite, which is to be evaporated and crystallized. On exposure the salt gradually changes into a sulphate.

Sulphuric acid added to the solution gives rise to an odor of burning sulphur, owing to the escape of sulphurous acid, and the liquid remains transparent, indicating the absence of calcium. For methods of determining sodium carbonate in sodium sulphite by C. E. Caspari and M. R. Moffat the reader is referred to *Proc. A. Ph. A.,* 1902; also *West. Drug.,* 1904, 59. Sodium sulphite has been replaced in the U. S. P. by the more stable exsiccated salt, which see.

Properties.—"Colorless, transparent, monoclinic prisms, efflorescent in dry air. Inodorous; taste saline and sulphurous. Soluble in 2 parts of *water;* insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of sodium and of sulphites. Aqueous solution neutral or faintly alkaline to *litmus;* on the addition of *hydrochloric acid* evolves sulphur dioxide, but does not become cloudy (absence of thiosulphate). 0.3 gramme dissolved in 30 millilitres of *N/10 solution of iodine* yields a solution which requires for complete decolorisation not more than 7.6 millilitres of *N/10 solution of sodium thiosulphate. Arsenic limit* 5 parts per million." *Br.*

Under the name of *Sodii Sulphis Exsiccatus* (*Exsiccated Sodium Sulphite*) the U. S. IX recognized sodium sulphite practically the same as that of the British pharmacopœia and defined it as containing "not less than 90 per cent. of Na_2SO_3 (126.07)." *U. S. IX.*

This salt may be readily prepared from the crystallized salt by heating the latter at a temperature slightly above 100° C. until an anhydrous residue of constant weight remains. It is more uniform in water content than the crystalline salt.

It was described as follows: "Exsiccated Sodium Sulphite occurs as a white powder; odorless, and having a cooling, saline, sulphurous taste Exposed to the air, it is slowly oxidized to sulphate. One Gm. of Sodium Sulphite dissolves in 3.2 mils of water at 25° C.; sparingly soluble in alcohol. An aqueous solution of the salt (1 in 10) is alkaline to litmus. At a red heat, the salt fuses to a reddish-yellow mass of sodium sulphate and sodium sulphide. To a non-luminous flame the salt imparts an intensely yellow color. Upon the addition of hydrochloric acid to the salt, sulphur dioxide is liberated, which is recognized by its odor, and by its blackening a strip of paper moistened with mercurous nitrate T.S. held in the escaping gas. Dissolve 1 Gm. of Exsiccated Sodium Sulphite in 10 mils of diluted hydrochloric acid and heat the solution sufficient to expel the gases; the liquid does not become turbid (*thiosulphate*). Dissolve 1 Gm. of the salt in 20 mils of diluted hydrochloric acid, evaporate the solution to dryness, and dissolve the residue in 50 mils of distilled water. Ten mils of this solution does not respond to the Test for heavy metals. Add 3 mils of nitric acid to 5 mils of an aqueous solution of the salt (1 in 25), cautiously evaporate the solution to dryness on a water bath, and treat the residue with a few cc. of distilled water and filter the liquid. On evaporating the filtrate and washings to dryness, this residue meets the requirements of the Test for arsenic.

"**Assay.**—Add about 0.3 Gm. of Exsiccated Sodium Sulphite, accurately weighed, to 50 mils of tenth-normal iodine V.S. in a glass-stoppered flask, agitate the mixture until complete solution results and titrate with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 90 per cent. of Na_2SO_3.

"Each mil of tenth-normal iodine V.S. used corresponds to 0.006304 Gm. of Na_2SO_3. Each gramme of Exsiccated Sodium Sulphite corresponds to not less than 142.8 mils of tenth-normal iodine V.S." *U. S. IX.*

A. H. Clark (*D. C.,* 1916, p. 376) has reported at length upon the keeping qualities of the anhydrous salt in comparison with the hydrated crystalline form. His conclusions are in favor of the greater stability of the dehydrated salt.

Uses.—According to the experiments of L. Pfeiffer (*A. E. P. P.,* xxvii), the sulphites are capable of causing death by paralyzing the heart and also the respiratory and other motor nerve centers, but are so rapidly and completely changed into the sulphates that unless given in enormous amount they exert very little influence upon the system; 96.5 per cent. of the sulphite was regained from the urine as a sulphate, and 86 per cent. passed out in five hours after ingestion. But, according to Kionka (*D. M. W.,* 1902, xxviii, p. 89), even in doses comparable to those used in the preservation of food the prolonged use produced in dogs serious symptoms of intoxication. Although the experiments of Sternberg have demonstrated that sodium sulphite has no germicidal powers, it appears to be distinctly toxic to the more highly organized fungoid parasites. It has been used in cases of *yeasty vomiting* with remarkable success. The matter vomited in these cases contains two microscopic fungi, called *Sarcina ventriculi* and *Torula cerevisiæ.* The remedy was first used at the suggestion of Graham of London, who supposed that the sulphurous acid, necessarily extricated from the salt in the stomach by the acid of the yeasty matter, would destroy the parasites. Sodium sulphite is sometimes used locally, especially in that species of *aphthous sore mouth* which is attributed to a parasitic vegetable. The wash may be made of a drachm of the salt to a fluidounce of water. It is said that the solution acts with surprising rapidity, a single application of it sometimes removing the disease in 24 hours. Astrié, an Italian physician, has proposed this salt as a remedy for the constitutional effects of mercury, when used in excess, on the ground that it has the power of rendering the metal soluble. It also has been largely given internally as an antizymotic (see *Sodii Thiosulphas*), but without general success.

Dose, of the official sodium sulphite, from, eight to thirty grains (0.5–2.0 Gm.).

SODII THIOSULPHAS. U. S.

SODIUM THIOSULPHATE Sod. Thiosulph
["Sodium Hyposulphite"]

"Sodium Thiosulphate contains not less than 63.07 per cent. and not more than 67.48 per cent. of $Na_2S_2O_3$, corresponding to not less than 99 per cent. of the crystallized salt [$Na_2S_2O_3.5H_2O$]." *U. S.*

Hyposulphite of Soda; Natrum Subsulfuresum (Hyposulfurosum); Hyposulphis Sodicus; Thiosulphas Natricus; Hyposulphite de Sodium, *Fr. Cod.;* Sulfite Sulfuré de Soude, *Fr.;* Natrium thiosulfuricum, *P. G.;* Natriumthiosulfat, Unterschwefligsaures Natron, *G.;* Hiposulfito sodico, *Sp.*

This salt is used in the United States and British Pharmacopœia as a test, and for the formation of the *Volumetric Solution of Sodium Thiosulphate.* It is found only in the Appendix of the Br. It is readily prepared, according to Walchner, by mixing a pound of dry sodium carbonate, in fine powder, with five ounces of sulphur, heating the mixture gradually in a porcelain vessel until the sulphur melts, and stirring the agglutinated mass, still kept hot, in order that every portion of it may come in contact with the air. The sodium sulphide first formed is thus converted into sodium sulphite. This is dissolved in water, and the filtered solution being boiled with sulphur becomes one of sodium thiosulphate, from which, after filtration and concentration, the salt is deposited in crystals. The latter part of the reaction is as follows:

$$Na_2SO_3 + S = Na_2S_2O_3$$

It may be obtained also by digesting the solution of sodium sulphite at a high temperature, but short of ebullition, with finely divided sulphur. It is made also by oxidizing sodium hydrosulphide, according to the following reaction:

$$2NaHS + 2O_2 = 2Na_2S_2O_3 + H_2O$$

It is also obtained as a by-product from the sulphur-containing residues of the LeBlanc soda process which is still employed in some parts of Europe.

Thiosulphuric acid exists only in combination, and its salts were formerly considered simply as sulphuretted sulphites. The true *hyposulphurous acid,* according to theory, would be H_2SO_2, while $H_2S_2O_3$ is more properly *thiosulphuric* acid, as it differs from sulphuric acid by the replacement of one oxygen atom by one sulphur atom.

Inasmuch as Schützenberger discovered the true hyposulphurous acid, H_2SO_2, exact chemical usage would demand that we give the distinguishing name thiosulphuric to what was formerly called hyposulphurous. Schützenberger himself called the newly-discovered acid *hydrosulphurous,* but this is not characteristic, and the correct name for "sodium hyposulphite" is sodium thiosulphate.

Description and Physical Properties.—"Colorless, odorless, transparent, monoclinic prisms. It is stable in the air below 33° C., but efflorescent in dry air above that temperature. It is slightly deliquescent in moist air. One Gm. of Sodium Thiosulphate is soluble in 0.5 cc. of water at 25° C. It is insoluble in alcohol. When rapidly heated, the salt liquefies. When heated slowly until it is effloresced, and afterwards at 100° C., it undergoes partial decomposition, loses all of its water of crystallization, and at about 220° C. is decomposed, sulphur being liberated, while a residue of sodium sulphide and sodium sulphate remains.

"An aqueous solution of Sodium Thiosulphate responds to the reactions for sodium, and for thiosulphates. An aqueous solution of Sodium Thiosulphate readily dissolves many compounds of silver (chloride, bromide, iodide, oxide, etc.) and discharges the color of solution of iodine or of starch iodide. The addition of hydrochloric acid to an aqueous solution of Sodium Thiosulphate produces a white precipitate of sulphur (distinction from *sulphite or bisulphite*).

"An aqueous solution of the salt (1 in 10) is neutral or faintly alkaline to litmus paper. An aqueous solution of Sodium Thiosulphate (1 in 20) is not rendered turbid by the addition of ammonium oxalate T.S. (*calcium*). Add 10 cc. of diluted hydrochloric acid to 1 Gm. of the salt, evaporate to dryness on a water bath, heat the residue with 50 cc. of distilled water, and filter: a 10 cc. portion of this filtrate meets the requirements of the test for *heavy metals.* Add 3 cc. of nitric acid to 5 cc. of an aqueous solution of the salt (1 in 25), evaporate the solution cautiously to dryness on a water bath, treat the residue with a few cc. of distilled water, filter the liquid, and evaporate the filtrate and washings to dryness: the residue meets the requirements of the test for *arsenic.*

"**Assay.**—Dissolve about 1 Gm. of Sodium Thiosulphate, accurately weighed, in 20 cc. of distilled water, and titrate with tenth-normal iodine, starch T.S. being used as indicator. Each cc. of tenth-normal iodine corresponds to 0.01581 Gm. of $Na_2S_2O_3$.

"Preserve in well-closed containers." *U. S.*

Its solution dissolves silver chloride and all water-insoluble compounds of that metal, except the sulphide, and that resulting from the decomposition of a silver salt by light. It has a similar relation to the insoluble salts of lead. Though without action on potassium iodide, it dissolves iodine, decomposes iodic acid with liberation of iodine, and destroys the blue color of starch iodide. In dissolving iodine it forms with it sodium iodide and sodium tetrathionate, as represented by the formula

$$2(Na_2S_2O_3) + I_2 = (NaI)_2 + Na_2S_4O_6$$

Its relations to iodine render it valuable as a means of estimating the quantity of free iodine, for which purpose it is used in the Pharmacopœias in the form of a volumetric solution.

In consequence of its peculiar solvent properties, it is much used in photography. The photographers employ it for the purpose of dissolving the unchanged silver iodide, or bromide, from the plate after the action of the light, and thus fixing the image already formed. It is also largely used as an "*antichlor*" in paper manufacture, to free the paper pulp from the excess of chlorine used in the bleaching. One of the most delicate tests is that of iodine with starch. The blue color produced by the mixture of very small quantities of these two substances in solution is instantly discharged by a solution containing a trace of the thiosulphate. If zinc or iron is dipped into an acidified solution of the thiosulphate, the liberated hydrogen at once reduces the sulphurous oxide which is in the solution to hydrogen sulphide, recognizable by lead acetate paper. This test will serve to show even traces of thiosulphate.

Uses.—In 1920 Ravaut of Paris recommended the use of sodium thiosulphate in the treatment of the *dermatitis* which sometimes follows arsphenamine injections. The value of the treatment has been confirmed by several investigators. Groehl and Myers (*T. G.*, 1924, xlviii, p. 691) found that after the intravenous injection of sodium thiosulphate in these cases there was a marked increase in the amount of arsenic in the urine and attribute the beneficial effect to stimulated excretion. Kuhn and Loevenhart (*J. P. Ex. T.*, 1925, xxv, p. 160) find, however, that sodium thiosulphate delays the elimination of arsenic; but that to a limited extent, at least, it protects animals against the toxic properties of this poison. They find that it also lowers the therapeutic efficiency of the organic arsenicals and conclude that its effect is due to the formation in the body of a less toxic compound with arsenic. Dennie and MacBride (*J. A. M. A.*, 1924, lxxxiii, p. 2082) recommend the internal use of sodium thiosulphate in other metallic poisonings, such as *lead* and *mercury*, but present no convincing evidence of its value.

Sodium thiosulphate is also useful as a topical application in many forms of *skin diseases.* Its beneficial effect is probably due in part to a reducing action, but in some, as in *ivy poisoning,* it appears to exercise an antipruritic action. Trousseau (*R. T.*, 1905, p. 136) has recommended sodium thiosulphate in five per cent. solution as a topical application in *blepharitis* and *conjunctivitis.*

Dose, ten to twenty grains (0.65–1.3 Gm.), three times a day simply dissolved in water, or in the form of syrup. For external use a drachm may be dissolved in a fluidounce of water.

SODIUM

SODIUM

"The metal sodium as met with in commerce. It should be preserved in well-stoppered bottles under mineral naphtha." *Br.*, 1898.

Sodium, *Fr.;* Natrium, Natronmetall, *G.;* Sodio, *It.*, *Sp.*

The metal sodium was discovered by Sir Humphry Davy in 1807, who obtained it in small quantity by decomposing soda by the agency of galvanic electricity. Sodium was formerly prepared on a large scale by igniting an intimate mixture of dry sodium carbonate, coal and chalk. The amount of metal obtained by this method is, however, not over 40 per cent. of the theoretical result. A much improved process was next brought out by Castner (*J. Soc. Chem. Ind.*, 1887, 174), in which an iron carbide, or a mixture of fine iron and coke, is used to reduce the caustic soda, according to the reaction:

$$6NaOH + FeC_2 = 2Na_2CO_3 + 6H + Fe + 2Na$$

The reduction of the sodium hydroxide takes place at a temperature of about 800° C., and is carried out in steel crucibles, each of which holds 5.6 kilos of sodium hydroxide and 1.97 kilos of carbide. The product of the reaction consists of about 4.85 kilos of sodium carbonate and 0.933 kilo of metallic sodium. This latter collects in a receiver connected with the top of the crucible, while the sodium carbonate is dissolved out from the residue and is causticized preparatory to being used again. This process in turn has been replaced by the electrolytic processes. The most successful of these is that of Castner, who uses an electrolyte of fused sodium hydroxide in an iron pot or crucible with an anode of iron and a cathode of copper. The sodium is reduced at a comparatively low temperature, and is ladled from the vessel into moulds. The process is carried out at present on a large scale by the Niagara Electro-Chemical Co., and at Oldbury, England, and several places in Germany.

Sodium is a soft, malleable, ductile solid, of a silver-white color. It possesses the metallic luster in a high degree, when protected from the action of the air, by which it is quickly tarnished and oxidized. Its sp. gr. when fused is 0.97 at 20° and 0.74 at the fusion point, which is 97.6° C. Its chemical affinities resemble those of potassium, but are less energetic. Like potassium, it has a strong attraction for oxygen. When thrown upon cold water it instantly fuses into a globule without inflaming, and traverses the surface in different directions with rapidity; on warm water it inflames. In both cases the water is decomposed, hydrogen is liberated, and sodium hydroxide generated. Like potassium, if exposed with a bright surface to the air, it undergoes a slow combustion, which renders it luminous in the dark. It combines with oxygen to form the monoxide, Na_2O, and a peroxide, Na_2O_2. This latter oxide is always formed when the metal is burned in the open air.

It is officially described as "A soft metal, rapidly oxidizing in the air, but showing a bright metallic surface when freshly cut. It violently attacks water or alcohol (90 per cent.), with evolution of hydrogen, little or no insoluble matter remaining. It imparts an intense yellow color to flame. Each gramme very cautiously added to water affords a solution which should require for neutralisation at least 42.6 cubic centimetres of the volumetric solution of sulphuric acid." *Br.*

Sodium salts are characterized by communicating to the blowpipe flame a rich yellow color which is the most distinguishing analytical characteristic of this element. Sodium salts are not readily precipitable. The least soluble salt is the pyroantimoniate, $Na_2H_2Sb_2O_7$, which requires 350 parts of cold water for solution. According to Ball (*Chem. Trans.,* 1909, 2126) a solution of bismuth potassium nitrite containing calcium nitrite forms a reagent capable of detecting as little as 0.01 mgm. of sodium, even in the presence of an excess of potassium, by the formation of a yellow precipitate.

$$Na_2O + H_2O = 2NaOH$$

For description of sodium dioxide, see under *Peroxides,* Part II.

Uses.—Sodium is the most nearly inert physiologically of all the elements. It is, therefore, the base of choice when it is desired to obtain the effects of various acid ions. For the effects of massive doses of sodium see under *Sodii Carbonas.*

SOLANUM. N. F.

SOLANUM Solan. [Horse-Nettle Berries]

"Solanum is the air-dried, ripe fruit of *Solanum Carolinense* Linné (Fam. *Solanaceæ*). Solanum contains not more than 5 per cent. of immature fruit and not more than 2 per cent. of foreign organic matter." *N. F.*

Horse Nettle; Sand Brier; Poisonous Potato; Apple of Sodom.

The horse nettle is a common perennial weed in waste places and sandy soil throughout the whole of the Eastern United States. Its erect, branched stem, about 2 or 3 feet in height, is armed with stout yellowish prickles which are also on the veins of the leaves. The corolla is violet and with the exserted yellow stamens makes an attractive contrast of color; the leaves are oblong, ovate, obtusely toothed or lobed; the fruit an orange yellow berry about ⅓ to ¾ of an inch in diameter.

Description and Physical Properties.—"*Unground Solanum.*—Globose, slightly depressed, somewhat shriveled and wrinkled in drying, from 0.8 to 2 cm. in diameter, orange-yellow, glabrous, fleshy, two-celled, many-seeded, calyx and pedicel usually persistent; calyx stellate pubescent, deeply incised, the five subdivisions ovate or ovate-lanceolate, acuminate and enclosing half or more of the berry; seeds orbicular, flat, yellow, smooth, shining. Odor pepper-like; taste bitter and acrid.

"*Powdered Solanum.*—Brownish; numerous fragments of seed coat composed of cells from 0.138 to 0.250 mm. in length with very sinuous, yellowish, lignified walls about 0.015 mm. in thickness; fragments of epicarp composed of cells with thick yellowish walls and a yellowish amorphous content; portions of sarcocarp composed of thin-walled, more or less collapsed cells some containing nearly spheroidal starch grains up to 0.012 mm. in diameter; tracheæ narrow with spiral or reticulate thickenings; occasional microcrystals." *N. F.*

For study of microscopic structure, see Johnson, *A. J. P.,* 1897, lxix, 76. G. A. Krauss (*A. J. P.,* 1890, p. 601 and 1891, p. 216) found two active principles corresponding probably to *solanine* and *solanidine* (see Part II), together with a characteristic organic acid to which he gives the name *solanic acid.* J. U. Lloyd believes that the alkaloid in this plant is not identical with solanine, and proposes to call it *solnine.* (*A. J. P.,* 1894, 161, and 1897, 108.)

Uses.—E. Q. Thornton (*T. G.,* xii, 1896) finds that in frogs this solanum produces stupor with tetanic spasms, not prevented by section of the cord. It is said to have long been used by the negroes of the South in the treatment of the so-called falling sickness, and in 1889 it was recommended by J. L. Napier as of value in *epilepsy.* H. C. Wood found that, although when given by itself its usefulness is very limited, as an adjuvant to the bromides it lessens the size of the doses necessary to keep the convulsions in check. Not less than a fluidrachm (3.75 cc.) of the fluidextract should be given three times a day. No unpleasant effects have been produced by it.

Dose, from thirty to sixty grains (2–4 Gm.).

Off. Prep.—Fluidextractum Solani, *N. F.*

SPIRITUS

SPIRITS

Alcoolats, *Fr.;* Geiste, *G.;* Spirito, *It.;* Espiritu, Solucion Alcoholica, *Sp.*

Spirits, as the term is here used, are alcoholic solutions of volatile principles formerly procured by distillation, but now frequently prepared by simply dissolving the volatile substance or substances in alcohol. The spirits as a rule are prepared by simple solution of the active substance in alcohol. A few are prepared by distillation as *Spiritus Frumenti* and *Spiritus Vini Vitis.* Some are therapeutic agents of value, others are employed merely as flavoring agents. These latter are sometimes confused with the "flavoring extracts" or "essences" used in culinary practice, but as a rule the official spirits are much stronger than the flavoring extracts of the same name, and in some cases, notably *Spiritus Amygdalæ* contain constituents which are not suitable for use in food products.

SPIRITUS ÆTHERIS. Br.

SPIRIT OF ETHER Sp. Æth. [Hoffmann's Drops]

Liquor Anodynus Mineralis Hoffmanni; Ether officinal alcoolisé, Ether sulfurique alcoolisé, Liqueur d'Hoffmann, *Fr.;* Spiritus Æthereus, *P. G.;* Aetherweingeist, Hoffmannsche Tropfen, *G.;* Etere con alcool, Liquore anodino di Hoffmann, *It.;* Eter sulfurico alcoholizado, Licor anodino mineral de Hoffmann, *Sp.*

"Ether, 500 *millilitres;* Alcohol (90 per cent.), 1000 *millilitres.* Mix. Specific gravity 0.802 to 0.806." *Br.*

This preparation is merely ether diluted with about twice its volume of alcohol. Because of the infrequency of its use and the simplicity of its preparation it was wisely omitted at the last revision of the U. S. The corresponding preparation of the German Pharmacopœia contains less ether, being made of one part of ether to three parts of alcohol, both by weight.

The spirit of ether is used chiefly as a carminative in *flatulent colic.* Although not so frequently employed as the former U. S. P. *compound spirits of ether,* which is now official in the N. F. (see *Spiritus Ætheris Compositus,* Part III), it has all the therapeutic virtues of that preparation. The Compound Spirit of Ether is commonly known as *Hoffmann's Anodyne.*

Dose, one to three fluidrachms (3.75–11.25 cc.).

SPIRITUS ÆTHYLIS NITRITIS.
U. S. (Br.)

SPIRIT OF ETHYL NITRITE Sp. Æth. Nitrit. [Spiritus Ætheris Nitrosi U. S. P. IX, Spirit of Nitrous Ether, Sweet Spirit of Niter]

"Spirit of Ethyl Nitrite is an alcoholic solution of ethyl nitrite containing not less than 3.5 per cent. and not more than 4.5 per cent. of $C_2H_5NO_2$." *U. S.* "Spirit of Nitrous Ether is an alcoholic solution containing not less than 1.52 or more than 2.66 per cent. by weight of ethyl nitrite, together with aldehyde and other allied substances. It should be kept in well-closed vessels; preferably in a cool dark place, and in small amber bottles." *Br.*

Spiritus Ætheris Nitrosi, *Br.;* Spiritus Nitri Dulcis; Spiritus Ætheris Nitrici; Spiritus Nitrico-æthereus; Ætheris Nitrosi Spiritus; Alcoholum Nitricum Æthereum; Ether Azoteux Alcoolisé, Liqueur anodine nitreuse, *Fr.;* Versüsster Salpetergeist, *G.;* Etere nitroso officinale, Spirito d'etere nitroso, *It.;* Espiritu de nitro dulce, *Sp.*

"Nitric Acid, 150 *millilitres;* Sulphuric Acid, 100 *millilitres;* Copper of commerce, in wire or turnings, 100 *grammes;* Alcohol (90 per cent.), *a sufficient quantity.* To one thousand millilitres of the Alcohol add gradually the Sulphuric Acid, and then one hundred and twenty-five millilitres of the Nitric Acid, stirring constantly. Transfer the mixture to a retort or flask, in which the fragments of copper have been placed, and to which is attached an efficient condenser with a receiver containing one thousand millilitres of the Alcohol. Surround the receiver with ice-cold water and distil gently at a temperature which is at first about 77° C., and rises to 80° C., but does not exceed 82° C., until the volume of liquid in the receiver has been increased to sixteen hundred millilitres. Then allow the contents of the retort to cool, introduce the remaining twenty-five millilitres of Nitric Acid, and resume the distillation as before, until the liquid in the receiver has been increased to seventeen hundred millilitres. Mix this liquid with one thousand millilitres of the Alcohol, or with as much as will make the product contain 2.66 per cent. by weight of ethyl nitrite when tested as described in the following paragraph." *Br.*

The U. S. P. X does not give any method for the preparation of this spirit. That which was previously official was based upon decomposition of sodium nitrate with sulphuric acid as follows: "Sodium Nitrite, *one hundred grammes;* Sulphuric Acid, *forty mils;* Monohydrated Sodium Carbonate, *six-tenths of a gramme;* Potassium Carbonate, completely deprived of water by heating, *three grammes;* Alcohol, Water, each, *a sufficient quantity.* Mix the sulphuric acid with *one hundred and twenty mils* of water, cool the liquid, add *eighty-five mils* of alcohol previously diluted with an equal volume of water, and introduce the solution into a 1000 mil flask, surrounded by a mixture of ice and water. Dissolve the sodium nitrite in *two hundred and eighty mils* of water, filter, and, having poured the filtrate into a separatory funnel, allow the liquid to slowly drop into the flask containing the acid mixture. When all has been added and the reaction is complete, allow any crystals which may have formed to settle at the bottom of the flask, and decant the cold mixture of ethyl nitrite and aqueous solution quickly to the previously cooled separatory funnel, and draw off and discard the aqueous liquid. Wash the separated ethyl nitrite, first with *twenty mils* of ice-cold water, and then remove any traces of acid by washing it with *fifteen mils* of ice-cold water, in which the monohydrated sodium carbonate has previously been dissolved. Carefully separate the ethyl nitrite from the aqueous liquid, and agitate it in a well-stoppered botle with the potassium carbonate to remove traces of water. Then cool the liquid, decant, and pour the ethyl nitrite immediately into a tared bottle containing *five hundred grammes* of alcohol. Ascertain the weight of the ethyl nitrite poured in the alcohol by noting the increase in weight of the tared bottle and contents, and then add enough alcohol to make the mixture weigh *twenty-two times* the weight of the ethyl nitrite added. Lastly, transfer the product to small, well-stoppered, dark, amber-colored bottles, and keep these in a cool place, remote from fire." *U. S. IX.*

The official spirit of nitrous ether is a mixture of nitrous ether or ethyl nitrite, $C_2H_5NO_2$, and alcohol (rectified spirit). For many years, spirit of nitrous ether was made by acting on alcohol with nitric acid, and the present British process is constructed on this plan. The U. S. P. VIII and IX processes differed essentially; in these, the use of nitric acid was abandoned, sodium nitrite being substituted as the source of the nitrous compound. Ethyl nitrite is readily generated by the reaction of nitric acid with alcohol; and it matters not whether the alcohol be mixed with nitric acid directly, or with the materials for generating it, namely, niter and sulphuric acid.

Many processes have been suggested for the preparation of this spirit by the retail pharmacist. All are equally subject to the criticism that they are difficult to carry out and none is capable of yielding a product which does not require assay and subsequent adjustment of strength. The appearance of the concentrated product in small sealed units, capable of easy use and affording a product of uniform strength has removed the necessity for an official process for this spirit.

Full details of former methods will be found in *U. S. D.*, 20th ed., p. 1049.

The reaction in the U. S. P. IX process may be expressed as follows:

$$2C_2H_5OH + 2NaNO_2 + H_2SO_4 = 2C_2H_5NO_2 + Na_2SO_4 + 2H_2O$$

Alcohol, sodium nitrite, and sulphuric acid when brought in contact yield ethyl nitrite, sodium sulphate, and water.

The nitric acid process may be explained as follows: One molecule of nitric acid, by reacting with one molecule of alcohol, forms one molecule of nitrous acid, one molecule of aldehyde, and one molecule of water, thus:

$$HNO_3 + C_2H_6O = HNO_2 + C_2H_4O + H_2O$$

The nitrous acid, as soon as formed, reacts with a second molecule of alcohol, so as to form one molecule of nitrous ether or ethyl nitrite, with separation of one molecule of water, according to the reaction:

$$C_2H_5.OH + HNO_2 = C_2H_5NO_2 + H_2O$$

In the process of the British Pharmacopœia the nitric acid is converted into nitrous acid by the reducing action of metallic copper and sulphuric acid, the reaction being:

$$HNO_3 + Cu + H_2SO_4 = HNO_2 + CuSO_4 + H_2O$$

The nitrous acid now reacts with the alcohol as in the previous reaction, so as to produce the nitrous ether. The object of using the sulphuric acid is to economize the nitric acid.

The present British formula rejects the sodium nitrite process for the preparation of the spirit, but introduces under *Liquor Ethyl Nitritis* a solution made by decomposing sodium nitrite in the presence of alcohol, and diluting the ethyl nitrite produced, with alcohol containing a little glycerin. It is unfortunate that both preparations were not made of the same strength, the solution containing 3 per cent., the spirit only 2 per cent., of ethyl nitrite; the *solution* contains no aldehyde, but the *spirit* is permitted to contain aldehyde and other substances.

Properties of Ethyl Nitrite.—Pure ethyl nitrite is pale yellow, has a pleasant ethereal and somewhat apple-like odor. It boils at 18° C., and has the sp. gr. 0.900 at 15.5° C. The density of its vapor is 2.627. Litmus is not affected by it. When it is mixed with an alcoholic solution of potassium hydroxide, potassium nitrite and alcohol are formed, without producing a brown color, showing the absence of aldehyde. It is soluble in 48 parts of water, and in all proportions in alcohol or rectified spirit. It is highly inflammable, and burns with a white flame without residue.

Ethyl nitrite in hermetically sealed glass tubes is found in commerce, affording a ready means of preparing small quantities of spirit of nitrous ether as referred to previously. The concentrated product deteriorates on keeping; as pure ethyl nitrite boils at 18° C., the tubes should be cooled and opened and the liquid immediately diluted with the proper quantity of alcohol to make spirit of nitrous ether, or they should be kept in a cool place until used. Clarence M. Kline, of Philadelphia, originated this method of protecting ethyl nitrite. In its pure and concentrated state it is never used in medicine.

Description and Physical Properties.—"A clear, mobile liquid of a pale yellow or faintly greenish-yellow tint. It has a fragrant, ethereal, pungent odor free from acridity, and a sharp, burning taste. It is volatile and inflammable, and rapidly decomposes on exposure to light and air. When freshly prepared or even after being kept for some time with but little exposure to light and air, it is neutral to dry litmus paper. When long kept or after having been exposed to light and air, it acquires an acid reaction. Specific gravity: not above 0.823 at 25° C.

"Immerse a test tube half filled with the Spirit in a water bath heated to 65° C. until it has acquired that temperature: the Spirit distinctly boils upon the addition of a few small pieces of broken glass. Effervescence does not result when a crystal of potassium bicarbonate is added to 5 cc. of the Spirit (*free acid*). Mix 10 cc. of the Spirit with 5 cc. of potassium hydroxide T.S. previously diluted with 5 cc. of distilled water: the mixture assumes a yellow color which does not turn decidedly brown within twelve hours (*aldehyde*).

"Preserve in small, well-stoppered, dark amber-colored bottles, in a cool, dark place, remote from fire." *U. S.*

"A transparent liquid, having a very faint yellowish tinge. Peculiar penetrating apple-like odor; taste characteristic. Specific gravity 0.838 to 0.842. When spirit of Nitrous Ether is carefully poured on an acidified strong aqueous solution of *ferrous sulphate* contained in a test-tube, a deep olive-brown coloration is produced at the surface of contact of the two liquids, widening as the tube is gently shaken. Does not effervesce, or only very slightly, when shaken with *sodium bicarbonate* (limit of acid). 10 millilitres mixed with 5 millilitres of *N/1 solution of sodium hydroxide* and 5 millilitres of *water* assume a yellow color, which does not become brown on standing twelve hours (limit of aldehyde). 1 volume shaken briskly at intervals during five minutes in a brine-charged nitrometer, with 1 volume of *solution of potassium iodide* and 1 volume of *diluted sulphuric acid,* yields at 15.5° C. and normal pressure not less than 4 or more than 7 volumes of nitric oxide gas, corresponding to not less than 1.52 or more than 2.66 parts by weight of ethyl nitrite in 100 parts by weight of the Spirit." *Br.*

Spirit of nitrous ether, when made by the nitric acid process, is never quite free from aldehyde, and, if the distillation be too long continued it is prone to contain a good deal of this substance, which afterwards becomes acetic acid by absorbing oxygen. The change goes on rapidly if the preparation be insecurely kept. Aldehyde, if in considerable proportion, may be detected by its imparting a pungent odor and an acrid flavor, and by the spirit assuming a brown tint on adding a weak solution of potassium hydroxide, owing to the formation of aldehyde resin (see official test).

The pharmacists should note specially that the U. S. P. requires this Spirit to be preserved in small, well-stoppered, dark, amber-colored bottles, in a cool and dark place. The former custom of keeping it in partially filled shop bottles in the regular stock must be abandoned if the preparation is to be dispensed of official strength. This is no hardship as the stock can be filled into small bottles at the time it is made and will then be ready for dispensing.

J. G. Roberts (*A. J. P.*, 1921, xciii, 324) reports upon the stability of spirit of nitrous ether after extensive experiments with various forms of exposure and keeping. He concludes that when the product is kept as directed by the U. S. Pharmacopœia the deterioration is slight. The same conclusions were reached by Kebler, Palkin and Ewing (*J. A. Ph. A.*, 1916, pp. 514 and 1327). See also *Ph. Wb.*, 1917, liv, 1052.

Assay.—The U. S. P. and the Br. Ph. quantitative test is based on Allen's method, differing only in the relative quantities of the reagents. (See paper by Curtman, *Proc. Missouri Pharm. Assoc.*, July, 1892; also *A. J. P.*, 1898, 273.)

"Transfer about 40 cc. of Spirit of Ethyl Nitrite, which has been previously shaken with 0.5 Gm. of powdered potassium bicarbonate, to a tared, 100 cc. measuring-flask, and weigh accurately. Add sufficient alcohol to bring the volume to exactly 100 cc., and mix thoroughly. Introduce into a nitrometer, exactly 10 cc. of the alcoholic solution, follow by 10 cc. of potassium iodide T.S. and afterwards by 5 cc. of diluted sulphuric acid. When the volume of gas has become constant (within thirty to sixty minutes), note the volume of gas collected. Multiply this volume in cc. by 0.307, and divide the product by one-tenth of the weight of the Spirit of Ethyl Nitrite taken. At standard temperature and pressure, the quotient represents the percentage of ethyl nitrite in the liquid. The temperature correction is 1/273 of the total percentage just found for each degree of temperature, added if the temperature is below, subtracted if above, 25° C. The barometer correction is 1/760 of the total percentage just found for each mm., added if above, subtracted if below, 760 mm." *U. S.*

The other methods in former use were defective in consequence of the complexity of the reaction or other factors causing variation. In the *J. A. Ph. A.*, 1916, p. 1327, Englehardt and Winters suggest a new method of estimation of the ethyl nitrite, based upon Dietze's potassium chlorate method as used in the Netherland Pharmacopœia, which avoids the use of the nitrometer and barometer and gives very good results. This method, however, has some drawbacks which impel the retention of the nitrometer method for official purposes.

Uses.—Sweet spirits of niter possesses the physiological properties of the other nitrites (see *Sodii nitris*). Its inhalation produces acceleration of the pulse with the characteristic leaden purplish color of the lips, mouth and finger tips, followed by flushing of the face, giddiness, nausea, muscular debility, and violent headache. It is rarely employed, however, to produce the full physiological action of the nitrites, its chief employment being to relax the blood vessels of the skin and thereby increase the flow of sweat. It is an extremely popular diaphoretic in mild *fevers*, especially in children. Because of its action on the circulation it also at times exercises a diuretic influence.

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

Off. Prep.—Mistura Glycyrrhizæ Composita, *U. S.;* Mistura Copaibæ, *N. F.;* Mistura Copaibæ et Opii, *N. F.*

SPIRITUS AMMONIÆ AROMATICUS.
U. S., Br.

AROMATIC SPIRIT OF AMMONIA Sp. Ammon. Arom.

Spiritus Ammoniæ Compositus; Spirit of Sal Volatile; Alcoolat ammoniacal aromatique, *Fr.;* Aromatischer Ammoniakgeist, *G.*

"Ammonium Carbonate, in translucent pieces, 34 Gm.; Ammonia Water, 90 cc.; Oil of Lemon, 10 cc.; Oil of Lavender, 1 cc.; Oil of Myristica, 1 cc.; Alcohol, 700 cc.; Distilled Water, a sufficient quantity, to make 1000 cc. Dissolve the ammonium carbonate in the ammonia water and 140 cc. of distilled water by gentle agitation, and allow the solution to stand for twelve hours. Dissolve the oils in the alcohol, contained in a 1000 cc. volumetric flask or cylinder, gradually add the ammonium carbonate solution, and enough distilled water to make the product measure 1000 cc. Set it aside in a cool place for twenty-four hours, occasionally agitating, and filter, using a covered funnel." *U. S.*

"Ammonium Carbonate, 100 *grammes;* Strong Solution of Ammonia, 200 *millilitres;* Oil of Nutmeg, 15 *millilitres;* Oil of Lemon, 20 *millilitres;* Alcohol (90 per cent.), 3000 *millilitres;* Distilled Water, 1500 *millilitres.* Place the Oil of Lemon, Oil of Nutmeg, and Alcohol with the Distilled Water in a retort; distil three thousand five hundred millilitres; then distil and separately collect an additional two hundred and twenty-five millilitres. Place the latter, together with the Ammonium Carbonate and the Strong Solution of Ammonia, in a bottle holding rather more than five hundred millilitres; securely cork the bottle and gently warm it in a water-bath to 60° C., shaking from time to time until all the salt has dissolved. Filter the resulting solution when cold through cotton wool, and gradually mix the filtrate with the portion first distilled." *Br.*

In both of these formulas ammonium carbonate and uncombined ammonia are used; but they differ in the relative proportion of the materials and the mode of conducting the process. The U. S. spirit is a mere solution of the ingredients in alcohol diluted with a small proportion of water, while the British contains so much of the ingredients as may rise in distillation and be condensed with the seven pints of spirit that result. The strength of the former is definite, that of the latter more or less indefinite, as a portion of the materials must be left behind. The advantage arising from distillation, however, is the avoidance of discoloration, one which is well worth considering although the spirit will always grow darker with age. The present preparation differs from that formerly official in the substitution of oil of myristica for oil of pimenta, it having been shown that oil of pimenta increased the tendency of the spirit to darken. Commercial oil of myristica frequently has a terebinthinate odor. Much care is needed to select for this preparation volatile oils that are fresh and of good quality. The translucent official ammonium carbonate, which is a mixture of bicarbonate and carbamate, does not dissolve in alcohol; the bicarbonate precipitates, and the carbonate, $NH_4HCO_3 + NH_4OH = (NH_4)_2CO_3 + H_2O$, dissolves. The object of the addition of free ammonia in the official process is to convert the insoluble bicarbonate into the carbamate, and it is directed that these shall be allowed to stand during *twelve hours* while this change is taking place. The effloresced ammonium carbonate of commerce having parted with some of its ammonia is a bicarbonate; hence, when it is used, unless more than the official proportion of the ammonia water be added, some of the ammonium salt will remain in the precipitate as ammonium bicarbonate.

The difficulty of precipitation which so many pharmacists complain of is thus explained. It is a useful precaution to permit the ammonium carbonate and ammonia water to remain in contact for twelve hours before diluting with the other ingredients; this will secure the entire conversion of the bicarbonate, and obviate the precipitation above noted. In addition to this, it is officially directed to set the mixed liquid aside, for twenty-four hours, before final filtration.

Description and Physical Properties.—"A nearly colorless liquid when freshly prepared, but gradually acquiring a yellow color. It has the taste of ammonia and an aromatic and pungent odor. Specific gravity: about 0.900 at 25° C.

"Preserve in glass-stoppered bottles, in a cool place. Alcohol content, by volume, 62 to 68 per cent." *U. S.*

"A nearly colorless transparent liquid. Odor and taste pungent and ammoniacal. Specific gravity 0.888 to 0.893. 20 millilitres require for neutralisation 25.4 millilitres of *N/1 solution of sulphuric acid,* corresponding to 2.16 grammes of ammonia, NH_3, in 100 millilitres of the Spirit. When 20 millilitres are mixed with 50 millilitres of *water* and excess of *solution of barium chloride,* the mixture heated to 70° C., the precipitate collected, washed until free from alkali, and dissolved in 20 millilitres of *N/1 solution of hydrochloric acid,* the solution thus obtained, after being boiled and cooled, requires for neutralisation not less than 7.2 or more than 8 millilitres of *N/1 solution of sodium hydroxide,* corresponding to not less than 2.35 or more than 2.51 grammes of acid ammonium carbonate and ammonium carbamate, calculated together as $N_3H_{11}C_2O_5$, in 100 millilitres of the Spirit." *Br.*

In handling this preparation on the large scale, copper vessels must never be used, as the preparation has a solvent effect upon the film of tarnish which is always present and thereby becomes contaminated, sometimes with the development of a bright green color. When this occurs, the preparation must either be thrown away or redistilled in a glass apparatus.

Uses.—Aromatic spirits of ammonia is much more widely used than the simple spirit because of its grateful taste and odor. It is used to correct *hyperacidity of the stomach* when not associated with inflammatory changes in the mucous membrane of that organ, and especially when there is *nausea* or *sick headache.* By virtue of its local irritant effect upon the mucous membrane of the stomach it will often reflexly excite the medulla and thereby relieve the feeling of *faintness.* It has, however, been enormously misapplied as a heart stimulant; as pointed out elsewhere (see *Aqua Ammoniæ*) although ammonia is a stimulant to the circulation it can act only when injected hypodermically.

Dose, thirty minims to a fluidrachm (1.8–3.75 cc.), sufficiently diluted.

Off. Prep.—Mistura Sennæ Composita, *Br.;* Tinctura Guaiaci Ammoniata, *N. F.;* Tinctura Valerianæ Ammoniata, *U. S.;* Liquor Sodæ et Menthæ, *N. F.*

SPIRITUS AMMONIÆ FŒTIDUS. Br.

FETID SPIRIT OF AMMONIA

Alcoolat ammoniacal fétide, Essence antihystérique, *Fr.;* Ammoniakalischer Stinkasantgeist, *G.*

"Asafetida, 75 *grammes;* Strong Solution of Ammonia, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Break the Asafetida into small pieces, and macerate it in a closed vessel in seven hundred and fifty millilitres of the Alcohol for twenty-four hours; distil until alcoholic vapors cease to be condensed; mix the distillate with the Strong Solution of Ammonia, and add sufficient Alcohol to produce the required volume." *Br.*

This is an alcoholic solution of the volatile oil of asafetida mixed with strong solution of ammonia, and is an energetic nervous stimulant and antacid, adapted to certain *hysterical conditions* associated with gastric weakness and acidity. It is one of the preparations formerly recognized by the British Colleges, and reinstated after having been dropped from the first British Pharmacopœia.

"A nearly colorless, transparent liquid with a strong odor of ammonia and of asafetida. Specific gravity 0.842 to 0.850. 25 millilitres require for neutralisation not less than 40 millilitres of *N/1 solution of sulphuric acid,* corresponding to not less than 2.75 grammes of ammonia, NH_3, in 100 millilitres of the Spirit." *Br.*

This preparation combines the carminative effect of asafetida with the antacid properties of ammonia. It may be used in gastric or intestinal *flatulence.*

Dose, thirty minims to a fluidrachm (1.8–3.75 cc.), to be largely diluted when administered.

SPIRITUS ANISI. U. S., Br.

SPIRIT OF ANISE Sp. Anisi

Essence of Anise; Teinture d'essence d'anis, *Fr. Cod.;* Anisgeist, *G.*

"Oil of Anise, 100 cc.; Alcohol, a sufficient quantity to make 1000 cc. Mix the oil with sufficient alcohol to make the product measure 1000 cc. Alcohol content, by volume, 80 to 87 per cent." *U. S.* "Oil of Anise, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 millilitres. Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

Dose, as a stomachic and carminative, from twenty to sixty minims (1.3–3.75 cc.), properly diluted.

SPIRITUS ARMORACIÆ COMPOSITUS. Br.

COMPOUND SPIRIT OF HORSERADISH

Esprit de Raifort composée, Alcoolat antiscorbutique, *Fr.;* Zusammengesetzter Meerrettiggeist, *G.*

"Horseradish Root, scraped, 125 *grammes;* Dried Bitter-Orange Peel, bruised, 125 *grammes;* Nutmeg, bruised, 3 *grammes;* Alcohol (90 per cent.), 625 *millilitres;* Distilled Water, 750 *millilitres.* Macerate the Horseradish Root in the Distilled Water for one hour, add the other ingredients, and distil one thousand millilitres. Specific gravity 0.917 to 0.927." *Br.*

This may be used advantageously as an addition to diuretic remedies, in *dropsy* attended with debility, especially in the case of drunkards.

Dose, from one to four fluidrachms (3.75–15 cc.).

SPIRITUS AURANTII COMPOSITUS. U. S.

COMPOUND SPIRIT OF ORANGE Sp. Aur. Co.

Teinture d'essence d'orange, Esprit d'orange composée, *Fr.;* Zusammengesetzter Orangegeist, *G.*

"Oil of Orange, 200 cc.; Oil of Lemon, 50 cc.; Oil of Coriander, 20 cc.; Oil of Anise, 5 cc.; Alcohol, a sufficient quantity to make 1000 cc. Mix the oils with sufficient alcohol to make the product measure 1000 cc.

"Preserve in dark amber-colored bottles.

"Alcohol content, by volume, 65 to 70 per cent." *U. S.*

This compound spirit has been introduced for the purpose of producing the orange flavor in making the official aromatic elixir, and in various N. F. elixirs. It will be found by physicians to be a useful and fragrant addition to prescriptions.

Off. Prep.—Elixir Aromaticum, *U. S.*

SPIRITUS CAJUPUTI. Br.

SPIRIT OF CAJUPUT

Teinture d'essence de Cajeput, Alcoolé d'essence de Cajeput, *Fr.;* Cajeputgeist, *G.*

"Oil of Cajuput, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

For an account of the medicinal properties and uses of oil of cajuput, of which this is simply an alcoholic solution, see *Oleum Cajuputi.*

Dose, from five to twenty minims (0.3–1.3 cc.), properly diluted.

SPIRITUS CAMPHORÆ. U. S., Br.

SPIRIT OF CAMPHOR Sp. Camph.

"Spirit of Camphor contains not less than 9.5 Gm. and not more than 10.5 Gm. of camphor in each 100 cc." *U. S.*

Tinctura Camphoræ, *U. S.* 1850; Tincture of Camphor; Solutum Camphoræ Alcoholicum; Alcohol Camphoratus; Teinture de camphre concentrée, *Fr. Cod.;* Esprit de Camphre, Alcool camphré, *Fr.;* Spiritus Camphoratus, *P. G.;* Kampherspiritus, *G.;* Alcohol Alcanforado, Solucion Alcoholica de Alcanfor, *Sp.*

"*Camphor,* 100 Gm.; *Alcohol,* a sufficient quantity, to make 1000 cc. Dissolve the camphor in about 800 cc. of alcohol and add enough alcohol to make the product measure 1000 cc. Filter if necessary." *U. S.*

"Camphor, 100 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. Specific gravity, 0.845 to 0.850. *Optical rotation* at 15.5° C., not less than + 4°." *Br.*

"**Tests for Purity.**—Specific gravity from 0.824 to 0.826 at 25° C. Add 0.05 Gm. of anhydrous potassium carbonate to 5 cc. of Spirit of Camphor: the potassium carbonate does not liquefy or adhere to the bottom of the vessel (*added water*).

"**Assay.**—Fill a 200 mm. polariscope tube with the Spirit of Camphor and take the mean of four or more readings of the rotation, setting the instrument at zero each time. The temperature correction for each degree of temperature is half a minute, added if above, subtracted if below, 25° C. Evaporate 60 cc. or more of the Spirit of Camphor in a dish, on a water bath, and when the camphor begins to solidify stir it with a glass rod until dry. Then transfer the camphor to a watch glass, cover it with an inverted funnel and place the watch glass on wire gauze 10 cm. above a Bunsen burner having a flame 4 cm. high. When the camphor has all sublimed, dissolve 2.5 Gm. of the sublimate in sufficient alcohol to make exactly 25 cc., and take the mean of four or more polariscope readings in a 200 mm. tube as before. The minutes of rotation of the Spirit of Camphor, divided by the minutes of rotation of the control test, and this multiplied by 10, shows the number of Gm. of camphor in 100 cc. of the Spirit of Camphor.

"Alcohol content, by volume, 80 to 87 per cent." *U. S.*

For other methods of assay, see *Ph. Centralh.*, 1901, 472 and 1915, 579; *J. S. C. I.*, 1919, xxxviii, 923a; and *Chem. Abs.*, 1919, xiii, 55.

The camphor content of the spirit is easily obtained by the official method when a polariscope is available, but the detection of the addition of water is a more difficult task. This has been worked out by Maiden and Elliot, and the results of the method published in the *J. A. Ph. A.*, 1914, p. 91.

Spirit of camphor is an excellent preparation, much used in *diarrhea,* and in *hysteria* and other forms of *nervous excitement.* Dilution with water precipitates the camphor, but when as in many cases it is desired to combine it with aqueous preparations, by dropping it into brandy or whisky and then adding water an eligible preparation is obtained; or the spirit of camphor may be dropped upon sugar and then mixed with water.

Dose, from ten to thirty minims (0.6–1.8 cc.).

Off. Prep.—Lotio Ammoniacalis Camphorata, *N. F.;* Mistura Opii et Chloroformi Composita, *N. F.;* Mistura Opii et Rhei Composita, *N. F.;* Tinctura Opii et Gambir Composita, *N. F.*

SPIRITUS CHLOROFORMI. U. S., Br.

SPIRIT OF CHLOROFORM Sp. Chlorof.

Chloric Ether, Spirit of Chloric Ether, *Br.;* Alcoolé de Chloroforme, *Fr.;* Chloroformspiritus, *G.*

"Chloroform, 60 cc.; Alcohol, a sufficient quantity to make 1000 cc. Mix the chloroform with sufficient alcohol to make the product measure 1000 cc. Preserve in dark amber-colored bottles.

"Alcohol content, by volume, 85 to 91 per cent." *U. S.* "Chloroform, 50 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve." *Br.*

It is to be regretted that the name Chloric Ether has been retained as a synonym in the British Pharmacopœia, 1914. There would be some reason for naming a mixture of chloroform and ether by the title chloric ether, but to use the term for an alcoholic solution of chloroform must inevitably cause confusion.

Chloric ether of the older works was a solution of variable strength of chloroform in alcohol, and was used as a general anesthetic. The practice has, however, very properly been abandoned, and the spirit of chloroform is now used as an internal remedy, especially in cases of *gastro-intestinal spasm* or *pain,* in which it acts as a local agent. The official aromatic elixir is an agreeable vehicle for its administration.

Dose, from ten to sixty minims (0.6–3.75 cc.).

SPIRITUS CINNAMOMI. U. S., Br.

SPIRIT OF CINNAMON Sp. Cinnam.

Teinture d'essence de Cannelle, Esprit de Cannelle, *Fr.;* Zimmtspiritus, *G.;* Spirito di cannella, *It.*

"Oil of Cinnamon, 100 cc.; Alcohol, a sufficient quantity to make 1000 cc. Mix the oil with sufficient alcohol to make the product measure 1000 cc.

"Alcohol content, by volume, 80 to 87 per cent." *U. S.*

"Oil of Cinnamon, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

The spirit of cinnamon is an agreeable aromatic cordial.

Dose, from ten to thirty minims (0.6–1.8 cc.) in water.

SPIRITUS FRUMENTI. U. S.

WHISKY Sp. Frum.

"Whisky is an alcoholic liquid obtained by the distillation of the fermented mash of wholly or partly malted cereal grains, and containing not less than 47 per cent. and not more than 53 per cent. by volume of C_2H_5OH, at 15.56° C. It must have been stored in charred wood containers for a period of not less than four years." *U. S.*

Eau de Vie de Graines, *Fr.;* Kornbranntwein, *G.;* Orzo Stillato, *It.*

The term "whisky" is a corruption of the Gaelic "usquebaugh" or more correctly "uisgebeatha," which signifies "water of life" and is said to have been first applied to the spirit obtained from barley in the Highlands of Scotland. As at present understood and as officially defined, whisky is the distilled spirit from the mash of various grains, including maize, wheat, rye and barley. In the United States it is generally made from corn or rye. The term is occasionally extended to other forms of ardent spirit; that resulting from the distillation of cider is frequently although incorrectly designated as "apple whisky."

In the preparation of whisky, the infusion of partially germinated grain (see *Maltum*), which is known as "mash," is made to ferment by the addition of yeast. This is submitted to distillation, the resulting product being denominated "low wine." By a second distillation it becomes purer and stronger and is known as "raw spirit" or "raw whisky." When stored in wooden vessels it undergoes slow oxidation losing the disagreeable odor and taste which it is apt to have when first distilled. It is generally believed that these changes involve the conversion of the aldehydic constituents of raw spirit into acids which unite with the higher alcohols of the fusel oil (see *Amyl Alcohol*, Part II) to form esters, the latter giving the improved taste and mellowness to aged whisky. The oxidation of the aldehydic constituents may be accomplished more rapidly by percolating the whisky through wood shavings. The peculiar flavor of Scotch whisky is due to the presence of small amounts of creosote and other constituents of smoke derived from the use of kiln-dried malt which has absorbed empyreumatic products.

When freshly distilled, whisky is colorless, but when stored in charred wooden casks it acquires its characteristic color from the carmelized "wood gum" of the barrel. During storage there is an increase in acidity, a loss of amyl alcohol and apparently a slight increase in the amount of furfural.

There are volatile principles naturally existing in the grains which are carried over in the successive distillations and give their characteristic flavor to the resulting spirit. These can scarcely be considered as impurities but there are others produced during the process of fermentation which seriously contaminate the product. Among these is the mixture known as fusel oil which is offensive both to smell and to taste. Minute proportions of acetic and butyric acids are often present in whisky and valeric acid has been reported.

A spurious or imitation whisky is often made by the addition of caramel or other coloring matter to alcohol and the addition of some genuine whisky to impart a characteristic flavor. This has led to considerable argument as to the definition of whisky, a question which can not be considered as entirely settled even at the present time although the question is not now as important as it was some years ago when the sale of whisky was only regulated by licensing provisions of the laws. What is a straight whisky, what is a blended whisky and what is an imitation whisky are the three fundamental questions. There is little argument over the first and the third of these questions. It is the second one upon which there is disagreement. *Straight whisky* is whisky which has been aged in wood for a sufficient length of time to ensure the changes by which the congeners of the alcoholic distillate are altered in a manner which produces the characteristic odor and taste distinctive of whisky, coloring matter from the charred oak barrels being at the same time taken up. *Imitation whisky* is an alcoholic liquid of approximately the same proof strength as whisky and colored and flavored in imitation of the same.

Blended whisky according to the original interpretation of Dr. H. W. Wiley, then head of the Bureau of Chemistry, is a mixture of straight whiskies of different types and varying degrees of maturity. This position was reversed by the U. S. Dept. of Agriculture officials in 1907 and the reversal was upheld by a decision of President Taft who acted as arbiter in the matter. The text of President Taft's decision, given Feb. 16, 1910, is as follows: "The term 'straight whisky' is well understood in the trade and well understood by consumers. There is no reason, therefore, why those who make straight whisky may not have the brand upon their barrels of straight whisky with further descriptive terms as 'Bourbon' or 'Rye' whisky, as the composition of the grain used may justify, and they may properly add, if they choose, that it is aged in the wood. Those who make whisky of 'rectified,' 'redistilled,' or 'neutral' spirits cannot complain if, in order to prevent frauds, they are required to use a brand which shall show exactly the kind of whisky they are selling. For that reason it seems to me fair to require them to brand their product as 'whisky made from rectified spirits,' or 'whisky made from redistilled spirits,' or 'whisky made from neutral spirits,' as the case may be; and if aged in the wood, as sometimes is the case with this class of whiskies, they may add this fact. A great deal of the liquor sold is a mixture of straight whisky with whisky made from neutral spirits. Now, the question is whether this ought to be regarded as a compound or a blend. The Pure Food Law provides that 'in the case of articles labelled, branded, or tagged so as to plainly indicate that they are compounds, imitations, or blends,' the term 'blend' shall be construed to mean a mixture of like substances, not excluding harmless coloring or flavoring ingredients used for the purpose of coloring and flavoring only. It seems to me that straight whisky and whisky made from neutral spirits, each with more than 99½ per cent. ethyl alcohol and water, and with less than half of one per cent. of fusel oil, are clearly a mixture of like substances, and that while the latter may have and often does have burnt sugar or caramel to flavor and color it, such coloring and flavoring ingredients may be regarded as for flavoring and coloring only, because the use of burnt sugar to color and flavor spirits as whisky is much older than the coloring and flavoring by the tannin of the charred bark. Therefore, where straight whisky and whisky made from neutral spirits are mixed, it is proper to call them a blend of straight whisky and whisky made from neutral spirits. This is also in accord with the decision of the British Royal Commission in the case which I have cited upon a similar issue. Neutral spirits made from molasses and reduced to potable strength has sometimes been called whisky, but not for a sufficient length of time or under circumstances justifying the conclusion that it is a proper trade name. The distillate from molasses used for drinking has commonly been known as rum. The use of whisky for it is a misbranding."

The following standards were then adopted by the Joint Standards Committee of the Association of Official Agricultural Chemists, and the American Society of National Food and Dairy Officials: *New whisky* is the properly distilled spirit from the properly prepared and properly fermented mash of malted grain, or of grain the starch of which has been hydrolyzed by malt; it has an alcoholic strength corresponding to the excise laws of the various countries in which it is produced, and contains in 100 liters of proof spirit not less than 100 grammes of the various substances other than ethyl alcohol derived from the grain from which it is made, and of those produced during fermentation, the principal part of which consists of higher alcohols estimated as amylic. *Whisky* (*potable whisky*) is new whisky which has been stored in wood not less than four years without any artificial heat save that which may be imparted by warming the storehouse to the usual temperature, and contains in 100 liters of proof spirit not less than 200 grammes of the substances found in new whisky, save as they are changed or eliminated by storage, and of those produced as secondary bodies during aging; and, in addition thereto, the substances extracted from the casks in which it has been stored. It contains, when prepared for consumption as permitted by the regulations of the Bureau of Internal Revenue, not less than 45 per cent. by volume of ethyl alcohol, and, if no statement is made concerning its alcoholic strength, it contains not less than 50 per cent. of ethyl alcohol by volume, as prescribed by law. *Rye whisky* is a whisky in the manufacture of which rye, either in a malted condition or with sufficient barley or rye malt to hydrolyze the starch, is the only grain used. *Bourbon whisky* is a whisky made in Kentucky from a mash of Indian corn and rye, and barley malt, of which Indian corn forms more than 50 per cent. *Corn whisky* is whisky made from malted Indian corn or of Indian corn the starch of which has been hydrolyzed by barley malt. *Blended whisky* is a mixture of two or more whiskys. *Scotch whisky* is *whisky* made in Scotland solely from barley malt, in the drying of which peat has been used. It contains in 100 liters of proof spirit not less than 150 grammes of the various substances prescribed for whisky exclusive of those extracted from the cask. *Irish whisky* is whisky made in Ireland, and conforms in the proportions of its various ingredients to Scotch whisky, save that it may be made of the same materials as prescribed for whisky, and the malt used is not dried over peat.

Neutral spirit is a grain distillate, of a high degree of purity and known as "silent spirit" on account of the ease with which it may be used as a blending ingredient without the production of a harsh and disagreeable odor.

Description and Physical Properties.—"A light to deep amber-colored liquid, having a characteristic odor and taste, and an acid reaction.

"Specific gravity: from 0.935 to 0.923 at 25° C.

"The residue obtained by evaporating 20 cc. of Whisky in a dish on a water bath is not completely soluble in 5 cc. of distilled water. Filter the solution and add to the filtrate a drop of diluted ferric chloride T.S. (1 in 10): a greenish-black coloration is produced (*indicating storage in wood barrels*). A 25 cc. portion of Whisky, diluted with 50 cc. of distilled water, requires for neutralization not less than 1.5 cc. and not more than 5 cc. of tenth-normal sodium hydroxide, using 3 drops of phenolphthalein T.S. as indicator. Mix 100 cc. of Whisky with 15 cc. of distilled water and slowly distil 100 cc., using an efficient condenser. Neutralize 50 cc. of the distillate with tenth-normal sodium hydroxide, using 5 drops of phenolphthalein T.S. as indicator, then add exactly 20 cc. more of the tenth-normal sodium hydroxide and boil for one hour under a reflux condenser. Cool and titrate the excess of alkali with tenth-normal sulphuric acid. Run a blank test, using distilled water in place of the distillate and make any necessary correction. The volume of tenth-normal sodium hydroxide consumed is not less than 1.7 cc. and more than 7 cc. (*esters*). To 5 cc. of the distillate add 2 cc. of sodium hydroxide T.S. and 5 drops of a freshly prepared aqueous solution of sodium nitroprusside (1 in 50), then add a slight excess of acetic acid: no violet tint is produced in one minute (*acetone*). A mixture of 0.5 cc. of the distillate with 5 cc. of distilled water meets the requirements of the test for *methanol* under *Alcohol*. Acidulate 10 cc. of Whisky with 5 drops of diluted hydrochloric acid and evaporate to 5 cc. Dilute with distilled water to 10 cc. and filter if necessary. The addition of iodine T.S. or mercuric potassium iodide T.S. yields no precipitate (*alkaloids*). Dilute 10 cc. of Whisky with 2 cc. of distilled water, transfer to a test tube, and shake gently for two minutes with 15 cc. of a mixture of 100 cc. of amyl alcohol, 3 cc. of phosphoric acid, and 3 cc. of distilled water, and allow the layers to separate completely: the lower aqueous layer is colorless or very nearly so (*caramel*). Mix 5 cc. of Whisky with 5 cc. of distilled water and shake the mixture with 10 cc. of purified petroleum benzin. Transfer the separated benzin to a dish of from 70 to 80 cc. capacity, add 1 cc. of sodium hydroxide solution (1 in 10), and evaporate to dryness on a water bath. Add to the dry residue 2 cc. of sulphuric acid, rotating the acid in the dish so that the residue will be completely moistened. Heat for two minutes on a water bath, and pour the solution into a dry test tube containing from 0.03 to 0.05 Gm. of resorcinol. Heat the mixture for three minutes at 160° to 170° C., shaking at intervals to dissolve all of the resorcinol. Then pour the solution into a mixture of 70 cc. of distilled water and 30 cc. of sodium hydroxide solution (1 in 10), adding more sodium hydroxide, if necessary, to make the mixture alkaline. The liquid shows no yellowish-green fluorescence after standing twenty-four hours (*diethylphthalate*). Mix 2 cc. of an aqueous solution of phloroglucinol (1 in 100) with 5 cc. of sodium hydroxide T.S. and add 2 cc. of Whisky: no red color is produced (*formaldehyde*). Mix 20 cc. of Whisky with 20 cc. of distilled water and shake the mixture with 10 cc. of ether. Allow the mixture to stand until separation takes place, separate the ether layer, and allow it to evaporate spontaneously on a watch glass: the residue has no disagreeable or irritating odor. Evaporate 20 cc. of Whisky in a dish on a water bath and dry the residue to constant weight at 100° C.: the weight of the residue does not exceed 0.10 Gm. This residue is not sticky, it has a slightly astringent taste but is not distinctly sweet or bitter (*glycerin, sugar, etc.*). Evaporate 10 cc. of Whisky to 5 cc. and dilute with 10 cc. of distilled water, acidulate with 5 drops of hydrochloric acid, and add 10 cc. of hydrogen sulphide T.S.: no precipitate is formed before or after rendering alkaline with ammonia T.S. (*heavy metals*). Place 2 cc. of mercuric sulphate T.S. in a test tube, add 5 drops of Whisky and heat the mixture just to boiling over a small Bunsen burner and remove it from the flame: no yellow precipitate is formed (*isopropyl alcohol*). The addition of an excess of bromine T.S. to 5 cc. of Whisky, diluted with an equal volume of distilled water, produces no precipitate (*phenols*)." *U. S.*

The alcoholic strength of whisky may usually be determined by taking the specific gravity directly, and calculating the alcoholic strength from the appropriate table. This method is only applicable, however, to straight whiskies, as the caramel, prune juice and other ingredients added to imitation and blended whiskies are disturbing factors. When working with unknown samples, therefore, it is customary to distil according to the directions in the U. S. P. method for determining alcohol.

In interpreting the results of the application of the U. S. P. tests for Spiritus Frumenti, the following points may be mentioned. A specimen which contains denaturants is unquestionably spurious. A specimen which is low in acidity, very light in color with no added caramel, is either an immature whisky or a straight whisky which has been reduced with silent spirit and water. This is the type legally recognized as a blended whisky even when caramel color is present but it does not meet the Pharmacopœial definition. A specimen which is low in acidity, but which contains caramel, and leaves an excessive amount of a sticky residue upon evaporation is an imitation whisky. Alcoholic strength is no criterion of the character of whisky, whatever.

Uses.—The therapeutic value of whisky depends chiefly upon the alcohol that it contains. Its advantage as an internal medicine probably depends on the characteristic flavor which makes it more acceptable to the palate and consequently less liable to cause gastric disturbance. It may be used for nearly all the therapeutic purposes both internally and externally for which alcohol of the same concentration is employed. (See *Alcohol Dilutum.*)

SPIRITUS GLYCERYLIS NITRATIS. U. S. (Br.)

SPIRIT OF GLYCERYL TRINITRATE Sp. Glyceryl. Nit. [Spirit of Nitroglycerin]

"Spirit of Glyceryl Trinitrate is an alcoholic solution containing not less than 1 per cent. and not more than 1.1 per cent. of $C_3H_5(NO_3)_3$. *Caution—Great care must be exercised in dispensing, handling, packing, transporting, and storing this Spirit, since a dangerous explosion may result if any considerable quantity of it is spilled, and the alcohol wholly or partly lost by evaporation. If, through accident, it is spilled, a solution of potassium or sodium hydroxide must be poured over it at once to effect partial decomposition.*" *U. S.*

Liquor Trinitrini, *Br.;* Solution of Trinitrin; Liquor Nitroglycerini; Spiritus Glonoini; Spirit of Glonoin; Solution of Nitroglycerin; Liquor Glonoini; Solution of Glonoin; Nitroglyceringeist, Glycerintrinitratlösung, *G.;* Solucion Alcoholica de Trinitrina, *Sp.*

The U. S. gives no process for this, that of the Br. is as follows:

"Trinitroglycerin of commerce, 1 *gramme;* Alcohol (90 per cent.), sufficient to produce 100 *millilitres.* Dissolve." *Br.*

Description and Physical Properties.—"A clear, colorless liquid, having the odor of alcohol. *Caution must be exercised in tasting it,* since even a small quantity is liable to produce a violent headache. The same effect is produced when it is applied to the skin.

"Specific gravity: 0.814 to 0.820 at 25° C. It is neutral to litmus paper. Heat about 10 cc. of Spirit of Glyceryl Trinitrate on a water bath with 1 cc. of potassium hydroxide T.S. until the alcohol is evaporated, and then heat a portion of the residue with about 1.5 Gm. of potassium bisulphate: the pungent odor of acrolein is evolved. Dissolve the remainder of the residue in 2 cc. of distilled water acidulated with diluted sulphuric acid, add a few drops of diphenylamine T.S., and pour the solution upon 2 cc. of sulphuric acid in a test tube so as to form a separate layer: a dark blue color is produced at the zone of contact. On mixing 10 cc. of the Spirit with 11 cc. of distilled water, both previously cooled to 15° C., a clear solution results. On now adding 2 cc. more of distilled water the mixture becomes turbid at 15° C.

"**Assay.**—Transfer about 5 cc. of the Spirit, accurately weighed, to a tared dish, protect it from dust, allow it to evaporate spontaneously, and dry the residue to constant weight over sulphuric acid. The weight of the residue corresponds to not less than 1 per cent. and not more than 1.1 per cent. of the weight of Spirit taken.

"Preserve in well-stoppered bottles, in a cool, dark place, remote from fire. Alcohol content, by volume, 88 to 95 per cent." *U. S.*

"A clear colorless liquid, neutral to *litmus*. Specific gravity 0.840. A mixture of 10 millilitres with an equal volume of *water*, cooled to 15.5° C., remains clear, but the further admixture of 1 millilitre of *water* causes opacity (presence of a due amount of glyceryl trinitrate). On further diluting with *water* and setting aside the mixture, there is deposited a liquid of oily consistence, one drop of which, absorbed by paper and struck with a hammer on a hard surface, explodes. This Solution contains 1 gramme of trinitroglycerin in 100 millilitres; 110 minims contain 1 grain." *Br.*

For a method of assaying this spirit, by Chas. Rice, see *Am. Drug.*, 1895, 6; also Nagelvoort's method, *A. J. P.*, 1894, 527. F. W. Heyl and J. F. Staley reviews the various methods for the estimation of nitroglycerin and gives comparative results of the assay of a large number of preparations and tablets. (*A. J. P.*, 1914, p. 195.) On account of the importance of nitroglycerin as a therapeutic agent, we append the following:

Nitroglycerin. Trinitrine. Glonoin. Glyceryl Trinitrate. $C_3H_5(NO_3)_3$.—When glycerin is gradually added in small portions at a time to a mixture of one part of strong nitric acid and three to four parts of concentrated sulphuric acid, and at a temperature kept low by artificial refrigeration, it is converted into a bright yellow liquid, which has remarkable explosive properties. Nitroglycerin was discovered in the year 1847 by Sobrero of Turin, who called it *pyroglycerine.* It was afterwards made a subject of study by de Vrij of the Netherlands, Gladstone, and Kopp, but did not attract general attention until 1867, when Alfred Nobel, a Swedish engineer, suggested its use for explosive purposes by mixing it with inert substances like kieselguhr or infusorial earth to make the product commercially known as *dynamite.* It is an almost colorless or slightly yellow liquid of a sp. gr. of about 1.6; inodorous; of a sweet, pungent, aromatic taste; very slightly soluble in water, but readily soluble in ether, alcohol, most immiscible solvents, and oils. According to J. R. Wagner, it does not freeze above –15.5° C. when quite pure, but as it occurs in commerce it solidifies on continued exposure to a temperature of 8° C., assuming the form of long needles, which are dangerous to handle, as they explode violently when gently broken. In the form of a solution it is not explosive. In the liquid state the mere contact of flame does not inflame or explode it; but concussion, or touching it with a red-hot iron, explodes it with great violence. Detonating mixtures, or exploding gunpowder, in its near vicinity, produce the same effect. By keeping, it undergoes partial decomposition, and in confined vessels the pressure of the accumulated gases which result is sometimes so great as to cause its explosion upon the slightest concussion. Its explosive force greatly exceeds that of gunpowder. According to Nobel, one volume of the fluid yields on explosion 10,384 volumes of gas, while one volume of gunpowder yields only 800 volumes. It has, therefore, been much employed in blasting rocks, in mining, quarrying, road making, etc., and its economical advantages have kept it in extensive use, notwithstanding the danger.

Nitroglycerin is formed by the introduction of the nitro-group (NO_2) in place of the three replaceable hydrogen atoms of the glycerin formula, according to the reaction:

$$C_3H_5(OH)_3 + 3(HNO_3) = C_3H_5,(NO_3)_3 + 3(H_2O)$$

The theoretical proportions of the reacting substances would be 100 parts by weight of glycerin and over 200 parts of absolute nitric acid. On the manufacturing scale about 25 per cent. excess of nitric acid is used. The sulphuric acid exceeds the nitric acid in amount by 1½ times. Nitroglycerin, being an ester, is readily saponified and rendered harmless when brought into contact with alkali hydroxides even in the cold. The reaction is as follows: $C_3H_5(NO_3)_3 + 3KOH = C_3H_5(OH)_3 + 3KNO_3$.

A complete and well illustrated article on nitroglycerin manufacture will be found in Molinari's Industrial Organic Chemistry, p. 223.

Uses.—The effects of nitroglycerin upon the system are precisely similar to those of the nitrites (see *Sodii Nitris*). According to the observations of Wallace and Ringer (*J. A. M. A.*, 1909, lii, p. 1629), the effects of one and one-half minims of the spirits of nitroglycerin come on within two or three minutes after taking by the mouth and endure for about one-half hour. The amount of the drug required to affect the system varies extraordinarily in different individuals. Murrell (*L. L.*, 1879, i, p. 80) has reported violent effects from one or two minims of the 1 per cent. solution. On the other hand, Kolipinski (*M. News*, 1890) reports a case in which two drachms of the official solution were taken without serious symptoms (amount somewhat doubtful). It is probable that in many of these cases in which large quantities have been ingested the drug was of inferior quality. Nitroglycerin is a volatile substance and unless evaporation is guarded against its preparations lose potency. The spirit of glyceryl nitrate is used in the same class of cases as sodium nitrite, but is employed where rapidity of action is important, as in *angina pectoris, threatened apoplexy, asthma, strychnine poisoning,* and the like. It has been enormously misused as a cardiac stimulant in various forms of collapse;

it should be remembered that its effect is always to lower blood pressure and it can do no good in any form of circulatory failure. It has been highly recommended in *hemoptysis,* its action being attributable to the consentaneous dilatation of the abdominal and contraction of the pulmonary vessels.

According to Ebright (*J. A. M. A.,* 1914, lxii, p. 201), workers in dynamite factories are subject to chronic nitroglycerin poisoning. The most characteristic symptom of this intoxication is throbbing headache, at times so violent that the patient may become maniacal. The pain is made worse by lying down and is not alleviated by either acetphenetidin or morphine. After some time the workers in these factories appear to develop an immunity to the poisoning.

Dose, of the spirit, from one to two minims (0.06–0.12 cc.).

Off. Prep.—Elixir Euphorbiæ Compositum, *N. F.*

SPIRITUS JUNIPERI. Br.

SPIRIT OF JUNIPER Sp. Junip.

Teinture d'essence de Genièvre, *Fr.;* Spiritus Juniperi, *P. G.;* Wachholderspiritus, *G.*

"Oil of Juniper, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter. This Spirit is of twice the strength of the corresponding preparation of the British Pharmacopœia, 1898." *Br.* This spirit has been omitted from the U. S. X; that formerly official was half the strength of the British preparation. The compound spirit (*Spiritus Juniperi Compositus*) was formerly recognized by the U. S. Its formula was: "Oil of Juniper, *eight mils;* Oil of Caraway, *one mil;* Oil of Fennel, *one mil;* Alcohol, *fourteen hundred mils;* Water, *a sufficient quantity,* to make *two thousand mils.* Dissolve the oils in the alcohol, and gradually add enough water to make the product measure *two thousand mils.*" *U. S. IX.*

This spirit is used chiefly as an addition to diuretic infusions.

Dose, from ten to twenty minims (0.6–1.2 cc.).

SPIRITUS LAVANDULÆ. U. S., Br.

SPIRIT OF LAVENDER Sp. Lavand.

Teinture d'essence de Lavande, *Fr.;* Spiritus Lavandulæ, *P. G.;* Lavandelspiritus, *G.*

"Oil of Lavender, 50 cc.; Alcohol, a sufficient quantity to make 1000 cc. Mix the Oil with sufficient alcohol to make the product measure 1000 cc.

"Alcohol content, by volume, 85 to 92 per cent." *U. S.*

"Oil of Lavender, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

Spirit of lavender is used widely as a perfume, and as an ingredient in other preparations. The perfume usually sold under the name of *lavender water* is not a distilled spirit, but an alcoholic solution of the oil, with the addition of other odorous substances. The following is given by Brande as one of the most approved recipes for preparing it. "Take of rectified spirit five gallons, essential oil of lavender twenty ounces, essential oil of bergamot five ounces, *essence of ambergris* [made by digesting one drachm of *ambergris* and eight grains of musk in half a pint of alcohol] half an ounce. Mix." The Br. spirit is double the strength of the U. S. preparation.

It is a grateful stimulant and carminative when administered in sweetened water.

Dose, of the U. S. Spirit, from ten to thirty minims (0.6–1.8 cc.); of the Br. Spirit, five to twenty minims (0.3–1.3 cc.).

Off. Prep.—Mistura Ferri Composita, *N. F.*

SPIRITUS MENTHÆ PIPERITÆ. U. S., Br.

SPIRIT OF PEPPERMINT Sp. Menth. Pip. [Essence of Peppermint]

Teinture d'essence de Menthe, *Fr. Cod.;* Esprit de Menthe; *Fr.;* Spiritus Menthæ Piperitæ, *P. G.;* Pfefferminzspiritus, Englische Pfefferminzessenz, *G.;* Alcohol de menta piperita, *Sp.*

"Oil of Peppermint, 100 cc.; Peppermint, bruised, 10 Gm.; Alcohol, a sufficient quantity to make 1000 cc. Macerate the peppermint leaves, freed as much as possible from stems, during one hour in 500 cc. of water, and then strongly express them. Mix 800 cc. of alcohol with the oil, add the moist, macerated leaves, and allow to stand during six hours with frequent agitation. Filter and pass sufficient alcohol through the filter to make the product measure 1000 cc.

"Preserve in amber-colored bottles. Alcohol content, by volume, 79 to 85 per cent." *U. S.*

"Oil of Peppermint, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

This is one of the numerous spirits that were made by distillation, but are now made of more uniform strength and better quality by simple solution of the oil in alcohol. The American spirit is green in color, but the British is almost colorless. P. H. Utech suggests the maceration of the peppermint in water for two hours, washing and draining, before adding to the solution of the oil; water soluble matter is removed and a more permanent green color produced. He recommends the same treatment for the spearmint in making spirit of spearmint, and the U. S. P. IX adopted this plan. It has long been popularly used under the name of *essence of peppermint.* The flavoring "extract" or "essence" as it is called is a much weaker preparation and contains but 3 per cent. by volume of the oil. It must not be confused with the official spirit. (See article by E. F. Kelly, *J. A. Ph. A.,* 1919, viii, 115.) The spirit of peppermint affords a convenient method of administering a dose of the volatile oil, being of such a strength that when dropped on loaf-sugar it may be taken without inconvenience. For a discussion of the methods of assay for this preparation (see a paper by H. L. Thompson, *A. J. P.*, 1916, lxxxviii, 303.)

Dose, ten to thirty minims (0.6–1.8 cc.), given as just mentioned, or mixed with sweetened water.

SPIRITUS MENTHÆ VIRIDIS. U. S.

SPIRIT OF SPEARMINT Sp. Menth. Vir.

Tinctura Olei Menthæ Viridis, *U. S.* 1850; Essence of Spearmint; Grüne Minzessenz, *G.*

"Oil of Spearmint, 100 cc.; Spearmint, bruised, 10 Gm.; Alcohol, a sufficient quantity to make 1000 cc. Macerate the spearmint leaves, freed as much as possible from stems, during one hour in 500 cc. of water, and then strongly express them. Mix 800 cc. of alcohol with the oil, add the moist macerated leaves, and allow to stand during six hours with frequent agitation. Filter, and pass sufficient alcohol through the filter to make the product measure 1000 cc.

"Preserve in amber-colored bottles. Alcohol content, by volume, 79 to 85 per cent." *U. S.*

The remarks made on the Spirit of Peppermint are equally applicable here.

Dose, ten to thirty minims (0.6–1.8 cc.).

SPIRITUS MYRISTICÆ. Br.

SPIRIT OF NUTMEG [Essence of Nutmeg]

Teinture d'essence de Muscade, *Fr.;* Muskatspiritus, *G.*

"Oil of Nutmeg, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

It is used chiefly for its flavor. (See *Oleum Myristicæ.*)

Dose, from five to twenty minims (0.3–1.3 cc.).

SPIRITUS ROSMARINI. Br.

SPIRIT OF ROSEMARY

Spiritus Anthos; Teinture d'essence de Romarin, *Fr.;* Rosmarinspiritus, *G.;* Alcohol de romero, *Sp.*

"Oil of Rosemary, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

This spirit is not official in the United States Pharmacopœia X. It is a grateful perfume, and is used chiefly as an odorous ingredient in lotions and liniments.

SPIRITUS VINI VITIS. U. S.

BRANDY Sp. Vin. Vit.

"Brandy is an alcoholic liquid obtained by the distillation of the fermented juice of sound, ripe grapes and containing not less than 48 per cent. and not more than 54 per cent. by volume of C_2H_5OH, at 15.56° C. It must have been stored in wood containers for a period of not less than four years." *U. S.*

Eau de Vie, *Fr.;* Branntwein, Schnapps, *G.;* Acquavite, *It.*

The term "brandy" has been applied generically to the ardent spirit obtained by the distillation of a fermented fruit juice. More frequently it is used in the official sense to designate grape brandy, that is, the liquor distilled from wine. This form of brandy is often known as *cognac,* from the name of a town in the Department of Charrente, France.

The process of manufacturing brandy is essentially the same as that for making whisky (see *Spiritus Frumenti*) except that it is distilled from fermented grape juice instead of the products of grains.

During the storage of the brandy the liquor undergoes analogous changes to those which take place in whisky. As brandy is not made from cereals or starchy materials, fusel oil is never present in the genuine article. As the wood containers are not charred, brandy is of a paler color than whisky and is apt to contain a larger proportion of tannic acid. Usually the color is increased by adding caramel.

An artificial or imitation brandy is sometimes made from alcohol by flavoring with *oil of cognac.* This latter is obtained by distillation from wine lees and is said to impart the characteristic brandy flavor. Such spurious liquor may be recognized by the absence of tannin and of aldehyde and an unusually high percentage of residue on evaporation due to the artificial coloring matter, and frequently by the characteristic odor of amyl acetate which is frequently used in factitious products.

Description and Physical Properties.—"A pale amber-colored liquid, having a characteristic odor and taste, and an acid reaction. Specific gravity: from 0.933 to 0.921 at 25° C.

"Evaporate 20 cc. of Brandy in a dish on a water bath, treat the residue with 5 cc. of distilled water, filter, and add to the filtrate a drop of diluted ferric chloride T.S. (1 in 10): a greenish-black coloration is produced (*indicating storage in wood barrels*). Evaporate 20 cc. of brandy in a dish in a water bath and dry the residue to constant weight at 100° C.: the weight of the residue does not exceed 0.30 Gm. A 25 cc. portion of Brandy, diluted with 50 cc. of distilled water, requires for neutralization not more than 3.8 cc. of tenth-normal sodium hydroxide, using 3 drops of phenolphthalein T.S. as indicator (*free acid*). Dilute 20 cc. of Brandy with 5 cc. of distilled water and slowly distil 20 cc. using an efficient condenser: the distillate meets the requirements of the tests for *acetone* and *methanol* under *Spiritus Frumenti.* Brandy meets the requirements of the tests for purity under *Spiritus Frumenti* beginning with the test for *alkaloids* but omitting the tests for *caramel* and for *glycerin, sugar, etc.*" *U. S.*

Uses.—It is commonly believed that brandy has a more constipating effect than whisky but there is no convincing evidence of the truth of this tradition. The medicinal virtues of the two liquors are probably essentially the same. Brandy has a somewhat more pleasing flavor to some persons and is therefore often superior in its acceptability to the stomach.

STAPHISAGRIÆ SEMINA. Br.

STAVESACRE SEEDS

"Stavesacre Seeds are the dried ripe seeds of Delphinium Staphisagria, *Linn.*" *Br.*

Staphisagria, *U. S. IX;* Staphysagriæ Semen; Semen Staphisagriæ, Staphidiagriæ or Pedicularis; Stavesacre Seeds; Staphisaigre, *Fr.;* Stephanskörner, Läusekörner, *G.;* Stafisagria, *It.*

Delphinium Staphisagria L., or stavesacre, is a handsome, annual or biennial plant, one or two feet high, with a simple, erect, downy stem, and palmate, five- or seven-lobed leaves, supported on hairy petioles. The flowers are bluish or purple, in terminal racemes, with pedicels twice as long as the flower, and bracteoles inserted at the base of the pedicel. The sepals are five in number, irregular, petal-like, the upper one being spurred at the base. The petals are four, irregular, the two upper having long spurs which are inclosed in the spur of the calyx, the two lower having short claws. The pistils form a many-seeded pod or capsule in fruit. Alike with the seeds of many other ranunculaceous plants, those of this species require planting soon after they ripen, if a good percentage of germination is to be obtained.

The plant is a native of the south of Europe. E. M. Holmes (*P. J.*, 1921, cvi, 265) calls attention to the remarkable fact that the plant in the English botanic gardens hitherto considered to be *Delphinium Staphisagria* is in reality another species, *i.e., Delphinium pictum* Willd. The author accounts for the absence of the true plant in botanic gardens partly by the fact that it is only half-hardy in Great Britain, while *D. pictum* is hardy, and partly by the reason that the illustrations in several works on medicinal plants—even in Bentley and Trimen's "Medicinal Plants"—are incorrect or unreliable. The two species are distinguished as follows: *D. Staphisagria* has very hairy stems, glandular hairs being mixed with the long spreading soft hairs; flowers that when well-developed have an ultramarine blue tint; a calyx with very short or almost obsolete spur; carpels containing only four or five seeds. *D. pictum* Willd. has shorter soft hairs, but no glandular hairs on the stems; the flowers are of a pale lilac color; the spur is as long as the calyx segments; each carpel contains ten or twelve seeds, and these are only half the size of those of *D. Staphisagria.* The true *D. Staphisagria* extends from Teneriffe around both the northern and southern coasts of the Mediterranean to Asia Minor. It is quite possible therefore, that varieties having blossoms of different tints may occur. The evidence obtainable, however, goes to show that the form of the plant from which the seed of commerce is obtained has clear blue flowers. (*Y. B. P.*, 1899, 300.) For description of other species of this genus, see *Delphinium.* The commercial supplies of this drug are imported from Leghorn, Italy.

Description and Physical Properties.—The seeds of stavesacre are officially described as "irregularly triangular or obscurely quadrangular, arched, blackish-brown when fresh, but becoming dull greyish-brown on keeping. Surface wrinkled and deeply pitted; kernel soft, whitish, oily. No marked odor; taste nauseous, bitter and acrid." *Br.* "Under the microscope, transverse sections of Staphisagria show an outer layer of nearly tabular, thick-walled, non-lignified cells, some being extended centrifugally, and forming the reticulations of the seed-coat; 2 or 3 rows of parenchyma cells with more or less irregular thin walls; a thin layer of very small, thick-walled cells with numerous, lattice-like or reticulate pores; endosperm large, composed of polygonal cells enclosing small aleurone grains and fixed oil, the latter forming in large globules on the addition of hydrated chloral T.S." *U. S. IX.*

The seeds of the field larkspur, *D. Ajacis* L., are recognized in the National Formulary (see *Delphinium*). These are readily distinguished, being about 2 mm. in length and of a black or blackish-brown color.

Constituents.—In 1819 Lassaigne and Feneulle isolated from staphisagria an alkaloid which they called delphinine. Marquis in 1877 obtained four bases, *delphinine* (crystalline), *delphinoidine* (amorphous), *delphisine* (crystalline), *staphisagrine* (amorphous). Kara-Stojanow (*In. Dis.*, Dorpat, 1890) asserted that delphinine and delphisine were identical. Keller (*A. Pharm.*, 1910, ccxlviii, 468) maintains that none of the above writers have separated delphinine in a pure state as is shown by the great variation in empirical formulæ which they give. Walz (*A. Pharm.*, 1922, cclx, p. 9) gives the formula for delphinine, $C_{34}H_{47}O_9N$.

If delphinine be rubbed up with an equal quantity of malic acid, and some drops of concentrated sulphuric acid added, there will be produced an orange-red color passing into rose, growing deeper after some hours, and finally changing from the edges to violet, and at last becoming cobalt blue. (Tattersall, *Chem. News*, 41.) It is stated that no other alkaloid and no other organic acid, except malic, affords this reaction. (*Pflanzenstoffe*, 2d ed., 1884, 617.) The total amount of alkaloids is about 1 per cent. Ahrens (*Ap. Ztg.*, 1899, 361) obtained from the residue of the seeds of *D. staphisagria*, from which delphinine, delphinoidine, delphisine and staphisagrine had been extracted, the alkaloid *staphisagroine* (*B. Chem. G.*, 1899, 1581). For Katz's process for extracting delphinine, see *Ph. Ztg.*, 1900, 735.

Uses.—The seeds were formerly used as an emetic and cathartic, but have been abandoned in consequence of their violence. A strong tincture has been employed as an embrocation in *rheumatism.* The ointment is used to destroy *lice* and the *itch-mite.* Staphisagria should never be used internally, and when it is applied externally, care should be exercised not to put it on an abraded surface, but only upon the unbroken epidermis. In some countries the seeds are used like Cocculus Indicus to intoxicate fish.

When given in poisonous doses to the lower animals, *delphinine* produces excessive salivation, followed by violent and repeated vomiting, great disturbance of respiration, failure of heart action, gradual enfeeblement of voluntary motion and of sensation, and a peculiar fibrillary spasm of the muscles of the abdomen, which is said to be characteristic of the poisoning. Elevation of temperature and glycosuria have both been noticed; death is said to occur always from failure of respiration, though the heart is greatly enfeebled and finally ceases in diastole. According to Gauthier, the period of depression of the heart and of sensibility is preceded by one of excitement. The pupils are dilated and the motor nerve finally paralyzed. (*L. M. R.*, Oct., 1887.) Turnbull, in his work *On the Medical Properties of the Ranunculaceæ,* states that pure delphinine externally acts like veratrine, but produces more redness and burning and less tingling than that substance. He has employed it in *neuralgia, rheumatism* and *paralysis.* It may be applied by friction, in the form of ointment or alcoholic solution, in proportions varying from ten to thirty grains of the alkaloid to an ounce of the vehicle, and the friction should be continued till a pungent sensation is produced.

Internally, *staphisagrine* is said to act like delphinine, except that it does not depress the heart so much or produce fibrillary contractions. Although cases of human poisonings have occurred with staphisagria, we know of none in which the result has been fatal. The symptoms are similar to those produced in the lower animals. Kobert states that the alkaloids of staphisagria all resemble aconitine in their action, but that delphinoidine has some narcotic action.

Off. Prep.—Unguentum Staphisagriæ, *Br.*

STILLINGIA. N. F.

STILLINGIA Stilling. [Queen's Root]

"Stillingia is the dried root of *Stillingia sylvatica* Linné (Fam. *Euphorbiaceæ*). Stillingia contains not more than 3 per cent. of foreign organic matter. Stillingia which has been stored for more than two years must not be used." *N. F.*

Silver Leaf, Queen's Delight, Yaw Root; Stillingie, *Fr., G.*

Stillingia sylvatica is an indigenous perennial herb with stems two or three feet high, and alternate, sessile, oblong or lanceolate-oblong, obtuse serrulate leaves, tapering at the base, and accompanied with stipules. The staminate and pistillate flowers are distinct upon the same plant. They are yellow, and arranged in the form of a spike, of which the upper part is occupied by the male, the lower by the female flowers. The staminate florets are scarcely longer than the bracteal scales. The plant grows in pine barrens from Maryland to Florida and west to Kansas and Texas, flowering in May and June. When wounded it emits a milky juice. The commercial supplies of this drug come from the southern United States.

Description and Physical Properties.—"*Unground Stillingia.*—When entire, terete, unequally tapering, rarely branched, usually in pieces, sometimes attaining a length of 40 cm. and from 0.5 to 3 cm. in diameter, externally reddish brown, longitudinally wrinkled; fracture very fibrous; internally the bark is light reddish brown, thick, spongy, finely fibrous, with numerous resin cells and easily separable from the porous, radiate wood; odor distinct; taste bitter, acrid and pungent.

"*Powdered Stillingia.*—Pinkish brown or light reddish brown; numerous starch grains from 0.005 to 0.045 mm. in diameter, mostly single, very variable in shape, and usually with a central cleft; numerous fragments, with more or less tabular secretion cells, containing a reddish brown, amorphous, resinous substance; fragments of tracheæ mostly with simple pores and associated with wood-fibers, the walls being very thin, lignified and possessing numerous, transverse, slit-like simple pores; bast-fibers long, narrow, the walls thick and slightly lignified; fragments of reddish brown cork cells; occasionally crystals of calcium oxalate in rosettes up to 0.070 in diameter." *N. F.*

The odor is slight, peculiar, and somewhat oleaginous, but in the recent root is said to be strong and acrimonious. The taste is bitterish and pungent, leaving an impression of disagreeable acrimony in the mouth and fauces. Holm gives an excellent illustrated article on the pharmacognosy of stillingia in *Merck's Rep.*, xx, p. 412.

W. Saunders has obtained from the root a volatile oil, which he found to possess the odor, taste and peculiar acrimony of the root in a high degree. He procured six and a quarter ounces from five pounds of the dried root. It had a thick consistence, and required the addition of alcohol to render it fit for manipulation. Wm. Bichy (*A. J. P.*, 1885, p. 529) found an alkaloid which he named *stillingine.* It was obtained as an amorphous powder, volatilizable on heating, forming a sulphate in fine scale-like crystals.

Uses.—In large doses stillingia is emetic and cathartic, but is rarely used for these purposes. Smaller quantities have been supposed to exercise an alterative effect upon the system and are used in *syphilitic* and *scrofulous* conditions. The drug is probably, however, without any real value.

Dose, half a drachm to a drachm (2.0–3.9 Gm.).

Off. Prep.—Fluidextractum Stillingiæ, *N. F.;* Elixir Corydalis Compositum (from Fluidextract), *N. F.;* Fluidextractum Stillingiæ Compositum, *N. F.;* Syrupus Stillingiæ Compositus, *N. F.*

STRAMONIUM. U. S. (Br.)

STRAMONIUM Stramon. [Jamestown Weed, Jimson Weed]

"Stramonium consists of the dried leaves and flowering tops of *Datura Stramonium* Linné (Fam. *Solanaceæ*). Stramonium yields not less than 0.25 per cent. of the alkaloids of Stramonium, contains not more than 3 per cent of stems over 8 mm. in diameter, and yields not more than 4 per cent. of acid-insoluble ash." *U. S.* "Stramonium Leaves are the dried leaves of Datura Stramonium, *Linn.*" *Br.*

Stramonii Folia, *Br.;* Stramonium Leaves; Herba Stramonii; Thornapple Leaves; Thorn, Devil's or Mad Apple; Apple of Peru; Stink-weed; Jamestown (Jimson) Lily; Devil's Trumpet; Derotry; Stramoine, Pomme-épineuse, Feuilles de Stramoine, *Fr.;* Folia Stramonii, *P. G.;* Stechapfelblätter, *G.;* Stramonio, *It.;* Estramonio (Hoja de), *Sp.*

The *thornapple* (*Datura Stramonium*) is an annual plant, of rank and vigorous growth, usually about three feet high, but in a rich soil attains a height of six feet or more. The root is large, whitish, and furnished with numerous rootlets. The stem is erect, round, smooth, somewhat shining, simple below, dichotomous above, with numerous spreading branches. The leaves are petiolate, five or six inches long, of an ovate-triangular form, irregularly sinuate and toothed at the edges, unequal at the base, dark green on the upper surface, and pale beneath. The flowers are large, axillary, solitary, and peduncled, having a green, tubular, pentangular, five-toothed calyx, and a white, funnel-shaped corolla with a long tube, and a wavy plaited border, terminating in five acuminate teeth. The upper portion of the calyx falls with the deciduous parts of the flower, leaving its base, which becomes reflected and remains attached to the fruit. This is a large, fleshy, ovoid, four-valved, four-locular capsule, thickly covered with sharp spines, and containing numerous flattened, reniform seeds, attached to a central placenta. It opens at the summit. The U. S. P. IX recognized the leaves of *Datura Tatula* L. as a second source of the drug but this has been dropped from the U. S. P. X. This species is indigenous to tropical America but naturalized on waste ground throughout the greater part of the Eastern United States and in the southwestern states. It differs from *D. stramonium* in having purplish stems, lavender colored flowers and capsules which are nearly equally prickly.

It is doubtful to what country *D. stramonium* originally belonged. Many European botanists have referred it to North America, while we in return trace it to the old continent. Nuttall considers it as having originated in South America or Asia, and it is probable that its native country is to be found in some part of the East. It is said to grow wild, abundantly in southern Russia, from the borders of the Black Sea eastward to Siberia. Its seeds, being viable for a long time, are taken in the earth put on shipboard for ballast from one country to another, not infrequently springing up upon the passage, and thus propagating the plant in all regions which have any commercial connection. In the United States it is usually found abundantly in the vicinity of cultivation frequenting dung heaps, the road sides and commons, and other places where a rank soil is created by the deposited refuse of towns and villages. Its flowers appear from May to July or August, according to the latitude. Where the plant grows abundantly, its vicinity may be detected by the rank odor which it diffuses to some distance around. Notwithstanding the abundance of the plant, it is being cultivated in order to obtain a drug which shall be of uniform quality. The Bureau of Plant Industry, U. S. Department of Agriculture, has conducted experiments on a large scale. Several hundred pounds of leaf were grown, cured by artificial heat in a tobacco barn, and marketed at a price in advance of the highest quoted figure. Mitlacher has reported his observations on the cultivation of stramonium in *Zeit. Oest. Apoth.*, i, p. 391. Miller has conducted comparative experiments on *D. stramonium* and *D. Tatula.* (*A. J. P.*, lxxiv, p. 446.)

All parts of it are active. The leaves, seeds, and root were formerly recognized by the U. S. P., the present U. S. P. recognizes both the leaves and the tops. These may be gathered at any time from the appearance of the flowers till the autumnal frost. In this country the plant is generally known by the name of *Jamestown* (*vulgo, Jimson*) *weed,* derived probably from its having been first observed in the neighborhood of that old settlement in Virginia. In India *Datura alba, D. ferox,* and *D. fatuosa* are employed as poisons. The last has been admitted to the Br. (See *Daturæ Semina.*) Under the names of *Man t'o lo fa, Wan t'o lo hua,* and *Nau yeung fa,* the Chinese use as a medicine the flowers of the *Datura alba;* according to Frank Browne, they contain 0.485 per cent. of hyoscine, free from other alkaloids. *El Bethene,* a Datura of the Sahara Desert, is capable of causing delirium, coma, and death, and it is probable that all the species of the genus are poisonous. A. R. L. Dohme (*Proc. A. Ph. A.*, 1894, 231) examined stramonium to determine the value in alkaloid of the various parts of the plant; he found that in general, the fresh parts yielded more than the dried parts; the stems contained the most alkaloid, the seeds next, then the leaves, and the roots the least of all.

The drug of commerce is collected for the most part from wild plants. It is best gathered while the plants are in flower, in summer. The supplies used in the United States have been obtained partly from native plants and to a large extent from plants growing in Europe. North Carolina, Germany, Holland, England and Italy have furnished the bulk of the supply used in this country.

The *fresh leaves* when bruised emit a fetid narcotic odor, which they lose upon drying. Their taste is bitter and nauseous. The leaves, if carefully dried, retain their bitter taste.

Description and Physical Properties.—"*Unground Stramonium*—More or less matted, wrinkled and crushed; leaves petiolate, ovate; apex acuminate, base unequal; margin sinuate, toothed or angled, the teeth few, acute and with rounded sinuses; the lamina usually shows small, circular perforations, surrounded by cork or sometimes filled with cork, surfaces usually sparsely hairy, the hairs mostly upon the veins; upper surface dark green, lower surface light green. Stems often flattened, longitudinally wrinkled, occasionally with one or more deep furrows: light greenish-brown to purplish-brown. Odor distinct, heavy and narcotic; taste unpleasant and nauseous.

"*Structure.*—Upper epidermis of thin-walled cells, with few stomata and hairs; palisade, 1-rowed, and resting upon a single row of small parenchyma cells extending through the middle of the blade, nearly every cell of the layer containing a rosette aggregate of calcium oxalate; spongy parenchyma loosely arranged; lower epidermis similar to the upper but more uneven and with more stomata, the latter slightly elevated and with guard cells nearly circular in outline and distinctly beaked. At the midrib and larger veins, epidermal walls thickened; a characteristic ridge of collenchyma just beneath the upper epidermis, large, rounded parenchyma cells with intercellular spaces; a bicollateral radial vascular structure with narrow, medullary rays.

"*Powdered Stramonium.*—Bright green to brownish-green; epidermal cells with wavy radial walls; stomata elliptical, about 0.025 mm. in length, usually with 3 neighboring cells, one smaller than the others; calcium oxalate in rosette aggregates, from 0.010 to 0.025 mm. in diameter, or in rodlike crystals, or in sphenoidal microcrystals; non-glandular hairs few, 2- to 6-celled, attaining a length of about 0.5 mm., the basal cell about 0.04 mm. in width, some of the cells more or less collapsed, the outer walls with numerous slight centrifugal projections; glandular hairs few, with 1- to 2-celled, usually curved stalks and 2- to 4-celled glandular heads; tracheæ annular or spiral. Stem fragments with annular or spiral tracheæ or tracheæ with simple or bordered pores associated with wood parenchyma or wood fibers; or fragments with long narrow unequally thickened collenchymatous cells associated with parenchyma cells, some of the latter containing sphenoidal microcrystals; bast fibers absent.

"**Assay.**—Proceed by Type Process B, using 10 Gm. of Stramonium in fine powder, ether-chloroform mixture for percolating the drug, and chloroform as the immiscible solvent for extracting the alkaloids from the aqueous liquid. Determine the alkaloids volumetrically. Each cc. of tenth-normal sulphuric acid corresponds to 0.02893 Gm. of the alkaloids of Stramonium (Proximate Assays).

"Ovate, petiolate, usually from ten to fifteen centimeters long, often unequal at the base; margin sinuate-dentate, apex acuminate. Upper surface dark greyish-green; under surface paler, and minutely wrinkled. Walls of the epidermal cells sinuous; stomata on both surfaces; on the lower surface, especially of young leaves, curved multicellular hairs with thin, warty walls, and also glandular hairs with unicellular or multicellular stalks; in the mesophyll numerous cluster-crystals of calcium oxalate. Characteristic odor; taste bitter, unpleasant. Ash not more than 18 per cent." *Br.*

J. S. Ward has found commercial stramonium leaves freely adulterated with those of *Carthamus helenioides* and *Xanthium Strumarium.* (*P. J.*, lxvi, 326.) E. M. Holmes states that the leaves of *Xanthium macrocarpum* were extensively substituted for European stramonium leaves from Spain in 1918 (*C. D.*, 1920, xcii, 908). The most common adulterants of American stramonium have been the leaves of *Xanthium strumarium* and excess stems. The former may be detected by their absence of rosette crystals and presence of rod-shaped crystals of calcium oxalate and especially by their short, non-glandular hairs, each exhibiting a broad basal cell and a pointed, frequently bent terminal cell. For a paper on the structure of the leaves of *D. stramonium, Atropa Belladonna,* and *Hyoscyamus niger* by Schlotterbeck and van Zwaluwenburg, see *Proc. A. Ph. A.*, 1897, 202. Holm has published an illustrated article on the morphology of stramonium (*M. R.*, xxii, p. 162). Rosenthaler has subjected the leaves of stramonium to pyroanalysis and obtained a distinctive and characteristic sublimate. (*B. P. G.*, xxi, p. 530.)

The seeds are small, kidney-shaped, pitted and wrinkled, flattened on the sides, of a dark-brown almost black color, inodorous unless bruised, and of the bitter, nauseous taste of the leaves, with some degree of acrimony. The testa is dull brownish-black, hard, and encloses a cylindrical curved embryo, which is embedded in a whitish oily albumen. They are much more energetic in their action on the system than are the leaves.

Constituents.—Geiger and Hesse in 1833 succeeded in isolating an alkaloid, to which the name *daturine* was given and which Trommsdorff has repeatedly procured by their process.

As was first shown by Von Planta in 1852, and since confirmed by many authorities, daturine is identical with hyoscyamine (see *Belladonna*). Ladenburg described two forms of the alkaloid which he called *heavy* and *light daturine,* but the former was probably a racemized hyoscyamine (atropine) formed during the process of isolation. There is also present traces of scopolamine but not in large enough quantity to influence the physiological activity.

H. C. Brill has studied *Datura alba* for alkaloidal content and effect of drying. (*Philippine Jour. Sci.* through *Chem. Abs.*, 1918, xii, 738.) Geo. P. Koch (*A. J. P.*, 1919, xci, 11) has done considerable research in the relative alkaloidal content of the stem and of the leaves of stramonium. He states that the whole plant, with or without the root, can be used without fear of the total alkaloidal content falling below the present U. S. P. standard.

Gérard (see *J. P. C.*, 1892, 8) studied *daturic acid* obtained from stramonium seed. D. Holde has, by means of benzene, extracted from stramonium seed 16.7 per cent. of a fixed oil. (*P. J.*, lxx, p. 90.) This has been examined by J. M. Baird and F. E. Sleeper, see *Proc. A. Ph. A.*, 1903, 324.

Uses.—Stramonium is so similar to belladonna in the symptoms produced by it in small or large doses, in its toxicity and its general physiological and therapeutic action, that the two drugs are practically identical. Furthermore, they are about the same strength in activity, so the preparations may be used in similar doses. Stramonium has been employed in all the conditions for which belladonna is more commonly used, but has acquired special repute in the treatment of *asthma,* this probably being due to the fact that the practice of smoking *Datura ferox* in that disease was introduced into Great Britain from the East Indies by General Gent, and that afterwards the English species was substituted for that employed in Hindostan. Formerly the roots were chiefly used, but at present the dried leaves and tops are exclusively employed. The beneficial effect is doubtless due to the presence of atropine which paralyzes the endings of the pulmonary branch of the vagus, thus relieving the bronchial spasm, for Gunther (*W. K. W.*, 1911, p. 748) has shown that the smoke from a stramonium cigarette containing 1.25 Gm. of stramonium leaves contains as much as 0.5 Mgm. of atropine. The leaves may be made up into cigarettes or smoked in a pipe, either with or without a mixture of tobacco; more commonly, however, the coarsely ground leaves are mixed with equal parts of potassium nitrate, in order to increase combustion, and burned in a saucer.

The seeds are more powerful than the leaves. The seeds were once officially recognized but the presence of a large amount of fixed oil made it difficult to extract them or to make stable preparations from them and the leaves have taken their place. They may be given in the dose of one-half to one grain (0.032–0.065 Gm.) twice a day; an extract made by evaporating the decoction, in one-quarter or one-half the quantity. The inspissated juice of the fresh leaves was formerly very commonly prescribed; but the alcoholic extract is now almost exclusively used when a solid form is desired. (See *Extractum Stramonii.*)

Dose, of the leaves, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Extractum Stramonii (Pilular and Powdered), *U. S.;* Tinctura Stramonii, *U. S., Br.;* Fluidextractum Stramonii, *N. F.*

STRONTII BROMIDUM. Br.

STRONTIUM BROMIDE Stront. Brom.

"Strontium Bromide may be obtained by neutralising dilute hydrobromic acid with strontium carbonate, evaporating and crystallising. It contains not less than 97 per cent. of pure strontium bromide, $SrBr_2,6H_2O$." *Br.*

Strontium Bromatum, *Fr. Cod.;* Bromure de Strontium, *Fr.;* Strontiumbromid, *G.;* Bromuro Estroncico, *Sp.*

This salt has been dropped from the U. S. P.

Properties.—Strontium Bromide occurs as "White acicular crystals, deliquescent. Taste saline, slightly bitter. Soluble in less than 1 part of *water,* and in *alcohol* (90 per cent.). Yields the *reactions* characteristic of bromides; an aqueous solution slowly deposits a crystalline precipitate on the addition of *solution of calcium sulphate.* A solution of 1 gramme in *water,* to which 5 millilitres of *solution of sodium acetate* and 3 millilitres of *acetic acid* have been added, does not become cloudy on the addition of 1 millilitre of *solution of potassium chromate* (absence of barium). 1 gramme dissolved in *water* requires for complete precipitation not less than 54.6 or more than 57 millilitres of *N/10 solution of silver nitrate.* 0.5 gramme moistened with *sulphuric acid* and gently ignited leaves a white residue weighing not less than 0.250 gramme. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million." *Br.*

The U. S. IX gave the following requirements: "The salt deliquesces in moist air but effloresces in very dry air. One Gm. of Strontium Bromide dissolves in 0.35 mil of water at 25° C.; soluble in alcohol; insoluble in ether. Its aqueous solution (1 in 20) is neutral to litmus. When quickly heated, the crystals at first melt, and at above 180° C. lose all of their water of crystallization. To a non-luminous flame the salt communicates a crimson color. Silver nitrate T.S. added to an aqueous solution of the salt (1 in 10) produces a yellowish white precipitate, insoluble in nitric acid or in a moderate excess of ammonia water. With calcium sulphate T.S. an aqueous solution of the salt (1 in 20) slowly forms a white precipitate of strontium sulphate, insoluble in dilute acids; the precipitation occurs more quickly with diluted sulphuric acid or a readily soluble sulphate. Add a few drops of ferric chloride T.S. and 1 mil of chloroform to 10 mils of an aqueous solution of the salt (1 in 20) and shake the mixture; the chloroform does not acquire a violet tint (*iodine*). Drop 1 mil of diluted sulphuric acid upon about 1 Gm. of the powdered salt; no yellow color appears at once (*bromate*). Dissolve 1 Gm. of Strontium Bromide and 1 Gm. of sodium acetate in 5 mils of distilled water, and render the solution slightly acid by the addition of from 3 to 5 drops (or a sufficient quantity) of diluted acetic acid. The solution, upon the addition of 5 drops of potassium dichromate T.S. and agitation, does not become cloudy within three minutes (*barium*). An aqueous solution of the salt does not respond to the Test for heavy metals." *U. S. IX.*

The U. S. IX also required that when assayed by the method for bromides it should show not less than 98 per cent. of $SrBr_2 + 6H_2O$.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.017778 Gm. of $SrBr_2 + 6H_2O$. Each gramme of Strontium Bromide corresponds to not less than 55.1 mils nor more than 56.6 mils of tenth-normal silver nitrate V.S." *U. S. IX.*

For further tests, see *Proc. A. Ph. A.*, 1897, 608.

Strontium bromide shows incompatibilities not shared by the other alkali bromides, from the fact that carbonates, citrates and sulphates form precipitates with strontium.

Uses.—Strontium bromide has been strongly commended as a substitute for potassium bromide in the treatment of *epilepsy* and allied conditions. It depends for its action on the nervous system upon the presence of bromine in it, and appears to act upon the nervous centers in much the same manner as does the corresponding salt of potassium. Its influence upon the general nutrition is much more favorable than is that of the potassium salt, and it is much less apt to produce the disagreeable effects of bromism. Moreover, it is less irritating to the gastro-intestinal mucous membranes, on which, indeed, it often seems to exert a beneficial influence. For these reasons many cases of epilepsy tolerate it much better than they do other bromides. In the experience of H. C. Wood, however, it seemed to be in its anticonvulsive influence among the least powerful and certain of its class. Possibly this result has been due to Wood not having employed it in sufficient dose, he never having administered more than two drachms a day, while the French observers affirm that it may be given with great advantage in the daily dose of three drachms. Strontium bromide is further stated by Sée to have an extraordinary influence in the reduction of the excretion of sugar in *diabetes,* and to be a valuable remedy in the treatment of *gastric dilatation* and *catarrh.*

Dose, fifteen to thirty grains (1–2 Gm.).

STRONTII SALICYLAS. U. S.

STRONTIUM SALICYLATE Stront. Salicyl.

"Strontium Salicylate, when dried to constant weight over sulphuric acid, contains not less than 99 per cent. of $Sr(C_7H_5O_3)_2.2H_2O$." *U. S.*

Strontium Salicylicum; Salicylate de Strontium, *Fr.;* Salicylsaures Strontium, Strontium Salicylat, *G.*

This salt may be obtained by the following process: Add 10 parts of salicylic acid to 100 parts of water, to the mixture add 5.3 parts of strontium carbonate; when the reaction is completed filter, partially evaporate and allow to crystallize.

Description and Physical Properties.—"A white, odorless, crystalline powder, having a somewhat sweet, saline taste. One Gm. of Strontium Salicylate is soluble in 19 cc. of water and in 61 cc. of alcohol, at 25° C. One Gm. is soluble in 3.7 cc. of boiling water and in 14 cc. of boiling alcohol.

"When heated, the salt is decomposed, giving off inflammable vapors and an odor of phenol, and finally leaving a residue of strontium carbonate and carbon. An aqueous solution of the salt (1 in 20) responds to the reactions for strontium, and for salicylates.

"An aqueous solution of the salt (1 in 30) is colorless. Add 1 cc. of diluted sulphuric acid to 10 cc. of an aqueous solution of Strontium Salicylate (1 in 50), and filter: the filtrate meets the requirements of the test for *heavy metals.* Agitate 2 Gm. of Strontium Salicylate with 10 cc. of diluted acetic acid, heat the mixture, cool, and filter: the filtrate, upon the addition of 5 drops of potassium dichromate T.S., does not become cloudy within three minutes (*barium*).

"**Assay.**—Place about 2 Gm. of Strontium Salicylate, previously dried to constant weight over sulphuric acid and accurately weighed, in a tared platinum crucible, and thoroughly carbonize it at a temperature not exceeding red heat. Dissolve the residue in 30 cc. of half-normal hydrochloric acid, and submit it to residual titration with normal sodium hydroxide, using methyl orange T.S. as indicator. Each cc. of half-normal hydrochloric acid corresponds to 0.09945 Gm. of $Sr(C_7H_5O_3)_2.2H_2O$.

"Preserve in well-closed containers, protected from heat and light." *U. S.*

Uses.—Strontium salicylate when taken internally is slowly decomposed in the alimentary canal with the liberation of salicylic acid, which acid, or its educts, can be detected in the urine shortly after administration. As a salicylate, the strontium salt is of especial value in subacute *rheumatic* affections, acting more slowly and persistently than most of the other allied salts. By some it is believed to have less tendency to disturb the digestion but Blankenhorn (*J. A. M. A.*, 1916, lvi, p. 331), from comparative studies in twenty-three cases of various diseases, has come to the conclusion that the toxic dose of strontium is the same as that of sodium salicylate, and that the strontium salt has no advantage in any way. It may be administered in capsule or in solution.

Dose, five to thirty grains (0.32–2.0 Gm.).

STROPHANTHINUM. U. S.

STROPHANTHIN Strophanthin.

"A glucoside or a mixture of glucosides obtained from *Strophanthus Kombe* Oliver (Fam. *Apocynaceæ*)." *U. S.*

Strophantine, *Fr. Cod.;* Strophanthin, *G.*

Preparation.—*Strophanthin* may be prepared by Fraser's process of depriving the ground seeds of fatty oil by percolation with petroleum benzin, making a tincture from the marc with 70 per cent. alcohol, distilling, evaporating and treating the extract with water; this solution is then filtered and the filtrate precipitated with tannic acid; the precipitate is washed, mixed with litharge, dried and exhausted with alcohol; by adding ether to the alcoholic liquid, strophanthin is precipitated. For an improved method, see Rowe, *J. A. Ph. A.*, 1916, v, 1183.

Description and Physical Properties.—"A white or yellowish powder containing varying amounts of water, which it does not lose entirely without decomposition. It is stable in the air. *Caution—Strophanthin is extremely poisonous.* Strophanthin is soluble in water and in diluted alcohol, but less soluble in dehydrated alcohol. It is nearly insoluble in chloroform, ether, and benzene.

"Solutions of Strophanthin are neutral to litmus paper, and are dextrorotatory. Sulphuric acid added to Strophanthin produces an emerald-green color, changing to brown. Add a trace of ferric chloride T.S. and a few cc. of sulphuric acid to an aqueous solution of Strophanthin (1 in 50): a red precipitate is produced, which turns dark green after one or two hours. A solution of 0.1 Gm. of Strophanthin in 15 cc. of distilled water, when mixed with 5 cc. of hot alkaline cupric tartrate solution, produces no precipitate. On heating an aqueous solution to 70° C. with a small amount of diluted hydrochloric acid, the Strophanthin is hydrolyzed into strophanthidin, which precipitates, and a sugar, capable of reducing alkaline cupric tartrate solution, which remains in solution. The ash from 0.1 Gm. is negligible.

"Preserve in well-closed containers, protected from light." *U. S.*

For further details of the various kinds of strophanthin and their properties, see *Strophanthus* and *Acocanthera.* Strophanthin is very susceptible to alkalies and both Levy and Cullen (*J. Ex. M.*, 1920, xxxi, 267) and Pomeroy and Heyl (*A. J. P.*, 1922, xciv, 479) have shown that ampules of strophanthin solution deteriorate very rapidly because of the alkali dissolved from the glass.

Uses.—Strophanthin fully represents the therapeutic properties of strophanthus. While occasionally used by the mouth it is usually employed where it is desirable to administer the drug by injection. On account of its intense local irritant effect the hypodermic injection is not to be recommended; the drug may, however, be thrown into the muscle substance or better, directly into a vein. In cases of severe *circulatory failure,* such as that seen in *pneumonia* and other infectious diseases, in *collapse* from *ether anesthesia,* and in *uremia,* striking results are often obtained by the intravenous injection of strophanthin. Bailey (*J. P. Ex. T.,* 1909, i, p. 349) finds the treatment of the utmost value as an emergency measure in broken compensation of *heart disease,* but not suitable for continuous use.

The confusion concerning the identity of the various strophanthins, as well as the extraordinary difference in their activity according to the channel of administration, has given rise to great diversity of statement as to the proper dosage of these glucosides. A long summary of the literature on this subject is given in *Merck's Report* for 1912, as a result of which the conclusion is reached that when given intravenously G-strophanthin is nearly twice as strong as the K-strophanthin (the official), but that when exhibited by the mouth G-strophanthin is very much weaker than the official. The conclusions reached from this article are that the maximum *daily* dose of these glucosides should not exceed for G-strophanthin, intravenously, one sixty-fourth of a grain (0.001 Gm.), by mouth, one-half grain (0.032 Gm.). Of the K-strophanthin, intravenously, one-fortieth grain (0.0016 Gm.), by mouth, one-twentieth of a grain (0.003.).

For a discussion of the various strophanthins, see *Strophanthus.*

Dose, one two-hundredth of a grain (0.0003 Gm.).

STROPHANTHUS. U. S. (Br.)

STROPHANTHUS Strophanth.

"Strophanthus is the dried, ripe seed of *Strophanthus Kombe* Oliver or of *Strophanthus hispidus* DeCandolle (Fam. *Apocynaceæ*), deprived of the awns. Strophanthus, in the form of the tincture, properly diluted and injected into the ventral lymph sac of a frog, has a minimum systolic dose (the minimum dose producing in one hour a stoppage of the ventricle of the heart in systole) not exceeding 0.00,006 cc. of tincture, equivalent to 0.00,000,05 Gm. of ouabain, for each gram of body weight of frog." *U. S.* "Strophanthus Seeds are the dried ripe seeds of Strophanthus Kombé, *Oliver,* freed from the awns." *Br.*

Strophanthi Semina, *Br.;* Strophanthus Seeds; Strophantus, *Fr. Cod.;* Semen Strophanti, *P. G.;* Strophanthussamen, *G.;* Strofanto, *It.;* Estrofanto (Semilla de), *Sp.*

The seeds of the various species of Strophanthus have been used by the African natives as arrow poisons. In 1861 the famous explorer and missionary, Doctor Livingston, described the method of use of poisoned arrows by the tribes on the Shiré River in East Africa near Mozambique. He says, "The poison used here, called Kombi, is obtained from a species of Strophanthus." Sir John Kurt obtained some of the seeds in the neighborhood of Lake Shirwa, from which this poison was prepared. These were identified by Oliver as being derived from a new species which he named *S. Kombe,* and remarked that the plant was closely allied to a species used for the same purpose at Sierra Leone on the west coast of Africa. Seeds of this plant, brought to Europe by a returning missionary named Waller, were studied by Fagge and Stevenson who found them to act as a cardiac poison similar to digitalis. In 1865 a French naval surgeon, Du Bellay, obtained some seeds that were used as arrow poisons in the neighborhood of the Gabun River on the western coast of Africa in the French Kongo, where it was known as Inée or Onaye. It was at first believed that these two poisons were derived from the same plant, but at present it seems that the *S. Kombe* grows solely in East Africa and that those which come from West Africa must be yielded by other species. For information concerning the history of Strophanthus and description of the plant, see monograph by Frazer (*Transactions of the Royal Society of Edinburgh,* 1890, xxxv, Part 4, p. 955). See also under *Acocanthera,* Part II.

There is no fixed principle of agreement in the several pharmacopœias. Meyer (*A. Pharm.,* 1908, p. 51) very correctly states that it is for the pharmacologist and therapeutist to determine the relative values of each of the seeds before it is possible to determine whether one species may be substituted for another. In Germany the seeds of *Strophanthus hispidus* are preferred because of their guaranteed purity. (*B. P. G.,* xviii, p. 284.) On the other hand, the British Pharmacopœia, the French Codex and the Swiss Pharmacopœia confine their official definitions to *S. Kombe.* The U. S. Pharmacopœia alone recognizes both species, the *S. hispidus* being added because of the arguments that have been advanced in this country as to the efficacy of these seeds. The literature in recent years on the question of strophanthus has been quite voluminous. Some of the more interesting articles are the following: Thoms (*Arb. a. d. Pharm. Inst. d. Univ. Berlin,* 1905, p. 74); Gilg (*Ibid.,* p. 59); Pabisch (*Zeit. Oest. Apoth. Ver.,* xlvii, p. 509); Gilg (*B. P. G.,* xviii, p. 284); Hartwich (*Ap. Ztg.,* xxvi, p. 94).

According to Engler and Prantl, there are twenty-eight recognized species of the genus found in Africa and Asia, extending to China, the East Indies, and the Philippines. The commercial drug is often largely composed of the seeds of other than the recognized official species, and may contain the seeds from related genera, especially those of *Kickxia africana* Benth. The seeds of *Kickxia africana* are without hairs, spindle-shaped, not flattened, twisted into an S-like shape, and with the base and the summit of the seed alike in their forms. On cross-section the cotyledons are seen much folded, while those of the strophanthus lie parallel one upon the other. The transverse section of the kickxia seed, when treated with concentrated sulphuric acid, first turns brown, then red, while the seeds of both kinds of strophanthus take on a green color. According to Stapf, the plant represents a new genus and should be known as the *Funtumia africana;* the only other species of the genus, *F. elastica,* yields India rubber.

The seeds of all the species of strophanthus apparently possess hairs that have a characteristic thickened base somewhat resembling those of nux vomica seeds. The tracing of the origin of the seeds is made more difficult by the fact that in Africa seeds from different regions are mixed before shipment. The seeds of *S. hispidus* enter commerce, as do also those of *S. glaber, S. Emini* Aschers and *S. Courmontii* Sacleux (*P. J.,* 1899, lxiii, p. 34). A white woolly strophanthus is said to be yielded by *S. Nicholsoni,* a species first characterized by Holmes (*P. J.,* 1897, lix, 208). *S. gratus* of Sierre Leone also contributes its seeds; also *S. glaber* contains ouabain.

Sharp (*P. J.,* 1912, lxxxviii, p. 159) has found that the seeds of the *S. Courmontii* are about one-fourth as poisonous to frogs as those of the *S. Kombe,* but their physiological effects are of a similar type. The seeds of the *S. Emini* Asch, he found to be almost without action upon the frog's heart. The seeds of the *S. Thalloni* and of the *S. Tarmentosus* A. DC., are also active.

S. hispidus when by itself takes the form of a bush, but usually occurs as a woody climber inhabiting the forests between the coasts and the center of the African continent. It reaches to the tops of the highest trees, coiling on the ground, and hanging in festoons from tree to tree. The stem is several inches in diameter. The flowers are cream-colored, yellow at the base, purplish-spotted above. They are grouped in terminal cymes. The lobes of their gamopetalous corollas are prolonged into very narrow tail-like ends being nine or more inches in length. The fruit, a pair of follicles from 10 to 17 inches long, is ripe in June, and is gathered by the natives, who scrape off the husks (epicarp and mesocarp) before drying, and preserve the more leathery internal inner covering (endocarp) with the enclosed seeds; hence the pods as they appear in commerce are smooth and of a tawny color. The seeds themselves are covered with long comose hairs, which, being deciduous, are apt to be lost before the escape of the seed from the pod. In preparing the arrow poison, the natives are said to pound the seeds deprived of their hairs to a pulp, add the adhesive sap of another plant, and simply smear the mixture for six inches along the point of the arrow. Game wounded by such an arrow is said to be rarely able to move a hundred yards, and the flesh is eaten without bad effect. Karsten has examined the *root* of *Strophanthus hispidus* and found that it contained *trigonelline, choline* and *strophanthin* in such small proportions that it will probably never be commercially valuable. (*B. P. G.,* 1902, 12, 241.)

Strophanthus occurs in commerce either in pods or as clean seeds. Helbing states (*P. J.,* March, 1887) that he has found the seeds to constitute about 37 per cent., the pod (endocarp) 37 per cent., and the hairs about 25 per cent., and says that the quality of the pods may be determined by examining the color of the pappus. If this is white and bright, the seeds and pods are in good condition.

Description and Physical Properties.—"*Unground Strophanthus Kombe.*—Oblong-lanceolate, flattened and obtusely edged; from 8 to 25 mm. in length, from 2.5 to 5 mm. in width, and from 0.5 to 2 mm. in thickness; the raphe ridge extending from near the center of one side to the apex; light brown with a distinct greenish tinge; silky lustrous owing to a dense coat of closely appressed hairs; fractured surface whitish and oily; taste very bitter.

"*Unground Strophanthus hispidus.*—Light to dark brown; otherwise resembling *S. Kombe* excepting that it is smaller and with fewer and smaller hairs.

"*Structure.*—Epidermis with numerous, unicellular hairs usually bent and arising in *S. Kombe,* from the center of the surface of the epidermal cell and in *S. hispidus,* from near the radial wall; endosperm of 9 to 30 rows of parenchyma cells; embryo consisting of a short straight caulicle, 2 long plano-convex cotyledons and a small radicle. Endosperm tissue usually colored dark-green with sulphuric acid.

"*Powdered Strophanthus.*—Grayish-brown to dark brown; epidermal cells with thickened, lignified radial walls; hairs slightly lignified and from 0.2 to 0.8 mm. in length, fragments of endosperm and cotyledons with fixed oil, aleurone grains and starch grains, the latter from 0.004 to 0.008 mm. in diameter; prismatic crystals of calcium oxalate in seed coat absent (*Strophanthus Courmontii* Sacleux)." *U. S.*

The seeds of *S. Kombe* are described in the British Pharmacopœia as "oval, acuminate, about fifteen millimetres long and four millimetres broad; flattened, narrow towards the base, which is obtuse; covered with silky appressed hairs; provided on one side with a longitudinal ridge running from the centre to the apex; of a greenish-fawn color. Kernel white and oily; cotyledons straight; endosperm narrow; in the seed-coats not more than an occasional crystal of calcium oxalate. Characteristic odor; taste very bitter. *Sulphuric acid* diluted with one-fifth of its volume of *water* colors the endosperm, and sometimes the cotyledons, dark green (presence of strophanthin)." *Br.*

At present strophanthus seeds are much less mixed than formerly. In 1892 Hartwich classified commercial strophanthus seeds (*A. Pharm.,* 1892, 401), in the following groups: (1) The official products yielded by *S. hispidus* or *S. Kombe,* which contain strophanthin and no crystals of calcium oxalate. (2) Those resembling the official seeds, but of different habitat—viz., Mozambique and Sierre Leone. (3) Those which contain calcium oxalate crystals, but no strophanthin—viz., Senegal, Lagos, Niger, German East Africa, Togoland, and Baol of Senegal. (4) A very hairy seed from the Upper Niger. The hairs vary in color from a silky white to brown; the embryo contains calcium oxalate crystals, but the seeds do not contain strophanthin. (5) Seeds which are said to be glabrous, but possess hairs in the region of the raphe. These include those from Lagos and Zambesi, and contain neither calcium oxalate crystals nor strophanthin. The seeds of *S. gratus* are recommended by E. Gilg as more easily recognized than the others and because it yields strophanthin more readily in crystalline form. (*B. P. G.,* 1904, 90.)

The seeds of *S. gratus* (Wall et Hook.) Franchet. are characterized by their uniform and reliable activity and it has been suggested that they may replace advantageously those of *S. Kombe.* They are obtained from plants growing in Senegal and the Congo, the same region in which *S. hispidus* is found. According to Gilg the seeds are spindle-shaped, being at the bases more or less rounded, although sometimes truncate. In the upper portion, they are sharply angular, sometimes being winged and gradually tapering at the summit. Externally the seeds are of a characteristic yellow or yellowish-brown. They vary in length from 11 to 19 mm., in breadth from 3 to 5 mm., and in thickness from 1 to 1.3 mm. In taste they are strongly and persistently bitter. On the addition of sulphuric acid to microscopic sections the latter are colored reddish or of a rose tint, changing to a deep red or violet. They contain the glucoside, ouabain.

The seeds of *S. Courmontii* Sacleux are 8 to 14 mm. in length, 2.5 to 3.5 mm. in breadth and 1 to 2 mm. in thickness; of a distinctly lanceolate form and decidedly brown color, often with the hairs rubbed off, but having a golden sheen when these remain, while the tint is dull and reddish when they are absent. The ridge on the ventral surface is indistinct and the arrangement of the hairs in longitudinal rows is now as apparent as in the official seed. They also contain crystals of calcium oxalate in abundance, which have been stated by some observers to be entirely absent from *S. Kombe* and *S. hispidus.* The statement of E. M. Holmes (*P. J.,* lxiv) that the seeds of *S. Kombe* and *S. hispidus* give with sulphuric acid a greenish reaction, while those of *S. Courmontii* give a reddish, and *S. elemi* a yellowish-brown changing into reddish, seems not to be absolutely accurate, for while the seed albumen of *S. Kombe* always gives the greenish reaction the cotyledons frequently are mottled with red and rarely give an entirely red reaction. (Perredes.) The strophanthus fruits are gathered when ripe, deprived of their epicarp and mesocarp and occasionally sent into commerce in this condition. More frequently, however, the seeds are separated from the pods, deprived of their awns and shipped both from West African and East African ports.

The sulphuric acid identification test for strophanthus has been improved by Bohrisch (*Ph. Ztg.*, 1918, lxiii, 318) who recommends the following manipulation: Thin cross-sections of the seeds placed on an object glass and treated with ether to remove the fat, are covered with one drop of sulphuric acid, containing ¼ of its weight water. The deep green coloration, indicating the presence of strophanthin, should, especially when some magnification is used, be observable in the endosperm and at least the outer portions of the embryo. When big sections (seeds cut in half) were used, the results of the test were very variable and indefinite. According to Karam Samaan (*C. D.*, 1919, xci, 802), two drops of concentrated sulphuric acid on a slab with 0.1 gramme of ammonium molybdate and a trace of strophanthin or strophanthin-containing residue gives a light brownish-green color which gradually develops into blue after 10 minutes. The intensity of the blue color reaches a maximum in 20 minutes and remains permanent, but may be destroyed instantaneously by addition of concentrated nitric acid.

Assay.—"Prepare a tincture by the official process and proceed as directed under *Tinctura Digitalis.*" *U. S.*

Several methods for the chemical assay of strophanthus have been suggested. These are all based on the principles of the extraction of the total glucosides and conversion into strophanthidin. Lampart and Mueller (*A. Pharm.*, ccli, 609) extract the drug with absolute alcohol, remove the oil from the percolate by means of petroleum ether and decompose the glucoside by boiling with hydrochloric acid.

Heacock (*Brit. and Col. Druggist,* 1911) percolates the drug first with petroleum ether to remove the oil and afterwards exhausts with 70 per cent. alcohol. The alcoholic extract is then partially evaporated, dissolved in an acidulated water, shaken out with ether, and the aqueous portion heated to 75° C. for one hour, and the strophanthidin formed during this period extracted with chloroform.

The Kombe seeds yield from one to two per cent. of glucosides.

Knudson and Dresbach (*J. P. Ex. T.*, 1922, x, 205) have presented evidence to show that the Baljet reaction (see under *Digitalis*) affords a criterion also for strophanthus.

None of the chemical standards are as yet sufficiently developed to be able to replace the biological assay which is official in the *U. S.* (for details of this see under *Digitalis*).

Constituents.—Hardy and Gallois in 1855 described in strophanthus a glucoside, *strophanthin,* and an alkaloid, *inœine.* The existence of the alkaloid has not been confirmed by subsequent investigators. The activity of the drug is undoubtedly due to the glucoside. The studies of Fraser (*A. J. P.*, 1889, 532), Thoms (*B. Chem. G.*, 1898, p. 534 and 1904, p. 104), Feist (*B. Chem. G.*, 1900, xxxiii, p. 2069), Brauns and Closson (*J. A. Ph. A.*, 1913, ii, p. 489) and others have apparently established the following facts: different species of strophanthus contain related but not identical glucosides. Thoms has suggested distinguishing these by the initials of the specific name, as *K-strophanthin* from the *S. Kombe, G-strophanthin* from the *S. gratus, E-strophanthin* from the *S. Emini, H-strophanthin* from the *S. hispidus.* The *G-strophanthin* is identical with ouabain (see under *Acocanthera,* Part II, also under *Reagents,* Part III). *S. Kombe* contains two glucosides, the more abundant being amorphous and having twice the molecular weight of the isomeric crystalline glucoside. These glucosides each have the empiric formula $C_{40}H_{56}O_{15}$ and when hydrolyzed yield *strophanthidin,* $C_{27}H_{38}O_7$, and a sugar.

There is evidence that the glucoside from the *S. hispidus* is identical with the amorphous principle from the *S. Kombe* (see Pomeroy and Heyl, *A. J. P.*, 1922, xcv, p. 479) although the matter cannot be considered definitely established.

Rowe (*T. G.*, 1917, xxxiii, p. 536) has shown that there is great difference in the toxicity of these various strophanthins. Ouabain is approximately twice as poisonous as *K-strophanthin,* although the relations vary greatly according to the animal and the method of administration employed. According to Tiffeneau (*B. Sc. Pharm.*, 1922, xxix, p. 68), the crystallized *K-strophanthin* is about one and one-half times as active as the amorphous variety.

For a discussion of the analytical differences of the several strophanthins and for the differentiation of strophanthin and ouabain, see *Pharm. Zeit.*, 1915, 159 and 174; and *J. P. C.*, 1921, 161.

Sieburg (*B. P. G.*, 1911, xxiii, 278) has found an acid saponin in *S. hispidus* which he calls *strophanthic acid.*

Uses.—As was first shown by Thomas R. Fraser (*J. A. P.*, vii, p. 141), strophanthus belongs to that group of cardiac poisons of which digitalis is the type. Its effects upon the circulation are so similar to that drug (see page 408) that it is only necessary to note the points of difference. Strophanthus is somewhat more rapid in its action and decidedly less permanent than digitalis; it causes relatively less reduction of the pulse rate and is generally believed to have less influence on the vasomotor mechanism. It appears to be absorbed from the intestinal tract with much less regularity than digitalis and therefore is less certain in its effects. Besides its action upon the circulation, strophanthus has a marked influence on intestinal peristalsis, according to Magnus (*A. G. P.*, 1905, cviii, p. 1), causing increased peristalsis and tone and under certain conditions tetanic spasm of the intestines. Probably because of this action it frequently produces diarrhea when used clinically. According to the early researches of Fraser it exercises a similar influence on all forms of muscle tissue including voluntary muscles. It is by some believed that strophanthus has a direct stimulating effect upon the kidney and is superior to digitalis as a diuretic, but the evidence in favor of this view is far from convincing. While it possesses some local anesthetic powers it is so highly irritant that it is practically unavailable for this effect.

Strophanthus is used in medicine solely for its influence on the circulation, especially in cases of *chronic heart weakness.* It is of value in exactly the same class of cases in which digitalis is employed and, although more likely to cause digestive disturbances, is frequently useful as an alternative or adjuvant to that drug. By some it is believed to be especially indicated in those cases complicated with dropsies, because of a belief in a greater diuretic power. In cases of threatening urgency the effects of strophanthus upon the circulation can be obtained almost immediately by means of the intravenous injection of its active principles (see *Strophanthinum*).

The question of the relative variability of potency in strophanthus as compared to digitalis cannot as yet be definitely answered. Although certain German investigators have claimed that strophanthus is more subject to wide range in power, Hatcher and Bailey (*J. A. M. A.*, 1909, lii, p. 5) have found that the tincture of strophanthus is much more uniform in this country than the tincture of digitalis.

Dose, of strophanthus, one-fourth to one grain (0.016–0.065 Gm.).

Off. Prep.—Extractum Strophanthi, *Br.;* Tinctura Strophanthi, *U. S. Br.*

STRYCHNINA. N. F., Br.

STRYCHNINE Strych.

"An alkaloid ($C_{21}H_{22}O_2N_2 = 334.30$) obtained from nux vomica, and also obtainable from other seeds of the *Loganiaceæ.*" *N. F.*

"Strychnine, $C_{21}H_{22}N_2O_2$, is an alkaloid, obtained from the seeds of Strychnos Nux-vomica, *Linn.*, and other species of Strychnos." *Br.*

Strychnia, Strychninum, ***Fr. Cod.;*** **Strychnin,** ***G.;*** **Stricnina,** ***It.;*** **Estricnina,** ***Sp.***

The U. S. X has omitted this base although two of the salts are recognized. It has been admitted to the N. F. No process for extracting strychnine is official as it can be made profitably only by the manufacturing chemist on a large scale. (See *U. S. D.*, 17th ed., p. 1295.) The method employed is, in brief, as follows: The powdered nux vomica is mixed with slaked lime and water added to make a paste which is then dried and exhausted with chloroform. From this the alkaloids are extracted by dilute sulphuric acid; this aqueous solution is then alkalized with ammonia and the precipitated alkaloids extracted with 25 per cent. alcohol which dissolves the brucine but leaves most of the strychnine. The latter is then purified by recrystallization.

J. F. Molyn proposed, previously to the extraction of strychnine, to subject nux vomica to fermentation, by which the saccharine and gummy matters of the seeds are decomposed, and lactic acid is formed, which decomposes the strychnine and brucine igasurates, producing with these bases very soluble lactates. For the particulars of this process, see *A. J. P.*, xix, 99, and for other processes see *U. S. D.*, 14th ed., p. 1456.

The bean of St. Ignatius yields strychnine more easily and more largely than nux vomica.

Description and Physical Properties.—As usually found in commerce, strychnine is a white or grayish-white powder. When rapidly crystallized from its alcoholic solution, it has the form of a white, granular powder; when slowly crystallized, that of elongated octohedra, or rhombic prisms with pyramidal summits.

"Strychnine occurs in colorless, transparent, prismatic crystals, or as a white, crystalline powder; odorless, permanent in the air. *Great caution must be used in tasting it and then only in very dilute solutions* which are exceedingly bitter. One Gm. of Strychnine dissolves in 6420 cc. of water, 136 cc. of alcohol, 5 cc. of chloroform, and in 180 cc. of benzene at 25° C.; also in 3100 cc. of boiling water, and 34 cc. of boiling alcohol; very slightly soluble in ether.

"Its saturated solutions are alkaline to litmus and are lævorotatory. Sulphuric acid containing 1 per cent. of ammonium vanadate produces with Strychnine a deep violet-blue color, changing to a deep purple, and finally to a cherry-red. A solution of about 0.1 Gm. of Strychnine in 2 cc. of sulphuric acid is not more than pale yellow (*readily carbonizable organic impurities*), but on adding a fragment of potassium dichromate, a deep blue color is momentarily produced, changing to deep violet, then to purplish red, cherry-red and finally to orange or yellow. Incinerate about 1 Gm. of Strychnine: not more than 0.1 per cent. of ash remains. One cc. of a mixture of equal volumes of nitric acid and distilled water, added to about 0.1 Gm. of Strychnine, may produce a yellow, but not a red or reddish color (*brucine*)." *N. F.*

"Colorless, transparent prismatic crystals, permanent in the air. Very slightly soluble in *water,* but sufficiently soluble to impart an intensely bitter taste; soluble in about 150 parts of *alcohol* (90 per cent.). *Sulphuric acid* forms with it a colorless solution which, on the addition of *nitric acid,* acquires not more than a faint pink color (limit of brucine). When a small fragment is dissolved in 2 or 3 drops of *sulphuric acid* on a white porcelain plate and a crystal of *potassium bichromate* is slowly moved through the solution, an intense violet color is produced, passing to red and yellow. No appreciable ash." *Br.*

Strychnine is so extremely bitter that it is perceptible to the taste in the proportions of one part in 700,000 of water. Although it contains two nitrogen atoms, strychnine is a monoacidic base. It has a melting point of 268° C. and an optical rotation of –132.07 in alcohol. When warmed with sodium ethoxide it takes up a molecule of water forming *strychninic acid* which is related to betaine. For account of the efforts to determine the chemical structure of strychnine see Henry, *Plant Alkaloids*, 1924, p. 182.

The identifying tests for strychnine often play an important part in forensic chemistry in connection with cases of suspected strychnine poisoning. Many references to the older tests, most of which have been found to be unreliable, will be found in *U. S. D.*, 20th ed., pp. 1072 and 1073.

The official sulphuric acid potassium dichromate reaction first discovered by Otto in 1839, has not been superseded as an identifying test, when other corroborative tests are positive and the suspected substance has been carefully tested to preclude the possibility of its being a mixture of other alkaloids, which can be done by the use of solvents. J. U. Lloyd in his novel "Stringtown on the Pike" used in an interesting manner a color reaction which he had discovered that produced a color which might deceive some who were working on a toxicological investigation in strychnine poisoning. *Lloyd's reaction* consists in adding sulphuric acid to a mixture of 1 part of hydrastine and 4 parts of morphine and adding a little potassium dichromate in the manner in which the color test for strychnine is made; colors are produced which somewhat resemble those given by strychnine, but a careful toxicologist could not be deceived. A controversy ensued upon the announcement of the reaction, participated in by Williams, Mayer, Wangerin, Wharton, and others, the result of which proved that the value of the official color test of strychnine had not been seriously assailed. (See *D. C.*, 1901, 28, 48; *Proc. N. Y. State Pharm. Assoc.*, 1901, 252; *Amer. Drug.*, 1903, 66.)

The adulterants and impurities reported in strychnine in the older literature are no longer of importance. The present methods of manufacture assure a pure alkaloid, and the Food and Drug Laws protect against the flagrant adulterations reported at a time when strychnine was largely used by trappers in the pioneer days of the West. For methods of distinction from brucine see *Nux Vomica.*

Incompatibilities.—Strychnine is precipitated from its solution by the ordinary alkaloidal reagents such as carbonates, tannic acid, etc. The most important incompatibility, however, is with the halogenic acids. It should never be prescribed in liquid form in combination with bromides, iodides, or chlorides, for fear of forming the insoluble strychnine hydrobromide, hydriodide, or hydrochloride. Several cases of poisoning have occurred through neglect of this precaution. A. B. Lyons (*A. J. P.*, Oct., 1877) records a case of poisoning through the patient's receiving in the last dose the greater portion of the strychnine hydrobromide, which had crystallized out.

Uses.—Strychnine is a stimulant to the whole central nervous system. The effects upon the brain are usually not well marked but in some individuals wakefulness often follows its use and the increased acuity of the special senses is further evidence of its stimulant action upon the cerebrum. The most direct symptom caused by strychnine is violent convulsions. These have been shown by McGuigan and Becht (*J. P. Ex. T.*, 1916, viii, 143) to be due to a simultaneous stimulation of both motor and sensory ganglia of the spinal cord. In the medulla the centers which show a special evidence of the stimulating effect of strychnine, are those governing respiration and vasomotion. While the increase in respiration caused by strychnine is not as great in the normal animal as after some other drugs, it seems to possess an extraordinary power of overcoming the effects of depressant poison. Clinically it is perhaps the most reliable respiratory stimulant which we possess. During the strychnic convulsion there is great rise in the blood pressure This is due in large part to the violent spasm of the muscles and consequent asphyxia, but even when the convulsions are prevented by the previous injection of curare the drug still produces a distinct rise in the arterial pressure, indeed in doses too small to cause convulsions there is still evidence of a stimulation of the vasomotor center. The experiments of Pilcher and Sollman (*J. P. Ex. T.*, 1915, vi, p. 331) indicate that the effect is due largely to an increased irritability of the center so that it responds abnormally powerfully to any exciting influence. Stewart and Rogoff (*J. P. Ex. T.*, 1919, xiii, 95) attribute the rise of pressure to stimulation of the adrenals. The effect of the drug upon the heart is not clearly understood. Although La Franca (*Z. E. P. T.*, 1911, ix, p. 436) found that strychnine increased the irritability and conductivity of the heart muscle the scientific evidence of any direct influence upon the heart is far from convincing. In large toxic dose strychnine causes a paralysis of the motor nerves similar to that produced by curare but it is improbable that this action can play any part in strychnine poisoning in the human being.

The convulsant effects of strychnine naturally suggest its use in *paralysis* but a moment's thought must convince anyone that in most forms of palsies it is incapable of benefit. When the loss of power depends upon the actual destruction of motor cells, as after apoplexy or poliomyelitis, it is evident that the drug can do no good because what does not exist cannot be stimulated. Or when there is a failure in the conducting power of the nerve, as in peripheral neuritis it is equally manifest that excitation of the spinal cells is futile. Indeed in spinal paralyses much harm may be done by irritating the inflamed tissue in the neighborhood of the area of destruction. On the other hand when the paralysis is due to the effect of depressant poisons circulating in the blood, as, for instance, in certain types of *chronic lead poisoning,* strychnine may prove of the utmost value. Like other bitters strychnine improves the appetite and digestion, but it has been enormously misused as a "general tonic." It is to be remembered that strychnine is essentially a stimulant leading to an increased functional activity with an expenditure, rather than a storing up, of reserve power. Such slight tonic effects as it may possess are due to the improved digestion and circulation. There is a common belief among clinicians that strychnine increases the peristaltic activity of the intestinal tract and hence it is frequently added to laxative mixtures, but the experimental evidence on this point is contradictory.

As a circulatory stimulant strychnine is useful in a wide variety of conditions such as *surgical shock, collapse* from hemorrhage, *poisoning* by such depressants as ether, chloroform, or alcohol, and the adynamic stages of *infectious fevers.* In some forms of *chronic heart disease,* especially in *myocarditis,* it seems to be clinically useful. Smith (*J. P. Ex. T.,* 1917, ix, 365) finds that it lessens irritability of the heart and may be of service therefore in extra systoles but is liable to be injurious in other forms of cardiac irregularities. Its value in *chronic bronchitis* in old and feeble subjects is probably also to be attributed to its effects upon the circulation. As a respiratory stimulant it is especially valuable in narcotic *poisoning,* as by *opium* or *chloral.* Strychnine is also asserted to be of much service in toxic *amblyopias,* especially that due to nicotine poisoning.

For ordinary purposes the dose of strychnine ranges from one-sixtieth to one-twentieth of a grain (0.0011–0.003 Gm.) but under many circumstances much larger quantities may be safely administered. Especially when used for its influence upon the circulation is it essential to give large doses. Many of the clinical reports of failure to influence the circulation with strychnine have doubtless been due to too small doses, thus Lucas (*American Journ. Dis. of Children,* 1914, vii) found that it required at least one-tenth of a grain to cause an appreciable change in the blood pressure. While others have reported distinct effects from somewhat smaller dose, the use of one-fortieth or one-thirtieth of a grain with the idea of having any marked influence upon the circulation is a delusion. In many cases it is essential to push the strychnine until marked exaggeration of the reflexes or even twitchings of the muscle affords a warning that the patient is approaching the toxic stage. Newburgh (*A. I. M.,* March, 1915) from studies on cases of pneumonia and typhoid fever concludes that it has no reliable effects on the circulation.

Poisoning.—The symptoms of strychnine poisoning come on usually with great suddenness and violence. Often without warning of any kind a patient falls in a violent convulsion. The convulsions are usually tonic in character, but are interrupted with periods of almost complete relaxation. They involve all the muscles of the body and are brought on by the slightest sensory impulses. During the spasm the body is rigid, usually arched backwards in the position of opisthotonos, the arms flexed, the face drawn into the *risus sardonicus.* Consciousness is not affected except as the result of the asphyxiation. During the period of convulsion the muscles of the chest are so firmly fixed that respiration is impossible and death may occur as the result of asphyxiation. In some cases, however, the fatal termination may be deferred for some hours and finally be the result of exhaustion. The ordinarily fatal dose probably lies between one-half and one grain, although much larger quantities may be recovered from under proper treatment.

In the *treatment* of strychnine poisoning it is to be remembered that the convulsions are of reflex origin and therefore all manipulations which are capable of furnishing the sensory stimulus must be sedulously avoided. For this reason no attempt should be made to empty the stomach; death has occurred during a convulsion brought on by the effort to pass a stomach tube. As a chemical antidote potassium permanganate is probably to be preferred, although Fantus (*J. A. M. A.,* 1915, lxiv) has reported favorable results in the lower animals from the use of Lloyd's reagent (silicated earth), and compound solution of iodine or tannic acid are also of value. The most important therapeutic measure is the control of the convulsions. For this purpose chloroform is probably the most efficient remedy. This drug should be administered to the stage of surgical anesthesia, after which chloral hydrate and potassium bromide may be given to continue the sedative effect. Amyl nitrite is also a useful agent because of the rapidity of its action; during the height of the convulsion, when there is no respiration, 3 to 5 minims may be given hypodermically.

In an investigation of the members of the pyridine series of bases by C. Greville Williams and W. H. Waters (*Proc. Roy. Soc.,* xxxii, p. 162, 1881), they found that β lutidine (dimethyl-pyridine, C_7H_9N) was antagonistic to strychnine and an apparent antidote. When injected into frogs already under the influence of strychnine, it arrested the convulsions; or if given first and then followed by a fatal dose of strychnine, it prevented the appearance of the tetanus. (Blyth, *Poisons, their Effects and Detection,* 1884, p. 319.)

Dose, one-sixtieth to one-fifteenth of a grain (0.0011–0.004 Gm.).

Off. Prep.—Syrupus Ferri Phosphatis cum Quinina et Strychnina, *Br.;* Elixir Ferri Pyrophosphatis, Quininæ et Strychninæ, *N. F.;* Liquor Hypophosphitum Compositus, *N. F.;* Elixir Pepsini, Bismuthi et Strychninæ, *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ, *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arseni Fortiores, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arseni Mites, *N. F.;* Pilulæ Laxativæ Compositæ, *N. F.;* Syrupus Ferri, Quininæ et Strychninæ Phosphatum, *N. F.;* Syrupus Hypophosphitum Compositus, *N. F.*

STRYCHNINÆ HYDROCHLORIDUM. Br.

STRYCHNINE HYDROCHLORIDE

"Strychnine Hydrochloride, $C_{21}H_{22}N_2O_2,HCl,2H_2O$, is the hydrochloride of the alkaloid strychnine." *Br.*

Strychninum Hydrochloricum; Hydrochlorate of Strychnine, *Br.*, 1885; Chlorhydrate de Strychnine, *Fr.;* Strychninhydrochlorid, Salzsaures Strychnin, *G.*

This salt of strychnine was made official for the first time in the Br. Ph. 1898; it is used in making *Liquor Strychninæ Hydrochloridi.* It is described as in "small, colorless, prismatic crystals. Soluble in 60 parts of *water.* Aqueous solution neutral to *litmus;* taste intensely bitter. Loses from 7 to 9 per cent. of its weight when dried at 110° C. Responds to the tests enumerated under 'Strychnina,' and yields the *reactions* characteristic of chlorides. No appreciable ash." *Br.*

In its physiological and therapeutic action, strychnine hydrochloride is equivalent to strychnine.

Dose, one-sixtieth to one-fifteenth of a grain (0.0011–0.004 Gm.).

Off. Prep.—Injectio Strychninæ Hypodermica, *Br.;* Liquor Strychninæ Hydrochloridi, *Br.*

STRYCHNINÆ NITRAS. U. S.

STRYCHNINE NITRATE Strych. Nit.

"The nitrate [$C_{21}H_{22}O_2N_2.HNO_3$] of an alkaloid obtained chiefly from nux vomica." *U. S.*

Azotate de Strychnine, Nitrate de Strychnine, *Fr.;* Strychninum nitricum, *P. G.;* Strychninnitrat, Salpetersaures Strychnin, *G.;* Nitrato di stricnina, *It.*

Preparation.—This salt may be made by dissolving a sufficient quantity of the alkaloid strychnine in diluted nitric acid until it is neutralized, evaporating the solution and crystallizing the strychnine nitrate.

Description and Physical Properties.—"Colorless, glistening needles or a white, crystalline powder. It is odorless and is stable in the air. *Caution—Strychnine Nitrate is extremely poisonous.* One Gm. of Strychnine Nitrate is soluble in 45 cc. of water, 150 cc. of alcohol, 50 cc. of glycerin, and in 105 cc. of chloroform, at 25° C. One Gm. is soluble in 10 cc. of boiling water and in 80 cc. of alcohol at 60° C. It is insoluble in ether.

"An aqueous solution of Strychnine Nitrate is lævorotatory. Dissolve about 0.05 Gm. of Strychnine Nitrate in 5 cc. of distilled water, add a few drops of ammonia T.S., and extract the liberated strychnine with 5 cc. of chloroform. Evaporate the chloroform to dryness on a water bath, cool, dissolve the residue in 2 cc. of sulphuric acid and add a fragment of potassium dichromate. On gently agitating the mixture, a blue color is momentarily produced, changing to violet, then to purplish-red, and finally to orange or yellow. An aqueous solution of the salt, when superimposed in a test tube, upon diphenylamine T.S., develops a blue color at the zone of contact. Strychnine Nitrate, heated with hydrochloric acid, produces a bright red color.

"A solution of 0.5 Gm. of Strychnine Nitrate in 25 cc. of distilled water requires not more than 0.5 cc. of fiftieth-normal sodium hydroxide for neutralization, using one drop of methyl red T.S. as indicator. Ash: not more than 0.1 per cent. A solution of 0.1 Gm. of Strychnine Nitrate in 5 cc. of sulphuric acid is not darker than pale yellow (*readily carbonizable substances*). The addition of 5 drops of silver nitrate T.S. to 20 cc. of an aqueous solution of Strychnine Nitrate (1 in 100), acidulated with 2 drops of diluted nitric acid, does not produce an opalescence at once (*chloride*), and no immediate turbidity is produced in 20 cc. of a similar solution by the addition of 5 drops of barium nitrate T.S. (*sulphate*). One cc. of a mixture of equal volumes of nitric acid and distilled water, added to about 0.1 Gm. of Strychnine Nitrate, may produce a yellow, but not a red or reddish color (*brucine*).

"Preserve in well-closed containers, protected from light." *U. S.*

Uses.—Strychnine nitrate has no advantage over the other soluble salts of strychnine.

Dose, one-sixtieth to one-fifteenth of a grain (0.0011–0.004 Gm.).

Off. Prep.—Syrupus Phosphatum cum Quinina et Strychnina, *N. F.;* Elixir Glycerophosphatum Compositum, *N. F.*

STRYCHNINÆ SULPHAS. U. S.

STRYCHNINE SULPHATE Strych. Sulph.

"The sulphate [$(C_{21}H_{22}O_2N_2)_2.H_2SO_4.5H_2O$] of an alkaloid obtained chiefly from nux vomica." *U. S.*

Strychniæ Sulphas, *U. S.* 1870; Strychninum Sulphuricum, *Fr. Cod.;* Sulfate de Strychnine, *Fr.;* Schwefelsaures Strychnin, Strychninsulfat, *G.;* Sulfato de estricnina, *Sp.*

Description and Physical Properties.—"Colorless or white crystals, or a white, crystalline powder. It is odorless and is efflorescent in dry air. *Caution—Strychnine Sulphate is extremely poisonous.* One Gm. of Strychnine Sulphate is soluble in 35 cc. of water, in 81 cc. alcohol, and in 220 cc. of chloroform, at 25° C. One Gm. is soluble in 7 cc. of boiling water and in 26 cc. of alcohol at 60° C. It is freely soluble in glycerin but insoluble in ether.

"An aqueous solution of Strychnine Sulphate is lævorotatory. Add a fragment of potassium dichromate to a solution of 0.1 Gm. of Strychnine Sulphate in 2 cc. of sulphuric acid. A deep blue color is momentarily produced, changing to deep violet, then to purplish red, cherry-red, and finally to orange or yellow. Sulphuric Acid containing 1 per cent. of ammonium vanadate produces with Strychnine Sulphate a deep violet-blue color, changing to a deep purple and finally to a cherry-red." *U. S.*

For information concerning the chemistry and uses of this salt, see *Strychnina.*

Strychnine Sulphate is incompatible with the ordinary alkaloidal reagents, also with sodium cacodylate, with sodium glycerophosphate, and with the iodides or bromides.

Dose, one-sixtieth to one-fifteenth of a grain (0.0011–0.004 Gm.).

Off. Prep.—Elixir Cinchonæ Alkaloidorum, Ferri, Bismuthi, et Strychninæ, *N. F.;* Elixir Ferri, Quininæ et Strychninæ, *N. F.*

STYRAX. U. S. (Br.)

STORAX [Liquid Storax]

"Storax is a balsam obtained from the trunk of *Liquidambar orientalis,* Miller, known in commerce as Levant Storax, or of *Liquidambar styraciflua* Linné, known in commerce as American Storax (Fam. *Hamamelidaceæ*)." *U. S.* "Prepared Storax is a viscid balsam obtained from the wounded trunk of Liquidambar orientalis, *Mill.,* purified by solution in alcohol, filtration, and evaporation of the solvent." *Br.*

Styrax Præparatus, *Br.;* Prepared Storax; Styrax Liquidus, Balsamum Storacis, Balsamum Styracis, Balsamum Styrax Liquidus; Styrax liquide, *Fr.;* Styrax, *P. G.;* Storax, Flüssiger Storax, *G.;* Storace liquido, *It.;* Estoraque liquido, *Sp.*

All species of the genus *Liquidambar* as well as those of a related genus, *Altingia,* yield *storax.* The product most valued, however, is that obtained from *L. orientalis* Miller.

The *oriental sweet-gum* (*Liquidambar orientalis*) is a tree from twenty to forty feet high. Its leaves are palmately 5-divided, serrate, perfectly smooth, bright green and shining on the upper and pale on the under surface. The flowers occur in globular, yellowish heads and its fruits are spherical heads of beaked capsules. The tree is a native of Asia Minor, in the southwestern parts of which it forms large forests.

The *L. Styraciflua,* commonly known as the *gum tree* (*Sweet Gum, Alligator Tree, Bilsted*), is one of our most beautiful native trees. It is found along the whole Atlantic coast from Connecticut southward to Central America. When full grown the tree reaches a height of 100 or sometimes even 150 feet. The flowers are apetalous and usually monœcious, the fertile ones being arranged in globular heads and the staminate flowers in conical clusters consisting of numerous small greenish heads. The leaves are palmately 5- to 7-lobed, the lobes being acuminate and finely serrate, star-shaped. There are two varieties besides the type species. The *L. Styraciflua Mexicana* has its leaves 3-lobed instead of 5- to 7-lobed as is common in the northern variety, and in the *L. Styraciflua macrophylla* of Central America the leaves are much larger than the type. The wood is hard and close-grained, of a reddish brown color. The exudate apparently was used by the aboriginal inhabitants of the continent; it was exported to Spain in large quantities in the 16th century for use both as a perfume and as a vulnerary. The resin which is commonly known as *liquidambar* or *copal balsam* or *copalm,* collects naturally under the bark in old trees, being rarely found in those less than 100 years old. Its use was revived during the scarcity of the oriental variety caused by the World War.

Although the sweet gum tree is of wide distribution, at the present time the American Storax is not produced in commercial quantities except in Honduras.

According to the researches of Moeller, storax is a pathological rather than a physiological product; when the young wood is injured secretion reservoirs are formed in which the storax is produced. (*O. Z.,* 1.) In collecting the drug the bark is first heavily bruised, so as to injure the cambium. Injury to the cambium stimulates the formation of numerous reservoirs or ducts in which the balsam is secreted and from which it seeps into the injured bark. After a time the outer bark is removed and the inner bark is scraped off. According to Maltass, this inner bark is first pressed cold in horse-hair bags, after which hot water is thrown over the bags and they are again pressed. Lieutenant Campbell states that the inner bark is first boiled with water, and, a portion of the balsam which rises having been skimmed off, is then pressed so as to extract the remainder. The residuary bark, after expression, is dried in the sun, and employed in various parts of Turkey for fumigation. It is the article formerly known in commerce as *Storax bark* or *Cortex Thymiamatis.* The formerly known "*Styrax calamitus*" consisted of coarsely ground *Cortex Thymiamatis* mixed with storax. The balsam is sent in casks to Constantinople, Smyrna, and other ports of the Levant.

American storax—sometimes known as *Copalm balsam*—varies in consistency from that of thin honey to a soft solid. It is more or less transparent, of a yellowish color, of a peculiar, agreeable, balsamic odor, and a bitter, warm, and acrid taste. By cold it becomes thicker and less transparent. It concretes also by time, assuming a darker color. It is sometimes collected in the form of tears, produced by the spontaneous concretion of the exuded juice. According to Jordan (*J. I. E. C.,* August, 1917), the resin of American storax averages higher in cinnamic acid than does the oriental variety. (See also Spokes, *J. A. Ph. A.*, 1920, ix, 1055.)

The *L. formosana* Hance also produces a resin resembling storax which has been analyzed by Tsuchihashi and Qasaki (*J. Soc. Chem. Ind.*, 1919, xxxviii, 646a). *L. Altingia* Bl. (*Altingia excelsa* Noronha), a tree which inhabits a very wide region in Southern Asia, yields a storax-like substance varying in color from white to red, sometimes called *Malay Storax* or *Rasamala Resin.* According to Tschirch and van Itallie, it differs from storax in the presence of benzoic and cinnamic aldehydes, the absence of ether and the small quantities of cinnamic acid in it. *L. storesin* is said also to be known in Eastern markets.

For account of the methods of collecting American storax see *Ph. Rund,* 1895, 57 and Watermyer, *Amer. Perf. and Essent. Oil Review,* July, 1919; Mahood and Gerry, *D. C.*, 1921, lxv, p. 3.

Description and Physical Properties.—" A semi-liquid, grayish to grayish-brown, sticky, opaque mass, depositing on standing a heavy dark brown layer (Levant Storax); or a semi-solid, sometimes a solid mass, softened by gently warming (American Storax). Storax is transparent in thin layers, has a characteristic odor and taste, and is heavier than water. Storax is insoluble in water, but soluble, usually incompletely, in an equal weight of warm alcohol. It is also soluble in acetone, carbon disulphide, and ether, some insoluble residue usually remaining.

" To about 0.5 Gm. of the cinnamic acid obtained in the assay add 5 cc. of diluted sulphuric acid, heat, and add potassium permanganate T.S.: the odor of benzaldehyde is evolved. A portion of the acid recrystallized from hot water melts between 134° and 135° C. Dry about 2 Gm. of well-mixed Storax, accurately weighed, for two hours at 100° C.: the loss in weight does not exceed 20 per cent. Dissolve about 10 Gm. of well-mixed Storax, accurately weighed, in 40 cc. of hot alcohol, filter through counterbalanced filters or a Gooch crucible, and wash the residue with small portions of hot alcohol until the washings are colorless or very nearly so: the residue after drying at 100° C. does not exceed 5 per cent. Evaporate the combined alcoholic filtrate and washings at a temperature not exceeding 60° C., and dry the residue for one hour at 100° C.: a yellow to brown residue of purified Storax remains, corresponding to not less than 70 per cent. of the weight of the Storax taken. The purified Storax thus obtained complies with the following tests: Dissolve about 1 Gm. of the purified Storax, accurately weighed, in 50 cc. of neutralized alcohol, add 0.5 cc. of phenolphthalein T.S., and titrate with half-normal sodium hydroxide: the acid number is from 56 to 85 for Levant Storax and from 38 to 85 for American Storax. Place about 2 Gm. of the purified Storax, accurately weighed, in a 250 cc. flask, mix with 50 cc. of purified petroleum benzin, add 25 cc. of half-normal alcoholic potassium hydroxide, and allow the mixture to stand twenty-four hours with frequent agitation. Then add 0.5 cc. of phenolphthalein T.S. and titrate the excess of alkali with half-normal hydrochloric acid. The saponification value thus obtained is not less than 160 and not more than 200.

" Boil about 2 Gm. of the purified Storax, accurately weighed, with 25 cc. of half-normal alcoholic potassium hydroxide for one hour under a reflux condenser. Neutralize with half-normal sulphuric acid, using 5 drops of phenolphthalein T.S. as indicator, and evaporate the alcohol on a water bath. Dissolve the residue in 50 cc. of distilled water and shake the solution with 20 cc. of ether. Shake the separated ether with 5 cc. of distilled water, add the washings to the aqueous solution, and reject the ether extract. Add to the aqueous solution 10 cc. of diluted sulphuric acid and shake with four successive portions of 20 cc. each of ether. Wash the combined extract with 5 cc. of distilled water, rejecting the water washings, transfer to a flask and distil off the ether. Add to the residue 100 cc. of distilled water, and boil vigorously for fifteen minutes under a reflux condenser. Filter while hot and allow the filtrate to cool to about 25° C.: white crystals of cinnamic acid separate. Filter the cinnamic acid on a Gooch crucible, applying a vacuum towards the end to drain the crystals completely. Repeat the extraction of the residue twice by boiling each time under a reflux condenser, as before described, with the filtrate from the preceding crystallization, and collect the additional cinnamic acid in the same crucible. Finally wash the cinnamic acid with two 10 cc. portions of ice cold water, dry at 80° C., and weigh. The weight of the cinnamic acid thus obtained corresponds to not less than 25 per cent. of the purified Storax taken." *U. S.*

" Brownish-yellow, viscous, transparent in thin layers. Entirely soluble in *alcohol* (90 per cent.) and in *ether.* Odor and taste agreeable and balsamic. Boiled with *solution of potassium chromate* and *sulphuric acid* it evolves an odor of benzaldehyde. Loses not more than 5 per cent. of its weight when heated in a thin layer on a water-bath for one hour. *Acid value* not less than 60 or more than 90; *ester value* not less than 100 or more than 146. Yields not less than 20 per cent. by weight of cinnamic acid when tested by the following process:—Dissolve 2.5 grammes of the Storax in 25 millilitres of *N/2 alcoholic solution of potassium hydroxide,* boil for one hour under a reflux condenser, neutralize with *N/2 solution of sulphuric acid,* remove the alcohol by evaporation, and dissolve the residue in 50 millilitres of *water. Shake* this aqueous solution with 20 millilitres of *ether;* after separation remove the ethereal layer, wash it with 5 millilitres of *water* and add the washings to the aqueous solution, rejecting the ethereal liquid. Acidify the aqueous solution with *diluted sulphuric acid* and shake it with four successive portions, each of 20 millilitres of *ether*. Mix the ethereal solutions, wash with a few millilitres of *water*, transfer to a flask and distil off the ether. To the residue add 100 millilitres of *water* and boil vigorously for fifteen minutes under a reflux condenser. Filter the solution while hot, cool to 15.5° C., and collect on a tared filter the crystals of cinnamic acid that have separated. Repeat the extraction of the residue with the filtrate at least three times, or until no more cinnamic acid is removed. Press the filter paper and crystals between blotting paper, dry in a desiccator over *sulphuric acid*, and weigh. Add to the weight of the crystals so ascertained 0.03 gramme (representing the average amount of cinnamic acid remaining dissolved in the aqueous liquid). The total weight is not less than 0.5 gramme." *Br.*

Storax melts with a moderate heat, and, when the temperature is raised, takes fire and burns with a white flame, leaving a light, spongy, carbonaceous residue. It imparts its odor to water, which it renders yellow and milky. Its active constituents are dissolved by alcohol and ether. Neumann obtained from 480 grains of storax 120 of aqueous extract, and from an equal quantity 360 grains of alcoholic extract. Containing volatile oil and resin, and yielding benzoic or cinnamic acid by distillation, it is entitled to rank as a balsam.

Both the Oriental and the American storax are often adulterated with turpentine, Burgundy pitch, castor oil or storax from which the cinnamic acid has been extracted. Such adulterated drug will fail to meet the official requirements especially the cinnamic acid test.

Constituents.—The most abundant constituent of storax is probably *storesin*, $C_{36}H_{55}(OH)_3$, discovered in 1877 by W. von Miller. This is present in two forms, designated respectively *alpha* and *beta*, both free and in the form of a cinnamic ester. These together make up from one-third to one-half of the resin. Storesin is an amorphous substance, melting at 168° C., readily soluble in petroleum benzin. *Cinnamic acid* both in the free state and in the form of esters constitutes an important part of the drug. Free cinnamic acid ranges from 5 to 15 per cent., but Löwe has reported a yield of as much as 23 per cent. Of the cinnamic esters, *cinnamyl cinnamate*, or *styracin*, $C_9H_7O_2.C_9H_9$, is present in the proportion of 5 to 10 per cent. It can be removed by ether, benzene, or alcohol after the separation from the resin of the cinnamic acid; it is insoluble in water, and volatile only in superheated steam. It crystallizes in tufts of long rectangular prisms, which melt at 38° C., but frequently do not solidify readily. By concentrated solution of potassium hydroxide, it is resolved into a cinnamate and cinnamic alcohol (*styrone*), $C_9H_{10}O$, which latter is not present in liquid storax. Of the other cinnamic esters the most important is *phenylpropyl cinnamate* which constitutes some 10 per cent. of the drug. There are present also small amounts of ethyl cinnamate and benzyl cinnamate. There is further found in liquid storax a hydrocarbon, C_8H_8, which exists in the resin as a liquid, and also in a polymeric form as a solid. The former, called *styrol, styrene*, or *cinnamene*, has a sp. gr. of 0.924, and a boiling point of 146° C. It is a colorless, mobile liquid, possessing the odor and burning taste of liquid storax. It has been formed synthetically, being *phenylethylene*, $C_6H_5.CH = CH_2$. When heated it polymerizes into the colorless, transparent solid, *metastyrol*, which, unlike styrol, is not soluble in alcohol or in ether. Lastly, there has been found in liquid storax, about 0.4 per cent. of a pleasant-smelling lævo-rotatory oil of the formula $C_{10}H_{16}O$, and traces of vanillin. For analyses of storax see Tschirch and Von Itallie (*A. Pharm.*, 1901, ccxxxix, p. 506) and Spokes (*J. A. Ph. A.*, 1920, ix, p. 1055).

Uses.—Styrax is a stimulating expectorant and feeble antiseptic, which was at one time used in various *pulmonic catarrhs*, also in *gonorrhea* and *leucorrhea*, but at present is very seldom used except as a constituent of the compound tincture of benzoin. Externally, mixed with two or three parts of olive oil, liquid storax was found by H. Schultze, of Magdeburg, to be very effective as a local remedy in scabies. The bark of the sweet gum tree has been used in the Southern and Western States in *diarrhea* and *dysentery*, especially in children. It is taken in the form of syrup, which may be prepared from the bark in the same manner as the syrup of wild cherry bark, according to the U. S. Pharmacopœia. The *dose* is a fluidounce (30 cc.) for an adult, repeated after each stool.

Dose, ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Tinctura Benzoini Composita, *U. S., Br.*

SUCCI

JUICES

Sucs végétaux, *Fr.;* **Kraütersäfte Pflanzensäfte,** *G.;* **Zumos,** *Sp.*

Though introduced to professional notice by Squire in the year 1835, and subsequently used by many practitioners, the juices were recognized but once by the U. S. Pharmacopœia (1870). They consist of the expressed juices of fresh plants, preserved by the addition of one-third of their bulk of alcohol. Considering the great inequality in strength, and, of course, the uncertainty in operation, of fresh juices themselves varying according to the soil, climate, mode of cultivation, season, and the age of the plant, it may be questioned whether they merit the prominence which has been given them in the past.

SUCCUS LIMONIS. Br.

LEMON JUICE

"Lemon Juice is the freshly expressed juice of the ripe fruit of Citrus Medica, *Linn.,* var. β Limonum, *Hook. f.*" *Br.*

Limonis Succus, *U. S. P. VIII;* Succus Citri; Suc de Citron, *Fr.;* Citronensaft, Limonensaft, *G.;* Succo di limone, *It.;* Zumo de limon, *Sp.*

For account of the botany of lemons see under *Limonis Cortex.* Although so closely related botanically to the lemon, the *lime*—the juice of which was recognized by the N. F. IV under the title of *Succus Citri*—is medicinally very much inferior. For description of lime-juice, see *U. S. D.,* 20th ed., p. 1467.

The juice is the part for which the fruit is most esteemed. It is sharply acid, with a peculiar grateful flavor, and consists chiefly of water, citric acid (from 6 to 10 per cent.), gum and sugar (from 3 to 4 per cent.), and inorganic salts (2.28 per cent.). It sometimes has in it a little volatile oil, derived by pressure from the rind. It is "a slightly turbid, yellowish liquid. Taste sharply acid. Specific gravity 1.030 to 1.040. 20 millilitres require for neutralisation not less than 20 and not more than 25.7 millilitres of *N/1 solution of sodium hydroxide,* corresponding to a proportion of not less than 7 and not more than 9 grammes of citric acid in 100 millilitres. The residue obtained on evaporation, dried at 110° C., yields not more than 3 per cent. of ash. 100 millilitres of Lemon Juice are neutralised by about 11.4 grammes of Potassium Bicarbonate, by about 9.5 grammes of Sodium Bicarbonate, and by about 16.5 grammes of Sodium Carbonate." *Br.*

As lemons cannot always be obtained, the juice is often kept in a separate state, but, from its liability to spontaneous decomposition, it speedily becomes unfit for medicinal use, and, though various means have been resorted to for its preservation, it can never be made to retain for any length of time its original flavor unaltered. One of the most effectual methods of preserving the juice is to allow it to stand for a short time after expression, until a coagulable matter separates, then to filter, and introduce it into glass bottles, with a stratum of almond oil or other sweet oil upon its surface. It will keep still better if the bottles containing the filtered juice be permitted, before being closed, to stand for fifteen minutes in a vessel of boiling water. Any method of preserving lemon juice which involves the use of heat injures its medicinal virtues, as these depend upon the presence of an unstable vitamin (see Part II). Another mode is to add one-tenth of alcohol and to filter. The juice may also be preserved by concentrating it either by evaporation with a gentle heat, or by exposure to a freezing temperature, which congeals the aqueous portion and leaves the juice much stronger than before. When used, it may be diluted to the former strength, but though the acid properties are retained, the flavor of the juice will be found to have deteriorated. Bottled lemon juice is frequently found to be preserved with sulphur dioxide, which dissolves in it to form sulphurous acid. The presence of this preservative interferes with some of its pharmaceutical uses and such a product should not be employed for medicinal purposes. Lemon syrup is another form in which the juice is preserved.

The proportion of citric acid in lemon juice varies greatly, ranging from 4.5 to nearly 9 per cent. Huerre reports (*J. P. C.,* 1919, xx, 5) lemon juice to average in each 100 cc.: citric acid, 7 to 7.5 Gm.; malic acid, 0.4 to 0.6 Gm.; sucrose, 0.4 to 0.5 Gm.; invert sugar, 1.8 to 2.0 Gm.; pectin, 0.4 Gm.; and ash 1.6 to 1.8 Gm. Robins (*C. D.,* 1896, 742) found the average yield of citric acid taken from a year's receipts was 35.23 grains in a fluidounce.

Commercial lemon juice often contains salts of organic acids other than citric; salts of inorganic acids; and albuminous, mucilaginous, saccharine, and other indifferent bodies; spirit is frequently added as a preservative, and mineral acids are not uncommonly employed as adulterants, although sulphur dioxide is more commonly used for this purpose and its presence is usually declared upon the label.

The proportion of citric acid in lime juice was required by the N. F. IV to be not less than 5 Gm. nor more than 10 Gm. to each 100 cc.

Uses.—Lemon juice is refrigerant, and, properly diluted, forms a refreshing and agreeable beverage in *febrile affections.* It may be given with sweetened water in the shape of lemonade, or may be added to the mildly nutritive drinks, such as albumen water, barley water, etc., usually administered in *fevers.* Locally applied it acts as an astringent due to its content of citric acid and has been used with benefit in *pruritus of the scrotum,* and in *sunburn.*

One of the most beneficial applications of lemon juice is the prevention and cure of *scurvy.* This disease today is regarded as due to the absence from the food of a water soluble vitamin (see Part II). This antiscorbutic vitamin is found abundantly in lemon juice and in orange juice, but according to Shick, Hume and Skelton (*L. L.,* Nov. 30, 1918) in only small proportions in the juice of the lime. Although it is abundantly demonstrated that this essential foodstuff is not citric acid, Harden and Zilber (*L. L.,* Sept. 7, 1918) have shown that it is rapidly destroyed when the juice is neutralized. The antiscorbutic vitamin is also sensitive to heat; according to Bassett-Smith (*L. L.,* Nov. 13, 1920, 997) heating for three-quarters of an hour to 58° C. greatly diminishes its value, but it is not appreciably affected by 5 minutes' boiling.

Off. Prep.—Syrupus Limonis, *Br.;* Trochiscus Acidi Carbolici, *Br.*

SUCCUS POMORUM. N. F.

FRESH APPLE JUICE Suc. Pomor.

"The freshly expressed juice of sound, ripe, sour apples, the fruit of cultivated varieties of *Pyrus Malus* Linné (Fam. *Rosaceæ*)." *N. F.*

The apple tree (*Pyrus Malus* L., *Malus communis* DC., *Malus Malus* (L.) Br.) probably originated in Europe and western temperate Asia, but has been cultivated from the most ancient times in all civilized parts of the temperate zone; it is even stated to have been grown in ancient Switzerland in the time of the lake dwellers. It is a small tree rarely exceeding 30 or 40 feet in height with crooked spreading branches and a dark brown rough bark. It is prone to hybridize with related species and it is probable that some of the cultivated varieties are the results of crosses with other species. The flower is white or sometimes tinged with pink, with a faint but pleasant fragrance. The fruit is a large pome which varies greatly in size, color and flavor as the result of cultivation. For medicinal purposes those varieties should be chosen which are rather firm in texture and sour in taste.

The Siberian *crab-apple, P. prunifolia* Willd., is also cultivated. Its fruit is smaller and more acid than the ordinary apple. The American or wild crab apple, *P. coronaria* L., is also cultivated to a small extent.

The expressed juice, commonly called *cider,* is a clear pale yellow liquid with a pleasant acidulous aromatic flavor. It must be obtained at the time that the cider is pressed and from reliable sources or an article preserved with sodium benzoate will be furnished by the grocer who sells large quantities of cider thus treated, for beverage purposes. It is adulterated by watering, by adding sugar or glucose, and in some cases cider has been entirely sophisticated by means of artificial flavoring and sweetening materials.

The fruit is approximately 85 per cent. of water, contains considerable amounts of sugar (7 to 8 per cent.) mostly fructose, a small amount of nitrogenous matter and a peculiar acid called *malic,* usually about a little less than 1 per cent. Pure *malic acid* (*oxysuccinic*), $C_4H_6O_5$, occurs as colorless crystals soluble in water and with a rather pleasant sour taste melting at 100° C. The characteristic flavor of the apple is chiefly due to amyl valerate.

The bark of the apple tree contains besides quercetin, the glucoside phlorizin (see Part II).

Uses.—The bark of the apple tree was at one time used as a tonic and also as an antiperiodic, but is probably of no therapeutic importance. The juice of the fruit or cider affords a pleasant acidulous drink and is slightly laxative. It is official for the purpose of preparing *ferric malate* which is the active ingredient of the ferrated extract of apples. *Iron malate* occurs in the form of brown hygroscopic scales soluble in either alcohol or water.

Off. Prep.—Extractum Ferri Pomatum, *N. F.*

SUCCUS SCOPARII. Br.

JUICE OF BROOM

Suc de Genet à Balais, *Fr.;* Besenginstersaft, *G.*

"Bruise fresh Broom Tops; press out the juice; to every three volumes of juice add one volume of Alcohol (90 per cent.); set aside for seven days; filter." *Br.*

For chemistry and therapeutic uses of this, see under *Scoparius.*

Dose, one to two fluidrachms (3.75–7.5 cc.).

SUCCUS TARAXACI. Br.

JUICE OF TARAXACUM

Suc de Pissenlit, *Fr.;* Löwenzahnwurzelsaft, Löwenzahnsaft, *G.*

"Bruise Taraxacum Root; press out the juice; to every three volumes of juice add one volume of Alcohol (90 per cent.); set aside for seven days; filter." *Br.*

Dose, two to four fluidrachms (8–15 cc.).

SUCROSUM. U. S. (Br.)

SUCROSE Sucros. [Saccharum U. S. P. IX, Sugar]

"A sugar [$C_{12}H_{22}O_{11}$] obtained from *Saccharum officinarum* Linné (Fam. *Gramineæ*) and other sources." *U. S.* "Refined Sugar is a crystallised sugar, $C_{12}H_{22}O_{11}$, obtained from the juice of the sugar-cane, sugar-beet, and other plants." *Br.*

Saccharum Purificatum, *Br.;* Refined Sugar; Cane Sugar. Saccharose; Saccharum Album; Sucre blanc officinal, *Fr, Cod.;* Sucre de Canne, Sucre de Betterave, *Fr.;* Saccharum, *P. G.;* Weisser Zucker; Zucker, Rohrzucker, *G.;* Zucchero, *It.;* Azucar refinado, *Sp.*

The *sugar cane, Saccharum officinarum,* is a perennial herb possessing a jointed, succulent rhizome, from which arises several glaucous, jointed, solid stems, from an inch to two inches in diameter, from six to twelve feet high, and containing a white and juicy pith. The color of the stem is yellow, greenish yellow, purple, or striped. The joints are about three inches apart, and give origin to the leaves, which embrace the stem at their base. The leaves are three or four feet long and about an inch wide, flat, acuminate, longitudinally striated, furnished with a white midrib, glabrous, finely dentate, and of a green color inclining to yellow. The flowers are pinkish, surrounded by a long silky down, and disposed in a large, terminal, nearly pyramidal panicle, composed of subdivided spikes, and two or three feet in length. The plant has a general resemblance to Indian corn. Four varieties are mentioned: 1, the *common,* with a yellow stem; 2, the *purple,* with a purple stem and richer juice; 3, the *gigantic,* with a very large light-colored stem; and 4, the *Otaheitan,* which was introduced into the West Indies from the island of Tahiti (Otaheite) by Bougainville and Bligh, and is distinguished by its greater height, the longer intervals between its joints, and the greater length of the hairs which surround the flowers.

Sugar cane was originally indigenous in all probability to India. It has been cultivated for its saccharine juice since remotest antiquity. At the present time it is cultivated in all tropical and sub-tropical countries. It was introduced into the West Indies by the Spaniards early in the 16th century, and these islands, especially Cuba, are now the world's largest producers.

The sugar cane is cultivated by cuttings, which are planted in rows, and which, by giving rise to successive shoots, furnish five or six crops before the plants require to be removed. At the end of a year or more the plant flowers, but before this takes place the canes are richest in sugar and are cut down. The quantity of sugar which they yield is variable. According to Avequin of New Orleans, the proportion of cane sugar in the recent stalk is about 10 per cent.; of uncrystallizable sugar from 3½ to 4 per cent. Cane juice is said to contain 17 per cent. of crystallizable sugar, though not more than 13 per cent. is extracted in practice.

The *Sugar beet* (*Beta vulgaris* L.) is extensively grown in temperate zones as a source of sugar, or saccharose. It is extensively grown in Europe and the western United States. The plant is a biennial resembling the ordinary garden beet. The varieties yielding sugar produce rather small tuberous roots, which are either yellowish or whitish internally. They yield 10 to 18 per cent. of sucrose, depending upon selection and cultivation.

Sucrose is also largely produced in Canada and the northern parts of the United States from the sap of the sugar maple (*Acer saccharinum*). This variety is never refined or purified as it owes its value as a confection and flavor to the impurities naturally present in the crude product. Cane sugar may be obtained from cornstalks, and from the *Chinese sugar cane,* or *Sorghum saccharatum,* which latter source for a time assumed some importance in Kansas and the Northwest. In India, sugar is made from the sap of different species of palm. Crude *palm sugar* is called *jaggery.*

Preparation and Purification.—The canes, when ripe, are cut down close to the earth, topped, and stripped of their leaves, and then crushed between a series of horizontally placed iron rollers in a mill, or they are cut in thin transverse slices and the juice extracted by diffusion with warm water. The juice, constituting 90 per cent. of the cane, though much less is actually obtained, is of a pale greenish color, sweet taste, and balsamic odor, and has a sp. gr. varying from 1.033 to 1.106. It usually contains from 15 to 20 per cent. of sucrose. As it runs out it is received in suitable vessels, and, being quickly removed, is immediately mixed with lime, in the form of milk of lime, in the proportion of about 1 part of the earth to 800 parts of the juice, and heated in a boiler to 60° C. The exact proportion of the lime cannot be determined, as the juice varies in quality in different seasons; but the manufacturer should aim at leaving the juice still slightly acid. The albuminous matter rises to the top, and forms a thick scum, from underneath which the liquid is drawn off by a cock into a copper boiler, where it is concentrated by heat, the scum being carefully skimmed off as it forms. When sufficiently concentrated, the juice is transferred to shallow vessels called coolers, from which, when it assumes a granular aspect, it is drawn off into wooden vessels with perforated bottoms, the holes in which are temporarily plugged. At the end of twenty-four hours the liquid is strongly agitated with wooden stirrers, in order to accelerate the granulation of the sugar, which is completed in six hours. The stoppers are now removed, and the syrup is allowed to drain off from the sugar. The substance obtained by the evaporation of cane juice is known as *brown sugar* or *muscovado;* it is a yellowish, crystalline and somewhat moist substance, which is decolorized and purified to form granulated sugar. The syrup, by a new evaporation, furnishes an additional portion of sugar, and the liquid which finally remains, incapable of yielding more sugar with advantage, is called *molasses.* Sugar produced in this way is called "open pan" sugar. It is now almost completely displaced by "vacuum pan" sugar.

In the production of raw sugars by the vacuum pan process, the juice, after "defecation" with lime and removal of excess of lime by carbonic acid gas, is run through large filters of bone black, and then into a vacuum pan for concentration. The vacuum pan is a large evaporating pan, closed above by a dome-like top, which connects with an exhausting steam pump, so that the liquid can be concentrated under very reduced pressure. The heat is supplied by coils of steam pipes which run through the interior of the pan. The saccharine juice is evaporated in this until it begins to crystallize, and even after this fresh portions are added, so that the crystals already formed grow by accretion of fresh material. After the crystallization is complete, the warm mixture of crystals and syrup is run into "centrifugals," to which a rapid motion of revolution is given, and the crystals so drained and dried.

There is no doubt that a large proportion of the sugar is lost in the ordinary process of manufacture. Nearly 20 per cent. is lost in even the most efficient of the processes. Melsens, of Brussels, proposed a process, which consists in the use of calcium bisulphite. This salt is alleged to act as an antiseptic, preventing the operation of any ferment; as an absorber of oxygen, opposing the action of that gas on the juice; as a clarifier, rendering insoluble at 100° C. all coagulable matters; as a bleacher of pre-existing coloring matters, and a preventative of the formation of new ones; and, lastly, as a substance furnishing a base to neutralize hurtful acids, which unite with the lime, displacing the weaker sulphurous acid. This process is now largely used, and calcium bisulphite is used in British Guiana and other sugar-producing countries in immense quantities. Emil Pfeiffer proposed another refining process, which consists in the use of acid calcium phosphate, an agent previously recommended by Brande. Reynoso considered alumina the best defecating agent, having succeeded by means of it in throwing down almost all impurities most hurtful. He adds the acid aluminum phosphate to the cane juice, and decomposes this with lime, by which the calcium phosphate is produced and alumina separated, and all these, with some lime in excess, cause the elimination of coloring and nitrogenous matters, so that there remain in the liquid only some of the salts which normally accompany the sugar in the juice.

The refining of raw sugar forms a distinct branch of business, and the methods pursued have undergone many improvements. The sugar which contains from 88 to 90 per cent. of sucrose is first "melted"—that is, dissolved in hot water—and then sometimes clarified by heating it with bullock's blood, although sulphites, phosphates, and other defecating agents referred to in preceding processes may be used. The clarified syrup is then strained through cloth filters, whereby it is rendered limpid. The clear straw colored syrup from the bag filters is then run into the char filters—that is, large percolators filled with freshly ignited bone black. In sugar refineries these are 25 or 30 feet in height and sometimes hold several thousand pounds of bone black each and some refineries have dozens of such units. The bone black may be reactivated several times by heating and is finally discarded and sold for fertilizing purposes. A bleaching compound known as *blankit* (*sodium hydrosulphite*) is sometimes used to spare the use of bone black filters. The syrup after filtration goes to the vacuum pans. By reduced pressure the syrup is made to boil at a lower temperature, and with a diminished contact of the air, and the loss of cane sugar by change into that which was uncrystallizable is in great measure avoided. Two, three, or even four vacuum pans may be coupled together so as to economize fuel, and the vapors arising from one made to heat the next, in which a more perfect vacuum exists, allowing of evaporation at still lower temperatures. Such a combination is called a double, triple, or quadruple effect apparatus.

At one time it was the custom to discontinue the decolorization process before an entirely white sugar was obtained, and then to add a small amount of ultamarine blue to overcome the yellow appearance of the granulated sugar. This process has practically been abandoned within recent years. The syrups of lowest quality are employed in forming inferior white sugar, from which a syrup finally drains containing so little cane sugar as not to repay the expense of extracting it. This constitutes *sugar-house molasses.* Good brown sugar, in the process of refining, yields over 75 or 80 per cent. of white sugar. A comprehensive historical article by C. A. Browne, on the development of the sugar industry is found in the *A. J. P.,* 1915, p. 10.

Commercial History.—*Cane sugar* was known to the ancients. It was originally obtained from India, where it was extracted from the sugar cane. About the period of the Crusades, the Venetians brought it to Europe; but at that time it was so scarce and costly as to be used exclusively as a medicine. Upon the discovery of the Cape of Good Hope and the maritime route to the East Indies, the commerce in sugar passed into the hands of the Portuguese. Subsequently the cultivation of the cane extended to Arabia, Egypt, Sicily, Spain, and the Canaries, and finally, upon the discovery of the New World, to America, where it was pursued with the greatest success, and continues to be so. In America it was produced most abundantly in the West Indies, which supplies also a part of the consumption of Europe. The Cuban production has grown rapidly in recent years, and is now over 3,000,000 tons annually. About an equal quantity is produced in Germany from beets. Considerable beet-sugar is also produced in the United States.

Classification of the Carbohydrates.—The term "sugars" is applied to a large number of carbohydrates. Emil Fischer has not only made numerous syntheses in this group, but has greatly widened our knowledge of the relations of the several sugars, permitting a more comprehensive classification than formerly. While no sugars are found in nature containing less than six atoms of carbon, synthetic compounds are formed belonging in the first, or monosaccharide, class which contain three, four, and five atoms of carbon, as well as others containing seven, eight, and nine atoms of carbon. The nomenclature of the sugars is based upon the fact that simple sugar molecules are distinguished by the Greek prefixes tri, tetra, penta, etc., indicating the number of carbon atoms in the molecule; thus, glycerose, $C_3H_6O_3$, is a triose, while dextrose, $C_6H_{12}O_6$, is a hexose. These are called *monosaccharoses, monosaccharides* or *monoses*. These simple sugar molecules are taken as the basis for a secondary classification based upon the number of monoses or simple sugar molecules represented in the molecular structure of the more complex members of the group. The Greek numerical prefixes are also used to distinguish these; thus, dextrose, $C_6H_{12}O_6$, is a monosaccharide, while sucrose, $C_{12}H_{22}O_{11}$, is a disaccharide produced by the union of two monosaccharide molecules with the elimination of water. Of the simple sugars, members ranging from three to nine carbon atoms are known (trioses to nonoses), while of the broader groupings, monoses, dioses, trioses, monosaccharides, etc.), contain respectively one, two, or three of the simple sugar molecules, while polyoses or polysaccharides contain an indefinite or larger number of monoses. The classification given below is based on that of Tollens.

I. MONOSACCHARIDES.

Trioses.—Glycerose, $C_3H_6O_3$ (prepared from glycerin by oxidation).

Tetroses.—Erythrose, $C_4H_8O_4$ (prepared from erythrite by oxidation).

Pentoses.—Arabinose, $C_5H_{10}O_5$ (prepared by the action of dilute sulphuric acid upon lævorotatory gum arabic; xylose, $C_5H_{10}O_5$ (prepared by boiling beech wood and jute with dilute acids); rhamnose or isodulcite, $C_5H_9(CH_3)O_5$, methyl pentose (obtained in the decomposition of glucosides like quercitrin).

Hexoses.—Glucose or dextrose, $C_6H_{12}O_6$; fructose or levulose, $C_6H_{12}O_6$; mannose, $C_6H_{12}O_6$ (obtained by the careful oxidation of mannite); galactose, $C_6H_{12}O_6$. Floridose (obtained by the hydrolysis of certain algæ).

Heptoses.—$C_7H_{14}O_7$. Manno-heptose (obtained artificially from the corresponding mannose); gluco-heptose (obtained artificially from the corresponding glucose).

Octoses.—$C_8H_{16}O_8$. Manno-octose (prepared from the corresponding mannose); gluco-octose (prepared from the corresponding glucose).

Nonoses.—$C_9H_{18}O_9$. Manno-nonose (prepared from the corresponding mannose); glucononose (prepared from the corresponding glucose).

II. DISACCHARIDES AND TRISACCHARIDES.

Tribioses and tetrabioses are as yet unknown.

Pentabioses.—Arabinose, $C_{10}H_{18}O_9$ (has been prepared by the moderated action of dilute sulphuric acid upon arabic acid).

Hexabioses.—Cane Sugar, $C_{12}H_{22}O_{11}$; milk sugar, $C_{12}H_{22}O_{11}$; maltose, $C_{12}H_{22}O_{11}$; isomaltose, $C_{12}H_{22}O_{11}$; trehalose, $C_{12}H_{22}O_{11}$.

Hexatrioses.—Meletriose or raffinose, $C_{18}H_{32}O_{16}$; melezitose, $C_{18}H_{32}O_{16}$.

III. POLYSACCHARIDES.

(*a*) *Crystallizable polysaccharides.*—Gentianose, lactosin.

(*b*) *Uncrystallizable polysaccharides.*—Starches, lichnin, inulin, glycogen, dextrin, natural gums, pectin substances, cellulose, lignin, tunicin.

The *glucosides* are substances closely related to the carbohydrates. They are of frequent occurrence in plant tissues and are characterized by the fact that when heated with dilute acids or dilute alkalies or subjected to the action of certain enzymes, they decompose into a glucose and an alcohol, phenol, aldehyde or nitrogen compound; hence they are probably ethers or ethereal derivatives of the monoses. (See *Amygdalin, Salicin,* etc.)

Artificial glucosides have been prepared by Fischer (*B. Chem. G.,* 1893) by the interaction of a monose and an alcohol in the presence of a dehydrating agent. Glucosides contain only carbon, hydrogen and oxygen except in the case of the cyanogenetic glucosides such as amygdalin, in which the nitrogen splits off as hydrocyanic acid.

Sucrose, in a pure state, is a solid of a peculiar grateful taste, permanent in the air, phosphorescent by friction, and of the sp. gr. 1.6.

Description and Physical Properties.—"White, hard, dry crystals or blocks, or a white, crystalline powder. It is odorless, has a sweet taste, and is stable in the air. One Gm. of Sucrose is soluble in 0.5 cc. of water and in 170 cc. of alcohol, at 25° C. One Gm. is soluble in slightly more than 0.2 cc. of boiling water. It is insoluble in chloroform and in ether.

"The specific rotation $[\alpha]_D$ of Sucrose determined at 20° C. in an aqueous solution containing in each 100 cc. 26 Gm. of Sucrose, previously dried to constant weight at 105° C., and using a 200 mm. tube, is not less than $+65.9°$. An aqueous solution of Sucrose (1 in 20) is neutral to litmus paper. Ash: not more than 0.05 per cent. An aqueous solution of Sucrose (1 in 1) is colorless or at most only faintly yellow when viewed horizontally against a white background through a vertical cylinder of colorless glass having an inside diameter of about 25 mm. When kept in large, well-closed, and completely filled bottles, the solution deposits no sediment on prolonged standing (*insoluble salts, ultramarine or Prussian blue*). Its aqueous solution (1 in 10) is not affected by the addition of an equal volume of hydrogen sulphide T.S. (*heavy metals*). Ten cc. portions of the solution (1 in 10), remain clear for at least one minute after the addition of 1 cc. of silver nitrate T.S. (*chloride*) or of ammonium oxalate T.S. (*calcium*). A 5 Gm. portion of Sucrose shows no more *sulphate* than corresponds to 0.3 cc. of fiftieth-normal sulphuric acid. Dissolve 20 Gm. of Sucrose in enough distilled water to make 100 cc. and filter the solution if necessary. To 50 cc. of clear liquid contained in a 250 cc. beaker, add 50 cc. of alkaline cupric tartrate solution, heat the mixture at such a rate that approximately four minutes are required to bring it to the boiling point, and boil for exactly two minutes. Add 100 cc. of cold, recently boiled distilled water, and collect and weigh the precipitated cuprous oxide in the following manner: Prepare a Gooch crucible with an asbestos layer. Thoroughly wash the asbestos with distilled water, followed successively by 10 cc. of alcohol and 10 cc. of ether, dry at 100° C. for thirty minutes, and weigh the prepared crucible. Filter the precipitated cuprous oxide through the crucible thus prepared, thoroughly wash the residue on the filter with hot distilled water, then with 10 cc. of alcohol, and finally with 10 cc. of ether, and dry it at 100° C. The weight of the cuprous oxide does not exceed 0.155 Gm., corresponding to not more than 0.5 per cent. of invert sugar." *U. S.*

"Colorless and inodorous crystals, or in crystalline masses. Readily and completely soluble in half its weight of *water,* forming a clear, colorless and odorless syrup which does not develop an unpleasant odor when acidified with *hypophosphorous acid* and allowed to stand for twenty-four hours; the syrup, heated to about 82° C. with *solution of potassio-cupric tartrate,* does not yield more than a trace of a red or yellow precipitate (absence of glucose). Yields no *reactions* for barium, strontium, calcium, chlorides or sulphates. Ash not more than 0.05 per cent." *Br.*

Its solution, when thick and strong, is called *syrup;* when alcohol is mixed with this the sugar is gradually deposited in crystals. An aqueous solution of sugar, kept in a warm place, has the property of corroding iron, partially immersed in it, just above the line where the surface of the liquid touches the metal, and the solution itself becomes impregnated with ferrous oxide, and of a deep red-brown color. A similar effect is produced on lead, but zinc and copper are but slightly acted on. A solution of sugar possesses the property also of dissolving a large quantity of calcium hydroxide, forming a compound called *calcium saccharate.* When a concentrated syrup is gently heated, and spirit added to it, the liquid, on cooling, forms white semi-transparent crystals of hydrated sugar, having the shape of oblique, four-sided prisms, and called *rock candy.* This is the purest form of sucrose commercially obtainable. When heated to 185° C., it melts into a viscid, colorless liquid, which on being suddenly cooled forms a transparent mass, called *barley sugar.* At a higher temperature, between 204.4° and 215.5° C., it loses two molecules of water, and is converted into a black syrupy liquid which is official in the N. F. as *Caramel.* At a still higher temperature it yields combustible gases, carbon dioxide, empyreumatic oil, and acetic acid, and there remains about one-fourth of its weight of charcoal, which burns without residue. Sugar renders the fixed and volatile oils to a certain extent miscible with water, which is probably a colloidal suspension; such mixtures are called *oleosaccharures.* When in solution, it is not precipitated by lead subacetate, a negative property which distinguishes it from most other organic principles.

Cane sugar may be distinguished from grape sugar by the fact that it does not reduce alkaline copper tartrate (see official tests), nor basic bismuth nitrate. See the official test above.

Action of Acids and Alkalies.—The mineral acids act differently on cane sugar according as they are concentrated or dilute. Strong nitric acid, with the assistance of heat, converts it into oxalic acid. (See *Oxalic Acid.*) The same acid, when weak, converts it into *saccharic acid,* $(CHOH)_4(COOH)_2$, confounded by Scheele with malic acid. Concentrated sulphuric acid chars it. Diluted hydrochloric acid, when boiled with cane sugar, converts it into a solid, brown, gelatinous mass. Weak sulphuric acid, by a prolonged action at a high temperature, converts cane sugar, first into uncrystallizable invert sugar, afterwards into grape sugar, and finally into *ulmin* and *ulmic acid.* The inversion of cane sugar by dilute acids is one of the most characteristic phenomena and is utilized in its quantitative estimation and is a factor in the changes which take place in many pharmaceutical preparations. It is called inversion because the sugar before the change takes place is dextrorotatory while after the operation it is lævorotatory. The reaction is as follows:

$$\underset{\text{Sucrose}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Dextrose}}{C_6H_{12}O_6} + \underset{\text{Levulose}}{C_6H_{12}O_6}$$

The reason for the lævorotatory power is that levulose is more strongly lævorotatory than dextrose is dextrorotatory. The amount of acid that will produce the change is very small indeed. One drop of hydrochloric acid will invert 1 lb. of sucrose in a few minutes at the optimum inversion temperature which is 80° C.

Commercial invert sugar which is used in food products and sometimes as an adulterant of honey, is usually prepared by the use of citric acid as an inversion medium, four ounces of citric acid being sufficient for 500 lbs. of sucrose. The sucrose of course must be in solution, the best density being about 1.3

A proprietary form of invert sugar is on the market under the name of *nulomoline.* Invert sugar is sweeter than sucrose and is the cause of the cloying sweetness of some syrups and preserves in which inversion has been produced by the natural acidity of the constituents.

Cane sugar unites with the alkalies and some of the alkaline earths, forming definite combinations which render the sugar less liable to change. It also unites with lead monoxide. Boiled for a long time with aqueous solutions of potassium hydroxide, the liquid becomes brown, formic acid is produced, and two new acids are generated,—one brown or black and insoluble in water, called *melassic acid,* the other colorless and very soluble, named *glucic acid.* Alkalies and the alkaline earths are said to lessen the rotatory power of sugar in relation to polarized light, but the sugar recovers its power when the alkali is saturated. (*J. P. C.*, 4e sér., iv, 314.) The action of acids and alkalies on cane sugar explains the way in which lime acts in the manufacture and refining of sugar. The acids naturally existing in the saccharine juice have the effect of converting the cane sugar into invert sugar, by which a loss of the sucrose is sustained. The lime, by neutralizing these acids, prevents this change. An excess of lime, however, must be carefully avoided, as it injures the product of cane sugar in both quantity and quality. The change in sugar which precedes fermentation, namely, the conversion of sucrose into the uncrystallizable invert sugar, points to the necessity of operating on the juice before that process sets in, and hence the advantage of grinding canes immediately after they are cut, and boiling the juice at once.

Molasses, sometimes Latinized in prescriptions as *Syrupus Fuscus*, is of two kinds, the West India and sugar-house. *West India molasses* is a black thick liquid, of a peculiar odor and sweet empyreumatic taste. When mixed with water and with the skimmings of the vessels used in the manufacture of sugar, it forms a liquor which, when fermented and distilled, yields *rum*. *Sugar-house molasses, golden drips*, or *grocer's syrup* is thicker than the West India molasses, and has a different flavor; as found in commerce, it is sometimes adulterated with glucose. Its sp. gr. is about 1.4 and it contains about 75 per cent. of solid matter. Both kinds of molasses contain uncrystallizable sugar, more or less cane sugar which has escaped separation in the process of manufacture or refining, and gummy and coloring matter. *New Orleans molasses* was formerly the most largely used variety, but has practically disappeared from the market, owing to the changed conditions of manufacture.

Uses.—Although sugar is so important a foodstuff to-day, it does not seem to have been widely employed in Europe until the tenth or eleventh century. It was known much earlier to the European writers, such as Dioscorides, who lived in the first century, by whom it seems to have been regarded as a sort of natural curiosity. Its food value is very high, commercial cane sugar yielding more than 4 calories of energy per gramme. It is not, however, directly utilizable by the body cells, but must first be inverted into dextrose or levulose; this is true also of the other disaccharides such as lactose and maltose. The latter, however, do not hydrolize in the same way; lactose yields both dextrose and levulose, maltose only dextrose. This inversion is accomplished in the system probably in part by the hydrochloric acid of the gastric juice, but chiefly by a specific ferment which is found throughout the whole small intestines. It occurs with great rapidity so that the body can derive energy from ingested cane sugar almost as rapidly as it can be absorbed. So rapidly, indeed, is sugar absorbed from the intestinal tract that eating large quantities of it may overwhelm the inability of the liver to withdraw the sugar from the blood and lead to hyperglycemia and the appearance of glucose in the urine; a condition which is known as alimentary glycosuria. Glucose and levulose are directly assimilable and the body can derive nourishment from them even when injected hypodermically or intravenously.

Magnus (*M. M. W.*, 1913, p. 406) claims that sugar has valuable antiseptic properties and recommends it in the treatment of various forms of *wounds*. *Schuecking's solution* consists of 0.08 per cent. of common salt, 0.033 per cent. of sodium saccharate ($C_{12}H_{21}O_{11}Na$) and in some cases also 0.003 to 0.015 per cent. calcium mono-saccharate. It is used for intravenous injection instead of physiological salt solution in *circulatory failure* and is said to directly stimulate the heart. Busacca (*Arch. di Farmacol. Sper.*, 1921, xxxi) finds that sucrose increased the amplitude of contractions of the frog's heart and has used it intravenously with asserted benefit in various forms of *heart disease*.

Sugar is much used for the purposes of preserving organic substances. It is probable that it acts by producing rapid exosmose of the fluids of the fermentative organisms, its diluted solution being in fact prone itself to undergo fermentative change. All the different kinds of sugar susceptible of the alcoholic fermentation have this power. In pharmacy, sugar is employed to render oils miscible with water, to cover the taste of medicines, to give pharmaceutical preparations consistency, to preserve them from change, and to protect certain ferruginous preparations from oxidation. Accordingly, it enters into the composition of several mixtures, pills, and powders, of syrups and confections, and of all the troches. *Molasses* is used as an excipient for pills, and on account of its hygroscopic properties it prevents hardening.

SULPHONETHYLMETHANUM. U. S. (Br.)

SULPHONETHYLMETHANE Sulphonethylmeth.

"Diethylsulphon-methylethylmethane $[(CH_3)$-$(C_2H_5)C(SO_2C_2H_5)_2]$." *U. S.* "Methylsulphonal, or diethyl-sulphone-methyl-ethyl-methane, $C_8H_{18}S_2O_4$, is an oxidation product of the mercaptol resulting from the condensation of ethyl-methyl-ketone with ethyl-mercaptan." *Br.*

Methylsulphonal, *Br.*; Methylsulphonal; Trional; Trionalum, *Fr. Cod.*; Methylsulfonalum, *P. G.*; Methylsulfonal, *G.*

The *disulphone* group of narcotics, to which belong both this and sulphonal, were introduced into medicine by Baumann and Kast in 1888. Chemically they may be regarded as methane in which two of the hydrogen atoms are replaced by ethyl-sulphone radicals ($SO_2C_2H_5$), the other two hydrogens being substituted by either ethyl or methyl groups,—in the present example one ethyl and one methyl.

Sulphonethylmethane is made by passing dry hydrochloric acid gas to saturation through a mixture of ethyl mercaptan and methyl ethyl ketone, then oxidizing the condensation product (methyl-ethyl-ketone mercaptol) by treating it with a 5 per cent. solution of potassium permanganate; the compound is purified by repeated crystallization from its solutions in boiling water.

Description and Physical Properties.—"Colorless, lustrous, odorless, crystalline scales, having a bitter taste in aqueous solution. One Gm. of Sulphonethylmethane is soluble in 200 cc. of water at 125° C. It is more soluble in boiling water; soluble in alcohol and in ether.

"A saturated aqueous solution of Sulphonethylmethane is neutral to litmus paper. It melts between 74° and 76° C. When strongly heated, it is decomposed with the evolution of sulphur dioxide. Heat about 0.1 Gm. of Sulphonethylmethane with an equal weight of powdered charcoal in a dry test tube: the characteristic, unpleasant odor of mercaptan is evolved.

"Ash: not more than 0.05 per cent. Boil 2 Gm. of Sulphonethylmethane with 100 cc. of distilled water until solution is complete: no odor develops. Cool the solution, add sufficient distilled water to restore the volume to 100 cc., filter, and to 20 cc. of the filtrate add 0.05 cc. of tenth-normal potassium permanganate: the pink color does not disappear at once (*readily oxidizable substances*). To 10 cc. of the filtrate obtained in the preceding test add a few drops of silver nitrate T.S.: no turbidity is produced at once (*chloride*). A 50 cc. portion of the same filtrate shows no more *sulphate* than corresponds to 1 cc. of fiftieth-normal sulphuric acid.

"Preserve in well-closed containers." *U. S.*

"A white crystalline powder; taste slightly bitter. Soluble in 320 parts of *water,* somewhat more soluble in dilute *alcohol.* Melting point from 76° to 76.5° C. At a red heat it decomposes with evolution of sulphur dioxide. When heated with *anhydrous sodium acetate* hydrogen sulphide is liberated. When boiled with *water* no offensive odor is developed (absence of mercaptan and mercaptol). 100 millilitres of a cold saturated aqueous solution do not immediately decolorise 1 drop of an aqueous solution (1 in 1000) of *potassium permanganate* (limit of readily oxidisable substances). No appreciable ash." *Br.*

The name methylsulphonal certainly appears to be a misnomer, as the product differs from sulphonal by the substitution of an ethyl group for one of the two methyl groups of sulphonal.

Uses.—The action of trional is very similar to sulphonal (*q.v.*) except that it is somewhat more powerful and prompt.

There appears to be no recorded case of fatal acute poisoning by trional. Sixty grains (3.9 Gm.) are said to have produced hematoporphyrinuria, but one hundred and twenty grains (7.7 Gm.) have been recovered from without very serious symptoms. Although trional is less prone than is sulphonal to cause chronic poisoning, a number of cases have occurred.

Sulphonethylmethane is used in medicine solely as a somnifacient. In doses of from fifteen to twenty grains (1.0–1.3 Gm.) it usually causes sleep in from half to an hour without unpleasant after effects. It may be administered as a powder, stirred up in half a glass of water, or enclosed in a gelatin capsule.

Dose, ten to twenty grains (0.65–1.3 Gm.).

SULPHONMETHANUM. U. S. (Br.)

SULPHONMETHANE Sulphonmeth.

"Diethylsulphon-dimethylmethane [$(CH_3)_2C(SO_2C_2H_5)_2$]." *U. S.* "Sulphonal, or dimethyl-methane-diethyl-sulphone, $C_7H_{16}S_2O_4$, may be obtained by oxidising mercaptol." *Br.*

Sulphonal, *Br.;* Diethylsulphon-dimethyl-methane; Acétoné-diéthylsulfone, *Fr.;* Sulfonalum, *P. G.;* Sulfonal, *G.* Sulfonale, *It.;* Sulfonal, *Sp.*

Preparation.—This compound belongs to the same group, to which belongs also trional. It may be made by the following processes. When anhydrous mercaptan (ethyl sulphydrate) and anhydrous acetone are mixed and a stream of dry hydrochloric acid gas passed through, the liquid gradually becomes turbid and separates into two layers, the upper being mercaptol (dithioethyldimethylmethane), the lower, diluted hydrochloric acid. The mercaptol is separated, washed, dried and purified by fractional distillation. The oxidation of the pure mercaptol to sulphonal is accomplished by potassium permanganate. It may also be prepared by the action of ethyl chloride on sodium thiosulphate, the resulting sodium ethyl thiosulphate being converted into ethyl mercaptan and acid sodium sulphate by the action of water. This conversion is made to take place in the presence of alcohol, hydrochloric acid, and acetone, the ethyl mercaptan being condensed to mercaptol, which is oxidized by potassium permanganate as in the foregoing method. A characteristic test is to fuse the sulphonal in a small dry test-tube, heat to about 280° C., and to the clear liquid add pyrogallic (or gallic) acid. The liquid becomes brown and gives off the characteristic odor of mercaptan or sulphur alcohol. Heating with potassium cyanide or even with powdered charcoal will effect the same decomposition.

Description and Physical Properties.—"Colorless, odorless crystals or a white, odorless powder. One Gm. of Sulphonmethane is soluble in 365 cc. of water, 60 cc. of alcohol, 11 cc. of chloroform, and in 64 cc. of ether, at 25° C. One Gm. is soluble in 16 cc. of boiling water and in 3 cc. of boiling alcohol. It is soluble in benzene.

"Sulphonmethane melts between 124° and 126° C. In other respects it responds to the tests for identity and purity under *Sulphonethylmethanum.*

"Preserve in well-closed containers." *U. S.*

The British Pharmacopœia gives the following description:

"Colorless, prismatic crystals. No odor; nearly tasteless. Soluble in 450 parts of cold *water,* in 15 parts of boiling *water,* and in 80 parts of *alcohol* (90 per cent.). Melting point 125° C. Aqueous solution neutral to *litmus.* When mixed with an equal weight of *potassium cyanide* and heated, the odor of mercaptan is evolved, and when to the solution of the product in *water* excess of *hydrochloric acid* and a few drops of *T. Sol. of ferric chloride* are added, a reddish color is developed. Evolves hydrogen sulphide when gradually heated with *anhydrous sodium acetate.* Yields no characteristic *reac-*

tions for chlorides or sulphates. No appreciable ash." *Br.*

Uses.—Sulphonal is used in medicine solely as a somnifacient. The sulphone hypnotics, as a group, have very little action on the system except as depressants to the higher cerebral centers. Although when given in very large dose they produce in the lower animals paresis and tremors, in quantities anywhere approaching the therapeutic dose they have almost no effect on man save to produce sleep. They are both characterized by the slowness of absorption and persistence of their action, although sulphonethylmethane is not quite so slow in its effects as sulphonmethane. Although usually not followed by disagreeable after effects, there sometimes remains some mental confusion and lassitude the following day. For some unknown reason it does not act happily in cases of heart disease and there have been reported sudden deaths in patients suffering from cardiac weakness following the use of sulphonal. It is best administered in the form of a powder stirred up in a glass of hot water or milk; it should never be exhibited in pill form.

While in single dose they are relatively safe somnifacients, when used continuously over long periods of time they give rise to serious forms of intoxication. This generally starts with constipation and vague neurasthenic pains. In the fully developed stage chronic sulphone poisoning is characterized by obstinate constipation with scaphoid abdomen, cramp-like pains in the extremities, ataxia, insomnia, and a peculiar discoloration of the urine which ranges from a faint pinkish hue to a deep port wine red. This discoloration is due to the presence of a pigment known as *hematoporphyrin*, which is probably derived from decomposition of the blood. The urine is also usually highly acid and may contain albumen and tube casts. The prognosis in chronic sulphone poisoning is always grave. In the treatment it is essential to open the bowels as promptly as possible; for this the most powerful purgatives are usually required, and their action may be assisted by high enemata. In order to hasten the elimination of the poison large quantities of water should be administered, both by mouth and by hypodermoclysis. The free use of alkalies has been recommended with the idea of correcting the acidity of the system; sodium bicarbonate may be added to physiological salt solution for hypodermic injection. Symptom treatment is rarely of any efficacy.

Because of the seriousness of the chronic poisoning by this drug—the mortality is upwards of 75 per cent.—and the insidiousness of its onset, sulphonal should never be used without interruptions for more than a week or ten days. Acute poisoning by sulphonal is rare, but Knapp has reported a case in which 450 grains produced death after unconsciousness lasting three days. Even after therapeutic doses occasionally a measles-like rash appears.

A. Falck reports that sulphonal may be recovered from decomposing animal matter after long contact (*J. S. C. I.*, 1919, xxxviii, 962A).

Dose, from ten to forty grains (0.65–2.6 Gm.).

SULPHUR LOTUM. U. S.

WASHED SULPHUR Sulphur Lot.

"Washed Sulphur, when dried to constant weight over sulphuric acid, contains not less than 99.5 per cent. of S." *U. S.*

Flores Sulphuris Loti; Sulphur Depuratum, Soufre Sublimé Lavé, Soufre Lavé, *Fr.;* Gereinigte Schwefelblumen, *G.;* Solfo sublimato e levato, *It.;* Azufre lavado, *Sp.*

"Sublimed Sulphur, 100 Gm.; Ammonia Water, 10 cc.; Water, a sufficient quantity. Pass the sublimed sulphur through a No. 30 sieve, mix it thoroughly with 100 cc. of water, add the ammonia water, and set the mixture aside for three days in a closed vessel, agitating occasionally. Then add 100 cc. of water, transfer the mixture to a strainer, and wash the sulphur with water until the washings cease to impart a blue color to red litmus paper. Then allow it to drain, press the residue strongly, dry it rapidly at a moderate heat in a drying closet, pass it through a No. 30 sieve." *U. S.*

Sublimed sulphur is frequently contaminated with small quantities of sulphuric acid and other impurities, and the object of the ammonia in the above process is to neutralize the acid—the salt being subsequently washed out—and to remove any arsenical contamination. (See *Sulphur Sublimatum.*)

Description and Physical Properties.—"A fine yellow powder, without odor or taste. It meets the requirements for solubility and identity under *Sulphur Sublimatum.* Agitate 2 Gm. of Washed Sulphur with 10 cc. of distilled water and filter: the filtrate is neutral to litmus paper (*acid or alkali*). The residue on ignition does not exceed 0.5 per cent. Digest 0.5 Gm. of Washed Sulphur for three hours with 10 cc. of ammonia T.S., filter the liquid, and evaporate the clear filtrate to dryness on a water bath. Add 1 cc. of nitric acid, and again evaporate to dryness. This residue meets the requirements of the test for *arsenic.*

"**Assay.**—Dry Washed Sulphur to constant weight over sulphuric acid and proceed as directed under *Sulphur Sublimatum.*

"Preserve in well-closed containers." *U. S.*

For description of chemical and therapeutic properties, see *Sulphur Sublimatum.*

Dose, one to three drachms (3.9–11.6 Gm.).

Off. Prep.—Pulvis Glycyrrhizæ Compositus, *U. S.;* Sulphuris Iodidum, *N. F.;* Tabellæ Sulphuris et Potassii Bitartratis, *N. F.*

SULPHUR PRÆCIPITATUM. U. S., Br.

PRECIPITATED SULPHUR Sulphur Præc. [Lac Sulphuris, Milk of Sulphur]

"Precipitated Sulphur, when dried to constant weight over sulphuric acid, contains not less than 99.5 per cent. of S." *U. S.* "Precipitated Sulphur is obtained by the action of hydrochloric acid upon a solution prepared by boiling together sulphur and lime in water." *Br.*

Magisterium Sulphuris; Soufre précipité, Magistère de Soufre, *Fr.;* Sulfur præcipitatum, *P. G.;* Schwefelmilch, *G.;* Solfo precipitato, *It.*

"Sublimed Sulphur, 100 Gm.; Lime, 50 Gm.; Hydrochloric Acid, Water, each a sufficient quantity. Slake the lime, and mix it thoroughly with 500 cc. of water. Add the sublimed sulphur, previously sifted, and, after thorough mixing, add 1000 cc. of water and boil the mixture in a porcelain or glass vessel during one hour, stirring or agitating the mixture very frequently, and replacing the water lost by evaporation. Then cover the vessel, and allow it to stand until the contents are cool and the supernatant liquid becomes clear. Carefully draw off the clear solution, and filter the remainder. To the united liquids add gradually and with constant stirring hydrochloric acid, previously diluted with an equal volume of water, until the liquid is nearly neutralized but still retains an alkaline reaction and a yellow color. Collect the precipitate on a strainer, and wash it until the washings are neutral to litmus paper and no longer give a precipitate upon the addition of ammonium oxalate T.S. Then dry the product rapidly and keep it in well-closed containers." *U. S.*

The process for *precipitated sulphur* was not changed in the last revision. The Br. Pharm. in its official definition outlines the method used in the U. S. preparation.

In the U. S. process three molecules of calcium oxide react with six atoms of sulphur to form two molecules of calcium disulphide and one of calcium thiosulphate;

$$3CaO + (S_2)_3 = 2CaS_2 + CaS_2O_3$$

On the addition of the hydrochloric acid, six atoms of sulphur are precipitated (four from the two molecules of calcium disulphide and two from the one molecule of calcium thiosulphate), and the calcium and oxygen unite with the hydrochloric acid, so as to form calcium chloride and water, according to the reaction:

$$2CaS_2 + CaS_2O_3 + 6HCl = 3CaCl_2 + 3H_2O + (S_2)_3$$

Hydrochloric acid is the most eligible precipitant for the sulphur, as it gives rise to calcium chloride, which is a very soluble salt and is easily washed away. Sulphuric acid is wholly inadmissible, as it produces calcium sulphate, which, from its sparing solubility, becomes necessarily intermingled with the precipitated sulphur.

Description and Physical Properties.—"A fine, amorphous powder, of a pale yellow color, without odor or taste.

"Precipitated Sulphur meets the requirements for solubility and identity under *Sulphur Sublimatum,* but it is more readily and completely soluble in carbon disulphide than the other forms of sulphur. Agitate 2 Gm. of Precipitated Sulphur with 10 cc. of distilled water, and filter: the filtrate is neutral to litmus paper (*acid or alkali*). The residue on ignition does not exceed 0.3 per cent. Digest 1 Gm. of Precipitated Sulphur for three hours with 10 cc. of ammonia T.S., and filter the liquid. Evaporate the clear filtrate to dryness on a water bath, add 1 cc. of nitric acid, and again evaporate to dryness: this residue meets the requirements of the test for *arsenic.*

"**Assay.**—Dry Precipitated Sulphur to constant weight over sulphuric acid and proceed as directed under *Sulphur Sublimatum.*" *U. S.*

"A greyish-yellow, soft powder, free from grittiness and from the odor of hydrogen sulphide. Under the microscope it is seen to consist of opaque globules, without any admixture of crystalline matter. Burns with a blue flame, forming sulphur dioxide, and leaving not more than 0.5 per cent. of fixed residue. When 10 grammes are mixed with *water,* filtered, and thoroughly washed, the mixed filtrate and washings require for neutralisation not more than 2 millilitres of *N/10 solution of sodium hydroxide* (limit of acidity). *Arsenic limit* 5 parts per million." *Br.*

The German test, that 1 Gm. of precipitated sulphur should completely dissolve in 5 Gm. of carbon disulphide, is trustworthy, according to Fittinger. From its color it was formerly called *lac sulphuris,* or *milk of sulphur.* It is insoluble in water, but dissolves in a boiling solution of potassium hydroxide, and in oil of turpentine by the aid of heat. When of a brilliant white color, the presence of calcium sulphate may be suspected, in which case the preparation will not be wholly volatilized by ignition. If pure, it communicates a harsh feel when rubbed between the fingers, owing to the friction of the particles. Precipitated sulphur differs from sublimed sulphur in being in a state of more minute division, and in its amorphous condition, sublimed sulphur being crystalline.

Colloidal sulphur, which is said to be physiologically much more active than ordinary sulphur, may be produced by passing H_2S into a solution of SO_2 and, after decantation, adding distilled water to the precipitated sulphur, which readily dissolves, and may be freed from SO_2 by subsequent dialysis. Lunan (*Am. Drug.,* 1917, lxiv, 495) gives the following process: Hydrochloric acid (10 per cent.), 22 cc.; sodium sulphide ($Na_2S.9H_2O$), 5 grammes; sodium sulphite ($Na_2SO_3.7H_2O$), 2.6 grammes; white of two eggs; sterilized water to 1 liter. Dissolve the sodium sulphide and sulphite each separately in 250 cc. of the water, mix and add the white of egg. To this solution add the hydrochloric acid, diluted with 250 cc. of the water. The mixture is then warmed slightly, and sufficient sterile water added to make the volume 1 liter and the solution carefully dialyzed to remove crystalloids. Theoretically, the product should contain 1 in 1000 of colloidal sulphur. The chemical action is explained as follows:

$$2Na_2S + 4HCl = 2H_2S + 4NaCl$$
$$Na_2SO_3 + 2H_2S + 2HCl = 2NaCl + 3S + 3H_2O$$

The presence of the albumin appears to prevent the aggregation of the sulphur into masses. In use the dose of 1 cc. (about 17 minims) is rendered isotonic by the addition of 0.2 cc. (about 3 minims) of 5.5 per cent. saline solution mixed immediately before injecting. *Sulfidal* and *sulfoform* are trade names for preparations of colloidal sulphur.

Uses.—Precipitated sulphur possesses medicinal properties similar to those of sublimed sulphur. Its state of extreme division renders it more readily suspended in liquids. A form easily suspended in water may be prepared by adding to the calcium polysulphide solution a solution of casein. The precipitated sulphur carries with it a little casein which communicates through its colloidal effect suspending properties to the sulphur. It is sometimes selected for forming sulphur ointments; these are lighter in color and smoother than those made with sublimed sulphur.

Dose, one to three drachms (3.9–11.6 Gm.).

Off. Prep.—Confectio Sulphuris, *Br.;* Trochiscus Sulphuris, *Br.;* Pasta Betanaphtholis, *N. F.;* Pasta Zinci Sulphurata, *N. F.*

SULPHUR SUBLIMATUM. U. S., Br.

SUBLIMED SULPHUR Sulphur Sublim.
[Flowers of Sulphur]

"Sublimed Sulphur, when dried to constant weight over sulphuric acid, contains not less than 99.5 per cent. of S." *U. S.* "Sublimed Sulphur may be obtained from native sulphur or sulphides." *Br.*

Flores Sulphuris; Brimstone; Soufre Sublimé, Fleur (Crême) de Soufre, *Fr.;* Sulfur sublimatum, *P. G.;* Schwefel, Schwefelblumen, Schwefelblüthe, *G.;* Solfo sublimato, *It.;* Azufre sublimado, Flor de Azufre, *Sp.*

Natural States.—Sulphur is very generally disseminated throughout the mineral kingdom, and is almost always present, in minute quantity, in animal and vegetable matter. Among vegetables, it is present in volatile oil of mustard and other cruciferous plants. It occurs in the earth either free or in combination. When free it is found in masses, translucent or opaque, or in the powdery form mixed with various earthy impurities. In combination it is usually united with certain metals, as iron, lead, mercury, antimony, copper, and zinc, forming compounds called sulphides. *Native sulphur* is most abundant in volcanic countries, and is hence called *volcanic sulphur.* Productive mines of sulphur are found in Sicily, but the output has declined in recent years. Sulphur exists as a mineral in widely separated localities in the United States. Two hundred miles south of Salt Lake City there is a deposit of sulphur two thousand feet square and of an unknown thickness, shafts having been sunk sixty feet without reaching the bottom. This sulphur is said to be free from arsenic and antimony and is a surface deposit. Much sulphur has been found in Mount Humboldt, Nevada, and Sulphur Mountain, as it is called, in the Yellowstone National Park, is largely composed of the mineral. The great bulk of the world's supply of sulphur is now produced from the mines in Louisiana and Texas which now yield (1922) approximately 1,000,000 tons annually. In the Frasch process, used in these mines, a well 25 cm. in diameter is sunk just as in boring for petroleum. This is lined with an iron pipe all the way to the rock formation underlying the sulphur deposit. In this tube are placed two aluminum lined concentric tubes which are driven to the lower portion of the sulphur layer but not entirely to the rock. The outer tube is then surrounded with water heated under pressure to 155° C., which melts the sulphur and forces it to ascend the middle tube as a liquid with a density of 2. A current of compressed air meets the sulphur and fills it with air bubbles which render it buoyant and it rises to the surface without the aid of a pump. The Louisiana sulphur is nearly 100 per cent. pure and is entirely free from arsenic, which is very advantageous for many industrial processes and for making pure sulphuric acid (see *Acidum Sulphuricum*). Sulphur exists in large quantities also in various localities in Japan.

Sicilian sulphur is usually extracted from the sulphur-containing earth by heating in covered mounds known as *calcaroni,* and collecting the melted sulphur or by extraction from the earth by superheated steam under several atmospheres' pressure.

The process of purifying the crude Sicilian sulphur consists in distilling the crude sulphur from a large cast iron still, set in brickwork over a furnace and furnished with an iron head. The head has two lateral communications, one with a chamber of brick-work, the other with an iron receiver immersed in water, which is constantly renewed to cool it sufficiently to cause the sulphur to condense in the liquid form. When the tube between the still and the receiver is shut, and that communicating with the chamber is open, the sulphur condenses on its walls in the form of an impalpable powder, and constitutes *sublimed sulphur,* or *flowers of sulphur.* If, on the other hand, the communication with the chamber be closed, and that with the receiver open, the sulphur will condense in the latter in the fused state and, when cast in cylindrical moulds, forms the *roll sulphur* of commerce.

In the island of Anglesea, and at Swansea, Wales, large quantities of sulphur are obtained from imported Spanish copper pyrites in the process for extracting the metal. The furnaces in which the ore is roasted are connected with chambers in which the volatilized sulphur is condensed.

A process for obtaining sulphur as a by-product from the residue of the manufacture of soda by the LeBlanc process, proposed by Max Schaffner, has been used in most of the soda factories of Germany, and has been introduced, to a greater or less extent, in England, France, and Belgium.

Crude foreign sulphur has come to this country principally from Messina, in Sicily, and the ports of Italy, but in recent years Japanese sulphur has been received on the Pacific coast. Roll sulphur and the flowers were formerly brought from Marseilles. Good Sicilian sulphur does not contain more than 3 per cent. of impurity, consisting chiefly of earths. The Louisiana sulphur has practically replaced much of the foreign sulphur.

Sulphur is a non-metallic element, existing in several allotropic states. In its ordinary state it is a brittle solid, of a pale yellow color, permanent in the air, and exhibiting a crystalline texture and shining fracture. It has a slight taste, and a perceptible odor when rubbed. When pure its sp. gr. is about 2, but it varies a little in density in its different allotropic states. It is a poor conductor of heat, and becomes negatively electric by friction. The melting point of sulphur varies with its allotropic state, which is readily altered by heat. Pure sulphur melts and sublimes at 114.5° C. If heated above its melting point, it undergoes, in proportion to the heat applied, a progressive change, which will cause it, upon slow cooling, to solidify at a temperature lower than that at which it was melted; and if it be remelted it will be found to have a higher melting point than before. Melted sulphur is perfectly limpid, and of a bright yellow color. When sulphur is melted, and, after partial cooling, the crust formed on its surface is pierced, and the fluid portion poured out, it may be obtained in slender monoclinic crystals, constituting an allotropic condition of the element. This variety, however, gradually passes back into the more permanent variety found in nature. When sulphur is heated above its melting point, it becomes deeper in color and less fluid. At 200° C. it has a deep brown color, and is so viscid that it cannot be poured from the containing vessel. If the temperature be still further increased, the sulphur resumes its fluidity, but retains its brown color. Finally, when the temperature reaches 448.4° C., it boils, forming a yellow vapor, and may be distilled. If melted sulphur, heated above 200° C., is suddenly cooled by being poured out into water, it becomes a reddish-brown plastic mass, with alteration of properties, called *soft sulphur* (*viscid sulphur*), which constitutes another allotropic variety, and is employed in taking impressions of medals, etc. This form of sulphur resumes the hard state, but not its original color, after the lapse of a few days, or suddenly if heated to 100° C.

Sulphur takes fire at about the temperature of 148.8° C., and burns with a blue flame, combining with the oxygen of the air, and giving rise to sulphurous oxide, SO_2. The combinations of sulphur are numerous, and are among the most powerful chemical agents. It forms with oxygen four oxides, *sulphurous oxide* (*sulphur dioxide*), SO_2, *sulphuric oxide* (*sulphur trioxide*), SO_3, *sulphur sesquioxide,* S_2O_3, and *sulphur heptoxide,* S_2O_7. The first two of these oxides, by their union with water, form *sulphurous acid,* H_2SO_3, and *sulphuric acid,* H_2SO_4, respectively. There are also known *hyposulphurous acid,* H_2SO_2, the corresponding oxide of which is not known, *thiosulphuric acid* (frequently spoken of as hyposulphurous acid), $H_2S_2O_3$, *persulphuric acid,* $H_2S_2O_8$, and a series of acids, $H_2S_2O_6$, $H_2S_3O_6$, $H_2S_4O_6$, and $H_2S_5O_6$, called the *thionic series.* It forms with hydrogen, hydrogen sulphide (hydrosulphuric acid or sulphuretted hydrogen), and with the metals, various *sulphides.* Some of the sulphides are analogous to oxyacids, others to basic hydroxides; and these different sulphides, by combining with one another, form compounds which, from their analogy to salts, are called Berzelius *sulphosalts.*

Description and Physical Properties.—"A fine, yellow powder having a faint odor and taste. Sublimed Sulphur is practically insoluble in water, and nearly insoluble in alcohol. One Gm. dissolves slowly and usually incompletely in about 2 cc. of carbon disulphide. One Gm. is soluble in about 70 cc. of chloroform, in 150 cc. of ether, and in 100 cc. of olive oil.

"At about 115° C. Sublimed Sulphur fuses to a yellow, mobile fluid, which upon further heating to about 162° C. becomes dark and viscid. In the air it burns to sulphur dioxide, which can be recognized by its characteristic odor. The residue in ignition does not exceed 0.5 per cent.

"**Assay.**—Dry about 1 Gm. of Sublimed Sulphur to constant weight over sulphuric acid, weigh accurately, and transfer to a flask containing 50 cc. of a solution of potassium hydroxide (1 in 10). Boil the mixture until the liquid is of a transparent, golden-yellow color and then dilute it with distilled water to measure exactly 250 cc. Oxidize 25 cc. of this diluted solution by the addition of solution of hydrogen dioxide in excess (using about 50 cc.), heat on a water bath for thirty minutes, acidulate the liquid with hydrochloric acid, dilute it with 250 cc. of distilled water, heat to boiling and add hot barium chloride T.S., in small portions, to the resulting liquid until no further precipitation takes place. Heat this mixture on a water bath for thirty minutes, collect the resulting precipitate on a filter, wash, dry, ignite, and weigh the barium sulphate. Carry out a blank determination, using the same amount of all of the reagents but omitting the Sulphur, and before making the final calculation deduct the amount of barium sulphate thus obtained from that obtained in the assay. The weight of the barium sulphate thus obtained, multiplied by

0.1373 indicates its equivalent of sulphur. Each Gm. of Sublimed Sulphur, previously dried, corresponds to not less than 7.243 Gm. of $BaSO_4$." *U. S.*

"A slightly gritty powder of a bright greenish-yellow color. Odorless and tasteless. Under the microscope it is seen to consist of irregular angular particles mixed with almost opaque globules. Burns with a blue flame, forming sulphur dioxide, and leaving not more than 0.25 per cent. of fixed residue. When 10 grammes are mixed with *water,* filtered, and thoroughly washed, the mixed filtrate and washings require for neutralisation not more than 5 millilitres of *N/10 solution of sodium hydroxide* (limit of acidity). *Arsenic limit* 5 parts per million." *Br.*

It is always contaminated with a little sulphuric acid, which is formed at the expense of the oxygen of the air contained in the subliming chambers. Accordingly, it always reddens litmus, and, if the acid is present in considerable quantity, sometimes cakes. It may be freed from acidity by careful washing with diluted ammonia water. (See *Sulphur Lotum.*)

Noyer (*Caoutchouc and Gutta Percha,* 1918, xv, 9661) states that in the commercial production of sublimed sulphur the deposit on the floor of the condensing chamber consists of a number of well defined layers possessing somewhat differing physical properties. He describes four distinct varieties and states that the term *"flowers of sulphur"* should be restricted to samples containing a minimum of 33 per cent. of sulphur insoluble in carbon disulphide. All other varieties should be called simply *"Sublimed Sulphur."*

Uses.—Elemental sulphur is free from local effect and is so insoluble that it cannot be absorbed, and hence exercises no effect upon the system. When taken into the alimentary canal, however, a portion of it unites to form hydrogen sulphide, which is an active agent. By virtue of its local irritant action upon the mucous membrane the latter substance provokes intestinal peristalsis and therefore sulphur exercises a laxative influence. The movements produced by it are soft, generally without griping, and it is a frequently used laxative in cases of *hemorrhoids.* A certain amount of the hydrogen sulphide formed may be absorbed; indeed it is asserted that the sweat of persons taking sulphur will cause a black deposit of sulphide upon silver coins. Although the therapeutic properties of hydrogen sulphide have not been clearly determined, sulphur has been widely used as an alterative, especially in *chronic rheumatism* and *gout.* Besides this, a portion of the sulphide will be eliminated through the mucous membrane of the respiratory tract and sulphur may therefore exercise a beneficial action in *chronic bronchitis* and *asthma.*

The most important uses, however, of sulphur are external. When brought in contact with the skin, especially in the presence of alkalies, a similar union of sulphur with hydrogen takes place as in the intestines. The alkaline sulphide thus formed is an active poison to various pathogenic parasites and sulphur is therefore a useful remedy in such diseases as *scabies, ringworm,* and *favus.* Besides this effect the sulphides by their local stimulating effect tend to overcome congestion in the skin and they have the power of softening the horny elements. For one or the other of these effects sulphur is a valuable remedy in a number of non-parasitic diseases of the skin, especially *acne, psoriasis, seborrhea,* etc. Locally it may be employed either in the form of a suspension or in an ointment in strengths of from 5 to 20 per cent. It is often incorporated in soaps. For local application the precipitated sulphur is the best because of its finely divided state. For internal administration either the washed or precipitated sulphur may be employed.

Soluble *colloidal sulphur* is asserted by Joseph (*Derm. Cb.,* 1913) and others to be superior to the official sulphur in the treatment of skin diseases. It is used in strengths of from 2 to 20 per cent. It has also been recommended by Bourges (*J. P. C.,* 1918, xvii, 243) internally in the treatment of *rheumatism.* It appears to be more toxic than the ordinary sulphur. (See Duhamel, *J. P. C.,* 1919, xx, 78). See under *Sulphur Precipitatum* for method of preparation.

According to Hannon of Brussels, *soft sulphur,* recently prepared, possesses valuable therapeutic properties, not as a laxative, but as a stimulant to the circulation, lungs, and skin, far more active than ordinary sulphur. The *dose* of soft sulphur is from twenty to fifty grains (1.3–3.2 Gm.), given in the form of pill. It has also been successfully employed for filling the hollows of *carious teeth.* (*P. J.,* xvii, 330.) Sublimed sulphur has been used with extraordinary success in South Africa and the Philippines in the treatment of *ameboid dysentery.* It acts probably by killing the ameba. It may be given in divided doses up to two hundred grains (13 Gm.) a day.

Much sulphur is consumed in the arts, principally in the manufacture of gunpowder and of sulphuric acid.

Dose, one to three drachms (3.9–11.6 Gm.).

Off. Prep.—Antimonium Sulphuratum, *Br.;* Confectio Sulphuris, *Br.;* Emplastrum Hydrargyri, *Br.;* Potassa Sulphurata, *Br.;* Pulvis Glycyrrhizæ Compositus, *Br.;* Sulphur Lotum, *U. S.;* Sulphur Præcipitatum, *U. S.;* Sulphuris Iodidum, *Br.;* Unguentum Sulphuris, *U. S., Br.;* Liquor Calcis Sulphuratæ, *N. F.;* Petroxolinum Sulphuratum, *N. F.;* Petroxolinum Sulphuratum Compositum, *N. F.;* Unguentum Sulphuris Alkalinum, *N. F.;* Unguentum Sulphuris Compositum, *N. F.*

SUMBUL. N. F.

SUMBUL [Musk-root]

"Sumbul consists of the dried rhizome and roots of *Ferula Sumbul* (Kaufmann), Hooker filius, or of other closely related species of

Ferula (Fam. *Umbelliferæ*) possessing a characteristic musk-like odor. Sumbul contains not more than 2 per cent. of foreign organic matter." *N. F.*

Sumbul Radix; Racine de Sumbul, *Fr.;* Sumbulwurzel, Moschuswurzel, *G.*

Under the name of *sumbul* or *jatamansi,* a root has long been used in India, Persia, and other parts of the East, as a perfume, an incense in religious ceremonies, and medicinally. It was the root of a then unknown plant, supposed to be umbelliferous, and, from the character of the root, to grow in low wet places. The plant is said to inhabit no part of British India, but the regions to the north and east of it, as Nepaul, Bootan, Pucharia, etc. The root is taken northward to Russia, and reaches the rest of Europe through Petrograd. The physicians of Moscow and Petrograd were the first to employ it on the continent of Europe. Granville first introduced it to the notice of the profession in Great Britain and in this country. It has also been imported into England from India, whither it was brought from a great distance. The species which yields the drug of commerce has not been definitely ascertained. The U. S. P. IX recognized *Ferula Sumbul* Hooker fil. as the source but this is denied by Holmes, although this author states it was probably the source of the original drug.

Ferula Sumbul was first discovered by the Russian Fedschenko in 1869, growing at an elevation of 3000 feet in the mountains which separate Russian Turkestan from Bucharia. The plant is a large umbellifer, reaching a height of eight feet, and having a solid, cylindrical, slender stem, which in the upper part gives origin to about twelve slender divaricate branches. The root-leaves are two and a half feet long, with short, channelled, broadly dilated, completely clasping petioles. They are triangular in outline, tripinnate, with the alternate divisions fine. The stem-leaves rapidly decrease in size until they become mere sheathing bracts. The flowers are polygamous, the fruit from three-eighths to one-half inch long by one-fourth inch wide; the mericarps oblong-oval, dorsally much compressed, thin, with three faint, thread-like, dorsal ridges; no dorsal vittæ, and commissural ones collapsed. J. E. Aitchison states (*Tr. Linn. Soc.,* ser. 2, *Bot.,* 69) that the root of *Ferula suaveolens,* which has only a faint musky odor, is one of the kinds exported from Persia to Bombay by the Persian Gulf.

The commercial supplies of Sumbul are imported from Turkey.

Description and Physical Properties.—"*Unground Sumbul.*—In transverse segments, attaining a length of 10 cm. and a diameter of 7 cm.; extremely light, floating in water; externally light brown to dark brown, longitudinally wrinkled and showing in the upper portions a smooth, grayish or brownish epidermal layer, occasionally with the short stem-bases attached; fracture short, fibrous, spongy; internally light yellow or brownish yellow, arrangement of wood irregular and with yellowish brown or blackish resinous patches frequently extending over the entire ends of the segments. Odor peculiar, musk-like; taste bitter and somewhat aromatic.

"*Powdered Sumbul.*—Grayish brown; exhibits numerous, irregular, brownish black fragments and well-defined isolated tracheæ, the latter with distinct end-walls, and mostly with reticulate thickenings and from 0.020 to 0.100 mm. in width; occasional fragments of polygonal epidermal cells with yellowish brown walls; numerous, nearly colorless, yellowish brown and reddish brown fragments consisting of a granular substance in which the cellular structure is not well defined; long, narrow fragments consisting of more or less collapsed sieve tissue; occasional fragments of well-defined parenchyma with a few, nearly spherical starch grains, from 0.003 to 0.012 mm. in diameter." *N. F.*

Constituents.—An elaborate analysis of sumbul by Heyl and Hart (*A. J. P.,* 1916, p. 546) showed in addition to the ordinary constituents of vegetable drugs, about 17 per cent. of resinous matter and 1 per cent. of volatile oil. The resinous matter consisted of a considerable proportion of a white acid resin which yielded upon hydrolysis vanillic acid and a substance resembling the volatile oil described below. From this resinous matter was also separated phytosterol, an unsaponifiable substance, $C_8H_{13}O$ and by saponification several fatty acids including *angelic* (*sumbulic*), valerianic, butyric, etc. The volatile oil had a specific gravity of 0.932 at 15° C., and on standing deposited a few yellow crystals of undetermined composition; it contained no sulphur. They also found traces of umbelliferone, both free and as a glucoside, and betaine.

For other analyses but less complete see Utech (*A. J. P.,* 1893, p. 465) and Hahn (*Proc. Penna. Phar. Assn.,* 1896, p. 75).

Uses.—Sumbul is supposed to have a quieting influence on the nervous system and is used in the treatment of various *hysterical* conditions. By many it is believed to have an especial relation to the pelvic organs and it is widely employed in *dysmenorrhea* and allied disorders. It has also been used as a stimulant to mucous membranes not only in *chronic dysenteries* and *diarrheas,* but in *chronic bronchitis,* especially with *asthmatic* tendency, and even in *pneumonia.*

Murawieff, of Russia, prepares the resin, which he considers to be the active principle, by macerating the root first in water, and then in a solution of sodium carbonate, washing it well with cold water, drying it, treating it with alcohol, filtering the tincture, adding a little lime and again filtering, separating the lime by sulphuric acid, agitating with animal charcoal, again filtering, distilling off nearly all the alcohol, mixing the residuum with water, driving off the remaining alcohol, and, finally, washing the precipitate with cold water, and drying it.

Dose, from fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Extractum Sumbul, *N. F.;* Tinctura Sumbul, *N. F.*

SUPPOSITORIA. U. S.

SUPPOSITORIES

"Suppositories are solid bodies of various weights and shapes, adapted for introduction into the different orifices of the human body, and melting or softening at body heat. The vehicles usually employed are oil of theobroma, glycerinated gelatin, or sodium stearate." *U. S.*

Suppositoires, *Fr. Cod.;* Suppositorien, Stuhlzäpfchen, *G.;* Supositorios, *Sp.*

Suppositories are solid bodies usually intended to be introduced into the rectum with a view either of evacuating the bowels by irritating the mucous membrane of the rectum, or of producing a specific effect on the neighboring parts or on the system at large. Suppositories are also made for vaginal or urethral administration. They fulfil the same indications as enemata, and are sometimes preferable from the facility of their application, and, when the object is to produce the peculiar effect of a medicine, from the smallness of their bulk, which facilitates retention. Their form may be cylindrical, conical, or spherical, the last being preferable when the bulk is small, or they may be in the shape of the modified cone with a tapering base, as recommended by H. S. Wellcome. (*Proc. A. Ph. A.,* 1893, p. 103.) This is the form now generally used when moulded suppositories are supplied. They should be of such a consistence as to retain their shape, but so soft as to incur no risk of wounding the rectum. Soap is not unfrequently employed in this way as a laxative, a piece of pure castile soap being cut to the proper shape and used as a suppository. Cacao Butter, originally recommended by A. B. Taylor (*A. J. P.,* 1852) is the most frequently used base (see *Oleum Theobromæ*). Rarely is it necessary to stiffen it but when such a material is employed, wax is usually selected, although cetaceum is preferable. If not more than 10 per cent. of the spermaceti is added, the value of the suppository is not very materially affected, although it melts more slowly, and consequently requires a longer time to act, than when the butter of cacao is used alone. Suppositories containing a considerable percentage of wax melt so slowly in the rectum as to be comparatively useless, or they may fail altogether to soften down, and be finally passed from the anus unchanged.

A critical study and contribution to the literature of suppository bases was published by Bruno Solomon (*Ph. Ztg.,* 1913, p. 502), who classifies them in general as (1) cacao butter, (2) fat and wax combinations, (3) glycerin and gelatin, agar, soap, etc. He prepares what he calls a *mother mass* of gelatin 50, distilled water 100, and glycerin 100. From this, modifications with agar-agar and soap, etc., may be subsequently prepared with the minimum of effort. The U. S. P. gives a formula for preparing suppositories with a glycerin gelatin base.

A very good method of mixing the oil of theobroma with the hardening material is by grating with an ordinary tin grater, such as used in kitchens, and mixing the coarse powders before melting, and W. G. Ewing has proposed rubbing the powders and the medicinal substance in a mortar together, dividing the plastic mass, and shaping it with the fingers. It is better to shape them with a spatula, and roll them upon a pill tile. This plan, although having its advantages, is, however, not equal to the official one of melting the ingredients and running them into moulds. The tendency of the hardened suppositories to adhere to the moulds may be overcome more or less perfectly by dusting the moulds with lycopodium powder, or greasing them well with olive oil, but it is far better to rely upon the natural contraction of the mass, caused by thoroughly cooling the moulds as lycopodium is a foreign substance which sometimes produces irritating effects, and oil sometimes makes them too soft, when used too freely. The moulds that open lengthwise, are now used almost exclusively in preference to the archaic individual moulds. The mould must be very cold, so as to chill the melted liquid at once and prevent any separation of its ingredients before cooling. It has also been recommended to form the excipient into the required shape, and then, while it is still soft, make an excavation from the base upward, into which the medicine may be introduced, and afterwards enclosed by a little of the cacao butter. But, as one of the objects of the excipient is an equable diffusion of the medicine, to prevent irritation, this method would be inapplicable to substances in any degree locally irritant. Hollow rectal suppositories made of pure cacao butter are on the market and have an extensive use; the medicinal ingredients are made into a soft mass rolled out on a slab or cut into pieces on a pill machine, inserted into the hollow chamber of the suppository and the cacao butter plug there fused in place with the use of gentle heat.

J. Percy Remington devised a suppository mould made of soft vulcanized rubber; it is used in the same manner as that employed for a metal mould, the advantage being mainly the facility of removal when the suppository is cold; a slight pressure with a twisting motion causes the soft rubber mould to open, and the suppository to drop out easily. (*Proc. New Jersey Pharm. Association,* 1906.)

The inventive genius of pharmacists has been industriously applied to the construction of suppository moulds, and there are now many varieties; the principle is much the same in all, however, but for convenience they may be classed as follows: 1. Individual moulds; these were among the first to be used. Half a dozen conical, hard-metal moulds, or made of paper, tin-foil, etc., are retained in an upright position in a tray containing ice-water. (See *A. J. P.*, 1861, p. 5, 1870, 392; *Proc. A. Ph. A.*, 1902, 501.) 2. Moulds which consist of two solid pieces of metal, hinged or temporarily joined, so that when the suppository is thoroughly cooled the parts may be separated and the suppository dropped out. (See *A. J. P.*, 1871, pp. 488, 563; 1879, p. 277; and *Proc. A. Ph. A.*, 1893, p. 103; 1902, 757.) 3. Soft rubber moulds. (See *Proc. New Jersey Pharm. Assoc.*, 1906.) 4. Moulds designed to be used through compression, more or less powerful. (*N. R.*, June, 1879, Jan. and March, 1880; also *Proc. A. Ph. A.*, 1897, p. 442.)

The weight—*i.e.*, the size—of rectal suppositories should vary according to the purposes for which they are employed. When they are to be used for infants and children, they should weigh from five to ten grains. The Br. Pharm. adopts the weight of 1 Gm. (fifteen grains).

Machines for making suppositories by cold compression are now available in a variety of forms, and, while they are more satisfactory for making stock suppositories, made up in large numbers, many retail pharmacists use them to advantage in dispensing suppositories on prescription. (For a discussion of such machines and their relative advantages see Remington, *Practice of Pharmacy.*) Compression is now recognized as an alternative method in the U. S. P. general article on suppositories.

The U. S. P. X directs as follows:

"For suppositories made with oil of theobroma the following general processes may be employed: Take of the Medicinal Substance, the prescribed quantity; Oil of Theobroma, grated, a sufficient quantity. Reduce the medicinal substance, if dry, to a very fine powder, or, if an extract, soften it with an appropriate liquid, then mix it thoroughly in a mortar with about an equal weight of grated oil of theobroma, and incorporate the remainder of the oil of theobroma until a homogeneous, plastic mass is obtained, adding, if necessary, a small quantity of expressed oil of almond or wool fat. Roll the mass on a graduated tile until a cylinder of the proper length is formed, divide this into the required number of equal parts, and with a spatula, or other mechanical aid, form them into the desired shape.

"If the process of cold compression is preferred, mix the medicinal substance in a suitable mortar with about an equal weight of grated oil of theobroma, as above directed, then thoroughly incorporate it with the remainder of the oil of theobroma, previously finely grated, chilling the mortar, if necessary, to preserve the pulverulent form of the mixture. Transfer the powdered mass to the cylinder of an appropriate suppository compressor and by the use of this apparatus prepare the desired number of compressed suppositories. If the process of fusion is preferred, mix the medicinal substance with about an equal weight of grated oil of theobroma, as above directed, then thoroughly incorporate it with the remainder of the oil of theobroma, previously melted by a gentle heat on a water bath, in a suitable vessel provided with a lip. Allow it to cool to about 38° C., and, when the mixture begins to congeal, pour it immediately into suitable well-cooled moulds. Keep the moulds at a freezing temperature until the suppositories have hardened and are ready to be removed. For suppositories containing chloral hydrate, phenol, or other substances which soften the vehicle, raise the melting point of the oil of theobroma by the addition of from 10 to 15 per cent. of spermaceti, but the melting point must not be raised above 37° C.

"For suppositories made with glycerinated gelatin the following process may be used: Take of: The Medicinal Substance, the prescribed quantity, Glycerinated Gelatin, Glycerin, Water, each, a sufficient quantity. Mix the medicinal substance, if solid and soluble in water or glycerin, or if a miscible liquid, with a little water, and add sufficient glycerin to make the weight of the mixture one-half that of the finished mass. Then thoroughly incorporate it with an equal weight of melted glycerinated gelatin, and pour it at once into suitable moulds which have been greased with a small quantity of petrolatum. Cool the moulds thoroughly before removing the suppositories. Moulds for urethral suppositories should be warmed sufficiently before pouring the mass to facilitate the proper filling of the mould. Suppositories having a firmer consistence may be prepared by substituting mucilage of acacia for a portion of the water or glycerin. If the medicinal substance is insoluble in water or glycerin, thoroughly triturate it in a warm mortar with a sufficient quantity of glycerin to make the weight of the mixture one-half that of the finished mass. Then thoroughly incorporate it with an equal weight of melted glycerinated gelatin, and pour it into suitable moulds as above directed. With bulky powders about one-half of the glycerin may be replaced with water before trituration. Glycerinated gelatin suppositories should be protected against the effects of heat, moisture, and dry air by keeping them in tightly-closed containers in a cool place.

"*Rectal Suppositories* should be cone-shaped, and when made from oil of theobroma should weigh about 2 Gm. If prepared with glycerinated gelatin, they should weigh about 4 Gm. *Urethral Suppositories* (*Bougies*) should be pencil-shaped, pointed at one extremity, and either 7 cm. in length, weighing about 2 Gm., or 14 cm. in length, weighing about 4 Gm., when made with glycerinated gelatin. If prepared with oil of theobroma they should weigh about one-half the above quantities. *Vaginal Suppositories* should be globular or oviform in shape, and weigh about 10 Gm. if made with glycerinated gelatin, and about 4 Gm. if made with oil of theobroma." *U. S.*

The U. S. Pharmacopœia gives no detailed formulæ for suppositories, except in one case, *Suppositoria Glycerini.*

Suppositories are used in medicine (1) for the purpose of obtaining the systemic action of drugs after their absorption, (2) for the local effects of their ingredients. There is an old superstition among the medical profession that systemically acting drugs introduced per rectum have more effect upon the pelvic organs than when given by the mouth, and suppositories of opium, belladonna, etc., are habitually recommended in the treatment of diseases of the bladder and uterus. This view, however, is patently erroneous. The per rectum channel of exhibiting systemically acting drugs may, however, be of service in those cases in which deleterious influence upon the stomach is feared. Speaking in a general way, quantities of about double the dose exhibited by the mouth may be given in the form of suppositories. As a means of obtaining the local action of astringents, anesthetics, or antiseptics, upon the mucous membrane of the rectum suppositories are very valuable.

SUPPOSITORIA ACIDI CARBOLICI. Br.

PHENOL SUPPOSITORIES

Carbolic Acid Suppositories; Suppositoires d'acide Phénique, *Fr.;* Phenol-suppositorien, *G.*

"Phenol, 0.8 gramme; White Beeswax, 0.5 gramme; Oil of Theobroma, *a sufficient quantity* for twelve suppositories each weighing about one gramme. Dissolve the Phenol in the Oil of Theobroma, previously melted, add the White Beeswax, and pour the melted mixture into suitable moulds; or let the mixture cool and then divide it into twelve equal parts, and press each into a conical or other convenient form for a suppository. Each of these Suppositories contains 0.067 gramme (about 1 grain) of Phenol." *Br.*

These suppositories may be used to obtain the local anesthetic and antiseptic effect of phenol. The wax is needed to offset the tendency to liquefy.

SUPPOSITORIA ACIDI TANNICI. Br.

TANNIC ACID SUPPOSITORIES

Suppositoires de Tannin, *Fr.;* Tanninsuppositorien, Tannin-Stuhlzäpfchen, *G.*

"Tannic Acid, 2.4 *grammes;* Oil of Theobroma, *a sufficient quantity* for twelve suppositories each weighing about one gramme. Melt the Oil of Theobroma; triturate the Tannic Acid intimately with a little of the Oil, and add to the remainder; stir well; as the mixture begins to thicken pour it into suitable moulds; or let the mixture cool and then divide it into twelve equal parts, and press each into a conical or other convenient form for a suppository. Each of these Suppositories contains 0.2 gramme (about 3 grains) of Tannic Acid." *Br.*

This remedy is especially applicable to cases of *piles* and *prolapsus of the rectum.*

SUPPOSITORIA BELLADONNÆ. Br.

BELLADONNA SUPPOSITORIES

Suppositoires de belladone, *Fr.;* Belladonnasuppositorien, *G.*

"Liquid Extract of Belladonna, 1.7 *millilitres;* oil of Theobroma, *a sufficient quantity* for twelve suppositories each weighing about one gramme. Evaporate the Liquid Extract of Belladonna to a syrupy consistence; mix with the Oil of Theobroma, previously melted; as the mixture begins to thicken pour it into suitable moulds; or let the mixture cool and then divide it into twelve equal parts, and press each into a conical or other convenient form for a suppository. Each of these Suppositories contains, approximately, 0.001 gramme (about 1/60 grain) of the alkaloids of Belladonna Root." *Br.*

SUPPOSITORIA GLYCERINI. U. S., Br.

SUPPOSITORIES OF GLYCERIN Supp. Glycerin.

Suppositoires de Glycérin, *Fr.;* Glycerinsuppositorien, *G.*

"Glycerin, 80 Gm.; Monohydrated Sodium Carbonate, 2 Gm.; Stearic Acid, 8 Gm.; Water, 10 cc.; to make about 30 suppositories. Dissolve the monohydrated sodium carbonate in the water and add it to the glycerin contained in a suitable vessel, placed in a water bath in such a way that the vessel is well immersed in the boiling water and its contents protected as much as possible from the steam of the bath. Add the stearic acid and heat the mixture for fifteen minutes or until the carbon dioxide ceases to be evolved, and the liquid is clear. Then pour the melted mass into suitable moulds, remove the suppositories when they are completely cold, and preserve them in tightly-stoppered glass vessels in a cool place." *U. S.*

"Gelatin, cut small, 14 *grammes;* Glycerin, 70 *grammes;* Distilled Water, *a sufficient quantity.* Soak the Gelatin in the Distilled Water for five minutes, or until thoroughly softened; drain well, add the Glycerin, dissolve on a water-bath and evaporate until the mixture weighs one hundred grammes. Pour the product into suitable moulds having capacities corresponding to two, four, or eight grammes of the Suppository, or of such other capacities as may be required. Each of these Suppositories contains 70 per cent. by weight of Glycerin." *Br.*

These were official for the first time in the U. S. P. 1890. Glycerin suppositories have come into extensive use, the object being to introduce glycerin into the rectum with a minimum amount of other ingredients. Stearic acid was selected on account of its forming with sodium carbonate the hardest soap attainable, thus permitting the introduction of a suppository containing at least 90 per cent. of glycerin, the water, added to dissolve the monohydrated sodium carbonate, and some of the glycerin being evaporated during the manipulation. This process was perfected by J. P. Remington. (See *Practice of Pharmacy.*) The British method, on account of the use of gelatin, permits the presence of only 70 per cent. of glycerin, the suppository not being firm enough for convenient application, and, in addition, the method of hydrating the gelatin is faulty. (*C. D.*, 1898, 831.) Instead of wrapping the suppositories in tin foil it will be found more satisfactory to insert each one in a small glass tube of the proper size, corked at both ends, or in small individual cylindrical vials. Some protection from the moisture in the air is necessary because of the hygroscopic character of glycerin. (See *P. J.*, 1895, 182; *Am. Drug.*, 1894, 91; *A. J. P.*, 1895, 599.)

Uses.—Glycerin suppositories are very much used to produce fecal discharges in *constipation.* They act by locally irritating the mucous membrane of the rectum, and are often satisfactory, though never really purgative. As an occasional remedy they are useful, but their habitual employment is probably injurious to the mucous membrane.

SUPPOSITORIA IODOFORMI. Br.

IODOFORM SUPPOSITORIES

Suppositoires d'Iodoforme, *Fr.;* Iodoformsuppositorien, *G.*

"Iodoform, in powder, 2.4 *grammes;* Oil of Theobroma, *a sufficient quantity* for twelve suppositories each weighing about one gramme. Proceed as directed for Suppositoria Acidi Tannici. Each of these Suppositories contains 0.2 gramme (about 3 grains) of Iodoform." *Br.*

These suppositories are valuable in cases of rectal inflammation and irritation. It is often possible by their use in *dysentery* to avoid the use of opium to a greater or less extent. They are especially serviceable to relieve the pain and itching of *hemorrhoids.*

SUPPOSITORIA MORPHINÆ. Br.

MORPHINE SUPPOSITORIES

Suppositoires de Morphine, Suppositoires morphinés, *Fr.;* Morphinumsuppositorien, Morphin-Stuhlzäpfchen, *G.*

"Morphine Hydrochloride, 0.2 *gramme;* Oil of Theobroma, *a sufficient quantity,* for twelve suppositories each weighing about one gramme. Proceed as directed for Suppositoria Acidi Tannici. Each of these Suppositories contains 0.017 gramme (about ¼ grain) of Morphine Hydrochloride." *Br.*

These may be used to obtain the systemic effects of morphine when, for any reason, it is undesirable to exhibit that drug by mouth.

SUPPOSITORIA PLUMBI COMPOSITA. Br.

COMPOUND LEAD SUPPOSITORIES

Suppositoires de Plomb composés, Suppositoires de Plomb opiacés, *Fr.;* Zusammengesetzte Bleisuppositorien, *G.;* Stuhlzäpfchen von Opium und Bleizucker, *G.*

"Lead Acetate, in powder, 2.4 *grammes;* Opium, in powder, 0.8 *gramme;* Oil of Theobroma, *a sufficient quantity,* for twelve suppositories each weighing about one gramme. Proceed as directed for Suppositoria Acidi Tannici. Each of these Suppositories contains 0.2 gramme (about 3 grains) of Lead Acetate, and 0.067 gramme (about 1 grain) of Opium." *Br.*

This irrational combination is occasionally used in *diarrhea* or *hemorrhoids.*

SYRUPI

SYRUPS

Sirops, *Fr. Cod.;* Sirupi, *P. G.;* Sirupe, *G.;* Sciroppi, *It.;* Jarabe, *Sp.*

Syrups are concentrated solutions of sugar in aqueous fluids, either with or without the addition of medicating or flavoring ingredients. When the solution is made with pure water, it is named *syrup* or *simple syrup;* when charged with one or more medicinal agents, it is called in general terms a *medicated syrup,* and receives its special designation from the substance or substances added.

Medicated syrups are prepared by dissolving sugar in infusions, vinegars, decoctions, expressed juices, fermented liquors, or simple aqueous solutions, or by adding a medicating substance, like a tincture or a fluidextract, to simple syrup. When the active constituents are not readily soluble in water, are associated with soluble matter which it is desirable to avoid, or are volatilized or decomposed by a heat of 100° C., they are sometimes extracted by diluted alcohol, the spirituous ingredient of which is subsequently driven off.

The process of percolation has been applied for the solution of the sugar and is offered as an alternative process in a few official preparations. This process offers several advantages over the older methods. The amount of labor attending the operation is greatly reduced, no heat is employed so that volatile constituents are not injured, and the finished syrup comes through clear and is protected from the usual contaminations attending straining, etc. For the mode of properly conducting this process the reader is referred to page 1062.

The quality and quantity of the sugar employed are points of importance. Official granulated sugar should always be employed.

In relation to the quantity of sugar, if in too small proportion, fermentation is apt to occur; if too abundant, crystallization. The Pharmacopœial formula calls for 850 Gm. of sugar to make 1000 cc. of syrup, the amount of water required being about 465 cc. This makes a stable preparation.

Syrups as formerly made by more or less empiric methods, checked finally by the use of a hydrometer (saccharimeter) have been replaced by those prepared according to definite procedure and affording products of uniformity.

When carefully prepared with the best refined sugar, syrups made by the hot process or by agitation in the cold usually require no other clarification than to remove any scum which may rise to their surface upon standing, and to pour them off from any dregs which may subside. But, as the sugar employed is seldom free from impurities, it may be best, as a rule, to remove the scum as it rises during the heating process, and to strain the syrup while hot through muslin or flannel. The percolation process avoids this necessity. Should syrups at any time lack the due degree of transparency, they may be filtered through paper if a hot water funnel is used, or, when likely to be injured by this treatment, may be clarified by other mechanical means, as mentioned under the head of *Syrupus*. The vicious habit practised not long ago by sugar refiners of "blueing" sugars by the use of ultramarine and other coloring agents has been discontinued by most sugar refiners. (See *A. J. P.*, 1901, 119.)

The medicated syrups are liable to undergo various alterations, according to their nature and mode of preparation. The acid syrups always contain invert sugar. Even at ordinary temperatures, acids in any amount, however small, slowly convert common sugar into invert sugar, which, being less soluble than the former, is often deposited in the form of crystalline grains. Excessive acidity soon causes a darkening of the syrup, due to caramelization of the sugar. Syrups containing too little sugar are subject to fermentation upon accidental inoculation with yeast cells which almost invariably occurs. Syrups sometimes undergo changes in which moulds are produced which appear on the surface as isolated colonies or as a continuous film. Those which contain too much, deposit a portion in the crystalline state, and the crystals, attracting the sugar remaining in solution, gradually weaken the syrup, and render it liable to the same change as when originally made with too little sugar. Such syrups which have undergone fermentation or moulding should never be used for pharmaceutical purposes, as no amount of reboiling can render them fit for use.

The percolation method for preparing syrups has come into general use. For some syrups it is to be preferred to the usual method of heating, and all syrups which contain a volatile principle, or one likely to be injured by heat, are preferably made by *percolation*. The details of the official method are given below. It was first recommended that a small piece of sponge should be used to close the lower orifice of the percolator, but this has advantageously been replaced by purified cotton.

To be successful in using the process, care in several particulars must be exercised. (1) The percolator should be cylindrical or semi-cylindrical, and cone-shaped as it nears the lower orifice. (2) The sugar must be coarse, else it will form into a compact mass, which the liquid cannot permeate. (3) The sponge or pledget must be introduced with care. If pressed too tightly in, it will effectually stop the process; if inserted too loosely, the liquid will pass too rapidly, and will, in consequence, be weak and turbid (not properly filtered). See also *Bull. Pharm.*, 1902, 1248. For a paper on *Fruit Syrups*, see *West. Drug.*, 1902, 182; *Proc. Penn. Pharm. Assoc.*, 1903, 196.

Syrups may be made rapidly (without heat) by putting the ingredients in a mechanical shaker or stirrer and agitating briskly.

"Rock Candy Syrup," the evaporated mother liquor left after crystallizing sugar in the form of large crystals, called "rock candy," has come largely into use in America. It varies much in quality as made by various manufacturers. It usually consists in part of invert sugar, and often contains added glucose. It should never be used for making the official syrups, and it should always be carefully tested before being used for any purpose. (See analyses by L. F. Kebler, in *A. J. P.*, 1895, 143.)

At best, syrups are apt to change, and various measures have been proposed for their preservation, but the best plan is to make small quantities of syrups at a time, and to keep them, unless when wanted for immediate use, in bottles quite full and well stoppered, which should be put in the cellar or other cool place. Glycerin is often used to aid in the preservation of syrups; in special cases this may be advantageous, but the solvent properties of glycerin must be remembered, and the finished preparation may possess properties (due to the glycerin) which are not found in syrups made without glycerin, and which may therefore be injurious in prescriptions. (See *West. Drug.*, 1898, 444.)

SYRUPUS. U. S., Br.

SYRUP [Sirup, Simple Syrup]

Syrupus Simplex; Syrupus Sacchari, s. Albus; Sirop de Sucre, Sirop simple, *Fr.*; Sirupus simplex, *P. G.*; Weisser Sirup, *G.*; Sciroppo semplice, *It.*; Jarabe simple, *Sp.*

"Sucrose, 850 Gm.; Distilled Water, a sufficient quantity to make 1000 cc. Insert into the neck of a percolator of suitable size a pledget of purified cotton, not too tightly, in such a manner that the cotton shall nearly fill the neck of the percolator, and moisten it with a few drops of distilled water. Place the sucrose in the percolator, make its surface level without shaking or jarring, then carefully pour upon it 450 cc. of distilled water, and regulate the flow of the liquid, if necessary, so that it will pass out in rapid drops. Collect the liquid in a 1000 cc. graduated container and return portions to the percolator if necessary until all of the sucrose has been dissolved. Then pass enough distilled water through the cotton to make the product measure 1000 cc. and mix thoroughly.

"Syrup may also be prepared in the following manner: Heat 450 cc. of distilled water to boiling, add the sucrose, and continue the heat cautiously, stirring until the sucrose is dissolved and the syrup has a temperature of 100° C. Then filter it through purified cotton and pass enough distilled water through the cotton to make the product measure 1000 cc. when cold.

"Specific gravity: about 1.313 at 25° C." *U. S.*

"Refined Sugar, 1000 *grammes;* Distilled

Water, sufficient to produce 1500 *grammes.* Heat together until dissolved; add sufficient Distilled Water to produce the required weight. Specific gravity 1.330. *Optical rotation* + 56° to + 58°." *Br.*

This syrup, when properly prepared, is inodorous, of a sweet taste without peculiar flavor, thick, viscid, nearly colorless, and perfectly transparent. It sometimes requires straining through muslin or it may be filtered through a pledget of cotton or often through paper.

Colorless "rock candy" forms an excellent source for pure syrup (the broken crystals can be procured cheaply from the manufacturers), and syrup entirely free from impurities is required in making such preparations as syrup of hydriodic acid, syrup of ferrous iodide, etc. Joseph L. Mayer (*J. A. Ph. A.*, 1916, p 712) shows that it is unfair to assume that commercial glucose is present as an adulterant of syrup, simply because it contains reducing sugar, for in a series of experiments conducted by him, working with both cold process and hot process syrups, the amount of invert sugar found after standing for one year, ranged from about 8 per cent. to over 40 per cent., depending entirely on the length of time of standing. Plette (*J. A. Ph. A.*, 1918, vii, 609) has found that, as far as the likelihood of inversion is concerned, there is no advantage in either the hot or cold process but that the change was less rapid if stored in a cold dark place. The grade of granulated sugar known as "crystal A" or as "Druggists' Dry Granular," is used with success in some parts of the country where it can be readily obtained. It is crystallized from the first runnings from the bone-black filters.

Syrup is very useful in the formulation of pills and mixtures, and in various other pharmaceutical operations in which sugar in solution is required.

The U. S. syrup is practically identical with that formerly official, being a trifle stronger, the sp. gr. being given as 1.313 at 25° C. That of the Br. syrup is 1.330 at 15.5° C., probably adapted to the climate of Great Britain, which is not so cold in winter as is ours, at least in the Northern and Middle States.

SYRUPUS ACIDI CITRICI. U. S.

SYRUP OF CITRIC ACID Syr. Acid. Cit.

Acidi Citri Sirupus; Syrupus Limonis, *Fr. Cod.;* Sirop d'Acide Citrique, Sirop Citrique, *Fr.;* Citronensaüre-sirup, *G.*

"Tincture of Lemon Peel, 10 cc.; Citric Acid, 10 Gm.; Distilled Water, 10 cc.; Syrup, a sufficient quantity to make 1000 cc. Dissolve the citric acid in the distilled water and mix the solution with 950 cc. of syrup. Add the tincture and enough syrup to make the product measure 1000 cc. Mix thoroughly. This preparation must not be dispensed if it has a terebinthinate odor or taste or shows other deterioration.

"Preserve in containers which have previously been washed with boiling water." *U. S.*

Syrup of citric acid is used solely as a vehicle. The British and several of the European Pharmacopœias still direct a syrup made from lemon juice. While this may have some advantage on the question of palatability it is so unstable that the U. S. Pharmacopœia, together with those of France, Belgium, etc., have used an "artificial" lemonade; in some of the Pharmacopœias the name of lemon syrup (or its foreign equivalent) is still retained, but in this country it would be illegal to so designate this preparation. The formula for the former U. S. syrup of lemon is given under *Syrupus Limonis.*

SYRUPUS ACIDI HYDRIODICI. U. S., Br.

SYRUP OF HYDRIODIC ACID Syr. Acid. Hydriod.

"Syrup of Hydriodic Acid contains not less than 1.3 Gm. and not more than 1.5 Gm. of HI in each 100 cc." *U. S.*

Sirop d'Acide Iodhydrique, *Fr.;* Jodwasserstoffsirup, *G.*

"Diluted Hydriodic Acid, 130 cc.; Sucrose, 450 Gm.; Distilled Water, a sufficient quantity to make 1000 cc. Mix the diluted hydriodic acid with 550 cc. of distilled water and dissolve the sucrose in this mixture by agitation. Add sufficient distilled water to make the product measure 1000 cc., and filter." *U. S.*

"Diluted Hydriodic Acid, 100 *grammes;* Distilled Water, 50 *millilitres;* Syrup, sufficient to produce 1000 *millilitres.* Mix." *Br.*

An unprotected aqueous solution of hydriodic acid is frequently unstable, the iodine being in time liberated, rendering it irritant and unfit for internal administration, and as it has been proved that syrup protects the acid efficiently, the 1880 Committee of Revision introduced the Syrup of Hydriodic Acid, with the view of furnishing a preparation which should remain if properly made and carefully preserved, for a long time unchanged. In the U. S. P. the syrup is made by dissolving sugar in diluted hydriodic acid and adding water, it having been proved that diluted hydriodic acid could be made so as to be reasonably permanent (see *Acidum Hydriodicum Dilutum*). Diluted simple syrup has been proved to make a more permanent syrup of hydriodic acid than syrup. Unofficial and proprietary forms of syrup of hydriodic acid are found in the market in which glycerin or glucose is the principal diluting constituent, the reason being given that the presence of these ingredients prevents discoloration. (*Proc. A. Ph. A.*, 1897, 221.)

Properties.—"A transparent, colorless, or not more than pale, straw-colored, odorless, syrupy liquid, having a sweet and acidulous taste. Specific gravity: about 1.185 at 25° C. Mix 5 cc. of Syrup of Hydriodic Acid with a few drops of starch T.S. and add 3 drops of chlorine T.S.: the liquid acquires a deep blue color. No blue color is produced in the syrup by starch T.S. alone (*free iodine*).

"**Assay.**—Place exactly 25 cc. of Syrup of

Hydriodic Acid in a flask, dilute it with 100 cc. of distilled water, add 40 cc. of tenth-normal silver nitrate, agitate the mixture, add 5 cc. of diluted nitric acid and 2 cc. of ferric ammonium sulphate T.S., and determine the residual silver nitrate by titration with tenth-normal potassium thiocyanate. Each cc. of tenth-normal silver nitrate corresponds to 0.01279 Gm. of HI." *U. S.*

Uses.—Syrup of hydriodic acid possesses the general therapeutic properties of the iodides, and is used by various practitioners to obtain alterative effects in *scrofula* and similar disorders. As it contains 1.4 per cent. by weight of absolute hydriodic acid, for practical purposes a teaspoonful may be said to represent about 0.75 of a grain of iodine or a little over 1 grain of potassium iodide. It is evident that the doses in which it is usually administered—from twenty to forty minims (1.3–2.5 cc.)—are too small. It should be well diluted at the time of administration, to prevent the possibility of injury to the teeth.

Dose, from one to two fluidrachms (3.75–7.5 cc.).

SYRUPUS AROMATICUS. Br.

AROMATIC SYRUP

Sirop Aromatique, *Fr.;* Aromatischer Sirup, *G.*

"Tincture of Orange, 250 *millilitres;* Cinnamon Water, 250 *millilitres;* Syrup, 500 *millilitres.* Mix the Tincture of Orange and Cinnamon Water; shake the mixture with a little *powdered talc;* filter; add the Syrup." *Br.*

This preparation of the Br. Ph., 1898, is practically a simple elixir (see *Elixir Aromaticum*); it has been introduced mainly as a vehicle or adjuvant.

SYRUPUS AURANTII. U. S., Br.

SYRUP OF ORANGE Syr. Aurant.

Syrup of Orange Peel; Sirop d'Ecorce d'Orange amère, *Fr.;* Sirupus Aurantii Corticis, *P. G.;* Pomeranzenschalensirup, Orangenschalensyrup, *G.;* Sciroppo di arancio, *It.;* Jarabe de corteza de naranja, *Sp.*

"Tincture of Sweet Orange Peel, 50 cc.; Citric Acid, 5 Gm.; Purified Talc, 15 Gm.; Sucrose, 820 Gm.; Distilled Water, a sufficient quantity to make 1000 cc. Triturate the purified talc with the tincture and citric acid, and gradually add 400 cc. of distilled water. Then filter, returning the first portions of the filtrate until it becomes clear, and wash the mortar and filter with enough distilled water to make the filtrate measure 450 cc. Dissolve the sucrose in this filtrate by agitation, and add enough distilled water to make the product measure 1000 cc. Mix thoroughly and strain. This preparation must not be dispensed if it has a terebinthinate odor or taste or shows other deterioration.

"Alcohol content, by volume, 2 to 5 per cent." *U. S.*

"Tincture of Orange, 125 *millilitres;* Syrup, sufficient to produce 1000 *millilitres.* Mix." *Br.*

The present U. S. process is an improvement over preceding formulas as the flavor is derived from the tincture of fresh orange peel and the alkaline magnesium carbonate of the U. S. P. VIII, which modified the flavor, has been replaced by inert talc, the latter being used as a distributing and filtering medium. The British preparation, which is a mere mixture of the tincture with syrup, is inferior. The syrup has an agreeable, slightly acid flavor, for which it is alone employed. For a process by E. E. Williams, using powdered pumice to disintegrate the orange peel, see *D. C.*, 1898, 125.

SYRUPUS AURANTII FLORUM. U. S. (Br.)

SYRUP OF ORANGE FLOWERS Syr. Aurant. Flor.

Syrupus Aurantii Floris, *Br.;* Sirop de Fleur d'Oranger, *Fr.;* Pomeranzenblüthensirup, *G.;* Jarabe de azahar, *Sp.*

"Orange Flower Water, 225 cc.; Sucrose, 850 Gm.; Distilled Water, a sufficient quantity to make 1000 cc. Mix the orange flower water with 225 cc. of distilled water, dissolve the sucrose in the mixture by agitation, without heat, and add sufficient distilled water to make the product measure 1000 cc. Mix thoroughly and strain. Syrup of Orange Flower Water may also be made in the following manner: Prepare a percolator in the manner described under *Syrupus.* Pour the mixture of orange flower water and water upon the sucrose, return the first portions of percolate until it runs through clear, and when all of the liquid has run through, follow it with distilled water until the sucrose is dissolved and the product measures 1000 cc. Mix thoroughly." *U. S.*

"Orange-flower water of commerce, undiluted, 150 *millilitres;* Refined Sugar, 300 *grammes;* Syrup, sufficient to produce 1000 *millilitres.* Mix the orange-flower water with the Refined Sugar in a closed vessel; stand in a moderately warm place, shaking occasionally till dissolved; then add sufficient Syrup to produce the required volume." *Br.*

The second U. S. process, by percolation, will be preferable here. This syrup is used chiefly for flavoring mixtures.

SYRUPUS CALCII LACTOPHOSPHATIS. Br.

SYRUP OF CALCIUM LACTOPHOSPHATE Syr. Calc. Lactophos.

Sirop de Lactophosphate (phospholactate) de chaux, *Fr.;* Calciumphospholactatsirup, *G.;* Jarabe de lactofosfato calcico, *Sp.*

"Calcium Lactate, 75 *grammes;* Concentrated Phosphoric Acid, 45 *millilitres;* Orange-flower water of commerce, undiluted, 25 *millilitres;* Refined Sugar, 700 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Mix the Calcium Lactate with four hundred millilitres of the Distilled Water, add the Concentrated Phosphoric Acid and stir until solution is complete, then add the orange-flower water, dissolve the Refined Sugar in the mixture without the aid of heat, and add sufficient Distilled Water to produce the required volume; filter." *Br.*

The U. S. no longer recognizes this syrup but a similar preparation has been admitted to the N. F. (see Part III).

This preparation is based upon the fact that freshly precipitated calcium phosphate is soluble in the presence of lactic acid. The calcium phosphate which is at first precipitated by the action between calcium lactate and the first portion of phosphoric acid is redissolved as more acid is added. The syrup sometimes deposits a gelatinous precipitate on keeping, which can usually be avoided by the addition of a small amount of hydrochloric acid. Calcium lactophosphate in the solid form is also recognized by the N. F. and is described elsewhere.

Dose, from one-half to one fluidrachm (2–4 cc.), representing from three to six grains of the lime salt.

Off. Prep.—Elixir Cinchonæ Alkaloidorum, Ferri, et Calcii Lactophosphatis, *N. F.;* Syrupus Calcii Lactophosphatis et Ferri, *N. F.*

SYRUPUS CASCARÆ AROMATICUS. Br.

AROMATIC SYRUP OF CASCARA

Sirop aromatique de Cascara Sagrada, *Fr.;* Aromatischer Amerikanisch-Faulbaumrindensirup, *G.*

"Liquid Extract of Cascara Sagrada, 400 *millilitres;* Tincture of Orange, 100 *millilitres,* Alcohol (90 per cent.), 50 *millilitres;* Cinnamon Water, 150 *millilitres;* Syrup, sufficient to produce 1000 *millilitres.* Mix." *Br.*

This was a new syrup in the Br. Pharm., 1898. It forms a convenient means of administering cascara, the alcohol being added to aid its preservation.

Dose, from one-half to two fluidrachms (1.8–7.5 cc.).

SYRUPUS CHLORAL. Br.

SYRUP OF CHLORAL

Sirop de Chloral, *Fr.;* Chloralhydratsirup, *G.;* Jarabe de hidrato de cloral, *Sp.*

"Chloral Hydrate, 200 *grammes;* Distilled Water, 200 *millilitres;* Syrup, sufficient to produce 1000 *millilitres.* Dissolve the Chloral Hydrate in the Distilled Water; add sufficient Syrup to produce the required volume. 10 millilitres of this Syrup contain 2 grammes of Chloral Hydrate; 1 fluid drachm contains 10.9 grains." *Br.*

Dose, one to two fluidrachms (3.75–7.5 cc.).

SYRUPUS CODEINÆ PHOSPHATIS. Br.

SYRUP OF CODEINE PHOSPHATE

Sirop de Codéine, *Fr.;* Kodeinsirup, *G.;* Sciroppo di codeina, *It.;* Jarabe de codeina, *Sp.*

"Codeine Phosphate, 5 *grammes;* Distilled Water, 15 *millilitres;* Syrup, sufficient to produce 1000 *millilitres.* Dissolve the Codeine Phosphate in the Distilled Water; add sufficient Syrup to produce the required volume. 10 millilitres of this Syrup contain 0.05 gramme of Codeine Phosphate; 1 fluid drachm contains 0.27 grain." *Br.*

This syrup is intended to furnish a convenient method of using codeine phosphate. A syrup of codeine, made from the sulphate is official in the N. F. (see *Syrupus Codeinæ,* Part III).

Dose, one-half to two fluidrachms (1.8–7.5 cc.).

SYRUPUS FERRI IODIDI. U. S., Br.

SYRUP OF FERROUS IODIDE Syr. Ferr. Iod. [Ferri iodidi syrupus P. I.]

"Syrup of Ferrous Iodide contains not less than 6.5 Gm. and not more than 7.5 Gm. of FeI_2 in each 100 cc., representing approximately 5 per cent. of FeI_2, by weight." *U. S.*

Syrup of Iodide of Iron; Syrupus Ferri Iodati Gallicus, *Fr. Cod.;* Sirop d'Iodure de fer, *Fr.;* Syrupus Ferri Jodati, *P. G.;* Eisenjodürsirup, *G.;* Sciroppo di protojoduro di ferro, *It.;* Jarabe de yoduro ferroso, *Sp.*

"Iron in the form of fine, bright wire, 20 Gm.; Iodine, 60 Gm.; Hypophosphorous Acid, 5 cc.; Sucrose, 850 Gm.; Distilled Water, a sufficient quantity to make 1000 cc. Place the iron in a flask having a capacity of about 500 cc., add the iodine and 200 cc. of distilled water, and shake the mixture occasionally, checking the reaction if necessary by placing the flask in cold water. When the liquid has acquired a green color and has lost the odor of iodine, heat it to boiling, and dissolve 100 Gm. of sucrose in hot liquid. Filter the solution at once into a flask, graduated to 1000 cc. and containing the remainder of the sucrose, and rinse the flask containing the iron with 240 cc. of hot distilled water, in divided portions, passing the rinsings successively through the filter. Agitate the mixture until the sucrose is dissolved, warming if necessary, cool to 25° C., add the hypophosphorous acid and enough distilled water to make the product measure 1000 cc. Mix well and strain." *U. S.*

"Iron, in wire, 15.0 *grammes;* Iodine, 41.4 *grammes;* Distilled Water, 75.0 *millilitres;* Glucose, 100.0 *grammes;* Syrup, sufficient to produce 1000.0 *grammes.* Add the Iron and the Iodine to fifty millilitres of the Distilled Water in a flask; shake occasionally, cooling if necessary. When the reaction is completed add the Glucose, heat on a water-bath for five minutes, mix, and while still hot filter into a tared vessel containing part of the Syrup. Rinse the flask and wash the filter-paper with the remaining twenty-five millilitres of the Distilled Water heated to boiling; add sufficient Syrup to produce the required weight." *Br.*

W. G. Toplis (*Proc. Penna. Pharm. Assn.,* 1916, p. 243) substitutes *Ferrum Reductum* for the card teeth officially directed in this process, with the result that the solution can be effected, ready for filtration, in less than ten minutes, working with the official proportions.

Properties.—"A transparent, pale yellowish-green, syrupy liquid, having a sweet, strongly ferruginous taste and slightly acid reaction. Specific gravity: about 1.37 at 25° C. Add a few drops of potassium ferricyanide T.S. to

5 cc. of Syrup of Ferrous Iodide: a blue precipitate is produced. Mix 5 cc. of Syrup of Ferrous Iodide with a few drops of starch T.S. and add three drops of chlorine T.S.; the liquid acquires a deep blue color. No blue color is produced in Syrup of Ferrous Iodide by starch T.S. alone (*free iodine*).

"**Assay.**—Place exactly 10 cc. of Syrup of Ferrous Iodide in a flask, dilute it with 30 cc. of distilled water, add 50 cc. of tenth-normal silver nitrate and 5 cc. of nitric acid, and heat on a water bath until the precipitate of silver iodide is yellow. Cool, add 2 cc. of ferric ammonium sulphate T. S., and determine the residual silver nitrate by titration with tenth-normal potassium thiocyanate. Each cc. of tenth-normal silver nitrate corresponds to 0.01548 Gm. of FeI_2.

"Preserve in completely filled, tightly-stoppered bottles." *U. S.*

"When 5 grammes of the Syrup are diluted with 20 millilitres of *water*, acidified with *nitric acid* and mixed with 20 millilitres of *N/10 solution of silver nitrate*, not less than 3.5 or more than 4.2 millilitres of *N/10 solution of ammonium thiocyanate* are required to produce a permanent red coloration, *solution of ferric sulphate* being used as indicator, corresponding to not less than 4.9 and not more than 5.1 grammes of ferrous iodide, FeI_2, in 100 grammes of the Syrup. 10 millilitres of this Syrup contain about 0.7 gramme of ferrous iodide; 1 fluid drachm contains 3.75 grains. It is of the strength required by the International Agreement, and is approximately of two-thirds the strength of the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

When the syrup is concentrated it becomes brown, and when evaporated to dryness forms a mass which may be called *saccharine ferrous iodide*, and which is not entirely soluble again, a little ferric oxide being left. This saccharine iodide, being protected by the sugar it contains, is not liable to the objections which apply to the pure solid salt (see *Ferrous Iodide*, Part II), and may be made into pills. (See *U. S. D.*, 19th ed., p. 1225, for *Ferri Iodidum Saccharatum.*)

Notes on examination of market samples and conclusions and recommendations as to methods of preservation, keeping qualities, etc., have been published by the following authors: L. A. Brown, *Proc. Ky. Ph. Assn.*, 1914, 61; W. C. Alpers, *J. A. Ph. A.*, 1914, 420; G. M. Beringer, *J. A. Ph. A.*, 1914, 970.

Uses.—Syrup of ferrous iodide combines the alterative action of iodine with the hematinic action of iron. It is a popular remedy in chronic types of *tuberculosis*, especially in the *scrofula* of children. It has, however, no advantage over an extemporaneous combination of an iodine with ferruginous tonic, and has the drawback that the dose of either ingredient cannot be altered singly.

Dose, for an adult, ten to forty minims (0.6–2.5 cc.); for a child of two years, two to eight minims (0.12–0.5 cc.).

SYRUPUS FERRI PHOSPHATIS. Br.

SYRUP OF FERROUS PHOSPHATE

Sirop de Phosphate de Fer, *Fr.;* Eisenphosphatsirup, *G.*

"Iron, in wire, 8.6 *grammes;* Concentrated Phosphoric Acid, 62.5 *millilitres;* Syrup, 700.0 *millilitres;* Distilled Water, sufficient to produce 1000.0 *millilitres.* Dilute the Concentrated Phosphoric Acid with an equal volume of Distilled Water in a small flask; add the Iron and heat very gently until dissolved. Filter into the Syrup, and pass sufficient Distilled Water through the filter to produce the required volume. 10 millilitres of this Syrup contain 0.17 gramme of anhydrous ferrous phosphate; 1 fluid drachm contains 1 grain." *Br.*

R. Wright (*P. J.*, 1893, 191) improved the formula, and this method is superior to the former cumbersome process of preparing a precipitate of ferric phosphate, and dissolving it in phosphoric acid. The syrup is a solution of ferrous phosphate protected by sugar. The sp. gr. is about 1.270. (Umney.) For its properties and uses, see *Ferri Phosphas.*

Dose, from one to two fluidrachms (3.75–7.5 cc.).

SYRUPUS FERRI PHOSPHATIS CUM QUININA ET STRYCHNINA. Br.

SYRUP OF PHOSPHATE OF IRON WITH QUININE AND STRYCHNINE

Easton's Syrup; Sirop Tonique d'Easton, *Fr.;* Eisenphosphatsirup mit Chinin und Strychnin, Eastonscher Sirup, *G.*

"Iron, in wire, 8.60 *grammes;* Concentrated Phosphoric Acid, 62.50 *millilitres;* Strychnine, in powder, 0.57 *gramme;* Quinine Sulphate, 14.80 *grammes;* Syrup, 700.00 *millilitres;* Distilled Water, sufficient to produce 1000.00 *millilitres.* Dilute the Concentrated Phosphoric Acid with an equal volume of Distilled Water in a small flask; add the Iron and heat very gently until dissolved; add the solution to the Strychnine and Quinine Sulphate previously triturated with thirty millilitres of the Distilled Water; when solution is complete filter the Syrup, and pass sufficient Distilled Water through the filter to produce the required volume. 10 millilitres of this Syrup contain 0.17 gramme of anhydrous ferrous phosphate, 0.148 gramme of Quinine Sulphate, and 0.057 gramme of Strychnine; 1 fluid drachm contains 1 grain of anhydrous ferrous phosphate, 4/5 grain of Quinine Sulphate, and 1/32 grain of Strychnine." *Br.*

This syrup is not official in the U. S. P. but a similar preparation is recognized by the N. F. (see Part III).

Uses.—This syrup has the medicinal activities of its ingredients, but is a very ineligible preparation, and has not even an agreeable taste to excuse its polypharmacy. It is known as *Easton's Syrup, Aitkin's Syrup, Syrup of* *the Three Phosphates,* and *Syrup of Triple Phosphates.*

Dose, one to two fluidrachms (3.75–7.5 cc.).

SYRUPUS GLUCOSI. Br.

SYRUP OF GLUCOSE

"Glucose, 250 *grammes;* Syrup, 500 *grammes.* Mix, by the aid of gentle heat." *Br.*

Sirop de Glycose, *Fr.;* Glykosesirup, *G.*

This was a new preparation of the Br. Ph., 1898. It may be used as a vehicle for syrups which contain chemical salts liable to discoloration through the action of light, but its principal use is to take the place of *treacle* or molasses so much used in British pharmacy as a pill excipient. (See *Pilulæ.*)

SYRUPUS IPECACUANHÆ. U. S.

SYRUP OF IPECAC Syr. Ipecac.

Sirop d'Ipécacuanha, *Fr. Cod.;* Sirupus Ipecacuanhæ, *P. G.;* Brechwurzelsirup, Ipecacuanhasirup, *G.;* Sciroppo di ipecacuanha, *It.;* Jarabe de Ipecacuana, *Sp.*

"Fluidextract of Ipecac, 70 cc.; Glycerin, 100 cc.; Syrup, a sufficient quantity to make 1000 cc. Mix the fluidextract with the glycerin, and add enough syrup to make the product measure 1000 cc. Mix thoroughly.

"Alcohol content, by volume, 1.5 to 2 per cent." *U. S.*

If strictly official fluidextract of ipecac is used in making this syrup, and the process is carried out in all its details, the syrup will remain transparent; but with fluidextracts which are not carefully made it may be necessary to allow the diluted fluidextract in the official process for making this syrup to remain for two or three days in a cool place before filtering, and adding to the sugar.

Although this syrup possesses all the virtues of ipecac, it is used almost exclusively as a nauseating expectorant in *acute bronchitis.*

Dose, for an adult, as an expectorant, from fifteen to thirty minims (0.9–1.8 cc.); as an emetic, half a fluidounce (15 cc.).

SYRUPUS LIMONIS. Br.

SYRUP OF LEMON

Syrupus Succus Citri; Sirop de Limon (de Citron), Sirop de suc de Limon (de citron), *Fr.;* Citronensirup, Citronensaftsirup, *G.;* Jarabe de limon, *Sp.*

"Lemon Peel, in thin slices or grated, 20 *grammes;* Alcohol (90 per cent.), *a sufficient quantity;* Lemon Juice, 500 *millilitres;* Refined Sugar, 760 *grammes.* Macerate the Lemon Peel in thirty millilitres of the Alcohol for seven days; press; filter; add sufficient of the Alcohol to produce forty millilitres. In the Lemon Juice, clarified by subsidence or filtration, dissolve the Refined Sugar by the aid of gentle heat; cool; add the forty millilitres of alcoholic liquid; mix." *Br.*

The U. S. P. 1880 syrup of lemon was dropped at the 1890 revision; as it is frequently used, the process is appended.

"Lemon Juice, recently expressed and strained, *forty parts;* Fresh Lemon Peel, *two parts;* Sugar, in coarse powder, *sixty parts;* Water *a sufficient quantity,* to make *one hundred parts.* Heat the Lemon Juice to the boiling point; then add the Lemon Peel, and let the whole stand, closely covered, until cold. Filter, add enough Water through the filter to make the filtrate weigh *forty parts,* dissolve the Sugar in the filtered liquid by agitation, without heat, and strain." *U. S.* 1880.

The addition of lemon peel to the preparation is an improvement, but the internal white portion of the peel should be carefully removed before adding to the hot lemon juice, or the finished syrup will have a bitter taste. (See *Limonis Cortex.*) This syrup forms a cooling and grateful addition to beverages in *febrile complaints,* and serves to conceal the taste of saline purgatives in solution.

SYRUPUS PICIS PINI. U. S.

SYRUP OF PINE TAR Syr. Pic. Pin. [Syrupus Picis Liquidæ U. S. P. IX, Syrup of Tar]

Syrupus Piceus; Sirop de Goudron, *Fr.;* Theersirup, *G.;* Jarabe de Brea, *Sp.*

"Rectified Oil of Tar, 1 cc.; Sucrose, 850 Gm.; Water, a sufficient quantity to make 1000 cc. Mix the oil with 450 cc. of water and agitate the mixture frequently during fifteen minutes. Then set aside for twenty-four hours, shaking it occasionally during that time. Filter, dissolve the sucrose in the clear filtrate, and add sufficient water to make the product measure 1000 cc. Mix thoroughly and strain." *U. S.*

This syrup has been improved by substituting in the place of tar itself, which was used in the U. S. IX, the liquid distillate known as oil of tar, which probably represents all the therapeutic virtues of the tar. Theoretically a teaspoonful of the syrup should represent approximately 1 minim of the oil of tar, but as this is not completely soluble in water and the undissolved portion is removed by filtration, the amount of active ingredient, will be somewhat less.

The change in this formula was made after considerable experimentation, in which it was found that when made from oil of tar the preparation possesses a pronounced odor and taste of tar, and the after taste is free from acridity.

Comparative tests showed the proportion of dissolved principles of tar to be greater in the preparation made from the oil by the present method, than in the preparation as formerly made from tar itself.

Syrup of tar is a popular stimulating expectorant in the milder forms of sub-acute or chronic *bronchitis.* In the doses ordinarily employed the quantity of active ingredient is, however, so small that the preparation can have scarcely any effect except as a flavoring agent.

Dose, from one to two fluidrachms (3.75–7.5 cc.).

SYRUPUS PRUNI VIRGINIANÆ.
U. S., Br.

SYRUP OF WILD CHERRY Syr. Prun. Virg.

Syrup of Virginian Prune, *Br.* 1898; Sirop d'Ecorce de Cerisier, *Fr.;* Wildkirschenrindensirup, *G.*

"Wild Cherry, in coarse powder, 150 Gm.; Sucrose, 800 Gm.; Glycerin, 50 cc.; Water, a sufficient quantity to make 1000 cc. Mix the glycerin with 200 cc. of water, moisten the wild cherry with 100 cc. of this mixture, pack it in a cylindrical percolator and pour the remaining 150 cc. of menstruum upon it. When this has disappeared from the surface of the drug, add enough water to saturate the powder and leave a stratum above it. Close the lower orifice, cover the percolator, and macerate the drug for twenty-four hours. Then allow the percolation to proceed slowly, allowing the percolate to drop into the sucrose contained in a bottle graduated to 1000 cc. and having a capacity of 2000 cc. Add enough water, as the menstruum, to make the combined sucrose and percolate measure 1000 cc., stopper the bottle, and dissolve the sucrose by agitation without heat. Restore the volume by adding enough water to make the product measure 1000 cc., and strain.

"Preserve in tightly-stoppered bottles, in a cool place." *U. S.*

"Wild Cherry Bark, in No. 20 powder, 150 *grammes;* Refined Sugar, in coarse powder, 750 *grammes;* Glycerin, 65 *millilitres;* Distilled Water sufficient to produce 1000 *millilitres.* Moisten the Wild Cherry Bark with Distilled Water; set aside for twenty-four hours in a closed vessel; pack in a percolator; percolate with Distilled Water until four hundred and fifty millilitres have been collected; dissolve the Refined Sugar in the percolated liquid, without heat; add the Glycerin and sufficient Distilled Water to produce the required volume." *Br.*

The British Pharmacopœia introduced this syrup into the 1898 edition. The process is modelled after the U. S. formula.

The U. S. process affords a handsome syrup with the virtues of the bark unimpaired by the injurious effects of heat. It is based upon a formula proposed by Procter and Turnpenny in *A. J. P.,* xiv, 27. The introduction of the glycerin into the receiving bottle instead of mixing it with the menstruum was dropped in the process of the U. S. P. The glycerin is not needed in the menstruum to increase the astringency of the syrup but it serves a useful purpose in keeping the infusion from decomposing and precipitating a reddish, insoluble substance in the receiving bottle. This syrup should never be made by adding fluidextract to simple syrup, as the fluidextract is likely to vary greatly in quality, and frequently precipitates when mixed with syrup, the syrup when made by the above process is far superior in flavor. It is largely used as a vehicle for cough mixtures.

Dose, one to four fluidrachms (3.75–15.0 cc.).

SYRUPUS RHEI. U. S., Br.

SYRUP OF RHUBARB Syr. Rhei

Sirop de Rhubarbe, *Fr.;* Sirupus Rhei, *P. G.;* Rhabarbersirup, Rhabarbersaft, *G.*

"Fluidextract of Rhubarb, 100 cc.; Spirit of Cinnamon, 4 cc.; Potassium Carbonate, 10 Gm.; Water, 50 cc.; Syrup, a sufficient quantity to make 1000 cc. Mix the spirit of cinnamon with the fluidextract, add the potassium carbonate, previously dissolved in the water, and add to this mixture enough syrup to make the product measure 1000 cc.

"Alcohol content, by volume, 5 to 6 per cent." *U. S.*

"Rhubarb, in No. 20 powder, 70.0 *grammes;* Oil of Coriander, 0.5 *millilitre;* Refined Sugar, 840.0 *grammes;* Alcohol (90 per cent.), 280.0 *millilitres;* Distilled Water, sufficient to produce 1000.0 *millilitres.* Mix two hundred and seventy millilitres of the Alcohol with three times its volume of Distilled Water. Moisten the Rhubarb with seventy millilitres of this diluted alcohol and set aside for twenty-four hours in a closed vessel; pack in a percolator; pass the remainder of the diluted alcohol slowly through the moistened powder; evaporate the percolate to four hundred and seventy-five grammes; filter; dissolve the Refined Sugar in the filtrate by the aid of heat; cool; add the Oil of Coriander dissolved in ten millilitres of the Alcohol; mix, and finally add sufficient Distilled Water to produce the required volume." *Br.*

The Br. process is a troublesome and imperfect method.

The U. S. syrup differs from that official before 1890 in several particulars, and, in our opinion, it is greatly improved; the activity of the rhubarb and the corrigent effects of the cinnamon are both secured without impairing the appearance of the finished syrup, while the simplicity of the manipulation must commend the process to all. In the Br. Pharm., 1914, oil of coriander replaced coriander fruit official in the former pharmacopœia.

The official syrup is a mild cathartic, adapted for use with infants, to whom it may be given in the dose of a fluidrachm (3.75 cc.).

Dose, for adults, two to three fluidrachms (7.5–11.25 cc.).

SYRUPUS RHEI AROMATICUS. U. S.

AROMATIC SYRUP OF RHUBARB Syr. Rhei Arom.
[Spiced Syrup of Rhubarb]

Sirop de Rhubarbe aromatique, *Fr.;* Gewürzter Rhabarbersaft, *G.*

"Aromatic Tincture of Rhubarb, 150 cc.; Potassium Carbonate, 1 Gm.; Syrup, a sufficient quantity to make 1000 cc. Dissolve the potassium carbonate in the tincture and add to the mixture enough syrup to make the product measure 1000 cc. Mix thoroughly.

"Alcohol content, by volume, 6 to 7 per cent." *U. S.*

A small amount of alkali is added here to prevent the syrup from becoming turbid.

The *aromatic syrup of rhubarb* is a warm stomachic laxative, too feeble for adult cases, chiefly used for the bowel complaints of infants, which are so frequent in our cities during the summer season. This preparation, or one analogous to it, has been long in use, under the name of *spiced syrup of rhubarb*. The dose for an infant with *diarrhea* is a fluidrachm (3.75 cc.), repeated every two hours until the passages indicate by their color that the medicine has operated. It should be borne in mind that the syrup, as prepared by the present formula, contains about 7 per cent. alcohol, which, though not injurious in most cases in which this syrup is used, might render it too stimulating in the very young infant.

Dose, one to three fluidrachms (3.75–11.25 cc.).

SYRUPUS RHŒADOS. Br.

SYRUP OF RED POPPY

Sirop de Coquelicot, *Fr. Cod.;* Sirop de Pavot rouge, *Fr.;* Klatschrosensaft, *G.*

"Red-Poppy Petals, 260 *grammes;* Refined Sugar, 720 *grammes;* Alcohol (90 per cent.), 50 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Add the Red-poppy Petals gradually to four hundred millilitres of Distilled Water kept hot upon a water-bath, stir frequently, and afterwards, the vessel being removed, infuse for twelve hours. Then press out the liquid; strain; add the Refined Sugar, and dissolve by the aid of heat. When nearly cold, add the Alcohol, and sufficient Distilled Water to produce the required volume." *Br.*

The object of introducing the petals into water heated by a water bath is that they may shrink by being scalded, as otherwise they could not be completely immersed in the quantity of water directed. After this has been accomplished, they should be immediately removed from the fire, lest the liquor become too thick and ropy. The fine red color of this syrup is its only recommendation. It is very liable to ferment; according to Enders, this can be obviated by evaporating the recently prepared syrup to dryness, keeping the powdered residue in well-stoppered bottles, and dissolving it, as wanted, in four-fifths of its weight of water.

Dose, as stated in the Br. Pharmacopœia, one-half to one fluidrachm (1.8–3.75 cc.).

SYRUPUS ROSÆ. Br.

SYRUP OF ROSE

Syrup of Roses; Syrupus Rosarum Rubrarum; Syrup of Red Rose; Sirop de Rose rouge, *Fr.;* Rosensirup, *G.*

Syrup of Rose was deleted from the U. S. P. IX, but the process was introduced into the National Formulary (see Part III).

"Dried Red-Rose Petals, 50 *grammes;* Refined Sugar, *a sufficient quantity;* Distilled Water, boiling, 500 *millilitres.* Infuse the Red-Rose Petals in the Distilled Water for two hours; strain; press; heat the infusion to the boiling point; filter; add to the filtrate twice its weight of Refined Sugar and dissolve by the aid of heat." *Br.*

Syrup of rose is mildly astringent, but is valued most for its fine red color, on account of which it is occasionally added to mixtures. The color is developed by the small amount of diluted sulphuric acid which is added.

Dose, a fluidrachm (3.75 cc.).

SYRUPUS SARSAPARILLÆ COMPOSITUS. U. S.

COMPOUND SYRUP OF SARSAPARILLA

Syr. Sarsap. Co.

Syrupus Sudorificus; Sirop de Salsepareille composé, *Fr. Cod.;* Sirop de Cuisinier, Sirop sudorifique, *Fr.;* Zusammengesetzter Sarsaparillsirup, *G.;* Jarabe de zarzaparrilla compuesto, *Sp.*

"Fluidextract of Sarsaparilla, 200.0 cc.; Fluidextract of Glycyrrhiza, 15.0 cc.; Oil of Sassafras, 0.2 cc.; Oil of Anise, 0.2 cc.; Methyl Salicylate, 0.2 cc.; Alcohol, 19.4 cc.; Syrup, 765.0 cc.; to make about 1000 cc. Mix the fluidextracts and add the alcohol, in which the methyl salicylate and the oils have been dissolved. Gradually add this solution to the syrup, and mix thoroughly.

"Alcohol content, by volume, 7.5 to 8.5 per cent." *U. S.*

In the original edition of the U. S. Pharmacopœia, published in 1820, a process for a syrup of sarsaparilla was adopted, intended to present the famous French *sirop de cuisinier.* This process has been variously modified from time to time, but the present preparation possesses any possible therapeutic virtues of the original preparation.

The preparation for years contained senna as one of its active constituents. This has now been omitted as unnecessary and even objectionable.

Uses.—The day has gone by when compound syrup of sarsaparilla is regarded by the medical profession as an active therapeutic agent. It has, however, a wide and proper use as a vehicle especially for the iodides and other saline drugs. It is also widely employed, especially in extemporaneous mixtures, to mitigate the unpleasant flavor of castor oil.

Kennedy (*Ph. Rec.,* 1888, 201) has shown that corrosive sublimate invariably yields a precipitate with this syrup, which he asserts may be prevented by the addition of sodium chloride. Potassium-mercuric iodide, which will be formed in the very frequently prescribed extemporaneous mixtures of corrosive sublimate, potassium iodide and compound syrup of sarsaparilla, does not form any such precipitate.

Off. Prep.—Syrupus Bromidorum, *N. F.*

SYRUPUS SCILLÆ, U. S., Br.

SYRUP OF SQUILL Syr. Scill.

Syrupus Aceti Scillæ; Sirop de Scille, *Fr.;* Meerzwiebelsirup, *G.*

"Vinegar of Squill, 450 cc.; Sucrose, 800 Gm.; Water, a sufficient quantity to make 1000 cc. Dissolve the sucrose in the vinegar of squill with the aid of a gentle heat, strain the syrup, and, when cold, add enough water through the strainer to make the product measure 1000 cc. Mix thoroughly." *U. S.*

"Vinegar of Squill, 175 *millilitres;* Refined Sugar, 650 *grammes;* Distilled Water, sufficient to produce 1000 *grammes.* Mix the Vinegar of Squill with an equal volume of Distilled Water. In the mixture dissolve the refined Sugar by the aid of gentle heat; add sufficient Distilled Water to produce the required weight." *Br.*

The heating should be performed as quickly as possible, to prevent undue loss of acetic acid.

The difference between the U. S. and Br. syrups is not so great as would seem from their formulas, because the British vinegar of squill is much stronger than the American.

This syrup is much employed as an expectorant, especially in combination with a solution of tartarized antimony. It is incompatible with ammonium carbonate, but not with ammonium chloride.

Dose, about from one-half to one fluidrachm (2–4 cc.).

SYRUPUS SCILLÆ COMPOSITUS. U. S.

COMPOUND SYRUP OF SQUILL Syr. Scill. Co. [Hive Syrup]

Coxe's Hive Syrup; Sirop de Scille composé, *Fr.;* Zusammengesetzter Meerzwiebelsirup, *G.*

"Fluidextract of Squill, 80 cc.; Fluidextract of Senega, 80 cc.; Antimony and Potassium Tartrate, 2 Gm.; Sucrose, 720 Gm.; Distilled Water, a sufficient quantity to make 1000 cc. Dissolve the antimony and potassium tartrate in 360 cc. of distilled water, add the fluidextracts, and allow the mixture to stand for twelve hours with occasional shaking. Filter, dissolve the sucrose in the clear filtrate by agitation, and add sufficient distilled water to make the product measure 1000 cc. Mix thoroughly and strain.

"Alcohol content, by volume, 7 to 8 per cent." *U. S.*

This is intended as a substitute for the popular preparation called *Coxe's hive syrup,* from which it differs chiefly in containing sugar instead of honey. Prepared as originally directed it invariably fermented from the want of sufficient concentration. The present formula is a decided improvement, fluidextracts of squill and senega being used. Percolation has been found very well adapted for dissolving the sugar and producing a transparent syrup. The present U. S. P. process has the merit of simplicity, but, unfortunately, the fluidextract of squill is never a wholly satisfactory preparation.

Compound syrup of squill was introduced into medicine a century ago by Dr. J. Redmond Coxe as a remedy for *croup,* which was then called "hives." It has been official in the U. S. since 1840. It has expectorant and diaphoretic properties, both of which depend upon its nauseating action, but in our opinion the use of drugs possessing such powerful systemic actions as do squill and antimony for their nauseating effect, especially in children, is not to be commended. The dose of this syrup for children is from two to twenty minims (0.12–1.3 cc.), according to the age, and it may be repeated in cases of croup every fifteen or twenty minutes until it causes vomiting.

Dose, for adults as an expectorant, from twenty to thirty minims (1.3–1.8 cc.).

SYRUPUS SENEGÆ. U. S.

SYRUP OF SENEGA Syr. Seneg.

Sirop de Polygala, *Fr.;* Sirupus Senegae, *P. G.;* Senegasirup, *G.*

"Fluidextract of Senega, 200 cc.; Ammonia Water, 10 cc.; Syrup, a sufficient quantity to make 1000 cc. Mix the ammonia water with the fluidextract, add the syrup, and mix well.

"Alcohol content, by volume, 9 to 10 per cent." *U. S.*

The syrup affords a very convenient mode of exhibiting senega in pectoral complaints. Owing to the pectinous principle present in senega, the syrup made directly from the root as in the process of 1870 was always turbid. It has been frequently pointed out that the addition of an alkali renders the syrup transparent, and the 1890 process directed the use of a small quantity of ammonia water, although, if the fluidextract of senega which contains alkali be used as in the U. S. P. X, this addition is unnecessary. This syrup may be given as a nauseating expectorant.

Dose, one or two fluidrachms (3.75 or 7.5 cc.).

SYRUPUS SENNÆ. U. S., Br.

SYRUP OF SENNA Syr. Senn.

Sirop de Séné, *Fr.;* Sirupus Sennae, *P. G.;* Sennasirup, *G.*

"Fluidextract of Senega, 250 cc.; Oil of Coriander, 5 cc.; Sucrose, 635 Gm.; Water, a sufficient quantity to make 1000 cc. Mix the oil of coriander with the fluidextract and gradually add 330 cc. of water. Allow the mixture to stand for twenty-four hours in a cool place, with occasional shaking, filter, and pass enough water through the filter to obtain 580 cc. of filtrate. Dissolve the sucrose in this liquid, and add sufficient water to make the product measure 1000 cc. Mix well and strain.

"Alcohol content, by volume, 5.5 to 6.75 per cent." *U. S.*

"Senna Leaves, 440.0 *grammes;* Oil of Coriander, 0.2 *millilitre;* Alcohol (90 per cent.), 2.0 *millilitres;* Refined Sugar, 540.0 *grammes;* Alcohol (20 per cent.), 760.0 *millilitres.* Moisten the Senna Leaves with four hundred and forty millilitres of the Alcohol (20 per cent.); pack tightly in a vessel which can afterwards be closed; set aside for three days; press strongly; reserve the liquid obtained; break up the marc; moisten it with one hundred and sixty millilitres of the Alcohol (20 per cent.); set aside for twenty-four hours; press strongly; add the liquid obtained to the portion previously reserved; break up the marc; mix it with the remainder of the Alcohol (20 per cent.); set aside for three hours; press again; evaporate the resulting liquid until it is reduced to such a volume that when added to the reserved liquid the whole measures four hundred and forty millilitres. Mix the evaporated liquid with the reserved liquid; heat the product in a covered vessel to 82° C. for a few minutes; set aside for twenty-four hours; filter, and pass Distilled Water through the filter until the filtrate measures four hundred and forty millilitres; add the Refined Sugar, and dissolve in a covered vessel by the aid of gentle heat; cool; add the Oil of Coriander dissolved in the Alcohol (90 per cent.); mix." *Br.*

The Br. preparation is much more concentrated than that of the U. S.

The process was improved in the U. S. P. VIII by simply adding the fluidextract and oil of coriander to syrup, and this process has been retained in the Ninth Revision.

Dose, of the U. S. syrup of senna, for an adult, from one to four fluidrachms (3.75–15.0 cc.); of the Br. syrup from one-half to two fluidrachms (2–7.5 cc.).

SYRUPUS TOLU. U. S. (Br.)

SYRUP OF TOLU Syr. Tolu [Syrupus Tolutanus U. S. P. IX]

Syrupus Tolutanus, *Br.;* Syrup of Balsam of Tolu; Sirop de Baume de Tolu, *Fr. Cod.;* Sirop balsamique, *Fr.;* Tolubalsamsirup, *G.,* Jarabe de balsamo de Tolu, *Sp.*

"Tincture of Tolu, 50 cc.; Magnesium Carbonate, 10 Gm.; Sucrose, 820 Gm.; Water, a sufficient quantity to make 1000 cc. Mix the tincture intimately with the magnesium carbonate and 60 Gm. of sucrose, in a mortar. Gradually add 430 cc. of water, with trituration, and filter. Dissolve the remainder of the sucrose in the clear filtrate with the aid of a gentle heat, strain the syrup while warm, and add sufficient water through the strainer to make the product measure 1000 cc. Syrup of Tolu may also be made in the following manner: Prepare a percolator as described under *Syrupus.* Pour the filtrate obtained as directed in the above formula upon the remainder of the sucrose contained in the percolator, return the first portions of the percolate until it runs through clear, and, when all of the liquid has passed, follow with water until the sucrose is dissolved and the product measures 1000 cc. Mix thoroughly.

"Alcohol content, by volume, 3.5 to 4.5 per cent." *U. S.*

"Balsam of Tolu, 25 *grammes;* Refined Sugar, 660 *grammes;* Distilled Water, sufficient to produce 1000 *grammes.* Add four hundred grammes of the Distilled Water, boiling, to the Balsam of Tolu; cover lightly and heat on a water-bath for half an hour, stirring frequently. Remove; add Distilled Water, if necessary, so that the liquid, when cold, measures four hundred millilitres. Filter the solution, add the Refined Sugar, dissolve by the aid of a water-bath, and finally add sufficient Distilled Water to produce the required weight." *Br.*

The U. S. VIII process, which has been continued in the present revision, introduced magnesium carbonate with much advantage, and has the further improvement of using the official tincture of tolu instead of making the syrup from the balsam by a special process. In the British process the soluble principles of the balsam are extracted by boiling it with water, but with great waste of the material, as the water dissolves but a small portion of the active matter.

Syrup of tolu is used chiefly to impart its agreeable flavor to mixtures. If a stronger preparation is desired, tincture of tolu may be added in the desired quantity, directing the bottle to be shaken.

Dose, one to four fluidrachms (3.75–15.0 cc.).

SYRUPUS URGINEÆ. Br.

SYRUP OF URGINEA

"Vinegar of Urginea, 175 *millilitres;* Refined Sugar, 650 *grammes;* Distilled Water, sufficient to produce 1000 *grammes.* Mix the Vinegar of Urginea with an equal volume of Distilled Water. In the mixture dissolve the Refined Sugar by the aid of gentle heat; add sufficient Distilled Water to produce the required weight." *Br.*

This syrup corresponds to the Syrup of Squill of the British Pharmacopœia and is used for the same purpose.

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

SYRUPUS ZINGIBERIS. U. S., Br.

SYRUP OF GINGER Syr. Zingib.

Sirop de Gingembre, *Fr.;* Ingwersirup, *G.*

"Fluidextract of Ginger, 30 cc.; Alcohol, 20 cc.; Magnesium Carbonate, 10 Gm.; Sucrose, 820 Gm.; Water, a sufficient quantity to make 1000 cc. Mix the fluidextract and alcohol, and triturate the liquid in a mortar with the magnesium carbonate and 60 Gm. of the sucrose. Then gradually add 430 cc. of water with constant trituration, and filter. Dissolve the remainder of the sucrose in the clear filtrate, with the aid of a gentle heat, strain the syrup while warm, and, when cold, add enough water through the strainer to make the product measure 1000 cc.

"Syrup of Ginger may also be made in the following manner: Prepare a percolator as described under *Syrupus.* Pour the filtrate obtained as directed in the above formula upon the remainder of the sucrose, return the first portions of the percolate, and, when all of the liquid has passed, follow with water until the sucrose is dissolved and the product measures 1000 cc. Mix thoroughly.

"Alcohol content, by volume, 3.5 to 4.5 per cent." *U. S.*

"Ginger, in powder, 25 *grammes;* Alcohol (90 per cent.), *a sufficient quantity;* Syrup, sufficient to produce 1000 *millilitres.* Prepare fifty millilitres of a strong tincture of the Ginger by the *process of percolation* with the Alcohol. To this add sufficient of the Syrup to produce the required volume." *Br.*

The U. S. P. process has been improved by the addition of magnesium carbonate as an aid in distributing the resinous fluidextract so as to facilitate its solution in water. It is practically a return to the U. S. 1870 method.

The British syrup, being made by the simple incorporation of an alcoholic tincture of the ginger with syrup, has of course all the strength of the ginger, but is inferior to the U. S. preparation in appearance and flavor. The old plan of using water as the menstruum for the drug has been abandoned, as the syrup thus made is encumbered with mucilage and starch, and consequently rendered more liable to decomposition. The syrup of ginger is much used as a warm stomachic addition to tonic and purgative infusions or mixtures, and to impart flavor particularly to carbonic acid water.

Dose, one to four fluidrachms (3.75–15.0 cc.).

TABELLÆ TRINITRINI. Br.

TRINITRIN TABLETS

Tablets of Nitroglycerin.

"Trinitrin Tablets are tablets of chocolate each weighing 0.300 gramme and containing 0.0005 gramme (0.5 milligram) of the trinitroglycerin of commerce. Each of these Tablets contains 0.5 milligram (approximately 1/130 grain) of the trinitroglycerin of comerce." *Br.*

A pill of nitroglycerin, made with althea and confection of rose, is recognized by the N. F. (see Part III). They afford a convenient mode of exhibiting glyceryl nitrate. The question of the stability of these tablets has frequently been brought up and many manufacturers have been penalized under the Food and Drug Act enforcement for supplying substandard tablets. Scoville (*J. I. E. C.,* 1915, 1054) states that nitroglycerin tablets containing less than 1/100 grain rapidly lose their strength on keeping, and suggests that this may be due to a finer attenuation of the nitroglycerin, thus favoring volatilization. As a second possible explanation the author calls attention to the two isomeric forms of nitroglycerin—a labile form melting at 2.8° C. and a stable form melting at 13.5° C. Nitroglycerin used in the paste form appears to be in a favorable condition owing to the presence of the solid matter and a trace of moisture, to forming the stable isomeride. Those tablets made from an alcoholic solution of nitroglycerin, appeared to be less stable than those made from the paste mixture. The subject was also investigated by a committee of the American Drug Manufacturers' Association in 1919 and the findings were to the effect that when the tablets are properly made there is no appreciable deterioration upon storage for a period of six months.

Dose, one to two tablets.

TALCUM PURIFICATUM. U. S.

PURIFIED TALC Talc. Purif.

"Purified talc is a purified native, hydrous magnesium silicate sometimes containing a small amount of aluminum silicate." *U. S.*

Talcum, *U. S. VIII;* Talc purifié, *Fr.;* Gereinigter Talc, *G.;* Talcum Venetum; Soapstone; Talc, *Fr. Cod.;* French Chalk; Creta Gallica; Talc de Venise, Craie de Briancon, *Fr.;* Talcum, *P. G.;* Talk, Talkstein, Speckstein, *G.*

Talc is a native acid metasilicate of magnesium (for account of other magnesium silicates, see Part II). It is found in various parts of the world; the largest producers being Vermont, New York and Virginia although considerable amounts are mined in other parts of the United States, in France, Austria and Italy (see Ladoo, *D. C.,* 1920, lxiv, 370). The finest quality is obtained in the Italian Alps. Talc is found in three forms, the foliaceous, fibrous and massive varieties. The latter occurs in irregular masses of a greenish-gray color, having a peculiar wax-like appearance of the surface, and giving when rubbed a greasy sensation to the skin. It is odorless, tasteless, and insoluble in water or in dilute solutions of the acids or alkaline hydroxides. Talc is largely used in the arts, especially in the manufacture of paper in which it is used as a filler.

When intended for medicinal or toilet uses the talc is first freed from limestone, marble or other similar impurities. It is then broken into small lumps and introduced into a disintegrator, where it is ground to a fine powder which is carried upwards into a vertical elevator pipe by means of a strong current of air, generated by a blower attached to the disintegrator. The most finely ground talc passes out of the top of the vertical pipe into a long canvas balloon and drops into a receiver below, as soon as the machinery stops. After adding perfume or desired medication the powdered talc if intended for toilet purposes is bolted through a fine sieve having 40,000 meshes to the square inch, being forced through by means of a rotating brush. For pharmaceutical uses it should not be in so fine a powder and requires to be purified by washing with hydrochloric acid. The present Pharmacopœia gives no process for its purification. That of the U. S. VIII was as follows:

"Talc, in fine powder, *five hundred grammes;* Hydrochloric Acid, *seventy-five cubic centimeters;* Water, *a sufficient quantity.* Mix the powdered Talc with about *twenty-five hundred cubic centimeters* of boiling Water, gradually add *fifty cubic centimeters* of the Hydrochloric Acid, and boil the mixture during fifteen minutes, then allow it to stand for fifteen minutes. Decant, and reject the supernatant liquid containing the finer particles of Talc in suspension, and again boil the residue with *twenty-five hundred cubic centimeters* of Water, mixed with the remainder of the Hydrochloric Acid, and allow it to stand for fifteen minutes. Again decant, and reject the finer suspended particles, and wash the coarser residue with Water by repeated decantation, until a portion of the wash-water, after filtering and acidifying with nitric acid, fails to become opalescent upon the addition of silver nitrate test solution. Then transfer the magma to a close linen or muslin strainer, allow it to drain, and dry it at 110° C." *U. S. VIII.*

Purified Talc is intended to replace magnesium carbonate, calcium phosphate, and other absorbent powders used to aid filtration, it having the advantage of insolubility, although its absorbent properties are deficient in comparison with magnesium carbonate. As much of the talc sold commercially has been bolted for use in toilet powders it is too fine for use as a filtering medium; the fine particles passing through the pores of the filter paper. For this reason the U. S. P. directs talc for filtering to be not finer than a No. 100 powder.

An interesting and valuable communication on the subject of filtering media is contributed to the *J. A. Ph. A.*, 1916, p. 506, by W. L. Scoville. In it he gives experimental data of the comparison of paper pulp, talc, infusorial earth and fuller's earth, in filtering aqueous solutions of alkaloids. He says that of the media experimented with, fuller's earth is the only one producing any marked change in the filtrate, and that it removes from 22 to 100 per cent. of alkaloidal substances from solution, depending upon the alkaloid and whether the liquid is acid, alkaline, or neutral. The "Mechanism of Filtration" is the title of an article by Hatchek (*J. S. C. I.*, 1908, p. 538), in which the effect of various filtering media is scientifically discussed and diagrammatically illustrated.

Description and Physical Properties.—"A very fine, white or grayish-white powder. It adheres readily to the skin. It is entirely free from grittiness and is unctuous to the touch.

"Mix 0.5 Gm. of Purified Talc with about 2 Gm. of anhydrous sodium carbonate and 2 Gm. of anhydrous potassium carbonate, heat the mixture in a platinum crucible until fusion is complete, the treat the resulting fused mass with hot distilled water. Then neutralize the liquid with diluted sulphuric acid, add another 10 cc. of the diluted acid, and evaporate the mixture until white fumes of sulphuric anhydride are evolved, and cool. Add 20 cc. of distilled water, boil the mixture, and filter. An insoluble residue of *silica* remains. The addition of ammonia T.S. and ammonium chloride T.S. to the filtrate may produce a white gelatinous precipitate of *aluminum hydroxide,* and the filtrate from this mixture on the addition of sodium phosphate T.S. yields a white, crystalline precipitate of magnesium ammonium phosphate.

"Purified Talc, when ignited at a red heat, loses not more than 5 per cent. of its weight. Boil 10 Gm. of Purified Talc with 50 cc. of distilled water for one-half hour, adding water from time to time to maintain approximately the original volume, and filter. The filtrate is neutral to litmus paper. One-half of this filtrate, when evaporated and dried at 110° C., yields not more than 0.005 Gm. of residue (*soluble substances*). The remaining half of this filtrate, after slightly acidulating with hydrochloric acid, does not yield a blue color upon the addition of potassium ferrocyanide T.S. (*iron*). Add 1 Gm. of Purified Talc to 20 cc. of diluted hydrochloric acid: no effervescence occurs (*carbonate*). Digest the mixture for fifteen minutes, and filter: a 10 cc. portion of the filtrate evaporated to dryness and ignited, leaves a residue weighing not more than 0.005 Gm. NOTE—Purified Talc is intended only as a filtering medium and for this purpose should not be finer than a No. 100 powder." *U. S.*

Uses.—Purified talc is used pharmaceutically (see above) and as a protecting, soothing powder to the skin. When in very fine powder it forms the basis of many of the proprietary toilet and infant powders, and is very valuable as a dusting powder in *intertrigo, prickly heat, pruritus,* and other conditions of dermal irritation.

Off. Prep.—Pulvis Talci Compositus, *N. F.*

TAMARINDUS. N. F., Br.

TAMARIND

"Tamarind is the partially dried ripe fruit of *Tamarindus indica* Linné (Fam. *Leguminosæ*), deprived of the brittle outer portion of the pericarp and preserved in sugar or syrup. Tamarind contains not more than 2 per cent. of foreign organic matter." *N. F.*

"Tamarinds are the fruits of Tamarindus indica, *Linn.*, freed from the brittle outer part of the pericarp and preserved with sugar." *Br.*

Fructus Tamarindorum; Tamarin, *Fr. Cod.;* Pulpa Tamarindorum cruda, *P. G.;* Tamarindemnus, Tamarinden, *G.;* Tamarindo, *It.;* Tamarindo (Pulpa de), *Sp.*

The tamarind, *Tamarindus indica* L., is the only known member of the genus *Tamarindus.* It is a large, spreading tree, attaining a height of 80 feet and with a trunk circumference up to 25 feet. It is indigenous to the upper Nile district of Africa and possibly southern Asia, and has been cultivated for centuries in tropical lands both for ornamental purposes and for its edible, acid fruits. The use of the latter as a laxative food was known to the ancient Hindus who imparted their knowledge concerning their properties to the Arabians. The Arabians introduced these fruits into Europe during the Middle Ages. At present, the tamarind is cultivated for the drug in India, West Indies and to a smaller extent in Florida. The tree possesses a brownish-gray, shaggy bark, alternate, paripinnate leaves with 20 to 40 oblong, opposite leaflets and pale yellow flowers arranged in lateral racemes. The fruit is a broad, compressed, reddish ash-colored pod, much curved, from two to six inches long, with numerous brown, flat, quadrangular seeds, contained in loculi formed by a tough membrane. Exterior to this membrane is a light-colored acid pulpy matter, between which and the shell are several somewhat branched tough ligneous strands, running from the stem to the extremity of the pod, the attachment of which they serve to strengthen. The shells are fragile and easily separated.

Calcutta appears to be the chief emporium for the tamarinds of the European markets. Tamarinds are also sent from Barbados and Antigua in the West Indies to England; when from this source they are preferred. The latter are known as West Indian tamarinds, and are obtained from *T. indica*, var. *occidentalis* Gärtn. They are of a light brown color, less cohesive and possess less acidity than the tamarinds from the Old World. Tamarinds are brought to us chiefly from the West Indies, where they are prepared by removing the epicarp, packing the decorticated fruits in layers in a cask, and pouring boiling syrup over them. A better mode, sometimes practised, is to place them in stone jars, with alternate layers of powdered sugar. They are said to be occasionally prepared in copper boilers. In India tamarinds are often prepared for market by stripping off the outer shell and pressing the pulpy interiors into a mass, with or without the addition of some salt as a preservative.

Properties.—Fresh tamarinds, which are sometimes brought to this country, have an agreeable, sour taste, without any mixture of sweetness. In the United States they are more usually met with in the preserved state; this is a dark-colored adhesive mass, consisting of syrup mixed with the pulp, membrane, and seeds of the pod, and having a sweet acidulous taste. The brown, flattish, quadrangular seeds, each enclosed in a tough membrane, should be hard, clean, and not swollen, the string-like fibers tough and entire, and the odor without mustiness.

Tamarind is officially described as "a pulpy mass of a light reddish brown color, changing with age to a dark brown, containing some branching fibers and numerous reddish brown, smooth, oblong or quadrangular, compressed seeds, each enclosed in a tough membrane; the pulp with parenchyma containing a few starch grains up to 0.020 mm. in diameter, calcium oxalate in rosettes up to 0.100 mm. in diameter, and crystal fibers with prisms of calcium oxalate up to 0.050 mm. in length. Odor distinct; taste sweet and agreeably acid." *N. F.*

"A reddish-brown, moist, sugary mass, containing strong branched fibres, and brown, shining seeds, each enclosed in a tough membrane. Taste agreeable, subacid. The pulp yields no characteristic *reactions* for copper." *Br.*

The Austrian Pharmacopœia excludes an article of a reddish-brown color. Some European Pharmacopœias limit the amount of seeds present and the Italian Pharmacopœia requires a minimum acid content.

K. Müller, after analyzing nine commercial varieties, gives the following figures for composition: Citric acid 4 to 6 per cent.; tartaric acid 5.3 to 8.8 per cent.; potassium bitartrate 4.7 to 6 per cent.; malic acid, traces only; insoluble matter 12 to 20 per cent.; seeds 1.5 to 38 per cent. (average 13.9). Copper may often be detected in preserved tamarinds, derived from the boilers in which they are prepared. Its presence may be ascertained by the reddish coat which it imparts to the blade of a spatula or other steel implement immersed in the tamarinds.

Uses.—Tamarinds are laxative and refrigerant, and infused in water form a highly grateful drink in febrile diseases. Convalescents often find the pulp a pleasant addition to their diet, and useful when a laxative action is desirable. It is sometimes prescribed in connection with other mild cathartics. Though frequently given with infusion of senna to cover its taste, it is said to weaken its purgative power, and the same observation has been made of its influence upon the resinous cathartics in general. For a formula for *fluidextract of tamarind,* see *Nat. Drug.*, 1892, 101.

Dose, a drachm to an ounce (3.9–31 Gm.).

Off. Prep.—Confectio Sennæ, *Br., N. F.*

TARAXACUM. N. F. (Br.)

TARAXACUM Tarax. [Dandelion]

"Taraxacum consists of the dried rhizome and roots of *Leontodon Taraxacum* Linné (Fam. *Compositæ*). Taraxacum contains not more than 2 per cent. of foreign organic matter and yields not more than 4 per cent. of acid-insoluble ash." *N. F.*

"Taraxacum Root is the fresh root of Taraxacum officinale, *Wiggers.* Collected in the autumn." *Br.*

Taraxaci Radix, *Br.;* Taraxacum Root; Dandelion Root; Blowball, Milk, Witch, or Yellow Gowan, Lion's-tooth, Cankerwort; Pissenlit, Dent de Lion, *Fr. Cod.;* Radix Taraxaci cum herba, *P. G.;* Löwenzahn, *G.;* Tarassaco, *It.;* Taraxacon, Diente de Leon, *Sp.*

The dandelion is a perennial herb native to Europe but now naturalized in many parts of the world, occurring almost ubiquitously in grassy places as a troublesome weed. Its subterranean portion consists of straight, fusiform root which in its upper part passes into an erect rhizome which sometimes branches into several secondary rhizomes. From the rhizome or its branches rosettes of coarsely pinnatifid leaves arise. These are usually runcinate, with the lobes toothed. The common name of the plant was derived from the fancied resemblance of its leaves to the teeth of a lion. The flower-stem rises from the midst of the leaves, six inches or more in height. It is erect, simple, naked, smooth, hollow, fragile, and terminated by a large golden-colored flower, which closes in the evening and expands with the returning light of the sun. The involucre is smooth and double, with the outer scales bent downward. The florets are very numerous, ligulate, and toothed at their extremities. The receptacle is flat and naked. The pappus is stipitate, and at the period of maturity is disposed in a spherical form, and is so light and feathery as to be easily borne away by the wind, with the achene attached. Another plant resembling the common dandelion, the achenes of which, however, are narrower and bright red or reddish brown, known as the *red-seeded dandelion,* is the product of *T. erythrospermum* Andrz., and is supposed by some to be naturalized from Europe. There seems little doubt but that the drug of commerce represents the rhizomes and roots of both of these species, as both often occur together and bear many features in common.

All parts of the plant contain a milky, bitterish juice, which exudes when they are broken or wounded. The leaves, when very young and blanched by the absence of light during their growth, are tender and not unpleasant to the taste, and are much used as a food. The Pharmacopœias recognize only the root. It should be full grown when collected, and should be employed in the recent state. That most esteemed is collected during the months of July, August, and September. The commercial supplies of Taraxacum are imported from Germany, Holland and England.

Description and Physical Properties.—"*Unground Taraxacum.*—Cylindrical or somewhat flattened, gradually tapering, usually in broken pieces, from 6 to 15 cm. in length and from 5 to 15 mm. in thickness; externally brown or blackish brown, longitudinally wrinkled, having numerous root and rootlet-scars; crown simple or branched with numerous leaf-bases showing annulate markings; fracture horny, short, non-fibrous. Odor slight or inodorous; taste bitter.

"*Structure.*—A porous, pale yellow, non-radiate wood from 1 to 4 mm. in diameter, surrounded by a light brown bark from 2 to 6 mm. in thickness, the latter containing concentric layers of laticiferous vessels and sieve tissues, alternating with whitish inulin-bearing parenchyma. The rhizome portions show a small pith.

"*Powdered Taraxacum.*—Light brown; parenchyma cells, large, thin-walled and containing irregular masses of inulin; fragments with yellowish brown laticiferous vessels; tracheæ reticulate; intermediate fibers non-lignified, with irregular, simple and oblique pores; starch wanting.

"Preserve Taraxacum in tightly closed containers." *N. F.*

"Fresh root frequently three decimetres or more long, and twelve millimetres or more thick, smooth and yellowish-brown externally, whitish within. Fracture short, the exposed surface showing a small yellow porous wood, surrounded by a thick nearly white cortex exhibiting a variable number of irregular concentric rings, from which a milky juice exudes. Inodorous; taste bitter." *Br.*

The roots of various plants have been largely substituted for dandelion in England and on the Continent by the herb gatherers, and we are informed that fraudulent substitution is not infrequent, in this country, of the root of *Cichorium Intybus* L., or *chicory.* It is rare to find chicory mixed with dandelion, the former being usually boldly substituted for the latter. Chicory rhizomes or roots are readily detected, upon fracture, by their radially arranged laticiferous vessels in the bark region. In dandelion these are arranged in concentric circles.

In 1839 Polex isolated a bitter crystalline principle which he called *taraxacin* and later Kromayer (1861) a second crystalline substance which he called *taraxacerin,* but F. B. Power (*C. D.,* 1912, p. 822) states that both of these substances are indefinite mixtures. The root contains in the fall about 25 per cent. of inulin but the quantity in the spring is considerably less; also about 17 per cent. of uncrystallizable sugar and a soluble carbohydrate called *levulin,* $C_6H_{10}O_5$. According to Vogel, the intra-cellular substance of the root consists chiefly of pectose, which is the result of a metamorphosis of the substance constituting the membrane of the cells. L. E. Sayre found that the yield of taraxacin varies in roots collected at different seasons. (See *Proc. A. Ph. A.,* 1893, 1894, 1895, 1896, 1897.) Power found in the air dried English root, an enzyme, essential oil, oily resin, fatty acids, including *melissic,* and *p-hydroxy-phenylacetic acid,* which had never before been isolated from a plant.

Uses.—Taraxacum was formerly supposed to possess cholagogic as well as diuretic powers. It has been used in various conditions accompanied with congested or *torpid liver.* There is, however, no sufficient reason for believing it possesses any therapeutic virtues. The dried root is sometimes mixed, in powder, with ground coffee, the taste of which covers that of the dandelion. It is roasted and powdered and then prepared in the same manner.

Dose, one to three drachms (3.9–11.6 Gm.).

Off. Prep.—Fluidextractum Taraxaci, *N. F.* (*Br.*); Extractum Taraxaci, *N. F., Br.;* Succus Taraxaci, *Br.;* Elixir Gentianæ Glycerinatum, *N. F.;* Elixir Taraxaci Compositum, *N. F.;* Elixir Eriodictyi Aromaticum, *N. F.;* Elixir Guaranæ, *N. F.*

TEREBENUM. U. S., Br.

TEREBENE Tereben.

"Terebene is a mixture of terpene hydrocarbons, chiefly dipentene and terpinene, obtained from oil of turpentine." *U. S.* "Terebene is a mixture of dipentene and other hydrocarbons, obtained by shaking oil of turpentine with successive quantities of sulphuric acid until optically inactive, and then distilling in a current of steam." *Br.*

Térébène, *Fr.;* Tereben, *G.*

This substance is produced by the action of sulphuric acid upon oil of turpentine. The sulphuric acid must be added gradually to the cooled oil of turpentine, in the proportion of one part of acid to twenty parts of oil, and after a day's standing the mixture is heated to boiling. After cooling, the oily layer is removed, freed from acid by calcium carbonate, and rectified. Some cymol is always produced at the same time, and by continued action of the acid the terebene is said to be entirely converted into cymol and colophene. Jayne and Chase (*A. J. P.*, 1887, p. 65) found an inactive camphor, boiling at about 200° C. (probably borneol), to be formed also, and the residue left on rectifying was principally *colophene.*

Description and Physical Properties.—"A colorless, thin liquid. It has a rather agreeable, thyme-like odor, and a somewhat terebinthinate taste. On exposure to light and air, Terebene gradually becomes resinified and acquires an acid reaction. It is practically insoluble in water, but miscible with chloroform, ether, and dehydrated alcohol. One cc. is soluble in 3 cc. of alcohol at 25° C.

"Specific gravity: 0.860 to 0.865 at 25° C. It boils between 160° and 172° C. Terebene does not redden blue litmus paper which has been moistened with alcohol. Its optical rotation does not exceed $+0.3°$ in a 100 mm. tube at 25° C. (*unaltered oil of turpentine*). After the determination of the boiling point, transfer the residue remaining in the distilling flask to a dish, by means of ether, and evaporate the liquid on a water bath: the residue remaining does not exceed 1 per cent. of the original weight of Terebene taken (*rosin*).

"Preserve in well-closed containers, protected from light." *U. S.*

"A colorless liquid. Agreeable odor; taste aromatic and terebinthinate. Specific gravity from 0.862 to 0.866. Soluble in 5 parts of *alcohol* (90 per cent.). *Optical rotation* at 15.5° C., $+1°$ to $-1°$. Distils between 156° and 180° C., leaving only a slight viscous residue (absence of excess of resin). Not more than 15 per cent. distils below 165° C." *Br.*

Power and Kleber (*Ph. Rund.*, 1894, 18) stated that pinene is not obtained by the action of sulphuric acid on oil of turpentine, that the boiling points 156° to 160° C. should be 170° to 185° C., and that the sp. gr. should be 0.855 instead of 0.862; also that terebene consists mainly of dipentene and terpinene with some cymol and camphene.

Uses.—Terebene is a valuable stimulant expectorant, first recommended by William Murrell (*B. M. J.*, Dec., 1885), in that form of *chronic bronchitis* often known as *winter cough.* It is very useful not only in cases of chronic bronchitis, but also in the *acute* disease, after the earlier stages have passed by. It probably exerts upon other mucous membranes the same action that it does upon that of the lungs, and it has been employed with asserted good results in *dyspepsia,* especially in the flatulent intestinal variety, and may be used in chronic or subacute inflammation of the genito-urinary tract. Its action upon the general system has not been investigated, but probably resembles that of oil of turpentine. It may be given in emulsion, or by dropping into half a teaspoonful of sugar. It is also sometimes administered in pastils or lozenges. It has been used by atomization, with asserted good results. Murrell (*B. M. J.*, July 24, 1884) states that terebene is an active antiseptic and germicide, one part in four hundred and fifty being able to keep in check the action of the yeast plant, and one part in five hundred having a very perceptible influence on the development of bacilli and paramœcia.

Dose, two to eight minims (0.12–0.5 cc.).

TEREBINTHINA. N. F.

TURPENTINE Terebinth.

"Turpentine is a concrete oleoresin obtained from *Pinus Palustris* Miller and from other species of *Pinus* (Fam. *Pinaceæ*). Turpentine contains not more than 2 per cent. of foreign matter." *N. F.*

White Turpentine; Thus Americanum; Common Frankincense; Terebinthina Communis; Terebinthina Pini, *Fr. Cod.;* Térébinthine du Pin, Térébinthine Commune, *Fr.;* Fliessharz, Terpentin, *G.;* Tremntina commune, *It.;* Trementino de Pino, *Sp.*

The word "turpentine" properly refers to the mixture of resin and volatile oil—whether liquid or concrete—which is obtained from coniferous trees. The word is sometimes, however, given a larger meaning and applied to similar oleoresins from other botanical families; in France it is applied to any oleoresin which does not contain benzoic or cinnamic acid.

The oleoresins from various species of pine trees have been used in the arts and in medicine from time immemorial in various parts of the world. They were collected from those species which were most abundant in each section. As a result there have been recognized a large number of turpentines which differ considerably among themselves both in their chemical and physical properties. At present the bulk of the world's supply of turpentine comes from America. Of the numerous varieties of turpentine we shall describe briefly, in addition to the official, those which are of medicinal importance.

The official turpentine is derived chiefly from the *Pinus palustris* and the *P. Tæda.* It occurs in the sap wood and is obtained by making incisions through the bark and wood and collecting the exudation in cavities or boxes made lower down on the trunk, from which it is dipped into barrels or other receptacles.

Pinus palustris Mill. (*P. australis* Michx. *f.*).—The names by which the tree is known in the Southern States are *long-leaved pine, yellow pine, Southern pine, hard pine, Virginia* *pine,* and *pitch pine;* but the first is the most appropriate. The leaves occur three in a group, being from ten to fifteen inches long, subtended at the base by a conspicuous scaly sheath from one to one and a half inches long and crowded at the ends of the branches. The cones are terminal, conical, and armed with a short recurved spine. This pine is a very large indigenous tree, growing in dry, sandy soils, from the southern part of Virginia to the Gulf of Mexico. It grows to a height of sixty or seventy feet, and the diameter of its trunk is about fifteen or eighteen inches for two-thirds of its height. This tree furnishes by far the greater proportion of the turpentine, tar, etc., consumed in, or exported from, the United States. (See *Pix Liquida.*)

Pinus Tæda L.—This is the *loblolly* or *old field pine* of the Southern States. "Leaves in threes, elongated, with elongated sheaths; strobiles oblong-conical, deflexed, shorter than the leaf; spines inflexed."

It is abundant in Virginia, where it occupies the lands exhausted by cultivation. It exceeds eighty feet in height, has a trunk two or three feet in diameter, and expands into a wide spreading top. The leaves are about six inches long, and of a light green color. It yields turpentine in abundance, but the quantity is less than that which flows from the preceding species.

Pinus Sabiniana Dougl., known as *nut-pine* or *digger-pine* (because the nut is largely consumed by the Digger Indians), yields, on being notched, a turpentine whose volatile oil is extensively used in California under the name of *abietene.* The *Pinus rigida,* or *pitch pine* of this country, and probably others besides those mentioned, are sometimes employed in the preparation of tar. *Pinus Teocoty* Cham. et Schlecht. yields a turpentine known as *Mexican* or *Brea turpentine,* which is used in Mexico.

A substance resembling manna, of a sweet, slightly bitter and terebinthinate taste, and actively purgative, exudes from incisions in *Pinus lambertiana,* of Oregon, and was used by the natives. Berthelot extracted from this product a principle, *pinite.* It is very sweet, but does not undergo the vinous fermentation. Pinite was for a long time classed among the sugars, but the latest researches seem to show that it is a hexahydric phenol derived from hexahydrobenzene. (*J. Am. C. S.,* 1891, xiii, 228.) The formula is $C_{17}H_{14}O_6$, and it is a methyl derivative of inosite. It is sometimes called *American Manna.*

Collection.—In former times, large quantities of turpentine were collected in New England, but the turpentine trees of that section have long been entirely exhausted, and our commerce has been until recently almost exclusively supplied from North Carolina and the southeastern parts of Virginia. Latterly attention was turned to the collection of this valuable product of Georgia and Florida, and now an abundant supply is derived from the vast pine forests which occupy the southern portion of our country bordering on the Gulf of Mexico.

During the winter, deep notches or excavations of the capacity of about three pints are made in the trunk of the tree three or four inches from the ground, and for about three feet above these so-called "boxes" the tree is deprived of its bark and some of the wood scraped off. Into these the turpentine or "crude" begins to flow about the middle of March, and continues to flow throughout the warm season, slowly at first, rapidly in the middle of summer, and more slowly again in the autumn, the tree being scraped every eight or ten days to prevent clogging. The liquid is removed from the "boxes" as they fill, and transferred into casks, where, if left, it gradually thickens, and ultimately acquires a soft solid consistence, but most of it is separated at once by distillation into the rosin and the volatile oil of turpentine.

When a tree is boxed, it is weakened and falls easily before the wind. To obviate the former destructive method, Herty has devised "the cup and gutter system." (See *Bulletin No. 40, Bureau of Forestry;* also *A. J. P.,* 1916, lxxxviii, 191.) By this method a small incision is made through the bark and a strip of galvanized iron is inserted. The turpentine flows along this strip and is caught in an earthenware receptacle much resembling a medium-sized flower pot inserted upon the tree. This method increases the yield of turpentine and has been adopted by some of the producers. E. S. Oliver (*National Drug.,* 1920, l, 394) describes a process which he claims gives double the output without injury to the trees. Large quantities of turpentine are now prepared directly from the stumps, roots, sawdust and wood of the trees which were wasted by the older or box method of collecting the oleoresin. "Wood" turpentine is not recognized as equivalent to "turpentine" by the Pure Food and Drugs Act, and must be labelled as "Wood Turpentine." The latter has a peculiar odor and is not used in medicine but is widely used in the arts. Wood turpentine is also produced as a by-product in the manufacture of sulphite cellulose.

Turpentine is likely to contain small pieces of bark, wood, or other impurity.

Composition.—Turpentine is a mixture of volatile oil and resin. In the recent state the proportion of volatile oil is about 7 per cent. but is less in old samples as the oil gradually oxidizes into resin.

Tschirch and Koritschoner (*A. Pharm.,* 1902) found the following constituents in white turpentine: *palabiennic acid,* $C_{13}H_{20}O_2$, 5 per cent.; *palabietinic acid,* $C_{20}H_{30}O_2$, which is crystalline, 6 to 7 per cent.; *α-* and *β-palabietinolic acids,* together 53 to 57 per cent. Both the latter are amorphous and are separated by the differing solubility of their lead salts. All the acids are soluble in sodium hydroxide solution. The portion of the resin insoluble in NaOH solution consists of essential oil, 20 to 22 per cent., and *paloresene,* 10 per cent., with traces of a bitter principle. The essential oil is dextrogyrate, while the resin itself and palabietinic acid are lævogyrate.

Properties.—The turpentines resemble one another in odor and taste, though distinguished by shades of difference. Liquid at first, they become thick and gradually solid by exposure, in consequence partly of the volatilization, partly of the oxidation of their essential oil. They are rendered more liquid or softened by heat, and at a high temperature take fire, burning with a white flame and much smoke. Water extracts only a minute proportion of their volatile oil. They are almost wholly soluble in alcohol and ether, and readily unite with the fixed oils. They yield by distillation a volatile oil, called *oil of turpentine,* the composition of which is essentially uniform, it being composed of several terpenes (pinene, dipentene, and sylvestrene) of the formula $C_{10}H_{16}$, the residue consisting exclusively of rosin. (See *Oleum Terebinthinæ* and *Resina.*)

White turpentine, as found in commerce, is yellowish white, of a peculiar somewhat aromatic odor, and a warm, pungent, bitterish taste. It is somewhat translucent, and of a consistence varying with the temperature. In the middle of summer it is almost semi-fluid and very adhesive; though brittle in the winter it is often so firm and hard as to be incapable of being made into pills without heat.

Description and Physical Properties.—"Turpentine occurs in yellowish, opaque masses, lighter internally, sticky and more or less glossy, brittle in the cold. Odor and taste characteristic.

"It is freely soluble in alcohol, ether, chloroform, or glacial acetic acid. Its alcoholic solution is acid to litmus. Dissolve about 1 Gm. of Turpentine, accurately weighed, in 25 cc. of alcohol and collect the insoluble residue, if any, on a filter which has been dried at 100° C. and weighed. Wash the residue and filter with about 25 cc. of alcohol and dry at 100° C. The weight of the residue does not exceed 2 per cent. (*mechanical impurities*)." *N. F.*

Schiff affirms that the odor of turpentine is due to the presence of a product of oxidation, probably a camphoric aldehyde, $C_{10}H_{16}O_3$, which, with the odor, may be removed by shaking the turpentine with sodium bisulphite. A non-odorless turpentine may also be obtained by washing with solution of sodium hydroxide and distilling in an atmosphere of carbon dioxide. From the experiments of Faure, of Bordeaux, it appears that some of the liquid turpentines, like copaiba, may be solidified by the addition of magnesia. (*Journ. de Chim. Méd.,* 1830, 94.) According to Thierry, the same result is obtained by the addition of calcium hydroxide. (*J. P. C.,* 3e sér., i, 315.)

Ed. Hirschsohn made experiments with the object of determining a reliable method for distinguishing artificial turpentine from the common, natural turpentine and larch turpentine; this becomes possible by the difference in the solvent effect of official ammonia water and alcohol, sp. gr. 0.863 at 15.6° C., upon them, under the conditions indicated in the following table:

Kind of Turpentine.	Ammonia Solution (sp. gr. 0.960), 1 p. turpentine and 5 p. ammonia solution.	Alcohol (sp. gr. 0.863), 1 p. turpentine and 3 p. alcohol.
Venice turpentine	Is not disintegrated; produces a milky fluid in the water bath.	Yields a nearly clear solution.
Common turpentine	Easily disintegrated, forming a milky mixture, then gelatinous, becomes clear in the water bath.	Large quantities are deposited, but the mixture becomes clear in the water bath.
Artificial turpentine	Is disintegrated, becomes clear in the water bath for a moment, then turbid.	Turbid solution and precipitation; turbid in the water bath with precipitation.

A mixture of common turpentine with larch (Venice) turpentine is recognized by the turbidity of, and precipitate from, the solution of 1 Gm. of the sample in 3 Gm. of alcohol sp. gr. 0.863. The same occurs if the common is replaced by artificial turpentine, but the latter is differentiated by ammonia, from the fact that in the presence of 20 to 30 per cent. of common turpentine the sample is easily disintegrated, and the solution becomes clear in the water bath, while in the presence of artificial turpentine the behavior is the same as with the pure Venice turpentine. (*Ph. Centralh.,* Nov. 26, 1903, 825 to 828.)

UNOFFICIAL TURPENTINES

European turpentine—the *Terebinthina vulgaris* of the old London Pharmacopœia—is furnished chiefly by *P. sylvestris* L. (*Scotch Pine, Norway Pine*) and *P. Pinaster* Soland. From the latter tree it is obtained largely in the maritime districts of the southwest of France, especially in the department of the Landes, and is exported from Bordeaux. Hence it is called in commerce *Bordeaux turpentine.* The substance which the French call *galipot,* or *barras,* is that portion of the turpentine which concretes upon the trunk of the tree when wounded, and is removed during the winter. This, when purified by melting with water and straining, takes the name of *yellow* or *white pitch,* and is sometimes substituted for *Burgundy pitch.* (See Part II.) European turpentine is whitish, turbid, thickish, and separates, upon standing, into two parts, one liquid and transparent, the other of a consistence and appearance like that of thickened honey. As found in European commerce, it often consists wholly of this latter portion. It speedily hardens on exposure in thin layers to the air. The most liquid specimens are completely solidified by the addition of one part of magnesia to thirty-two parts of the turpentine (*J. P. C.*, xxv, 499.) Tschirch and Bruening (*A. Pharm.*, 1900, ccxxxvii, 630) find this oleoresin to have the following composition: 6 to 7 per cent. of *pimarinic acid,* $C_{14}H_{22}O_2$; 8 to 10 per cent. of *pimaric acid,* $C_{20}H_{30}O_2$; 48 to 50 per cent. of *alpha-* and *beta-pimarobic acids,* $C_{18}H_{26}O_2$; 5 to 6 per cent. of *bordoresin,* together with traces of *succinic acid.* The acid resins are soluble in sodium hydroxide solution, the pimarinic acid being separable from the other two by its property of forming with ammonium carbonate a water-soluble double salt. The volatile oil consists of two fractions, the larger fraction, amounting to about 85 per cent. of the whole, distilling easily. It is scarcely ever given internally, but furnishes large quantities of oil of turpentine and rosin. We do not import it into this country.

Venice Turpentine (*Larch Turpentine*).—The N. F. formerly recognized under the title of *Terebinthina Laricis* "the viscid oleoresin obtained from *Larix europœa* De Candolle (Fam. *Pinaceæ*)." *N. F.*

The genus *Larix* differs from all the other coniferous trees in that its leaves are deciduous. The European Larch (*Larix decidua* Mill., *L. europœa* DC.), from which this oleoresin is obtained, is a large tree found especially in the mountainous regions of Europe and Siberia. The leaves are narrowly linear, about one inch in length, in fascicles on short scaly branches and the cones ovoid and a little longer than the leaves. It yields, besides the *Venice turpentine* of commerce, a peculiar sweetish substance called in France *Briancon manna* which exudes spontaneously and concretes upon the bark. When the larch forests of Russia take fire, a juice exudes from the trunk during their combustion, which concretes and is called *Orenburg gum.* It is wholly soluble in water.

The oleoresin is collected in France and southern Tyrol during the spring by boring holes into the wood of the trees and plugging. The plugs are later removed and the oleoresin collected in suitable containers. The commercial supplies are chiefly imported from France and Italy.

Venice turpentine was described by the N. F. IV as "a nearly transparent yellowish or yellowish green, thick liquid heavier than water, and having a distinctive odor and a bitter characteristic taste. Completely soluble in alcohol, glacial acetic acid, acetone or chloroform. Almost entirely soluble in petroleum benzin with the separation of a light flocculent deposit. One part of Venice turpentine dissolves completely and forms a clear solution in 3 parts of 80 per cent. alcohol. It may possess a slight, greenish fluorescence when viewed by reflected light but exhibits no violet or purple fluorescence (*rosin oil*). Dissolve 5 Gm. of Venice turpentine in 25 cc. of alcohol, add a few drops of phenolphthalein T.S. and render the solution slightly alkaline by the addition of a 10 per cent. solution of potassium hydroxide. The resulting solution is clear and transparent and no separation of oily drops occurs (*rosin oil*). Its acid number is not more than 80 when determined as directed in the U. S. Pharmacopœia IX." *Pinaceæ*)." *N. F. IV.*

It does not readily concrete on exposure, is not solidified by one-sixteenth of magnesia, and is entirely soluble in alcohol. H. Beckurts and W. Brueche found the specific gravity at 15° C. from 1.060 to 1.190; acid number from 76 to 101 (Kremel found from 68 to 70.3); ester number from nothing to 6; saponification number from 81 to 101, and the iodine number from 137 to 149. (*A. Pharm.*, 1892, ccxxx, 83.) It yields on an average 15 per cent. of essential oil, which has been found to be nearly pure *pinene.* The residual resin is soluble in two parts of warm alcohol of 57 per cent., and more copiously in absolute alcohol.

Tschirch and Wiegel (*A. Pharm.*, 1900, pp. 401, 487) found in larch turpentine from 60 to 64 per cent. of acid resins soluble in soda, from 20 to 22 per cent. of volatile oil, and from 14 to 15 per cent. of indifferent resin. The acid resins consist mainly of two isomeric amorphous bodies, *a*- and *b*-larinolic acid, $C_{18}H_{26}O_2$, and a smaller quantity of the crystalline *laricinolic acid,* $C_{20}H_{30}O_2$. The greater portion of the volatile oil boils between 155° and 170° C.; a smaller quantity of higher boiling sesquiterpene commencing to boil at 190° C. The recently distilled oil has the sp. gr. 0.872, and possesses a characteristic turpentine odor. It is soluble in all proportions in alcohol and other solvents.

What is sold under the name of Venice turpentine, in commerce, is usually quite brown, and is a factitious substance prepared by dissolving rosin in oil of turpentine. According to G. Fabris the nature of these spurious Venice turpentines can readily be detected by dissolving 5 Gm. of the sample in 20 cc. of 95 per cent. alcohol, adding a few drops of phenolphthalein and sufficient of a 10 per cent. solution of potassium hydroxide to render it alkaline. With genuine Venetian turpentine a clear solution is obtained, while the spurious drug yields a turbid solution from which on standing, drops of oily resin separate.

Finnan Turpentine, the oleoresin of *Pinus sylvestris,* is found by Tschirch and Niederstadt to consist of: 1.5 per cent. *silveolic acid,* $C_{14}H_{20}O_2$; 58 to 60 per cent. of *a-silvinolic acid,* $C_{15}H_{26}O_2$, and *β-silvinolic acid* ($C_{14}H_{24}O_2$); 20 to 21 per cent. of *resene;* 15 per cent. of volatile oil; and traces of bitter principle and succinic acid. Silveolic acid is crystalline; α- and β-silvinolic acids are both amorphous. The volatile oil has the sp. gr. 0.840 at 15° C., is soluble in all proportions in alcohol, ether, and chloroform, and is neutral when recently distilled, but becomes acid when exposed to the air. (*A. Pharm.*, 1901, ccxxxix, 167.)

Jura Turpentine.—A. Tschirch and E. Bruening have determined the following constituents of the oleoresin of *Picea vulgaris:* From 2 to 3 per cent. of *picea-pimarinic acid,* $C_{18}H_{20}O_2$; from 1.5 to 2 per cent. of *picea-pimaric acid,* $C_{20}H_{30}O_2$; from 48 to 50 per cent. of α- and *β-picea-pimarolic acid,* $C_{25}H_{44}O_2$; from 32 to 33 per cent. of volatile oil; from 10 to 12 per cent. of resene, $C_{21}H_{36}O$; and traces of succinic acid, coloring matter and bitter principle. (*A. Pharm.,* 1900, ccxxxviii, 616.)

Tschirch and Weigel (*A. Pharm.,* 1900, 401, 487) investigated *Strassburg turpentine*—the oleoresin of *Abies Picea;* it contains from 8 to 10 per cent. of an acid resin, *abietinic acid,* $C_{13}H_{20}O_2$; from 1.5 to 2 per cent. of a crystalline acid resin, *abietolic acid,* $C_{20}H_{28}O_2$; from 46 to 50 per cent. of two amorphous isomeric acid resins, α- and *β-abietinolic acid,* $C_{16}H_{24}O_2$; from 12 to 16 per cent. of a neutral resin, *abieto-resin;* and from 28 to 30 per cent. of volatile oil, together with traces of succinic acid, bitter principle, coloring matter, moisture and impurities. The oil when recently distilled has the sp. gr. 0.860, boiling between 148° and 165° C.; the major fraction distils between 162° and 163° C. It has a greenish fluorescence and a lemon-like odor. When the oleoresin is distilled with potassium hydroxide a pleasant rose or orange-flower odor is developed, possibly due to the liberation of a fragrant alcohol.

In Japan, the exudation from the *Pinus densiflora* Sieb. et Zucc., and that from the *Pinus Thunbergii* Parl. are used under the respective names of *akamatsu* and *kuromatsu.* They are said to contain about 18 per cent. of oil and 81 per cent. of resin. The distilled oil is bright and colorless, having an odor somewhat different from that of the European oil of turpentine. It boils at from 155° to 156° C., and has a specific gravity of a little under 0.87. Its index of polarization is from 55° to 61° (dextrogyrate). The resin cannot be distinguished from the European.

Uses.—The physiological activities of the turpentines depend upon their volatile oils (see *Oleum Terebinthinæ*). They are so inconvenient of administration and so variable in their activity that at present they are almost never used internally. They are occasionally used externally for their local irritant effects, but even for this are inferior to corresponding dilutions of the volatile oil. Solid turpentines are used like resin sometimes to stiffen ointments where a stimulating effect is not undesirable.

TEREBINTHINA CANADENSIS. Br.

CANADA TURPENTINE

"Canada Turpentine is the oleo-resin obtained from Abies balsamea, *Mill.*" *Br.*

Canada Balsam, Balsam of Fir; Balsamum Canadense; Baume du Canada, *Fr. Cod.;* Térébenthine du Canada, *Fr.;* Canadischer Terpentin, *G.;* Canadischer Balsam, Canadischer Terpentin, *G.;* Trementina del Canada, *It.*

Terebinthina Canadensis, Br., is collected in Canada and the State of Maine from the *Abies balsamea,* by breaking the vesicles which naturally form upon the trunk and branches, and receiving their liquid contents in a bottle.

Abies balsamea (L.) Mill., (*A. balsamifera* Michaux).—This is the *American silver fir,* or *balm of Gilead tree* or *Fir Balsam* inhabiting Canada, Nova Scotia, Maine, and the mountainous regions farther south. It is an elegant tree, seldom rising more than forty feet, with a tapering trunk, and numerous branches, which diminish in length in proportion to their height and form an almost perfect cone. The leaves are six or eight lines long, inserted in rows on the sides and tops of the branches, narrow, flat, rigid, bright green on their upper surface, and of a silvery whiteness beneath. The cones are large, erect, nearly cylindrical, of a purplish color, and covered with a resinous exudation, which gives them a glossy, rich, and beautiful appearance.

Several other species of Abies are important. The *A. Picea* Lindl. (*Abies pectinata* of De Candolle, *Pinus picea* of Linnæus), or *European silver fir,* growing in the mountainous regions of Switzerland, Germany, and Siberia, yields the *Strassburg turpentine* (*Térébenthine d'Alsace* or *des Vosges*), which is much used in some parts of Europe. By the distillation of its cones with water it also affords a variety of oil of turpentine called in France *essence de templine.* By boiling the young branches of the allied *Picea Mariana* (Mill.), B. S. P. (*Pinus nigra* Link.), or *black* or *bog spruce* of this country, and evaporating the decoction, the *essence of spruce* is prepared. It is a thick, molasses-like liquid, with a bitterish, acidulous, astringent taste, and is used for making *spruce beer.* (See *U. S. D.,* 19th edition, page 1244.)

Abies Fraseri Lindley, commonly called *double fir* and *she-balsam* occurs at high elevations in the mountains of Tennessee and North Carolina. The tree is noted for its hardiness, and is used for ornamental purposes. It is also said to have been used to furnish a balsam of fir similar to that obtained from *A. balsamea,* but the data concerning this are obscure.

Abies Douglasii Lind. (*Pseudotsuga Taxifolia* Brit.).—From this a *Balsam of Fir* of the Pacific Slope has been obtained; it is a turpentine similar to Canada balsam and is extensively sold under the names *Oregon Balsam* or Oregon Balsam of Fir. Roberts and Becker (*Proc. P. P. A.,* 1913, p. 328) state that Canada balsam is thicker than Oregon balsam, dries to a solid, transparent film, while Oregon balsam remains sticky, has a lower acid value than Oregon balsam, and solidifies when mixed with 20 per cent. of magnesium oxide, which Oregon balsam does not.

Russian White Pitch, "Belji var," "Sos nowaja Smold," which is probably derived from the Siberian Fir, *Abies Pichta* Forb. (*Picea obovata* Ledeb.), contains, according to A. Tschirch, two free resin acids, the amorphous, *beljiabiennic acid,* $C_{13}H_{20}O_2$, and the crystalline, *beljiabietinic acid* besides *beljiresene,* $C_{13}H_{36}O$ and an essential oil. (*A. Pharm.,* Nov., 1902.)

Properties.—Canada turpentine is "pale yellow or greenish-yellow, transparent, viscous. Agreeable terebinthinate odor; taste feebly bitter and acrid. Dries very slowly to a transparent varnish when exposed to the air. Solidifies when mixed with about one-sixth of its weight of *heavy magnesia* moistened with a little *water.*" *Br.*

"It is completely soluble in ether, chloroform, or benzene." *U. S. VIII.*

For a paper on its miscibility in alcohol, by J. E. Morrison, see *Proc. A. Ph. A.,* 1894, 309. By time and exposure it becomes thicker and more yellow, and finally solid. It is usually brought into market in bottles under the name of *Canada balsam* or *balsam of fir.* Under the microscope the hard balsam is found to be entirely free from any granular or crystalline structure. In Europe it is sometimes called *balm of Gilead,* from its supposed resemblance to that celebrated medicine. The term *balsam,* as at present understood, is improperly applied to it, as it contains no benzoic or cinnamic acid, and is in fact a true turpentine, consisting chiefly of resin and volatile oil. Bonastre obtained from 100 parts of Canada turpentine 18.6 parts of volatile oil, 40.0 of resin easily dissolved by alcohol, 33.4 of sub-resin of difficult solubility in that fluid, 4.0 of caoutchouc similar to sub-resin, and 4.9 of bitter extractive and salts, besides traces of acetic acid. Flückiger found in 100 parts, 24 parts of an essential oil, $C_{10}H_{16}$, with a very small proportion of an oxygenated oil, 60 parts of a resin soluble in boiling alcohol, and 16 parts of a resin soluble only in ether. (*Pharmacographia,* 2d ed., 614.) Emmerich obtained by fractional distillation of the oil, *bornyl* or *terpinyl acetate, pinene,* and a fragrant liquid resembling oil of lemon. (*A. J. P.,* 1895, 135. See also a paper by Hunkel, *A. J. P.,* 1895, 9.) The chief distinction between it and *Strassburg turpentine,* which is sometimes sold for it in commerce, is in the odor.

According to Tschirch, Wiegel and Bruening, Canada turpentine contains about 63 per cent. of acid resins, from 23 to 24 per cent. of volatile oil, and from 11 to 12 per cent. of indifferent resin. The acid portion consists of four acids, of which one—*canadinic acid,* $C_{19}H_{34}O_2$—is obtained by treating the oleoresin with ammonium carbonate, with which it combines; a small amount of crystalline *canadolic acid,* $C_{19}H_{28}O_2$, and two amorphous isomeric acids — *a-* and *β-canadinolic acids,* $C_{19}H_{30}O_2$—which constitute the main portion of the acid resins. The indifferent resin has the formula $C_{21}H_{40}O$. The greater part of the volatile oil boils between 160° and 167° C. (*A. Pharm.,* 1900, Aug. and Sept., 401, 411 and 487.)

Uses.—The medicinal properties of this resembles that of the other turpentines. It is little used as a therapeutic agent by the medical profession although it is a popular folk remedy in the regions it inhabits being used as a vulnerary and internally for coughs. It is largely employed as a cement for glassware and as a permanent mounting medium for histological specimens.

TERPINI HYDRAS. U. S.

TERPIN HYDRATE Terpin Hyd.

"A dihydric alcohol [$C_{10}H_{18}(OH)_2.H_2O$]." *U. S.*

Terpinum, *Fr. Cod.;* Dihydrate de Térébenthène, Hydrate de Terpilène, *Fr.;* Terpinum Hydratum, *P. G.;* Terpinhydrat, *G.;* Terpina, *Sp.*

In making terpin hydrate a mixture of four parts of rectified oil of turpentine, three parts of alcohol (sp. gr. 0.863), and one part of nitric acid is put in large, shallow porcelain dishes and allowed to stand for three or four days. The crystals which have formed are then collected and allowed to drain thoroughly; they are then pressed between sheets of absorbent paper, and crystallized from a cold solution in 95 per cent. of alcohol. The product is about 12 per cent. of the original turpentine oil. E. T. Hahn proposed the use of methyl alcohol (sp. gr. 0.801) in place of alcohol, in making terpin hydrate. (*A. J. P.,* 1897, 73.) L. Krentmann states that good results are obtained by replacing the alcohol in the process with hydrogen dioxide solution and subjecting the mixture poured into shallow dishes to light and air. The temperature should be carefully regulated so that the range will be between 15° and 20° C.

The anhydrous *terpin* $C_{10}H_{18}(OH)_2$, obtained from it by the loss of water, has the characters of a glycol. Dipentene dihydrochloride is its hydrochloric acid ether. By the loss of water the terpin then becomes *terpineol,* $C_{10}H_{17}(OH)$, a liquid with an aromatic odor resembling lilac, and finally yields dipentene, terpinene, or terpinolene, according to the conditions of its treatment. Bouchardat and Voiry obtained terpineol in crystals which melt at 35° C. and remain in superfusion for long periods. (*Ann. Ch. Ph.,* 1893, 103.) For Wallach's researches on crystallized terpineol, see *P. J.,* 1893, 2.

The yield of crystallizable material is largely dependent upon the temperature at which the reaction is allowed to proceed. If the temperature be too high, polymerization of the turpentine takes place; if too low, the yield is insufficient.

Properties.—"Colorless, lustrous crystals, or a white powder. It has a slight odor, and is efflorescent in dry air. One Gm. of Terpin Hydrate is soluble in about 200 cc. of water, 13 cc. of alcohol, 135 cc. of chloroform, and in 140 cc. of ether, at 25° C. One Gm. is soluble in about 34 cc. of boiling water, in 3 cc. of boiling alcohol, and in about 1 cc. of boiling glacial acetic acid. When slowly heated to about 100° C., Terpin Hydrate sublimes in fine needles. It loses its water of crystallization at 100° C. It is also slowly dehydrated by drying over sulphuric acid.

"Preserve in well-closed containers, in a cool place.

"When quickly heated, Terpin Hydrate melts between 115° and 117° C. with the loss of water. Add a few drops of sulphuric acid to a hot aqueous solution of Terpin Hydrate: the liquid becomes turbid and develops a strongly aromatic odor.

"Terpin Hydrate has no odor of turpentine, and its hot aqueous solution (1 in 100) is not acid to litmus paper. Ash: not more than 0.05 per cent." *U. S.*

The pharmacy of terpin hydrate seems to be much misunderstood if one may judge by the liquid preparations on the market purporting to contain amounts of terpin hydrate impossible to be held in solution by the alcoholic strength of the preparation. It requires about 40 per cent. of alcohol in the finished preparation to hold in solution an amount of terpin hydrate corresponding to one grain to each fluidrachm.

Uses.—Terpin was first physiologically investigated by Lépine, in 1855, who found it to act both upon the mucous membranes and upon the nervous system in a manner similar to the oil of turpentine. It has since been used in *chronic bronchitis* and in the advanced stages of *acute bronchitis,* especially when the secretion is unusually free; also in *chronic cystitis* and *gonorrhea.*

Dose, two to five grains (0.13–0.32 Gm.), from four to six times a day, in pill or in emulsion.

Off. Prep.—Elixir Terpini Hydratis, *N. F.;* Elixir Terpini Hydratis et Creosoti, *N. F.*

TERRA SILICEA PURIFICATA. U. S.

PURIFIED SILICEOUS EARTH Ter. Sil. Purif. [Purified Kieselguhr, Purified Infusorial Earth]

"A form of silica (SiO_2) consisting of the frustules and fragments of diatoms, purified by boiling with diluted hydrochloric acid, washing, and calcining. It contains not more than 10 per cent. of water." *U. S.*

Kieselguhr is a form of earth consisting of fragments of frustules, or shells, of diatoms—which are microscopical unicellular algæ. Chemically it is an amorphous silicon dioxide and is therefore related to quartz which is a crystalline silica (see *Silex,* Part II). It is found in large deposits of greater or lesser purity in many parts of the world. It should not be confounded with kaolin whose chemical composition and physical properties are quite different.

Description and Physical Properties.—"A very bulky and very fine, odorless powder; white or light gray to pale buff in color. It readily absorbs moisture, retaining about four times its weight of water without the mixture becoming fluid. Purified Siliceous Earth is insoluble in water, acids, or in dilute solution of the alkali hydroxides.

"When ignited its color is not darkened (*organic impurities*), nor does it lose more than 10 per cent. of its weight (*moisture*). Digest 1 Gm. of Purified Siliceous Earth for fifteen minutes with 20 cc. of diluted hydrochloric acid, and filter: a 10 cc. portion of the filtrate, evaporated to dryness and ignited, leaves not more than 0.005 Gm. of residue. Boil 10 Gm. of Purified Siliceous Earth with 50 cc. of distilled water during ten minutes, replace any water lost by evaporation, and filter: the filtrate is colorless and neutral to litmus paper, and on adding 5 drops of potassium ferrocyanide T.S. to 5 cc. of the filtrate no blue color is produced (*soluble iron*). Add 1 Gm. of Purified Siliceous Earth to 25 cc. of diluted hydrochloric acid: no effervescence occurs (*carbonate*). Boil the mixture for ten minutes, replacing any water lost by evaporation, and filter: the addition of a few drops of barium chloride T.S. to the filtrate produces no turbidity (*sulphate*).

"Preserve in tightly-closed containers." *U. S.*

Uses.—Kieselguhr has widespread technical uses on account of its valuable physical properties. Chief among these are its chemical inertness and its power of absorbing large amounts of liquid. It is used to absorb nitroglycerin in the manufacture of dynamite; in transporting sulphuric acid as it forms a pulverulent compound containing 75 per cent. of sulphuric acid. It is also used as an absorbent for liquid manures. It is also used in fireproofing and insulating work because of its incombustibility and non-conductivity. It is used in polishing powders and soaps and in the composition of phonograph records. It differs importantly from the clays in that it has very slight *ad*sorbing powers. Because of this fact it is valuable in pharmacy as a filtering medium. It is difficult to obtain it of U. S. P. quality because none of the firms supplying it seem to be interested enough in it to remove the traces of iron and soluble impurities which are frequently observed in the commercial article. It may easily be purified by the same method as described under *Talcum.* It is also used in making dermatologic pastes.

THEOBROMINÆ SODIO-SALICYLAS. U. S. (Br.)

THEOBROMINE SODIO-SALICYLATE Theobrom. Sodio-Sal.

"A mixture of sodium theobromine [$C_7H_7O_2N_4Na$] and sodium salicylate [$NaC_7H_5O_3$] in approximately molecular proportions. It yields, when dried to constant weight at 110° C., not less than 46.5 per cent. of theobromine [C_7H_8-

O_2N_4] and not less than 35 per cent. of salicylic acid [$HC_7H_5O_3$]." *U. S.* "Theobromine and Sodium Salicylate, $Na_2C_{14}H_{12}N_4O_5$, may be obtained by combining sodium hydroxide, theobromine, and sodium salicylate in molecular proportions. Should be preserved in stoppered, amber-colored bottles." *Br.*

Theobrominæ et Sodii Salicylas. Theobromine and Sodium Salicylate, *Br.;* Theonasal; Diuretinum; Diuretin; Salicylas Natrii et Theobrominae Sodicae; Theobrominonatrium. Salicylicum, *G.*

Theobromine is a basic principle found in the chocolate bean (see *Cacao Præparata*). It was discovered by Woskresensky, who obtained it by the following method: The kernels are exhausted with water by means of the water bath; the solution is strained through linen, precipitated by lead acetate, and filtered; the filtered liquor is freed from lead by hydrogen sulphide, and evaporated; the brown residue is treated with boiling alcohol, and the liquor filtered while hot. Upon cooling, the theobromine is deposited in the form of a reddish-white powder, which is rendered colorless by repeated crystallization. Keller obtained it still purer by heating the powder between two watch glasses, by which a brilliant white sublimate was obtained. According to O. Donker and C. Treumann, theobromine is contained not only in the cotyledons but also in the shells of the cacao seeds. Four kilos of the latter yielded 13.5 Gm. of pure theobromine.

F. P. Stroup (*Proc. Penna. Ph. A.,* 1919, 161) has suggested the potassium dichromate sulphuric acid test as a means of distinguishing between caffeine and theobromine. With caffeine a bright bluish-green color immediately appears, while with theobromine the color change is at first purple, subsequently changing to an olive green, and finally to the same bluish-green produced by caffeine.

Theobromine is a *dimethyl xanthin* (dimethyloxypurin) isomeric with theophylline and differing in the location of the methyl groups which in theophylline are in the 1–3 position and in theobromine are in the 3–7 position. It is found in cacao beans in amounts ranging from 0.9 to 3.0 per cent., and in very much smaller amounts in kola nuts. It is also related to caffeine, which is a tri-methyl xanthin.

Theobromine may combine with either bases or acids. The official preparation is a mixture of theobromine-sodium and sodium salicylate.

Properties.—"A white, odorless powder, having a sweetish, saline, and somewhat alkaline taste. It gradually absorbs carbon dioxide from the air with the liberation of theobromine, becoming incompletely soluble in water. It also frequently develops a characteristic odor. One Gm. of Theobromine Sodio-Salicylate is soluble in 1 cc. of water at 25° C. It is slightly soluble in alcohol.

"An aqueous solution of Theobromine Sodio-Salicylate (1 in 20) is strongly alkaline to litmus paper and to phenolphthalein T.S. When ignited, Theobromine Sodio-Salicylate yields a residue which colors a non-luminous flame intensely yellow and effervesces with acids. An aqueous solution of Theobromine Sodio-Salicylate (1 in 100), slightly acidulated with acetic acid, becomes violet on the addition of ferric chloride T.S. To about 0.05 Gm. of the precipitate obtained in the assay for Theobromine add 1 cc. of hydrochloric acid and about 0.1 Gm. of potassium chlorate and evaporate to dryness on a water bath: a reddish-yellow residue remains which becomes purple when moistened with a drop of ammonia T.S.

"Dried to constant weight at 110° C., Theobromine Sodio-Salicylate loses not more than 10 per cent. (*water*). A freshly prepared aqueous solution of Theobromine Sodio-Salicylate (1 in 20) is colorless or nearly colorless and is clear or at most opalescent. One-tenth Gm. of Theobromine Sodio-Salicylate dissolves in 2 cc. of sulphuric acid without effervescence (*carbonate*) and without producing more than a slight color (*readily carbonizable substances*). Dissolve 1 Gm. of Theobromine Sodio-Salicylate in 10 cc. of distilled water, add a few cc. of sodium hydroxide T.S., and shake the mixture with 10 cc. of chloroform. Separate the chloroform layer, evaporate it to dryness on a water bath, and dry to constant weight at 80° C.: the weight of the residue so obtained does not exceed 0.005 Gm. (*caffeine*).

"Preserve in well-closed containers." *U. S.*

"A white amorphous powder. No odor; taste sweetish and alkaline. Soluble in 1 part of *water;* soluble in *alcohol* (90 per cent.); insoluble in *ether,* and in *chloroform.* Aqueous solution (1 in 4) alkaline to *litmus* and colorless; when acidified with *acetic acid* yields a violet coloration with *T. Sol. of ferric chloride;* when neutralized with *hydrochloric acid* gives a white precipitate of theobromine, and the filtrate from this, on the addition of more of the acid, gives a precipitate of salicylic acid; the precipitated theobromine, washed with a little *water,* yields, when treated with *potassium chlorate* and *hydrochloric acid* as described under 'Caffeina,' a purple color. The aqueous solution also yields precipitates with *T. Sol. of mercuric chloride,* with solutions of alkaloidal salts, and with *N/10 solution of iodine.*" *Br.*

"**Assay for Theobromine.**—Dissolve about 2 Gm. of Theobromine Sodio-Salicylate, previously dried to constant weight at 110° C. and accurately weighed, in 10 cc. of warm distilled water, and titrate the solution with normal hydrochloric acid, using phenolphthalein T.S. as indicator: not more than 5.5 cc. of normal hydrochloric acid is required to neutralize 2 Gm. of the dried Theobromine Sodio-Salicylate. The solution should now be slightly alkaline to litmus paper or be made so by the addition of one or two drops of very dilute ammonia water. Allow to stand at from 20° to 25° C. for three hours, stirring occasionally, transfer the precipitate of theobromine to a dried and weighed filter of 9 cm. diameter, wash the precipitate and filter with four successive portions of 5 cc. each of ice-cold distilled water, and dry to constant weight at 100° C. To the weight of precipitate thus obtained add 0.13 Gm. (the approximate quantity of theobromine remaining in the liquid and washings). The total weight corresponds to not less than 46.5 per cent. of the weight of dried Theobromine Sodio-Salicylate taken. About 0.2 Gm. of the precipitate obtained in the assay for theobromine volatilizes when slowly heated, leaving only a negligible residue.

"**Assay for Salicylic Acid.**—Dilute the filtrate and washings obtained in the assay for theobromine with distilled water to exactly 50 cc., transfer 25 cc. of the liquid to a separator, add 10 cc. of diluted sulphuric acid, and extract the liberated salicylic with four successive portions of 25, 15, 10 and 5 cc. each of chloroform. Pass the chloroform solutions through a filter previously moistened with chloroform, and wash the filter and the stem of the funnel with a few cc. of hot chloroform. Evaporate the combined chloroform solutions to about 5 cc. at a temperature not exceeding 60° C., add 25 cc. of diluted alcohol which has been previously neutralized with tenth-normal sodium hydroxide, using 3 drops of phenolphthalein T.S. as indicator, and titrate with tenth-normal barium hydroxide until the pink color is restored. Each cc. of tenth-normal barium hydroxide corresponds to 0.01381 Gm. of salicylic acid ($HC_7H_5O_3$).

"Preserve in well-closed containers." *U. S.*

"Yields not less than 40 per cent. of theobromine and 35 per cent. of salicylic acid when tested by the following process: Dissolve 2 grammes of the Salicylate of Theobromine and Sodium in 10 millilitres of warm *water*, slightly acidify with *diluted hydrochloric acid*, add *solution of ammonia* until the reaction is faintly alkaline, and set aside for three hours at about 15.5° C., stirring frequently. Collect the precipitated theobromine on a tared filter, wash twice with 10 millilitres of *water*, dry at 100° C., and weigh the precipitate; it weighs not less than 0.8 gramme. Acidify the filtrate and washings with *hydrochloric acid*, shake with two successive quantities, each of 10 millilitres, of *ether*, evaporate the mixed ethereal solutions, dry the residue at 60° C., and weigh; it weighs not less than 0.7 gramme." *Br.*

Uses.—The effects of theobromine upon the system are very similar to those produced by caffeine except that it has relatively little influence upon the central nervous system. Because of this fact it is much less liable to produce wakefulness—although in some sensitive individuals it does act as a cerebral stimulant—and is not useful as a respiratory stimulant. The most important effect of theobromine upon the system is an increase in the secretion of urine. The mechanism of this action is doubtless the same as that of caffeine. Theobromine also is a powerful stimulant to the voluntary muscles, but because of its feeble effect upon the central nervous system is less useful than caffeine for the purpose of overcoming fatigue. It is used in medicine as a diuretic, especially in cases of *dropsy*. It is superior to caffeine in that because of its feeble influence over the central nervous system much larger doses can be administered than are permissible with caffeine.

Dose, from five to ten grains (0.32–0.65.), repeated at short intervals up to thirty or forty grains (2.0–2.6 Gm.) in 24 hours.

THEOPHYLLINA. U. S.

THEOPHYLLINE Theophyll.

"Dimethylxanthine [$C_5H_2(CH_3)_2.O_2N_4.H_2O$ 1:3]." *U. S.*

Theocin; Theophyllinum, *G.*

Theophylline belongs to a group of organic compounds related to uric acid and known as diureides or xanthin bases. It is also known as 1–3, dimethyl, 2–6, dioxypurine, and differs from caffeine in having one less methyl group. It forms crystalline salts with hydrochloric and nitric acids and with a number of metallic chlorides. It forms a soluble compound with sodium hydroxide. Caffeine may be prepared from it by methylation. Theophylline occurs in the mother liquors after extraction of caffeine from tea. It may be recovered by precipitating as a sparingly soluble compound with silver, which is later decomposed by hydrogen sulphide. The amount found naturally in tea is so small that most of the commercial product is of synthetic origin. It is made from ethyl cyanoacetate, which is the starting point for the synthesis of a number of the xanthine bases.

Description and Physical Properties.—"A white, crystalline, odorless powder having a bitter taste. It is stable in the air. One Gm. of Theophylline is soluble in 120 cc. of water and in 80 cc. of alcohol, at 25° C. It is more readily soluble in hot water; sparingly soluble in ether. It is readily soluble in solutions of potassium hydroxide and in ammonia water.

"Theophylline melts between 269° and 272° C. To about 0.01 Gm. of Theophylline, contained in a porcelain dish, add 1 cc. of hydrochloric acid and 0.1 Gm. of potassium chlorate, and evaporate to dryness on a water bath: on inverting the dish over a vessel containing a few drops of ammonia T.S., the residue acquires a purple color which is destroyed by fixed alkalies. An aqueous solution of Theophylline yields with tannic acid T.S. a precipitate which is soluble in an excess of the reagent.

"A saturated aqueous solution of Theophylline is neutral to litmus paper. Theophylline loses not more than 9.5 per cent. when dried to constant weight at 100° C. (*water*). The ash from 0.1 Gm. is negligible. Two-tenths Gm. of Theophylline dissolves in 5 cc. of sulphuric acid without producing more than a faint yellow color (*readily carbonizable substances*). A clear solution is produced when 0.2 Gm. of Theophylline is dissolved in 5 cc. of potassium hydroxide T.S. or in 5 cc. of ammonia T.S. (*difference from caffeine, theobromine, or paraxanthine*)." *U. S.*

Uses.—In its effects upon the system, theophylline acts almost the same as its isomer, theobromine, and is used in medicine for precisely the same purposes. It appears, however, to be somewhat more irritant to mucous membrane, and is therefore more actively diuretic and also more likely to produce gastric disturbances. When used continuously over considerable periods of time the primary diuretic influence of theophylline may disappear, and the quantity of the urine return to its former low level, this despite increased doses of the drug. The explanation of this clinical observation is not yet forthcoming.

This drug is used more frequently in the form of one of its soluble compounds (see *Theocine Compounds,* Part II).

Dose, three to five grains (0.2–0.32 Gm.).

THUJA. N. F.

THUJA [Arbor Vitæ]

"Thuja consists of the dried, leafy, young twigs of *Thuja occidentalis* Linné (Fam. *Pinaceæ*). Thuja contains not more than 2 per cent. of its stems over 4 mm. in diameter or other foreign organic matter. Only the recently dried drug should be used." *N. F.*

Thuya; White Cedar; Arbor Vitæ; Herba Thujæ; Cèdre Blanc, *Fr.*; Lebensbaum, Weisses Ceder, *G.*

Arbor vitæ is a coniferous tree characterized by the appressed-imbricated leaves, the pointless cone-scales, and the broad wings extending all around the seeds. It attains a height of 20 m., and grows in swampy grounds from New Brunswick to Manitoba, south to North Carolina and Illinois, often forming extensive "cedar swamps." In Canada and the extreme northern parts of the United States it has been erroneously called *white cedar,* a name often applied to *Chamæcyparis thyoides* (L.) B. S. P., which latter is more properly called *Southern white cedar.* The wood is reddish, soft, fine-grained, and very durable and is much used for telegraph poles. The leaves, or small twigs invested with the leaves, have an agreeable, balsamic odor, specially when rubbed, and a strong, balsamic, camphoraceous, bitter taste. The commercial supplies of the drug are obtained from North Carolina, Virginia and Michigan.

Description and Physical Properties.—"*Unground Thuja.*—Twigs fan-shaped, flattened, bearing the scale-like, imbricated leaves appressed in four rows; leaves of the edges boat-shaped, the intermediate flat, those at the tips of the twigs very broad, the lower elongated, all bearing conspicuous glands on the back. Odor strongly balsamic, aromatic and pungent; taste camphoraceous, terebinthinate and bitter.

"*Powdered Thuja.*—Greenish to brownish green consisting chiefly of fragments composed of chlorenchyma and epidermal cells with broadly elliptical stomata from 0.025 to 0.040 mm. in length, the latter with guard cells having lignified walls; numerous long fibers with thick lignified walls and simple oblique pores." *N. F.*

A. Kawalier, of Vienna, found in them volatile oil, a bitter principle called *pini-picrin,* $C_{22}H_{36}O_{11}$—which occurs also in *Pinus sylvestris*—sugar, gelatinous matter, a variety of wax, resin, and tannic acid; also a peculiar crystallizable glucoside, *thujin,* to which he gives the formula $C_{20}H_{22}O_{12}$. It is of a citron-yellow color and an astringent taste, soluble in alcohol, inflammable, and when its alcoholic solution is heated with diluted hydrochloric or sulphuric acid it splits up into glucose and *thujigenin,* and by continuing the reaction another molecule of water is taken up by the latter and *thujetin,* $C_{14}H_{14}O_8$, is formed. The same chemist determined that the tannic acid of this plant is identical with *pinitannic acid,* which he had previously obtained from the leaves of *Pinus sylvestris* L. Thuja leaf oil is of a yellowish-green color and occurs to the extent of 0.5 to 1 per cent. The chief constituents are *alpha-pinene, lævo-fenchone,* and the isomeric ketone *dextro-thujone* which also occurs in the volatile oils of tansy, worm wood and sage. The specific gravity is 0.910 to 0.935; optical rotation $-5°$ to $-15°$; ester value 18 to 25.

Uses.—At one time thuja was used as an internal remedy in the treatment of intermittent fevers, rheumatism, etc., but is today no longer employed for this purpose. It is mildly counter-irritant and is sometimes used as a local application in rheumatic states. Howe (*Eclectic Med. Journ.,* 1880) recommends the local application of a tincture in the treatment of *warts, condylomata,* and other foreign growths, even asserting its value in *epithelioma* and *nævus.* Sicard and Larue (*Gaz. des Hop.,* 1909) state that the injection of a tincture into warts will cause their rapid disappearance. Thuja is occasionally employed internally in menstrual disorders, which perhaps finds some justification in the experiments of Prochnow (*A. I. P. T.,* xxi, p. 314) who found that it had a stimulating effect upon the isolated uterus similar to that of hydrastis. It has also been used especially by the eclectic physicians in various urinary disorders such as *enuresis* and irritability of the bladder. A yellowish-green volatile oil, which may be obtained from the leaves by distillation, has been used with success in *worms.* According to Hildebrand both fenchone and thujone act as stimulants to the heart muscle. (*A. E. P. P.,* xlviii.) F. K. Bailey has reported a case of poisoning in a girl, aged fifteen, who took sixteen drops of the oil of white cedar, and directly afterwards fell unconscious, with clonic spasms followed by epileptiform convulsions lasting at intervals for several hours. Long-continued irritation of the stomach resulted. (*N. R.*, 1872.)

Dose, from fifteen to forty-five grains (1–3 Gm.).

Off. Prep.—Fluidextractum Thujæ, *N. F.*

THYMOL. U. S., Br.

THYMOL

"A phenol [$C_6H_3.CH_3.OH.C_3H_7$ 1:3:4]." *U. S.* "Thymol, or isopropyl-metacresol, $C_{10}H_{14}O$, is a substance obtained from the volatile oils of Thymus vulgaris, *Linn.*, Monarda punctata, *Linn.*, and Carum copticum, *Benth. and Hook. f.* Purified by recrystallisation from alcohol." *Br.*

Acidum Thymicum; Thymic Acid; Methylpropylphenol; Camphre de Thym, Acide Thymique, *Fr.;* Thymolum, *P. G.;* Thymiansaure, Thymolkampher, *G.;* Timolo, *It.;* Timol, *Sp.*

This substance has attracted considerable attention from its possession of powerful antiseptic properties. It may be obtained by submitting the volatile oils of several plants to a prolonged refrigeration, under the influence of which it crystallizes. Thus, it has been obtained from *Monarda didyma* Linn., *M. punctata* Linn., *Thymus zygis* Linn. var. *gracilis* Boiss., *Ptychotis ajowan* (see *Oleum Ajowan*), *Mosula Japonica* and *Carum copticum* Benth. et Hook. filius. *Ocimum viride* Willd., a plant which is used in Liberia as an antiperiodic, and is said to be especially valuable owing to the fact that when growing in a room it will drive mosquitoes out of the apartment, as well as the medicinally active *O. gratissimum* of India, probably depend for their activities upon thymol. (*Proc. A. Ph. A.*, xxvi, 168.) Thymol is obtained from any of the oils in which it occurs by distilling off from these the larger part of the hydrocarbons and adding warm sodium hydroxide solution to the residue, which combines with the thymol. The mixture is diluted after a time with hot water, which causes the unattacked oil to rise to the top. From the sodium hydroxide solution hydrochloric acid sets the thymol free. This collects as an oily layer, which on cooling will crystallize if a crystal of thymol is added.

A process has been patented by M. Dinesman for making *synthetic thymol* from *p*-cymol (see *Ph. Centralh.*, Oct., 1901, 650).

Description and Physical Properties.—"Large, colorless, transparent crystals, having an aromatic, thyme-like odor, and a pungent, aromatic taste. One Gm. of Thymol is soluble in about 1000 cc. of water, about 1 cc. of alcohol, 0.7 cc. of chloroform, 1.5 cc. of ether, and in 1.7 cc. of olive oil, at 25° C. It is soluble in glacial acetic acid and in fixed or volatile oils.

"Thymol melts between 48° and 51° C., remaining liquid at a considerably lower temperature. Thymol is heavier than water, but when liquefied by fusion it is lighter than water. An alcoholic solution of Thymol (1 in 20) is neutral to litmus paper, and is optically inactive.

"When Thymol is triturated with about an equal weight of camphor or menthol, the mixture liquefies. Dissolve a very small crystal of Thymol in 1 cc. of glacial acetic acid, and add 6 drops of sulphuric acid and 1 drop of nitric acid: the liquid assumes a deep bluish-green color by reflected light. Heat about 1 Gm. of Thymol in a test tube in a water bath with 5 cc. of a 10 per cent. solution of sodium hydroxide: a clear, colorless, or pale red solution is formed, which becomes darker on standing, without the separation of oily drops. Upon the addition of a few drops of chloroform to this solution and agitating the mixture, a violet color is produced. Volatilize about 2 Gm. of Thymol on a water bath: not more than 0.05 per cent. of residue remains." *U. S.*

"Large, oblique prismatic crystals, sinking in water at 15.5° C. Melting point from 50° to 51° C. Completely volatilised on a water-bath. Odor recalling that of thyme; taste pungent, aromatic. Almost insoluble in *water;* freely soluble in *alcohol* (90 per cent.), in *ether,* and in *solution of sodium hydroxide.* A solution of Thymol in half its volume of *glacial acetic acid,* warmed with an equal volume of *sulphuric acid,* assumes a reddish-violet color." *Br.*

Robert Meldrum (*Chem. News,* cxi, 193) has attempted to reconcile the conflicting melting points which have been ascribed to thymol and states that the variations and wide range recorded are due to supercooling. He gives the correct solidifying point at 48.2° to 49.2° C. Moles and Marquina (*J. S. C. I.*, 1919, xxxviii, 388A) propose a method of assay for thymol based upon iodometric titration.

Uses.—Thymol was originally introduced as a disinfectant for the same range of purposes for which phenol is employed. The advantage claimed for it was a more agreeable odor. Its drawbacks are its strong local irritant effect and its sparing solubility in water. Concerning its antibacterial powers the findings of different investigators have been contradictory, thus Cooper (*B. M. J.*, 1912, i, p. 1235) finds that in the presence of organic matter it is eight times as powerful as phenol and in the absence of organic matter twenty-five times as strong. On the other hand Schmidt (*Z. P. C.*, 1910, lxvi, p. 412) asserts that it has no germicidal value against vigorous bacteria. It is probably superior to phenol in antibacterial power. It is to-day rarely employed as a surgical disinfectant, but is an ingredient in many of the antiseptic mixtures intended for use upon mucous cavities, such as the National Formulary *Antiseptic Solution.* Its value for these purposes, however, is greatly reduced because of its powerful local irritant action; it is scarcely possible to apply it in stronger solution than one part in a thousand without considerable discomfort. Thymol is also used as a gastro-intestinal disinfectant in *fermentative gastritis, enteritis,* and similar conditions. For this purpose it may be given in doses of two to five grains (0.13–0.32 Gm.) several times a day.

Perhaps the most important modern use of thymol is as a vermifuge. It is efficient against the *tape-worm* and probably all forms of intestinal parasites, but is especially employed against the *hook-worm*. For this purpose it is necessary to use it in such large doses that there is danger of poisoning unless absorption be guarded against. The method employed by the Porto Rican Commission as reported by Schultz (*J. A. M. A.*, 1911, lvii, p. 1102) was as follows: If the patient be fairly robust, from fifteen to thirty grains (1–2 Gm.) were given mixed with an equal quantity of sugar of milk, and administered on an empty stomach; this dose is repeated in two hours, and two hours later followed by a vigorous purge, either magnesium sulphate or compound cathartic pills. It is essential that the intestines be as empty as possible as the presence of various foodstuffs encourages absorption. Castor oil should be avoided as the cathartic for a similar reason. The symptoms of thymol poisoning are nausea, vomiting, headache, ringing in the ears, dizziness, muscular weakness, thready pulse, and fall of bodily temperature.

Dose, two to fifteen grains (0.13–1.0 Gm.).

Off. Prep.—Cataplasma Kaolini, *N. F.;* Liquor Antisepticus, *N. F.;* Liquor Aromaticus Alkalinus, *N. F.;* Nebula Aromaticus, *N. F.;* Nebula Thymolis, *N. F.;* Petroxolinum Sulphuratum Compositum, *N. F.;* Pulvis Antisepticus, *N. F.*

THYMUS. N. F.

THYME

"Thyme consists of the dried leaves and flowering tops of *Thymus vulgaris* Linné (Fam. *Labiatæ*). Thyme contains not more than 3 per cent. of stem over 1 mm. in diameter or other foreign organic matter and yields not more than 4 per cent. of acid-insoluble ash." *N. F.*

Garden Thyme; Common Thyme; Herba Thymi *P. G.;* Thymian, *G.;* Thym, *Fr.;* Tomillo, *Sp.*

The thyme is a small shrub growing to a height of about a foot, with ascending, brown to purplish, branches and oblong-lanceolate, grayish-green leaves; the pale purple flowers are strongly bilabiate and arranged in dense cymes both axillary and terminal. The plant is a native of south-central Europe and is widely cultivated in France, Germany, Spain and the United States. The commercial supplies of the crude drug come chiefly from Italy, Spain and France.

The whole plant is aromatic and yields from about 0.5 per cent. of a volatile oil, which is official (see *Oleum Thymi*). This oil contains as its most important ingredient thymol, but it is stated that the oil from the Spanish plant yields carvacrol, rather than thymol with which it is isomeric.

Description and Physical Properties.—"*Unground Thyme.*—Stems quadrangular, about 0.5 mm. in diameter, grayish brown or purplish in color, pubescent, nodes from 5 to 20 mm. apart, occasionally with the opposite leaves attached; leaves linear, linear-lanceolate, or ovate, oblong, from 0.5 to 6 mm. in length and from 0.5 to 2 mm. in breadth, summit acute, base obtuse tapering into a petiole from 0.5 to 2 mm. in length, margin revolute, upper surface grayish green, puberulent, with numerous one-celled, thick-walled, non-glandular hairs; lower surface grayish, pubescent, with non-glandular, one- to four-celled, thick-walled, rough simple hairs, up to 0.135 mm. in length and usually curved at the first joint in the bases; numerous compound glandular secreting hairs, with short one-celled stalk occurring chiefly on the upper surface and depressed in the cuticle, which give the leaf a glandular-punctate appearance; inflorescence in about twelve-flowered axillary whorls; flowers polygamous, calyx tubular, about 4 mm. in length, ovoid or slightly curved on the lower side near the base, from nine- to twelve-nerved, pubescent, the throat bearded with straight simple hairs up to 1 mm. in length, bilabiate, upper lip three-toothed, lower lip with two hairy, ascending attenuate divisions, corolla about twice as long as the calyx, purplish, smooth within, slightly pubescent without, upper lip emarginate, lower spreading and three-lobed, stamens slightly didynamous and exserted, stigma bifid; nutlets about 0.5 mm. in diameter, spheroidal and finely tuberculate. Odor agreeable, aromatic; taste aromatic and warming.

"*Powdered Thyme.*—Light green; short sharp-pointed unicellular non-lignified non-glandular hairs about 0.060 mm. in length; 2- to 3-celled non-lignified, uniseriate, non-glandular hairs of two types, both with papillose walls, one from 0.200 to 0.300 mm. in length with the apical cell sharp-pointed, the other with the apical cell somewhat curved or hooked; glandular hairs of two types, one with a short stalk embedded in the epidermal layer and a unicellular head, the other with an 8- to 12-celled head but without a stalk; fragments of leaf tissue composed of chlorenchyma with vascular tissue and epidermal cells with broadly elliptical stomata the latter about 0.025 mm. in length; fibers with thick lignified walls and simple pores; pollen grains, nearly spheroidal about 0.020 mm. in diameter." *N. F.*

The chief adulterants of thyme have been the leaves and flowering tops of *Origanum creticum* or "*Spanish hops*" and of *O. Dictamnus* or "*Cretan Dittany.*" The former may be detected by its yellowish-brown stems, palmately 5-veined, ovate leaves, papillated nutlets and oil containing carvacrol; the latter by its elliptical, densely hairy leaves and volatile oil containing pulegone.

Uses.—The therapeutic value of thyme probably depends entirely upon its volatile oil and it is very doubtful whether the whole plant has any advantage over the volatile oil. Of recent years, however, it has come into considerable popularity, largely because of the advertisement of a proprietary preparation, as a remedy for *bronchitis* and especially *whooping cough.*

Dose, from thirty to sixty grains (2–4 Gm.).

Off. Prep.—Fluidextractum Thymi, *N. F.;* Syrupus Thymi, *N. F.;* Syrupus Thymi Compositus, *N. F.*

THYMOLIS IODIDUM. U. S.

THYMOL IODIDE Thymol. Iod.

"Thymol Iodide is a mixture of iodine derivatives of thymol, principally dithymol-diiodide [$(C_6H_2.CH_3.C_3H_7.OI)_2$], containing, when dried to constant weight over sulphuric acid, not less than 43 per cent. of iodine." *U. S.*

Dithymoldiiodide; Aristol; Aristolum; Diiodothymolum; Diiodo dithymolum, *Fr. Cod.;* Dithymol Biiodé, *Fr.;* Dithymoljodid, Annidalin, Thymotol, *G.;* Timol Biyodado, Aristol, *Sp.*

Preparation.—*Thymol Iodide* contains about 45 per cent. of iodine; it is the product of the condensation of two molecules of thymol and the substitution of the hydrogen in the hydroxyl group in each by iodine. It may be prepared by decomposing a solution of iodine in potassium iodide by an alcoholic solution of thymol. The Cincinnati Academy of Pharmacy published the following formula for thymol iodide: Thymol, 50 Gm.; potassium iodide, 58 Gm.; sodium hydroxide, 50 Gm.; water, to make 500 cc.; solution of chlorinated soda, to make 3000 cc. Dissolve the thymol, potassium iodide, and sodium hydroxide in sufficient water, add the solution of chlorinated soda, collect the precipitate on a filter and wash it with water until it is free from chlorides. Remove the precipitate and dry it carefully at a temperature not exceeding 20° C. Reduce it to powder and keep it in a well-stoppered dark bottle. (*Am. Drug.,* 1898, 130.) The French Codex directs that two solutions be made, one by dissolving 16 Gm. of sodium hydroxide and 15 Gm. of thymol in sufficient water to make the solution measure 300 cc. The other solution is made by dissolving 60 Gm. of iodine and 80 Gm. of potassium iodide in enough water to make the solution measure 300 cc., the latter solution is added gradually to the alkaline solution of thymol with constant stirring; the resulting brown precipitate is washed with water and the product dried between 40° and 50° C.

The structural formula of thymol iodide usually assumes the compound to be a hypoiodous ether of the phenolic group. J. Bonjault contests this view and states that the iodine replaces the hydrogen of the hydrocarbon nuclei. (*J. P. C.,* 1918, xvii, 221.)

Description and Physical Properties.—"A reddish-brown or reddish-yellow, bulky powder with a very slight, aromatic odor. Thymol Iodide is insoluble in water and in glycerin; slightly soluble in alcohol; readily soluble in chloroform, ether, collodion, and in mixed or volatile oils, usually leaving a slight residue. It is insoluble in cold or in hot solutions of the fixed alkali hydroxides. When heated with concentrated sulphuric acid, it is decomposed with the separation of iodine.

"Heat about 0.5 Gm. of Thymol Iodide, accurately weighed, in a porcelain crucible until charred, cool, add 5 drops of sulphuric acid, and ignite to constant weight: not more than 1.5 per cent. of residue remains. Digest 0.1 Gm. of Thymol Iodide with 50 cc. of warm, distilled water for 10 minutes, filter, cool, add 5 drops of diluted nitric acid and 1 cc. of silver nitrate T.S.: the turbidity produced, if any, is not greater than that in a control test made with 1 cc. of a solution containing 0.002 Gm. of potassium iodide (*soluble iodides*). Shake 0.5 Gm. of Thymol Iodide with 10 cc. of distilled water and filter the mixture: the filtrate is not alkaline to litmus paper (*alkalies*), nor is it colored blue upon the addition of a few drops of starch T.S. (*free iodine*).

"**Assay.**—Mix thoroughly about 0.25 Gm. of Thymol Iodide, previously dried to constant weight over sulphuric acid and accurately weighed, with about 3 Gm. of anhydrous potassium carbonate. Place the mixture in a platinum crucible, cover with about 1 Gm. of anhydrous potassium carbonate, and heat moderately, gradually increasing the heat, but not exceeding a dull redness, until the mass is completely carbonized. Extract the residue with boiling distilled water and wash it on a filter with boiling distilled water until the washings cease to produce an opalescence with silver nitrate T.S. Heat the combined washings, which measure about 150 cc., on a water bath and add an aqueous solution of potassium permanganate (1 in 20) in small portions, until the hot liquid remains permanently pink. Add just enough alcohol to remove the pink tint, cool to room temperature, dilute to 200 cc., mix well, and filter through a dry filter, rejecting the first 50 cc. of filtrate. To 100 cc. of the subsequent clear filtrate, add about 1 Gm. of potassium iodide (free from iodate) and an excess of diluted sulphuric acid, and titrate the liberated iodine with tenth-normal sodium thiosulphate, adding starch T.S. near the end of the titration. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.002115 Gm. of iodine.

"Preserve in well-closed containers, protected from light." *U. S.*

Osseward (*Proc. A. Ph. A.,* 1901, 176) obviates the difficulty of obtaining smooth ointments of thymol iodide (which most dispensers have experienced when proceeding in the usual way) by adding sufficient ether to 1 oz. of thymol iodide placed in a dry mortar, to form a paste, then stirring in 1 oz. of olive oil until a smooth paste is obtained; the ether can be dissipated during the stirring, and this 50 per cent. mixture used in making ointments by incorporating with fatty substances.

Uses.—Thymol iodide is used as a non-toxic and non-irritant dusting powder for *wounds.* It has the same range of usefulness for this purpose as iodoform over which it has the great advantage of being comparatively odorless. According to Shamberg and Kolmer (*J. A. M. A.*, 1914, lxii, p. 1950), it restrains the growth of *Staphylococcus aureus* when present in the proportion of 0.5 per cent. Despite, however, its superiority in direct antiseptic action to iodoform, it is not held in as high esteem by most surgeons. It is also used as a dusting powder in various moist *skin diseases,* such as weeping eczemas, and Daxenberger (*Heilkunde,* 1908) recommends a 10 per cent. solution in olive oil as a local application in *atrophic rhinitis* and *fissure in ano* as well as various *skin diseases.*

Dose, from two to three grains (0.13–0.2 Gm.).

THYROIDEUM. U. S. (Br.)

THYROID Thyroid. [Thyroideum Siccum U. S. P. IX]

“Thyroid is the cleaned, dried, and powdered thyroid gland, previously deprived of connective tissue and fat. It is obtained from domesticated animals which are used for food by man. Thyroid contains not less than 0.17 and not more than 0.23 per cent. of iodine in thyroid combination, and must be free from iodine in inorganic or any other form of combination than that peculiar to the thyroid gland. One part corresponds to approximately 5 parts of the fresh glands.” *U. S.* “Dry Thyroid is a powder prepared from the fresh and healthy thyroid glands of the sheep. Remove the external fat and connective tissue from the thyroid glands taken from the sheep immediately after killing. Cut the glands across, and reject any which contain cysts, are hypertrophied, or are otherwise abnormal. Mince finely the healthy glands, and dry at a temperature of 30° to 40° C.; powder the dried product; remove all fat by washing with *petroleum spirit;* again dry the residue.” *Br.*

Thyroideum Siccum, *Br.;* Dried Thyroids; Glandulæ Thyroideæ Siccæ; Desiccated Thyroid Glands, Schilddrüsen, Getrocknete Schilddrüsen, *G.*

The thyroid body is a glandular structure found in all mammals, located in the front of the neck. It consists of two oval lobes usually connected by an “isthmus” and differs considerably in size even in animals of the same species. The human thyroid averages from 30 to 40 Gm. in weight, but in the condition known as goiter, sometimes forms a huge tumor. The gland secretes a substance necessary for the health of the animal, which is poured directly into the blood vessels with which it is richly supplied. Its use as a medicine is because of the secretion retained in it.

Description and Physical Properties.—“A yellowish, amorphous powder, having a slight, characteristic odor.

“Thyroid contains not more than 6 per cent. of moisture. Ash: not more than 5 per cent.” *U. S.*

“A light, dull-brown powder, with a very faint meat-like odor and taste; free from any flavor of putrescence. Liable to become damp on exposure to the air, and to deteriorate.” *Br.*

Assay.—“Mix 1 Gm. of Thyroid in a nickel crucible of about 125 cc. capacity, with 15 Gm. of a mixture composed of 138 parts by weight of anhydrous potassium carbonate, 106 parts of anhydrous sodium carbonate, and 75 parts of potassium nitrate. Spread an additional 5 Gm. of this fusion mixture evenly over the surface. Heat the crucible over a free Bunsen flame until no further carbonization is observed, cool, and dissolve the residue in about 150 cc. of distilled water, warming to hasten solution. Transfer this solution to an Erlenmeyer flask of about 500 cc. capacity, and add approximately 50 cc., or its equivalent, of a fresh solution of chlorinated soda (containing 2.5 per cent. of chlorine by weight). Treat the mixture with enough phosphoric acid, diluted with an equal volume of distilled water, to produce an appreciable yellow tint of free chlorine, add about 10 cc. more of phosphoric acid, diluted with an equal volume of distilled water, and boil for one-half hour or until the volume has been reduced to about 150 cc. Cool the liquid, add 10 cc. of a freshly prepared aqueous solution of potassium iodide (1 in 100), and titrate the liberated iodine with freshly prepared two-hundredth-normal sodium thiosulphate, starch T.S. being used as indicator just before the end of the reaction. Each cc. of two-hundredth-normal sodium thiosulphate used corresponds to 0.0001058 Gm. of iodine derived from thyroid glands.” *U. S.*

Various attempts to develop a biological method for the standardization of thyroid preparations have been made. The two most promising are those based upon (1) the metamorphosis of tadpoles and (2) alterations in susceptibility towards acetonitrile.

It is well established that thyroid feeding hastens the development of tadpoles into frogs. Rogoff (*J. P. Ex. T.,* 1917, x, p. 199) has developed a method based upon this principle which he claims will detect variations of 10 per cent. in the activity of preparations. Jensen (*Ph. Era,* 1921, liv, p. 143) suggests the use of the axolotl (*Ambystoma Mexicanum*). This is an amphibian which normally does not develop beyond the larval (tadpole) stage but, according to Jensen, if fed with thyroid gland undergoes a similar metamorphosis to other amphibians. The acetonitrile test was brought forward by Hunt and Seidl (*J. P. Ex. T.,* 1910, ii, p. 15). They found that thyroid feeding alters the resistance of mice to certain poisons, diminishing the susceptibility to acetonitrile but increasing them to morphine. They have suggested the lessening of the sensitiveness to acetonitrile as a test of the activity of samples of the drug.

The attempt to isolate an active principle from the thyroid has engaged the attention of physiological chemists for more than thirty years. In 1895 Baumann (*Zeit. P. C.,* xxi) described a principle, *thyroiodine* (*iodothyrine*), which possessed many of the physiological properties of the gland, but it was subsequently shown not to be a pure chemical individual. Pick and Pilenes (*Z. E. P. T.*, 1909, vii, p. 518) prepared a thyro-globulin by precipitation from an aqueous extract by means of ammonium sulphate. In 1915 Kendall separated a crystalline substance *thyroxin,* which has received official recognition, but it is not yet definitely established as the sole active constituent (see *Thyroxinum*).

Uses.—The thyroid gland is one of those organs, called endocrine, which furnish an internal secretion necessary for the health of the body. Its congenital absence leads to the condition called *cretinism,* which is chiefly characterized by: a failure of growth both mental and physical, a lack of ossification in the bones, general sluggishness, the deposit in the subcutaneous tissues of a peculiar jelly-like material, which causes an appearance resembling that of general dropsy, and usually sub-normal temperatures. Its removal in adults leads to an analogous symptom-complex called *myxedema.* In this state there is the same deposit beneath the skin giving the appearance of a dropsy, from which, however, it can be differentiated by the fact that the skin does not pit on pressure. There is mental sluggishness, a slowing of the pulse and usually a lowering of the bodily temperature. It is probable that there are diseased conditions of the system in which there is a partial but not complete failure of its secretion. The symptoms supposed to indicate such a state of hypo-thyroidism are a thick dry skin, loss of hair, depression of sexual functions, accumulation of fat, increased tolerance for sugar, and a subnormal body temperature. The administration of the thyroid body or its active principle to healthy animals causes an increase in the metabolism with consequent tendency for elevation of the temperature and a loss of body weight. There is usually increased rapidity of the pulse, nervous restlessness often with tremors, and a tendency to insomnia. The loss in bodily weight is due chiefly to the oxidation of the adipose tissue, but is accompanied, especially when the diet is restricted, by destruction of the nitrogenous (protein) substances of the body. There is usually also an increase in the number of mononuclear leukocytes of the blood. Although the single dose produces no very obvious changes in the bodily functions, Asher and Flack (*Z. B.*, 1911, lv, p. 83) have shown that the injection of this drug increases the irritability of the vasomotor center which observation has been confirmed by other observers. It is this increased sensitiveness that causes the extreme reaction to epinephrine, which is sometimes used as a diagnostic test (see under *Diagnostic Tests,* Part II).

As a medicine the thyroid is used first to combat those symptoms which are due to the absence of its secretion, either partial or complete, congenital or acquired. In addition to those symptoms already described as *myxedema* and *cretinism,* there are many physicians who attribute various obscure chronic disorders, especially those that occur during the climacteric, to diminished activity of the thyroid gland and consequently recommend the use of this drug. Because of the fact that thyroid feeding causes a loss of weight, it has been largely used in cases of *obesity,* even those that are not dependent on thyroid deficiencies. Many of the "antifat" nostrums upon the market contain thyroid. While there is no doubt that the thyroid will cause a loss of excessive corpulence, the injudicious use of it is accompanied with considerable danger, especially of the production of cardiac disturbances which may seriously injure the health. Means (*J. A. M. A.*, 1921, lxxvii, p. 792) strongly deprecates the use of the thyroid in any case of obesity, which is not due to subnormal metabolism.

In addition to these states in which the drug is obviously of value, it has been used in a more or less empiric manner in a large number of other disorders. There are indeed few diseases, either acute or chronic, for which the thyroid gland has not been recommended by someone. Among those conditions in which there is more or less suggestive evidence of its usefulness may be mentioned uterine disorders, especially *metrorrhagia;* certain types of *chronic nephritis* (see Epstein, *A. J. M. S.*, 1922, clxiii, p. 167); diseases of the bones as *ununited fractures, osteomalacia,* and *rheumatoid arthritis,* certain skin diseases especially *psoriasis, hay fever, asthma, cancer, hemophilia,* etc.

In myxedema it is generally well to begin with relatively large doses, about five grains (0.32 Gm.), until the accumulated symptoms due to the prolonged lack of thyroid secretion have abated, and afterwards continue the use of the drug in smaller quantities. For other conditions it is generally well to begin with smaller doses, one or two grains (0.06–0.12 Gm.), three times a day, gradually increasing if necessary, until palpitation of the heart or excessive nervousness indicates that the physiological limit or the therapeutic purpose is obtained. In any case, during the administration of the drug the occurrence of any of the symptoms of hyper-thyroidism should be the immediate signal for the withdrawal of the drug.

Among the various preparations of thyroid upon the market may be mentioned the following: *Iodothyrin* (*thyro-iodine*) appears commercially diluted with milk sugar to a strength equal to that of the fresh gland. The dose is ten to thirty grains (0.65–2.0 Gm.). *Thyroprotein,* standardized to contain 0.33 per cent. of iodine. *Thyraden,* dose two to eight grains (0.13–0.5 Gm.). *Thyrein,* said to be identical with iodothyrin. *Thyroidin,* a commercial preparation corresponding to the official dried gland. *Thyreoidin* Notkin, dose, one-sixth grain (0.01 Gm.).

It is said also to be useful for hypodermic administration in the form of a one-half per cent. solution. *Thyron* or *tyron,* prepared by treating thyroid gland with tannic acid.

Dose, of dried thyroids, from one to five grains (0.06–0.32 Gm.).

THYROXINUM. U. S.

THYROXIN Thyrox.

"Thyroxin [$(C_8H_5ONI_3).C_2H_4COOH$] is an active principle obtained from the thyroid gland, and contains not less than 63 per cent. of iodine." *U. S.*

This substance was discovered by E. C. Kendall (*J. Bi. Chem.,* 1915, xx, p. 501) who has also determined its chemical constitution to be a di-iodo-dihydroxy-indol (*J. A. M. A.,* 1918, lxxi, p. 871). The proportion in the thyroid body is from 0.025 per cent. to 0.001 per cent. It is prepared by first treating fresh or desiccated thyroid with a hot aqueous 5 per cent. solution of sodium hydroxide. The liquid is then filtered to separate insoluble soaps and the filtrate is cooled and acidified. The precipitate, which comprises only about 1 per cent. of the weight of the glandular substance used, is redissolved in sodium hydroxide solution and reprecipitated with hydrochloric acid. This second precipitate is then dried, dissolved in 95 per cent. alcohol and the liquid is carefully neutralized with sodium hydroxide. The solution is then filtered and the filtrate treated with a saturated aqueous solution of barium hydroxide, after another filtration carbon dioxide is passed into the liquid to remove barium. The filtered alcoholic solution is then subjected to distillation to recover the alcohol, the residue acidified with hydrochloric acid and the precipitate collected and dissolved in a weak solution of sodium hydroxide in strong alcohol. The solution is again treated with carbon dioxide, this time to precipitate sodium carbonate, and the alcohol again removed and recovered by distillation; upon standing a mono-sodium salt of thyroxin separates. This is further purified by a repetition of the foregoing precipitation processes, dissolving it in alkaline alcohol and using acetic acid as the precipitating agent. By this process about one ounce of thyroxin is obtained from over three tons of fresh thyroids.

Description and Physical Properties.—"White or slightly yellow, needle-like, odorless crystals or powder. Thyroxin is insoluble in water and practically insoluble in alcohol or other usual organic solvents, but in the presence of mineral acids it dissolves in alcohol. It is soluble in solutions of the alkali hydroxides and when alkaline solutions are saturated with sodium chloride the sodium salt of thyroxin separates.

"Ignite a few milligrams of Thyroxin with about 0.1 Gm. of sodium carbonate, dissolve the residue in 2 cc. of distilled water, acidulate with acetic acid, add 1 cc. of chloroform and a few drops of chlorine T.S.: the chloroform acquires a violet color.

"The ash from 0.01 Gm. is negligible. Dry about 0.02 Gm. of Thyroxin over sulphuric acid for twenty-hour hours: the loss in weight is negligible (*water*). Shake 0.01 Gm. of Thyroxin with 10 cc. of distilled water during five minutes, and filter. Acidulate the filtrate with one drop of diluted nitric acid, and add 3 drops of tenth-normal silver nitrate: the turbidity so produced is not greater than that produced in a control test by one drop of fiftieth-normal hydrochloric acid (*soluble iodides*).

"**Assay.**—Mix about 0.02 Gm. of Thyroxin, previously dried over sulphuric acid for twenty-four hours and accurately weighed, with about 0.5 Gm. of anhydrous potassium carbonate in a small platinum crucible. Cover the mixture with an additional 1 Gm. of anhydrous potassium carbonate, and heat gradually until it is completely decomposed. Treat with distilled water and transfer to a 100 cc. graduated flask. Heat the solution on a water bath and add potassium permanganate solution (1 in 20), drop by drop, until the liquid remains pink. Then add, drop by drop, just enough alcohol to discharge the pink color, cool, and dilute to the mark with recently boiled and cooled distilled water. Mix well and filter through a dry filter into a dry flask rejecting the first 20 cc. of the filtrate. To 50 cc. of the filtrate add about 0.5 Gm. of potassium iodide and 30 cc. of diluted sulphuric acid, and titrate the liberated iodine with two-hundredth-normal sodium thiosulphate, using starch T.S. as indicator towards the end. Correct for any iodine liberated in a blank made with the same quantities of distilled water, sulphuric acid, and potassium iodide. Each cc. of two-hundredth-normal sodium thiosulphate corresponds to 0.0001058 Gm. of iodine." *U. S.*

Uses.—While it seems well established that thyroxin is a pure chemical substance and that it possesses some of the physiological properties of the thyroid secretion, especially the power of increasing the metabolic rate, Hunt (*A. J. P.,* 1923, lxiii, p. 257 and *J. P. Ex. T.,* xxi, p. 199) has reached the conclusion that it does not fully represent the physiological activity of the thyroid gland. He found that in proportional dose it had less effect upon the development of growing animals and also was less efficient in protecting mice against his acetonitrile test. The drug must be regarded as still in the experimental stage, but it is being used with apparent success in the treatment of many of those conditions in which the whole gland is of service. It may be administered either by mouth or by intravenous injection.

Dose, from one three-hundredth to one-fiftieth of a grain (0.2 to 1 Mgm.). Jackson (*Illinois Med. J.,* 1925) has found that 50 milligrammes of thyroxin, administered intravenously, is required to bring the basal metabolic rate of a myxedematous patient to within normal limits. A variable daily dose of from 0.8 to 2 milligrammes of thyroxin by mouth is required to maintain this level. It is stated that 1 milligramme (1/60 grain) daily in a normal person if continued will eventually cause toxic symptoms.

TINCTURÆ. U. S.

TINCTURES

"Tinctures are liquid preparations made by extracting the useful principles from vegetable or animal drugs by appropriate menstrua or solvents containing alcohol. Tincture of ferric chloride and tincture of iodine are exceptions, being alcoholic solutions of chemicals." *U. S.*

Teintures (Alcooliques) Alcoolés, *Fr.;* Tinkturen, *G.;* Tinture alcooliche, *It.;* Tinturas alcoholicas, *Sp.*

Tinctures, in the pharmaceutical sense of the term, are alcoholic solutions of medicinal substances, prepared by maceration, digestion, or percolation. Solutions in spirit of ammonia and ethereal spirit are embraced under the same denomination, but are severally distinguished by the titles of *ammoniated tinctures* and *ethereal tinctures.* The advantages of alcohol as a menstruum are that it dissolves principles which are sparingly, or not at all, soluble in water, and contributes to their preservation when dissolved, while it leaves behind some inert substances which are dissolved by water. In no instance, however, is dehydrated alcohol employed. Because of the slight amount of water in it, official alcohol dissolves more or less of substances which are insoluble in dehydrated alcohol, while its solvent power in relation to bodies soluble in that fluid is sufficient for all practical purposes. A hydroalcoholic menstruum is often preferable to official alcohol, as it is capable of extracting a larger proportion of those active principles of plants which require an aqueous menstruum, while at the same time it is strong enough to prevent spontaneous decomposition, and has the advantages of being cheaper and less stimulating. In such cases the proper proportion of alcohol in the menstruum has been determined experimentally. Official diluted alcohol, which is of approximately the same strength as proof spirit, is frequently directed as a menstruum for tinctures. The diluted alcohol of the different Pharmacopœias is not of the same strength; that of the United States consists of equal volumes of official alcohol and water, and has the sp. gr. of about 0.936 at 15.56° C., while the British has four official diluted alcohols—70, 60, 45, and 20 per cent. Undiluted alcohol, or rectified spirit as it was formerly called, is preferred as a solvent when the substance to be extracted or dissolved is nearly or quite insoluble in water, as in the instances of resins, camphor, and the essential oils. The presence of water is here injurious, by diluting the menstruum, which interferes with its solvent power. Thus, water added to an alcoholic solution of one of these bodies produces a precipitate. Diluted alcohol, or proof spirit, is employed when the substance is soluble both in alcohol and in water; or when one or more of the ingredients are soluble in the one fluid and one or more in the other, as in the case of vegetable bodies which contain extractive or tannin, or the natural salts of the alkaloids, or gum united with resin or volatile oil. As these include the greater number of medicines from which tinctures are prepared, diluted alcohol is most frequently used. In the preparation of the tinctures, the drug should be dry, and properly comminuted. It is usually better in a moderately fine than in a very fine powder; the proper degree of pulverization varies according to the ease with which the menstruum extracts the soluble principles. The recommendations of the International Protocol included the use of the 70 per cent. alcohol for the various tinctures, but as this has not proven to be the best menstruum for some drugs, the U. S. P. has not always followed the suggestion.

"Tinctures of potent drugs are made of the strength of 10 Gm. of drug in 100 cc. of tincture, to conform to the Brussels Protocol. The other tinctures vary in the proportion of drug in the finished tincture, but many of these are made of the strength of 20 Gm. of drug in 100 cc. of tincture. Tinctures, with few exceptions, are made by percolation. Maceration or solution is preferred when, from its physical character, the drug is not suitable for percolation. The majority of official tinctures are prepared by one of the type processes described. The process to be followed is directed in each formula with such modification as may be necessary. A number of drugs require special manipulation for the preparation of satisfactory tinctures, and the formulas for these will be found in full in the text. Where it has been possible to standardize the tinctures, standards and assays have been provided. Tinctures should be stored in tightly-stoppered bottles, in a cool place, protected from light." *U. S.*

Type Process P—Percolation.—"Moisten the powdered drug or mixed drugs designated in the formula with a sufficient quantity of the prescribed menstruum to render it evenly and distinctly damp and to maintain it so after macerating for six hours in a tightly-covered container. Transfer it to a precolator, pack it firmly, unless otherwise directed, and pour on enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for twenty-four hours. Then allow the percolation to proceed slowly, gradually adding sufficient of the menstruum to make the finished tincture measure 1000 cc., and mix thoroughly.

"*Modification for Assayed Tinctures.*—In tinctures that are directed to be assayed, allow the percolation to proceed until the percolate measures 950 cc. Assay a portion of this percolate as directed and from the alkaloidal content thus determined, or from the biological activity, ascertain by calculation the strength of the remainder of the liquid, and, make the finished tincture conform to the required standard, adding sufficient of the menstruum if necessary, and mix thoroughly." *U. S.*

Type Process M—Maceration.—"Macerate the drug or mixed drugs designated in the formula in a stoppered container, in a moderately warm place, with 750 cc. of the prescribed solvent (unless a different amount is specified in the formula). Continue the maceration with frequent agitation during three days or until active constituents of the drug are practically extracted. Transfer the mixture to a filter, and, when the liquid has drained off, gradually wash the residue on the filter with enough of the solvent directed to make the filtrate measure 1000 cc., and mix thoroughly." *U. S.*

The British Pharmacopœia in the *Appendix IX* (see Part III) has provided detailed instruction for both percolation and maceration processes.

Tinctures were at one time universally prepared by maceration or digestion. The U. S. Pharmacopœia formerly directed maceration at ordinary temperatures, and extended the period to two weeks. In several instances in which maceration is ordered in the U. S. Pharmacopœia, maceration for three days is directed, but the Br. process requires seven days. When circumstances require that the tincture should be speedily prepared, digestion may be resorted to. Care should always be taken to keep the vessels well stoppered, in order to prevent the evaporation of the alcohol. The materials should be frequently shaken during the digestion or maceration, and this caution is especially necessary when the substance acted on is in the state of powder. The tincture should not be used until the maceration is completed, when it should be separated from the dregs either by simply filtering it through paper, or, when force is requisite, by expressing it through linen, and filtering.

The plan of preparing tinctures by percolation has been extensively adopted, and has been found to answer well when skilfully executed. In the present edition of our Pharmacopœia, percolation has been adopted as the rule, maceration being directed in some instances in which it was deemed preferable.

The method of making tinctures by diluting fluidextracts, except in a few special cases, is not to be recommended. The menstruum directed for the fluidextract is most frequently not identical with that used for the tincture, and precipitation of active constituents often ensues when this easy method is employed. Owing to the larger dose of the tinctures, and consequently less degree of concentration, a larger proportion of water can be used in their menstrua than in fluidextracts, and this is a distinct advantage, as tinctures are frequently prescribed in combination with aqueous solutions.

Another mode of exhausting medicines by spirit has been proposed by H. Burton. It consists in suspending in the solvent, immediately under its surface, the solid matter contained loosely in a bag. The liquid in contact with the bag, becoming heavier by impregnation with the matters dissolved, sinks to the bottom; its place is supplied with a fresh portion, which in its turn sinks, and thus a current is established, which continues until the solid substance is exhausted or the liquid saturated. During the maceration the bag should be occasionally raised above the surface of the liquor in the bottle, allowed to drain, and then again immersed. It is asserted that the period of maceration is much shortened in this way. For this mode of preparing tinctures Samuel Gale proposed the use of a cylindrical stoneware vessel with a diaphragm capable of being supported at different heights by projections from the inner surface of the jar, with corresponding notches in the diaphragm, to permit its easy passage to the lower ledges. The material is to be placed upon the diaphragm and kept covered with the menstruum.

Tinctures prepared by adding alcohol to the expressed juices of plants have been long in use on the continent of Europe, and have been brought into notice in Great Britain. They are sometimes called in England *preserved vegetable juices.* This method of preparing tinctures has, however, been abandoned by both the U. S. and Br. Pharmacopœias. Preserved juices are often energetic, yet it is obvious that tinctures prepared from the fresh plant must be still more so, as they contain necessarily not only the soluble active matter of the juice, but also that which, when the juice is expressed, is left in the solid residue of the plant. For further information see *U. S. D.,* 19th ed., p. 1293.

A process for making tinctures from fresh drugs was official in the U. S. P. VIII. It was deleted from the U. S. P. IX, but introduced into the National Formulary under the heading *Tincturæ Medicamentorum Recentium* (see Part III).

Tinctures should be kept in bottles accurately stoppered, in order to prevent evaporation, which might in some instances be attended with serious inconvenience, by increasing their strength beyond the official standard.

Medicines which act in small doses are most conveniently administered in tinctures, as the proportion of alcohol in which they are dissolved is usually insufficient to produce an appreciable effect. Those which must be given in large doses should be cautiously employed in this form, lest the injury done by the menstruum should more than counterbalance their beneficial operation. This remark is particularly applicable to chronic cases, in which the use of tinctures is apt to lead to the formation of habits of intemperance. The tinctures of the weaker medicines are more frequently given as adjuvants of other remedies than with the view of obtaining their own full effects upon the system.

Progressive pharmacy demands greater uniformity and simplicity in the processes, and hence in the present U. S. P. practically all of the tinctures have been brought into two classes, 20 and 10 Gm. of drug per 100 cc. The potent tinctures employ 10 Gm. per 100 cc. in order to comply with the recommendations of the Brussels Conference of 1902 for the unification of the strength of Potent Remedies.

A tabulated comparison of the tinctures of the P. G. IV and P. G. V as to sp. gr., extractive percentage and alkaloidal content, is available for those to whom it would be of value in the Yearbook of the *A. Ph. A.*, 1913, p. 84.

TINCTURA ACONITI. U. S., Br.

TINCTURE OF ACONITE Tr. Aconit. [Aconiti tinctura P. I.]

"Tincture of Aconite, administered subcutaneously to guinea pigs, has a minimum lethal dose of not less than 0.00,035 cc. and not more than 0.00,045 cc. for each Gm. of body weight of guinea pig." *U. S.* "Tincture of Aconite contains in 100 millilitres 0.04 gramme of the ether-soluble alkaloids of Aconite Root." *Br.*

Tinctura Aconiti Radicis, *U. S.* 1870; Tincture of Aconite Root; Teinture d'Aconit (Racine), *Fr. Cod.;* Tinctura Aconiti, *P. G.;* Akonittinktur, Eisenhuttinktur, *G.;* Tinctura di aconito, *It.;* Tintura alcoholica de aconito, *Sp.*

"Aconite, in fine powder, 100 Gm.; to make about 1000 cc. Prepare a Tincture by Type Process P as modified for assayed tinctures, using a mixture of 7 volumes of alcohol and 3 volumes of water as the menstruum. Adjust the volume of the finished Tincture to conform to the above biological standard.

"Alcohol content, by volume, 61 to 65 per cent." *U. S.*

"Aconite Root, in No. 40 powder, 150 *grammes;* Alcohol (70 per cent.), *a sufficient quantity.* Moisten the powder with seventy-five millilitres of the Alcohol, and produce, by the *percolation process,* one thousand millilitres of a strong tincture. Determine the proportion of ether-soluble alkaloids present in this strong tincture, by evaporating one hundred millilitres to dryness in a shallow porcelain evaporating basin, and proceeding as directed under 'Aconiti Radix.' Dilute the remainder of the strong tincture with sufficient of the Alcohol to produce a tincture of Aconite containing 0.04 gramme of ether-soluble alkaloids in 100 millilitres of the Tincture. Examined by the foregoing process Tincture of Aconite is found to contain in 100 millilitres 0.04 gramme of the ether-soluble alkaloids of Aconite Root. *Limit of error* 0.002 gramme in excess or defect. This Tincture is of approximately the same strength as the Tinctura Aconiti of the International Agreement, and about twice as strong as the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

There is a very material difference in the strength of the tinctures of the U. S. and Br., that of the latter being apparently 50 per cent. stronger than the International Protocol, while the U. S. adheres to the 10 per cent. standard. On the other hand, the difference is probably not so great because the American standard for aconite root is higher than that of the Br.

Assay.—The Br. gives a method for determining the proportion of alkaloids in this tincture (see above) but as pointed out elsewhere (see under *Aconitum*) the chemical assay of this drug or its preparations is of little practical value (see Dohme, *J. A. Ph. A.*, 1921, x, 428) and has been omitted from the U. S. P.

Of the various methods that have been suggested for standardizing aconite by biological experiment only two seem of any practical value.

The first of these—in fact probably the oldest of all biological methods of standardizing—is that suggested by the late Doctor Squibb which is based upon the peculiar effects of aconite on peripheral sensory nerve endings. The principle of the method consists in determining the lowest dilution in which a given sample taken into the mouth of the experimenter produces the first perceptible degree of tingling in the tongue. The method may be carried out as follows: After rinsing the mouth with distilled water 4 cc. (1 fluidrachm) of an aqueous solution, representing one part of aconite *root* to 600 parts of water, is taken into the anterior part of the mouth and held there for one minute and then expelled. If the drug is of standard quantity there is produced in a few minutes a characteristic sensation, too faint to be properly called tingling and yet closely allied to it. If, at the end of fifteen minutes, there is no distinct sensation the drug may be deemed below standard and stronger solutions tested in the same manner. On the other hand, if it produces a sharp, distinct, tingling it is stronger than normal and less concentrated solutions should be tested. It is evident that personal susceptibility must play a considerable part in this method and it is necessary for the experimenter to standardize himself by determining his sensitiveness towards a sample of known potency. Although the method may seem rather crude to the chemist accustomed to the exactitude of physical measurements, Roth has found (*J. A. Ph. A.*, 1913, ii, 705) that it may be made to yield very satisfactory results.

The second method, which has the advantages of eliminating the personal factor and also of allowing the test of several samples simultaneously, is the method which has been adopted by the Pharmacopœia based upon the fatal dose for guinea pigs.

The official directions for this assay process are as follows: "Use guinea pigs weighing from 275 Gm. to 325 Gm. each and in good health. Dilute the Tincture with distilled water to make the dose about 1 cc., and inject into the guinea pig under the skin of the abdomen. The standard dose must kill within six hours at least two of every three guinea pigs injected." *U. S.*

In carrying out the assay it is convenient to make a preliminary test using four guinea-pigs, which are injected respectively with doses of 0.3, 0.4, 0.45 and 0.5 milligramme, of the tincture, per gramme of body weight. The syringe for the injection should be graduated in tenths of a cc., such as the so-called tuberculin syringe. We believe that the use of such syringe is more convenient than first measuring the fluid into another vessel. In making the injection, care should be taken not to penetrate the abdominal wall, as absorption from the peritoneal cavity is so rapid that the results would be very different; the fluid should be injected immediately beneath the skin and outside the abdominal muscles. If in the preliminary series, just mentioned, none of the animals survive the drug is too strong, but if none of them die it is too weak. In either case a second series of preliminary tests should be made using doses either larger or smaller, according to the results of the first series. If, however, some of the animals survive and some die, a second series of tests should be made, using doses of 0.35, 0.38, 0.4, 0.4, 0.42, 0.45. Of these six animals, at least one should survive and at least four die. For literature on this assay see Swanson and Walters (*J. A. Ph. A.*, 1923, xii, 957).

For a paper on Tincture of Aconite, by M. I. Wilbert, see *Proc. A. Ph. A.*, 1902, 348.

There was formerly employed in the United States, and at one time recognized by the N. F., a preparation known as *Fleming's Tincture of Aconite,* which represented 70 per cent. of aconite root.

Uses.—A tincture of aconite thoroughly represents the drug and is the most frequently prescribed preparation for internal use. It is occasionally employed externally as an addition to liniments, but it is not to be recommended for this purpose as toxic symptoms have been reported from its external application.

Swanson and Walters (*loc. cit.*) have shown that tincture of aconite deteriorates rapidly, but states that the addition of acetic acid prevents this change.

Dose, five to fifteen minims (0.3–1 cc.).

Off. Prep.—Dentilinimentum Aconiti Compositum, *N. F.;* Deutilinimentum Aconiti et Iodi Compositum, *N. F.*

TINCTURA ALSTONIÆ. Br.

TINCTURE OF ALSTONIA

"Alstonia, in No. 20 powder, 125 *grammes;* Alcohol (60 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

This tincture represents whatever therapeutic properties alstonia bark may possess. It is used in *malaria.*

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA ARNICÆ FLORUM. Br.

TINCTURE OF ARNICA FLOWERS

Teinture d'Arnica, *Fr. Cod.;* Tinctura Arnicae, *P. G.;* Arnikatinktur, *G.;* Tintura di Arnica, *It.;* Tintura alcoholica de arnica, *Sp.*

The U. S. X has dropped this tincture but a similar preparation has been admitted to the N. F. (see Part III).

"Arnica Flowers, in No. 20 powder, 100 *grammes;* Alcohol (45 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with two hundred *millilitres* of the Alcohol, and complete the *percolation process.*" *Br.*

Either alone, or diluted with water, soap liniment, etc., tincture of arnica is often applied popularly to *bruises, sprains, tumors* and local *rheumatic pains,* under the impression that it has extraordinary healing powers. It probably acts merely as a counter-irritant. On some skins it produces a violent eczematous inflammation.

Dose, one-half to one fluidrachm (2–4 cc.).

TINCTURA ASAFŒTIDÆ. U. S. (Br.)

TINCTURE OF ASAFETIDA Tr. Asafœt.

Tinctura Asafetidæ, *Br.;* Teinture (alcoolé), d'Asafœtida, *Fr. Cod.;* Asanttinktur, Stinkasanttinktur, *G.;* Tinctura alcoholica de asafetida, *Sp.*

"Asafetida, bruised, 200 Gm.; to make 1000 cc. Prepare a Tincture by Type Process M, using alcohol as the solvent.

"Alcohol content, by volume, 78 to 85 per cent." *U. S.*

"Asafetida, bruised, 200 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Macerate the Asafetida in a closed vessel with *seven hundred and fifty millilitres* of the Alcohol for seven days, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

This tincture becomes milky on the addition of water, in consequence of the separation of the resin.

Dose, thirty minims to a fluidrachm (2–4 cc.).

Off. Prep.—Mistura Magnesii, Asafœtidæ et Opii, *N. F.*

TINCTURA AURANTII AMARI. U. S. (Br.)

TINCTURE OF BITTER ORANGE PEEL

Tr. Aurant. Amar.

Tinctura Aurantii, *Br.;* Tincture of Orange; Teinture d'Orange amère (Ecorce), *Fr.;* Tinctura Aurantii, *P. G.;* Pomeranzentinktur, Pomeranzenschalentinktur, *G.*

"Bitter Orange Peel, in moderately coarse powder, 200 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, using a mixture of 3 volumes of alcohol and 2 volumes of water as the menstruum.

"Alcohol content, by volume, 53 to 56 per cent." *U. S.*

"Fresh Bitter-Orange Peel, cut small, 250 *grammes;* Alcohol (90 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

It is the peel of the Seville orange that is directed in this process, and the outer part only is active. The two tinctures differ because of the fact that the Br. "orange peel" is only of the outer layer, while the U. S. includes also the inner, white, portion of the rind. The U. S. tincture has a greenish-brown color and a bitterish taste, the latter due to the presence of hesperidin from the inner layer of the rind. The Br. tincture of orange more closely resembles the U. S. *Tinctura Aurantii Dulcis* in sensible properties. The tincture of bitter orange peel is employed as a flavoring agent to infusions, decoctions, and mixtures.

Off. Prep.—Syrupus Aromaticus, *Br.;* Syrupus Aurantii, *Br.;* Elixir Aurantii Amari, *N. F.*

TINCTURA AURANTII DULCIS. U. S.

TINCTURE OF SWEET ORANGE PEEL
Tr. Aurant. Dulc.

Alcoolature d'Orange, *Fr. Cod.;* Teinture de Zeste d'Orange douce, *Fr.;* Apfelsinenschalentinktur, *G.*

"Sweet Orange Peel, the outer yellow rind, grated from the fresh fruit, 500 Gm.; to make 1000 cc. Prepare a Tincture by Type Process M, macerating the drug in 1000 cc. of alcohol and completing the preparation with alcohol. Use purified cotton as the filtering medium." *U. S.*

This tincture was designed to furnish a highly flavored alcoholic preparation of orange and has no medicinal properties. It is used as a pleasant adjuvant and flavoring agent.

On account of its alcoholic content and its lack of medicinal properties tincture of sweet orange peel is one of the preparations coming under the restrictions of the Volstead Act as regards its manufacture and sale. The volatile oil content has been found to be between 0.5 and 1.0 per cent.

Off. Prep.—Syrupus Aurantii, *U. S.*

TINCTURA BELLADONNÆ. U. S., Br.

TINCTURE OF BELLADONNA LEAVES Tr. Bellad.
[Tinctura Belladonnæ Foliorum, U. S. IX. Belladonnæ tinctura P. I.]

"Tincture of Belladonna yields, from each 100 cc., not less than 0.027 Gm. and not more than 0.033 Gm. of the alkaloids of belladonna leaves." *U. S.* "Tincture of Belladonna contains in 100 millilitres 0.035 *gramme* of the alkaloids of Belladonna Leaves." *Br.*

Tincture of Belladonna; Teinture de feuille de Belladone, *Fr.;* Belladonnatinktur, *G.;* Tintura alcoholica de belladonna, *Sp.*

"Belladonna Leaves, in moderately coarse powder, 100 Gm.; to make about 1000 cc. Prepare a Tincture by Type Process P as modified for assayed tinctures, using diluted alcohol as the menstruum, and adjust the volume of the finished Tincture by the addition of diluted alcohol to make each 100 cc. contain 0.03 Gm. of the alkaloids of belladonna leaves." *U. S.*

"Belladonna Leaves, dried and in No. 20 powder, 100 *grammes;* Alcohol (70 per cent.) sufficient to produce 1000 *millilitres.*

"Moisten the Belladonna Leaves with one hundred millilitres of the Alcohol, and complete the *percolation process.* Determine the proportion of alkaloids contained in the tincture so prepared by the Br. process below." *Br.*

Assay.—"Proceed by Type Process D, taking 100 cc. of Tincture of Belladonna, use chloroform as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal sulphuric acid corresponds to 0.02893 Gm. of the alkaloids of belladonna leaves (Proximate Assays).

"Alcohol content, by volume, 44 to 47 per cent." *U. S.*

"Evaporate 100 millilitres in an evaporating basin on a water-bath until it measures about 10 millilitres, add, if necessary, sufficient *alcohol* (90 per cent.) to dissolve any separated substance and transfer to a separator, rinsing the dish with a little *water.* Add 10 millilitres of *water,* 20 millilitres of chloroform, and 2 millilitres of *solution of ammonia.* Shake well and separate the chloroformic layer. Repeat the extraction with two successive portions of 10 millilitres of *chloroform.* Mix the chloroformic solutions, and shake them with 10 millilitres of *N/1 solution of sulphuric acid* diluted with twice its volume of *water.* Separate the chloroformic solution. Repeat the shaking with a further 10 millilitres of the acidified water. Mix the acid solutions, add 20 millilitres of *chloroform* and 4 millilitres of *solution of ammonia.* Shake well, draw off the chloroformic solution into a beaker, and repeat the extraction with two further portions, each of 10 millilitres, of *chloroform.* Allow the mixed chloroformic solutions to evaporate, dry the residue on a water-bath for thirty minutes, dissolve it in 10 millilitres of *N/20 solution of sulphuric acid* and titrate with *N/20 solution of sodium hydroxide,* using *tincture of cochineal* as indicator. Deduct the number of millilitres of alkaline solution required from 10, and multiply the difference by 0.01446; the product will be the weight in grammes of the alkaloids contained in 100 millilitres of the tincture. This quantity should be not less than 0.035 gramme. Should the tincture contain more than this proportion it must be diluted with the necessary quantity of Alcohol (70 per cent.).

"Examined by the foregoing process, Tincture of Belladonna is found to contain in 100 millilitres 0.035 gramme of the alkaloids of Belladonna Leaves. *Limit of error* 0.002 gramme in excess or defect. This Tincture contains seven-tenths of the proportion of alkaloids contained in the Tincture of Belladonna of the British Pharmacopœia, 1898. It may be used when the Tinctura Belladonnæ of the International Agreement is required." *Br.*

In the U. S. P., 1890, the name of this tincture was changed to *Tinctura Belladonnæ Foliorum,* for the sake of greater precision, but the tenth revision has returned to the older name and dropped the unnecessary "Foliorum."

The tincture is an efficient preparation when made from the recently dried leaves and assayed by the official process.

Dose, from five to fifteen minims (0.3–0.9 cc.).

TINCTURA BENZOINI. U. S.

TINCTURE OF BENZOIN Tr. Benz.

Teinture (alcoolé) de Benjoin, *Fr.;* Tinctura Benzoës, *P. G.;* Benzoëtinktur, *G.;* Tintura di benzoino, *It.;* Tintura alcoholica de benjui, *Sp.*

"Benzoin, in moderately coarse powder, 200 Gm.; to make 1000 cc. Prepare a Tincture by Type Process M, using alcohol as the solvent.

"Alcohol content, by volume, 75 to 83 per cent." *U. S.*

A popular toilet preparation—sometimes known as *Lac Virginis* (*Lait virginal, Jungfrausmilch*) is made by mixing rose water, glycerin and tincture of benzoin. Some difficulty occurs in this preparation from the separation of the resin. Hensel (*D. C.,* 1915, 509) states when 3 ounces of water were placed in a four-ounce prescription bottle and one-half drachm of tincture of benzoin was rapidly delivered (five seconds) on the surface of the water, followed by vigorous shaking, he obtained a permanent emulsion which showed no signs of separation after ten days. He found that he could, by the same manipulation, mix as much as 1½ ounces of tincture of benzoin with 12 ounces of water and obtain a permanent emulsion if 13½ ounces of glycerin were immediately added to the mixture. He explains the successful emulsification by the theory that the heat of solution of the mixture lessens the adhesive force of the separated resin, thus separating it into an almost colloidal condition.

Tincture of benzoin possesses the therapeutic properties of that drug but it is rarely prescribed by the medical profession.

Dose, fifteen to thirty minims (0.9–1.8 cc.).

Off. Prep.—Unguentum Picis Compositum, *N. F.*

TINCTURA BENZOINI COMPOSITA. U. S., Br.

COMPOUND TINCTURE OF BENZOIN Tr. Benz. Co.

Tinctura Balsamica, Balsamum Commendatoris, Elixir Traumaticum; Friar's Balsam; Teinture balsamique, *Fr. Cod.;* Baume du Commandeur de Permes, *Fr.;* Persischer Wundbalsam, *G.;* Tintura alcoholica de Benjui, *Sp.*

"Benzoin, in moderately coarse powder, 100 Gm.; Aloe, in moderately coarse powder, 20 Gm.; Storax, 80 Gm.; Tolu, 40 Gm.; to make 1000 cc. Prepare a Tincture by Type Process M, using alcohol as the solvent.

"Alcohol content, by volume, 74 to 80 per cent." *U. S.*

"Benzoin, in powder, 100 *grammes;* Prepared Storax, 75 *grammes;* Balsam of Tolu, 25 *grammes;* Aloes, 20 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.*

"Macerate the Benzoin, Storax, Balsam of Tolu, and Aloes with eight hundred millilitres of the Alcohol in a closed vessel for two days, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

Uses.—Compound tincture of benzoin is chiefly employed both for its antiseptic and protective effect as a local application to minor *wounds, chapped hands* or *nipples, indolent ulcers,* etc. It is the *balsamum traumaticum* of the older Pharmacopœias, and may be considered as a simplified form of certain complex compositions, such as *baume du commandeur, Wade's balsam, Balsam de Maltha, Friar's balsam, Jesuit's drops, Turlington's balsam,* etc., which were formerly in great repute, and are still esteemed by the people, as pectorals and vulneraries. The compound tincture of benzoin is precipitated by water. A variety of *court plaster* is made by applying to black silk, by means of a brush, first a solution of isinglass, and afterwards an alcoholic solution of benzoin.

It is occasionally employed internally as a stimulating expectorant in *chronic bronchitis.* More frequently it is used as an inhalant by adding a teaspoonful of the tincture to a pint of hot water and breathing the vapors; this mode of treatment is especially useful in the early stages of *acute bronchitis.* It has also been recommended in *chronic dysentery* with the idea that it would exercise its local action upon the ulcerated surface of the colon, but is of doubtful utility.

Dose, fifteen to sixty minims (0.9–3.75 cc.).

TINCTURA BERBERIDIS. Br.

TINCTURE OF BERBERIS

"Berberis, in No. 60 powder, 100 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.*

"Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.* This tincture is used as a bitter tonic.

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA BUCHU. Br.

TINCTURE OF BUCHU

Teinture (alcoolé) de Buchu, *Fr. Cod.;* Teinture de Bucco, *Fr.;* Buchutinktur, *G.*

"Buchu Leaves, in No. 20 powder, 200 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture has the virtues of buchu leaves.

Dose, from one to two fluidrachms (3.75–7.5 cc.), either simply diluted with water or as an addition to the infusion of the leaves.

TINCTURA CALUMBÆ. U. S., Br.

TINCTURE OF CALUMBA Tr. Calumb.

Tinctura Colombo; Teinture (alcoolé) de Colombo, *Fr. Cod.;* Kolombotinktur, *G.;* Tintura alcoholica de colombo, *Sp.*

"Calumba, in coarse powder, 200 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, packing the moistened drug moderately and using a mixture of 3 volumes of alcohol and 2 volumes of water as the menstruum.

"Alcohol content, by volume, 53 to 56 per cent." *U. S.*

"Calumba Root, in No. 20 powder, 100 *grammes;* Alcohol (60 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

This tincture was doubled in strength at the U. S. P. (VIII) in order to bring it into the class of 20 per cent. non-potent tinctures. The British tincture, 1914, retains the strength of 10 Gm. of drug in each 100 cc.

Joseph Ince recommended that the tincture be prepared from the root as found in commerce, without further slicing or powdering it. Made as he proposes, the tincture is clear and bright; while if the powdered root is used it will be very turbid, even after filtration. (*P. J.*, xiv, 491.) No. 20 powder is now directed instead of the No. 50 powder used in older Pharmacopœias.

Tincture of calumba is used as a bitter stomachic.

Dose, of the U. S. tincture one-half to one fluidrachm (1.8–3.75 cc.), of the Br. tincture one to two fluidrachms (3.75–7.5 cc.).

TINCTURA CANNABIS INDICÆ. Br.

TINCTURE OF CANNABIS INDICA

Tinctura Cannabis, *U. S. IX;* Tincture of Cannabis; Tincture of Indian Hemp; Tincture of Hemp; Teinture de Chanvre de l'Inde, *Fr.;* Indischhanftinktur, *G.*

"Extract of Indian Hemp, 50 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve." *Br.*

Tincture of cannabis has been dismissed from the U. S. It can be physiologically standardized by the method described under *Cannabis.*

Dose, five to twenty minims (0.3–1.3 cc.), to be gradually increased until some effects are experienced.

Off. Prep.—Tinctura Chloroformi et Morphinæ Composita, *Br.;* Mistura Chloroformi et Morphinæ Composita, *N. F.*

TINCTURA CANTHARIDIS. U. S. (Br.)

TINCTURE OF CANTHARIDES Tr. Canthar. [Cantharidis tinctura P. I.]

Tinctura Cantharidini, *Br.;* Tincture of Cantharidin; Tincture of Spanish Flies; Teinture de Cantharide, *Fr. Cod.;* Tinctura Cantharidum, *P. G.;* Spanischfliegentinktur, *G.;* Tinctura di cantaridi, *It.;* Tinctura alcoholica de cantaridas, *Sp.*

"Cantharides, in fine powder, 100 Gm.; Glacial Acetic Acid, 50 cc.; Alcohol, a sufficient quantity to make 1000 cc. Moisten the cantharides with a mixture of the glacial acetic acid and 50 cc. of alcohol. Transfer it to a covered percolator and allow to macerate for twenty-four hours, then percolate slowly, using alcohol as the menstruum, until the Tincture measures 1000 cc.

"Alcohol content, by volume, 82 to 87 per cent." *U. S.*

"Cantharidin, 0.1 *gramme;* Chloroform, 10.0 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000.0 *millilitres.* Dissolve the Cantharidin in the Chloroform, and add sufficient of the Alcohol to produce the required volume. This tincture contains approximately one-seventh of the proportion of Cantharidin contained in the Tinctura Cantharidis of the International Agreement; it contains approximately the same proportion of Cantharidin as the Tinctura Cantharidis of the British Pharmacopœia, 1898." *Br.*

This is a very difficult preparation to make in that cantharides is not easily extracted by any solvent suitable for making a tincture. The U. S. IX prepared it by extraction with boiling alcohol, using a reflux condenser to avoid loss of the solvent. Scoville (*J. A. Ph. A.*, 1917, vi, 798) found that it was impossible to exhaust cantharides with alcohol because of the slight solubility of cantharidin in that menstruum. He reported the results of extraction by means of a Soxhlet apparatus with a menstruum of 150 cc. of acetic ether and 5 cc. of glacial acetic acid for 100 Gm. of drug, the extraction continuing until a few drops yielded no residue on spontaneous evaporation. Twelve to eighteen hours were required in most cases, depending on the fineness of the drug. After adjusting the volume of extract to 150 cc., alcohol was added to make 1000 cc. and after 24 hours it was filtered. The finished tincture represented 10 per cent. of the drug in an alcoholic menstruum containing 15 per cent. acetic ether and 0.5 per cent. acetic acid, by volume. Three specimens assayed respectively 83 per cent., 93 per cent., and 95 per cent. of the theoretical strength. He concluded that the drug should be either slowly percolated with 10 volumes of acetic acid and 90 volumes of alcohol, or should be extracted with ethyl acetate and acetic acid as outlined above. The British tincture, 1914, is made by dissolving the blistering principle, cantharidin, in chloroform and alcohol. It is about the strength of the tincture of the Br. Pharm., 1898. It is decidedly weaker than the U. S. preparation.

Tincture of cantharides is frequently used in mixtures of castor oil and alcohol in the so-called hair tonics, and when made with diluted alcohol turbidity results. The official tincture is double the strength of that of the U. S. P. 1890 and is now in conformity with the provisions of the International Protocol. It is the most convenient form for the internal use of Spanish flies, the virtues of which it possesses to their full extent. (See *Cantharis.*) If made with diluted alcohol, when long kept it deposits fatty matter, cantharidin in rhomboidal tables, and other crystals of a quite different form. It is occasionally employed externally as a rubefacient; but its liability to vesicate should be taken into consideration.

Dose, of the U. S. tincture, one to three minims (0.06–0.2 cc.); of the Br., two to five minims (0.12–0.3 cc.).

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TINCTURA CAPSICI. U. S., Br.

TINCTURE OF CAPSICUM Tr. Capsic.

Tincture of Cayenne Pepper; Teinture de Piment des Jardins, *Fr.;* Tinctura capsici, *P. G.;* Spanischpfeffertinktur, *G.*

"Capsicum, in moderately coarse powder, 100 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, using a mixture of 95 volumes of alcohol and 5 volumes of water as the menstruum.

"Tincture of Capsicum should meet the requirements of the following test: Mix 10 cc. of the Tincture with 40 cc. of alcohol in a stoppered flask, and dilute 0.1 cc. of the clear liquid with 140 cc. of distilled water containing 10 per cent. of sucrose. Five cc. of this dilution swallowed at one time will produce a distinct sensation of pungency in the mouth and throat of at least two out of three individuals.

"Alcohol content, by volume, 84 to 88 per cent." *U. S.*

"Capsicum, in No. 20 powder, 50 *grammes;* Alcohol (60 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

The U. S. P. tincture is double the strength of the British. The alcoholic strength of the menstruum is of unusual proportions, 19 volumes of alcohol to 1 volume of water, the reason for this is that, on account of oleoresinous constituents of capsicum, alcohol is required and on account of a small quantity of a constituent soluble in water and insoluble in alcohol a little water must be added to the menstruum to prevent cloudiness. It is used in atonic conditions of the stomach, especially in *alcoholic gastritis.* It may also be used locally in various sluggish conditions of the throat and for the various purposes for which red pepper is applicable. (See *Capsicum.*) Applied by means of camel's-hair pencil to the *relaxed uvula,* it sometimes produces contraction and relieves prolapsus of that part.

Dose, of the U. S. tincture, five to ten minims (0.3–0.6 cc.); of the Br. preparation, ten to twenty minims (0.6–1.3 cc.).

Off. Prep.—Tinctura Chloroformi et Morphinæ Composita, *Br.;* Mistura Chloroformi et Morphinæ Composita, *N. F.;* Mistura Opii et Chloroformi Composita, *N. F.;* Mistura Opii et Rhei Composita, *N. F.*

TINCTURA CARDAMOMI. U. S.

TINCTURE OF CARDAMOM Tr. Cardam.

Teinture de Cardamome, *Fr.;* Kardamomentinktur, *G.*

"Cardamom Seed, in moderately coarse powder, 200 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, using diluted alcohol as the menstruum.

"Alcohol content, by volume, 44 to 46 per cent." *U. S.*

The strength of this tincture was doubled in the U. S. P. (VIII) in order to bring it into the 20 per cent. class; it is an agreeable, not very strong, aromatic, and may be advantageously added to tonic and purgative infusions.

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA CARDAMOMI COMPOSITA. U. S., Br.

COMPOUND TINCTURE OF CARDAMOM

Tr. Cardam. Co.

Teinture de Cardamome composée, *Fr.;* Zusammengesetzte Kardamomentinktur, *G.*

"Cardamom Seed, in moderately coarse powder, 20 Gm.; Cinnamon, in fine powder, 25 Gm.; Caraway, in moderately coarse powder, 12 Gm.; Cochineal, in fine powder, 5 Gm.; to make 1000 cc. Prepare a Tincture by Type Process M, macerating the mixed powders in 750 cc. of a mixture of 50 cc. of glycerin and 950 cc. of diluted alcohol, and completing the preparation by using first the remainder of the mixture prepared as directed above, and then diluted alcohol.

"Alcohol content, by volume, 45 to 47 per cent." *U. S.*

"Cardamom Seeds, in No. 20 powder, 14 *grammes;* Caraway Fruit, in No. 20 powder, 14 *grammes;* Cinnamon Bark, in No. 20 powder, 28 *grammes;* Cochineal, in No. 20 powder, 7 *grammes;* Glycerin, 100 *millilitres;* Alcohol (45 per cent.), sufficient to produce 1000 *millilitres.* Moisten the mixed powders with fifty millilitres of the Alcohol, and prepare, by the *percolation process,* eight hundred and fifty *millilitres* of tincture. Add the Glycerin and sufficient of the Alcohol to produce the required volume." *Br.*

This is a very agreeable aromatic tincture, occasionally used as a carminative, but more frequently as an addition to mixtures, infusions, etc., which it renders pleasant to the taste and acceptable to the stomach. It is one of the most highly prized vehicles, not merely because of its pleasant flavor, but also on account of its beautiful color. The substitution of glycerin in the U. S. formula of 1880 for the honey formerly used was an improvement, as it increases the stability of the preparation.

This is one of the preparations which, on account of its attractive flavor and low medicinal value, is included under the restrictive provisions of the Volstead Act.

Dose, one to two fluidrachms (3.75–7.5 cc.).

TINCTURA CASCARILLÆ. Br.

TINCTURE OF CASCARILLA

Teinture de Cascarille, *Fr.;* Kaskarilltinktur, *G.*

"Cascarilla, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred and fifty *millilitres* of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture has the properties of cascarilla, but is seldom, if ever, used in this country.

Dose, from thirty minims to two fluidrachms (1.8–7.5 cc.).

TINCTURA CHIRATÆ. Br.

TINCTURE OF CHIRETTA

Tincture of Chirata; Teinture de Chirette, *Fr.;* Chirettatinktur, *G.*

"Chiretta, in No. 40 powder, 100 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture is used as a bitter tonic. Although no longer recognized by the U. S. P., it is still prescribed in this country. The tincture of the U. S. 1890 was of twenty per cent. strength.

Dose, from one to two fluidrachms (3.75–7.5 cc.), three or four times a day.

TINCTURA CHLOROFORMI ET MORPHINÆ COMPOSITA. Br.

COMPOUND TINCTURE OF CHLOROFORM AND MORPHINE

"Chloroform, 75 *millilitres;* Morphine Hydrochloride, 10 *grammes;* Diluted Hydrocyanic Acid, 50 *millilitres;* Tincture of Capsicum, 25 *millilitres;* Tincture of Indian Hemp, 100 *millilitres;* Oil of Peppermint, 2 *millilitres;* Glycerin, 250 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Mix the Chloroform, Tincture of Capsicum, Tincture of Indian Hemp, Oil of Peppermint, and Glycerin, with four hundred and fifty *millilitres* of the Alcohol, and dissolve the Morphine Hydrochloride in the mixture; add the Diluted Hydrocyanic Acid, and sufficient of the Alcohol to produce the required volume. This Compound Tincture contains in 1 millilitre 7.5 centimils of Chloroform, 1 centigram of Morphine Hydrochloride, and 5 centimils of Diluted Hydrocyanic Acid; it contains in 10 minims ¾ minim of Chloroform, 1/11 grain of Morphine Hydrochloride, and ½ minim of Diluted Hydrocyanic Acid." *Br.*

This is the official substitute for *chlorodyne,* the well-known British nostrum. It does not differ from the process of the Br. Pharm. 1898, except that the oil of peppermint was increased from 1.5 cc. to 2 cc. It is much stronger than the *Mistura Opii et Chloroformi Composita* of the N. F. (see Part III).

Dose, from five to fifteen minims (0.3–0.9 cc.).

TINCTURA CINCHONÆ. U. S., Br.

TINCTURE OF CINCHONA Tr. Cinch.

"Tincture of Cinchona yields, from each 100 cc., not less than 0.8 Gm. and not more than 1 Gm. of the alkaloids of cinchona." *U. S.* "Tincture of Cinchona contains in 100 millilitres 1 gramme of the alkaloids of Red Cinchona Bark." *Br.*

Tincture of Peruvian Bark; Teinture de Quinquina Rouge, *Fr.;* Tinctura Chinæ, *P. G.;* Chinatinktur, *G.;* Tintura di china, *It.;* Tintura alcoholica de Quina, *Sp.*

"Cinchona, in moderately coarse powder, 200 Gm.; to make about 1000 cc. Prepare a Tincture by Type Process P as modified for assayed tinctures, using as the first menstruum a mixture of 75 cc. of glycerin, 675 cc. of alcohol, and 250 cc. of water, and completing the percolation with a mixture of 2 volumes of alcohol and 1 volume of water. Adjust the volume of the finished Tincture to make each 100 cc. contain 0.9 Gm. of the alkaloids of cinchona.

"Alcohol content, by volume, 60 to 64 per cent." *U. S.*

"Red Cinchona Bark, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.), a sufficient quantity. Moisten the powder with two hundred *millilitres* of the Alcohol; set aside for seven days in a closed vessel; percolate with more of the Alcohol, until seven hundred *millilitres* of percolate have been collected; press the marc; add the expressed liquid to the percolate; set aside for twenty-four hours; filter." *Br.*

The U. S. formula is based on the suggestion of A. B. Taylor to include glycerin in the menstruum. This yields a fairly stable preparation in contrast to the unsatisfactory character of the tinctures made by various other processes.

Assay.—"Proceed by Type Process C, taking 25 cc. of Tincture of Cinchona to which is added 5 cc. of diluted hydrochloric acid before evaporation, use 200 cc. of ether-chloroform mixture, and decant an aliquot portion of 160 cc. of the ethereal solution representing 20 cc. of Tincture. Use chloroform for the final extraction and determine the alkaloids gravimetrically (Proximate Assays)." *U. S.*

"Take ten millilitres of the strong tincture so prepared, and determine the proportion of alkaloids contained in it by the process described under 'Extractum Cinchonæ Liquidum.' Add to the bulk of the strong tincture such a quantity of the Alcohol that 100 millilitres of the resulting Tincture contain 1 gramme of the alkaloids of Red Cinchona Bark. Examined by the process described under 'Extractum Cinchonæ Liquidum' Tincture of Cinchona is found to contain in 100 millilitres 1 gramme of the alkaloids of Red Cinchona Bark. *Limit of error* 0.05 gramme in excess or defect." *Br.*

Tincture of cinchona is rarely employed, but may be used as a bitter tonic. As an antiperiodic it has been entirely superseded by the salts of quinine.

Dose, from one to two fluidrachms (3.75–7.5 cc.).

Off. Prep.—Tinctura Cinchonæ Composita, *Br.*

TINCTURA CINCHONÆ COMPOSITA. U. S., Br.

COMPOUND TINCTURE OF CINCHONA Tr. Cinch. Co.

"Compound Tincture of Cinchona yields, from each 100 cc., not less than 0.4 Gm. and not more than 0.5 Gm. of the alkaloids of cinchona." *U. S.* "Compound Tincture of Cinchona contains in 100 millilitres 0.5 gramme of the alkaloids of Red Cinchona Bark." *Br.*

Compound Tincture of Peruvian Bark; Huxham's Tincture of Bark; Whytt's Tincture; Elixir Roborans Whytii; Teinture de Quinquina Composée, Elixir Febrifuge de Huxham, *Fr.;* Tintura Chian Composita, *P. G.;* Zusammengesetzte Chinatinktur, *G.;* Tintura Alcoholica de Cortezade Naranja Compuesta, *Sp.*

"Cinchona, in moderately coarse powder, 100 Gm.; Bitter Orange Peel, in moderately coarse powder, 80 Gm.; Serpentaria, in fine powder, 20 Gm.; to make about 1000 cc. Prepare a Tincture by Type Process P as modified for assayed tinctures, using as the first menstruum a mixture of 75 cc. of glycerin, 675 cc. of alcohol, and 250 cc. of water, and complete the percolation with a mixture of 2 volumes of alcohol and 1 volume of water. Adjust the volume of the finished Tincture to make each 100 cc. contain 0.45 Gm. of the alkaloids of cinchona.

"Alcohol content, by volume, 58 to 64 per cent.

"**Assay.**—Proceed by Type Process C, taking 50 cc. of Compound Tincture of Cinchona, to which is added 5 cc. of diluted hydrochloric acid before evaporation, use 200 cc. of ether-chloroform mixture, and decant an aliquot portion of 160 cc., representing 40 cc. of the Tincture. Use chloroform for the final extraction and determine the alkaloids gravimetrically (Proximate Assays)." *U. S.*

"Dried Bitter-Orange Peel, bruised, 50 *grammes;* Serpentary Rhizome, in No. 40 powder, 25 *grammes;* Cochineal, in powder, 3 *grammes;* Tincture of Cinchona, 500 *millilitres;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Mix the solid ingredients with five hundred millilitres of the Alcohol; set aside in a closed vessel for seven days, shaking frequently; strain, and then press; mix the two liquids thus obtained; add the Tincture of Cinchona, and sufficient of the Alcohol to produce the required volume; set aside for twenty-four hours; filter. Examined by the process described under 'Extractum Cinchonæ Liquidum' Compound Tincture of Cinchona is found to contain in 100 millilitres 0.5 gramme of the alkaloids of Red Cinchona Bark. *Limit of error* 0.05 gramme in excess or defect." *Br.*

This is the preparation commonly known by the name of *Huxham's tincture of bark.* The use of glycerin is an improvement, precipitation being thus largely prevented as in the case of the simple tincture of cinchona. The process for the British tincture presents some novel features. Half of the quantity of the tincture is first made from four of the ingredients; this is then mixed with an equal bulk of tincture of cinchona. The reason for this was probably to avoid assaying a mixed product during the process; but the final test has to deal with the finished tincture, and the utility of the whole method is doubtful.

As this tincture is directed to be made by percolating definite amounts of red cinchona, bitter orange and serpentaria with alcohol, glycerin and water, but assayed only for cinchona alkaloids it is obvious that the adjustment may reduce the proportion of bitter orange, serpentaria and glycerin materially and prevent uniformity in different lots of compound tincture. Nitardy (*J. A. Ph. A.,* 1919, viii, 114) suggests making the tincture in two portions, "the first representing one-half of the volume of the finished tincture and containing all of the bitter orange peel and serpentaria, the other representing the cinchona adjusted to proper strength (double that of the compound tincture) and these mixed in equal volumes, would produce a product that would be more nearly uniform" than the present official method.

Compound tincture of cinchona is an excellent bitter tonic, useful for its local effect on the stomach but too feeble in the principles of cinchona to serve when the systemic action of the drug is required.

Dose, one to two fluidrachms (3.75–7.5 cc.).

Off. Prep.—Gargarisma Guaiaci Composita, *N. F.*

TINCTURA CINNAMOMI. Br.

TINCTURE OF CINNAMON Tr. Cinnam.

Teinture (alcoolé) de Cannelle, *Fr. Cod.;* Tinctura Cinnamomi, *P. G.;* Zimmttinktur, *G.;* Tintura alcoholica de canela, *Sp.*

"Cinnamon Bark, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture has, unfortunately, been dismissed from the U. S. but is recognized by the N. F. (see Part III). By long keeping it is prone to gelatinize and become unfit for use. It is an agreeable flavoring to other tinctures and because of its astringent powers is especially used in *diarrhea* mixtures.

Dose, one to two fluidrachms (3.75–7.5 cc.).

Off. Prep.—Elixir Taraxaci Compositum, *N. F.;* Mistura Rhei Alkalina, *N. F.*

TINCTURA COCCI. Br.

TINCTURE OF COCHINEAL

Teinture (alcoolé) de Cochenille, *Fr. Cod.;* Cochenilletinktur, *G.*

"Cochineal, in powder, 100 *grammes;* Alcohol (45 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

This is valued chiefly for imparting color to liquid preparations; four or five per cent. of this tincture will give a deep red color. (See *Coccus.*)

Dose, from five to fifteen minims (0.3–1 cc.).

TINCTURA COLCHICI. U. S., Br.

TINCTURE OF COLCHICUM Tr. Colch. Sem. [Tinctura Colchici Seminis U. S. IX, Colchici tinctura, P. I.]

"Tincture of Colchicum yields, from each 100 cc. not less than 0.036 Gm. and not more than 0.044 Gm. of colchicine." *U. S.*

Tincture of Colchicum Seed; Teinture de Colchique, *Fr. Cod.;* Tinctura Colchici, *P. G.;* Zeitlosentinktur, *G.;* Tintura alcoholica de colquico, *Sp.*

"Colchicum Seed, in moderately coarse powder, 100 Gm.; to make about 1000 cc. Prepare a Tincture by Type Process P as modified for assayed tinctures, using a mixture of 3 volumes of alcohol and 2 volumes of water as the menstruum, and adjust the volume of the finished Tincture to make each 100 cc. contain 0.04 Gm. of colchicine.

"Alcohol content, by volume, 54 to 57 per cent." *U. S.*

"Colchicum Seeds, in No. 30 powder, 100 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with fifty millilitres of the Alcohol, and complete the *percolation process.* This Tincture is of approximately the same strength as the Tinctura Colchici of the International Agreement, and is of one-half the strength of the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

Assay.—"Evaporate 150 cc. of Tincture of Colchicum on a water bath to about 15 cc., cool, and dissolve the residue in sufficient distilled water to make 290 cc. Add 10 cc. of solution of lead subacetate, and agitate the mixture frequently during one hour. Filter off 200 cc. and proceed as directed under *Golchici Semen,* beginning with the word 'Add.'" *U. S.*

This is another tincture in which it is difficult to extract the drug satisfactorily with any appropriate menstruum. Some of the processes formerly recommended included the use of a hot menstruum. This is unsatisfactory. The present official method has been found to give an efficient preparation when carefully followed.

This tincture possesses the properties of colchicum, and may be given whenever that medicine is indicated, but the fluidextract, containing less alcohol, is generally preferred.

Dose, from ten to thirty minims (0.6–1.8 cc.), to be repeated with caution.

TINCTURA CUBEBÆ. Br.

TINCTURE OF CUBEBS

Teinture de Cubèbe, *Fr. Cod.;* Kubebentinktur, *G.*

"Cubebs, in No. 20 powder, 200 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

The U. S. P. has not recognized this tincture for many years, but it is official in the N. F. (see Part III). While this tincture represents the therapeutic virtue of cubeb, it is an inelegant form of administering that drug.

Dose, one to two fluidrachms (3.75–7.5 cc.).

TINCTURA DATURÆ SEMINUM. Br.

TINCTURE OF DATURA SEEDS

"Datura Seeds, in No. 20 powder, 250 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the bruised Datura Seeds with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture well represents the activities of datura seeds.

Dose, five to fifteen minims (0.3–0.9 cc.).

TINCTURA DIGITALIS. U. S., Br.

TINCTURE OF DIGITALIS Tr. Digit. [Digitalis tinctura P. I.]

"Tincture of Digitalis, injected into the ventral lymph sac of a frog, has a minimum systolic dose of not less than 0.0055 cc. and not more than 0.0065 cc., equivalent to not less than 0.00,000,046 Gm. and not more than 0.00,000,054 Gm. of ouabain, for each Gm. of body weight of frog." *U. S.*

Tincture of Foxglove; Teinture de Digitale, *Fr. Cod.;* Tinctura Digitalis, *P. G.;* Fingerhuttinktur, *G.;* Tintura di digitale, *It.;* Tintura alcoholica de digital, *Sp.*

"Digitalis, in fine powder, 100 Gm.; to make about 1000 cc. Pack the Digitalis firmly in a cylindrical glass percolator, provided with a stop-cock, and arranged with a cover and a receptacle suitable for volatile liquids, and percolate slowly with purified petroleum benzin until a few drops of the percolate evaporated from filter paper leave no greasy stain. Reject the benzin percolate. Remove the drug from the percolator and expose it to the air until the odor of benzin is no longer noticeable. Prepare from this a tincture by Type Process P as modified for assayed tinctures, using a mixture of 4 volumes of alcohol and 1 volume of water as the menstruum. Adjust the volume of the finished Tincture to conform to the above biological standard.

"Alcohol content, by volume, 67 to 72 per cent." *U. S.*

"Digitalis Leaves, in No. 20 powder, 100 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.* This tincture is of approximately the same strength as the Tinctura Digitalis of the International Agreement, and is of four-fifths the strength of the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

Assay.—"Use healthy frogs of the same species (*Rana pipiens* Schreber) and of a fairly uniform size (20 to 30 Gm.).

"*Storage.*—Before use, the frogs should be stored in constant temperature tanks kept in a cool room, preferably where the temperature does not rise above 15° C. The bottom of the tanks should be covered with running water. The day before the frogs are to be used, a sufficient number should be taken from the storage tanks and placed in a tank, the temperature of which is approximately 20° C. One hour before the assay, they are weighed to within 0.5 Gm. and placed in wire cages or containers in a tank containing water to the depth of about 1 cm. (½ inch), the water being kept at a uniform temperature of 20° C. during the assay.

"*Dosage.*—The doses of the tincture to be given the frogs are calculated according to the weights of the frogs and are injected into the ventral lymph sac by means of a pipette or glass syringe which is graduated in hundredths of a cubic centimeter. The injection is made into the lymph sac through the floor of the mouth, care being taken not to puncture the skin. The amount of fluid to be injected into the different frogs should be as uniform in quantity as possible, approximately 0.015 cc. for each Gm. of body weight of frog. In case the alcohol content in any preparation after dilution is higher than 20 per cent., the preparation may be subjected to careful evaporation and subsequent addition of distilled water until the original volume is restored and the alcohol content is not above the per cent. named. The animal is replaced in its cage in the tank after injection, the temperature being maintained at 20° C. About fifty-eight minutes from the time of injection, each frog is pithed, the heart is exposed, and its condition examined. For the correct end reaction, at the expiration of one hour from the time of injection, the ventricle must be in systolic standstill, while the auricles are widely dilated. Following mechanical stimulations, feeble contractions may occur in the auricles and localized contractions in the ventricle, but no general contraction is allowable. If, when the lymph sac is opened to expose the heart, any of the injected drug is found unabsorbed, the animal must be discarded and not considered in the results obtained." *U. S.*

For details of carrying out this assay and description of other methods of standardization see under *Digitalis.*

It is well established that tincture of digitalis is more liable to deterioration than well kept leaves. According to the investigations of Pittenger (*J. A. Ph. A.*, 1918, vii, 1031), the loss of strength may be anywhere from nothing to 12 per cent. a month, the average being about 20 to 30 per cent. a year. The factors which influence the rapidity of deterioration he could not discover; it did not seem to depend on the strength of alcohol employed in its extraction.

According to Focke, light accelerates the change. (See also Eberhardt and Eldred, *J. A. Ph. A.*, 1914, iii, p. 38.)

Uses.—Tincture of digitalis probably represents the crude drug better than any other official preparation. The beginning dose is ordinarily from five to fifteen minims (0.3–0.9 cc.) three or four times a day, increased cautiously as circumstances demand. Very much larger single doses may be employed, thus as high as a fluidrachm may occasionally be given at a dose if not repeated.

It should be remembered that, as with most of the tinctures, one minim is equivalent to about two drops.

Dose, from five to thirty minims (0.3–1.8 cc.).

TINCTURA ERGOTÆ AMMONIATA. Br.

AMMONIATED TINCTURE OF ERGOT

Tinctura Secalis Cornuti Ammoniata; Teinture Ammoniacale de Seigle Ergoté, *Fr.;* Ammoniakalische Mutterkorntinktur, *G.*

"Ergot, in No. 20 powder, 250 *grammes;* Solution of Ammonia, 100 *millilitres;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Mix the Solution of Ammonia with nine hundred millilitres of the Alcohol; moisten the powder with one hundred millilitres of this mixture, and percolate with the remainder; press the marc; mix the expressed liquid with the percolate; add sufficient of the Alcohol to produce the required volume; set aside for twenty-four hours; filter." *Br.*

This is a new official tincture of the Br. Ph., 1898; it differs from the tincture recommended by the British Pharmaceutical Conference in the use of solution of ammonia in place of aromatic spirit of ammonia. Its value is very questionable as the alkalies appear to destroy the activity of ergot.

Dose, from one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA FERRI CHLORIDI.
U. S., Br.

TINCTURE OF FERRIC CHLORIDE Tr. Ferr. Chlor.
[Tincture of Iron]

"A hydro-alcoholic solution containing about 13 per cent. of ferric chloride [$FeCl_3$], corresponding to not less than 4.48 per cent. of Fe." *U. S.*

Tinctura Ferri Perchloridi, *Br.;* Tincture of Chloride of Iron; Tinctura Ferri Muriatis; Tincture of Perchloride of Iron; Tinctura of Muriate of Iron; Tinctura Ferri Sesquichloridi; Teinture de Perchlorure de fer, *Fr.;* Tinctura Ferri Chlorati, *P. G.;* Eisenchloridtinktur, *G.*

"Solution of Ferric Chloride, 350 cc.; Alcohol, a sufficient quantity to make 1000 cc. Mix the solution with enough alcohol to make 1000 cc." *U. S.*

"Strong Solution of Ferric Chloride, 250 *millilitres;* Alcohol (90 per cent.), 250 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Mix." *Br.*

This is one of many official preparations in which there has been great variation in the methods of preparing it during the century of its official recognition. It was originally made by weight instead of volume. The free acidity causes the development of a small proportion of an ester which gives a peculiar flavor to the tincture and probably modifies in some degree its influence on the system. For this reason it is preferable to keep the tincture for some time before dispensing.

Description and Physical Properties.—"A bright, amber-colored liquid, having a slightly ethereal odor, a very astringent, styptic taste, and an acid reaction. Specific gravity: about 1.00 at 25° C. The Tincture responds to the reactions for ferric iron, and for chlorides. After the Tincture has been exposed for some time to daylight, it yields a greenish or greenish-blue color with potassium ferricyanide T.S. (presence of some *ferrous salt,* due to reduction). Mix 3 cc. of the Tincture with 10 cc. of ferrous sulphate T.S., and carefully superimpose this mixture upon 3 cc. of sulphuric acid contained in a test tube: the zone of contact does not assume a brown or reddish-brown color (*nitrate*).

"**Assay.**—Place about 5 cc. of Tincture of Ferric Chloride in a tared weighing bottle, weigh accurately, transfer it to a tall beaker, and evaporate to dryness on a water bath. Add to the residue 2 cc. of hydrochloric acid and 5 cc. of solution of hydrogen dioxide, and again evaporate to dryness. Dissolve this residue in 3 cc. of hydrochloric acid, and transfer to a 250 cc. glass-stoppered flask by means of 25 cc. of distilled water. Add about 1 Gm. of potassium iodide, and allow the mixture to stand for thirty minutes at a temperature of 40° C., the flask being securely stoppered while it is being warmed. Cool the solution, add 100 cc. of distilled water, and titrate the liberated iodine with tenth-normal sodium thiosulphate. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.005584 Gm. of Fe.

"Preserve in amber-colored, glass-stoppered bottles, protected from light." *U. S.*

The tincture is decomposed by the alkalies, alkaline earths and their carbonates, astringent vegetable infusions, and mucilage of acacia, which produces with it a brown semi-transparent jelly. All these substances are, therefore, incompatible with it in prescriptions.

Bestucheff's tincture, which is much used in Europe, is simply a solution of ferric chloride in a mixture of one measure of ether and three measures of alcohol. (See *Tinctura Ferri Chloridi Etherea,* N. F.)

Uses.—Tincture of chloride of iron has in the past been attributed with curative properties verging on the mystical. Thus it has been supposed to exercise a specific action in *erysipelas, diphtheria,* and other infectious diseases. Its value in these states, however, is, to say the least, questionable. In *Bright's disease* it has been used not only for its chalybeate effect but with the idea that its astringent action would lessen the quantity of albumin in the urine. As it is an active coagulant of albumin, however, it cannot exist in the blood and therefore can never reach the kidney unchanged; any beneficial effect which may follow its employment in diseases of the kidney is of the same nature as that which is produced by other preparations of iron, namely, an enrichment of the hemoglobin content of the blood. In *anemias* it acts as a chalybeate, but is inferior to many other salts of iron. In the first place a dose of fifteen minims represents only approximately 0.7 grain of iron. In the second place, because of its high astringency and local irritant effect it cannot be administered in large quantities without producing disturbances in the stomach. Locally it is valuable as an astringent in *hemorrhages* and passive congestions of the mucous membrane. Mixed with equal parts of glycerin and water it may be applied by means of a swab with benefit in various types of *pharyngitis.* Its use as a gargle is not to be recommended as its acidity makes it injurious to the teeth.

Dose, five to thirty minims (0.3–1.8 cc.), which may be gradually increased.

Off. Prep.—Liquor Ferri et Ammonii Acetatis, *U. S.;* Elixir Chloridorum, *N. F.*

TINCTURA GAMBIR COMPOSITA. U. S. (Br.)

COMPOUND TINCTURE OF GAMBIR Tr. Gambir Co. [Compound Tincture of Pale Catechu]

Tinctura Catechu, *Br.;* Tincture of Catechu; Teinture de Cachou, *Fr. Cod.;* Tinctura Catechu, *P. G.;* Katechutinktur, *G.*

"Gambir, in moderately coarse powder, 50 Gm.; Cinnamon, in fine powder, 25 Gm.; to make 1000 cc. Prepare a Tincture by Type Process M, using diluted alcohol as the solvent.

"Alcohol content, by volume, 44 to 47 per cent." *U. S.*

"Catechu, in powder, 200 *grammes;* Cinnamon Bark, bruised, 50 *grammes;* Alcohol (45 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

The British tincture (1898) was increased to 20 per cent. in the proportion of catechu, and is now four times the strength of the U. S. tincture.

This is a grateful astringent tincture, useful in all cases to which gambir is applicable and in which small quantities of spirit are not objectionable. It is especially employed in the treatment of *diarrhea.* It sometimes gelatinizes when kept, and becomes unfit for use.

Dose, of the U. S. tincture of gambir, two to four fluidrachms (7.5–15.0 cc.); of the British tincture of catechu, one-half to two fluidrachms (1.8–7.5 cc.).

Off. Prep.—Tinctura Opii et Gambir Composita, *N. F.*

TINCTURA GELSEMII. Br.

TINCTURE OF GELSEMIUM Tr. Gelsem.

Teinture de Gelsemium, *Fr.;* Gelsemiumtinktur, *G.*

Gelsemium was dropped at the tenth revision of the U. S. but both it and the tincture are recognized by the N. F.

"Gelsemium Root, in No. 40 powder, 100 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with fifty millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

For Farr and Wright's method of estimating this tincture, see *C. D.,* 1892, 263.

Dose, from five to twenty minims (0.3–1.3 cc.).

TINCTURA GENTIANÆ COMPOSITA. U. S., Br.

COMPOUND TINCTURE OF GENTIAN
Tr. Gentian. Co.

Teinture de Gentiane Composée, *Fr.;* Zusammengesetzte Enziantinktur, *G.*

"Gentian, in moderately coarse powder, 100 Gm.; Bitter Orange Peel, in moderately coarse powder, 40 Gm.; Cardamom Seed, in moderately coarse powder, 10 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, packing the mixed drugs moderately, using as the first menstruum a mixture of 100 cc. of glycerin, 500 cc. of alcohol and 400 cc. of water, and completing the percolation with diluted alcohol.

"Alcohol content, by volume, 43 to 47 per cent." *U. S.*

"Gentian Root, cut small and bruised, 100.0 *grammes;* Dried Bitter-Orange Peel, bruised, 37.5 *grammes;* Cardamom Seeds, in powder, 12.5 *grammes;* Alcohol (45 per cent.), 1000.0 *millilitres.* Prepare by the *maceration process.*" *Br.*

There has always been difficulty from precipitation in this tincture; glycerin has been added to the menstruum to overcome this annoyance, but it is only partially successful.

This is an elegant bitter, much used in *dyspepsia,* and as an addition to tonic mixtures in debilitated states of the digestive organs. There is, however, much danger of its abuse by alcoholics, especially in chronic cases.

Dose, one to two fluidrachms (3.75–7.5 cc.).

TINCTURA GUAIACI AMMONIATA. Br.

AMMONIATED TINCTURE OF GUAIAC
Tr. Guaiac. Ammon.

Ammoniated Tincture of Guaiacum; Tinctura Guaiaci Composita; Teinture de Gaiac ammoniacale, *Fr.;* Ammoniakalische Guajaktinktur, *G.*

"Guaiacum Resin, in powder, 200 *grammes;* Oil of Nutmeg, 3 *millilitres;* Oil of Lemon, 2 *millilitres;* Strong Solution of Ammonia, 75 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Mix the Strong Solution of Ammonia with seven hundred millilitres of the Alcohol; add the Guaiacum Resin; set aside in a closed vessel for forty-eight hours, shaking frequently; filter; dissolve the Oil of Lemon and Oil of Nutmeg in the filtrate, and pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

A similar preparation is recognized by the N. F.

The British Pharmacopœia, 1898, improved the process for this tincture by abandoning the distilled aromatic spirit of ammonia, used as a menstruum by the former British authority, and substituting alcohol containing solution of ammonia and volatile oils, the proportion of oil of lemon having been reduced 60 per cent.

This tincture is celebrated in the treatment of *chronic rheumatism,* and is frequently also used in *amenorrhea.* It is precipitated by water, and should be administered emulsified with gum, so that the guaiac may be held in suspension.

Dose, from one to two fluidrachms (3.75–7.5 cc.).

TINCTURA HAMAMELIDIS. Br.

TINCTURE OF HAMAMELIS

Teinture (alcoolé) de Hàmamélis, *Fr.;* Hamamelistinktur, *G.;* Tintura alcoholica de hamamelis, *Sp.*

"Hamamelis Bark, in No. 20 powder, 100 *grammes;* Alcohol (45 per cent.), sufficient to produce 1000 millilitres. Moisten the powder with fifty millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

Dose, from thirty to sixty minims (1.8–3.75 cc.).

TINCTURA HYDRASTIS. Br.

TINCTURE OF HYDRASTIS Tr. Hydrast.
[Tincture of Golden Seal]

Teinture (alcoolé) de Hydrastis, *Fr.;* Hydrastistinktur, *G.;* Tintura alcoholica de hidrastis, *Sp.*

"Liquid Extract of Hydrastis, 100 *millilitres;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Mix." *Br.*

This tincture was dropped at the tenth revision of the U. S. because it was felt that hydrastis was so feeble that the effects of the tincture were due chiefly to its alcohol. The former U. S. tincture was twice the strength of the Br. It was made as follows: "Hydrastis, in No. 60 powder, *two hundred grammes* to make about *one thousand mils.* Prepare a Tincture by Type Process P, as modified for assayed tinctures, using a mixture of *two volumes* of alcohol and *one volume* of water as the menstruum and adjusting the volume of the finished Tincture so that each *one hundred mils* contains 0.4 Gm. of the ether-soluble alkaloids of hydrastis." *U. S. IX.*

This tincture is too feeble to be of any real therapeutic value.

Dose, from one to two fluidrachms (3.75–7.5 cc.).

TINCTURA HYOSCYAMI. U. S., Br.

TINCTURE OF HYOSCYAMUS Tr. Hyosc. [Tincture of Henbane Hyoscyami tinctura P. I.]

"Tincture of Hyoscyamus yields, from each 100 cc., not less than 0.0055 Gm. and not more than 0.0075 Gm. of the alkaloids of hyoscyamus." *U. S.*

Teinture de Jusquiame, *Fr.;* Bilsenkrauttinktur, *G.;* Tintura alcoholica de beleno, *Sp.*

"Hyoscyamus, in moderately coarse powder, 100 Gm.; to make about 1000 cc. Prepare a Tincture by Type Process P as modified for assayed tinctures, using diluted alcohol as the menstruum. Adjust the volume of the finished Tincture to make each 100 cc. contain 0.0065 Gm. of the alkaloids of hyoscyamus. Alcohol content, by volume, 44 to 46 per cent.

"**Assay.**—Proceed by Type Process D, taking 250 cc. of Tincture of Hyoscyamus, evaporate to about 25 cc., use chloroform as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal sulphuric acid corresponds to 0.02893 Gm. of the alkaloids of hyoscyamus (Proximate Assays)." *U. S.*

"Hyoscyamus Leaves, in No. 20 powder, 100 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture possesses the activities of hyoscyamus.

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA IODI. U. S. (Br.)

TINCTURE OF IODINE Tr. Iodi.

"An alcoholic solution of iodine and potassium iodide containing, in each 100 cc., not less than 6.5 Gm. and not more than 7.5 Gm. of I, and not less than 4.5 Gm. and not more than 5.5 Gm. of KI." *U. S.*

Tinctura Iodi Mitis, *Br.;* Weak Tincture of Iodine; **Tinctura Iodi Fortis,** *Br.;* Strong Tincture of Iodine; Tinctura Iodinii, *U. S.*, 1870; Teinture d'iode, *Fr. Cod.;* Tinctura Jodi, *P. G.;* Jodtinktur, *G.;* Solucion alcoholica de yodo, *Sp.*

"Iodine, 70 Gm.; Potassium Iodide, 50 Gm.; Distilled Water, 50 cc.; Alcohol, a sufficient quantity to make 1000 cc. Dissolve the potassium iodide in the distilled water contained in a bottle graduated to 1000 cc., add the iodine, and agitate the mixture until solution is effected. Then add sufficient alcohol to make 1000 cc. of Tincture, and mix thoroughly.

"Preserve in tightly-stoppered bottles, using only glass or rubber stoppers. Alcohol content, by volume, 82 to 84 per cent." *U. S.*

The British Pharmacopœia 1914 recognizes two tinctures of iodine; a strong, containing 10 per cent. of free iodine, and a weak representing 2.5 per cent. of iodine. The formulas for these are as follows:

Tinctura Iodi Mitis (*Weak Tincture of Iodine*).

"Iodine, 25 *grammes;* Potassium Iodide, 25 *grammes;* Distilled Water, 25 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve the Potassium Iodide and Iodine in the Distilled Water; add sufficient of the Alcohol to produce the required volume." *Br.*

"10 millilitres of the Tincture, diluted with 20 millilitres of *water,* require for decolorisation not less than 19.2 or more than 19.8 millilitres of *N/10 solution of sodium thiosulphate.* This Weak Tincture contains 0.025 gramme of Iodine in each millilitre; 1 minim contains about $^{1}/_{44}$ grain. It is not of the same strength as the Tinctura Iodi of the International Agreement. It contains the same proportion of Iodine as the Tinctura Iodi of the British Pharmacopœia, 1898." *Br.*

Tinctura Iodi Fortis (*Strong Tincture of Iodine*).

"Iodine, 100 *grammes;* Potassium Iodide, 60 *grammes;* Distilled Water, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve the Potassium Iodide and the Iodine in the Distilled Water; add sufficient of the Alcohol to produce the required volume." *Br.*

"Five millilitres of the Tincture, diluted with 20 millilitres of *water,* require for decolorisation not less than 38.4 or more than 39.6 millilitres of *N/10 solution of sodium thiosulphate.* This Strong Tincture contains 0.1 gramme of Iodine in each millilitre; 1 minim contains about $^{1}/_{11}$ grain. It is of approximately the same strength as the Tinctura Iodi of the International Agreement. It contains approximately the same proportion of Iodine as the Liquor Iodi Fortis of the British Pharmacopœia, 1898." *Br.*

The iodine should be thoroughly dried before being weighed out. The tincture should be kept in well-stoppered bottles, in order to prevent the evaporation of the alcohol. It should never be dispensed in cork-stoppered vials, because of the destructive action of the iodine on the cork; rubber or glass stoppers should be used.

Assay for Potassium Iodide.—"Measure exactly 5 cc. of Tincture of Iodine, evaporate in a tared dish or watch glass on a water bath, and then add several small successive portions of water, drop by drop, until all of the iodine has volatilized and a white residue remains. The residue should weigh not less than 0.225 Gm. and not more than 0.275 Gm. and should respond to the tests for identity found under *Potassii Iodidum.*

"**Assay for Iodine.**—Measure exactly 5 cc. of the Tincture, dilute with 25 cc. of distilled water, and titrate the solution with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.01269 Gm. of I." *U. S.*

L. F. Kebler (*J. Ind. & E. C.*, 1913, p. 484) reports the results of analyses of a number of samples collected in pharmacies in the District of Columbia in which the iodine content ranged from 1.97 Gm. to 9.26 Gm. in 100 cc. and the potassium iodide content from 0.0 to 6.82 Gm. in 100 cc. Such variations of course are due to carelessness, or dishonesty, in making it and not to changes or deterioration taking place in the properly made article which has been found by numerous investigators to be a very stable preparation.

J. W. Mardin (*J. A. P. A.*, 1913, p. 1464) gives a method of determining the alcohol in this preparation by a series of factors based upon the alterations in sp. gr. produced respectively by potassium iodide and iodine and gives tables which may be consulted for the determination by this method.

Tincture of iodine when made with plain alcohol and no potassium iodide, as is done in numerous foreign Pharmacopœias, and was formerly the practice in the U. S. P., is a very unstable preparation. The alcohol reacts with the iodine to form ethyl iodide. This has the effect of making the tincture more readily miscible with water, but the per cent. of free iodine drops to one-half of its original amount in a very short time. It was discovered that the use of a certain proportion of potassium iodide stabilized the preparation very satisfactorily. The potassium iodide in this preparation, therefore, is not used for its solvent effect but as a preservative ingredient.

If the tincture is exposed to the air, as in an imperfectly stoppered bottle, it will gain appreciably in strength as the alcohol volatilizes much more rapidly than does the iodine. Such a preparation should not be applied to the skin for fear of producing blisters or burns.

Uses.—Tincture of iodine is now employed almost exclusively for its local effects. It is a powerful local irritant acting somewhat slowly but with great persistence. If applied too freely it will produce an acute dermatitis with desquamation of the cuticle. It is a favorite remedy as a counter-irritant in inflammations of the joint, especially when of a more or less chronic type, thus it is widely employed in *sprains* after the stage of acute inflammation has subsided, in *chronic rheumatism, arthritis deformans, gout, chilblains, myalgias,* and the like. In *scrofulous glands* and chronic rheumatic conditions it is often applied with the idea of obtaining the constitutional action of the iodine from absorption through the skin as well as the local counter-irritant effect. While it is true that if evaporation is guarded against perceptible amounts of iodine may be absorbed, after the application of the tincture to the skin, as ordinarily employed, the quantity taken up by the system is insignificant. The irritant action of tincture of iodine is also made use of for the obliteration of serous cavities, as in the radical cure of *hydrocele* or *ovarian dropsies.*

As pointed out elsewhere, iodine is a powerful germicide and within the last few years the tincture of iodine has become a valuable addition to the surgeon's armamentarium against infections. It is very widely used for the purpose of sterilizing the skin, before operation or for hypodermic injections. For disinfecting *wounds* the U. S. tincture should be diluted with equal parts of water; the weaker tincture of the Br. is a satisfactory strength for this purpose. It is also employed as a local remedy in the treatment of *erysipelas,* but its application requires some caution and it is better to surround the inflamed surface with a border of the tincture, embracing a portion of both the sound and diseased skin with the idea of preventing the progress of the inflammation, than to attempt a complete cure by covering the whole surface affected.

Luc has found the inhalation of the fumes from slightly warmed tinctures very useful in *coryza.*

Under the erroneous title of *colorless tincture of iodine* various combinations manufactured from tincture of iodine have been prepared. These preparations are calculated to mislead practitioners, for they contain no free iodine and therefore have not the therapeutic virtues of the official tincture, but are variable mixtures consisting principally of ammonium iodide and various other compounds of iodine. (See *Tinctura Iodi Decolorata,* N. F., Part III.)

Lugol's solution (*Liquor Iodi Compositus*) is a much preferable preparation for the internal administration of iodine.

Dose, one to five minims (0.06–0.3 cc.).

TINCTURA JALAPÆ. Br.

TINCTURE OF JALAP

Teinture (alcoolé) de Jalap, *Fr. Cod.;* Jalapentinktur, *G.*

"Jalap, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.), *a sufficient quantity.* Moisten the powder with one hundred millilitres of the Alcohol; pack in a percolator; gradually add more of the Alcohol until six hundred millilitres of percolate have been collected; press the marc; add the expressed liquid to the percolate; set aside for twenty-four hours; filter. Determine the amount of Jalap Resin present in ten millilitres of the strong tincture so prepared by the process described under 'Jalapæ Resina,' and dilute the remainder of the strong tincture with sufficient of the Alcohol to produce a Tincture of Jalap containing 1.5 grammes of the Resin in 100 millilitres. When 10 millilitres of the Tincture, concentrated by evaporation, are mixed with eight times their volume of *water,* the resin thus separated, washed with *water* and dried at a gentle heat, weighs not less than 0.145 or more than 0.155 gramme." *Br.*

This tincture is no longer official in the U. S. Pharmacopœia, but is in the N. F. (see Part III).

This tincture is now prepared on the basis of proportion of resin, not of crude drug, as formerly. It possesses the medicinal virtues of jalap, and is sometimes added to cathartic mixtures.

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA JALAPÆ COMPOSITA. Br.

COMPOUND TINCTURE OF JALAP

Aqua Vitæ Germanica; Tintura Alcoholica de Jalapa Composita, *Sp.*

"Jalap, in No. 40 powder, 80 *grammes;* Scammony Resin, in powder, 15 *grammes;* Turpeth, in No. 40 powder, 10 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the mixed powders with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture is also official in the N. F. IV (see Part III). It is a harsh but active purgative, capable of producing serious effects if given in over-dose.

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA KALADANÆ. Br.

TINCTURE OF KALADANA

"Kaladana, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the alcohol, and complete the *percolation process.*" *Br.*

This is a new tincture of the British Pharmacopœia 1914. It is used as a cathartic in doses of one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA KINO. U. S., Br.

TINCTURE OF KINO Tr. Kino

Teinture (alcoolé) de Kino, *Fr. Cod.;* Kinotinktur, *G.*

"Kino, 100 Gm.; to make 1000 cc. Place the kino in a capacious flask, and pour on it 500 cc. of boiling water. Agitate the mixture thoroughly, and heat it for one hour on a water bath containing boiling water, shaking it frequently. Allow the liquid to cool, add enough recently boiled water to make the product measure 500 cc., and add 500 cc. of alcohol. Stopper the flask, set it aside in a cool place for twenty-four hours, and then decant the mixture through cheese cloth.

"Preserve in a cool, dark place, in small bottles, tightly stoppered. Alcohol content, by volume, 45 to 47 per cent." *U. S.*

"Kino, in powder, 100 *grammes;* Glycerin, 150 *millilitres;* Distilled Water, 250 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Mix the Glycerin and the Distilled Water; rub the Kino in a mortar with a sufficient quantity of the mixture to form a smooth paste, gradually adding the remainder of the mixture; transfer to a closed vessel; add five hundred millilitres of the Alcohol; set aside for twelve hours, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

An important operation in the process of the U. S. Pharmacopœia is the employment of heat. This is due to the researches of Edmund White (*P. J.*, 1903, May, 644, and Nov., 702), who with David Hooper showed that the gelatinization of tincture of kino is due to an enzyme or oxydase present in the kino; the activity of this is destroyed by heat. This very simple procedure makes it unnecessary to comment upon the numerous formulas which filled the pharmaceutical literature of bygone years, in which all sorts of expedients were resorted to, in order to prevent the gelatinization of this preparation, which almost invariably occurred and which was a constant source of loss to the pharmacist. Tincture of kino is one of the most frequently prescribed astringents, especially in the treatment of *diarrhea.*

Dose, one to two fluidrachms (3.75–7.5 cc.).

Off. Prep.—Tinctura Kino et Opii Composita, *N. F.*

TINCTURA KRAMERIÆ. U. S., Br.

TINCTURE OF KRAMERIA

Tincture of Rhatany; Teinture Ratanhia, *Fr. Cod.;* Tinctura Ratanhiæ, *P. G.;* Ratanhiatinktur, *G.*

"Krameria, in moderately coarse powder, 200 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, using diluted alcohol as the menstruum.

"Alcohol content, by volume, 40 to 45 per cent." *U. S.*

"Krameria Root, in No. 40 powder, 200 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

It is stated that the tincture made from Pará rhatany furnishes a clear solution on the addition of water, while that from Peruvian root yields a turbid mixture.

The same precaution should be observed in keeping this tincture as is recommended for tincture of kino. It is a good preparation in cases which admit of the use of small quantities of alcohol.

Dose, one or two fluidrachms (3.75 or 7.5 cc.).

TINCTURA LAVANDULÆ COMPOSITA. U. S., Br.

COMPOUND TINCTURE OF LAVENDER Tr. Lavand. Co. [Compound Spirit of Lavender]

Spiritus Lavandulæ Compositus, *U. S.* 1870; Lavender Drops; Teinture de Lavande composée, *Fr.;* Zusammengesetzte Lavendeltinktur, *G.*

"Oil of Lavender, 8 cc.; Oil of Rosemary, 2 cc.; Cinnamon, in moderately coarse powder, 20 Gm.; Clove, in moderately coarse powder, 5 Gm.; Myristica, in moderately coarse powder, 10 Gm.; Red Saunders, in moderately coarse powder, 10 Gm.; to make 1000 cc. Prepare a Tincture by Type Process M, macerating the mixed drugs in a mixture of 750 cc. of alcohol, in which the oils have been dissolved, and 250 cc. of water. Complete the preparation with a menstruum of 3 volumes of alcohol and 1 volume of water.

"Alcohol content, by volume, 67 to 72 per cent." *U. S.*

"Oil of Lavender, 5.0 *millilitres;* Oil of Rosemary, 0.5 *millilitre;* Cinnamon Bark, bruised, 10.0 *grammes;* Nutmeg, bruised, 10.0 *grammes;* Red Saunders Wood, rasped, 20.0 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000.0 *millilitres.* Macerate the solid ingredients and the Oils with nine hundred millilitres of the Alcohol for seven days, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

The compound tincture of lavender of the U. S. Pharmacopœia is nearly twice the strength of the British preparation, although it is made with a menstruum weaker in alcohol. When properly prepared it is an excellent preparation to be used for *gastric uneasiness, nausea,* and *flatulence.*

Dose, from thirty minims to a fluidrachm (1.8–3.75 cc.).

TINCTURA LIMONIS. U. S., Br.

TINCTURE OF LEMON Tr. Limon. [Tincture Limonis Corticis U. S. P. IX]

Alcoolature de Citron, *Fr. Cod.;* Teinture de Zeste de Citron, *Fr.;* Citronenschalentinktur, *G.;* Alcohol de Corteza de Cidra, *Sp.*

"Lemon Peel (the outer yellow rind, grated from the fresh fruit), 500 Gm.; to make 1000 cc. Prepare a Tincture by Type Process M, macerating the drug in 1000 cc. of alcohol, and complete the preparation with alcohol. Use purified cotton as the filtering medium.

"Alcohol content, by volume, 70 to 75 per cent." *U. S.*

"Lemon Peel, cut small, 250 *grammes;* Alcohol (90 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

This tincture was doubled in strength at the 1898 revision of the Br. Pharm., but is still only about one-half the strength of the U. S. tincture. It is made with strong alcohol instead of proof spirit formerly used. It forms a grateful aromatic addition to tonic infusions, etc.

Dose, from one to two fluidrachms (3.75–7.5 cc.).

Off. Prep.—Syrupus Acidi Citrici, *U. S.*

TINCTURA LOBELIÆ. U. S.

TINCTURE OF LOBELIA Tr. Lobel. [Lobeliæ tinctura P. I.]

Teinture de Lobélie, *Fr. Cod.;* Tinctura Lobeliae, *P. G.;* Lobelientinktur, *G.;* Tintura di lobelia, *It.;* Tintura alcoholica de lobelia, *Sp.*

"Lobelia, in moderately coarse powder, 100 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, using diluted alcohol as the menstruum.

"Alcohol content, by volume, 44 to 47 per cent." *U. S.*

For method of assay, see *C. D.,* 1893, 454; also *P. J.,* 1895, 141.

It possesses the emetic and narcotic properties of lobelia, and is much used in *asthma.* A saturated tincture is strongly recommended by A. Livezey as a local application in *erysipelas,* and in the *eczematous eruption* of *Rhus poisoning.* (*B. M. S. J.,* lv, 262.)

Dose, as an expectorant, fifteen to thirty minims (0.9–1.8 cc.).

TINCTURA LOBELIÆ ÆTHEREA. Br.

ETHEREAL TINCTURE OF LOBELIA

Teinture ethérée de Lobélie enflée, *Fr.;* Ætherische Lobelientinktur, *G.*

"Lobelia, in No. 40 powder, 200 *grammes;* Spirit of Ether, sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred *millilitres* of the Spirit of Ether, and complete the *percolation process.*" *Br.*

It should be noted that this tincture is twice the strength of the U. S. tincture and the International Protocol.

Dose, from five to fifteen minims (0.3–0.9 cc.).

TINCTURA MYRRHÆ. U. S., Br.

TINCTURE OF MYRRH Tr. Myrrh.

Teinture (alcoolé) de Myrrhe, *Fr. Cod.;* Tinctura Myrrhae, *P. G.;* Myrrhentinktur, *G.;* Tintura di mirra, *It.;* Tintura alcoholica de mirra, *Sp.*

"Myrrh, in moderately coarse powder, 200 Gm.; to make 1000 cc. Prepare a Tincture by Type Process M, using alcohol as the solvent.

"Alcohol content, by volume, 83 to 88 per cent." *U. S.*

"Myrrh, in coarse powder, 200 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Macerate the Myrrh with eight hundred millilitres of the Alcohol in a closed vessel for seven days, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

The strength of this tincture was increased 60 per cent. at the revision of the British Pharmacopœia (1898) and is now equivalent to the U. S. preparation.

Official alcohol is preferable to diluted alcohol as a solvent of myrrh, because it forms a perfectly clear tincture, which is not attainable with the latter menstruum. The addition of water to the tincture renders it turbid. According to E. B. Shuttleworth (*A. J. P.,* xliii, 369), the gum which is left behind in making the tincture may be utilized for making mucilage. The tincture of myrrh is used solely as a local application to stimulate *indolent and foul ulcers, spongy gums, aphthous sore mouth,* and *ulcerations of the throat.*

Dose, from fifteen to thirty minims (0.9–1.8 cc.).

TINCTURA NUCIS VOMICÆ. U. S., Br.

TINCTURE OF NUX VOMICA Tr. Nuc. Vom. [Strychni tinctura P. I.]

"Tincture of Nux Vomica yields, from each 100 cc., not less than 0.237 Gm. and not more than 0.263 Gm. of the alkaloids of nux vomica." *U. S.* "Tincture of Nux Vomica contains in 100 millilitres 0.125 gramme of strychnine." *Br.*

Teinture (alcoolé) de Noix vomique, *Fr. Cod.;* Tinctura Strychni, *P. G.;* Brechnusstinktur, Krähenaugentinktur, *G.;* Tintura di noce vomica, *It.;* Tintura alcoholica de nuez vomica, *Sp.*

"Nux Vomica, in moderately coarse powder, 100 Gm.; to make about 1000 cc. Prepare a Tincture by Type Process P as modified for assayed tinctures, using a mixture of 10 cc. of acetic acid, 750 cc. of alcohol, and 240 cc. of water as the first menstruum, and completing the percolation with a mixture of 3 volumes of alcohol and 1 volume of water. Adjust the volume of the finished tincture by the addition of sufficient of the second menstruum to make each 100 cc. contain 0.25 Gm. of the alkaloids of nux vomica. Cool the Tincture in a proper container by exposure to a temperature of 5° C., and filter.

"Alcohol content, by volume, 67 to 72 per cent." *U. S.*

"Liquid Extract of Nux Vomica, 50 *milli-*

litres; Distilled Water, 150 *millilitres;* Alcohol (90 per cent.), sufficient to produce 600 *millilitres.* Mix; filter if necessary. Examined by the process described under 'Extractum Nucis Vomicæ Liquidum,' Tincture of Nux Vomica is found to contain in 100 millilitres 0.125 gramme of strychnine. *Limit of error* 0.005 gramme in excess or defect. This Tincture contains in each millilitre 1.25 milligrams of strychnine; each fluidrachm contains about $^1/_{16}$ grain. It contains approximately the same proportion of strychnine as the Tinctura Nucis Vomica of the International Agreement, and one-half of that contained in the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

Assay.—"Proceed by Type Process D, taking 50 cc. of Tincture of Nux Vomica, use chloroform as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal sulphuric acid corresponds to 0.0364 Gm. of the alkaloids of nux vomica (Proximate Assays)." *U. S.*

Great variations in procedure have marked the course of this tincture in the former editions of the U. S. P. As made from a standardized extract or a fluidextract the strength was usually satisfactory but the color of the preparation was too variable. The present U. S. P. method affords a product which is uniform both in appearance and alkaloidal content.

The British Pharmacopœia standardizes the liquid extract, and makes its tincture from it of such strength that 100 cc. shall contain 0.125 Gm. of strychnine.

The amount of strychnine in this tincture is so small that it is not to be recommended for producing the systemic effects of that alkaloid. Its most important use is as a bitter tonic in *gastric atony.*

Dose, of the tincture, ten to thirty minims (0.6–1.8 cc.), to be increased if necessary.

Off. Prep.—Elixir Phosphori et Nucis Vomicæ, *N. F.*

TINCTURA OLIVERI CORTICIS. Br.

TINCTURE OF OLIVER'S BARK

"Oliver's Bark, in No. 40 powder, 100 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with fifty millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture has been used in Australia for a number of years and is now official in the Br. Pharm. 1914. It possesses the properties of an aromatic like cinnamon.

The *dose* is from one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA OPII. U. S., Br.

TINCTURE OF OPIUM Tr. Opii [Tinctura Opii Deodorati U. S. P. IX, Laudanum, Tincture of Deodorized Opium, Opii tinctura P. I.]

"Tincture of Opium yields, from each 100 cc., not less than 0.95 Gm. and not more than 1.05 Gm. of anhydrous morphine." *U. S.*

"Opium contains in 100 millilitres 1 gramme of morphine, calculated as anhydrous." *Br.*

Tinctura Thebaica, Tinctura Meconii, Tinctura Extracti Opii; Teinture d'Extrait d'Opium, *Fr. Cod.;* Teinture (alcoolé) d'Opium, Teinture thébaïque, *Fr.;* Tinctura Opii Simplex, *P. G.;* Einfache Opiumtinktur, *G.;* Tintura di oppio, *It.;* Tintura alcoholica de opio, *Sp.*

There has been a marked change in the formula for this tincture in the U. S.; the preparation at present official under the name of Tincture of Opium is practically the same as that which was recognized previously as Tincture of Deodorized Opium and the plain Tincture of Opium, corresponding to the Br. preparation, has been entirely omitted.

"Granulated Opium, 100 Gm.; Paraffin, 50 Gm.; Alcohol, 200 cc.; Water, a sufficient quantity to make about 1000 cc. Heat 500 cc. of water to boiling, pour it on the granulated opium contained in a suitable vessel, and stir the mixture frequently during twenty-four hours. Transfer the mixture to a percolator, and, when the original menstruum has ceased to drop, continue the percolation slowly, gradually adding water until the opium is exhausted. Concentrate the percolate by evaporation on a water bath until it measures 150 cc., add the paraffin, and continue the heating until this is entirely melted. Beat the mixture thoroughly and set it aside to cool. When cool, pierce a hole through the top layer of paraffin and drain off the liquid, add to this 600 cc. of water, and filter, add the alcohol to the filtered liquid, and wash the residual paraffin and the filter with small portions of water until the combined liquids measure 950 cc. Assay a portion of this liquid as directed below, and, from the morphine content thus determined, ascertain by calculation the amount of anhydrous morphine in the remainder of the liquid, and adjust the volume of the finished Tincture by the addition of a mixture of 1 volume of alcohol and 4 volumes of water, to make each 100 cc. contain 1 Gm. of anhydrous morphine.

"Alcohol content, by volume, 17 to 19 per cent." *U. S.*

"Opium, 200 *grammes;* Alcohol (90 per cent.), Distilled Water, of each, *a sufficient quantity.* Rub the Opium to a paste with five hundred *millilitres* of Distilled Water, previously heated to at least 90° C.; set aside for six hours; add five hundred *millilitres* of the Alcohol; mix thoroughly; set aside in a covered vessel for twenty-four hours; strain, and then press; mix the two liquids thus obtained; set aside for twenty-four hours; filter. Determine the proportion of morphine, calculated as anhydrous, in the strong tincture so prepared by the following process:" *Br.*

Assay.—"Evaporate 80 cc. of Tincture of Opium on a water bath until the alcohol is removed. Then proceed as directed in the assay under *Opium,* beginning with the word 'transfer.' The result of the assay indicates the amount of morphine obtained from 40 cc. of the Tincture of Opium." *U. S.*

"Pour 40 millilitres of the liquid into a porcelain dish; evaporate on a water bath until the volume is reduced to about 10 millilitres; mix the residual liquid in a mortar with 1 gramme of freshly slaked *lime;* dilute the mixture with water to 41 *millilitres;* set aside for half an hour, stirring from time to time. Filter off 25 millilitres of the liquid (representing 25 millilitres of the strong tincture) through a plaited filter, having a diameter of about one decimetre, into a convenient vessel; add 2.5 millilitres of *alcohol* (90 per cent.) and 15 millilitres of *ether;* shake the mixture; add 1 gramme of *ammonium chloride;* shake well and frequently during half an hour; set aside for twelve hours for the morphine to separate. Counterbalance two small filters; place one within the other in a small funnel in such a way that the triple fold of the inner filter shall be superposed upon the single fold of the outer filter; wet them with *ether;* remove the ethereal layer of the liquid in the vessel as completely as possible by means of a small pipette, and transfer it to the filter; rinse the vessel with 8 millilitres of *ether,* again transferring the ethereal layer, by means of the pipette, to the filter; wash the filter with a total amount of 5 millilitres of *ether* added slowly, and in portions; let the filter dry in the air; pour upon it the liquid in the bottle, in portions, in such a way as to transfer the granular crystalline morphine as completely as possible to the filter. When all the liquid has passed through, wash the remainder of the morphine from the vessel with *morphinated water.* Wash the crystals with *morphinated water* until the washings are free from color; allow the filter to drain and dry it first at 60° C., and finally at 115° C. for two hours. Weigh the crystals in the inner filter, counterbalancing by the outer filter. Take 0.2 gramme of the crystals, and titrate, with *N/10 solution of sulphuric acid,* as directed under 'Opium.' Add to the weight of anhydrous morphine obtained, as indicated by the titration, 0.025 gramme, a portion representing the average loss of morphine during the process. Having thus ascertained the proportion of morphine calculated as anhydrous, present in 25 millilitres of the strong tincture, dilute the remainder of the latter with sufficient of a mixture of Alcohol (90 per cent.) and Distilled Water, in equal volumes, to produce Tincture of Opium containing 1 gramme of morphine, calculated as anhydrous, in 100 millilitres. Examined by the foregoing process, Tincture of Opium is found to contain in 100 millilitres 1 gramme of morphine, calculated as anhydrous. *Limit of error* 0.05 gramme in excess or defect. This Tincture contains in 100 millilitres 1 gramme of morphine, calculated as anhydrous; 110 minims contain 1 grain of the same. It is of approximately the same strength as the Tinctura Opii of the International Agreement, and is about one-third stronger than the corresponding preparation of the British Pharmacopœia, 1898. Tincture of Opium may be prepared with any variety of opium containing a known percentage of morphine, calculated as anhydrous, provided that the percentage is not less than seven and a half, and provided that the resulting Tincture of Opium responds to the foregoing test." *Br.*

There were formerly a number of official liquid preparations of opium of the same drug strength, *i.e.,* the *vinegar,* the *wine,* the *tincture* and the *deodorized tincture.* The vinegar and wine have been long since dismissed from the official list.

The deodorized tincture had its origin in *Battleys sedative-drops,* a proprietary preparation of a century ago.

The advantages of a preliminary treatment of the opium or its extract with a solvent capable of removing waxy, fatty and caoutchouc-like constituents of the drug, without diminishing the content of narcotic alkaloids was soon appreciated. Methyl acetate, ether, paraffin and benzin have all been suggested and used. The latter, however, has the advantage of cheapness and yields a very satisfactory product. The large increase in the use of the deodorized tincture has led to the replacement by it, as an official article, of the plain tincture previously known and used.

About two-thirds of the opium used in the preparation of the tincture are dissolved, the residue consisting chiefly of inert matter, but containing traces of morphine. According to the requirements of the Pharmacopœia, 10 minims of this tincture will contain about one-tenth of a grain of morphine. Because of the other narcotic principles of opium, however, the clinical effects are somewhat stronger; the narcotic action of ten minims of the tincture of opium (0.6 cc.) is nearly equivalent to one-sixth of a grain (0.01 Gm.) of morphine. Its action differs slightly from that of pure morphine, it being more constipating and more nauseating. As pointed out under opium the other alkaloids present seem to lessen the depressant effect of morphine upon the respiratory center so that the crude drug is a somewhat safer form of narcotic than pure opium.

The tincture of opium is probably the best of the official preparations where the effects of the whole drug are desired. It should be recollected that a fluidrachm of laudanum will yield on an average about one-hundred and twenty drops. When long kept with occasional exposure to the air, it becomes thick from the evaporation of a portion of the alcohol and the deposition of solid matter. If given in this state, it often acts with unexpected energy, and death has resulted in infants from doses which would have been entirely safe if the tincture had not been concentrated in this way.

Dose, five to ten minims (0.3–0.6 cc.).

Off. Prep.—Linimentum Opii, *Br.;* Tinctura Camphoræ Composita, *Br.;* Tinctura Opii Ammoniata, *Br.;* Linimentum Opii Compositum, *N.*

F.; Lotio Plumbi et Opii, *N. F.;* Mistura Carminativa, *N. F.;* Mistura Copaibæ et Opii, *N. F.;* Mistura Magnesiæ, Asafœtidæ et Opii, *N. F.;* Mistura Opii et Chloroformi Composita, *N. F.;* Mistura Opii et Rhei Composita, *N. F.;* Tinctura Opii et Gambir Composita, *N. F.*

TINCTURA OPII AMMONIATA. Br.

AMMONIATED TINCTURE OF OPIUM

Scotch Paregoric; Teinture d'Opium ammoniacale, *Fr.;* Ammoniakalische Opiumtinktur, *G.*

"Tincture of Opium, 100 *millilitres;* Benzoic Acid, 20 *grammes;* Oil of Anise, 5 *millilitres;* Solution of Ammonia, 200 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve the Oil of Anise and the Benzoic Acid in six hundred millilitres of the Alcohol; add the Tincture of Opium and the Solution of Ammonia; mix; filter; add sufficient of the Alcohol to produce the required volume. This Tincture contains in 100 millilitres 0.1 gramme of morphine, calculated as anhydrous; 110 minims contain about 1/10 grain of the same. It contains approximately one-tenth less morphine than that contained in the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

This is an old preparation of the Edinburgh Pharmacopœia, formerly used in Scotland under the name of *Paregoric Elixir.* It differs, however, both in composition and in strength, from the very popular preparation known as Paregoric in the United States.

Dose, from thirty minims to a fluidrachm (1.8–3.75 cc.).

TINCTURA OPII CAMPHORATA. U. S. (Br.)

CAMPHORATED TINCTURE OF OPIUM Tr. Opii Camph. [Paregoric, Opii tinctura benzoici P. I.]

Tinctura Camphoræ Composita, *Br.;* Compound Tincture of Camphor; Paregoric Elixir; Tinctura Thebaica Benzoica; Elixir Parégorique, Teinture d'Opium Camphrée, *Fr.;* Tinctura Extracti Opii Camphorata, Elixir Paregoricum, Tinctura Opii benzoïca, *P. G.;* Benzoësaurehaltige Opiumtinktur, *G.*

"Powdered Opium, 4 Gm.; Benzoic Acid, 4 Gm.; Camphor, 4 Gm.; Oil of Anise, 4 cc.; to make 1000 cc. Prepare a Tincture by Type Process M, macerating the ingredients in a mixture of 40 cc. of glycerin and 950 cc. of diluted alcohol, completing the preparation with diluted alcohol.

"Alcohol content, by volume, 43 to 46 per cent." *U. S.*

"Tincture of Opium, 50 *millilitres;* Benzoic Acid, 5 *grammes;* Camphor, 3 *grammes;* Oil of Anise, 3 *millilitres;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Dissolve the Benzoic Acid, Camphor, and Oil of Anise in nine hundred *millilitres* of the Alcohol; add the Tincture of Opium and sufficient of the Alcohol to produce the required volume; filter if necessary. This Compound Tincture contains in 10 millilitres 5 milligrammes (0.005 gramme) of morphine, calculated as anhydrous; and in each fluid drachm about one thirty-seventh of a grain of the same. It contains approximately one-tenth more morphine than the Tinctura Opii Benzoica of the International Agreement, and one-tenth more than was contained in the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

This is widely employed with the idea that it is a mild anodyne for the relief of *cough, nausea,* and abdominal *pains.* As its narcotic effects depend, however, entirely upon the opium which it contains its mildness is due solely to the fact that it is usually given in relatively small doses. In *diarrheas* the effect of the opium is somewhat enhanced by the camphor. The superstition that it is especially suited for children is senseless; if morphine be indicated for infants the alkaloid itself is just as useful if given in equivalent dose. One-half a fluidounce of either the United States or British tincture contains about nine-tenths of a grain of powdered opium.

Although this preparation is exempted from the provisions of the Harrison Anti-Narcotic Act, it has been frequently used by opium habitues when other forms of the narcotic are unobtainable and few pharmacists will sell more than one ounce to a customer.

Dose, for an infant, from five to twenty minims (0.3–1.3 cc.); for an adult, from one to four fluidrachms (3.75–15.0 cc.).

Off. Prep.—Mistura Glycyrrhizæ Composita, *U. S.;* Mistura Pectoralis, Stokes, *N. F.*

TINCTURA PICRORHIZÆ. Br.

TINCTURE OF PICRORHIZA

"Picrorhiza, cut small and bruised, 250 *grammes;* Alcohol (45 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

Although "this Tincture is of twice the strength of the corresponding preparation of the Indian and Colonial Addendum, 1900," *Br.,* the proportion of alcohol in this tincture is too large for it to be available as an antiperiodic; it is used as a bitter tonic.

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA PODOPHYLLI. Br.

TINCTURE OF PODOPHYLLUM

Teinture de Résine de Podophyllum, *Fr.;* Podophyllintinktur, *G.*

"Podophyllum Resin, 36.5 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Add the Podophyllum Resin to nine hundred *millilitres* of the Alcohol, and set aside for twenty-four hours, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

The introduction of this tincture is of doubtful utility.

Dose, five to fifteen minims (0.3–0.9 cc.).

TINCTURA PODOPHYLLI INDICI. Br.

TINCTURE OF INDIAN PODOPHYLLUM

"Indian Podophyllum Resin, 36.5 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Add the Indian Podophyllum Resin to nine hundred millilitres of the Alcohol, and set aside for twenty-four hours, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

This has been introduced to afford a substitute in the Asiatic provinces for the tincture of podophyllum.

Dose, five to fifteen minims (0.3–0.9 cc.).

TINCTURA PRUNI VIRGINIANÆ. Br.

TINCTURE OF WILD CHERRY

Tincture of Virginian Prune; Teinture d'Ecorce de Cerisier, *Fr.;* Wildkirschenrindentinktur, *G.*

"Wild Cherry Bark, in No. 20 powder, 200 *grammes;* Alcohol (90 per cent.), 565 *millilitres;* Distilled Water, 365 *millilitres;* Glycerin, 100 *millilitres.* Mix the powder with the Distilled Water; set aside in a closed vessel for twenty-four hours; add the Alcohol, and complete the *maceration process;* add the Glycerin to the product." *Br.*

This was a new official tincture of the Br. Pharm., 1898; its utility is doubtful. The English name has been changed from Virginian Prune to Wild Cherry in the Br. Pharm., 1914. The use of the glycerin serves to retard precipitation.

Dose, from one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA PYRETHRI. Br.

TINCTURE OF PYRETHRUM Tr. Pyreth.
[Tincture of Pellitory]

Teinture de Pyrèthre, *Fr. Cod.;* Bertramwurzeltinktur, *G.*

"Pyrethrum Root, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred and fifty millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture is a powerful local irritant, and is an ingredient in several mouth and tooth washes. For its uses, which are purely external, see *Pyrethrum.*

TINCTURA QUASSIÆ. Br.

TINCTURE OF QUASSIA

Teinture de Quassia, *Fr.;* Quassiatinktur, *G.*

"Quassia Wood, rasped, 100 *grammes;* Alcohol (45 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

This tincture is no longer recognized by the U. S. That formerly official was twice as strong as the Br. It was prepared as follows: "Quassia, in No. 50 powder, *two hundred grammes,* to make *one thousand mils.* Prepare a Tincture by Type Process P, using a mixture of *one volume* of alcohol and *two volumes* of water as the menstruum." *U. S. IX.*

It may be employed as an addition to tonic infusions or mixtures. It has the advantage of being free from tannin, and may be given in conjunction with salts of iron.

Dose, one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA QUILLAIÆ. Br.

TINCTURE OF QUILLAIA

Teinture de Quillaya, Teinture d'Ecorce de Panama, *Fr.;* Seifenrindentinktur, *G.*

Tincture of quillaja has been deleted from the U. S., but is official in the N. F. (see Part III).

"Quillaia Bark, in No. 20 powder, 50 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with twenty-five millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture is almost exclusively used as an emulsifying agent. Its medicinal activity, however, limits its use. (See *Quillaja.*)

Dose, from one-half to one fluidrachm (1.8–3.75 cc.).

TINCTURA QUININÆ. Br.

TINCTURE OF QUININE

Teinture de Quinine, *Fr.;* Chinintinktur, *G.*

"Quinine Hydrochloride, 20 *grammes;* Tincture of Orange, 1000 *millilitres.* Dissolve." *Br.*

Quinine sulphate was replaced in this preparation by the hydrochloride in the 1885 Br. Pharmacopœia, because, as pointed out by Wright (*Y. B. P.,* 1884, 537), the sulphate was not always soluble in the proportion of tincture of orange peel ordered.

Dose, a fluidrachm (3.75 cc.) (about equal to one and two-tenths grains of quinine hydrochloride).

TINCTURA QUININÆ AMMONIATA. Br.

AMMONIATED TINCTURE OF QUININE

Teinture Ammoniacale de Quinine, *Fr.;* Ammoniakhaltige Chinintinktur, *G.*

"Quinine Sulphate, 20 *grammes;* Solution of Ammonia, 100 *millilitres;* Alcohol (60 per cent.), 900 *millilitres.* Mix the Solution of Ammonia with the Alcohol; add the Quinine Sulphate; shake until a clear solution is produced; set aside for three days; filter." *Br.*

Dose, one fluidrachm (3.75 cc.), representing about one and two-tenths grains of quinine sulphate.

TINCTURA RHEI. U. S. (Br.)

TINCTURE OF RHUBARB Tr. Rhei

Tinctura Rhei Composita, *Br.;* Compound Tincture of Rhubarb; Teinture de Rhubarbe, *Fr. Cod.;* Rhabarbertinktur, *G.;* Tintura di rabarbaro, *It.*

"Rhubarb, in moderately coarse powder, 200 Gm.; Cardamom Seed, in moderately coarse powder, 30 Gm.; to make 1000 cc. Prepare a

Tincture by Type Process P, using a mixture of 100 cc. of glycerin, 500 cc. of alcohol, and 400 cc. of water as the first menstruum, completing the percolation with diluted alcohol.

"Alcohol content, by volume, 43 to 46 per cent." *U. S.*

"Rhubarb, in No. 20 powder, 100.0 *grammes;* Cardamom Seeds, in No. 20 powder, 12.5 *grammes;* Coriander Fruit, in No. 20 powder, 12.5 *grammes;* Glycerin, 100.0 *millilitres;* Alcohol (45 per cent.), sufficient to produce 1000.0 *millilitres.* Moisten the solid ingredients with one hundred millilitres of the Alcohol, and prepare, by the *percolation process,* eight hundred and fifty millilitres of tincture. Add the Glycerin, and sufficient of the Alcohol to produce the required volume." *Br.*

Like several other tinctures, this is one which has been found difficult to stabilize. Glycerin minimizes the tendency to precipitate. The precipitate is in part chrysophanic acid which is one of the less valuable medicinal constituents of the drug, so a small amount of precipitation in this preparation may be disregarded.

Dose, from one to two fluidrachms (3.75–7.5 cc.).

Off. Prep.—Mistura Opii et Rhei Composita, *N. F.*

TINCTURA RHEI AROMATICA. U. S.

AROMATIC TINCTURE OF RHUBARB
Tr. Rhei Arom.

Teinture (alcoolé) de Rhubarbe aromatique, *Fr.;* Aromatische Rhabarbertinktur, *G.*

"Rhubarb, in moderately coarse powder, 200 Gm.; Cinnamon, in moderately coarse powder, 40 Gm.; Clove, in moderately coarse powder, 40 Gm.; Myristica, in moderately coarse powder, 20 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, using a mixture of 100 cc. of glycerin, 500 cc. of alcohol, and 400 cc. of water as the first menstruum, completing the percolation with diluted alcohol.

"Alcohol content, by volume, 43 to 46 per cent." *U. S.*

This is the tincture which is used in making the aromatic syrup of rhubarb. It is preferable to separate the preparations, as it is occasionally desirable to prescribe the tincture without the admixture with syrup, while the pharmacist will always prefer to make the tincture in quantity and keep it on hand, since it is permanent, and add to it syrup to make the aromatic syrup when needed.

Dose, for an adult, from one-half to one fluidrachm (1.8–3.75 cc.).

Off. Prep.—Syrupus Rhei Aromaticus, *U. S.*

TINCTURA SCILLÆ. U. S., Br.

TINCTURE OF SQUILL Tr. Scill.

"Tincture of Squill, injected into the ventral lymph sac of a frog, has a minimum systolic dose of not less than 0.0055 cc., and not more than 0.0065 cc., equivalent to not less than 0.000,000,46 Gm. and not more than 0.000,000,54 Gm. of ouabain, for each Gm. of body weight of frog." *U. S.*

Teinture de Scille, *Fr. Cod.;* Meerzwiebeltinktur, *G.;* Tintura alcoholica de escila, *Sp.*

"Squill, in coarse powder, 100 Gm.; Alcohol, Water, each, a sufficient quantity to make about 1000 cc. Moisten the drug with sufficient menstruum, prepared by mixing 3 volumes of alcohol and 1 volume of water, and macerate in a closed vessel in a moderately warm place for twenty-four hours, stirring occasionally. Then transfer it to a percolator, shake it down evenly without packing, and pour on enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for twenty-four hours. Then allow the percolation to proceed slowly, gradually adding sufficient of the same menstruum until the percolate measures 950 cc. Assay a portion of this percolate as directed below, and, from the result thus obtained, adjust the volume of the finished Tincture by the addition of menstruum to conform to the above biological standard.

"Alcohol content, by volume, 64 to 67 per cent.

"**Assay.**—Proceed as directed under *Tinctura Digitalis.*" *U. S.*

"Squill, bruised, 200 *grammes;* Alcohol (60 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

The tincture represents the virtues of squill probably better than any other official preparation.

Dose, from ten to twenty minims (0.6–1.3 cc.).

TINCTURA SENEGÆ. Br.

TINCTURE OF SENEGA

Teinture de Polygala de Virginie, *Fr.;* Senegatinktur, *G.*

"Senega Root, in No. 40 powder, 200 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

The Br. Pharm. 1898 increased the strength of this preparation 60 per cent. The tincture is efficient, but it is hardly needed while recourse can be had to the fluidextract or the syrup.

Dose, from thirty minims to two fluidrachms (1.8–7.5 cc.).

TINCTURA SENNÆ COMPOSITA. Br.

COMPOUND TINCTURE OF SENNA

Elixir Salutis; Teinture de Séné composée, Teinture de Séné aromatique, Elixir de Salut, *Fr.;* Zusammengesetzte Sennatinktur, *G.*

"Senna Leaves, in No. 20 powder, 200 *grammes;* Caraway Fruit, in No. 20 powder, 25 *grammes;* Coriander Fruit, in No. 20 powder, 25 *grammes;* Glycerin, 100 *millilitres;* Alcohol (45 per cent.), sufficient to produce

1000 *millilitres.* Moisten the solid ingredients with two hundred and fifty millilitres of the Alcohol, and prepare, by the *percolation process,* eight hundred and fifty millilitres of tincture. Add the Glycerin and sufficient of the Alcohol to produce the required volume." *Br.*

The Br. Pharm. 1898 increased the proportion of senna in this preparation 60 per cent.

This tincture is the *elixir salutis* of the old Pharmacopœias. It is a warm cordial purgative, useful in *costiveness* attended with flatulence, and in *atonic gout,* especially when occurring in intemperate persons. It is also added to cathartic infusions and mixtures. Tincture of senna yields a yellow scaly deposit, containing white crystals of calcareous salts. (Ménière.)

Dose, from two to four fluidrachms (7.5–15 cc.).

TINCTURA SERPENTARIÆ. Br.

TINCTURE OF SERPENTARY

Teinture de Serpentaire de Virginie, *Fr.;* Schlangenwurzeltinktur, *G.*

" Serpentary Rhizome, in No. 40 powder, 200 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture is little other than a feebly aromatic, alcoholic stimulant. The Br. Pharm. 1898 increased the strength of this preparation 60 per cent.

Dose, thirty minims to two fluidrachms (1.8–7.5 cc.).

TINCTURA STRAMONII. U. S., Br.

TINCTURE OF STRAMONIUM Tr. Stramon.

" Tincture of Stramonium yields, from each 100 cc., not less than 0.0225 Gm. and not more than 0.0275 Gm. of the alkaloids of stramonium." *U. S.*

Tincture of Stramonium Leaves; Teinture de Stramoine (feuille), *Fr.;* Stechapfelblättertinktur, *G.*

" Stramonium, in moderately coarse powder, 100 Gm.; to make about 1000 cc. Prepare a Tincture by Type Process P as modified for assayed tinctures, using diluted alcohol as the menstruum, and adjust the volume of the finished Tincture by the addition of diluted alcohol to make each 100 cc. contain 0.025 Gm. of the alkaloids of stramonium.

" Alcohol content, by volume, 44 to 47 per cent.

" **Assay.**—Proceed by Type Process D, taking 100 cc. of Tincture of Stramonium, use chloroform as the solvent, and determine the alkaloids volumetrically. Each cc. of tenth-normal sulphuric acid corresponds to 0.02893 Gm. of the alkaloids of stramonium (Proximate Assays)." *U. S.*

" Stramonium Leaves, in No. 20 powder, 200 *grammes;* Alcohol (45 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

The British tincture is now double the strength of the U. S. P. tincture.

Dose, from ten to twenty minims (0.6–1.3 cc.); of the British tincture, five to ten minims (0.3–0.6 cc.).

TINCTURA STROPHANTHI. U. S., Br.

TINCTURE OF STROPHANTHUS Tr. Strophanth. [Strophanthi tinctura P. I.]

" Tincture of Strophanthus, injected into the ventral lymph sac of a frog, has a minimum systolic dose of not less than 0.00,005,5 cc. and not more than 0.00,006,5 cc., equivalent to not less than 0.00,000,046 Gm. and not more than 0.00,000,054 Gm. of ouabain, for each Gm. of body weight of frog." *U. S.*

Teinture de Strophantus, *Fr. Cod.;* Tinctura Strophanthi, *P. G.;* Strophanthustinktur, *G.;* Strophanthussamentinktur, *G.;* Tinctura di strofanto, *It.;* Tintura alcoholica de estrofanto, *Sp.*

" Strophanthus, in moderately coarse powder, 100 Gm.; to make about 1000 cc. Pack the Strophanthus in a cylindrical glass percolator, provided with a stop-cock and arranged with a cover and a receptacle suitable for volatile liquids, and percolate it slowly with purified petroleum benzin until a few drops of the percolate, evaporated from filter paper, leave no greasy stain. Reject the benzin percolate. Remove the powdered drug from the percolator, and expose it to the air until the odor of benzin is no longer noticeable. Prepare from this a tincture by Type Process P as modified for assayed tinctures, using alcohol as the menstruum, and allowing the moistened drug to macerate for forty-eight hours before starting the percolation, instead of twenty-four hours as directed in Type Process P. Adjust the volume of the finished Tincture to conform to the above biological standard. Alcohol content, by volume, 88 to 92 per cent.

" **Assay.**—Proceed as directed under *Tinctura Digitalis.*" *U. S.*

" Strophanthus Seeds, in No. 30 powder, dried at 45° C., 100 *grammes;* Ether, *a sufficient quantity;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Pack the powder in a percolator; moisten with the Ether, and macerate for twenty-four hours; then allow percolation to proceed, continuing the addition of the Ether until the liquid passes through colorless. Remove the marc from the percolator, and dry it, gradually heating it to 50° C. Again reduce it to powder, repack in the percolator, and moisten with the Alcohol. Macerate for forty-eight hours, then pour on successive quantities of the Alcohol, percolating slowly, until five hundred millilitres of percolate are obtained; add sufficient of the Alcohol to produce the required volume. This Tincture is made with four times the proportion of Strophanthus Seeds ordered for the corresponding preparation of the British Pharmacopœia, 1898. It is of approximately the same strength as the Tinctura Strophanthi of the International Agreement, but in the case of the latter Tincture, the seeds are not treated with ether for the removal of fat and resins." *Br.*

H. Helch found diluted alcohol yielded the best tincture, the one with highest strophanthin content; that extraction with strong alcohol apparently tended to decompose strophanthin into strophanthidin; that tinctures made from seed defatted with petroleum ether had no higher strophanthin content than tinctures made from natural seed. (*Chem. Abs.*, 1919, xiii, 496.) Karam Samaan (*C. D.*, 1919, xci, 802) has also come to the like conclusion that strong alcohol can not extract the activity of strophanthus and recommends the use of 65 per cent. alcohol. The use of petroleum benzin in the U. S. P. IX and ether in the Br. P. for the preliminary exhaustion of the drug is to effect the removal of the fixed oil which interferes with the stability of the preparation unless previously removed. By these expedients a preparation which was formerly very unsatisfactory, on account of its turbid and unsightly condition, has been very much improved.

In spite of the researches which are quoted above the official menstruum for the U. S. P. X tincture of strophanthus is strong alcohol.

It is stated that when tincture of strophanthus is mixed with water and allowed to stand, the active principles undergo hydrolysis with the formation of a toxic substance, the identity of which has not yet been established. (*Schweiz. Apoth. Zeit.* through *Pract. Drug.*, 1916, p. 39.)

The question of deterioration of the tincture of strophanthus has been the subject of some difference of opinion. In the experiments of Pomeroy and Heyl (*A. J. P.*, 1922, xciv, p. 479) there was no appreciable deterioration when properly stored even after a period of five years, and according to Hatcher and Baily (*J. A. M. A.*, 1909, lii, p. 5), it is much more uniform in strength than tincture of digitalis.

Uses.—The tincture of strophanthus fully represents the crude drug and may be used for all the purposes for which strophanthus is serviceable.

Dose, three to eight minims (0.2–0.5 cc.).

TINCTURA TOLU. U. S. (Br.)

TINCTURE OF TOLU Tr. Tolu. [Tinctura Tolutana U. S. IX, Tolu Tincture]

Tinctura Tolutana, *Br.;* Tinctura Balsami Tolutani; Tincture of Balsam of Tolu; Teinture de Baume de Tolu, *Fr. Cod.;* Tolubalsamtinktur, *G.*

"Tolu, 200 Gm.; to make 1000 cc. Prepare a Tincture by Type Process M, using alcohol as the solvent.

"Alcohol content, by volume, 80 to 85 per cent." *U. S.*

"Balsam of Tolu, 100 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve the Balsam of Tolu in eight hundred *millilitres* of the Alcohol; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

The British tincture (1914) is half the strength of the U. S. P. tincture.

The tincture of tolu has the properties of the balsam, and may be employed as an addition to expectorant mixtures in *chronic bronchitis,* but the proportion of alcohol is too large to allow of its advantageous use in some cases. It is used in preparing the syrup of tolu. In smaller quantities it is often employed to flavor cough mixtures. It is precipitated by aqueous liquids.

Dose, one-half to two fluidrachms (1.8–7.5 cc.).

Off. Prep.—Syrupus Tolu, *U. S.*

TINCTURA URGINEÆ. Br.

TINCTURE OF URGINEA

"Urginea, bruised, 200 *grammes;* Alcohol (60 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

This tincture was introduced into India and is intended to be used in place of squill.

The *dose* is five to fifteen minims (0.3–0.9 cc.).

TINCTURA VALERIANÆ. U. S.

TINCTURE OF VALERIAN Tr. Valer

Teinture de Valériane, *Fr. Cod.;* Tinctura Valerianæ, *P. G.;* Baldriantinktur, *G.;* Tinturo di valeriana, *It.*

"Valerian, in moderately coarse powder, 200 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, using a mixture of 3 volumes of alcohol and 1 volume of water as the menstruum.

"Alcohol content, by volume, 66 to 70 per cent." *U. S.*

The tincture possesses the properties of valerian, but cannot be given in some cases, so as to produce the full effects of the root, without stimulating too highly, in consequence of the large proportion of spirit.

Dose, one to four fluidrachms (3.75–15.0 cc.).

TINCTURA VALERIANÆ AMMONIATA. U. S., Br.

AMMONIATED TINCTURE OF VALERIAN Tr. Valer. Ammon.

Tinctura Valerianæ Composita; Teinture de Valériane ammoniacale, *Fr.;* Ammoniakalische Baldriantinktur, *G.*

"Valerian, in moderately coarse powder, 200 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, using aromatic spirit of ammonia as the menstruum.

"Alcohol content, by volume, 62 to 65 per cent." *U. S.*

"Valerian Rhizome, in No. 40 powder, 200 *grammes;* Oil of Nutmeg, 3 *millilitres;* Oil of Lemon, 2 *millilitres;* Solution of Ammonia, 100 *millilitres;* Alcohol (60 per cent.), 900 *millilitres.* Mix the liquid ingredients, and, using the mixture as a menstruum, prepare by the *maceration process.*" *Br.*

The proportion of valerian was increased 60 per cent. in the Br. Pharm. 1898, and the aromatic spirit of ammonia replaced by alcohol, solution of ammonia, and volatile oils.

The ammonia in this preparation is thought to assist the solvent powers of the alcohol, while it co-operates with the valerian in medicinal action. The quantity of valerian was very judiciously increased one-third in the U. S. revision of 1880. The tincture is employed as an antispasmodic in *hysteria* and other *nervous diseases.*

Dose, from thirty minims to a fluidrachm (1.8–3.75 cc.).

TINCTURA VALERIANÆ INDICÆ AMMONIATA. Br.

AMMONIATED TINCTURE OF INDIAN VALERIAN

"Indian Valerian Rhizome, in No. 40 powder, 200 *grammes;* Oil of Nutmeg, 3 *millilitres;* Oil of Lemon, 2 *millilitres;* Solution of Ammonia, 100 *millilitres;* Alcohol (60 per cent.), 900 *millilitres.* Mix the liquid ingredients, and, using the mixture as a menstruum, prepare by the *maceration process.*" *Br.*

This tincture was introduced into the Br. Pharm. 1914 to be used in India and elsewhere in place of ammoniated tincture of valerian.

Dose, thirty minims to one fluidrachm (1.8–3.75 cc.).

TINCTURA VERATRI VIRIDIS. U. S.

TINCTURE OF VERATRUM VIRIDE Tr. Verat. Vir.

Tinctura Veratri; Tincture of Green Hellebore; Tincture of American Hellebore; Teinture (alcoolé) de Vératre, *Fr.;* Tinctura Veratri, *P. G.;* Nieswurzeltinktur, *G.*

"Veratrum Viride, in moderately coarse powder, 100 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, using alcohol as the menstruum.

"Alcohol content, by volume, 88 to 92 per cent." *U. S.*

The U. S. tincture of American hellebore of 1890 was of the same strength as *Norwood's tincture,* which was prepared by its author from fresh drug (240 grains for each fluidounce of alcohol), and was supposed to be saturated. The present tincture represents 10 per cent. of the drug, in conformance with the recommendations of the Brussels Congress concerning potent tinctures (see *Tincturæ*).

For uses see *Veratrum Viride.*

Dose, ten to thirty minims (0.6–1.8 cc.).

TINCTURA ZINGIBERIS. U. S., Br.

TINCTURE OF GINGER Tr. Zingib. [Tincture of Jamaica Ginger]

Teinture de Gingembre, *Fr.;* Tinctura Zingiberis, *P. G.;* Ingwertinktur, *G.*

"Ginger, in moderately coarse powder, 200 Gm.; to make 1000 cc. Prepare a Tincture by Type Process P, using a mixture of 850 cc. of alcohol and 150 cc. of water as the menstruum.

"Alcohol content, by volume, 74 to 78 per cent." *U. S.*

"Ginger, in No. 40 powder, 100 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

The strength of this tincture was reduced at the 1880 revision one-third, to bring it into the 20 per cent. class; this is not a disadvantage, however, in view of the introduction of the fluidextract, and the dose is not now inconveniently large.

The tincture of the British Pharmacopœia is still too weak in the proportion of ginger, being only half the strength of the U. S. tincture. In consequence of the mucilaginous matter contained in ginger, the tincture made with diluted alcohol or proof spirit is apt to be turbid, and the drug is incompletely exhausted of its resinous and oily constituents. Official Jamaica ginger only should be used; for, while a darker-colored preparation is made when the inferior varieties are substituted, the apparent increase in strength is due to coloring matter, and not to the presence of a larger amount of volatile oil or resin. It has been shown by carefully conducted experiments that the addition of a small proportion of water to the alcoholic menstruum may be made without injury to the strength of the preparation in terms of resinous matter and flavor.

Tests for Purity.—The U. S. gives the following organoleptic test: "Evaporate 10 cc. of Tincture of Ginger to dryness in a small flask. Add 5 cc. of half-normal alcoholic potassium hydroxide, and boil the mixture gently for thirty minutes under a reflux condenser. Remove the condenser, and evaporate the alcohol on a water bath. Then add 50 cc. of distilled water to the residue, agitate the mixture, filter, transfer the aqueous filtrate to a separatory funnel, and shake it out with 25 cc. of ether. Evaporate the separated ether solution spontaneously by adding it, a few drops at a time, to the center of a watch glass, and cautiously apply the tip of the tongue to the dry residue. The taste should be slightly camphoraceous but not sharp or bitingly pungent (*capsicum or similar pungent substitute*)." *U. S.*

This is another of the numerous alcoholic preparations of the U. S. P. that have been placed on the interdicted list by the Prohibition authorities.

The tincture of ginger is a useful carminative, and may often be beneficially added to tonic and purgative infusions or mixtures in debilitated states of the alimentary canal. It is in this country largely used for the preparation of a syrup of ginger, for which purpose, however, the fluidextract is official, and is better even than the strong tincture of the Br. Pharmacopœia 1885, which was dropped at the 1898 revision.

Dose, eight to forty minims (0.5–2.5 cc.).

Off. Prep.—Acidum Sulphuricum Aromaticum, *U. S., Br.*

TOLU. U. S. (Br.)

TOLU [Balsamum Tolutanum U. S. P. IX, Balsam of Tolu]

"Tolu is a balsam obtained from *Toluifera Balsamum* Linné (Fam. *Leguminosæ*)." *U. S.* "Balsam of Tolu is a solid balsam obtained from incisions made in the trunk of Myroxylon toluiferum, *H. B. and K.*" *Br.*

Balsamum Tolutanum, *Br.;* Balsamum Americanum; Resina Tolutana; Baume de Tolu, Baume de Carthagène, *Fr.;* Tolubalsam, *G.;* Balsamo Tolutano, Balsamo del Tolu, *It.;* Bálsamo de Tolu, *Sp.*

This balsam, like balsam of Peru, has been the subject of much controversy. This is not only seen in the distinct sources above given by the U. S. and British Pharmacopœias, but is rendered more confusing by the fact that the German Pharmacopœia prescribes "the air hardened balsam of *Myroxylon balsamum* (L.) Harms var. *genuinum* Baillon." In addition to this Tschirch regards the tree yielding balsam of Tolu like that of the tree yielding balsam of Peru, merely physiological varieties of *Toluifera Balsamum* L.

Toluifera Balsamum L. (*Myroxylon toluiferum* H. B. and K.) is a tree with spreading crown, somewhat like *Toluifera Pereiræ,* differing from it mainly by its habit of branching about 14–16 m. above ground, in having leaves with fewer leaflets and in bearing dense racemes of flowers each with a tubulary calyx. Most of the balsam is obtained in the province of Tolu along the Magdalena River in Colombia.

The balsam is said to be produced normally in the tree only in young growing tissues such as the young twigs and leaves, and to be formed in the older tissues only as the result of injuries received. It is procured by making V-shaped incisions in the trunk quite through the bark. The juice is received in small calabash cups, which are inserted in slight excavations beneath the point of the two vertical incisions meeting at the lower end; and Weir has seen as many as twenty cups at a time on one tree. The collectors go from tree to tree, emptying the cups into flasks of raw-hide. In these skin vessels the balsam is shipped to Cartagena and Savanilla where it is transferred to cylindrical tin cans, containing 10 to 25 pounds and exported.

Schaer has reported on *Myrocarpus Balsam* (*Cabureiba Balsam,* of Piso; *Baume du Perou en coques,* of Guibourt), and concludes that it has intermediate properties between balsam of Tolu and balsam of Peru. It did not contain cinnamic acid and the benzoic acid which he obtained had a melting point from 3° to 4° higher than normal benzoic acid. (*A. Pharm.,* 1909, p. 176.)

Description and Physical Properties.—As first imported, balsam of Tolu has a soft tenacious consistence, which varies considerably with the temperature. By age it becomes hard and brittle like rosin. It is shining, translucent, of a reddish or yellowish-brown color, a highly fragrant odor, and a warm, somewhat sweetish and pungent, but not disagreeable taste. Exposed to heat, it melts, inflames, and diffuses an agreeable odor while burning. It is entirely soluble in volatile oils.

"A brown or yellowish-brown, plastic solid, transparent in thin layers and brittle when old, dried, or exposed to cold. It has a pleasant, aromatic odor resembling that of vanilla, and a mild aromatic taste. Tolu is nearly insoluble in water and in petroleum benzin. It is soluble in alcohol, chloroform, and ether. It dissolves in solutions of the fixed alkalies, usually leaving an insoluble residue.

"An alcoholic solution of Tolu (1 in 20) is acid to litmus paper. Shake about 1 Gm. of Tolu with 25 cc. of carbon disulphide, allow it to stand for thirty minutes, filter the liquid, and evaporate 15 cc. of the filtrate to dryness. The residue thus obtained, when dissolved in glacial acetic acid, does not show a green color on the addition of a few drops of sulphuric acid (*rosin*). The remaining portion of the filtrate, when shaken with an equal volume of an aqueous solution of copper acetate (1 in 1000), does not acquire a green color (*rosin or copaiba*). Dissolve about 1 Gm. of Tolu, accurately weighed, in 50 cc. of neutral alcohol, add 1 cc. of phenolphthalein T.S., and titrate the solution with half-normal alcoholic potassium hydroxide. The acid number thus obtained is not less than 112 and not more than 168. Add sufficient half-normal alcoholic potassium hydroxide to the neutralized liquid obtained in the preceding test to make the total volume of the volumetric alkali solution exactly 20 cc., heat the liquid on a water bath for half an hour under a reflux condenser, and cool. Mix this liquid with 200 cc. of distilled water, or more if necessary, and titrate the excess of potassium hydroxide with half-normal sulphuric acid. The total volume of half-normal potassium hydroxide corresponds to a saponification value of not less than 154 and not more than 220." *U. S.*

"A soft, tenacious solid when first imported, becoming harder and finally brittle. Transparent and yellowish-brown in thin films. Pressed between pieces of glass with the aid of heat, and examined with a lens, it exhibits crystals of cinnamic acid. Odor fragrant, especially when warmed; taste aromatic and slightly acid. Soluble in *alcohol* 90 per cent.), the solution being acid to *litmus. Acid value* 107.4 to 147.2; *saponification value* 170 to 202. If 5 grammes are gently warmed with three successive portions of 25, 15, and 10 millilitres of *carbon disulphide,* the solution yields, when evaporated to dryness, a distinctly crystalline residue, which, when tested as described under 'Styrax Præparatus' yields not less than 1.25 grammes of balsamic acids." *Br.*

The carbon disulphide test is based upon Braithwaite's researches upon spurious balsams of Tolu. (See *P. J.,* 1895, 145; also 1897, 307.)

Hatchett states that when dissolved in the smallest quantity of solution of potassium hydroxide it loses its own characteristic odor and acquires that of the clove pink. G. L. Ulex gives as a test of the purity of the balsam, that if heated in sulphuric acid it dissolves without disengagement of sulphurous acid, and yields a cherry-red liquid. A modification of this test is that of R. A. Cripps (*P. J.*, xix, 1888), who states that by a comparative test of the suspected balsam with a pure specimen 1 per cent. of storax or other resinous adulterant can be detected. Thirty grammes of the sample are digested in carbon disulphide for fifteen minutes with gentle warmth, the clear liquid decanted, evaporated to dryness, and dissolved in sulphuric acid. A bright red rose color is produced, remaining rose for a length of time if the balsam be pure, rapidly becoming brown if the balsam has been adulterated.

Constituents.—Tolu balsam like that of Peru is a mixture of resinous matter with cinnamic and benzoic acids and esters of these acids. The proportion of resinous matter is larger than in Peru balsam, amounting to 75 or 80 per cent. It consists, according to Tschirch and Oberlander (*A. Pharm.*, 1894, 599), largely of the esters of an alcohol, *toluresinotannol.* The total aromatic acids, according to Cocking and Kettel (*P. J.*, 1918), amount to about 36 per cent., of which some 12 per cent. is free cinnamic acid and 8 per cent. free benzoic. When distilled with water it yields a small quantity, 1.5 to 3 per cent., of a highly aromatic volatile oil. Deville in 1841 found this oil to consist largely of a liquid principle to which he gave the name of *tolene* but which is probably identical with phellandrene ($C_{10}H_{16}$). This volatile oil, according to Parry (*Chemistry of Essential Oils*, etc., 1919), has the following characteristics: Sp. gr., 0.949 to 1.080; optical rotation, -2 to $+1$; refractive index, 1.5440 to 1.5600; acid number, 5 to 20; ester number, 175 to 210. The oil contains benzyl bonzoate, benzyl cinnamate, phellandrene, and farnesol. A factitious balsam described by R. V. Mattison (*A. J. P.*, 1876, 51) contained 63 per cent. of storax.

Tolu balsam is sometimes adulterated with rosin and pine resins, both of which are readily detected, as they are soluble in carbon disulphide and benzol. The Balsam of Tolu of commerce is sometimes deficient in alcohol-soluble contents. Occasionally, the cans of shipment of tolu contain large pieces of red brick with enough melted balsam poured in to completely cover the bricks and fill the cans.

Uses.—Balsam of Tolu is a feeble stimulant expectorant; the syrup of Tolu is much used, on account of its agreeable flavor, as the basis of cough mixtures. Old and obstinate *catarrhs* are said to be sometimes greatly relieved by the inhalation of the vapor proceeding from an ethereal solution of this balsam. The best form of administration is that of emulsion, made by triturating the balsam with mucilage and loaf sugar, and afterwards with water.

Dose, ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Syrupus Tolu, *U. S.* (from the tincture), *Br.;* Tinctura Benzoini Composita, *U. S., Br.;* Tinctura Tolu, *U. S., Br.*

TONGA. N. F.

TONGA

"Tonga is a mixture of equal parts of the bark of *Premna arborea* (Forster filius) Farwell (Fam. *Verbenaceæ*) and of the root of *Epipremnum pinnatum* (Linné) Engler (Fam. *Araceæ*). Tonga contains not more than 5 per cent. of foreign organic matter." *N. F.*

The natives of the Fiji Islands have long employed a mixture of two barks as a medicine.

Epipremnum pinnatum (L.) Engler (*Rhaphidophora Vitiensis* Schott.) (Fam. *Araceæ*) is a climbing shrub which grows in various islands of the Malaysian region.

Premna Taitensis Schauer (*Scrophulariodes arborea* Forst. f., *P. arborea* (Forst. f.) Farwell, n. comb.), is a verbenaceous tree with opposite leaves, cymose flowers and drupaceous fruits, indigenous to the Fiji, Tonga and other islands of the Pacific. The natives of these islands call it "*Yoro*" and "*Awalho.*"

Description and Physical Properties.—"*Unground Tonga.*—In small chips or quills up to about 11 cm. in length, 2 cm. in width and 3 mm. in thickness, outer surface of chips brownish with numerous prominent, irregular longitudinal ridges some of which are of a pale yellow color giving the surface a striated appearance; fracture hard and short. Root: in cylindrical pieces up to about 6 cm. in length and about 3 cm. in diameter; outer surface light yellowish brown to dark brown with the light yellowish cork partially exfoliated; numerous root-scars or root remains along one surface; internally very fibrous and tough. Taste slight; odor slight.

"*Powdered Tonga.*—Dark brown; spiral or scalariform tracheæ with lignified walls, the spiral tracheæ from 0.020 to 0.080 mm. in diameter, the scalariform tracheæ from 0.150 to 0.250 mm. in diameter; numerous simple to many-compound starch grains, the simple grains spheroidal or ellipsoidal up to about 0.020 mm. in diameter; numerous fragments composed of long lignified fibers with thick porous walls associated with rectangular medullary ray cells with lignified walls and large simple pores; fragments composed of starch bearing parenchyma associated with thick-walled stone-cells with simple or branching pores or non-lignified fibers the latter frequently branched and resembling two parallel fibers, one longer than the other, united near the middle by a short connecting portion, the whole structure with a continuous lumen; numerous fragments of cork tissue some of which are composed of cells with lignified walls; calcium oxalate in crystal fibers or in rosettes, the latter up to 0.095 mm. in diameter." *N. F.*

The presence of a liquid alkaloid, tongine, has been reported but there is no definite information concerning it.

Uses.—This drug was introduced to the medical profession by Ringer and Murrell (*L. L.*, 1880, ii) as a remedy for *neuralgia.* A few authors reported favorably on its effect but it has not achieved the confidence of the medical profession. A proprietary preparation asserted to contain tonga has been used for rheumatism. What claim the drug has to official recognition is a mystery.

Dose, given by the N. F., thirty grains (2 Gm.).

Off. Prep.—Fluidextractum Tongæ, *N. F.;* Elixir Tongæ et Salicylatum, *N. F.*

TOXITABELLÆ HYDRARGYRI CHLORIDI CORROSIVI. U. S.

POISON TABLETS OF CORROSIVE MERCURIC CHLORIDE Toxitabel. Hydrarg. Chlor. Corr. [Corrosive Sublimate Tablets, Bichloride Tablets]

"Tablets of an angular shape, not discoid, each having the word *'Poison'* and the skull and cross bones design distinctly stamped upon it. Each tablet weighs about 1 Gm. and contains not less than 0.45 Gm. and not more than 0.55 Gm. of corrosive mercuric chloride ($HgCl_2$), the remainder consisting chiefly of either sodium chloride [NaCl] or ammonium chloride [NH_4Cl]. The tablets are to be colored blue, preferably with sodium indigotindisulphonate. Poison Tablets of Corrosive Mercuric Chloride are to be dispensed in securely stoppered glass containers on the exterior of which is placed a red label bearing the word *'Poison'* and a statement indicating that the Tablets contain the required amount of corrosive mercuric chloride." *U. S.*

Hydrargyrum Bichloratum Compressum; Pastilli Sublimati.

Assay.—"Proceed as directed under *Hydrargyri Chloridum Corrosivum,* using one tablet and washing the sulphide with distilled water until the filtrate is colorless and until a 5 cc. portion of the washings, acidulated with nitric acid, yields no turbidity on the addition of a few drops of silver nitrate T.S. The weight of the mercuric sulphide obtained, multiplied by 1.167, indicates its equivalent in corrosive mercuric chloride. Tablets of Corrosive Mercuric Chloride may also be assayed as directed under the electrolytic method." *U. S.*

Uses.—The convenience of tablets of corrosive sublimate for the preparation of antiseptic solutions, and their wide use, has led to the introduction of such a tablet into the Pharmacopœia. Because of the large number of cases of poisoning through the inadvertent swallowing of these tablets, in the place of compressed tablets of certain drugs which may have a somewhat similar appearance, it has become highly desirable that these tablets be made in such a form as to render such a mistake less liable. A variety of suggestions for this purpose have been made; among the most popular shapes are the oblong or coffin-shaped, and the triangular tablets. As the solution formed by these tablets is colorless, in order that the solution shall not be confounded with harmless drugs, the tablets are directed to be colored blue by the addition of sodium indigotindisulphonate, or other dye.

A bluish color is greatly preferable to a pink dye, which is sometimes used, not only because it is less liable to be confused with reddish colored drugs but because various confections are often colored red. Despite these precautions, however, it is probable that cases of poisoning by mercuric chloride, either accidental or intentional, will continue to occur from time to time. The physician, therefore, should exercise the greatest reserve in allowing tablets of corrosive sublimate to get into the hands of his patients and the pharmacist should be exceedingly careful in selling and dispensing them. The official tablet contains 0.5 Gm. (8.0 grains) of corrosive sublimate; one of them dissolved in one pint of water (500 cc.) makes a solution of 1 to 1000. The addition of sodium chloride in these tablets aids in the solution of the mercuric chloride.

TRAGACANTHA. U. S., Br.

TRAGACANTH Trag. [Gum Tragacanth]

"Tragacanth is the dried gummy exudation from *Astragalus gummifer* Labillardière, or other Asiatic species of *Astragalus* (Fam. *Leguminosæ*)." *U. S.* "Tragacanth is a gummy exudation obtained by incision from Astragalus gummifer, *Labill.*, and some other species of Astragalus. Known in commerce as Syrian tragacanth." *Br.*

Gummi Tragacanthæ vel Astragalorum; Gomme Adragante, *Fr. Cod.;* Tragacantha, *P. G.;* Tragant, Traganth, *G.;* Gomma adragante, Dragante, *It.;* Gomo tragacanto, *Sp.*

Tragacanth is one of the oldest drugs in the Materia Medica. It was known in the days of Theophrastus, who described it three centuries before the Christian Era. It has been official in every edition of the U. S. P. since 1820.

The Astragalus plants are herbs or low shrubs with odd-pinnate, rarely simple leaves, white, yellow or purple flowers, arranged in racemes or spikes and membranous, or fleshy fruits.

Numerous species belonging to the genus *Astragalus* yield a gummy matter having the properties of *tragacanth.* The drug known in commerce by that name was at first erroneously supposed to be obtained from *A. Tragacantha* L. (*A. massiliensis* Lam.), which grows in southern Europe and northern Africa and is now said to yield no gum. It was afterwards ascribed, on the authority of Tournefort, to a species (*A. creticus* Lam.) which grows in Crete and Ionia, and on that of Olivier, to *A. verus,* which inhabits Asia Minor, Armenia, and Northern Persia. Labillardière described a species by the name of *A. gummifer* which he found growing on Mount Libanus in Syria, and from which tragacanth exudes. Lindley received two specimens of plants, said to be those which furnish tragacanth in Turkestan, one of which proved to be *A. gummifer* of Labillardière which was said to yield a white variety, and the other a new species, which he called *A. strobiliferus,* and which was said to yield a red and inferior product. The fact seems to be that the commercial drug is collected from various sources; and it is affirmed that all the species of Astragalus with thorny petioles are capable of producing it. These form a natural group, and so closely resemble one another that botanists have found some difficulty in distinguishing them. They are very abundant on the mountains of Asia Minor, and, according to information received by M. J. Léon Soubeiran from Balansa, a scientific traveller who derived his knowledge from personal observation, the gum-producing species are closely analogous to the *A. creticus* of Lamarck. It is in the Anti-Taurus range that the gum is chiefly collected. Transverse incisions are made, near the base of the stem, into the medullary tissues, which alone yield the gum. This exudes very slowly, flowing at night, and ceasing during the day; two weeks usually elapse before the pieces are large enough for collection. The shape of the pieces is influenced by the rapidity of the exudation, and the lines on their surface indicate the daily concretion.

According to a recent report from the Revenue Commissioner of Mesopotamia, Tragacanth is collected by tapping the small Astragalus shrubs which grow in the mountainous regions of southern Persia and from thence through the entire mountainous region which runs northwest along the frontiers of Mesopotamia, including northern Arabistan, the Luristan–Pust-i-Kut country and Kurdistan. In collecting the gum, the Kurds are said to first burn all the leaves off the shrubs, then expose the roots, cut incisions in the roots and leave for a week or more; they then return and collect the gum which exudes from the roots, the gum obtained from the first tapping is of superior quality, that from subsequent tappings being inferior and of yellow colors. The Kurds bring the gum to Suleimanaya, an important collecting center in Kurdistan. Here it is bought by local merchants who export it to Bagdad, from whence it is exported to Europe and America. (*A. J. P.,* 1920, 38.) The section *Tragacantha* of the genus *Astragalus* includes the principal species which yield gum tragacanth.

According to Haussknecht, tragacanth is yielded by the following species of Astragalus: *A. adscendens* Boiss. et Hausskn. (southern Persia); *A. leioclados* Boiss. (in middle and western Persia, by Ispahan and Hamadan); *A. brachycalyx* Fisch. (Kurdistan and Luristan); *A. gummifer* Labill. (widely distributed from Lebanon to Armenia and in the northern regions of the Euphrates and Tigris); *A. microcephalus* Willd. (the same as *A. gummifer* Labill., and also in Asia Minor); *A. pycnocladus* Boiss. et Hausskn. (particularly in western Persia); *A. stromatodes* Bge. (in Achyr Dagh, in Northern Syria); *A. kurdicus* Boiss. (Aintab). Other species that yield a tragacanth gum are *A. heratensis* Bge., of the Khorasan Mountains, which yields a gum known as "kutira," and *A. parnassi* Boiss. var. *cyllenea,* found on the mountains of Peloponnesus.

Harris states that the best Smyrna tragacanth is produced in Asia Minor. It is not, however, collected in the immediate vicinity of Smyrna, but comes from Karahissar, Jalowadsch, and even farther in the interior, where the plant grows wild. This kind of gum consists of white, yellow, and red, hardened pieces, which have become congealed after oozing out of the bush or tree in the hot sun of a Levantine summer. The gum is secured in a similar manner as opium by an incision in the branch. This is done in the spring and summer of each year, and the gum is usually scraped in September, when the first rains begin to fall.

The nature of the incision influences the shape of the pieces of tragacanth. The color is influenced both by the length of time consumed in drying on the bark and by the sequence of the tapping. The first tapped gum is always lighter than that of subsequent tappings. The commercial supplies of tragacanth used in this country are imported chiefly from London. Small quantities come direct from Shiraz, Persia and Bombay, India. During the last twenty years the gum tragacanth trade of Smyrna has decreased.

Tragacanth occurs either in flaky, leaf-like pieces, irregularly oblong or roundish, or in tortuous vermicular filaments, rounded or flattened, rolled up or extended. In commerce certain varieties of tragacanth are recognized and usually known by the name of the locality from which they have been produced or through which they have entered commerce. The ordinary tragacanth, tragacanth in sorts, sometimes known as *traganton* or *common tragacanth,* occurs in irregular pieces; Smyrna tragacanth appears usually in broad, thick flakes, yellowish or brownish; Syrian tragacanth, also called Leaf Gum, in thin, ribbon-like, white flakes, is obtained in Kurdistan and Persia. This is the best grade on the market.

Vermiform tragacanth occurs in thin, narrow, vermiform bands which are usually twisted or coiled. It is obtained largely in north Morea from *Astragalus cylleneus* Boiss. et Heldr. From the researches of Hugo von Mohl, which have been confirmed by Wigand (*A. J. P.,* xxxi, 243) it would seem that tragacanth is not a secretion of the plant, but the result of the transformation of the cells of the pith and those of the medullary rays which traverse the ligneous part of the stem and older branches. (*A. J. P.,* xxxi, 243.)

Description and Physical Properties.—"*Unground Tragacanth*—In flattened, lamellated, frequently curved fragments or in straight or spirally twisted linear pieces from 0.5 to 2.5 mm. in thickness; whitish to light brown, translucent and horny; fracture short; rendered more easily pulverizable by heating to 50° C.; inodorous; taste insipid, mucilaginous.

"*Structure*—A mass showing the distorted and swollen lamellæ of mucilaginous walls and a few starch grains.

"*Powdered Tragacanth*—White; angular fragments of mucilage with circular or irregular lamellæ; starch grains from 0.003 to 0.025 mm. in diameter, spherical to elliptical, with occasional 2- to 4-compound grains, many of the grains being swollen and more or less altered. The powder shows few or no fragments of lignified vegetable tissue (*Indian gum*).

"Add 1 Gm. of Tragacanth to 50 cc. of distilled water: it swells and forms a smooth, nearly uniform, stiff, opalescent mucilage free from cellular fragments. Shake 2 Gm. of Tragacanth with 100 cc. of water until fully swollen and free from lumps, then add 2 Gm. of powdered sodium borate, and shake the mixture thoroughly until the salt is dissolved: the mucilage does not lose its transparency, nor exhibit any change in consistence, and on pouring is not slimy or stringy even after standing twenty-four hours (*foreign gums*). Boil 1 Gm. of Tragacanth with 20 cc. of water until a mucilage is formed, then add 5 cc. of hydrochloric acid, and again boil the mixture for five minutes: it develops no pink or red color (*Indian gum*)." *U. S.*

"Thin flattened flakes, irregularly oblong, or more or less curved, marked on the surface by concentric ridges. Frequently two and a half centimetres long, and twelve millimetres wide. White or pale yellowish-white, somewhat translucent. Horny, fracture short. Inodorous; almost tasteless. Sparingly soluble in *water,* but swelling into a gelatinous mass, which may be tinged violet or blue by *N/10 solution of iodine.* Ash not more than 4 per cent." *Br.*

It is hard and more or less fragile, but difficult of pulverization, unless exposed to a freezing temperature, or thoroughly dried, and powdered in a heated mortar at the temperature of 50° C. Its sp. gr. is 1.384. Introduced into water, it absorbs a certain proportion of that liquid, swells very much, and forms a soft adhesive paste, but does not dissolve. If agitated with an additional quantity of water, this paste forms a uniform mixture; but in the course of one or two days the greater part separates, and is deposited, leaving a portion dissolved in the supernatant fluid. Tragacanth is wholly insoluble in alcohol. It appears to be composed of two different constituents, one soluble in water and resembling gum arabic, the other swelling in water, but not dissolving. To separate the soluble from the insoluble part requires agitation with separate portions of water; the solutions are to be decanted and filtered, and the process is to be continued until water ceases to dissolve anything.

Constituents.—The chemistry of tragacanth needs further study. According to O'Sullivan (*Proc. Chem. Soc.,* 1901) the soluble part—which is the greater portion—is made up chiefly of polyarabinan-trigalactan-geddic acid; this yields on hydrolysis, arabinose, galactose and *geddic acid.* The insoluble part is mostly *bassorin,* $(C_{11}H_{20}O_{10})_n$; bassorin acted on by baryta water forms two isomers, alpha- and beta-tragacanthan-xylan-bassoric acid which on hydrolysis yield *tragacanthose,* xylose and *bassoric acid.*

There is present also small amounts of cellulose, starch and protein substances.

It is stated by S. H. Maltass that tragacanth is adulterated, in the Levant, with worthless gums brought from Armenia and Caramania, which, as they are originally of a dark color and destitute of the flaky form of the genuine gum, are broken into small fragments and whitened by means of lead carbonate before being mixed with the tragacanth. Hanbury states, in confirmation of this, that he has detected lead in the *small tragacanth* imported into London. (*P. J.,* xv, 20.) Gum tragacanth has been recently admixed with and substituted by inferior gums from India and Persia, obtained from *Cochlospermum* and *Sterculia* species which have been imported under the names of Indian-, Karaya-, Kuteera-, Kadaya-, and Maura gum. Among these have been the gums of *Cochlospermum gossypium* DC. (Fam. *Bixaceæ*) and *Sterculia urens* (Fam. *Sterculiaceæ*). These occur in irregular vermiform or rounded tears having a dull, rough surface and pale brownish or pinkish-brown pieces, some of which have adherent bark. C. O. Ewing in *J. A. Ph. A.,* 1918, 789 states that karaya gum absorbs large quantities of water, swelling considerably and forming a tasteless, nearly colorless mucilage. A 1 per cent. mucilage of karaya had a viscosity about like a 3/4 per cent. mucilage of tragacanth. The adhesiveness of a 1 per cent. tragacanth mucilage is superior to that of a 1 per cent. karaya mucilage. As an emulsifying agent, karaya appears good though from one-third to one-half more should be used and it may be objectionable sometimes because of its acidity. It is detected by the official tests. The powdered drug is not only adulterated with the Indian gum, but with powdered acacia, dextrin, wheat and corn-starch. Payet gives a test for the detection of acacia in powdered tragacanth which depends on the brown color produced by the oxidase of the former when brought in contact with an aqueous solution of guaiacol in the presence of hydrogen dioxide. (*Ann. de Chim. Analyt.,* x, p. 63.)

Uses.—Tragacanth is demulcent, but, on account of its difficult solubility, is not often given internally. The great viscidity which it imparts to water renders it useful for the suspension of heavy insoluble powders, and it is also employed in pharmacy to impart consistence to troches, for which it answers better than does gum arabic, and in making emulsions, although for these purposes it is inferior to acacia. It is also used for its demulcent action in *pharyngitis* by allowing a piece of the gum to dissolve slowly in the mouth. It is officially employed as the basis of many of the troches.

Off. Prep.—Glycerinum Tragacanthæ, *Br.;* Mucilago Tragacanthæ, *U. S., Br.;* Pulvis Tragacanthæ Compositus, *Br.;* Glyceritum Tragacanthæ, *N. F.*

TRIFOLIUM. N. F.

TRIFOLIUM Trifol. [Red Clover Blossoms]

"Trifolium is the dried inflorescence of *Trifolium pratense* Linné (Fam. *Leguminosæ*). Trifolium contains not more than 2 per cent. of foreign organic matter." *N. F.*

Red Clover, Clover, Trefoil; Trèfle Rouge, *Fr.;* Klee, Rothklee, *G.;* Trifoglio, *It.*

The clovers are so well known as not to require any extended description. The official species, which is a native of Europe but widely cultivated in the U. S., is characterized by its sessile papilionaceous flowers in dense heads, sweet-scented, and with a purplish corolla which withers after flowering; the stems are ascending and somewhat hairy. The three ovate leaflets are notched at the end and marked on the upper side with a pale spot.

The drug comes chiefly from the southern Appalachian district and from Germany.

Description and Physical Properties.—"*Unground Trifolium.*—Heads ovoid with rounded summit, mostly from 12 to 25 mm. in length and width, shriveled, purplish and more or less brown from drying, consisting of many small papilionaceous flowers, crowded together and clothed at the base with broad, pointed ciliate stipules of a pale green color with darker veins, and which may or may not be accompanied by diminutive trifoliate leaves. Flowers from 12 to 15 mm. in length, longer than the four, nearly equal calyx teeth and shorter than the narrower fifth calyx tooth; calyx-teeth subulate, tapering; petals united into a tube below, the standard longer than the wings but when recurved appearing shorter; stamens diadelphous (nine and one); style slender. Odor faintly aromatic and somewhat tea-like; taste sweetish, then slightly bitter.

"*Powdered Trifolium.*—Brownish red to greenish red; numerous long, sharp-pointed unicellular non-glandular hairs with thick, non-lignified walls, the latter somewhat roughened by slight centrifugal projections; smooth, nearly spheroidal pollen grains from 0.020 to 0.048 mm. in diameter; fragments of epidermis with stomata the latter from 0.013 to 0.023 mm. in length; fragments of corolla tissue composed of closely packed polygonal cells, each cell filled with a rhombohedron of calcium oxalate, the latter up to 0.017 mm. in length." *N. F.*

The clover blossoms have been subjected to an elaborate analysis by Power and Salway (*Tr. Chem. Soc.,* 1910, xcvii, p. 231). They found a number of new phenolic substances including *pratol,* which is apparently an hydroxy-methoxy-flavone. It has a melting point of 253° C. *Pratensol* which is present in much smaller proportions has a melting point of 210° C. In addition they found three glucosides, *trifolin, isotrifolin* and one, unnamed, that yielded quercetin on hydrolysis.

Uses.—Clover was at one time attributed with alterative and anti-spasmodic properties and used in *whooping-cough* and *scrofula.* It has also been used in the form of ointments and local application to *ulcers.* It also enters into the composition of some anti-asthmatic cigarettes. There is, however, no sufficient reason to suspect it of any medicinal virtue.

TRILLIUM. N. F.

TRILLIUM Trill. [Beth Root]

"Trillium consists of the dried rhizome and root of *Trillium erectum* Linné and other species of *Trillium* (Fam. *Lilaceæ*). Trillium contains not more than 2 per cent. of foreign organic matter." *N. F.*

Beth Root; Birth Root; Wake Robin.

The trilliums are attractive native lilies easily recognized by their stout simple stem which bears at the summit a whorl of three broadly ovate leaves and a large terminal flower. The flower which appears in late spring, in the official species, is composed of three herbaceous sepals and three larger ovate petals usually of a brownish purple color. The fruit is a three-celled, six-angled red berry.

The commercial supplies of this drug are obtained chiefly from North Carolina, Virginia, Indiana and Missouri.

Description and Physical Properties.—"*Unground Trillium.*—Rhizome oblique, globular, oblong or obconical, truncate below, terminated at the top by a small bud surrounded by a sheath of scarious leaf bases, annulated by leaf scars and fissured by stem scars; from 0.6 to 5 cm. in length and from 1 to 3 cm. in width, more or less compressed laterally; rootlet scars in several concentric rows on the under side in the upper portions; externally yellowish to reddish brown; internally of a pale yellow; fracture somewhat uneven with a hard and close texture or a more or less spongy appearance. Odor distinct; taste bitter and acrid with a sensation of warmth in the throat, and when chewed causing an increased flow of saliva.

"*Powdered Trillium.*—Pale yellowish white; consisting chiefly of fragments composed of parenchyma some of which are elongated and contain raphides of calcium oxalate up to 0.225 mm. in length, others being nearly isodiametric, more or less thin-walled and containing mostly simple, nearly spheroidal altered or unaltered starch grains, the latter up to 0.020 mm. in diameter; fragments of epidermal tissue composed of cells with reddish brown porous walls; tracheæ with spiral or reticulate markings." *N.F.*

Reid (*A. J. P.,* 1892, p. 67) found in trillium 4.86 per cent. of a saponin, also an acid crystalline principle which gave a purplish brown reaction with sulphuric acid and a light green with sulphuric acid and potassium dichromate. Prendergast (*Am. Drug.*, Nov., 1886) believes that there is present a glucoside similar to convallamarin. The drug also contains volatile oil and an astringent principle, probably a tannin.

Uses.—The term birthroot appears to have been applied to this substance by the early settlers because of the fact that the American Indians used it as an aid to parturition. From this aboriginal use the early settlers came to employ the drug in the treatment of various uterine disorders, as *metrorrhagia* and *menorrhagia*. It is also employed in the treatment of various *hemorrhages* both locally and internally, and as an astringent in *diarrhea*. It is today, however, almost never employed except as an ingredient of the compound elixir of viburnum.

Dose, one-half to one drachm (2–4 Gm.).

Off. Prep.—Elixir Viburni Opuli Compositum, *N. F.;* Fluidextractum Trillii, *N. F.*

TRINITROPHENOL. U. S. (Br.)

TRINITROPHENOL Trinitrophen. [Picric Acid]

"$C_6H_2(OH)(NO_2)_3$ 1:2:4:6." *U. S.* "Picric Acid may be obtained by the action of nitric acid and sulphuric acid on phenol, and contains not less than 99 per cent. of tri-nitrophenol, $C_6H_2(NO_2)_3OH$." *Br.*

Acidum Picricum, *Br.;* Carbazotic Acid; Nitrophenic Acid, Acide Picrique, *Fr. Cod.;* Acide Carbazotique, *Fr.;* Pikrinsaüre, Bittersaüre, *G.*

Trinitrophenol is obtained by the action of nitric acid on indigo, silk, leather, wool, aloes, benzoin, Australian gum, and other substances, or, as the name indicates, from phenol (carbolic acid). It may be cheaply prepared by adding crude carbolic acid, impure phenol gradually to strong nitric acid and heating, when, on standing, the picric acid will crystallize out; but in practice it is now almost always made by dissolving crystallized phenol in strong sulphuric acid, and adding either nitric acid or sodium nitrate to the resultant phenolsulphonic acid. The reaction is as follows:

$$C_6H_5OH + H_2SO_4 = C_6H_4OH.HSO_3 + H_2O$$

$$C_6H_4OH.HSO_3 + 3HNO_3 = C_6H_2OH(NO_2)_3 + H_2SO_4 + 2H_2O$$

Its salts crystallize readily, and explode when heated. The potassium salt is so sparingly soluble that an alcoholic solution of the acid has been used as a test for this alkali. It is largely used in dyeing, producing magnificent yellow colors, and, in connection with indigo or Prussian blue, different shades of green. The salts which picric acid forms with potassium and sodium are yellow and bitter, and are much used in the arts. They are, however, violent explosives, and as such have produced very serious consequences. Picric acid itself is also a powerful explosive which is used in modern warfare, not as a propellant, but as the exploding charge in shells, a detonator being necessary to explode it. It was first used extensively during the Boer War under the name of *Lyddite.* A saturated aqueous solution of picric acid is a very delicate test for albumin. (See *Esbach's Reagent,* Part III.) *Ammonium picrate* is universally preferred for internal use. It crystallizes in rhombic scales, which are somewhat more soluble than the corresponding potassium salt.

Description and Physical Properties.—" Pale yellow, rhombic prisms or scales. It is odorless and has an intensely bitter taste. *Caution—Trinitrophenol explodes when heated rapidly or when subjected to percussion.* For safety in transportation Trinitrophenol is usually mixed with from 10 to 20 per cent. of water. Before applying the tests described below, dry the Trinitrophenol to constant weight over sulphuric acid. One Gm. of Trinitrophenol is soluble in 78 cc. of water, 12 cc. of alcohol, 35 cc. of chloroform, 65 cc. of ether, and in 10 cc. of benzene, at 25° C. One Gm. is soluble in 15 cc. of boiling water.

" Trinitrophenol melts between 121° and 123° C. An aqueous solution of Trinitrophenol is acid to litmus paper. An aqueous solution of Trinitrophenol (1 in 100) has a yellow color, which becomes more intense on the addition of alkalies, and red on the addition of ammonium sulphide T.S. or a solution of an alkaline cyanide. An aqueous solution of Trinitrophenol is precipitated by solutions of most alkaline salts.

" Add 5 drops of barium chloride T.S. to 10 cc. of an aqueous solution of Trinitrophenol (1 in 100): the liquid does not at once become opalescent (*sulphate*). Dissolve 2 Gm. of Trinitrophenol in 50 cc. of benzene, collect the insoluble residue, if any, on a small counterpoised filter, or in a Gooch crucible with an asbestos layer, which has been dried at 100° C. and weighed, and wash the residue and filter with benzene until the washings are colorless: the residue, dried at 100° C., does not exceed 0.2 per cent.

" Preserve in well-stoppered bottles, in a cool place, remote from fire." *U. S.*

" Bright yellow crystalline powder. Inodorous; taste very bitter. Soluble in 90 parts of *water,* and in 10 parts of *alcohol* (90 per cent.), forming intensely yellow solutions which stain the skin yellow. Melting point 122° C. 2 grammes dissolved in hot *water* require for neutralisation 17.3 millilitres of *N/2 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator." *Br.*

Uses.—Trinitrophenol is germicidal, astringent, and apparently stimulates epithelial growth. According to Ehrenfried (*J. A. M. A.*, 1911, lvi, 412), a saturated aqueous solution (1.2 per cent.) destroys the *Bacillus pyocyaneus* in less than one minute and the *Staphylococcus pyogenes aureus* in two minutes. In the experiments of Schamberg and Kolmer (*L. L.*, 1911, ii, p. 1397) it showed itself four times as active as phenol while Tidy (*L. L.*, 1915, clxxxix, 604) gives its phenol coefficient as 6.

Internally trinitrophenol is comparatively feeble in its effects upon the system. It is absorbed probably as a sodium salt and eliminated chiefly through the urine to which it imparts an intense yellow color. After large doses the skin and mucous membranes are also stained yellow. In toxic quantities it causes in the lower animals destruction of the red blood corpuscles, but this effect has not been reported in man. The symptoms of poisoning as observed in human beings have been vomiting, diarrhea (the matters ejected being stained yellow), strangury and often anuria; in severe cases stupor with convulsions followed by collapse have also been noted. A very common symptom, even after not extremely large doses, is itching of the skin frequently associated with an eczematous eruption. Ehrenfried states that 15 to 30 grains are sufficient to cause toxic symptoms. It should be remembered that the drug may be absorbed after its local application in sufficient quantities to produce constitutional effects.

Internally picric acid has been used in the treatment of *trichinosis* and *malaria,* but is probably without any value. It is capable of destroying intestinal parasites, either *tapeworm* or *roundworm,* but has no advantage over other vermifuges. The practical value of trinitrophenol in medicine is as a local agent. It is strongly recommended for the sterilization of the skin preceding operations (see Farr, *Annals of Surg.,* 1921, lxxiii, p. 13). While by some used as an antiseptic dressing for superficial *wounds,* it is especially prized in *burns* of the first and second degree and is also useful for its astringent and antiseptic action in *ulcers* with free discharge. Wilcox (*Archives of Pediatrics,* 1913, xxx) recommends it very highly in the treatment of various skin diseases, especially acute *eczema, intertrigo,* and *herpes labialis.* In local *hyperidrosis,* especially of the feet, it has long been recognized as a standard remedy. Picric acid is also highly recommended by a number of ophthalmologists in the treatment of *injuries of the cornea,* due to caustic agents, such as quick-lime and the mineral acids. It has also been employed in simple *conjunctivitis* and in *trachoma.* For the latter purpose Ohlemann (*Wochens. f. Ther. u. Hyg. d. Auges,* 1910, p. 103) recommends a 2 per cent. ointment which is applied directly to the lid, after previous cocainization if necessary.

For surgical purposes from one-half to one per cent. is generally used. In skin diseases the aqueous solution may be either painted over the lesion or sometimes gauze moistened with the solution applied. In sweating feet a dusting powder containing 2 per cent. of picric acid with talc is sometimes used. The great drawback of the remedy is its powerful staining properties.

In skin diseases when the epiderm is unbroken it may be desirable to use stronger solutions in which case a hydro-alcoholic menstruum is employed.

Picric acid poisoning is quite common among workers engaged in the manufacturing of high explosives (see Hamilton, *J. A. M. A.,* 1917, lxviii, 1447). In some cases this is manifested by dermatitis, often quite severe and resistant to treatment. The inflammation of the skin in these cases bears a strong resemblance to that seen in ivy poisoning and at times is accompanied with marked constitutional disturbances, such as headache, loss of appetite, nose bleed, and fever. There is in many of these cases more or less leukocytosis. In other patients the symptoms are chiefly gastro-intestinal; abdominal cramps, diarrhea, vomiting and headache being the most common manifestations. The inhalation of the dust by these workers produces a bronchitis accompanied with a dry hacking cough, often with expectoration of blood, and signs of irritation of the throat.

Dose, one-half to one grain (0.032–0.065 Gm.).

TRITICUM. N. F. (Br.)

TRITICUM Tritic. [Couch Grass, Dog Grass]

"Triticum consists of the dried rhizome and roots of *Agropyron repens* (Linné) Beauvois (Fam. *Gramineæ*). Triticum contains not more than 2 per cent. of foreign organic matter and yields not more than 3 per cent. of acid-insoluble ash." *N. F.*

"Couch Grass is the dried rhizome of Agropyron repens, *Beauv.,* freed from remains of leaves and rootlets." *Br.*

Agropyrum, *Br.;* Rhizoma Graminis; Radix Graminis; Dog Grass, Quick-grass, Quitch, Twitch-grass, Witch-grass, Quickens; Chiendent Officinal, Petit chiendent, *Fr. Cod.;* Queckenwurzel, Grasswurzel, *G.;* Grama (Rizoma de), *Sp.*

This grass, originally a native of Europe, now abounds in meadows and cultivated grounds in the northern United States, where it is often very troublesome as a weed. It is specifically characterized by its creeping rootstock, the leaves being flat, thin and finely veined, and the flowering glumes being glabrous or scabrous. It is probable that the rhizomes of a number of other grasses share the medicinal properties of *Agropyron repens.* Of these the Scotch or Bermuda grass, *Capriola Dactylon* (L.) Kuntze, is probably as effective as the official species.

Much spurious triticum has appeared upon the market recently. Most of it can be readily distinguished from the official drug by the presence of abundant starch in the spurious article.

The commercial supplies of triticum come largely from England and Germany.

Description and Physical Properties.—"*Unground Triticum.*—Rhizome; usually in pieces from 4 to 12 mm. in length and from 1 to 2.5 mm. in diameter; externally light yellow or yellowish brown, longitudinally furrowed, smooth, lustrous, nodes with circular leaf-scars, a few root-scars and occasional slender roots; fracture tough, fibrous; internally lemon-yellow and with a large, hollow pith. Roots filiform, irregularly branching, attaining a length of about 5 cm. and not more than 0.5 mm. in thickness, light brown or yellowish brown, frequently covered with long root hairs. Odor slight, aromatic; taste sweetish.

"*Structure.*—A single layer of strongly lignified epidermal cells showing in surface view characteristic twin-cells having strongly silicified walls and giving a ball and socket appearance; a hypodermis of from 3 to 6 rows of cells with strongly lignified walls; a cortex of from 10 to 16 rows of thin-walled parenchyma cells, occasionally with nearly spherical starch grains up to 0.015 mm. in diameter, or with irregular masses of a more or less soluble carbohydrate; among the parenchyma cells and near the hypodermis occur small, widely separated fibro-vascular bundles, each with a closed sheath of fibers; an endodermis, the lateral and inner walls of the cells moderately thickened, strongly lignified and somewhat porous; several layers of fibers immediately inside the endodermal ring, in which are imbedded an interrupted circle of about 10 to 12 collateral fibro-vascular bundles having large tracheæ; adjoining these are usually 8 to 10 rows of parenchyma cells with a few fibrovascular bundles and a pith in which the parenchyma cells are more or less broken or absent.

"*Powdered Triticum.*—Light yellowish; consisting of irregular, lignified fragments; numerous fragments showing tracheæ with annular or spiral thickenings or marked with simple pores and associated with long, narrow, rather thin-walled, strongly lignified sclerenchymatous fibers; fragments of epidermis made up of cells rectangular in outline, the longer walls considerably thickened, strongly lignified and marked with numerous transverse pores; ends of epidermal cells usually separated from each other by a very narrow cell with thin walls and few pores, numerous fragments of parenchyma rectangular in outline and with thin, porous walls." *N. F.*

"Rhizome pale yellow, rigid, from two to two and a half millimetres in diameter, usually in pieces from three to six millimetres long. Strongly furrowed longitudinally, hollow except at the nodes. Contains no starch. No odor; taste slightly sweet." *Br.*

The morphology of triticum has been described by Holm (*M. R.*, xix, p. 65). The chief adulterant for Triticum is the rhizomes and roots of *Cynodon Dactylon* L. (*Capriola Dactylon* (L.) Kze.), commonly known as *Bermuda-*, or *Bahama-Grass*, a native of Europe but naturalized in America. For a detailed distinction between this article and triticum, see Zufall, *J. A. Ph. A.*, 1919, p. 472. Small (*A. J. P.*, 1919, xci, 685) asserts that there is practically no true triticum on the market; the commercial article being sold for it is practically all Bermuda grass.

The Austrian Pharmacopœia has a requirement of not less than 30 per cent. of aqueous extractive for this drug.

Triticum contains dextrose and levulose to the extent of some 2 or 3 per cent., also a dextrorotatory sugar of undetermined identity, gum and inosite. According to Alsberg, Viehover and Yewey (*J. A. Ph. A.*, 1919, 469) triticum contains two glucosides, one of which yields vanillin on hydrolysis, also a carbohydrate resembling inulin which has been named *triticin.* The ash contains much silica.

Uses.—Triticum is never exhibited for the purpose of affecting the general system, but only for its influence upon the genito-urinary organs. It is much used by some surgeons in *irritable bladder,* and also in *cystitis.* It is one of the least stimulant of the remedies of its class, and may be employed very freely. In Europe its decoction is said to be used to a considerable extent as a diluent and slightly nutritious drink.

Dose, from two to four drachms (4–8 Gm.) or more.

Off. Prep.—Fluidextractum Tritici, *N. F.;* Decoctum Agropyri, *Br.;* Extractum Agropyri Liquidum, *Br.;* Elixir Sabal et Santali Compositum, *N. F.*

TRITURATIONES. U. S.

TRITURATIONS

"Unless otherwise directed, Triturations are to be prepared according to the following formula: The Substance, 10 Gm.; Lactose, in moderately fine powder, 90 Gm.; to make 100 Gm. Weigh the medicinal substance and the lactose separately; then place the substance, previously reduced, if necessary, to a moderately fine powder, in a mortar. Add about an equal measure of lactose, mix well by means of a spatula, and triturate the powders thoroughly together. Then add fresh portions of the lactose, from time to time, until the whole is added, and continue the trituration after each addition until the substance is intimately mixed with the lactose and reduced to a fine powder." *U. S.*

This general formula has been introduced into the Pharmacopœia in order that a definite and uniform method be authorized of making a class of powders which has come into use in various sections of our country. While the necessity of giving recognition to the class may be questioned by many, the importance of securing uniformity in composition is evident.

TROCHISCI.

TROCHES

Lozenges; Pastilli, Rotulae, *P. G.;* Pastillen, Plätzchen, *G.;* Pastiglie, *It.*

Troches or *lozenges* are small, dry, solid masses, usually of a flattened shape, consisting for the most part of powders incorporated with sugar and mucilage. They are designed to be held in the mouth and dissolved slowly in the saliva, and are, therefore, adapted for the administration of those medicines only which do not require to be given in large quantities and which are destitute of any very disagreeable flavor.

Lozenges were formerly much more used and more skilfully prepared in Europe than in this country, but at present those manufactured here are fully equal to the imported lozenges. Tragacanth, from the greater tenacity of its mucilage, is better suited for their formation than gum arabic. The following directions for preparing them are taken from the *Dictionnaire des Drogues*. A mucilage of tragacanth is first prepared with cold water and strained. With this the powders, including sugar, are thoroughly mixed by rubbing upon a marble slab, and are thus formed into a paste, which is spread out by means of a roller upon the surface of the marble, previously powdered over with a mixture of sugar and starch. The thickness of the mass is rendered uniform by a frame upon which the ends of the roller rest. The upper surface is now dusted with sugar and starch, and the mass is divided into small cakes by means of a punch. These cakes are placed upon paper, and, having been exposed to the air for twelve hours, are carried into a drying room moderately heated. When perfectly dry, they are thrown upon a sieve to separate the sugar and starch, and are then enclosed in boxes. Lozenges may be prepared from almost any medicine which it is advisable to administer in this form. The following typical formula may be found useful.

Take citric acid, in powder, a drachm; powdered sugar eight ounces; oil of lemon twelve minims; mucilage of tragacanth a sufficient quantity. Form them in the manner above directed into troches of twelve grains each. Lozenges are sometimes made by saturating blank lozenges with aromatic spirits. Black-currant paste has come into use largely as a basis for troches because of its official recognition in the British Pharmacopœia. For formulas for lozenges with current paste basis, see *U. S. D.*, 19th edition, page 1297.

Lozenges of a cylindrical shape are extensively used, having a basis of licorice, gum, and sugar, and the manufacture of these is now an important industry.

The Br. Pharmacopœia, 1914, adopted four bases for lozenges, as follows: fruit basis, rose basis, simple basis, and tolu basis. It will be noticed that in the British formulas the quantity of active ingredients for each lozenge is stated and the kind of basis indicated. This is done merely to avoid repetition.

PREPARATION WITH FRUIT BASIS.

"Take five hundred times the quantity of the drug ordered for one lozenge. Mix it with 6.5 grammes of Tragacanth and 26 grammes of Refined Sugar, both in fine powder. Add sufficient of the black-currant paste of commerce to produce 650 grammes, beat into a uniform mass, divide into 500 equal lozenges and dry in a hot-air chamber at a moderate temperature." *Br.*

PREPARATION WITH ROSE BASIS.

"Take five hundred times the quantity of the drug ordered for one lozenge. Treat it as described under 'Preparation with Simple Basis,' previously mixing with the Refined Sugar 0.025 millilitre of Oil of Rose." *Br.*

PREPARATION WITH SIMPLE BASIS.

"Take five hundred times the quantity of the drug ordered for one lozenge, mix it with 496 grammes of Refined Sugar and 19.5 grammes of Gum Acacia, both in fine powder. Make the mixture into a paste with 35 millilitres of Mucilage of Gum Acacia and a sufficient quantity of Distilled Water, divide into 500 equal lozenges and dry in a hot-air chamber at a moderate temperature." *Br.*

PREPARATION WITH TOLU BASIS.

"Take five hundred times the quantity of the drug ordered for one lozenge; dissolve such salts of alkaloids as may be ordered in 10 millilitres of Distilled Water; mix the solution with 482 grammes of Refined Sugar and 19.5 grammes of Gum Acacia, both in fine powder. Incorporate 10 millilitres of Tincture of Balsam of Tolu, and any other drugs ordered for the lozenges. Make into a paste with 35.5 millilitres of Mucilage of Gum Acacia and a sufficient quantity of Distilled Water; divide into 500 equal lozenges and dry in a hot-air chamber at a moderate temperature." *Br.*

TROCHISCUS ACIDI BENZOICI. Br.

BENZOIC ACID LOZENGE

Tablettes de l'Acide Benzoique, *Fr.;* Benzoesäurepastillen, *G.*

"Benzoic Acid, 0.03 *gramme.* Mix with the *Fruit Basis* to form a Lozenge." *Br.*

This is a stimulant and antiseptic lozenge useful in *chronic pharyngitis,* and other passive congestions of the buccal cavity.

TROCHISCUS ACIDI CARBOLICI. Br.

PHENOL LOZENGE

Tablettes de l'Acide Phénique, *Fr.;* Phenolpastillen, *G.*

"Phenol, in powder, 15 *grammes;* Refined Sugar, in powder, 500 *grammes;* Gum Acacia, in powder, 45 *grammes;* Tragacanth, in powder, 15 *grammes;* Lemon Juice, 45 *millilitres.* Mix. Divide into five hundred lozenges. Dry them in a hot-air chamber at a moderate temperature. Each lozenge contains 0.03 gramme of Phenol, or approximately one-half grain. It is of one-half the strength of the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

This lozenge affords an excellent means of obtaining the antiseptic and local anodyne effect of phenol in *acute pharyngitis, stomatitis,* and similar infections of the mouth and throat.

TROCHISCI ACIDI TANNICI. U. S. (Br.)

TROCHES OF TANNIC ACID Troch. Acid. Tann.

Trochiscus Acidi Tannici, *Br.;* Tannic Acid Lozenge; Tannin Lozenges; Tablettes de Tannin, *Fr.;* Tanninpastillen, *G.*

"Tannic Acid, 6 Gm.; Sucrose, in fine powder, 65 Gm.; Tragacanth, in very fine powder, 2 Gm.; Orange Flower Water, a sufficient quantity to make 100 troches. Triturate the powders until they are thoroughly mixed, form a mass with orange flower water, and divide it into 100 troches." *U. S.*

"Tannic Acid, 0.03 *gramme.* Mix with the *Tolu Basis* to form a Lozenge." *Br.* (See above.)

These are useful in *relaxation of the uvula,* and in *chronic angina,* being allowed slowly to dissolve in the mouth. Each U. S. troche contains about one grain (0.065 Gm.) of the acid; the Br. about half a grain (0.032 Gm.).

TROCHISCI AMMONII CHLORIDI. U. S.

TROCHES OF AMMONIUM CHLORIDE Troch. Ammon. Chlor.

Tablettes de Chlorhydrate d'Ammoniaque, *Fr.;* Chlorammoniumpastillen, *G.*

"Ammonium Chloride, in fine powder, 10 Gm.; Extract of Glycyrrhiza, in fine powder, 20 Gm.; Tragacanth, in very fine powder, 2 Gm.; Sucrose, in fine powder, 40 Gm.; Syrup of Tolu, a sufficient quantity to make 100 troches. Triturate the powders until they are thoroughly mixed; form a mass with syrup of tolu, and divide it into 100 troches." *U. S.*

Each troche contains about one and a half grains (0.096 Gm.) of ammonium chloride.

These troches are largely used in *congested conditions of the pharynx and larynx.*

TROCHISCUS BISMUTHI COMPOSITUS. Br.

COMPOUND BISMUTH LOZENGE

Troches of Bismuth; Tablettes de Sous-nitrate de Bismuth, *Fr. Cod.;* Bismuthpastillen, *G.*

"Bismuth Oxycarbonate, 0.15 *gramme;* Heavy Magnesium Carbonate, 0.15 *gramme;* Precipitated Calcium Carbonate, 0.30 *gramme.* Mix with the *Rose Basis* to form a Lozenge." *Br.*

These may be used to obtain the effects of bismuth subcarbonate on the stomach, as well as of the magnesium and calcium carbonates as an antacid, two or more being administered for a dose. They may also be found useful in *chronic inflammation of the throat and esophagus.*

TROCHISCUS CATECHU. Br.

CATECHU LOZENGE

"Catechu, 0.06 *gramme.* Mix with the *Fruit Basis* to form a Lozenge." *Br.*

This lozenge was introduced into the Br. Pharm., 1914. It is mildly astringent.

TROCHISCUS FERRI REDACTI. Br.

REDUCED IRON LOZENGE

Tablettes de Fer Réduit par l'Hydrogène, Tablettes de Fer, *Fr.;* Eisenpastillen, *G.*

"Reduced Iron, 0.06 *gramme.* Mix with the *Simple Basis* to form a Lozenge." *Br.*

From one to three of the lozenges may be taken for a dose.

TROCHISCUS GUAIACI RESINÆ. Br.

GUAIACUM RESIN LOZENGE

Tablettes de Résine de Gayac, *Fr.;* Guajakharzpastillen, *G.*

"Guaiacum Resin, 0.2 *gramme.* Mix with the *Fruit Basis* to form a Lozenge." *Br.*

TROCHISCUS IPECACUANHÆ. Br.

IPECACUANHA LOZENGE

Tablettes d'Ipécacuanha, *Fr. Cod.;* Brechwurzelpastillen, *G.;* Pastiglie d'ipecacuana, *It.*

"Ipecacuanha Root, in powder, 0.015 *gramme.* Mix with the *Simple Basis* to form a Lozenge." *Br.*

TROCHISCUS KINO EUCALYPTI. Br.

EUCALYPTUS KINO LOZENGE

Eucalyptus Gum Lozenge, Red Gum Lozenge; Tablettes de Kino d'Eucalypte, *Fr.;* Eucalyptuskinopastillen, *G.*

"Eucalyptus Kino, 0.06 *gramme.* Mix with the *Fruit Basis* to form a lozenge." *Br.*

A similar lozenge is recognized by the N. F. (See *Trochisci Eucalypti Gummi,* Part III.)

A popular astringent lozenge used in *sore throat* and relaxed conditions of the mouth.

TROCHISCUS KRAMERIÆ. Br.

KRAMERIA LOZENGE

Krameria Lozenge, Rhatany Lozenge; Tablettes de Ratanhia, *Fr.;* Ratanhiapastillen, *G.*

"Extract of Krameria, 0.06 *grdmme.* Mix with the *Fruit Basis* to form a Lozenge." *Br.*

TROCHISCUS KRAMERIÆ ET COCAINÆ. Br.

KRAMERIA AND COCAINE LOZENGE

Rhatany and Cocaine Lozenge; Tablettes de Ratanhia et de Cocaine, *Fr.;* Ratanhia- und Cocain-pastillen, *G.*

"Extract of Krameria, 0.060 *gramme;* Cocaine Hydrochloride, 0.003 *gramme.* Mix with the *Fruit Basis* to form a Lozenge. This Lozenge contains 0.003 gramme of Cocaine Hydrochloride, or approximately $^1/_{20}$ grain." *Br.*

TROCHISCUS MORPHINÆ. Br.

MORPHINE LOZENGE

Tablettes de Chlorhydrate de Morphine, Tablettes de Morphine, *Fr.;* Morphinpastillen, *G.*

"Morphine Hydrochloride, 0.002 *gramme.* Mix with the *Tolu Basis* to form a Lozenge. This Lozenge contains 0.002 gramme of Morphine Hydrochloride, or approximately $^1/_{32}$ grain." *Br.*

This is an undesirable preparation, as the local action of morphine is insignificant. Any sedative effect in *cough* will be due to the systemic absorption of the drug.

TROCHISCUS MORPHINÆ ET IPECACUANHÆ. Br.

MORPHINE AND IPECACUANHA LOZENGE

Tablettes de Morphine et d'Ipécacuanha, *Fr.;* Morphinpastillen mit Brechwurzel; Morphin und Brechwurzel-pastillen, *G.*

"Morphine Hydrochloride, 0.002 *gramme;* Ipecacuanha Root, in powder, 0.006 *gramme.* Mix with the *Tolu Basis* to form a Lozenge. This Lozenge contains 0.002 gramme of Morphine Hydrochloride, or approximately 1/32 grain." *Br.*

This tablet is used as an expectorant. Its effects are the same as would be those of its ingredients if administered in solution. Each lozenge contains one-thirtieth of a grain (0.002 Gm.) of morphine salt, and one-tenth of a grain (0.006 Gm.) of ipecacuanha.

TROCHISCUS POTASSII CHLORATIS. Br.

TROCHES OF POTASSIUM CHLORATE Troch. Pot. Chlorat.

Trochisci Potassii Chloratis, *U. S. IX;* Potassium Chlorate Lozenge, Chlorate of Potash Lozenges; Tablettes de Chlorate de Potasse, *Fr.;* Kaliumchloratpastillen, Pastillen von Chlorsaurem Kali, *G.;* Pastiglie di clorato di potassio, *It.;* Tabletas de clorato potasico, *Sp.*

These troches have been dropped at the last revision of the U. S. The formula of the U. S. IX was "Potassium Chlorate, in fine powder, *fifteen grammes;* Sugar, in fine powder, *sixty grammes;* Tragacanth, in fine powder, *three grammes;* Water, *a sufficient quantity,* to make *one hundred troches.* Mix the sugar with the tragacanth by trituration in a mortar; then transfer the mixture to a sheet of paper, and by means of a bone or wooden spatula mix it with the potassium chlorate, being careful to avoid unnecessary trituration or pressure, which might cause the mixture to ignite or explode. Lastly form a mass with water and divide it into *one hundred troches." U. S. IX.*

"Potassium Chlorate, 0.2 *gramme.* Mix with the *Rose Basis* to form a Lozenge." *Br.*

These lozenges are employed as mildly stimulant and astringent in cases of *sore throat,* although in commercial usage the official troches are almost entirely replaced by compressed tablets of potassium chlorate.

TROCHISCUS SANTONINI. Br.

SANTONIN LOZENGE

Trochisci Santonini, *U. S. VIII;* Troches of Santonin; Tablettes de Santonine, *Fr. Cod.;* Pastilli Santonini, *P. G.;* Santoninpastillen, *G.;* Pastiglie de santonina, *It.;* Tabletas de santonina, *Sp.*

"Santonin, 0.06 *gramme.* Mix with the *Simple Basis* to form a Lozenge." *Br.* (See p. 1168.)

Troches of santonin are also official in the N. F. V (see Part III).

The N. F. process is faulty in the direction that the santonin be in fine powder. The longer the absorption of santonin is delayed in the intestines the more prolonged and consequently the more effective is its vermicidal influence. As soon as it is absorbed it ceases to act upon the worm, and becomes a more or less deleterious substance in the system. A dose of santonin in crystals which is not poisonous may become somewhat toxic when given in fine powder. The proportion of crystals in the lozenge mass (2½ per cent.) is not sufficient to prevent the formation of a good lozenge from a pharmaceutical point of view. The National Formulary lozenge contains about half a grain (0.032 Gm.) of santonin. The Br. formula calls for about one grain (0.065 Gm.).

Dose, for an adult, of the Br. lozenge, from one to three lozenges.

TROCHISCUS SULPHURIS. Br.

SULPHUR LOZENGE

Tablettes de Soufre, *Fr. Cod.;* Schwefelpastillen, *G.*

"Precipitated Sulphur, 150 *grammes;* Acid Potassium Tartrate, in powder, 30 *grammes;* Refined Sugar, in powder, 275 *grammes;* Gum Acacia, in powder, 30 *grammes;* Tincture of Orange, 30 *millilitres;* Mucilage of Gum Acacia, 30 *millilitres.* Mix the Tincture of Orange with the powders; add the Mucilage of Gum Acacia to form a suitable mass. Divide into five hundred Lozenges. Dry them in a hot-air chamber at a moderate temperature. Each Lozenge contains 0.3 gramme of Precipitated Sulphur, or approximately 5 grains." *Br.*

Dose, from one to six lozenges. (See *Sulphur Sublimatum.*)

TURPETHUM. Br.

TURPETH

"Turpeth is the dried root and stem of Ipomœa Turpethum, *R.Br.*" *Br.*

Radix Turpethi; Turpeth Root; Indian Jalap; Trivrit; Nisoth, Turbith, *Fr.;* Turbit (Raiz de), *Sp.*

Ipomœa Turpethum (*Operculina Turpethum* (L.) Peter) (Fam. *Convolvulaceæ*) is a convolvulaceous plant which is found throughout India, the Malay Archipelago, China, Ceylon, Australia, and is occasionally cultivated in botanical gardens as an ornamental plant. There are two varieties, viz., *Sveta* or white turpeth, and *Kirshna* or black turpeth, the former being preferred as a mild cathartic. The black variety is said to be a powerful drastic.

According to Mérat and De Lens, the root itself formerly came into commerce, but at present turpeth consists of the root and stem of the plant cut into short lengths, usually from 1.5 to 5 cm. in diameter; the central woody portion is often removed by splitting the bark on one side. The pieces are cylindrical, somewhat twisted and externally of a dull gray color. A transverse section shows a porous central wood surrounded by a broad cortical portion, containing yellowish-brown resin cells, laticiferous vessels and crystals of calcium oxalate. The fracture is short in the cortex and fibrous in the central portion. The drug has a faint odor and a nauseous taste, which is perceptible only after it has been some time in the mouth.

"In cylindrical pieces of varying length, from one to five centimetres wide, often split on one side and deprived of the central portion; longitudinally furrowed; dull grey or brown. Fracture of the bark short, of the wood fibrous; internally usually pale grey. In transverse section, a porous wood surrounded by a thick bark in which abnormal wood-bundles are frequently present. Slight odor; taste nauseous, slowly developed." *Br.*

Turpeth contains a yellow coloring matter and a small amount of volatile oil but its important medicinal effect depends upon its resin of which it contains about 5 or 10 per cent. A part of this, which is soluble in ether, seems to be of complex nature; it has been called *turpethein* but is probably very similar to the resin known as convolvulin. The principal resin, however, is that known as *turpethin.* This does not dissolve in ether but does in alcohol, to which it imparts a brown color not removable by animal charcoal; it has been given the formula $C_{34}H_{56}O_{16}$. To obtain it pure, the alcoholic solution is concentrated; the resin precipitated by, and afterwards boiled with, water, then dried, reduced to powder, digested with ether, and finally redissolved by absolute alcohol and thrown down by ether. After being treated several times in this way, it is obtained in the state of a brownish resin, yielding on pulverization a gray powder, which strongly irritates the mucous membrane of the nostrils and mouth, and is fusible at 182.2° C. It is inflammable, burning with a smoky flame and emitting irritant vapors. With strong bases it acts like jalapin, takes up water, and is transformed into a soluble acid, *turpethic acid,* $C_{34}H_{60}O_{18}$, while with dilute acids it is decomposed into *turpetholic acid,* $C_{16}H_{32}O_4$, and glucose. (*J. P. C.,* 4e sér., i, 236.)

Turpeth root is purgative, somewhat less powerful than jalap, and rather slow in its action.

Dose, five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Tinctura Jalapæ Composita, *Br.*

ULMUS. U. S.

ELM [Elm Bark, Slippery Elm]

"Elm is the dried inner bark of *Ulmus fulva* Michaux (Fam. *Ulmaceæ*)." *U. S.*

Red Elm, Moose-elm, Indian Elm; Cortex Ulmi Interior, Ulmi Cortex; Orme Fauve, Ecorce d'Orme, *Fr.;* Ulmenrinde, Rüsterrinde, *G.*

The *slippery elm* (*Ulmus fulva*) is a lofty tree, fifty or sixty feet in height, with a trunk fifteen or twenty inches in diameter. The bark of the trunk is brown, that of the branches rough and whitish. The leaves are petiolate, oblong-ovate, acuminate, nearly equal at the base, unequally serrate, pubescent, and very rough on both sides. The buds, a fortnight before their development, are covered with a dense russet down. The flowers, which are apetalous, appear before the leaves, are sessile, and in clusters at the extremities of the young shoots. The clusters of flowers are surrounded by scales, which are downy like the buds. The calyx is also downy. The stamens are five, short, and of a pale rose color. The fruit is a membranaceous samara, enclosing in the middle one round seed, destitute of fringe.

Ulmus fulva is indigenous, growing in all parts of the United States north of the Carolinas, but most abundantly west of the Allegheny Mountains. It extends westward to the Dakotas and northward to western Quebec and Lake Huron. It flourishes in open, elevated situations, and requires a firm, dry soil. From the *white elm* (*U. americana* L.) it is distinguished by its rough branches, its larger, thicker, and rougher leaves, its downy buds, and the character of its flowers and seeds. Its period of flowering is in April. The inner bark, separated from the cortex, is the part used. Elm bark is gathered in the spring, deprived of the cork and part of the cortex, sawed into oblong pieces and dried. It is packed in bundles which are bound at each end with wire. Large quantities are collected in the Lower Peninsula of Michigan.

Fremontia californica Torr., or *California Slippery Elm,* is not botanically allied to *Ulmus fulva;* its bark is said, however, to have the same properties as slippery elm bark, and to be used for a similar purpose.

Description and Physical Properties.—"*Unground Elm.*—Usually broad, flat, oblong pieces, from 1 to 4 mm. in thickness; outer surface pale brown, roughened by longitudinal striæ and partially detached bundles of bast-fibers and with occasional thin, dark brown patches of adhering cork; inner surface light yellowish-brown, finely striate, fracture fibrous, with projections of fine bast-bundles; odor distinctive; taste mucilaginous.

"*Structure.*—Bast-fibers in small bundles or individual and arranged in numerous tangential rows alternating with rows of mucilage cells, the latter from 0.1 to 0.4 mm. in diameter; medullary rays 4 to 6 cells wide and bearing starch; sieve associated with parenchyma cells, the latter containing starch or prismatic monoclinic crystals or twin crystals of calcium oxalate, the crystal cells frequently so elongated and the crystals superimposed as to form short, non-lignified crystal-fibers.

"*Powdered Elm.*—Very light brown; bast-fibers numerous, very long, usually broken, up to 0.025 mm. in diameter, thick-walled, unlignified or with only a thin outer sheath of the wall lignified; calcium oxalate prisms from 0.010 to 0.035 mm. in length; starch grains spheroidal or polygonal, usually from 0.003 to 0.015 mm.

in diameter, occasionally up to 0.25 mm. in length; mucilage fragments numerous, frequently lamellated; brown-walled cork cells few or absent.

"Macerate 1 Gm. of finely powdered Elm with 40 cc. of water for one hour: the mixture is of a thick mucilaginous consistence and of a light brown color." *U. S.*

Ulmus abounds in mucilaginous matter, which it readily imparts to water. The mucilage is precipitated by solutions of lead acetate and subacetate, but not by alcohol. It contains a variety of tannin which colors iron solutions green, in amount about 6.5 per cent. according to Rink, or, according to Davy, a little less than 3 per cent.

Much of the bark brought into the market is of inferior quality, imparting comparatively little mucilage to water. It has the characteristic odor of the genuine bark, but is much less fibrous and more brittle, breaking abruptly when bent, instead of being capable, like the better kinds, of being folded lengthwise without breaking. To what this inferiority is owing, whether to difference in the species or the age, or to circumstances in the growth of the tree producing it, we are unable to state. Ground elm bark is said to be adulterated, usually with substances containing starch. Roberts found commercial specimens which possessed considerable of a brownish outer bark still adhering to them. One specimen was partly mouldy and had considerable adhering wood. (*Proc. Penn. Ph. Assoc.,* 1913, p. 85.) The following test, devised by Geo. M. Beringer, seems to have practical value: Ten grains of ground or pulverized elm bark, thoroughly shaken with one fluidounce of water, will, if pure and of good quality, in fifteen minutes form a thick jelly-like mass of a fawn color.

Elm bark has the property of preserving fatty substances from rancidity, a fact known to the Indians, who prepared bear's fat by melting it with the bark, in the proportion of a drachm of the latter to a pound of the former, keeping them heated together for a few minutes, and then straining off the fat.

Uses.—The elm bark is an excellent demulcent, formerly largely employed, but today used chiefly in the form of lozenges to relieve *irritation of the pharynx.* A warm infusion is a popular folk remedy in the treatment of *diarrheas, coughs,* etc. This is made by stirring an ounce of the powdered bark in a pint of hot water with which it forms a mucilage that may be drunk *ad libitum.*

It is commonly used as a drink in the form of infusion. (See *Mucilago Ulmi.*) The powder may be used stirred in hot water, with which it forms a mucilage more or less thick according to the proportion added. The bark also serves as an emollient application in cases of *external inflammation.* For this purpose the powder may be formed into a poultice with hot water, or the bark itself may be applied, previously softened by boiling. McDowell, of Virginia, recommended slippery elm bark for the dilatation of *fistulas* and *strictures* (*Med. Examiner,* i, 244); subsequently H. R. Storer, of Boston, used it advantageously for *dilating the os uteri* (*B. M. S. J.,* liii, 300), and A. Abbe, of the same place, succeeded in curing with it a case of *stricture of the rectum* (*B. M. S. J.,* liv, 349).

Off. Prep.—Trochisci Ulmi, *N. F.*

UNGUENTA.

OINTMENTS

Salves; Pomati; Pommades, Onguents, *Fr.;* Salben, *G.;* Pomatas, Unguentos, *It.;* Pomadas, Unguentos, *Sp.*

These are fatty substances, softer than cerates, of such a consistence that they may be readily applied to the skin by inunction. When ointments are prepared by merely mixing medicinal substances with simple ointment, hydrous wool-fat, lard, or petrolatum, care should be taken, if the added substance be a powder, that it be brought to the finest possible state of division before being incorporated with the unctuous matter. If soluble in water or in alcohol, it may often be advantageously rubbed with a little of one of these liquids. Gritty matter should not be allowed to enter these preparations. On the large scale manufacturers frequently make use of "paint mills" for making this class of preparations. When an extract is added, if not uniformly soft, it should be made so by trituration with water or alcohol, according to its nature. Many of the ointments become rancid if long kept, and should, therefore, be prepared in small quantities at a time, or only when wanted for use. The tendency to rancidity may be in a considerable degree counteracted by imbuing the unctuous vehicle with benzoin, elm bark or with poplar buds, as recommended by Deschamps; but care should be taken that there be no therapeutic objection to the admixture.

It has been proposed to substitute glycerin for oils and fats in the preparation of ointments, either wholly or in part; but ointments thus prepared are altogether unfit for application by inunction, as a portion of the glycerin remains upon the skin, producing a rough sensation of adhesiveness, very different from the softness caused by oleaginous matter, and in some skin diseases glycerin in an ointment would be positively injurious, due to its dehydrating properties which make it irritating.

Linnett (*Pract. Drug.,* 1917, p. 34) finds hydrogenated oil an ideal ointment base, being a good carrier, quickly absorbed, practically non-rancid, and economical. He gives several formulas for ointments with this base. A large number of combinations of oleates, fats or glycerin with various other substances have been recommended as ointment bases. It is extremely doubtful, however, whether any of these possess real superiority to the official preparations.

The cerates having been abolished as a class in the British Pharmacopœia, a few of the individual articles have been transferred to the ointments, making the definition of the latter class of preparations, as given above, not exactly applicable to all the individual substances at present included among them in that Pharmacopœia. We consider no substance to be strictly entitled to the name of ointment which is not of such a consistence as to adapt it to application to the skin by friction or inunction.

Ointments should be dispensed in glass, porcelain, or queensware pots or jars, or, if for temporary use, in tight wooden boxes. A very convenient method of dispensing soft ointments is in compressible tubes. These tubes are similar to those used for holding artists' colors, and have the advantage of shielding the ointment from the oxidizing action of the air while allowing the use of the desired quantity. Vanderkleed and Heidlberg (*Proc. P. P. A.*, 1913, p. 312) state that the only satisfactory method of determining whether or not the proper degree of subdivision has been attained is by the use of the microscope, and call attention to some of the precautionary measures which should be taken in order to obtain correct results. Their article is illustrated by numerous photographic representations of ointments of different degrees of fineness.

Uses.—The choice of base for ointments will vary according to the purpose for which the ointment is intended. We may divide the uses of ointments into three groups; (1) for influence upon the epiderm either as protectives or to retain active medicaments in contact with the skin; (2) to carry drugs into the true skin or subcutaneous tissues for antiseptic or anesthetic action; and (3) to introduce drugs into the circulation.

For the first purpose it is obvious that an ointment base is desirable which will tend to cling to the skin. For this reason those which become completely liquid at the bodily temperature are as a rule less desirable. On the other hand if the base is too stiff it will not be easily spread. Also a certain degree of stickiness is desirable. Wool-fat possesses in eminent degree a proper consistency for remaining where it is placed. If not modified with some emollient, however, it is rather difficult to spread and also has an objectionable odor. For the second purpose the base requires the power of penetrating the epiderm. It seems probable that, other things being equal, those fats which liquefy at the body temperature will be taken up by the superficial layers of the skin more readily, a view which has received some experimental confirmation. Various investigators have attempted to solve this problem experimentally. Sutton (*B. M. J.*, 1908, May 23, p. 1225) applied ointments of scarlet dye made with various bases and after a period of 3 or 4 hours excised pieces of the skin and examined them microscopically to see how deeply the stain had penetrated. He found that lard and goose grease gave the best penetration, wool-fat penetrated but slightly, although when mixed with equal parts of olive oil it gave a fair degree of penetration. Petrolatum penetrated scarcely at all unless applied with friction.

Gardiner (*B. M. J.*, 1912, i, p. 238) rubbed ointments containing various stains into the shaven skin of guinea pigs and then examined the skin microscopically to observe the depth of penetration. He found that olive oil penetrated more deeply than any substance with which he experimented, but that goose grease and lard also penetrated well. Petrolatum remained limited to the very superficial portions of the skin. Wool-fat, while it penetrated somewhat more deeply than petrolatum, was noticeably behind lard. Wild (*B. M. J.*, 1911, ii, p. 161) employed a very different method to study this subject. He rubbed pure ointment bases into the skin for a measured time and then scraped off what was left on the skin and weighed. The difference between the quantity taken and that recovered he considered to represent the amount absorbed. He found that petrolatum was absorbed practically not at all, that of lard or olive oil about 15 per cent., and of hydrous wool-fat about 20 per cent., but that the absorption of the latter was noticeably less if it was deficient in water. The question of which base is best for endermic administration of systemic drugs has been the subject of considerable discussion. It may be pointed out, however, that no one base can serve as the best for all drugs. The question of absorption from an ointment into the blood stream involves two very distinct factors; in the first place the penetration of the medicament through the skin, and secondly the partition coefficient between the solvent properties of the fatty base and the watery basis of the blood. Even if the ointment carrying the active medicament in fatty solution goes through the skin to the capillary blood vessels, it is obvious that the blood will take away more quickly from the ointment those drugs which are more soluble in water. It is probably this fact that has led to some of the contrary results by different experimenters. One, for example, using iodine will recommend a certain base, while the second investigator using salicylic acid as a test drug will reach quite the opposite conclusions. For endermic absorption each drug offers a separate problem.

UNGUENTUM. U. S.

OINTMENT Ung. [Simple Ointment]

Unguentum Adipis, *U. S.* 1860; Unguentum Simplex; Pommade simple, *Fr.*; Unguentum cereum, *P. G.*; Wachssalbe, *G.*

"Yellow Wax, 200 Gm.; Benzoinated Lard, 800 Gm.; to make about 1000 Gm. Melt the yellow wax, add the benzoinated lard, heat gently until liquefied, and stir the mixture until it congeals.

"Note.—For use in southern latitudes and during the warm season in other localities, 50

Gm. of the benzoinated lard (or more if necessary) may be replaced by an equal quantity of yellow wax." *U. S.*

Yellow wax was used in this ointment in the U. S. P., 1890, and objection was made to the color of the ointment. It has been very properly replaced by white wax and the lard is now benzoinated.

This is emollient, and is occasionally employed as a mild dressing to blistered or excoriated surfaces, but more frequently as a vehicle, it being the basis of several official ointments.

UNGUENTUM ACIDI BORICI. U. S., Br.

OINTMENT OF BORIC ACID Ung. Acid. Bor.

Boric Ointment; Pommade de l'Acide Borique, *Fr.;* Unguentum Acidi Borici, *P. G.;* Borsalbe, *G.;* Pomada de Acido Borico, *Sp.*

"Boric Acid, in fine powder, 100 Gm.; Yellow Wax, 50 Gm.; Petrolatum, 850 Gm.; to make about 1000 Gm. Melt the yellow wax, add the petrolatum, and heat gently until liquefied. Gradually add the warm liquid to the boric acid, contained in a warm mortar, triturating thoroughly, and stir the mixture until it congeals." *U. S.*

"Boric Acid, in powder, 10 *grammes;* Paraffin Ointment, white, 90 *grammes.* Melt the Paraffin Ointment; sift in the Boric Acid; stir until cold." *Br.*

Theodore Faber (*Ph. Ztg.,* 1914, p. 163) finds that boric acid in ointments may be readily and accurately estimated by the method of Jörgensen, in which it is converted into glycerin boric acid and estimated by titration with normal potassium hydroxide volumetric solution, as in the official method for estimating boric acid, the operation being carried out at a temperature sufficiently high to melt the fat, the presence of which may be disregarded.

Uses.—This ointment is widely used both as an emollient to the skin and for its protective effect on superficial *wounds* and *abrasions.* It is popularly, although with doubtful correctness, supposed to possess valuable antiseptic and healing powers. The prevalent belief that it has antiseptic properties because of the boric acid in it has no scientific support.

UNGUENTUM ACIDI SALICYLICI. Br.

SALICYLIC ACID OINTMENT

Pommade d'Acide Salicylique, *Fr.;* Salicylsalbe, *G.*

"Salicylic Acid, in powder, 2 *grammes;* Paraffin Ointment, white, 98 *grammes.* Melt the Paraffin Ointment; sift in the Salicylic Acid; stir until cold." *Br.*

According to Bourjet (*Th. M.,* 1893) salicylic acid is absorbed into the system more readily from ointments made with the true fats than from those made with a petrolatum base, but as this ointment is used chiefly for its local effect upon the epiderm, the question of its penetration is of little importance.

UNGUENTUM ACIDI TANNICI. U. S.

OINTMENT OF TANNIC ACID Ung. Acid. Tann.

Pommade d'Acide tannique, Pommade de Tannin, *Fr.;* Tanninsalbe, *G.*

"Tannic Acid, 20 Gm.; Glycerin, 20 Gm.; Ointment, 60 Gm.; to make about 100 Gm. Dissolve the tannic acid in the glycerin with the aid of a gentle heat, and mix the solution thoroughly with the ointment, avoiding the use of iron utensils." *U. S.*

Ointment of Tannic Acid was doubled in strength at the U. S. P., 1890, revision. It is an excellent application in many cases of *piles* and *prolapsus ani,* also for *flabby ulcers.*

UNGUENTUM ACONITINÆ. Br.

ACONITINE OINTMENT

Pommade d'Oléate d'Aconitine, Pommade d'Aconitine, *Fr.;* Akonitinoleatsalbe, Akonitinsalbe, *G.;* Pomada de Aconitina, *Sp.*

"Aconitine, 2 *grammes;* Oleic Acid, 16 *grammes;* Prepared Lard, 82 *grammes.* Triturate the Aconitine with the Oleic Acid, and gently warm the mixture until dissolved; add the Prepared Lard; mix. This Ointment contains 2 per cent. of Aconitine. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

For the uses of this preparation the reader is referred to the articles on *Aconitum* and *Aconitina.* Care must be taken not to apply it too freely nor to an abraded or ulcerated surface, lest it produce serious constitutional effects.

UNGUENTUM AQUÆ ROSÆ. U. S., Br.

OINTMENT OF ROSE WATER Ung. Aq. Ros.

Rose Water Ointment; Unguentum Emolliens; Galen's Cerate, Cold-cream; Cerat de Galien, Ceratum Galeni, *Fr. Cod.;* Cérat cosmétique, Crême froide, *Fr.;* Unguentum leniens, *P. G.;* Cold Cream, *G.*

"Spermaceti, 125 Gm.; White Wax, 120 Gm.; Expressed Oil of Almond, 560 Gm.; Sodium Borate, in fine powder, 5 Gm.; Stronger Rose Water, 190 Gm.; to make about 1000 Gm. Reduce the spermaceti and the white wax to fine pieces and melt them on a water bath, add the expressed oil of almond, and stir, continuing the heat until the mixture is uniformly melted. Dissolve the sodium borate in the stronger rose water warmed on a water bath to the temperature of the melted wax and fat, and add the warm solution gradually to the melted mixture, stirring it rapidly and continuously until it congeals and becomes of uniform consistence. Ointment of Rose Water must be free from rancidity. If the Ointment has been chilled, warm it slightly before attempting to incorporate other ingredients with it. Preserve in pure tin, collapsible tubes." *U. S.*

"Rose Water, 20.0 *millilitres;* White Beeswax, 18.0 *grammes;* Purified Borax, 1.0 *gramme;* Almond Oil, 61.0 *grammes;* Oil of Rose, 0.1 *millilitre.* Melt the White Beeswax in the Almond Oil; add, with constant stirring, the Borax previously dissolved in the Rose Water; add the Oil of Rose, and continue to stir until cold." *Br.*

This preparation is a white, very soft, and elegant ointment, deriving a grateful odor from the rose water, which remains incorporated with the other constituents if kept enclosed in glazed vessels. We have found it an improvement to add oil of rose in the proportion of one drop to eight ounces, and, when made in the official quantity, to use an instrument known as the "Dover egg-beater" for giving it the desired creamy appearance. In larger amounts an ice cream churn or one of the mechanical mixing devices sold for mixing or emulsifying is well adapted for this purpose.

"Cold cream" is not recognized in the U. S. Pharmacopœia as an official synonym for ointment of rose water. This course became necessary because of the large number of unofficial ointments of varying composition popularly exploited as cold creams, and these were frequently dispensed, when physicians' prescriptions directed Ointment of Rose Water. The commercial cold creams must be made from substances which are not liable to rancidity, and paraffin oil, liquid petrolatum, white petrolatum, etc., largely form the basis of such, but the official ointment is to be preferred for use in prescriptions. W. C. Alpers furnishes the following formula for a cold cream which is more permanent than the official ointment. One hundred and fifty parts of white wax is melted in 600 parts of paraffin oil with the aid of a gentle heat; 9 parts of borax is dissolved in 240 parts of water; the two fluids are brought to a uniform temperature, not exceeding 60° C., and the aqueous solution is poured into the oily one in a continuous stream, stirring gently for a minute or two; then 1 part of oil of geranium and a little oil of rose are added while stirring, and the product while still warm is poured into jars. The cold cream so obtained is white, soft and smooth, pleasantly odorous, keeps well in the heat of summer and the cold of winter, and becomes only slightly thinner in summer.

Uses.—This ointment is a popular and valuable emollient and base. It is sometimes applied unmedicated to *chapped hands* and other irritated states of the skin. More frequently it is used as a base for more active medicaments, being highly prized not only on account of its odor but for its peculiar consistency which makes it easy to spread; a few substances are incompatible with borax and should not be combined with it. The commercial cold creams, made with petrolatum base, do not possess the therapeutic virtues and should never be substituted for ointment of rose-water.

UNGUENTUM ATROPINÆ. Br.

ATROPINE OINTMENT

Pommade d'Oléate d'Atropine, Pommade d'Atropine, *Fr.;* Atropinoleatsalbe, Atropinsalbe, *G.*

"Atropine, 2 *grammes;* Oleic Acid, 8 *grammes;* Prepared Lard, 90 *grammes.* Triturate the Atropine with the Oleic Acid, and gently warm the mixture until dissolved; add the Prepared Lard; mix. This Ointment contains 2 per cent. of Atropine. In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

For the uses of this ointment, see under *Belladonna* and *Atropina.* Caution must be observed that the ointment shall not come in contact with abraded, ulcerated, or wounded surfaces, and that it be not applied too freely to sound skin.

UNGUENTUM BELLADONNÆ.
U. S., Br.

BELLADONNA OINTMENT Ung. Bellad.

Pomatum; Pommade Belladonée, *Fr.;* Belladonnasalbe, Tollkirschensalbe, *G.;* Pomada de Belladonna, *Sp.*

"Pilular Extract of Belladonna, 10 Gm.; Diluted Alcohol, 5 cc.; Wool Fat, 30 Gm.; Yellow Wax, 5 Gm.; Petrolatum, 50 Gm.; to make about 100 Gm. Triturate the extract with the diluted alcohol until a smooth mixture is obtained, add the wax, wool fat, and petrolatum, which have been melted together on a water bath, and mix thoroughly." *U. S.*

"Liquid Extract of Belladonna, 80 *millilitres;* Benzoated Lard, 60 *grammes;* Wool Fat, 20 *grammes.* Evaporate the Liquid Extract of Belladonna on a water-bath until it is reduced to twenty grammes; mix with the Benzoated Lard and Wool Fat. This Ointment contains 0.6 per cent. of the alkaloids of Belladonna Root. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoinated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

This is a convenient form for the external application of extract of belladonna. Care must be taken in preparing it that the extract employed have the due consistence, and be free from lumps; the purpose of the diluted alcohol is to assure the even distribution of the belladonna.

The most important use of this ointment is as a local application in *hemorrhoids.*

UNGUENTUM CANTHARIDINI. Br.

CANTHARIDIN OINTMENT

Unguentum Irritans, Unguentum ad Fonticulos; Onguent de Cantharides, *Fr.;* Spanischfliegensalbe, *G.*

"Cantharidin, 0.1 *gramme;* Chloroform, 10.0 *millilitres;* Benzoated Lard, 290.0 *grammes.* Dissolve the Cantharidin in the Chloroform; add the solution to the Benzoated Lard, previously melted; stir until cold. This Ointment contains 0.033 per cent. of Cantharidin, which is approximately two-thirds of the proportion of Cantharidin contained in the Unguentum Cantharidis of the British Pharmacopœia, 1898. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

This ointment is intended as a dressing for blisters, not to produce vesication. The U. S. Committee of Revision wisely deleted this preparation many years ago, as it was frequently prescribed under the impression that it was equal in strength to the cerate, in fact, identical with it, and disappointment resulted. Such a preparation should be left to extemporaneous prescription. *Dupuytren's ointment,* employed as a local application to *prevent the loss of hair,* was made by macerating a drachm of Spanish flies in a fluidounce of alcohol, and incorporating one part of the tincture thus formed with nine parts of lard.

UNGUENTUM CAPSICI. Br.

CAPSICUM OINTMENT

Pommade de Piment das Jardins, *Fr.;* Spanisch-Pfeffersalbe, *G.*

"Capsicum Fruit, bruised, 25 *grammes;* Hard Paraffin, 10 *grammes;* Soft Paraffin, 75 *grammes;* Prepared Lard, 10 *grammes.* Digest on a water-bath for one hour, stirring occasionally; strain; stir until cold. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

This is an active counter-irritant which may be used in the place of liquid liniments in *sprains, bruises, rheumatism,* and other inflammations.

UNGUENTUM CETACEI. Br.

SPERMACETI OINTMENT

Pommade de baleine, *Fr.;* Walrathsalbe, *G.*

"Spermaceti, 20 *grammes;* White Beeswax, 8 *grammes;* Liquid Paraffin, 72 *grammes.* Melt together, and stir until cold." *Br.*

This ointment is employed as a mild dressing for *blisters, wounds,* and *excoriated surfaces,* or as the basis for carrying more active ingredients. It should be made in small quantities at a time, as it is apt to become rancid when long kept.

UNGUENTUM CHAULMOOGRÆ. Br.

CHAULMOOGRA OINTMENT

"Chaulmoogra Oil, 10 *grammes;* Hard Paraffin, 40 *grammes;* Soft Paraffin, white, 50 *grammes.* Melt the Hard and Soft Paraffins together; add the Chaulmoogra Oil; stir until cold." *Br.*

This is intended for its local effects; it is not suitable for obtaining the systemic actions of chaulmoogra oil. (See *Oleum Chaulmoogra.*)

UNGUENTUM CHRYSAROBINI. U. S., Br.

CHRYSAROBIN OINTMENT Ung. Chrysarobin.

Pommade de Chrysarobine, *Fr.;* Chrysarobinsalbe, *G.*

"Chrysarobin, 6 Gm.; Hydrous Wool Fat, 94 Gm.; to make about 100 Gm. Triturate the chrysarobin with the hydrous wool fat, previously melted, heat the mixture on a water bath for twenty minutes, with occasional stirring, strain, and stir until the Ointment congeals." *U. S.*

"Chrysarobin, in powder, 4 *grammes;* Soft Paraffin, 96 *grammes.* Triturate the Chrysarobin with a portion of the Soft Paraffin until smooth; gradually add the remainder, mixing thoroughly by trituration." *Br.*

The U. S. ointment is now considerably stronger than the British ointment. The base has been changed in the U. S. X from lard to wool-fat.

It is a valuable agent in *psoriasis, ringworm,* and other *diseases of the skin,* but has the great drawback of leaving a permanent stain upon the linen. It is more easily made by dissolving the chrysarobin in a little hot benzene, mixing this rapidly with a portion of the melted wool-fat (or petrolatum), and subsequently stirring before adding the rest of the base.

UNGUENTUM COCAINÆ. Br.

COCAINE OINTMENT

Pommade d'Oléate de Cocaine, *Fr.;* Cocainoleatsalbe, *G.*

"Cocaine, 4 *grammes;* Oleic Acid, 16 *grammes;* Prepared Lard, 80 *grammes.* Triturate the Cocaine with the Oleic Acid, and gently warm the mixture until the alkaloid is dissolved; add the Prepared Lard; mix. This Ointment contains 4 per cent. of Cocaine. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

UNGUENTUM CREOSOTI. Br.

CREOSOTE OINTMENT

Pommade Créosotée, *Fr.;* Kreosotsalbe, *G.*

"Creosote, 10 *grammes;* Hard Paraffin, 40 *grammes;* Soft Paraffin, white, 50 *grammes.* Melt the Hard and Soft Paraffins together; add the Creosote; stir until cold." *Br.*

The British ointment is more than twice as strong as that official in the U. S. P., 1870, which was made by mixing half a fluidrachm of creosote with a troyounce of lard. For the use of this ointment, see *Creosotum.* It may sometimes be advantageously diluted with lard when found to irritate.

UNGUENTUM EUCALYPTI. Br.

EUCALYPTUS OINTMENT

Pommade d'Eucalypte, *Fr.;* Eukalyptussalbe, *G.*

"Oil of Eucalyptus, 10 *grammes;* Hard Paraffin, 40 *grammes;* Soft Paraffin, white, 50 *grammes.* Melt the Hard and Soft Paraffins together; add the Oil of Eucalyptus; stir until cold." *Br.*

This ointment is used as a stimulant to indolent *ulcers* and in *skin diseases.*

UNGUENTUM GALLÆ. U. S., Br.

NUTGALL OINTMENT Ung. Gall.

Gall Ointment; Ointment of Galls; Pommade de Noix de Galle, *Fr.;* Galläpfelsalbe, *G.*

"Nutgall, in very fine powder, 20 Gm.; Ointment, 80 Gm.; to make about 100 Gm. Rub the nutgall with the ointment, gradually added, until they are thoroughly mixed. Avoid the use of iron utensils." *U. S.*

"Galls, in powder, 20 *grammes;* Benzoated Lard, 80 *grammes.* Triturate the Galls with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

Care should be taken to have the nutgall in very fine powder and thoroughly sifted. This ointment is used chiefly in *piles* and *prolapsus ani,* and in *flabby* or *indolent ulcers.*

Off. Prep.—Unguentum Gallæ cum Opio, *Br.*

UNGUENTUM GALLÆ CUM OPIO. Br.

GALL AND OPIUM OINTMENT

"Gall Ointment, 92.5 *grammes;* Opium, in powder, 7.5 *grammes.* Triturate the Opium with a portion of the Gall Ointment until smooth; gradually add the remainder, mixing thoroughly by trituration. This Ointment contains 7.5 per cent. of Opium." *Br.*

This combination of galls and opium is sometimes employed for *hemorrhoids* but is not a very happy combination. From two to four per cent. of camphor is sometimes added.

UNGUENTUM HAMAMELIDIS. Br.

HAMAMELIS OINTMENT

Pommade de Hamamélis, *Fr.;* Hamamelissalbe, *G.*

"Liquid Extract of Hamamelis, 10 *millilitres;* Wool Fat, 60 *grammes;* Soft Paraffin, 30 *grammes.* Mix by trituration in a warm mortar." *Br.*

This was one of the "Additions" to the British Pharmacopœia, 1885, and afterwards introduced into the Br. Pharm., 1898, 1914. It is, in our opinion, of doubtful utility, but may be applied to *sprains.*

UNGUENTUM HYDRARGYRI AMMONIATI. U. S., Br.

OINTMENT OF AMMONIATED MERCURY Ung. Hydrarg. Ammon. [White Precipitate Ointment]

Unguentum Præcipitati Albi; Ointment of White Precipitate; Pommade de Chloramidure de Mercure, *Fr.;* Unguentum Hydrargyri Album, *P. G.;* Weisse Quecksilbersalbe, *G.*

"Ammoniated Mercury, in very fine powder, 10 Gm.; Liquid Petrolatum, 10 Gm.; Hydrous Wool Fat, 40 Gm.; White Petrolatum, 40 Gm.; to make about 100 Gm. Triturate the ammoniated mercury with the liquid petrolatum until the mixture is smooth, add the white petrolatum, previously melted, mix thoroughly with the hydrous wool fat, and stir the mixture until it congeals." *U. S.*

"Ammoniated Mercury, in powder, 5 *grammes;* Benzoated Lard, 95 *grammes.* Triturate the Ammoniated Mercury with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. This Ointment is of approximately one-half the strength of the corresponding preparation of the British Pharmacopœia, 1898. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

The Br. Pharm., 1914, reduced the strength of this ointment and it is now one-half the strength of the U. S. preparation.

It is used chiefly as a stimulant and parasiticide in cutaneous eruptions, such as *scabies, ringworm, chronic eczema,* and *porrigo.*

UNGUENTUM HYDRARGYRI COMPOSITUM. Br.

COMPOUND MERCURY OINTMENT

"Mercury Ointment, 40 *grammes;* Yellow Beeswax, 24 *grammes;* Olive Oil, 24 *grammes;* Camphor, in flowers, 12 *grammes.* Mix the Yellow Beeswax, Olive Oil, and Mercury Ointment with the aid of heat; add the Camphor; triturate until cold. This Ointment is of approximately three-fifths the strength of the corresponding preparation of the British Pharmacopœia, 1898. (See Appendix XII, Part III, *Unguenta,* and *Oleum Olivæ*)." *Br.*

The addition of camphor to mercurial ointment has been thought to soften it and promote absorption of the mercury, but that it has such an effect is very doubtful.

UNGUENTUM HYDRARGYRI FORTIUS. U. S.

STRONGER MERCURIAL OINTMENT Ung. Hydrarg. Fort. [Unguentum Hydrargyri U. S. P. IX]

"Stronger Mercurial Ointment contains not less than 49 per cent. and not more than 51 per cent. of Hg." *U. S.*

Unguentum Neapolitanum; Pomatum Hydrargyricum Gallicum, *Fr. Cod.;* Pommade Mercuriel à parties egales, Onguent Napolitain, *Fr.;* Pomada Mercurial Simple, *Sp.*

"Mercury, 500 Gm.; Oleate of Mercury, 20 Gm.; Prepared Suet, 230 Gm.; Benzoinated Lard, 250 Gm.; to make about 1000 Gm. Triturate the oleate of mercury in a warm mortar, with the mercury added gradually, and when the globules are completely divided and distributed, set it aside for about fifteen minutes. Melt the lard and suet, allow the mixture to partially cool, add about 25 Gm. of it to the mercurial mixture, and continue the trituration until globules of mercury are no longer visible under a lens magnifying ten diameters. Then add the remainder of the lard and suet, and mix thoroughly." *U. S.*

As the name "Unguentum Hydrargyri" is applied all over Europe to an ointment containing only 30 per cent. of mercury the revisers of the U. S. X felt that the name of this ointment, containing 50 per cent. of the metal, should be changed in order to avoid conflict with the Protocol Internationale; at the same time in order to avoid confusion in this country it was felt necessary to add also a limiting adjective to the ointment which corresponds to the internationally accepted strength (see *Unguentum Hydrargyri Mite*). The formula of this is practically unchanged from that of the U. S. IX.

The U. S. official formula is particularly adapted to the extemporaneous preparation of this ointment, it having been shown that the extinguishment of the mercury is facilitated by the use of oleate of mercury, while its presence probably adds to the efficiency of the ointment. Oleic acid was suggested by Leo Eliel (see *Indiana Pharmacist,* 1888) in the proportion of 1 per cent. for the extinction of the mercury. The addition of 4 per cent. of compound tincture of benzoin aids in the preservation of the ointment. The trituration should not be accompanied with pressure, a light, rapid motion of the pestle being most effective. In the preparation of mercurial ointment, care is requisite that the mercury should be completely extinguished. The trituration is usually performed upon the large scale in a marble mortar, as it is difficult to keep iron so clean as not to impart more or less oxide to the ointment. The mercury is known to be extinguished when a portion of the mass, rubbed upon paper, exhibits no metallic globules under a magnifying glass of ten diameters. The operation cannot be considered as satisfactorily accomplished when the globules are invisible merely to the naked eye. To facilitate the process which is very tedious, the addition of various substances has been proposed, calculated to hasten the disappearance of the metal. (For the details of many of these older processes see *U. S. D.,* 19th ed., p. 1310.)

E. R. Squibb prepared this ointment by succussion in an apparatus which agitates the mixture of fats and mercury until the metal is extinguished. When prepared with lard alone, the ointment is liable, in hot weather, to become so soft as to allow the metal to separate. Hence the official use of suet, and even a larger proportion might be employed, during the summer season. The ointment is preferably made by machinery on the large scale. The fatty matters, kept in the fluid state by a heat of about 37.7° C., are triturated with the metal by means of two iron balls which are driven rapidly around in a circular trough by steam power. The extinguishment of the mercury is thus effected in about twelve hours. For an account of many expedients that have been proposed to facilitate the extinguishment of the metal, see a paper by Dieterich. (*A. J. P.,* 1880.)

Mercurial ointment has when freshly prepared a bluish color, which becomes darker with age. It was at one time believed to contain the mercury in the state of mercurous oxide, but it is now generally admitted that by far the greater part of it exists in a state of minute division and not of chemical combination. It has been shown, however, that the metal does become slightly oxidized, and the change of color which the ointment undergoes with age is attributable to further oxidation. If the ointment be kept long melted in a narrow vessel, metallic mercury subsides, and an oily liquid floats upon the surface. The same change takes place if the ointment is kept for a long time in too warm a place. Christison states that he has examined various samples of the ointment, and never failed to detect mercurial oxides, and he has inferred from his observations that the oxide amounts to rather more than 1 per cent. But the proportion is variable, according to the age and mode of preparation of the ointment.

"**Assay.**—Mix about 1 Gm. of Stronger Mercurial Ointment, accurately weighed, in a suitable flask with 20 cc. of water and 20 cc. of nitric acid, and warm the mixture gently until red fumes cease to be evolved and the solution is colorless. Cool, add 100 cc. of distilled water and 2 cc. of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium thiocyanate until a permanent reddish color is produced. Each cc. of tenth-normal potassium thiocyanate corresponds to 0.01003 Gm. of Hg." *U. S.*

Uses.—Mercurial ointment is intended for the introduction of mercury into the general system, especially for the treatment of *syphilis.* There has been some question as to the method of the absorption of mercury after inunction; there can be no question of the fact of absorption. It has been suggested that what occurs is really a volatilization of mercury and inhalation of it. Schamberg from experiments on rabbits (*J. A. M. A.,* 1918, lxx, 142) came to the conclusion that while there might be some volatilization, the bulk of the mercury that entered the system did so through the skin. The matter appears to have been definitely settled by the observations of Cole, Gericke and Sollmann (*J. A. M. A.,* 1921, lxxvii, p. 2002) who perfected a method of inunction in which the ointment was rubbed into the skin for thirty minutes and at the end of this period the skin was cleansed with benzin which would remove any mercurial ointment that might remain on the outside. They produced salivation in three-fourths of the cases in which this method was employed. Attention may be called to the observation of Cole and Litman (*J. A. M. A.,* Nov. 8, 1919) that a calomel ointment is of no therapeutic value in syphilis probably because of its slight absorption through the skin. It has also been employed as a resolvent in local affections, as in the case of *venereal buboes,* and of *chronic glandular swellings,* with the thought that it may operate directly by being applied in the course of the absorbents passing through the enlarged glands.

It is best absorbed if applied over those areas of the body where the skin is thin, as the bend of the elbows or knees, or the groins. The friction should on each occasion be continued till the ointment is not visible on the skin. When frequently rubbed upon the same part, it is prone to produce a disagreeable eruption, which interferes with its continued application, and it is therefore advisable to apply it to different parts if used on successive days. Mercurial ointment has been employed, with some success, to prevent the maturation of the *small pox pustule,* and the consequent pitting. For this purpose it may be applied to the face or other part, thickly spread on patent lint or muslin, care being taken to prevent the access of air to the covered part. To be successful it must be applied before the third or fourth day of the eruption. The ointment has been recommended also in *erysipelas* and in *chilblains.*

Dose, one-half to one drachm (2–4 Gm.). It is usually dispensed in dosage packets, each wrapped separately in waxed paper.

Off. Prep.—Unguentum Hydrargyri Dilutum, *U. S.*

UNGUENTUM HYDRARGYRI IODIDI RUBRI. Br.

MERCURIC IODIDE OINTMENT

Ointment of Mercuric Iodide; Ointment of Red Iodide of Mercury; Pommade d'Iodure Mercurique, *Fr.;* Jodquecksilbersalbe, *G.*

"Red Mercuric Iodide, in powder, 4 *grammes;* Benzoated Lard, 96 *grammes.* Triturate the Red Mercuric Iodide with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

This ointment is employed as a dressing to indolent *scrofulous* and *syphilitic ulcers.*

UNGUENTUM HYDRARGYRI MITE. U. S.

MILD MERCURIAL OINTMENT Ung. Hydrarg. Mit. [Unguentum Hydrargyri Dilutum U. S. P. IX, Diluted Mercurial Ointment, Blue Ointment, Hydrargyri unguentum P. I.]

"Mercurial Ointment contains not less than 29 per cent. and not more than 31 per cent. of Hg." *U. S.*

Unguentum Hydrargyri, *Br.;* Mercury Ointment; Unguentum Mercuriale; Blue Ointment; Unguentum Coeruleum; Pomatum Hydrargyricum Dilutum, *Fr. Cod.;* Pommade Mercurielle Faible, *Fr.;* Unguentum Hydrargyri Cinereum, *P. G.;* Grauesalbe, Quecksilbersalbe, *G.;* Pomada Mercurial, *Sp.*

"Stronger Mercurial Ointment, 600 Gm.; Petrolatum, 200 Gm.; Ointment, 200 Gm.; to make about 1000 Gm. Mix the ingredients thoroughly.

"**Assay.**—Proceed as directed under *Unguentum Hydrargyri Fortius.*" *U. S.*

"Mercury, 30 *grammes;* Benzoated Lard, 65 *grammes;* Prepared Suet, 5 *grammes.* Triturate until metallic globules cease to be visible. This Ointment is of approximately three-fifths the strength of the corresponding preparation of the British Pharmacopœia, 1898; it is of the same strength as the Unguentum Hydrargyri of the International Agreement. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

This ointment was introduced into the U. S. P. (8th Rev.) to correspond to the recommendations of the International Conference; it should be kept in a cool place in the summer, as otherwise the mercury may separate on account of the softening of the fatty vehicle.

A substitute for *blue ointment* has been proposed by a French pharmacist, which is made as follows: 23.5 Gm. of mercuric chloride is triturated with 8.1 Gm. of sodium sulphocyanate and enough lanolin and petrolatum to make 100 Gm. The sulphocyanate reduces the mercuric chloride with the production of metallic mercury in a finely divided state and the resulting preparation is said to be very similar in its effect to blue ointment and to be much more easily prepared. (*Bull. Pharm.,* 1914, 306.)

The U. S. mild mercurial ointment is used only for the destruction of parasites and vermin on the skin. It is not suited for producing the systemic action of mercury as the petrolatum base does not so readily penetrate the skin. For anti-syphilitic inunctions the strong mercurial ointment should be employed. The British preparation may be used for either purpose.

UNGUENTUM HYDRARGYRI NITRATIS. Br.

MERCURIC NITRATE OINTMENT

Ointment of Nitrate of Mercury; Unguentum Citrinum; Citrine Ointment; Unguentum Hydrargyri Citrinum; Pommade Citrine, *Fr. Cod.;* Onguent Citrin, *Fr.;* Quecksilbernitratsalbe, Gelbe Quecksilbersalbe, *G.*

"Mercury, 10 *grammes;* Nitric Acid, 30 *millilitres;* Prepared Lard, 40 *grammes;* Olive Oil, 70 *grammes.* Dissolve the Mercury in the Nitric Acid without the aid of heat, shaking gently from time to time. Heat the Prepared Lard and Olive Oil together on a sand-bath, so that the mixture when transferred to a heated earthen jar, capable of holding ten times the quantity, is at a temperature of about 150° C. Add the cold mercurial solution very gradually, stirring constantly with a glass or wooden spatula to promote the disengagement of fumes. Keep the mixture at a temperature of not less than 90° C. until frothing ceases, then stir until cold. (See Appendix XII, Part III, *Unguenta,* and *Oleum Olivæ.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

The chemical changes which take place in the preparation of this ointment are complex.

They differ somewhat according to the circumstances under which the operation is performed; for example, according to the proportion and strength of the acid, the nature of the fatty matter, and the degree of heat employed. In the British process the mercury, in the first step of the process, is converted into a mixture of mercuric and mercurous nitrate by the addition of nitric acid in excess, with the loss of some of the free nitric acid through deoxidation. When the acid mercurial solution is added to the fatty matter, a reaction takes place, which results in the fat being oxidized at the expense of the free nitric acid, nitrogen dioxide and nitrogen tetroxide being at the same time liberated, and the olein of the fat is converted into elaidin, which change is recognized by the beautiful orange color of the fat. But the degree to which these changes take place is influenced greatly by the temperature to which the mixture is exposed. If this be low, there is little or no escape of gas; if elevated, there is a copious evolution of nitrous fumes. In the former case the changes are obviously less considerable than in the latter.

As formerly prepared, this ointment, though at first beautifully yellow and of the proper consistence, soon began to change, acquiring in time a dirty-greenish and mottled color, and becoming so hard and friable as to be unfit for use unless mixed with lard. These results were ascribed to various causes, and many different modifications of the process were proposed in order to obviate them. The present official process was based on Rother's formula (*A. J. P.*, xlii, 420). The value of this process lies principally in the fact that the olein of the oil is first converted into elaidin by the addition of nitric acid alone and the application of heat; when the reaction has ceased and the basis of citrine ointment, as it might be called, is prepared, and nearly cold, the mercurial solution is added. In this way decomposition of the mercuric nitrate is avoided, as it is not subjected to heat, and the result is an ointment which will retain its color and consistence a long time. Care must be taken that the heat applied be not too great. Gas is extricated at 82.2° C., and at 100° C. escapes so abundantly that the mixture boils over unless the vessel is very large. (Alsop.) Besides, if the heat be too great, a portion of the mercury will be reduced, and the color of the ointment impaired. When large quantities of materials are operated upon, the reaction which occurs produces of itself a sufficient heat. It should always be sufficient to produce a copious extrication of gas. The ointment should be prepared in a glass, porcelain, or well-glazed earthen vessel, and a glass rod or a wooden spatula should be employed for stirring the mixture. Under no circumstances should an iron or steel spatula or stirrer be used in its preparation, because of the contamination and discoloration due to the action of the acid upon the iron.

Uses.—This ointment is much and very advantageously employed, as a stimulant and alterative application, in *porrigo* or *tinea capitis, impetigo larvalis, psoriasis, sycosis, pityriasis,* certain forms of *chronic eczema,* and various other eruptive affections. It is an active parasiticide and antiseptic, highly stimulating and generally should be diluted with lard, unless in very sluggish cases. Some care is requisite in its use, to avoid the risk of salivation. When hard and friable, it must be rubbed up with fresh lard before it can be applied. An ointment prepared with lard and nitric acid, called *Alyon's ointment,* after the person who first prepared it, was formerly much used in cases similar to those in which the citrine ointment is now employed. The *ointment of nitric acid* of the former Edinburgh and Dublin Pharmacopœias was of this character.

Off. Prep.—Unguentum Hydrargyri Nitratis Dilutum, *Br.*

UNGUENTUM HYDRARGYRI NITRATIS DILUTUM. Br.

DILUTED MERCURIC NITRATE OINTMENT [Diluted Ointment of Nitrate of Mercury]

"Mercuric Nitrate Ointment, 20 *grammes;* Soft Paraffin, yellow, 80 *grammes.* Mix by trituration." *Br.*

UNGUENTUM HYDRARGYRI OLEATI. Br.

MERCURIC OLEATE OINTMENT

Pommade d'Oléate Mercurique, *Fr.;* Quecksilberoleatesalbe, *G.*

"Oleated Mercury, 25 *grammes;* Benzoated Lard, 75 *grammes.* Mix by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

UNGUENTUM HYDRARGYRI OXIDI FLAVI. U. S., Br.

OINTMENT OF YELLOW MERCURIC OXIDE
Ung. Hydrarg. Oxid. Flav.

"NOTE.—The strength of this Ointment has been reduced from 10 per cent. of Yellow Mercuric Oxide to 1 per cent." *U. S.*

Yellow Mercuric Oxide Ointment; Pomatum Hydrargyri Oxydati Flavi, *Fr. Cod.;* Pommade d'oxyde de mercure jaune, *Fr.;* Gelbe Quecksilberoxydsalbe, *G.;* Pomadada de Oxido Mercurico Amarillo, *Sp.*

"Yellow Mercuric Oxide, in very fine powder, 1 Gm.; Liquid Petrolatum, 1 Gm.; Hydrous Wool Fat, 10 Gm.; Petrolatum, 88 Gm.; to make about 100 Gm. Triturate the yellow mercuric oxide with the liquid petrolatum until the mixture is smooth, add the hydrous wool fat in divided portions, and incorporate the mixture thoroughly with the petrolatum. All contact with iron utensils or containers must be avoided." *U. S.*

"Yellow Mercuric Oxide, in powder, 2 *grammes;* Soft Paraffin, yellow, 98 *grammes.*

Triturate the Yellow Mercuric Oxide with a portion of the Soft Paraffin until smooth; gradually add the remainder, mixing thoroughly by trituration." *Br.*

Sjöström (*Ph. Ztg.,* 1915, 554) gives the following method for the assay of this ointment. 1.0 Gm. of the ointment is dissolved in 25 cc. of ether. The solution, in a glass-stoppered bottle, is mixed with 25 cc. potassium iodide solution (1+9), 20 cc. N/10 hydrochloric acid, and 1 cc. phenolphthalein solution, then titrated, shaking vigorously, with N/10 potassium hydroxide. 1 cc. N/10 hydrochloric acid = 0.01083 Gm. mercuric oxide, phenolphthalein as indicator. The method depends on the property of potassium iodide combining with finely divided mercuric oxide immediately and quantitatively according to the equation

$$3KI + HgO + H_2O = KHgI_3 + 2KOH.$$

The potassium hydroxide formed may be determined in the usual manner. The method is useful for ointments of any percentage of mercuric oxide and gives very exact results.

Uses.—This is the least irritant of the official ointments of the mercurial salts. It possesses the disinfectant and local stimulating properties of the mercury preparations and is used in various skin diseases, especially in *eczema* of the auditory canal or eye-lid, and in *hordeolum.* The U. S. ointment has been greatly reduced in strength and is now only half as strong as the Br. preparation.

UNGUENTUM HYDRARGYRI OXIDI RUBRI. Br.

RED MERCURIC OXIDE OINTMENT
[Red Precipitate Ointment]

Unguentum Præcipitati Rubri; Pommade d'oxyde de Mercure rouge, *Fr. Cod.;* Pommade de Lyon, Pommade de Précipité rouge, Baume ophthalmique rouge, *Fr.;* Unguentum Hydrargyri Rubrum, *P. G.;* Rothe Quecksilbersalbe, *G.;* Pomada de Oxido Mercurico Rojo, *Sp.*

"Red Mercuric Oxide, in powder, 10 *grammes;* Paraffin Ointment, yellow, 90 *grammes.* Melt the Paraffin Ointment; sift in the Red Mercuric Oxide; stir until cold." *Br.*

Red Precipitate Ointment was deleted from the U. S. P. IX but has been added to the N. F. (see Part III). It has been largely replaced in medical practice by Yellow Mercuric Oxide Ointment, which is a more desirable preparation.

The red mercuric oxide here referred to is that prepared from the nitrate and usually called *red precipitate.* It is important that the oxide should be thoroughly pulverized before being mixed with the lard, as otherwise it might prove injurious in cases of ophthalmia, in which it is sometimes used. When great care is taken to have the red oxide very finely pulverized, the color is more yellowish than is usual. This ointment loses its fine red color when kept long, probably in consequence of the conversion of the red oxide into the black, or its reduction to the metallic state. It is best to prepare it in small quantities at a time. The U. S. P. (8th Rev.) process was an improvement over the process of the U. S. P. 1890, particularly in the choice of the vehicle.

Ointment of red mercuric oxide is more highly stimulating than that of the yellow oxide and is used for different purposes. It is employed in *indolent and foul ulcers,* and *various skin diseases.* It may be diluted with lard if found too stimulating.

UNGUENTUM HYDRARGYRI SUBCHLORIDI. Br.

MERCUROUS CHLORIDE OINTMENT
[Calomel Ointment]

Unguentum Calomelanos, *Br.* 1864; Ointment of Subchloride of Mercury; Ointment of Calomel; Pomatum Hydrargyri Chlorati, *Fr. Cod.;* Pommade de Calomél, *Fr.;* Quecksilberchlorürsalbe, *G.;* Pomada de Cloruro Mercurioso Precipitado, *Sp.*

"Mercurous Chloride, 20 *grammes;* Benzoated Lard, 80 *grammes.* Triturate the Mercurous Chloride with a portion of the Benzoated Lard, until smooth; gradually add the remainder, mixing thoroughly by trituration. This Ointment is of twice the strength of the corresponding preparation of the British Pharmacopœia, 1898. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

Uses.—While ointments of calomel are often of much value in the same class of cases for which the yellow oxide is employed, this ointment is far too strong. We believe ointments of this character might well be left to extemporaneous prescription.

UNGUENTUM IODI. U. S., Br.

IODINE OINTMENT Ung. Iodi

Unguentum Iodinii, *U. S.* 1870; Pommade d'iodure de potassium iodée, *Fr. Cod.;* Pommade d'Iode, *Fr.;* Jodsalbe, *G.;* Pomada de Yoduro Potasico Yodada, *Sp.*

"Iodine, 4 Gm.; Potassium Iodide, 4 Gm.; Glycerin, 12 Gm.; Wool Fat, 80 Gm.; to make about 100 Gm. Triturate the iodine and potassium iodide, preferably in a glass mortar with the glycerin until dissolved, gradually incorporate the wool fat, and mix thoroughly. All contact with metallic utensils or containers must be avoided." *U. S.*

"Iodine, 4 *grammes;* Potassium Iodide, 4 *grammes;* Glycerin, 12 *grammes;* Prepared Lard, 80 *grammes.* Triturate the Iodine, Potassium Iodide, and Glycerin in a glass or porcelain mortar; add the Prepared Lard; mix thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

It has been stated that if there were no potassium iodide and glycerin present in iodine ointment, that 95 per cent. of the iodine would be "absorbed" by the lard in a short time. Some absorption and diminution of strength in iodine content does take place even in the present formula. It would seem, therefore, that the Br. preparation is distinctly superior to that of the U. S.

Miles Shimer (*Proc. P. P. A.*, 1915, p. 304) suggests that by keeping the iodine, potassium iodide and glycerin already made up as a stock solution, the dispensing of U. S. P. iodine ointment is much more expeditiously accomplished.

The change of base in the U. S. X formula seems to us peculiarly unfortunate. Hirschfeld and Pollio (*Arch. f. Derm. u. Syph.*, 1904, lxxii, p. 163) found that iodides were readily absorbed from ointments made with either petrolatum or lard, although scarcely at all from those made from wool-fat. Guttmann (*Z. K. M.*, 1887, xii, p. 276) found that the absorption from lard was superior to that from wool-fat.

Uses.—Ointment of Iodine is useful both for the local counter-irritant effect of the element and as a means of obtaining the constitutional action of the iodides. It is commonly believed that this ointment exercises a local resolvent action and it is therefore employed in various forms of *arthritis, goiter, scrofulous swellings of the glands,* and other *chronic tumefactions.*

When rubbed upon the skin it imparts to it an orange color, which, however, slowly disappears with the absorption of the iodine. When continued for some time it occasionally produces a pustular eruption upon the portion of skin to which it is applied. It has also been recommended in *chilblains.* The ointment should be prepared only when wanted for use, for it undergoes change if kept, losing its deep orange-brown color and becoming pale upon its surface, due to the combination of part of the iodine with the fat.

UNGUENTUM IODOFORMI. U. S., Br.

IODOFORM OINTMENT Ung. Iodof.

Pommade d'Iodoforme, *Fr.;* Jodoformsalbe, *G.;* Pomada de Yodoformo, *Sp.*

"Iodoform, 10 Gm.; Wool Fat, 20 Gm.; Petrolatum, 70 Gm.; to make about 100 Gm. Triturate the Iodoform with the previously melted petrolatum until dissolved, incorporate the wool fat, and mix thoroughly." *U. S.*

"Iodoform, in powder, 10 *grammes;* Prepared Lard, 90 *grammes.* Triturate the Iodoform with a portion of the Prepared Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

It is important to have the iodoform in very fine powder, as officially directed, and, owing to the powerful odor of iodoform, it is usual to add oil of bitter almond or one of the other volatile oils, balsam of Peru, or a similar substance, to render the odor less unpleasant.

UNGUENTUM LANÆ COMPOSITUM. Br.

COMPOUND WOOL-FAT OINTMENT [Emollient Ointment]

"Prepared Lard, 40 *grammes;* Wool Fat, 40 *grammes;* Paraffin Ointment, 20 *grammes.* Melt together; stir until cold. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

The addition of the paraffin ointment to wool-fat overcomes the stickiness which is so frequently an obstacle to the employment of that emollient.

UNGUENTUM MYROBALANI. Br.

MYROBALAN OINTMENT

"Myrobalans, in powder, 20 *grammes;* Benzoated Lard, 80 *grammes.* Triturate the Myrobalans with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

This is used as a local astringent.

Off. Prep.—Unguentum Myrobalani cum Opio, *Br.*

UNGUENTUM MYROBALANI CUM OPIO. Br.

MYROBALAN AND OPIUM OINTMENT

"Myrobalan Ointment, 92.5 *grammes;* Opium, in powder, 7.5 *grammes.* Triturate the Opium with a portion of the Myrobalan Ointment until smooth; gradually add the remainder, mixing thoroughly by trituration. This Ointment contains 7.5 per cent. of Opium." *Br.*

UNGUENTUM PARAFFINI. Br.

PARAFFIN OINTMENT

Pommade de Paraffin, *Fr.;* Paraffinsalbe, *G.*

"Hard Paraffin, 27 *grammes;* Soft Paraffin, 70 *grammes;* White Beeswax, 3 *grammes.* Melt together; stir until cold. When Paraffin Ointment is used as the basis of white ointments it should be prepared with the white variety of Soft Paraffin; and when used for colored ointments it should be prepared with the yellow variety of Soft Paraffin. (See Appendix XII, Part III, *Unguenta.*)" *Br.*

This is recognized by the Br. for use as a vehicle in the exhibition of various medicaments.

UNGUENTUM PHENOLIS. U. S. (Br.)

OINTMENT OF PHENOL Ung. Phenol. [Ointment of Carbolic Acid]

Unguentum Acidi Carbolici, *Br.;* Carbolized Petrolatum; Pomatum Phenoli, *Fr. Cod.;* Pommade de Phénol, Vaseline Phéniquée, *Fr.;* Karbolsalbe, Phenolsalbe, *G.;* Pomada de Acido Ferrico, *Sp.*

"Phenol, 2 Gm.; Yellow Wax, 5 Gm.; Petrolatum, 93 Gm.; to make about 100 Gm.

Melt the yellow wax and phenol on a water bath, add the petrolatum, and stir the mixture until it congeals." *U. S.*

"Phenol, 3 *grammes;* Paraffin Ointment, white, 97 *grammes.* Melt the Paraffin Ointment; in it dissolve the Phenol; stir until cold." *Br.*

The base of this ointment has been changed in the U. S. X to one composed largely of petrolatum. This is an improvement as the researches of McMaster have shown that a petrolatum solution of phenol is germicidal, while one in true fats is not. At the same time the proportion of phenol has been slightly reduced which is also an advantage; the Br. ointment is too strong for most purposes.

It is a useful antiseptic for small wounds and sores of various types.

UNGUENTUM PICIS PINI. U. S. (Br.)

TAR OINTMENT Ung. Pic. Pin. [Unguentum Picis Liquidæ U. S. P. IX]

Unguentum Picis Liquidæ, *Br.;* Pommade de Goudron, *Fr. Cod.;* Theersalbe, *G.;* Pomada de Brea, *Sp.*

"Pine Tar, 50 Gm.; Yellow Wax, 15 Gm.; Petrolatum, 35 Gm.; to make about 100 Gm. Melt the yellow wax, add the petrolatum, and to the melted mixture add the pine tar, previously warmed, and incorporate thoroughly. Strain the mixture through muslin, and stir until it congeals." *U. S.*

"Tar, 70 *grammes;* Prepared Lard, 5 *grammes;* Yellow Beeswax, 25 *grammes.* Melt together; stir until cold. (See Appendix XII, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

The U. S. X. has modified the formula of this ointment by the substitution of petrolatum for the lard formerly official. It is considerably lower in content of tar than the British preparation.

This ointment is highly useful as a stimulant application in various *scaly* and *scabby eruptions,* particularly in *psoriasis* and *chronic eczema* and also for its anti-parasitic effect in *tinea capitis* or similar *skin diseases.* In the last-mentioned affection it should be applied night and morning, and in bad cases the patient should constantly wear a cap thickly coated internally with the ointment. In some cases it requires dilution with an equal quantity of lard to avoid irritation.

UNGUENTUM PLUMBI IODIDI. Br.

LEAD IODIDE OINTMENT

Lead Iodide Ointment; Pommade d'Iodure de Plomb, *Fr. Cod.;* Jodbleisalbe, *G.;* Pomado de Yoduro Plumbico, *Sp.*

"Lead Iodide, in powder, 10 *grammes;* Benzoated Lard, 90 *grammes.* Triturate the Lead Iodide with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

For the uses of this ointment, see *Plumbi Iodidum.* It is also official in the N. F. (see Part III).

UNGUENTUM PLUMBI OLEATIS. U. S.

OINTMENT OF LEAD OLEATE Ung. Plumb. Ol. [Unguentum Diachylon U. S. P. IX]

Unguentum Plumbi Hebræ; Hebra's Lead Ointment; Diachylon Ointment; Onguent Diachylon, Pomade de Diachylon, *Fr.;* Unguentum diachylon, *P. G.;* Bleipflastersalbe, Diachylonsalbe, *G.*

"Lead Oleate Plaster, 50 Gm.; Oil of Lavender, 1 Gm.; White Petrolatum, 49 Gm.; to make about 100 Gm. Melt together the lead oleate plaster and the white petrolatum by applying a gentle heat, strain the mixture, allow it to cool but not congeal, add the oil of lavender, and stir the Ointment until it is cold." *U. S.*

This ointment has been largely used by dermatologists in *eczema* and other *skin diseases.* It is frequently called *"Unguentum Diachylon Hebræ,"* on account of its extensive use by Hebra, of Vienna. Vulpius states that the ointment used at Hebra's clinic, made according to the following formula, is very superior and will keep for weeks: Twenty parts of litharge are heated with sufficient water and eighty parts of olive oil until the reaction is completed, when one part of oil of lavender is added to the strained and cooling mass. Our experience with the ointment made by this formula is that the tendency to rancidity constitutes its greatest objection, and in warm weather it is impossible to keep it longer than a few days. If even slightly rancid, it is unfit for use in most cases.

The official ointment is the same as that of the U. S. IX, which has proven fairly stable and has given satisfaction. Other suggested modifications may be found in the *U. S. D.,* 20th ed., p. 1177.

UNGUENTUM PLUMBI SUBACETATIS. Br.

LEAD SUBACETATE OINTMENT

"Strong Solution of Lead Subacetate, 12.5 *grammes;* Wool Fat, 25.0 *grammes;* Hard Paraffin, 12.5 *grammes;* Soft Paraffin, 50.0 *grammes.* Melt together the Wool Fat and the Hard and Soft Paraffins; stir until nearly cold; add the Strong Solution of Lead Subacetate, and continue to stir until cold." *Br.*

The white petrolatum, wool-fat and paraffin now used in this ointment are preferable to the lard and cottonseed oil formerly employed, as they are free from the great objections to the former official cerate, of proneness to rancidity, and discoloration. This cerate received the name by which it is commonly known from Goulard, by whom it was employed and recommended. (See also *Ceratum Plumbi Subacetatis,* N. F., Part III.)

The ointment of subacetate of lead was formerly largely used in *excoriations, burns, scalds,* and *chilblains,* but is infrequently employed at present.

UNGUENTUM POTASSII IODIDI. Br.

POTASSIUM IODIDE OINTMENT

Ointment of Potassium Iodide; Pommade d'Iodure de Potassium, *Fr. Cod.;* Unguentum Kalii jodati, *P. G.;* Jodkaliumsalbe, Kaliumjodidsalbe, *G.*

"Potassium Iodide, 10.0 *grammes;* Potassium Carbonate, 0.6 *gramme;* Distilled Water, 9.4 *grammes;* Benzoated Lard, 80.0 *grammes.* Dissolve the Potassium Iodide and Potassium Carbonate in the Distilled Water; mix the solution, gradually, with the Benzoated Lard, in a slightly warmed mortar. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

The former ointments of potassium iodide became discolored by time in consequence of the liberation of iodine. This was due to rancidity in the lard, and the slightest change in the fat would produce some discoloration. It was prevented in the U. S P. 1880 by the sodium thiosulphate, which also produces traces of sodium iodide and sulphur. The addition of potassium carbonate by the present Br. Pharmacopœia is made with the same object.

The *Bulletin de Pharmacie du Nord* recommended a concentrated solution of potassium iodide in glycerin as a basis for this ointment. One gramme of the salt is dissolved in two and a half grammes of hot glycerin, and the solution mixed with the fatty constituent in the proper proportion. The advantages of this method are that the ointment is free from crystals, and the salt more readily absorbed. The glycerin would probably not be objectionable in most cases, and potassium carbonate could be added, if desired. Ointment of potassium iodide is employed for the discussion of *goiters, scrofulous tumors,* and other *indolent swellings,* and is sometimes preferred to the ointment of iodine, as it does not, like that, discolor the skin. It does not, however, possess the antiseptic nor counter-irritant properties of the free iodine.

UNGUENTUM STAPHISAGRIÆ. Br.

STAVESACRE OINTMENT

Onguent de Staphisaigre, *Fr.;* Stephanskörnersalbe, *G.*

"Stavesacre Seeds, 20 *grammes;* Yellow Beeswax, 10 *grammes;* Benzoated Lard, 85 *grammes.* Crush the Stavesacre Seeds; digest the crushed seeds with the Benzoated Lard on a water-bath for two hours; strain and press through calico; melt the Beeswax in the liquid mixture; stir until cold. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

This ointment is but half the strength of that official in the British Pharmacopœia 1885; it is said to be non-irritant, and is largely used in Great Britain for destroying *body-lice,* also in *scabies* and *prurigo.*

UNGUENTUM SULPHURIS. U. S., Br.

SULPHUR OINTMENT Ung. Sulphur.

Pomatum Sulfuratum, Unguentum Sulfuratum Simplex; Pommade Soufrée, *Fr. Cod.;* Schwefelsalbe, *G.*

"Sublimed Sulphur, 15 Gm.; Benzoinated Lard, 85 Gm.; to make about 100 Gm. Rub the sublimed sulphur, which must be free from gritty particles, with a small portion of the benzoinated lard until smooth, and incorporate uniformly the remainder of the benzoinated lard with the sulphur mixture." *U. S.*

"Sublimed Sulphur, 10 *grammes;* Benzoated Lard, 90 *grammes.* Triturate the Sublimed Sulphur with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

Washed sulphur was substituted in the U. S. P., 1890, for the sublimed sulphur of the former Pharmacopœia; the change was of questionable utility and the U. S. P. has returned to the use of sublimed sulphur. It has been found that the acid products resulting from the slight decomposition in sublimed sulphur have value as parasiticides. The disagreeable odor may be partially concealed by oil of lemon or oil of bergamot.

This ointment affords a ready means of obtaining the local action of sulphur. For discussion of its properties, see *Sulphur.*

UNGUENTUM ZINCI OLEATIS. Br.

ZINC OLEATE OINTMENT

Pommade d'oléate de zinc, *Fr.;* Zinkoleatsalbe, *G.*

"Zinc Sulphate, 30 *grammes;* Hard Soap, in shavings, 90 *grammes;* Distilled Water, boiling, Soft Paraffin, white, of each, *a sufficient quantity.* Dissolve the Zinc Sulphate in sixty millilitres of the Distilled Water. Dissolve the Hard Soap in six hundred millilitres of the Distilled Water. Mix the solutions; heat to boiling; allow the melted zinc oleate so produced to rise to the surface; cool until it solidifies; pour off the aqueous liquid; boil the zinc oleate with successive quantities of Distilled Water until the washings afford not more than a slight *reaction* for sulphates; reduce the cake thus obtained to a coarse powder; dry at a temperature below 60° C., melt on a water-bath with an equal weight of the Soft Paraffin; stir until cold." *Br.*

This ointment was radically changed in the Br. Ph., 1898, revision; instead of using zinc oleate made from oleic acid and zinc oxide, a process is ordered which directs the zinc oleate to be made by double decomposition between zinc sulphate and sodium oleo-stearate (hard soap). The product is a white, fine precipitate; it is, however, not a pure oleate, but a zinc oleo-stearate or oleo-palmitate.

This preparation has therapeutic properties similar to those of the ointment of zinc oxide, but is a little more stimulating. It is especially useful in *chronic eczema* and similar *cutaneous eruptions.*

UNGUENTUM ZINCI OXIDI. U. S. (Br.)

OINTMENT OF ZINC OXIDE Ung. Zinc. Ox. [Zinc Ointment]

Unguentum Zinci, *Br.;* Ointment of Zinc; Unguentum de Nihilo Albo; Pommade d'Oxyde de Zinc, Cérat épulotique, *Fr.;* Unguentum Zinci, *P. G.;* Zinksalbe, *G.;* Pomada de Oxido Zincico, *Sp.*

"Zinc Oxide, in very fine powder, 20 Gm.; Paraffin, 15 Gm.; White Petrolatum, 65 Gm.; to make about 100 Gm. Rub the zinc oxide, which must be free from gritty particles, with about one-fourth of the melted paraffin and white petrolatum in a previously warmed container, and with this incorporate the remainder of the melted mixture. If necessary, strain the Ointment while warm, and stir until it congeals." *U. S.*

"Zinc Oxide, 15 *grammes;* Benzoated Lard, 85 *grammes.* Mix by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

The assay of this ointment for its zinc oxide content may be easily accomplished, according to J. L. Mayer (*Proc. N. Y. P. A.*, 1913, p. 226) by igniting a weighed portion of the ointment and weighing the resulting zinc oxide. Care should be taken, after combustion has begun, to withdraw the burner and allow the sample to burn quietly until all inflammable matter is consumed. If the resulting oxide is not white in color it may be moistened with nitric acid and re-ignited. The same procedure will serve for the assay of ointment of zinc stearate.

The British ointment is weaker in the proportion of zinc oxide than that of the U. S. Pharmacopœia, the former containing about 15 per cent., the latter 20 per cent. *Commercial* zinc oxide should not be used, as it is usually gritty, and it is difficult to make a smooth ointment with it. Commercial zinc oxide is sometimes contaminated with lead to an appreciable amount and for that reason alone should not be employed in making this important and widely used ointment; the many expedients that have been suggested by various writers, such as the use of a paint mill or of a flat iron, or trituration with oil or with glycerin, are unnecessary if official zinc oxide is employed and the directions of the Pharmacopœia followed.

The change in the base of this important ointment from lard to petrolatum was made by the U. S. X after consultation, by questionnaire, with the members of the American Dermatological Society. Nevertheless we feel that the new ointment will have somewhat different therapeutic action from that formerly official. With a lard base the fat is largely absorbed and leaves a protective deposit of zinc oxide on the skin; with the new formula the petrolatum being almost non-absorbable the skin remains more greasy. The new preparation has the advantage of not becoming rancid.

To what the peculiar virtues of this ointment are due is not certainly known. The emollient effect of the base and the protective action of the metallic salt are obviously important properties, but the ointment seems to have some other influence on the skin; perhaps the zinc may exert a mild antiseptic or astringent action. However it acts, it is one of the most widely employed unguents in a large variety of diseases and irritations of the skin.

URGINEA. Br.

URGINEA [Indian Squill]

"Urginea consists of the younger bulbs of Urginea indica, *Kunth,* collected soon after the plants have flowered, divested of their dry, outer, membranous coats, cut into slices, and dried. When powdered should be kept quite dry over quicklime." *Br.*

Urginea indica is a plant resembling *Urginea maritima* (see *Scilla*) but produces a smaller tunicated bulb. Urginea indica grows in sandy soil near the sea coast throughout India and also extends to the lower Himalayas. The medicinal properties of the drug are apparently identical with the squill of the Greeks. The outer coats are quite inert and should be removed as indicated in the definition of the Br. Pharm.

"Curved or sickle-shaped strips, separated or connected, several together, to a portion of the shortened axis; usually one to five centimetres long and five to ten millimetres wide; yellowish-white, fleshy, often longitudinally ribbed; tough when slightly moist, but brittle and pulverisable when dry. No odor; taste bitter and acrid." *Br.*

The bulbs of *Urginea indica* are rounded, conical or pear-shaped and about the size of an onion; tunicated, consisting of fleshy coats which enclose each other completely; color whitish; taste bitter and acrid.

Uses.—The bulbs of Indian squill have long been used in India for purposes similar to that for which the official squill is employed in Europe and America, but no sufficient chemical examinations have been made to prove the identity of the Indian and European drugs.

Dose, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Acetum Urgineæ, *Br.;* Oxymel Urgineæ (from Vinegar), *Br.;* Pilula Ipecacuanhæ cum Urginea, *Br.;* Pilula Urgineæ Composita, *Br.;* Syrupus Urgineæ, *Br.;* Tinctura Urgineæ, *Br.*

UVA URSI. U. S. (Br.)

UVA URSI [Bearberry]

"Uva Ursi is the dried leaf of *Arctostaphylos Uva-ursi* (Linné) Sprengel (Fam. *Ericaceæ*). Uva Ursi contains not more than 5 per cent.

of its stems or other foreign organic matter." *U. S.* "Bearberry Leaves are the dried leaves of Arctostaphylos Uva-ursi, *Spreng.*" *Br.*

Uvæ Ursi Folia, *Br.;* Barren Myrtle, Mountain Box, Rockberry; Kinnikinnic; Busserole, Raisin d'Ours, *Fr.;* Folia Uvae Ursi, *P. G.;* Bärentraubenblätter, *G.;* Uva Ursina, *It.;* Gayuba, *Sp.*

The *uva ursi,* or *bearberry,* is a low evergreen shrub, with trailing stems, the young branches of which rise obliquely upward for a few inches. The leaves are scattered, upon short petioles, from half an inch to an inch long, obovate, or oblong-spatulate, acute at the base, obtuse at the apex, entire, with a rounded margin, thick coriaceous, smooth, shining, deep green on their upper surface, paler and covered with a network of veins beneath; furnished especially near the margin or near the midrib with minute hairs, which are usually abundant in young leaves, but may be few or absent in old leaves, especially those which have been much handled. The flowers, which stand on short reflexed peduncles, are in small clusters at the ends of the branches. The calyx is small, five-parted, reddish, and persistent. The corolla is urceolate, reddish-white, or white with a red lip, transparent at the base, contracted at the mouth, and divided at the margin into five short reflexed segments. The stamens are ten, with short filaments and bifid anthers; the ovary round, with a style longer than the stamens, and a simple stigma. The fruit is a small, round, depressed, smooth, glossy red berry, with an insipid mealy pulp and five cohering seeds.

This humble but hardy shrub inhabits the northern latitudes and high mountains of Europe, Asia, and America. On the American continent it extends from Hudson Bay as far southward as New Jersey and Pennsylvania, in some parts of which it grows in abundance. It prefers a barren soil, flourishing on gravelly hills and elevated sandy plains. The leaves are the only part used in medicine. They should be gathered in autumn, and only the green leaves selected. The present commercial supplies of this drug are partly imported from Spain and partly obtained from plants growing wild in California and the northwestern states.

In Europe the uva ursi is adulterated with the inert leaves of the *Vaccinium Vitis-Idæa* L. (*Cowberry, Mountain Cranberry*); these may be distinguished by being obovate, having revolute margins which are sometimes slightly toothed, and the presence of fine blackish dots or bristly points upon their lower surface. Leaves of the *Chimaphila umbellata* (L.) Nutt., sometimes found among the uva ursi, may be readily detected by their greater length, their cuneiform-lanceolate shape, and their serrate edges.

Arctostaphylos glauca Lindl., *manzanita,* is a small tree or shrub indigenous in California, where it generally grows in dry and rocky places on the west of the mountain ranges. The leaves appear to possess properties similar to those of the official species. (See Flint, *A. J. P.,* 1873, p. 187.) The fruit of *A. arguta* Zucco, a Mexican species, is said to be a narcotic poison.

Description and Physical Properties.—"*Unground Uva Ursi.*—Usually unbroken, obovate, oblong or spatulate, from 12 to 30 mm. in length, from 5 to 13 mm. in breadth; apex obtuse or rounded; margin entire, slightly revolute; base cuneate, tapering into a short, stout petiole; upper surface dark green, glabrous and shiny, finely reticulate; under surface yellowish-green and slightly pubescent, especially on the midrib; coriaceous; fracture short; odor slightly aromatic, tea-like; taste astringent and somewhat bitter.

"*Powdered Uva Ursi.*—Olive green; epidermal cells polygonal, those of the lower surface showing broadly elliptical stomata about 0.04 mm. in length, surrounded by 5 to 8 neighboring cells; cells of mesophyll with chloroplastids and frequently irregular masses of a carbohydrate; fragments of fibro-vascular bundles with spiral tracheæ associated with narrow, strongly lignified, sclerenchymatous fibers and frequently also with crystal-fibers showing mono-clinic prisms, from 0.006 to 0.030 mm. in diameter; numerous fragments made up of cells having a yellowish-brown content colored a bluish-black upon the addition of ferric chloride T.S.

"Place 0.1 Gm. of powdered Uva Ursi on a watch crystal, cover with another watch crystal, and gently heat the powder: a crystalline sublimate of hydroquinonone is formed, consisting of long rods and feather-like aggregates which polarize light with a brilliant play of colors. Macerate 1 Gm. of powdered Uva Ursi with 10 cc. of boiling water, shake the mixture occasionally until cold, and filter: the filtrate yields a grayish-purple precipitate upon the addition of a few drops of ferrous sulphate T.S." *U. S.*

"Obovate or spatulate, about two centimetres long, yellowish-green, coriaceous, entire, shortly petiolate. Upper surface glabrous, shining, reticulate; veinlets depressed. Slight odor; taste very astringent." *Br.*

The commercial drug frequently consists of the entire plants and therefore contains a large quantity of stems. The latter should not be present, according to the official definition, in greater amount than five per cent. Farwell states that the leaves are sometimes very dark or blackish-green, which is probably due to carelessness in drying. (*M. R.,* xvii, p. 35.) Holm has contributed an interesting article on the morphology of the plant. (*M. R.,* xx, p. 95.)

Uva ursi leaves contain—besides tannic and gallic acids, quercetin, bitter extractive resin, gum, fatty matter, and salts of potassium and calcium—two glucosides, *arbutin,* $C_{12}H_{16}O_7$, and *ericolin,* $C_{34}H_{56}O_{21}$, and a crystalline principle, *urson,* $C_{20}H_{34}O_2$. There is present also a small amount of volatile oil which is probably a decomposition product of ericolin. The tannin is so abundant (6 or 7 per cent.) that the leaves are used for tanning in Russia.

Arbutin is widely diffused in the species of *Ericaceæ,* such as species of *Vaccinium, Rhododendron,* and *Chimaphila,* also in *Epigæa repens* L., and *Gaultheria procumbens* L. Arbutin occurs in long, acicular, colorless crystals, united in tufts, and of a bitter taste. It is soluble in water, alcohol, and ether, fusible at 195° C., without action on vegetable colors, and not precipitated by ferric salts or by lead acetate or subacetate. It is a glucoside, being resolvable by emulsin, or more rapidly by boiling with sulphuric acid, into glucose and *hydroquinone,* $C_6H_6O_2$ (*arctuvine* of Kawalier). Schiff has shown that arbutin is almost always accompanied by *methylarbutin,* $C_{12}H_{15}(CH_3)O_7 + H_2O$. This latter compound has been made synthetically by Schiff (*B. Chem. G.,* 1882, p. 1841) by acting upon arbutin with methyliodide and potassium hydroxide in methyl alcohol solution, and purely synthetically by Michael (*B. Chem. G.,* 1885, p. 118) by the action of methylhydroquinone and acetochlorhydrose. It is decomposed by dilute acids into glucose and methylhydroquinone. Upon heating 1 part of arbutin with 8 parts of manganese oxide, 2 parts of sulphuric acid, and 1 part of water, it gives off the penetrating odor of quinone. The aqueous solution is rendered blue by a small quantity of solution of ferric chloride and green by a larger quantity. It dissolves in sulphuric acid, forming a colorless solution, turning red after a short time; a trace of nitric acid turns this solution yellow-brown. A good test for arbutin is that of Jungmann: Phosphomolybdic acid added to an alkaline solution of arbutin gives a blue color.

A. G. Perkin has obtained from the leaves of uva ursi a yellow coloring principle of the composition $C_{15}H_{10}O_7$, crystallizing in glistening yellow needles. On fusion with alkali, phloroglucinol and protocatechuic acid were formed. Though resembling quercetin in these points, it forms deep green solutions with diluted potassium hydroxide. (*A. J. P.,* 1898, 584.) Shippee and Fogele (*Chem. News,* 1918, cxvii, 254) analyzed the fruit of uva ursi commonly known as *red bearberry* or *kinnikinic* and report protein 4 per cent., sugars (chiefly levulose) 21 per cent., a dark gummy substance and 2.9 per cent. of ash.

Uses.—Uva ursi is used to-day almost exclusively in the treatment of catarrhs of the urinary tract, especially *acute cystitis.* Although by some it is believed to exercise an astringent and alterative influence on these membranes, it is probable that its action is simply that of a mild antiseptic. Lewin (*V. A. P. A.,* 1883, xcii, p. 517) attributes its virtues to the arbutin which is decomposed in the system liberating hydroquinone. Bass, however (*Z. E. P. T.,* 1912, x, p. 120), is doubtful whether enough hydroquinone can appear in the urine to exercise any antiseptic effect. But whether or not its virtue is due to arbutin or some other principle, the clinical evidence is strong that uva ursi is a useful drug in these conditions. Formerly it was also employed in *gravel, nephritis, urethritis,* and *menorrhagia,* but has been largely abandoned. Because of the formation of hydroquinone in the body the urine often acquires a greenish color from the use of uva ursi.

Arbutin has been employed in medicine not only for its antiseptic effect but also as a diuretic in doses of from one to three grains (0.065–0.2 Gm.).

Dose, powdered uva ursi, from twenty grains to a drachm (1.3–3.9 Gm.), but the fluidextract is usually preferred.

Off. Prep.—Fluidextractum Uvæ Ursi, *U. S.;* Infusum Uvæ Ursi, *Br.;* Elixir Buchu Compositum (from Compound Fluidextract of Buchu), *N. F.;* Fluidextractum Buchu Compositum, *N. F.*

VACCINUM VARIOLÆ. U. S.

SMALLPOX VACCINE Vaccin. Var. [Virus Vaccinicum U. S. P. IX, Glycerinated Vaccine Virus, Jennerian Vaccine]

Vaccine Virus; Impfstoff, *G.;* Virus vaccin, *Fr.;* Vaccino, Virus di vacca, *It.;* Vacuna, *Sp.*

Though constantly used by the medical profession for more than a century, this article was first admitted into the United States Pharmacopœia in the Ninth Revision. Vaccination against smallpox is the oldest and the surest method of preventive medicine, directed against a specific disease. Its efficacy was first proven by Jenner in England in 1796, and soon corroborative evidence was supplied from America, notably by Waterhouse of Boston. Up to the middle of the nineteenth century, the vaccine material was commonly taken from the arm of a person previously vaccinated and thus carried on from patient to patient. At present the calf serves exclusively in this country as the animal for propagating the virus to be used on human subjects; the danger of transmitting some other latent disease of man at the same time is thus avoided. Other improvements which have occurred in the course of time are the use of the more potent pulp, instead of the lymph of the vesicle on the calf, and especially the use of glycerin as a preservative. The glycerin is allowed to act on the virus for a numer of days before use, and by this means the bacteria, normally present on the skin of the calf from which the virus is taken, are very greatly reduced in number. Phenol and ether have also been used to obtain a nearly sterile vaccine. The only form of dispensing now allowed is in the sterile capillary tube.

"Smallpox Vaccine consists of a glycerinated suspension of the vesicles of vaccinia or cowpox which have been obtained from healthy vaccinated animals of the bovine species. The vesicles must be removed and the vaccine must be prepared under aseptic conditions. The vesicles must be removed from the animal at the time of maximum potency, thoroughly triturated and made into a smooth suspension with an aqueous solution of glycerin. This solution shall not be acid to bromcresol purple T.S. or distinctly alkaline to phenol red T.S.

"Smallpox Vaccine must be prepared in an establishment licensed by the Secretary of the Treasury of the United States. The following precautions must be observed in licensed establishments.

"No vaccine shall be used from any animal having a communicable disease, other than vaccinia. Animals used for propagating Smallpox Vaccine must have been previously subjected to a tuberculin test and must have been held at least seven days in quarantine under daily veterinary inspection prior to vaccination. After the vaccine pulp is removed from each animal, a necropsy shall be performed, permanent records of which shall be kept. Each lot of Smallpox Vaccine shall be examined to determine its freedom from undue bacterial content and a special examination shall be made of each lot to determine the absence of tetanus organisms and other pathogenic anaerobes. Permanent records must be kept of these examinations. The finished product must be placed in sterile containers that comply with the requirements of the law and of the regulations established by the United States Public Health Service.

"Each package of Smallpox Vaccine must bear upon the label the name of the product, the name, address, and license number of the manufacturer, and a statement of the date beyond which the contents cannot be relied upon to yield their specific results. The label must also bear the lot number of the Vaccine, and directions concerning the storage of the package below 5° C.

"Smallpox Vaccine loses potency rapidly, even at moderate temperature. It must therefore be kept at the lowest possible temperature, preferably below 0° C., and never above 5° C." *U. S.*

The propagation of vaccine virus requires sterile laboratory equipment and careful technic throughout. The animals must be tuberculin tested, repeatedly inspected and kept very clean; the removal, grinding, and distribution of the vaccine into its final containers are strict aseptic operations.

Uses.—To appreciate what vaccination has done for mankind, it is necessary to consider the era before vaccination, when having had smallpox was one of the evidences of maturity, and the toll of lives yearly demanded by this disease was a constant drain on every class of humanity. In more recent times the regions where vaccination is little practiced are conspicuous for the number of pock-marked faces; opposition to vaccination was so general in Montreal that when in 1886 a Pullman car conductor brought smallpox from Chicago, an epidemic broke out which in nine months killed 3164 persons. As a contrast to this may be cited the experience of smallpox hospitals, where doctors, nurses, and attendants never having had smallpox are kept immune by vaccination. Smallpox among the unvaccinated is the most contagious disease known, yet vaccination is often too lightly regarded in that it is carelessly performed and no attention is given the patient after the operation. Any wound is liable to complications; a wound intentionally given should be particularly guarded against infection. Vaccination by scarification or cross-hatching, which forms an ulcerating area of appreciable extent—and the use of vaccination shields or other inappropriate after-care are the most frequent causes of sore arms. To vaccinate, the skin of the upper arm near the insertion of the deltoid muscle should be cleansed and dried. Soap and water followed by alcohol, or ether may be used for this purpose, but no stronger antiseptic should be applied. The cotton or cloth with which the skin is wiped should be sterile and nothing else allowed to touch the site. The capillary tube may be wiped with alcohol, the ends broken inside the bulb, and the glycerinated virus expelled by the bulb to form a line on the cleansed skin. Drawing the skin tight by grasping the arm beneath, a single incision about one quarter of an inch long and parallel with the arm is made through the virus. This incision may be made with a flamed needle or other sterile instrument and should penetrate the papillary layer, but preferably not draw blood. The virus should be thoroughly rubbed into the incision with a smooth sterile instrument, such as the side of the needle. No other incision or cross-scratching should be made unless there will be no opportunity for revaccination; in the latter case similar single incisions may be made on either side of the first and at least an inch away; other tubes should be used for this purpose. By this means the pustulation is limited so that large confluent crusts are not formed and deep ulceration with the tendency to secondary infection is avoided. Another method which produces even a smaller wound, but is surely successful only with very fresh virus is inoculation by the twisting abrasion. A dentist's drill (sterilized each time by flaming or other method) is used for this purpose. A slight twirling motion between the thumb and forefinger causes this instrument when pressed against the skin to give a shallow area denuded of epidermis, but without bleeding, no larger than a pinhead. To this the virus can be applied and rubbed in as above described. The vaccination area should dry (not in direct sunlight) for fifteen minutes or half an hour before being covered with clothing. The arm must be kept clean, dressed aseptically when the vesicle appears, and, when pustulation ensues, treated antiseptically. No dressing should be allowed to remain on the arm more than forty-eight hours. The arm should be seen by the physician on the third, sixth and ninth day at least, to determine the character of the reaction, and as often as may be necessary thereafter to insure rapid healing of the wound. It is preferable if the whole process can take place without the crust breaking. Vaccination is a surgical procedure and is worthy not only of the painstaking asepsis of a skilled physician, but of his intelligent after-care as well. If never previously vaccinated, the patient usually shows a papule about the fourth day, a vesicle about the fifth, and a pustule the eighth. Re-vaccination may be more rapid in its course, and correspondingly milder; in some cases a small papule is seen on the second day, subsiding without further progress. These abortive accelerated reactions may be taken as indicative of a degree of immunity.

The protection given by vaccination is relative, not absolute, and re-vaccination should be done when exposure to smallpox takes place or is threatened. All infants, except in the presence of eczema or marasmus, should be vaccinated before teething begins; re-vaccination should be performed before entering school and again at the age of fifteen.

Vaccine virus is the most rapidly deteriorating product likely to be carried by the pharmacist, and should be kept in the coldest part of an ice-box, at a temperature preferably below 0° C. and never above 5° C.

VALERIANA. U. S. (Br.)

VALERIAN Valer.

"Valerian consists of the dried rhizome and roots of *Valeriana officinalis* Linné (Fam. *Valerianaceæ*). Valerian contains not more than 5 per cent. of foreign organic matter and yields not more than 10 per cent. of acid-insoluble ash." *U. S.* "Valerian Rhizome is the dried rhizome and roots of Valeriana officinalis, *Linn.* Collected in the autumn." *Br.*

Valerianæ Rhizoma, *Br.;* Valerian Root; Radix Valerianæ Minoris, R. Valerianæ Sylvestris, R. Valerianæ Montanæ; Common, Garden, Cat's or Great Wild Valerian, All-heal, Garden Heliotrope; St. George's Herb; Summer Heliotrope, Herb Bennet, Vandal Root; Racine de Valériane, Valériane, *Fr.;* Radix Valerianae, *P. G.;* Wilde Baldrianwurzel, Baldrianwurzel, *G.;* Valeriana, *It.;* Valeriana (Rizoma de), *Sp.*

Official or common valerian (*Valeriana officinalis*) is a large, handsome, herbaceous plant, with a perennial rhizome, and an erect, round, channelled stem, from two to four feet high, furnished with opposite pinnate leaves, and terminating in flowering branches. The leaves of the stems are attached by short, broad sheaths; the radical leaves are larger and long petiolate. In the former the leaflets are lanceolate and partially dentate, in the latter elliptical and deeply serrate. The flowers are small, white or rose-colored, quite fragrant, and disposed in terminal corymbs interspersed with pear-shaped bracts. The number of the stamens is three. The fruit is a capsule containing one oblong-ovate, compressed seed. The plant is a native of Europe, where it grows either in damp woods and meadows or on dry elevated grounds. As found in these different situations, it presents characters so distinct as to have induced some botanists to make two varieties. Dufresne makes four, of which three prefer marshy situations. The variety which affects a dry soil (*sylvestris* L. Ph.) is not more than two feet high, and is distinguished by its narrow leaves.

The valerian plant is cultivated to some extent in New England and New York, and on an extensive scale in England, and various parts of Europe and in Japan. In this country it will grow in light, well-prepared, and well-drained soil, and is propagated by dividing the roots in the fall and setting these portions in rows about two feet apart. (*D. C.*, lvi, p. 134.) In Europe it appears to be grown in a clayey soil. (*Pac. Pharm.*, vii, p. 297.) Mitlacher reports on the results of his experiments on the cultivation of valerian. (*Zeit. Oest. Apoth. Ver.*, l, p. 459.)

Valeriana mexicana DC.—According to the *Nueva Farmacopea Mexicana,* the roots of this plant contain a large percentage of valeric acid, which they yield readily and economically. In Mexican commerce they are said to occur in slices or fleshy disks about four centimeters or more in diameter, or in voluminous tubercles. Externally the color is grayish-yellow, internally yellow; the odor is strong and disagreeable, the taste bitter. R. McLaughlin (*A. J. P.*, 1893, 329) found 3.3 per cent. of oil in the Mexican valerian root. (See also *Schim. Rep.*, April, 1897.)

Japanese Valerian. Kesso Root.—This, formerly believed to be the product of *Patrinia scabiosæfolia* Link, is now said to be obtained from *V. officinalis* var. *latifolia* Miq. It yields a volatile oil. (*P. J.*, xx, 837; xxi, 1069.) The rhizome, sometimes known as *Valerianæ Radix Majoris,* is obtained from *V. Phu* L., of southern Europe, and western Asia. It is from 4 to 6 inches long, ½ inch in thickness, brown, annulated with numerous yellowish roots, and a feeble, valerian-like odor and taste.

The root should be collected in spring, before the stem begins to shoot, or in the autumn, when the leaves decay. It should be dried quickly, and kept in a dry place. It consists of numerous, long, slender, brittle, cylindrical, thick-barked rootlets, issuing from an erect tuberculated rhizome. The drug of commerce comes chiefly from England, Belgium and Germany.

Description and Physical Properties.—"*Unground Valerian.*—Rhizome upright, from 2 to 4 cm. in length, and from 1 to 2 cm. in diameter, usually cut longitudinally into 2 to 4 pieces; externally yellowish-brown or dark brown, upper portion with stem bases and frequently with a short horizontal branch or stolon, and from the outer surface arise numerous slender, brittle roots; fracture of rhizome short and horny; internally light brown, with a thick bark and narrow central cylinder; odor of valeric acid, becoming stronger upon aging; taste sweetish, camphoraceous and somewhat bitter.

"*Structure.*—Root with a single epidermal layer of papillose cells, some being modified to root hairs; a hypodermal layer bearing secretion cells with suberized walls and usually containing numerous small globules and occasionally small prismatic crystals; cortical parenchyma, the cells filled with starch, some of the cells near the hypodermis containing a few oil globules; an endodermis of thin-walled cells surrounding a pericambium; a central cylinder with usually 3 to 5 fibro-vascular bundles. Older roots with a large pith of starch-bearing parenchyma, a secondary thickening in the fibro-vascular bundles and a periderm of a few layers of cells. Rhizome with a thin periderm, a cortical parenchyma with scattered fibro-vascular bundles, a layer of altered cells of the endodermis, numerous, more or less twisted, collateral, fibro-vascular bundles and a large pith.

"*Powdered Valerian.*—Light brown to grayish-brown; starch grains numerous, from 0.003 to 0.020 mm. in diameter, spherical, plano-convex, polygonal, 2- to 4-compound and each usually with a central cleft; tracheal fragments, the walls having simple and bordered pores or scalariform and reticulate thickenings, accompanied by narrow fibers, the walls of the latter being thin, porous, and strongly lignified; occasional fragments of epidermis with root-hairs, and fragments of cork." *U. S.*

"Rhizome short, erect, entire or sliced, dark yellowish-brown externally, whitish internally. Roots numerous, about seven to ten centimetres long, of the same color as the rhizome, slender, brittle. Strong, characteristic, disagreeable odor; taste unpleasant, camphoraceous, slightly bitter. Ash not more than 10 per cent." *Br.*

The roots of *Valeriana Phu* L., and *V. dioica* L., are said to be sometimes mingled with those of the official plant. According to Ebermayer, in Germany various ranunculaceous roots are a dangerous adulterant of valerian; they may be readily detected by their want of the peculiar odor of the official root. According to M. O. Raveil, the valerian in the markets of Paris has been largely adulterated with the roots of *scabious* (*Scabiosa succisa* L., and *S. arvensis* L.). They are shorter than the genuine root, with larger radicles, less rough, little or not at all striated, very brittle, with a white amylaceous fracture. The roots are inodorous in themselves, but are very apt to acquire odor from contact with the valerian. (*J. P. C.*, xxvi, 209.)

The odor in the fresh root is pleasantly aromatic, but in the dried is stronger and less agreeable. Cats are strongly attracted by it. The taste is at first sweetish, afterwards bitter and aromatic.

Trommsdorff found it to consist of 1.2 parts of volatile oil, 12.5 of a peculiar extractive matter, soluble in water, insoluble in ether and alcohol, and precipitated by metallic solutions, 18.75 of gum, 6.25 of a soft odorous resin, and 63 of lignin. Of these constituents the most important is the *volatile oil.* This occurs only in the subepidermal cells of the root. It is lævorotatory, of a pale greenish color, of the sp. gr. 0.934, with the pungent odor of valerian, and an aromatic taste. It becomes yellow and viscid by exposure. Schimmel & Co. (*Schim. Rep.*, April, 1897) summarize their researches upon valerian oil from different sources: In the oil from Dutch and Thuringian roots, the amount varying from 0.5 to 1 per cent., they find pinene, camphene, borneol, bornyl formate, bornyl acetate, and *bornyl isovalerate,* together with a sesquiterpene and an alcohol, $C_{15}H_{26}O$. In the oil from Japanese roots (amounting to from 6 to 6.5 per cent.), they find pinene, camphene, dipentene, terpineol, borneol, bornyl acetate, bornyl isovalerate, and *kessyl acetate.* Trommsdorff ascertained the existence in the oil of *valeric acid.* (See Part II.) The acid does not pre-exist in the oil, but is produced by the decomposition of its borneol ester. Söderberg (*P. J.*, 1918, ci, 120) assays valerian root by steam distillation, neutralization of the distillate, shaking out with ether, distilling the ethereal solution and drying the oily residue in a desiccator. He reports from 2.00 to 3.18 per cent. of oil present.

Goris and Vischniac (*C. R. A. S.*, 1921, clxxii, 1059) confirm the statement of Chevalier that valerian root contains two alkaloids, of which one is soluble in ether (*chatinine*) and the other insoluble in ether (*valerine*) but soluble in chloroform.

Uses.—Valerian is used as a sedative to the higher nerve centers in conditions of *nervous unrest, hysteria, hypochondriasis, neuralgic pains,* and the like. The virtues of the plant seem to depend chiefly on the esters of valeryl which are contained in the volatile oil. According to Chevalier (*Nouv. Rem.*, 1912, xxix, p. 169), the volatile oil of valerian is a depressant to the whole central nervous system, including both the motor and psychical centers of the brain and the motor cells of the spinal cord. The experiments of Macht and Giu (*J. P. Ex. T.*, 1921, xviii, p. 361) upon rats suggest that the cerebral sedative action of valerian is a reflex from the olfactory organs. The esters contained in this drug are unstable bodies and in the process of drying largely oxidized with the formation of valeric acid. As the latter is practically without physiological action much of the virtue of the plant is lost during the drying process. Probably for this reason preparations of this drug are very uncertain in their activity and valerian has largely fallen into disrepute. Chevalier has introduced the juice of the fresh root which he asserts is a valuable remedy not only for the conditions mentioned above, but even as a narcotic in *insomnia* and an anticonvulsant in *epilepsy.* The dose of this juice, which has been introduced under the name of *energetene of valerian,* is one to three coffee-spoonfuls. It appears also to have some slight influence upon the circulation, slowing the heart and increasing its force, and causing a rise in blood pressure, and has been used in the treatment of *cardiac palpitations.*

Dose, twenty to forty grains (1.3–2.6 Gm.). The dose of the oil of valerian, which is occasionally employed, is four to five minims (0.25–0.3 cc.).

Off. Prep.—Tinctura Valerianæ, *U. S.;* Tinctura Valerianæ Ammoniata, *U. S., Br.;* Fluidextractum Valerianæ, *N. F.*

VALERIANÆ INDICÆ RHIZOMA. Br.

INDIAN VALERIAN RHIZOME

"Indian Valerian Rhizome is the dried rhizome and roots of Valeriana Wallichii, *DC.*" *Br.*

Valeriana Wallichii is a perennial herb growing in the temperate Himalayas and in the Khasia Mountains. The rhizome is more largely used as a perfume than in medicine. It is used in preparations for the hair and the dried rhizome is used as an incense. It is officially described as follows: "Rhizome curved, about five centimetres long, from five to ten millimetres thick, dull brown, with raised transverse leaf-scars, numerous prominent root-scars and a few thick roots; the crown bearing the remains of petioles. Fracture short. In transverse section, dark with a large pith and diffuse ring of small wood-bundles. Strong, characteristic, disagreeable odor; taste unpleasant, camphoraceous." *Br.*

According to Lindenberg (*Ph. Z. R.,* 1886), Indian valerian is practically identical in its composition with the European drug, but contains a slightly larger amount of volatile oil. It may be employed in the same class of cases as valerian.

Off. Prep.—Tinctura Valerianæ Indicæ Ammoniata, *Br.*

VANILLA. N. F.

VANILLA Vanill. [Vanilla Bean]

"Vanilla is the cured, full-grown, unripe fruit of *Vanilla planifolia* Andrews (Fam. *Orchidaceæ*). Vanilla should be preserved in a cool place where it will not become brittle. Vanilla which has become brittle should not be used." *N. F.*

Vanille, *Fr. Cod.;* Fructus Vanillae, *P. G.;* Vanille, *G.*

Vanilla planifolia is a tall, perennial climbing epiphyte, with a very long, smooth, dark green stem, much branched, and furnished at the nodes with aerial roots, which cling to the tree or the wooden framework supporting the plant. The dark green, tough leaves are alternate, oval, sessile, attenuate at the apex, fleshy and veinless. The pale greenish-yellow, sessile flowers are about two inches in diameter, and occur in loose, axillary racemes of twenty or more blossoms. The fruit is a slender capsule, seven or eight inches long, filled with an oily mass containing numerous small, black, shining seeds.

This plant is a native of Mexico, but is now widely cultivated throughout the tropics and in greenhouses. Mexico, the Seychelles, Réunion and Society Island yield the bulk of the beans of commerce. It does well from the sea-level up to two thousand feet of altitude, requiring for its perfection, however, a moist, hot climate, with an habitual dry summer spell which seems to be necessary to bring good flowering. It is propagated by means of cuttings, sometimes two or three feet in length, but preferably from ten to twelve feet long, taken from growing shoots; these are planted after the dry season is over and should produce flowers in two years. Preferably placed upon trees, but sometimes on long stakes, trellises, wire supports, etc., the slip is placed with one end on the ground, covered with leaves or some light top dressing. In many cases the vines are planted so closely as scarcely to leave room for cultivators to pass, but it has been found that under these circumstances the vanilleries are especially liable to destructive fungous diseases. As the flower does not fertilize itself, fertilization (pollination) by hand is necessary; it is usually performed by women and children. In most localities not more than thirty fertilized flowers should be left to a plant. The pods reach their full size in from five weeks to eight months, according to the altitude of the locality and to the amount of shade. The first indication of ripening is a slight yellowing of the whole pod; as soon as this occurs the pods should be picked, and sorted, and the curing process commenced. If left to ripen further the pods are prone to split and otherwise deteriorate. For the purpose of curing them the pods are kept in a heated room for some days, then transferred to a cooler one and finished at ordinary temperature. During the process, which lasts some months, there is a loss of 70 to 80 per cent. of weight. For details as to culture, see articles by S. J. Galbraith in *Bulletin* 21, 1898, U. S. Department of Agriculture, Division of Botany, and by A. Franchère, *Bul. Econ. Gouvt. Gen. Madagascar,* vol. ii, No. 2, p. 122, 1914. The practice of curing the beans by placing them under blankets in the sun is still in vogue, but that of using a regulated artificial heat is more certain, and it is the modern method.

When thoroughly cured the beans are sorted according to length, those that have split or become otherwise defective being separated. They are then tied into bundles, which are wrapped in sheet lead or placed in small metallic boxes. In doing this it is essential that the bundle be wrapped in a thin vegetable parchment paper, as chemical action occurs when the beans come in contact with the metal.

Fruits which have not been picked early enough are inferior and are frequently cut into short pieces and sold as "cuts." If by chance the fruit should be picked too early the quality of the resulting product is distinctly inferior. The fruit as first picked has no aroma, the *vanillin* during the process of curing being produced from the glucoside *coniferin* in the interior of the fruit.

The cultivation of vanilla has extended from Mexico and South America throughout the tropics, so that at present, although the wild plant is abundant in the Mexican States of Vera Cruz and Oaxaca the vanilla of the markets comes almost exclusively from vanilleries. Holland is supplied from Java plantations; France from Tahiti, Madagascar, Réunion, Guadeloupe, and other of her colonies. From Mauritius and the Seychelles the product goes to London. In the markets most of the varieties are known by the name of the country in which they are produced. The finest of the varieties is the Mexican, although of recent years the Bourbon beans have so improved that they almost rival it in strength and flavor.

Of *Mexican vanilla,* the first quality occurs in pods from 15 to 20 cm. long, flattened, 6 to 8 mm. in diameter, with the lower end slightly attenuated, the upper end gradually tapering for about a quarter of the length of the pod, usually curved and slightly twisted near the point. The color is dark brown, the pods fairly plump, the surface ridged longitudinally, and with an incrustation of fine crystals beginning at the ends, gradually extending; when fresh somewhat viscid, but always roughish to the touch. For an interesting account of the Mexican vanilla plant by Charles E. Hires, see *A. J. P.,* 1893, 576. Cunningham states that the best quality of Mexican beans are those plucked in January and February but that much of the crop consists of beans plucked in October and November. Four classes of Mexican beans occur in commerce, viz., large-fine, small-fine, zacate and basura.

Of the Mexican vanillas the most valuable variety is the *papantha* bean, called *ley,* or *vainilla mansa* by the Spaniards; it consists of cylindrical, somewhat flattened pods, six or eight inches long, three or four lines thick, nearly straight, narrowing towards the extremities, bent at the base, shining and dark brown externally, wrinkled longitudinally, soft and flexible, and containing within their tough shell a soft black pulp, in which numerous minute, black, glossy seeds are embedded. It has a peculiar, strong, agreeable odor, and a warm, aromatic, sweetish taste. The interior pulp portion is most aromatic. In it are more or less numerous, minute crystals. Another variety, called *vainilla simarona* by the Spaniards, is smaller, of a lighter color, and less aromatic. The pods are said to be very dry and to contain no vanillin. According to Schiede, it is yielded by a distinct species, the *Vanilla sylvestris* Schiede. A third variety is the *vainilla pompona* of the Spaniards (*boba vainilla,* or *plátano vainilla*). In this, the pods are from 12 to 18 cm. long, from 12 to 18 mm. broad, shaped somewhat like a plantain, almost always open, very dark brown or nearly black, soft, viscid, and of a strong odor. Schiede states that it is the product of the *Vanilla Pompona* Schiede. The variety *vainilla vezacate* is said to be derived from pods gathered long before maturity. (*Nueva Farmacopea Mexicana.*) The *vainilla pompona* of the Spaniards is evidently the *vanillons* of European commerce, which are usually from 10 to 13 cm. long and from 15 to 25 mm. in diameter, frequently sharply angled, brown to red-brown in color, usually split open and free from efflorescence. Owing to the transverse markings by twine with which they have been wrapped during the process of curing, the beans have a peculiar twisted appearance. Their odor, which resembles that of heliotrope, is due to the presence in them of *heliotropin,* in lieu of *vanillin.*

Bourbon or *Indian Ocean vanilla,* produced in the Isle of Réunion, resembles Mexican vanilla, but is scarcely so long in the tapering portions, is of a dark brown almost black color, is not so firm as the Mexican, has the surface smooth and waxy, and soon becomes covered with a coating of acicular crystals known as "frost." The odor of this vanilla is said to resemble that of Tonka bean rather than that of Mexican vanilla.

The *Seychelles* and *Mauritius vanilla* (*inferior Bourbon* of the trade) has the pods about six inches in length, not over a quarter of an inch in width, and characterized by the pale color, the faint odor, and a smooth but not waxy surface.

South American or *Guadeloupe vanilla* resembles the Mexican bean, but is usually recognizable, when the bean is entire, by the latter being broad and flattened, usually half an inch or more wide, slightly tapering at the lower end, and at the upper sharply attenuated an inch or so at the point. It has a reddish brown color, and is of a rank odor. It is very pulpy, with a surface intermediate in feel between the Bourbon and the Mexican, and having but few crystals. One variety of this vanilla, sold under the name of *vanillons,* has the odor of heliotrope and is much used by perfumers and tobacco manufacturers.

Tahiti vanilla has its pods from six to seven inches long, flat, from three-eighths to half an inch wide, with a reddish-brown color. They are almost destitute of vanilla flavor, and have an odor suggesting heliotrope. It is said they contain piperonal and also vanillin. According to Constantin and Bois (*P. J.,* 1915, xcv, 360), there are two other sorts of vanilla grown in Tahiti; one is from a plant that they regard as a variety of *V. planifolia* from which it differs in the characters of foliage and the shape of the labellum in the flower; they propose to call it *V. planifolia* var. *Augusta.* The third sort has a flavor resembling that of the Java bean and a pleasant odor with an after-taste of heliotrope. They have not seen the flowers of this.

Java vanilla, which is almost exclusively consumed in Holland, has a pod from four to six inches long, with a flavor as fine as that of the Mexican bean, and a much stronger odor.

Description and Physical Properties.—"*Unground Vanilla.*—Fruit linear, flattened, from 15 to 35 cm. in length and from 5 to 9 mm. in width; apex terminating in a flat circular scar; gradually tapering, more or less bent and curved or hooked at the bases, or in the Tahiti variety, broad in the middle and tapering towards either end, the base closely resembling the summit; externally blackish brown, longitudinally wrinkled, moist-glossy; occasionally with an efflorescence of vanillin in the form of acicular crystals or monoclinic prisms; frequently with narrow, elliptical or irregular, more or less wrinkled, dark-brown patches of cork, occasionally split into three parts near the tip, flexible and tough, one-celled, containing a blackish brown pulp and numerous blackish brown seeds; the latter being flattened, irregularly triangulate or nearly circular in outline; reticulate and varying from 0.25 to 0.3 mm. in diameter. Odor and taste characteristic and very agreeable.

"*Structure.*—Epidermis with a somewhat thickened outer cuticularized layer having occasionally rounded or conical masses of an excretion of a gum-like substance; a layer of collenchyma of one or two rows of cells; a thick sarcocarp composed of parenchyma cells in which is imbedded an interrupted circle of fibrovascular bundles; the parenchyma cells are deeply undulate in outline and usually contain a thin protoplasmic layer enclosing numerous oily globules or may contain bundles of raphides of calcium oxalate; the individual crystals varying from 0.2 to 0.4 mm. in length; some of the parenchyma cells are specially modified and distinguished by their somewhat thickened walls with long, oblique, slit-like pores or the thickening may extend in the form of broad, spiral bands; in the fibro-vascular bundles the phlœm is central, being more or less surrounded by a few tracheæ, the walls possessing slit-like pores or spiral thickenings, and at the outside of the bundle is a closed circle of fibers, the walls being thin, strongly lignified, provided with numerous, transverse, simple pores, the outer wall of the outer row of fibers being irregular or sinuate; from the inner walls of the endocarp arise the placentæ bearing numerous brownish red or blackish seeds, and from the cells of the endocarp also arise numerous long, nearly straight hairs, the ends being rounded, the hairs being more or less matted together by a gummy or resinous mass in which some of the seeds are held; in mounts made in chloral hydrate T.S. or potassium hydroxide T.S., the immature, brownish red seeds show a deeply reticulate seed-coat, with cells of an oblong-polygonal form in surface view.

"Place a few of the crystals, occurring as an efflorescence on the fruit, on a microscope slide or watch crystal and add a drop of phloroglucinol T.S. and hydrochloric acid; the solution immediately acquires a carmine-red color (distinction from *benzoic acid*). The amount of extractive yielded to dilute alcohol should not be less than 12 per cent." *N. F.*

A characteristic test for the vanillin crystals which occur as an efflorescence on the fruit is as follows: On a microscope slide or watch crystal, place a few crystals and add a drop of phloroglucinol T.S. and hydrochloric acid; the solution immediately acquires a carmine-red color (distinction from *benzoic acid*). The amount of extractive which vanilla of good quality yields to dilute alcohol should not be less than 12 per cent. Nor should it yield more than 6 per cent. of ash.

Vanilla beans from which the vanillin has been removed by means of a solvent are sometimes offered for sale. The fraud is to be detected by the absence of flavor and odor. Such beans, and also beans of an inferior quality, are sometimes "improved" in appearance and in odor by the use of benzoic acid. For the detection of this fraud the pharmacist should avail himself of the fact that while the crystals of benzoic acid are flattened and rhomboidal and generally lie upon the bean, those of vanillin are usually acicular and stand out at right angles from the surface of the fruit. The absence of the crystalline coating on the vanilla beans seems to be no proof of inferiority, for Henri Lecomte affirms that it is not rarely absent in the best Mexican bean. (*B. Sc. Pharm.*, 1901.)

Constituents.—The vanilla fruit when fresh possesses none of the pleasant aroma which we associate with the fruit, the odor being developed during the process of curing. There is present in the fruit the glucoside *coniferin* and two ferments. Under the action of these successively, the coniferin is first changed into *coniferyl alcohol* and thence into vanillin. Coniferin has been separated in the pure state not only from this plant but from several species of pine trees (see *Pinus Strobus*). Coniferin forms white crystalline needles having a composition of $C_{16}H + 2H_2O$. These are efflorescent in dry air and when anhydrous have a melting point of 185° C. Coniferin is practically insoluble in cold water, but soluble in alcohol and slightly so in hot water, its solution having a bitter taste. It may be hydrolyzed by either sulphuric or chromic acid as well as by the ferments found in the vanilla bean. (See *Vanillinum.*) H. Lecomte (*J. P. C.*, 1903, 343) studied the conditions which bring about the formation of vanillin. According to his researches, there exist in the vanilla plant two ferments, which differ in a marked degree from each other in their functions. The one, an oxydase, is present in the individual organs of the plant, such as the leaves, shoots and their aqueous extracts, in the green and ripe fruit, and in the prepared commercial fruit. The second ferment is contained in the sap of the vanilla, and acts as a hydrolyzing ferment. Both ferments, the oxydase as well as the one possessing the hydrolytic action, appear to be necessary for the formation of vanillin in the plant, and their action may possibly be explained thus: During the preparation the coniferin produced by the plant is split up into glucose and coniferyl alcohol. This process would explain also the occurrence of grape-sugar in vanilla. The oxydase then converts the coniferyl alcohol into vanillin.

Tiemann and Haarmann obtained from Mexican vanilla 1.69 per cent. of vanillin, from Réunion vanilla 2.48 per cent., from Java vanilla 2.75 per cent.

Uses.—Vanilla is used solely as a flavoring agent; it is an ingredient of several N. F. preparations.

Vanilla Poisoning.—Cases of violent gastro-intestinal irritation from eating vanilla ices have been reported. Most of these undoubtedly were due to tyrotoxicon, a ptomaine produced in decomposing milk; but if the one reported by Rosenthal (*P. J.*, xv, p. 24) be accurately stated it must be allowed that in some instances the vanilla itself is at fault. In this connection the reports of Claverie (*J. P. C.*, Supp. 1908, xxv) of violent dermatitis in workmen handling vanilla beans is of interest. He attributes the symptoms to the oily exudate of the vanilla pods.

Off. Prep.—Tinctura Vanillæ, *N. F.*

VANILLINUM. U. S.

VANILLIN Vanillin.

"Methylprotocatechuic aldehyde [$C_6H_3.CHO.OCH_3.OH$ 1:2:4]." *U. S.*

Vanilline, *Fr. Cod.;* Aldehyde Vanillique, *Fr.;* Vanillin, Vanillekampher, *G.*

Preparation.—Vanillin was first obtained from vanilla by Gobley, who, by exhausting vanilla with 85 per cent. alcohol, evaporating the resulting tincture to an extract, softening this with water, and agitating in a flask with ether so long as it gave color to that fluid, then evaporating the ethereal liquid and treating the residue with boiling water, obtained on the evaporation of the water a crop of crystals having the odor of vanilla. It is now recognized to be the methyl ether of protocatechuic aldehyde, $C_8H_8O_3$, and is widely diffused in the vegetable kingdom; it occurs in the sugar beet, the flower of the potato, and the woody tissues of several plants. Vanillin oxidizes slowly in damp air to *vanillic acid,* $C_8H_8O_4$; when heated with diluted hydrochloric acid to 200° C., it breaks up into methyl chloride and protocatechuic acid.

Vanillin was first synthetically prepared from *coniferin,* $C_{16}H_{22}O_8$, a principle discovered by Hartig in the cambium layer of coniferous trees and later discovered in *asparagus.* When coniferin is hydrolyzed it yields dextrose and *coniferyl alcohol,* $C_{10}H_{12}O_3$. Either *coniferin* or coniferyl alcohol yield *vanillin* when subjected to oxidation by the action of sulphuric acid and potassium dichromate. The reaction in the latter case is as follows:

$$C_{10}H_{12}O_3 + O = C_8H_8O_3 + C_2H_4O$$

Vanillin is also produced synthetically from eugenol, the chief constituent of oil of cloves, by the action of acetic anhydride, to convert it into acetyl-eugenol, $C_{10}H_{11}(C_2H_3O)O_2$. This is then oxidized by means of potassium permanganate which results in the production of acetyl-vanillin, which is later converted into vanillin by the action of sodium hydroxide.

Description and Physical Properties.—"Fine, white, or only very slightly yellowish, needle-like crystals, having an odor and taste resembling vanilla. One Gm. of Vanillin is soluble in 100 cc. of water and in about 20 cc. of glycerin, at 25° C. One Gm. is soluble in 16 cc. of water at 80° C. It is freely soluble in alcohol, chloroform, and ether.

"Vanillin is easily dissolved by aqueous solutions of alkali hydroxides, and from these solutions, when not too dilute, it is precipitated at once by the addition of acids. Vanillin melts between 80° and 82° C. Its aqueous solution is acid to litmus paper and is optically inactive. A saturated aqueous solution of Vanillin gives a blue color with ferric chloride T.S. On boiling the mixture, the blue color changes to brown, and on cooling, a white, or nearly white precipitate of dihydrodivanillin separates. Vanillin is extracted completely from its solution in ether by shaking with a saturated, aqueous solution of sodium bisulphite, from which it is precipitated by the addition of sulphuric acid. A cold aqueous solution of Vanillin gives with lead acetate T.S. a white precipitate of a lead compound of vanillin, which is soluble in hot water.

"Ash: not more than 0.05 per cent. Warm 0.1 Gm. of Vanillin with a concentrated alcoholic solution of sodium hydroxide, add a drop of chloroform, and again warm: the odor of phenylisocyanide is not perceptible (*acetanilid*).

"Preserve in well-closed containers, protected from light." *U. S.*

A new qualitative test and colorimetric method for the quantitative estimation of vanillin has been described by Clarence Estes (*J. I. E. C.*, 1917, ix, p. 142) which depends upon the effect of the addition of solution of acid nitrate of mercury under certain conditions. A violet to violet-red color is produced, which is unlike that produced by any organic compound likely to be present as an accidental or interfering substance. The results of the application of the author's method directly to flavoring extracts of known composition agreed closely with the gravimetric figures.

Uses.—According to Grasset, vanillin produces in frogs spinal convulsions, followed by paralysis due to a direct action upon both the spinal cord and motor nerves. It has been suggested as a stomachic and excito-motor given in doses of three-fourths of a grain (0.048 Gm.).

(*A. Pharm.*, Aug., 1896.) Neither it nor vanilla, however, are used for other than flavoring purposes. The fact that while the vanilla beans have steadily risen in price for a number of years that of the artificial vanillin has enormously fallen, indicates that as a flavoring agent vanillin is not equal to the natural product. It is said that articles flavored with it leave a peculiar, disagreeable after-taste and retain their flavor only a very short time.

Off. Prep.—Elixir Amygdalæ Compositum, *N. F.;* Elixir Vanillini Compositum (from Compound Spirit), *N. F.;* Spiritus Vanillini Compositus, *N. F.*

VERATRINA. N. F.

VERATRINE Veratrin. [Veratria]

"A mixture of alkaloids obtained from the seed of *Asagræa officinalis* (Chamisso and Schlechtendal) Lindley (Fam. *Liliaceæ*)." *N. F.*

Vératrine Officinale, *Fr. Cod.;* Veratrinum, *P. G.:* Veratrin, *G.;* Veratrina, *It.*, *Sp.*

Veratrine has been deleted from the U. S. X and the Br. 1914, but has been introduced into the N. F. A process for its preparation will be found in the *U. S. D.,* 19th ed., pp. 1327 and 1328.

For description of the plant from which this substance is obtained see *Sabadilla,* Part II.

Veratrine is a mixture of all the alkaloids of sabadilla seeds. (See *Sabadilla,* Part II.) These, as far as determined at present, are: *cevadine* (*crystallized veratrine*), $C_{32}H_{49}O_9N$; *cevine* (*sabadinine*), $C_{27}H_{43}O_8N$; *veratridine* (*amorphous veratrine*), $C_{37}H_{53}O_{11}N$; *cevadilline* (*sabadilline*), $C_{34}H_{53}O_8N$; and *sabadine,* $C_{29}H_{51}O_8N$. Of these alkaloids the most important, from the therapeutic standpoint at least, appear to be cevadine and veratridine; the other alkaloids being much less active physiologically. Wright and Luff (*Tr. Chem. Soc.,* 1879, xxxv, 425) have found about 0.1 per cent. of cevadine. According to MacBeth and Robinson (*Tr. Chem. Soc.,* 1922, cxxi, p. 1574), its anhydrous crystals melt at 205° C.; it is insoluble in water but soluble in hot alcohol, their solutions being dextrorotatory. Veratridine is an amorphous varnish-like substance with a melting point of 180° C. It may be separated from the other alkaloids by precipitating an ethereal solution of the latter with light petrolatum. For further information concerning these alkaloids consult Freund (*B. Chem. G.,* 1899, xxxii, 800 and 1904, xxxvii, 1946); Frankfortes (*Am. Chem. J.,* 1898, xx, p. 361) and Hess and Mohr (*B. Chem. G.,* 1919, lii, 1984).

Two acids have also been found in sabadilla—the *sabadillic* or *cevadic acid* of Pelletier and Caventou, forming needle-like crystals fusing at 20° C., and the *veratric acid* of Merck, which Koerner showed to be dimethylprotocatechuic acid.

Description and Physical Properties.—"Veratrine is a white, or grayish white, amorphous powder, odorless, but causing intense irritation and sneezing when even a minute quantity reaches the nasal mucous membrane. *Great caution must be used in handling it.* It is slightly hygroscopic. One Gm. of Veratrine dissolves in 1760 cc. of water, 2.8 cc. of alcohol, 0.7 cc. of chloroform, and in 4.2 cc. of ether at 25° C.; also in 1345 cc. of water at 80° C.; insoluble in petroleum benzin.

"Its alcoholic solution is alkaline to moistened litmus paper. Triturate about 0.05 Gm. of Veratrine with 2 cc. of sulphuric acid in a glass mortar; the yellow or orange-red solution exhibits by reflected light a greenish fluorescence, which becomes more intense upon the addition of an equal volume of sulphuric acid. Upon standing, the solution gradually assumes a deep red color. Sulphuric acid, when heated with Veratrine, gives a cherry-red color. Sulphuric acid added to a mixture of one part of Veratrine and six parts of sucrose produces a green color which changes to blue, and finally the mixture becomes colorless. No weighable ash remains on incinerating 0.1 Gm. of Veratrine. An alcoholic solution of Veratrine (1 in 20) remains clear after the addition of platinic chloride T.S. (*Various foreign alkaloids.*)

"Preserve it in well-closed containers, protected from light." *N. F.*

Uses.—Probably because of its unfortunate name it has been assumed by some that veratrine represents the therapeutic virtues of veratrum. Its physiological action, however, differs greatly from that of veratrum, and if it possess any therapeutic usefulness it is certainly not for the conditions for which veratrum is employed.

Veratrine is an intense local irritant and somewhat locally anesthetic. Rubbed upon the skin it excites a sensation of warmth and a peculiar tingling. Sometimes an evanescent blush is produced and still more rarely an eruption upon the skin, but generally no decided signs of inflammation are evinced. When taken into the mouth it produces an almost insupportable sense of acrimony, and snuffed up the nostril it produces violent sneezing, and when taken into the stomach in large doses it causes violent vomiting, serous purging with intense burning in the mouth and throat and general muscular weakness. It is a powerful muscle poisoning and if given in sufficient dose in the lower animals it causes an extraordinary prolongation of the contraction of the striated muscles; the time required for relaxation of voluntary muscles may be 20 or 30 times as long as normal. A similar influence is exerted upon the ventricular muscles, at least in the frog, but the slowing of the heart rate seen in warm blooded animals seems to be due chiefly to stimulation of the cardio-inhibitory center. Death in mammals is generally due to depression of the respiration.

The only justifiable therapeutic use of veratrine is as an anodyne counter-irritant in *neuralgias* and various forms of *arthritis.* Even for this purpose it has no advantages sufficient to offset the dangers of systemic poisoning which might follow from its absorption.

Dose, one-thirtieth of a grain (0.002 Gm.).

Off. Prep.—Oleatum Veratrinæ, *N. F.;* Unguentum Veratrinæ, *N. F.*

VERATRUM VIRIDE. U. S.

VERATRUM VIRIDE Verat. Vir. [Green Hellebore, American Hellebore]

"Veratrum Viride consists of the dried rhizome and roots of *Veratrum viride* Aiton (Fam. *Liliaceæ*). Veratrum Viride contains not more than 5 per cent. of its stems or other foreign organic matter, and yields not more than 4 per cent. of acid-insoluble ash." *U. S.*

Big or False Hellebore, Swamp Hellebore, Indian Poke, Itch-weed, Tickle-weed, Bugbane; Vératre vert, *Fr.;* Grüner Germer, *G.;* Vedegambre verdo, *Sp.*

In the several revisions of the U. S. Pharmacopœia, *veratrum* has been handled in a vacillating manner. In 1880 and 1890 the drug was restricted to that obtained from *V. viride.* In 1900 both *V. viride* and *V. album* were recognized, this being done for reason of the large importations of *Veratrum album,* there being no practical method of distinguishing between these two drugs. The U. S. Pharmacopœia IX wisely restricted the definition, in the interest of uniform medicine, to *V. viride* and the present revision continues the distinction. This, however, may offer some practical commercial difficulties as it is not always easy to differentiate its substitution by *V. album,* and certainly it is almost impossible to detect an admixture with the European drug.

That the two species are very closely allied, and the two rhizomes histologically, chemically, and toxicologically very similar is indisputable, but similarity is not identity. The European plant seems to be more actively poisonous than is the American, and has been said by some chemists to contain a larger proportion of the alkaloids. It usually also has a distinctly greater action upon the intestinal tract and it is probable that the proportionate amounts of the alkaloids differ in the two species. The conclusions reached in an elaborate physiological research made by H. C. Wood and H. C. Wood, Jr., for the Committee of Revision of the U. S. VIII (*A. J. M. S.,* May, 1899) was that the drugs can scarcely be distinguished physiologically, but that the European plant is more likely to disturb the intestines and that in the absence of any cogent reason for recognizing *V. album, Veratrum viride* should alone be retained.

The American hellebore, *Veratrum viride,* has a perennial, thick, fleshy rhizome, the upper portion of which is tunicated, the lower solid, and beset with numerous whitish roots. The stem is annual, cylindrical, striated, pubescent, and solid, from three to six feet in height, furnished with bright green leaves, and terminating in a panicle of greenish-yellow flowers. The leaves gradually decrease in size as they ascend. The lower are from six inches to a foot long, oval, acuminate, plaited, nerved, and pubescent, and embrace the stem at their base, thus affording it a sheath for a considerable portion of their length. Those on the upper part of the stem, at the origin of the flowering branches, are oblong-lanceolate. The panicle consists of numerous flowers, distributed in racemes with downy peduncles. Each flower is accompanied by a downy, pointed bract, much longer than its pedicel. The perianth consists of six oblong or oblanceolate, acute segments, thickened on the inside at their base, with the three alternate segments longer than the others. The six stamens have recurved filaments and roundish two-lobed anthers. The ovary is ovoid, tricarpellary; styles three and persistent. Some of the flowers have only the rudiments of pistils. Those on the upper end of the branchlets are barren, those below fruitful. The fruit is a three-lobed capsule, three-celled, and containing flat imbricated seeds. This indigenous species of veratrum inhabits swamps, wet meadows, and the banks of mountain streamlets. It is more abundant northward, but reaches as far south as Georgia. From May to July is the season for flowering. It is doubtful whether the rhizome should be collected in autumn or just before flowering. It should be thoroughly dried and carefully preserved, as otherwise it deteriorates.

The commercial supplies of the drug are obtained from North Carolina, Virginia, Illinois and Michigan.

Veratrum album L. (*V. viride* Roehl., but not *V. viride* Aiton.).—The specific difference between this plant, which is a native of Europe and northern Asia, and *V. viride* of North America has been questioned by various botanists, but prominent taxonomists still regard the two species as distinct. (See *Index Kewensis;* also Engler and Prantl.) *V. album* resembles closely the American species, but is distinguished by its smaller leaves by possessing flowers with shorter pedicels and ovate perianth segments. The rhizome of *V. nigrum* of central Europe is said to be sometimes substituted for that of *V. album,* but is much smaller. According to the Pharmacographia, that of the Mexican species, *V. frigidum* Schl., exactly resembles that of *V. album.*

Description and Physical Properties.—"*Unground Veratrum Viride.*—Rhizome more or less conical, from 2 to 7 cm. in length, from 1.5 to 3 cm. in diameter, externally light to dark brown or brownish-black; frequently bearing at the summit numerous, thin, closely-arranged leaf bases, otherwise rough and wrinkled and somewhat annulate from scars of bud scales; inodorous; taste bitter and acrid. Roots numerous, nearly cylindrical, from 3 to 8 cm. in length and from 1 to 4 mm. in diameter, usually brittle, whitish, and more or less starchy.

"*Structure.*—The rhizome shows an outer layer of brownish cork-like cells; parenchyma containing raphides of calcium oxalate and starch; a continuous layer of endodermal cells; vascular bundles arranged in interrupted circles, single bundles scattered throughout the central parenchyma and also in the cortex. The root shows epidermal cells with lignified thickened outer and radial walls; parenchyma similar to that of rhizome; endodermal cells with inner and radial walls thickened and slightly lignified, with U-shaped cavity about one-third the cell width.

"*Powdered Veratrum Viride.*—Grayish-brown to dark brown, strongly sternutatory; starch grains numerous, from 0.003 to 0.020 mm. in diameter, spherical or ellipsoidal, single or 2- to 3-compound; raphides from 0.015 to 0.150 mm. in length; tracheæ scalariform or reticulate, often with lemon-yellow contents and associated with slightly lignified porous fibers; cork fragments few, reddish-brown or brownish-black." *U. S.*

It has been asserted that the color of *V. album* is much lighter than that of *V. viride,* but this certainly is practically incorrect, however it may apply to carefully preserved specimens. Very commonly the roots have been removed from commercial *V. album,* while in America they are generally allowed to remain on the rhizomes. According to R. H. Denniston, no microscopic differences can be detected in the rhizomes, but in the roots distinction is possible owing to the fact that directly beneath the epidermis in the *V. viride* the collenchyma region consists of but two or three rows of large, irregular and distorted cells, while in *V. album* this region is generally made up of seven to eight rows of rounded, thicker-walled and smaller cells, which are not in the least distorted. Any such test is, of course, inapplicable to the drug in powder. According to Viehoever, Keenan and Clevenger in the roots the endodermal cells of *V. viride* possess a U-shaped lumen whereas those of *V. album* possess a V-shaped lumen, further, the aerenchyma of *V. viride* shows air-spaces surrounded by disorganized parenchyma more pronounced than in *V. album.* These authors have found, during their investigation of *V. viride, V. album* and *V. californicum,* that the histological characters of the rhizomes and roots of these species vary to a considerable degree, showing a tendency to overlap in single instances. (*J. A. Ph. A.,* 1921, p. 581.) From a critical study of the published investigations thus far carried out on *V. viride* and *V. album,* we venture the opinion that no differences have been shown to exist between these two plants or their rhizomes or roots, which could not be explained on purely ecological grounds.

The pharmacognosy of *V. viride* has been well illustrated by Bastin (*A. J. P.,* 1895, p. 196). The structure of *V. album* has been presented by Meyer (*Arch. d. Pharm.,* 1882, p. 81; and in "*Wissenschaftliche Drogenkunde,*" vol. 2, p. 46). Rosenthaler has submitted veratrum to pyroanalysis and has obtained a sublimate which is in part crystalline and gives a yellowish-red color with sulphuric acid. (*Apoth. Zeit.,* xxviii, p. 991.)

Constituents.—The chemistry of *Veratrum viride* is rather confused, partly because of its complexity and partly because of the botanical similarities with the *V. album.* The latter has, in recent years at least, been more studied by chemists than the *V. viride,* but the physiological actions and the botanical relation of the two plants are so similar, that it is probable that they contain approximately the same alkaloids. The most abundant of the alkaloids is *jervine,* which is present in the proportion of from 0.1 to 0.3 per cent., but which H. C. Wood, Jr. (*J. A. M. A.,* 1906, xlvii, p. 2061), has shown to be physiologically relatively feeble. *Jervine,* $C_{26}H_{37}O_2N$, was first separated in a pure state by Wright and Luff (*Tr. Chem. Soc.,* 1878, xxxiii, p. 341) although the substance previously reported by Bullock under the name of *viridine* was probably an impure form of it. It crystallizes with 2 molecules of water and has a melting point of 241° C., according to Bredemann (*Ap. Ztg.,* 1906, xxi, p. 53). It has been reported in both species of veratrum (Pehkschen, *A. J. P.,* 1891). *Pseudojervine,* $C_{29}H_{43}O_7N$, and *rubijervine,* $C_{26}H_{43}O_2N$ (*veratroidine* of Bullock), which also occur in both species, are physiologically almost completely inert. The most active substance as yet isolated is *protoveratrine,* $C_{32}H_{51}O_{11}N$. It crystallizes in rectangular tablets with a melting point of 245° to 250° C. It was found by Salzberger (*A. Pharm.,* 1890, ccviii, p. 462) in the *V. album,* but has not yet been demonstrated in the *V. viride. Protoveratridine,* $C_{26}H_{45}O_8N$, has also been reported by Salzberger in the white hellebore; it is non-toxic. Traces of cevadine have been reported in *V. viride* and also of *Veradridine,* $C_{37}H_{53}O_{11}N$.

Assay.—The alkaloids of veratrum vary so greatly in their toxicity that a chemical assay is of very little use as an indication of the strength of the drug. At the same time there is evidence of considerable variation in the strength of different samples of the drug. Pilcher (*A. J. P.,* 1917, xliv, p. 1) reports variations of more than 100 per cent. between different preparations supposedly of the same strength. He has employed as test animals both guinea pigs and frogs. In the latter he found a very marked seasonal variation. In view of this fact and also that the toxic effects in man are upon the respiratory center, the guinea pig method would seem more serviceable. Pittenger has worked out details for the bio-assay of veratrum and suggests as a standard for the fluidextract an M. L. D., for the guinea-pig, of 0.05 Gm. per 250 Gm. body weight in 24 hours after hypodermic injection. He finds among samples tested a range of from 16 to 250 per cent. of standard. Rowe (*J. A. Ph. A.,* 1925, xiv, p. 24) prefers white mice as test objects. His standard is an M. L. D. of 0.25

milligramme per gramme body weight, which does not greatly differ from that of Pittenger.

Uses.—The various alkaloids present in veratrum act upon the system in very different manners, and none of them appears to exercise exactly the same action as the whole drug. According to H. C. Wood (*Phila. Medical Times,* 1874, iv, p. 737), jervine is a depressant to the respiratory center, to the vasomotor center, and to the heart muscle, and also lowers reflex activity by an effect upon the spinal cord, and rubijervine is chiefly a stimulant to the cardio-inhibitory mechanism, but has also a depressant action upon the respiratory center. According to Eden (*A. E. P. P.,* 1892, xxix, p. 440), small doses of protoveratrine stimulate cardiac inhibition thereby causing a lowering of the blood pressure. In large doses there is a secondary paralysis of inhibition accompanied by rise in the pressure. In large quantities it also exercises a poisonous effect upon the voluntary muscles similar to that of veratrine. Rubijervine is present in such small proportions (according to Breideman, *J. P.,* 1906, lxxxiv, 0.053 per cent.) and is so feeble a substance that it is improbable that it plays any part in the physiological action of the drug. Jervine although present in larger quantities (0.34 per cent.), according to H. C. Wood, Jr., is less poisonous than the drug itself. Protoveratrine, although present in small amounts (0.06 per cent., according to Breideman), is an extremely toxic substance and is the most important of the ingredients at present known. It appears to differ, however, in some of its properties from the whole drug.

When a moderate dose of veratrum is introduced into the system, the most marked change produced is reduction in the rate of the pulse accompanied with a fall in the arterial pressure. At the same time there may be some slowing in the respiration. With proper doses the slowing of the pulse is extreme and we have seen, in the lower animals, even complete arrest of the heart at this stage of the poisoning. The slowing of the pulse does not occur if the pneumogastric nerves have been divided previous to the injection of the drug, and is at once abolished either by section of these nerves or by the administration of atropine. It must be regarded, therefore, as due to stimulation of the cardio-inhibitory center. The reduction in the arterial tension in the normal animal may, therefore, be attributed to the slowing of the pulse. The conclusions of H. C. Wood, Jr. (*U. P. M. B.,* March, 1908), that contrary to the older views, veratrum does not lower arterial tone, have been confirmed by the experiments of Pilcher and Sollmann (*J. P. Ex. T.,* 1915, vii, p. 295) on animals, and by the observations of Collins (*A. I. M.,* 1915, xvi, pp. 54–58) on man. After toxic doses of veratrum there is a late paralysis of the intra-cardiac terminals of the pneumogastric nerve and consequent increase in the pulse rate with at first a rise of the blood pressure followed by a fall. This toxic fall in the blood pressure appears to be due to a direct depressant action upon the heart muscle. There is, following the toxic dose, also marked reduction in the respiratory activity, death being due eventually to failure of this function.

Veratrum was introduced into medicine about a century ago by the group of physicians who called themselves "eclectics." By them it was attributed with mysterious "adenagic" virtues and used in all sorts of inflammatory diseases. Later under the belief that it dilated the blood vessels and hence would relieve various local congestions, regular practitioners employed it largely in the treatment of *pneumonia, peritonitis,* and other sthenic *fevers.* While it is still employed to some extent in this type of disorder, our knowledge of its physiological action indicates that its true field of usefulness is rather in chronic, than in acute, diseases. Thus it is a very valuable agent for the reduction of excessively *high blood pressure* in *arteriosclerosis, interstitial nephritis,* and other conditions of hypertension; in cases with feeble myocardia it should be used cautiously because the stimulation of the cardio-inhibitory mechanism predisposes to cardiac dilatation. For the same purpose it is often employed in threatened *apoplexy,* in *chronic endocarditis,* especially in those in which there is considerable degree of cardiac hypertrophy, and in the so-called *irritable heart* seen in soldiers and athletes. In *exophthalmic goiter* and various other forms of *tachycardia* it is frequently of great service to reduce the pulse rate and prevent the heart exhausting itself in excessive activity. In certain of these conditions its line of usefulness more or less parallels that of digitalis. It differs, however, sharply from that drug, in that while digitalis tends to increase the tone of the heart muscle, veratrum rather diminishes cardiac tone. Veratrum has also been used widely by obstetricians in the treatment of *puerperal eclampsia.* Whether its benefit in this condition is to be attributed to a depressant action upon the motor cord, as some believe, or whether it be due to a lowering of the blood pressure, is as yet uncertain. The dose of veratrum must be gauged by the effect it produces; in general it may be said that if it does not slow the pulse no benefit will be received by the patient. The drug should therefore be pushed until evidence of its action is seen in the reduction of the pulse rate. Ordinarily from one to three minims (0.06–0.2 cc.) of the fluidextract may be given every two or three hours until it manifests its action. It should be remembered, however, that in some cases the cardio-inhibitory mechanism is refractory to the action of the drug and no dose will slow the pulse, and if given incautiously it may do great harm. Fortunately in most instances if given in too large dose it will manifest its toxic action by nausea before any more serious symptoms are produced.

Toxicology.—The symptoms of veratrum poisoning are vomiting accompanied with great nausea and much retching. There is profound prostration with muscular weakness, the skin bedewed with perspiration and pale in color, the pulse, in the milder cases, or in the early stage of the severe cases, is extremely slow and easily compressible, later, in the severe types of poisoning, it may become rapid and irregular. The respirations are often shallow and sometimes stertorous. Frequently there is much complaint of dizziness and in a few cases there has been dilatation of the pupil with disturbance of vision. Because of the promptness with which vomiting comes on even very large single doses of veratrum may be recovered from, thus Buckingham (*A. J. M. S.*, 1865) reports a case in which recovery followed a teaspoonful of the fluidextract. But when repeated large doses have been taken, the poisoning is much more dangerous.

In the treatment of veratrum poisoning if the patient be vomiting it is well to give a couple of glasses of water in order to thoroughly cleanse the stomach, at the same time twenty grains (1.3 Gm.) of tannic acid may be exhibited as an imperfect chemical antidote. If for any reason vomiting has not occurred it should be at once provoked or the stomach washed out by means of a stomach pump. The patient must be kept in a horizontal position and should not be allowed to sit up to vomit. After washing out the stomach in the manner described above, efforts should be made to stop the vomiting by the use of counter-irritation over the epigastrium and the cautious employment of morphine. But since when the drug proves fatal death is due to the respiratory arrest the latter should not be given in too large doses. If seen in the early stages when the pulse is slow, atropine is a remedy of great value antagonizing the effect of the veratrum upon the pneumogastric nerve and at the same time checking the excessive sweating and stimulating the respiratory center. Other active respiratory stimulants, such as hypodermic injections of ammonia and strychnine, may be employed, and if the bodily temperature is low it should be maintained by the external application of heat.

Dose, one to two grains (0.065–0.13 Gm.).

Off. Prep.—Fluidextractum Veratri Viridis, *N. F.;* Tinctura Veratri Viridis, *U. S.*

VERBASCI FLORES. N. F.

MULLEIN FLOWERS Verbasc. Flor.

"Mullein Flowers consist of the dried corollas, with adhering stamens, of *Verbascum phlomoides* Linné, or of *Verbascum thapsiforme* Schraeder (Fam. *Scrophulariaceæ*). Mullein Flowers contain not more than 2 per cent. of foreign organic matter. Flowers which have become brown should not be used." *N. F.*

Great Mullein; Mullein Dock; Flores Thapsi barbati; Bouillon Blanc (Fleurs de), Molène, *Fr.;* Flores Verbasci, *P. G.;* Wollkrautblumen, Koenigskersenblumen, *G.*

Off. Prep.—Species Pectorales, *N. F.*

VERBASCI FOLIA. N. F.

MULLEIN LEAVES [Verbasc. Fol.]

"Mullein Leaves are the dried leaves of *Verbascum Thapsus* Linné (Fam. *Scrophulariaceæ*). Mullein Leaves contain not more than 2 per cent. of foreign organic matter and yields not more than 4 per cent. of acid-insoluble ash." *N. F.*

The mullein is a common weed native to Europe but abundantly naturalized in the United States, growing in open fields on stony hillsides. It is a tall, biennial herb reaching a height of 3 or 4 feet, terminating in a dense cylindrical spike of yellow flowers. The leaves are alternate and decurrent on the stem which is stout and simple. The whole plant is covered with a thick woolly pubescence. The corolla is rotate, almost regular and deeply five-lobed.

Folia Verbasci, *Fr. Cod.;* Feuilles de Bouillon Blanc, *Fr.;* Wollkrautblatter, *G.*

Description and Physical Properties.—The flowers are described as follows: "Corolla light yellow, the outer surface grayish with a fine, soft, woolly indumentum, the inner surface sparsely hairy and finely veined; tube of the corolla 1 or 2 mm. in length and almost equally broad, the limb from 14 to 30 mm. in width, between wheel-shaped and saucer-shaped, obscurely two-lipped, the unequal lobes rounded, obovate. Stamens five, borne on the base of the corolla, shorter than the corolla, two of them longer than the other three, the filaments thick and fleshy, more or less pilose, especially the three shorter ones, usually orange-colored. Stamen-hairs cylindrical, unicellular, non-branching, surface minutely reticulate, apex rounded, frequently enlarged. Pollen grains smooth, triangular and more or less rounded, from 0.025 to 0.035 mm. in diameter. Odor peculiar, agreeable; taste mucilaginous, not agreeable.

"The flowers impart a yellow color to boiling water, and a rather permanent green color with dilute sulphuric acid, the latter color becoming brown upon the addition of alkalies." *N. F.*

The N. F. gives the following description of the leaves.

"*Unground Mullein Leaves.*—Obovate with narrowed base, or varying to oblong or oblong-lanceolate, without a true petiole, obtuse or tending toward acuteness at the summit, from 1 to 6 dm. in length and from 3 to 15 cm. in width; very thick, rather tough when damp, brittle when dry, light yellowish gray or greenish gray, densely long-tomentose, with numerous, multicellular, branching, non-glandular hairs. Nearly odorless; taste mucilaginous and slightly bitter.

"*Powdered Mullein Leaves.*—Dark green; numerous branching multicellular slightly lignified hairs consisting of an upright, jointed central stalk with whorls of from 2 to 8 radiating lateral cells arising at the joints or apex, the lateral cells measuring up to 0.600 mm. in length; glandular hairs with a 1-celled stalk and a unicellular head, the latter from 0.020 to 0.030

mm. in diameter; numerous fragments consisting of epidermal cells with broadly elliptical stomata, the latter from 0.020 to 0.030 mm. in length and chlorenchyma associated with fibrovascular tissue." *N. F.*

According to Kobert (*Ph. Wb.*, 1918, lv, p. 49), the *V. Thapsus* contains several saponins. According to L. Rosenthal (*P. J.*, July, 1902), the seeds of *Verbascum sinuatum* L., which are used in Greece as a fish poison, contain 6.13 per cent. of a saponin. Traces of the same substance were found in the fruits of *V. phlomoides* L. and *V. thapsiforme* Schrad.

Uses.—Mullein leaves are demulcent and emollient, and are thought to possess anodyne properties, which render them useful in pectoral complaints. On the continent of Europe, an infusion of the flowers, strained in order to separate the rough hairs, is considerably used in mild *catarrhs.* An oil, produced by saturating olive oil with mullein flowers, during prolonged exposure to the sun, is used as a local application in Germany for *piles* and other *mucous membrane inflammations.* The mullein oils sold in pharmacies are of this nature, or some of them alcoholic tinctures. The dried leaves are sometimes smoked to relieve irritation of the respiratory mucous membranes; fomentations with mullein leaves also have some repute as anodynes. Internally, the decoction (an ounce to the pint, flowering tips) may be taken in the quantity of from four to six fluidounces.

Dose, from one to two drachms (4–8 Gm.).

Off. Prep.—Fluidextractum Verbasci Foliorum, *N. F.*

VIBURNUM OPULUS. N. F.

VIBURNUM OPULUS Viburn. Op.
[High Bush Cranberry Bark, Cramp Bark]

"Viburnum Opulus is the dried bark of *Viburnum Opulus* Linné var. *americanum* (Miller) Aiton (Fam. *Caprifoliaceæ*). Viburnum Opulus contains not more than 5 per cent. of adhering wood or other foreign organic matter." *N. F.*

High Bush Cranberry; Cramp-Bark; Wild Guelder Rose; Rose Elder; Squaw Bush; Pincushion Tree; Cherry-wood; Obier, *Fr.;* Wasserholderinde, Wasserschwelke, *G.*

Viburnum Opulus L. var *americanum* Ait. (*V. americanum* Mill.), *cranberry bush* or *high bush cranberry,* belongs to the section of the genus which has peduncled cymes, light red, acid, roundish drupes, with very flat orbicular not sulcate stones, palmately veined leaves, and scaly winter buds. It is a large bush, reaching the height of ten feet, growing in low grounds from New Brunswick far westward, and southward to Pennsylvania. The leaves are from three- to five-ribbed, strongly three-lobed, broadly wedge-shaped or truncate at the base, with the spreading pointed lobes mostly toothed in the sides and entire in the sinuses. The petioles bear two glands at the apex. The *snow-ball tree,* or *Guelder rose,* represents the var. *sterile* DC. in which the whole inflorescence has been turned into a mass of showy sterile flowers.

Description and Physical Properties.—"*Unground Viburnum Opulus.*—In strips, or occasionally in quills or chip-like fragments, the bark attaining a thickness of 3 mm.; outer surface of the thinner pieces of a light gray color with crooked, longitudinal, purplish brown stripes and very small brown lenticels, the thicker pieces purplish red or occasionally blackish, except when very young, and more or less finely fissured or thinly scaly; inner surface varying in color from yellowish to rusty-brown, with very short oblique striæ, except where the outer wood layer adheres; fracture short and weak, the fractured surface mostly whitish, varying to pale brown in the inner layer, rusty brown in the outer layer, covering the green tangential layer of phelloderm. Odor slight and characteristic; taste mildly astringent and decidedly bitter.

"*Structure.*—An outer corky layer of 5 to 25 rows of cells, the walls being nearly colorless, frequently thickened on the inner surface, individual cork cells from 0.015 to 0.045 mm. in radial diameter and from 0.030 to 0.075 mm. in tangential diameter; middle bark of about 10 rows of cells containing a brownish yellow, amorphous substance, small starch grains or chloroplastids; medullary rays one to two cells in width, usually not more than one-cell wide; inner bark with occasional groups of bast fibers composed of 1 to 10 cells, the walls being very thick, non-lignified, lamellated and finely porous; adhering wood with large tracheæ having scalariform or reticulate thickenings, and being surrounded by wood fibers with thick lignified walls.

"*Powdered Viburnum Opulus.*—Light grayish brown, consisting of irregular fragments; polygonal cork cells, with thin, colorless walls; parenchyma with rosettes of calcium oxalate, from 0.010 to 0.040 mm. in diameter; starch grains mostly in parenchyma cells and up to 0.010 mm. in diameter; fragments of parenchyma containing a brownish yellow amorphous substance; occasional tracheal fragments associated with lignified wood fibers, bast fibers and stone-cells." *N. F.*

The bark described in the U. S. P. VIII as "Viburnum Opulus" was that of *Acer spicatum* Lam., commonly known as *mountain maple,* or *false cramp-bark* as shown first by Satter and Farwell. Farwell states that as early as the nineties, *A. spicatum* was mistaken for *true cramp-bark* (*V. Opulus*) and that from then on until 1913, this bark represented the commercial cramp-bark. He gives detailed distinctions between mountain maple and true cramp-bark in an elaborately illustrated article (*Bull. of Pharm.*, 1913, 65). Viehoever, Ewing and Clevenger, in 1918, again called attention to the extent of the substitution of *A. spicatum* for *Viburnum Opulus.* They state that the barks as well as the preparations can be distinguished by the different color reactions of the tannins in the barks with iron salt, these being blue in *A. spicatum* and green in *Viburnum* (*J. A. Ph. A.*, 1918, p. 944). Despite the ruling of the U. S. Dept. of Agric. that all material labelled "cramp-bark" must represent the bark of *V. Opulus* var. *americanum,* substitution still continues, probably due to the synonym "cramp-bark" being commonly used for *A. spicatum* in the southern Appalachians, where much of this substitute drug is collected. The bark of *Acer spicatum* may readily be distinguished from that of *Viburnum Opulus* var. *americanum* by its fibrous fracture, absence of a valeric acid odor, especially when triturated in a mortar with phosphoric acid, and by its inner structure which exhibits numerous lignified, sclerenchyma fibers in cortex, pericycle and phloem as well as scattered monoclinic prisms of calcium oxalate. The bark of an *elder* has recently been reported as being used to adulterate cramp-bark (*Proc. N. W. D. A.*, 1921, 215).

For studies of Viburnum barks, see *A. J. P.*, 1895, 378, 394; also *Ph. Post.*, 35, 773.

Heyl (*J. A. Ph. A.*, 1922, xi, 329) found in the resinous extract a number of fatty acids, including acetic, caproic, valeric, palmitic, etc., and traces of a paraffin, myricyl alcohol and two phytosterols; in the water soluble extract he found acetic and valeric acids, tannin and sugar. There was also indications of a small amount of glucoside but no alkaloid.

It contains valeric acid, an enzyme, and viburnin (see *Viburnum prunifolium*).

Uses.—The berries of this plant are used to a considerable extent as a substitute for the ordinary cranberry, and are antiscorbutic, but there is no sufficient reason to believe the bark has any medicinal properties of any kind. It is occasionally employed with other drugs in functional uterine disorders but Pilcher and Burman (*J. A. M. A.*, 1916, lxvii, 490) has shown that it has no effect on the uterus. *V. obovatum* Walt., a tree shrub growing from Virginia southward, is said to be an antiperiodic. (*A. J. P.*, 1878.)

Dose, thirty to sixty grains (2–4 Gm.).

Off. Prep.—Elixir Viburni Opuli Compositum, *N. F.;* Fluidextractum Viburni Opuli, *N. F.;* Tinctura Viburni Opuli Composita, *N. F.;* Elixir Aletridis Compositum, *N. F.;* Elixir Heloniadis Compositum, *N. F.*

VIBURNUM PRUNIFOLIUM. N. F. (Br.)

VIBURNUM PRUNIFOLIUM Viburn. Prun.
[Black Haw, Viburnum]

"Viburnum Prunifolium is the dried root bark of *Viburnum prunifolium* Linné (Fam. *Caprifoliaceæ*). Viburnum Prunifolium contains not more than 7 per cent. of wood or other foreign organic matter and yields not more than 3 per cent. of acid-insoluble ash." *N. F.*

"Black Haw is the dried bark of Viburnum prunifolium, *Linn.*" *Br.*

Viburnum, *Br.;* Black Haw; Stagbush; Sheep-berry; Sloe; Viburno (Corteza de), *Sp.*

Viburnum prunifolium is a very handsome shrub or small tree which is quite common in the Middle and Southern United States, east of the Mississippi, flowering in May and ripening in the early autumn its ovoid or oblong blackish fruit. It is specifically characterized by its short pointed winter buds, by its acuminate, sharply serrulate, ovate leaves on long, slender glabrous, often narrow margined petioles. Its sessile, white flowered cymes are 2 to 5 inches broad and bear oval bluish-black drupes slightly over one-third inch in length.

Viburnum Lentago L., *Sheep Berry,* or *Nanny Berry,* resembles the previous species, but has the winter buds longer pointed, and its leaves stouter petioled with a distinctly wavy margined petiole. Its geographical limit overlaps that of *V. prunifolium,* but extends much further westward and northward, even to Hudson Bay and Manitoba. The bark of *V. dentatum* L., or *Arrow wood,* is said to be sometimes substituted for the official drug. Most of the commercial supply of *V. prunifolium* is obtained from western North Carolina.

Description and Physical Properties.—"*Unground Viburnum Prunifolium.*—In irregular, transversely curved or quilled pieces, from 1.5 to 6 cm. in length, and from 0.5 to 1.5 mm. in thickness; outer surface grayish brown, or, where the outer cork has scaled off, brownish red, longitudinally wrinkled; inner surface reddish brown, longitudinally striated; fracture short but uneven, showing in bark which is young or of medium thickness, a dark brown cork, a brownish red outer cortex, and a whitish inner bark in which are numerous light yellow groups of cells. Odor strong, sourish; taste distinctly bitter and somewhat astringent.

"*Structure.*—Outer bark of variable thickness composed of somewhat lignified cork cells, many of the latter with a brownish amorphous content; middle bark chiefly composed of tangentially elongated cortical parenchyma; inner bark with nearly straight medullary rays up to 2 cells in width and separated by sieve and parenchyma tissue; middle and inner bark with numerous groups of stone cells and characteristic rifts between the parenchyma; parenchyma cells containing either oil globules, brownish amorphous masses, starch grains, or calcium oxalate occasionally in monoclinic prisms, usually in rosette-aggregates, the latter often occurring in the inner bark in rows of cells.

"*Powdered Viburnum Prunifolium.*—Dark brown; numerous rounded or elongated stone cells, from 0.040 to 0.150 mm. in length, with thick, porous, lignified walls; calcium oxalate in rosette-aggregates or occasionally monoclinic prisms from 0.010 to 0.040 mm. in diameter; numerous fragments of lignified cork tissue;

fragments composed of parenchyma cells containing simple starch grains from 0.003 to 0.015 mm. in diameter; bast fibers few." *N. F.*

"In quills or curved pieces, one to four millimetres thick; dull brown or reddish-brown. Outer surface longitudinally wrinkled or, in older bark, with shallow fissures and scaly; inner surface longitudinally striated, reddish-brown. Fracture granular. In transverse section, a dark brown outer portion and a whitish or reddish bast with numerous groups of sclerenchymatous cells. Slight odor; taste astringent and bitter." *Br.*

The morphology of *Viburnum prunifolium* is well illustrated by Holm in *M. R.*, xxii, p. 35. Illustrations of the bark of the several species of viburnum are given in Kraemer's "*Scientific and Applied Pharmacognosy*"; also see *P. J.*, 1903, lxx, p. 197. Lloyd states that the bark of all native species of viburnum are collected by root diggers and sold under the name of black haw. (*Ph. Rev.*, xxiii, p. 333.) The bark of the root is preferred to that of the stem and the official definition formerly limited the drug to the root bark. Farwell reported the substitution of the genuine drug by the bark of some other species of viburnum than those specified by the Pharmacopœia. The bark is much darker than the official bark and consisted largely of stem bark. (*M. R.*, xvii, p. 35.) Youngken has reported a recent substitute which is collected in western North Carolina as "Shonny Haw bark" and which is stated by McManus to be collected from *V. nudum* L.

Herman van Allen found the following constituents in viburnum: (1) a brown resinous body, of a very bitter taste, from which it was found impossible to separate the sugar; (2) a greenish-yellow resin, or neutral principle, of a bitter taste, slightly soluble in water, freely so in alcohol, called by Krämer *viburnin;* (3) valeric acid; (4) a tannic acid giving a greenish-black color with ferric salts; (5) oxalic acid; (6) citric acid; (7) malic acid; (8) sulphates; (9) calcium, magnesium, potassium, and iron chlorides. (*A. J. P.*, 1880, 443.) As the result of elaborate investigation, T. Shennan (*Royal Coll. Phys. Lab. Rep.*, Edinburgh, vi, 1897) concludes that the *Viburnum prunifolium* contains *viburnic—i.e.*, valeric—acid, and a non-volatile alkaloid which, however, he failed to obtain in a pure condition. For examination of this bark by Heyl and Barkenbus see *J. Am. Chem. Soc.*, 1920, xlii, 1744.

Uses.—Viburnum has been used quite largely in the treatment of *dysmenorrhea, after-pains,* and other uterine disorders. Pilcher (*A. I. M.*, Jan., 1917), however, has shown that in the doses ordinarily employed it has no effect of any kind on the uterine muscle. Hager and Becht (*J. P. Ex. T.*, 1919, xiii, 61) have reached similar conclusions.

R. L. Payne, Jr., has found that when given in toxic amount to the lower animals viburnum produces muscular weakness, ending in complete paralysis with loss of reflex action, which he believes to be due to an influence upon the motor side of the spinal cord. In warm blooded animals there is also marked lowering of the arterial pressure, believed by Payne to be the result of a direct action of the drug upon the heart. Experiments of Payne have in a measure been confirmed by those of T. Shennan, but as the latter took six drachms of the fluidextract within thirty minutes, with no demonstrable effect except a doubtful decrease of the rate and force of the pulse, it is plain that the drug is very feeble.

Dose, thirty to sixty grains (2.0–3.9 Gm.).

Off. Prep.—Fluidextractum Viburni Prunifolii, *N. F.* (*Br.*); Elixir Viburni Prunifolii, *N. F.*

VINA MEDICATA

MEDICATED WINES

Vins médicinaux, Œnolés, *Fr.;* Medicinische Weine, *G.*

All wines were deleted from the U. S. P. IX. The Br. Pharm. 1914 retains sherry wine as a menstruum, and also an "Orange Wine" (see *Vinum Aurantii*).

The reported advantages of wine as a pharmaceutical menstruum are that, in consequence of the alcohol it contains, it dissolves substances insoluble in water, and, to a certain extent, resists their tendency to spontaneous change, while at the same time it is less stimulating than strong or diluted alcohol, owing to its smaller proportion of alcohol. The acid which it usually contains serves in some instances to increase its solvent power. But most wines, particularly the light varieties, are liable to undergo decomposition, and even the strongest acquire such a liability from the principles which they extract from vegetable substances; so that medicated wines, though they keep better than infusions or decoctions, are inferior in this respect to the tinctures. The proportion of alcohol, moreover, is not constant, and the preparations, therefore, made with them lacked uniformity. The medicated wines, in consequence of their liability to change, should be prepared in small quantities, from wine of proper identity and strength, and should be kept in a cool place. *Detannated wine* may be best made by digesting the wine with casein which has the advantages of milk, formerly used, without its diluting effect or the introduction of foreign and undesirable constituents. Gelatin has also been used successfully for the same purpose, but is somewhat inferior to casein, which is now obtainable either in the soluble or insoluble form. The former should be used and the latter form may be made soluble by the careful use of an alkali. Ferric hydroxide should never be used for detannating wines, for, while it successfully removes the tannin, it also removes other valuable constituents and the acid of the wine always takes up a little of the iron so that a slightly ferruginous preparation results, which is usually undesirable.

VINUM ANTIMONIALE. Br.

ANTIMONIAL WINE

Wine of Antimony; Vin antimonié, Vin émétique, Vin stibié, *Fr.;* Vinum Stibiatum, *P. G.;* Brechwein, *G.;* Vino emetico, *Sp.*

" Tartarated Antimony, 4 *grammes;* Distilled Water, boiling, 40 *millilitres;* Sherry, sufficient to produce 1000 *millilitres.* Dissolve the Tartarated Antimony in the Distilled Water, and add sufficient Sherry to produce the required volume." *Br.*

Considerable difficulty is often experienced in effecting a solution of tartar emetic in wine, and precipitation is likely to occur after the solution has been effected. These results are undoubtedly due to the variability in the amount of tannic acid in wines of different type and quality. Paris stated that he had seen the decomposition of the tartar emetic so complete that no traces of the salt could be detected in the supernatant liquid. The difficulty is not avoided by the plan adopted in the Br. of first dissolving the antimonial in water and then adding the wine; for, even allowing that the solution may be accomplished, the same ingredients are present, and their mutual reaction must ultimately result in the same effects. The proper course is to select perfectly pure crystallized tartar emetic, and wine which is low in tannic acid content, to make a permanent solution.

The advantages of antimonial wine are that it affords the means of administering minute doses of tartar emetic, and that it is more permanent than an aqueous solution of that salt, which is liable to spontaneous decomposition. It is used only as a diaphoretic or expectorant.

Dose, from ten to thirty minims (0.6–1.8 cc.).

VINUM AURANTII. Br.

ORANGE WINE

Vin d'Ecorce d'orange amère, *Fr.;* Pomeranzenwein, *G.;* Vino de Corteza Naranja amarga, *Sp.*

" Orange Wine is made by the fermentation of a saccharine solution to which Fresh Bitter-Orange Peel has been added." *Br.*

This is officially described as " a vinous liquid, having a golden sherry color, and a taste and aroma derived from the Bitter-Orange Peel. Contains from 12 to 14 per cent. by volume of ethyl hydroxide. Not more than slightly acid to *litmus.* When 50 millilitres are made alkaline with *solution of sodium hydroxide,* evaporated to a small bulk, acidified with *hydrochloric acid,* and shaken with *benzene,* the residue obtained on evaporating the benzene solution, when dissolved in *water,* does not assume a violet color on the addition of a drop of *T. Sol. of ferric chloride* (absence of salicylic acid). Yields not more than the slightest characteristic *reactions* for sulphites." *Br.*

This wine is used as a vehicle, and is the official menstruum for several Br. preparations.

VINUM COLCHICI. Br.

COLCHICUM WINE

Vinum Colchici Cormi, *N. F. IV;* Wine of Colchicum corm; Vinum Colchici Radicis, *U. S.* 1890; Wine of Colchicum Root; Vin de Bulbe de Colchique, *Fr.;* Zeitlosenknollenwein, *G.;* Vino con colchico, *It.*

" Colchicum Corm, in No. 20 powder, 200 *grammes;* Sherry, 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

In *gout* this wine is frequently given in connection with magnesium sulphate. It is a violent poison in overdoses. Two fluidrachms and a half (9.3 cc.) of it are said to have caused death.

Dose, ten to forty minims (0.6–2.5 cc.).

VINUM FERRI. Br.

IRON WINE

Vinum Chalybeatum, s. Martiatum; Eisenwein, Stahlwein, *G.*

" Iron, in wire, 50 *grammes;* Sherry, 1000 *millilitres.* In a closed vessel partially immerse the Iron in the Sherry; continue the maceration until the filtered liquid responds to the following test:—Evaporate 50 millilitres to dryness, incinerate the residue, heat the ash with *hydrochloric acid* diluted with an equal volume of *water,* filter, wash the filter paper with *water,* and add to the mixed filtrate and washings excess of *solution of ammonia.* Collect the precipitate, wash, dry and ignite; the residue weighs not less than 0.089 or more than 0.215 gramme, representing a proportion of not less than 0.125 or more than 0.300 gramme of iron, calculated as iron, Fe, in 100 millilitres of the Wine." *Br.*

(See also *Vinum Ferri Citratis.*)

When wine is made to react on metallic iron with presence of air, the metal is oxidized, and then unites with the excess of acid of the potassium bitartrate, which is the characteristic salt of wines. The ferruginous salt, therefore, formed is iron and potassium tartrate, or the tartarated iron of the Br. Pharmacopœia, and this was the old method of preparing the Wine of Iron. But it is obvious that the strength in iron cannot be entirely uniform, as the quantity dissolved must depend on the proportion of the bitartrate in the wine, which is variable, and on various circumstances of the manipulation. In consideration of these objections, it was thought best, in the Br. formula of 1864, to substitute a simple solution in the wine, of the iron and potassium tartrate already formed, and to abandon the old tedious formula. But it is obvious that a solution of the ferruginous salt in wine is not exactly the same as the wine of iron prepared with the metal, as it contains the potassium bitartrate unaltered. For this and other reasons, the Br. Pharmacopœia has returned to the old method.

Dose, one to four fluidrachms (3.75–15.0 cc.).

VINUM FERRI CITRATIS. Br.

WINE OF IRON CITRATE

Vinum Ferri, *N. F. IV;* Wine of Iron; Vinum Chalybeatum, Wine of Ferric Citrate; Vin Chalybé, Œnolé ferrugineux, Vin ferrugineux, *Fr.;* Eisenwein, *G.;* Vino de Citrato Ferricoamonico, *Sp.*

"Iron and Ammonium Citrate, 18 *grammes;* Orange Wine, sufficient to produce 1000 *millilitres.* Dissolve. Shake occasionally for three days; filter." *Br.*

Dose, one to four fluidrachms (3.75–15.0 cc.).

VINUM IPECACUANHÆ. Br.

IPECACUANHA WINE

Wine of Ipecac; Vin d'Ipécacuanha, *Fr.;* Brechwurzelwein, *G.*

"Liquid Extract of Ipecacuanha, 50 *millilitres;* Sherry, 950 *millilitres.* Mix; set aside for forty-eight hours; filter." *Br.*

This wine is much weaker than that formerly recognized by the N. F. IV.

Wine of ipecac possesses all the medicinal properties of the root, and may be used as a substitute when it is desirable to administer the medicine in a liquid form. It is much used as an expectorant and a diaphoretic, and the effects of the Dover's powder may be obtained by combining it with a liquid preparation of opium.

Dose, expectorant, ten to thirty minims (0.6–2 cc.); emetic, four to six fluidrachms (16–20 cc.).

VINUM QUININÆ. Br.

QUININE WINE

Vin de Quinine, *Fr.;* Chininwein, *G.;* Vino de Quina, *Sp.*

"Quinine Hydrochloride, 2 *grammes;* Orange Wine, 875 *millilitres.* Dissolve; filter if necessary." *Br.*

The Br. Ph., 1898, replaced quinine sulphate used in the 1885 process by quinine hydrochloride on account of the greater solubility of the latter. Each fluidounce contains one grain of quinine hydrochloride.

Dose, one-half to one fluidounce (15–30 cc.).

VINUM XERICUM. Br.

SHERRY WINE Vin. Xeric.

"Sherry is a Spanish wine." *Br.*

Sherry wine is not official in either the U. S. P. or N. F.

"Pale yellowish-brown, containing not less than 16 per cent. by volume of ethyl hydroxide. Contains in 100 millilitres not less than 0.1 or more than 0.2 gramme of volatile acids, calculated as acetic acid, $HC_2H_3O_2$, and not less than 0.3 or more than 0.45 gramme of fixed acids, calculated as tartaric acid, $H_2C_4H_4O_6$, when tested by the following process:—(1) Titrate 25 millilitres of the Sherry with *N/5 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator, and note the number (*a*) of millilitres of the former solution required. (2) Introduce 25 millilitres of the Sherry with 25 millilitres of *water* into a flask capable of holding 200 millilitres and attach a condenser; add 0.5 gramme of *tannic acid,* and distil gently until about 25 millilitres have been collected. Then pass a current of steam through the residual liquid in the flask, and continue the distillation until about 200 millilitres in all have been collected. Titrate the distillate with *N/5 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. The number (*b*) of millilitres of the former solution required is not less than 2.1 or more than 4.2, representing a proportion of not less than 0.1 or more than 0.2 gramme of volatile acids, calculated as acetic acid, $HC_2H_3O_2$, in 100 millilitres of the Sherry. Deduct the number (*b*) of millilitres required in (2) from the number (*a*) of millilitres required in (1). The difference is not less than 5 or more than 7.5, representing a proportion of not less than 0.3 or more than 0.45 gramme of fixed acids, calculated as tartaric acid, $H_2C_4H_4O_6$, in 100 millilitres of the Sherry. When 50 millilitres of the Sherry are made alkaline with *solution of sodium hydroxide,* evaporated to a small bulk, acidified with *hydrochloric acid* and shaken with *benzene,* the residue obtained on evaporating the benzene solution, when dissolved in *water,* does not assume a violet color on the addition of a drop of *T. Sol. of ferric chloride* (absence of salicylic acid)." *Br.*

XANTHOXYLI FRUCTUS. N. F.

PRICKLY ASH BERRY Xanthox. Fruct.

"Prickly Ash Berry is the dried fully grown fruit of *Xanthoxylum americanum* Miller (Northern Prickly Ash) or *Xanthoxylum Clava-Herculis* Linné (Southern Prickly Ash) (Fam. *Rutaceæ*). Prickly Ash Berry contains not more than 2 per cent. of foreign organic matter." *N. F.*

For information concerning these shrubs see next article.

Description and Physical Properties.—The berries are officially described as follows: "*Unground Prickly Ash Berry.*—Capsules with short stalks (*X. Americanum*) or without stalk (*X. Clava-Herculis*); ellipsoidal, fleshy, gray-brown, dehiscent; carpels two, convex, apex short pointed; seed one or two, oblong black, shining and wrinkled from drying. Taste pungent, warm, aromatic and on chewing leave a tingling sensation on the tongue; odor when breathing upon, faintly aromatic resembling that of citral.

"*Powdered Prickly Ash Berry.*—Dark brown; numerous fragments of pericarp tissue showing large oil cavities and vascular tissue surrounded by parenchyma cells, the latter containing irregular masses or sphaerocrystals of hesperidin; fragments of the inner layer of pericarp composed of narrow, irregular, elongated cells with thick lignified walls and simple pores; polygonal cells of the seed coat with dark brownish walls; numerous globules of volatile oil." *N. F.*

Xanthoxylum berries do not appear to contain any active substance other than a volatile oil. They probably have no therapeutic effect except that of a mild aromatic.

Dose, as given in the N. F., fifteen grains (1 Gm.).

Off. Prep.—Fluidextractum Stillingiæ Compositum, *N. F.;* Syrupus Stillingiæ Compositus, *N. F.*

XANTHOXYLUM. N. F.

XANTHOXYLUM Xanthox. [Prickly Ash Bark]

"Xanthoxylum is the dried bark of *Xanthoxylum americanum* Miller, known in commerce as Northern Prickly Ash Bark, or *Xanthoxylum Clava-Herculis* Linné, known in commerce as Southern Prickly Ash Bark (Fam. *Rutaceæ*). Xanthoxylum contains not more than 2 per cent. of foreign organic matter." *N. F.*

X. amercianum; Toothache Tree, Angelica Tree, Suterberry, Pellitory Bark, Yellow-wood; Clavalier, Frêne épineux, *Fr.;* Zahnwehholz, Zahnwehrinde, *G.*
X. Clava-Herculis; Sea Ash, Hercules' Club, Pepper-wood.

The *Xanthoxylum* (or more properly *Zanthoxylum*) *Americanum* Miller (X. *fraxineum* Willd.) or *Northern Prickly Ash* is a shrub from five to twenty-five feet in height, with alternate branches, which are covered with strong, sharp, scattered prickles. The leaves are alternate and pinnate, consisting of four or five pairs of leaflets, and an odd terminal one, with a common footstalk, which is sometimes prickly on the back, and sometimes unarmed. The leaflets are nearly sessile, ovate, acute, slightly serrate, and somewhat downy on their under surface. The flowers, which are small and greenish, are disposed in sessile clustered cymes near the origin of the young shoots. The plant is polygamous, some shrubs bearing both male and perfect flowers, others only female. The number of stamens is five, of the carpels three or four in the perfect flowers, about five in the pistillate. The capsules are stipitate, oval, punctate, of a greenish-red color, with two valves, each with one oval blackish seed. It grows in woods and in moist shady places from Quebec to Georgia, Mississippi and Nebraska. The flowers appear in April and May, before the foliage. The leaves and capsules have an aromatic odor, recalling that of oil of lemon.

Botanists are not agreed concerning the distinction of the genus *Fagara* from *Zanthoxylum.* The most important character separating them seems to be the absence of sepals in *Zanthoxylum.* Most of the species of the genus *Fagara* are tropical trees.

Z. Clava-Herculis L. [*Fagara Clava-Herculis* (L.) Small, *Z. carolinianum* Lam.], or *Southern Prickly Ash,* is a small tree. Its bark is armed with warty prickles, and large conical cork wings occur on the branches and the petioles. The alternate leaves have from seven to eleven ovate-lanceolate, crenate-serrulate, unequal-sided leaflets, smooth and shining on the upper surface. It grows on dry soil, westward as far as western Texas, and perhaps into Mexico, eastward to the Atlantic coast, and northward to southern Virginia, especially affecting the coast region.

The fruits (*Prickly ash berries*) of both of the official species probably contain the same principles found in the barks. The dried berries are recognized by the N. F. V under the name of *Xanthoxyli Fructus,* and are described below.

There has been much confusion in regard to the nomenclature of the prickly ashes. *Aralia spinosa* L., or angelica tree, which grows in the Southern States, is occasionally confounded with *Z. Clava-Herculis,* in consequence partly of being sometimes called, like the latter, *prickly ash.* Its bark is nearly smooth externally, is beset with slender prickles in transverse rows and has a taste different from that of *F. Clava-Herculis.* Besides the official trees, the bark of *F. flava* (Vahl) Frug. and Urban (*Z. caribæum* S. Wats.), the *satin-wood* of semi-tropical Florida and the West Indies, has appeared in commerce under the name of *yellow Hercules' club* or *yellow thorn.* This bark is thin, with an odor like that of Angustura bark, a bitter, disagreeable, acrid taste, and a canary-yellow color, which it imparts to the saliva when chewed. It would seem, also, that under the name of *prickly yellow wood, yellow wood,* or *fustic,* the products of other West Indian xanthoxylums and allied plants find their way into commerce.

Zanthoxylum veneficum Bailey, of Australia, is, according to J. H. Maiden, a violent convulsive poison, 5 grains of the extract being a fatal dose for a cat. *Zanthoxylum scandens* is said to be used by the natives of Java as a fish poison, and according to Van der Haar, contains an alkaloid. (*P. J.,* 1902, lxxi, 134; lxxiii, 814.)

The N. F. gives the following description of the bark:

"*Unground Northern Xanthoxylum.*—In transversely curved fragments or quills from 2 to 15 cm. in length; bark from 0.5 to 2 mm. in thickness; outer surface light gray to brownish gray with grayish patches of foliaceous lichens; longitudinally wrinkled and with numerous whitish lenticels; the cork occasionally abraded, showing the yellowish or orange, inner bark; inner surface yellowish white, finely longitudinally striate and usually with numerous, bright, shining crystals; fracture short, uneven. Odor slight; taste bitter, acrid, becoming pungent.

"*Structure.*—An outer corky layer consisting of from 4 to 20 rows of cells, the tangential walls being more or less thickened and lignified; a wide stratum of collenchyma inside of the cork cambium composed of from 8 to 10 rows of tangentially elongated cells, with very thick walls and containing plastids; a more or less indistinct row of endodermal cells beneath which occur small groups of primary bast-fibers; the inner bark consists of numerous parenchyma cells among which are included large oil-secretion reservoirs, and occasionally a few stone cells, separated by medullary rays which are mostly one cell in width; the parenchyma cells as well as the oil-secretion reservoirs contain numerous colorless oily globules. Scrapings from either the inner or outer surface show numerous rod-shaped crystals and flat prisms, from 0.015 to 0.250 mm. in length, which polarize light with a display of bright colors.

"*Unground Southern Xanthoxylum.*—In transversely curved or irregular, oblong, flattened pieces, or in quills from 2 to 40 cm. in length, bark from 1 to 4 mm. in thickness; outer surface light gray to brownish gray, marked by numerous large barnacle-shaped projections of cork, from 0.5 to 3.5 cm. in thickness and numerous elliptical lenticels; otherwise with grayish patches of foliaceous lichens; inner surface light yellowish brown to olive-brown, obscurely longitudinally striate and free from crystals. Odor and taste as in Northern Prickly Ash Bark.

"*Structure.*—A strong development of lignified cork in successive layers, the layers being separated by several rows of narrow tabular cells strongly thickened on the tangential walls; beneath the cork cambium occurs a thin layer of collenchyma followed by the outer tissues of the primary cortex and consisting of small groups of rather large stone cells and occasional, scattered groups of bast-fibers and parenchyma; the inner bark consists of parenchyma, a more or less indistinct sieve tissue among which are numerous, large, light yellowish oil-secretion reservoirs, medullary rays 1 or 2 cells in width and occasional groups of stone cells and bast-fibers; starch grains numerous, occurring in the parenchyma cells and medullary rays; calcium oxalate chiefly in monoclinic prisms occurring in crystal fibers and in parenchyma cells of the primary cortex.

"*Powdered Xanthoxylum.*—Light grayish brown, irregular fragments of cork cells, nearly colorless and strongly lignified, fragments of parenchyma containing eight small nearly spherical starch grains 0.002 to 0.010 mm. in diameter, oily globules or monoclinic prisms of calcium oxalate the latter 0.010 to 0.045 mm. in length; stone cells up to 0.150 mm. in length in small groups, with thick, colorless walls and frequently containing a reddish brown substance; bast fibers few and non-lignified. In the Northern Prickly Ash, the stone cells and the fragments of cork are relatively few." *N. F.*

Southern Prickly Ash has been adulterated with the bark of *Aralia spinosa* which can be readily detected by the sharp spines which are closely set and not mounted on corky cones. The bark of a tropical American species, X. *Ochroxylum* DC., has been the subject of a pharmacognostical study by Leprince. (*Repert. Pharm.*, 1912, xxiv, p. 215.)

W. L. Cliffe after careful examination demonstrated that the bark of Southern prickly ash exceeded that of the Northern prickly ash in active properties. (*A. J. P.*, 1901, 562.)

Constituents.—The Xanthoxylum barks contain berberine and probably one or more other alkaloids, which may be derivatives of berberine. There is some doubt whether the alkaloids of the two species are identical.

In 1826 Chevalier and Pellatan found in the Southern prickly ash (X. *Clava-Herculis*) a yellow alkaloidal substance which they called *xanthopicrit;* subsequently Perrins (*J. Chem. Soc.*, 1862, xv, 339) showed this to be berberine. G. H. Colton (*A. J. P.*, 1880, p. 191) separated from the Southern prickly ash, tastless, colorless, silky acicular crystals, soluble in alcohol, ether, and chloroform, less soluble in benzene, and insoluble in water.

The first to report an alkaloid in the bark of the *x. americanum* (Northern prickly ash) was Edward Staples who in 1829 isolated a colorless crystalline substance which he named *xanthoxyline.* This finding was confirmed by J. V. Lloyd in 1876. Subsequently, from the same plant Edward T. Moffet (*A. J. P.*, 1886, 417) obtained a supposed alkaloid in yellow crystals, soluble in alcohol and chloroform, insoluble in petroleum benzin, ether, and benzene. This was probably berberine.

The identity of the alkaloids from the two species was generally assumed until the analysis of Eberhardt. (*A. J. P.*, 1890, 231.) He obtained from the Southern prickly ash a colorless crystalline principle agreeing in solubilities with that of Colton. On analysis it gave figures indicating the formula $C_{20}H_{19}O_6$ or $C_{30}H_{28}O_9$. At the same time he analyzed a sample of Lloyd's crystalline principle from X. *americanum*, which had been preserved in the museum of the Philadelphia College of Pharmacy, and found for it the formula $C_{29}H_{27}O_8$. Numerous reactions also indicated that the two principles were different. Thus, Lloyd's crystals (xanthoxyline) dissolve in concentrated sulphuric acid with light red color, and on the addition of an excess of water produce a whitish precipitate which is taken up by chloroform; the crystals from the X. *Clava-Herculis* dissolve in concentrated sulphuric acid with dark red color, and on dilution separate a purplish precipitate, which is not taken up by chloroform. Lloyd's principle melts, moreover, at 129.5° C., while Eberhardt's melts at 110° C.

X. senegalense (*artar root*) was analyzed by Giacosa and Soave (*A. J. P.*, 1890, 500), who found a fixed oil, a neutral crystalline substance, melting at 120° C., and two alkaloids. The first of these they call *artarine,* and give to it the formula $C_{20}H_{17}O_4N$ (which makes it agree with *berberine*), or $C_{21}H_{23}O_4N$, in which case they consider that it may be *methylhydroberberine.* The second alkaloid, crystallizing in blood-red needles, they did not analyze. In X. *Ochroxylum,* Leprince (*B. Sc. Pharm.*, 1912, xviii, 337) found an alkaloid, *xantherine,* allied to berberine. (See also *P. J.*, 1917, xcviii, 275.)

In *Z. caribæum,* the lactone *carixanthide,* $C_{12}H_{24}O$, has been found. In *Z. carolinianum,* the lactone *carolixanthide,* $C_{20}H_{19}O_6$, has been reported. In *Z. americanum* Witte found *xanthoxyloin,* $C_{14}H_{14}O_4$. Giacosa and Soave extracted from *Z. senegalense,* a lactone, $C_{13}H_{10}O_3$. Streglitz believes this to be identical with *xanthotoxin,* found by him in the fruit of the same species and to which he ascribes the formula $C_{12}H_8O_4$.

Several species of this genus, including the official, yield volatile oils (see *Schim. Rep.,* April, 1911, p. 50).

Uses.—Xanthoxylum is stimulant, producing, when swallowed, a sense of heat in the stomach, and a tendency to diaphoresis. It is thought to resemble mezereum and guaiac in its remedial action, and is given in the same diseases. As a remedy in *chronic rheumatism,* it enjoys some reputation in this country. The bark, used as a masticatory, is a popular remedy for *toothache.* Xanthoxylum is also occasionally employed as a gastro-intestinal stimulant in atonic *dyspepsia, flatulence,* and serous *diarrhea.*

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Fluidextractum Xanthoxyli, *N. F.;* Elixir Corydalis Compositum, *N. F.;* Elixir Hydrastis Compositum, *N. F.*

ZEA. N. F.

ZEA [Corn Silk]

"Zea consists of the fresh styles and stigmas of *Zea Mays* Linné (Fam. *Gramineæ*). Zea should be collected when the corn is in milk and used in the green condition for the manufacture of pharmaceutical preparations." *N. F.*

Corn Silk; Stigmata Maydis, Mais, *Fr. Cod.;* Filament de Mais, *Fr.;* Maispistille, *G.*

This drug is the so-called "silk" of the ear of ordinary *Indian corn* or *maize,* cultivated in the warmer temperate and subtropical countries of the world.

Description and Physical Properties.—"In slender filaments from 10 to 20 cm. in length, and about 0.4 mm. in diameter; of a light green, purplish red, yellow or light brown color; stigmas bifid, the segments very slender, frequently unequal and from 0.4 to 3 mm. in length.

"*Structure.*—Styles consisting for the most part of parenchyma and two parallel vascular bundles with narrow, spiral or annular tracheæ; the epidermal cells rectangular, many of these being extended into multicellular hairs, the latter being from 0.2 to 0.8 mm. in length, the basal portion consisting of two to five united cells, the upper portion being usually unicellular; the cells of the hairs are rich in cytoplasm and usually contain a small, spherical nucleus; the purplish red styles contain a purplish red cell sap.

"Digest a small portion of the fresh styles and stigmas in diluted alcohol and filter; a pale purplish red solution is produced, separate portions of which, on the addition of acids, become distinctly purplish or yellowish red; on the addition of alkalies, green; on the addition of ferric chloride T.S., olive-green changing to greenish brown; and on the addition of an aqueous solution of alum, bluish or purplish, the color being quite permanent." *N. F.*

Rademaker and Fischer (*A. J. P.,* 1886, p. 369) determined the presence of 2.25 per cent. of *maizenic acid* in dried corn silk. It was first described, however, by Vautier. It is freely soluble in water, alcohol and ether, but insoluble in benzin. Rademaker and Fischer found, in addition to the acid, fixed oil, resin, chlorophyll, sugar, gum, extractive, albuminoids, phlobaphene salt, cellulose and water.

Uses.—Zea is employed in *acute* and *chronic cystitis* and in the bladder irritation of *uric acid* and *phosphatic gravel.* It has also been employed in *gonorrhea,* and has been affirmed by Landreux to be a useful diuretic and even cardiac stimulant in the *dropsy of heart disease.* It probably is, however, of little value.

Concerning the activity of *maizenic acid* we have little definite knowledge, but it probably represents whatever physiological power the drug possesses; it has been given in the *dose* of one-eighth of a grain (0.008 Gm.).

Dose, one to three drachms (3.9–11.6 Gm.).

Off. Prep.—Fluidextractum Zeæ, *N. F.;* Elixir Sabal et Santali Compositum, *N. F.*

ZEDOARIA. N. F.

ZEDOARY

"Zedoary is the dried rhizome of *Curcuma Zedoaria* (Bergius) Roscoe (Fam. *Zingiberaceæ*). Zedoary contains not more than 2 per cent. of foreign organic matter." *N. F.*

Zedoaria; Zedoaire, *Fr. Cod.;* Radix Zedoariæ, Rhizoma Zedoariæ, *P. G.;* Zitterwurzel, *G.*

The plant which produces this rhizome is closely related to that which produces turmeric (see *Curcuma,* Part II) and is, like that species, a native of India. It chiefly differs from *Curcuma longa* by its handsomely variegated leaves, pungent rhizome and upper bract leaves which are white and tinged with carmine. The plant is widely cultivated in India, Ceylon and China for its medicinal rhizome which is collected, washed and cut into circular disks and dried. The commercial supplies reach this country through Bombay and Trieste.

Formerly there were two kinds of zedoary, the long and the round, distinguished by the old official titles of *radix zedoariæ longæ* and *radix zedoariæ rotundæ.* The *long zedoary* was in slices, from 2.5 to 7.5 cm. in length, and from 1 to 2.5 cm. thick, obtuse at the extremities and exhibiting the remains of the radical fibers. The *round* alone is now found in commerce.

Description and Physical Properties.—"*Unground Zedoary.*—Usually cut into transverse rounded sections, twisted and wrinkled, from 1 to 4 cm. in diameter, and from 5 to 10 mm. in thickness; externally grayish brown, hairy, rough, with few root scars; transverse surface pale reddish, to gray-brown; a distinct dark circular endodermis separates the cortex from the central cylinder; the stele contains numerous, orange-colored resin cells, and irregularly distributed lighter colored fibrovascular bundles which are fewer in the cortex; fracture short, somewhat mealy and waxy. Odor aromatic, camphor-like; taste aromatic, warm, slightly bitter.

"*Structure.*—A thick cork, a thin epidermis with numerous characteristic hairs, the latter thick-walled, 1- to 6-celled, up to 1 mm. in length and often thicker in the middle than at the base; the parenchyma of the cortex and of the central cylinder rich in starch; secretion cells isodiametric with suberized walls, contents colorless or yellowish; the endodermis of small, thin-walled quadrangular cells, the fibro-vascular bundles collateral, more numerous in the central cylinder and nearer the endodermis; few bast-fibers in the cortex and no crystal cells.

"*Powdered Zedoary.*—Numerous starch grains, ovoid, from 0.010 to 0.070 mm. in length and from 0.007 to 0.030 mm. in thickness, having the point of origin of growth in the smaller end of the grain; numerous characteristic, thick-walled hairs; rich in parenchyma; very few bast fibers; no calcium oxalate crystals or stone cells." *N. F.*

Zedoary yields a volatile oil, when distilled with water, and contains a pungent soft resin and bitter extractive.

Uses.—Zedoary has a local effect upon the digestive organs similar to, but milder, than that of ginger and is occasionally employed as a gastro-intestinal stimulant in *flatulent colic* and other debilities of the digestive organs. Its official recognition, however, is due to the fact that it was an ingredient in the original Warburg's tincture and N. F. modifications.

Dose, ten to thirty grains (0.6–2 Gm.).

Off. Prep.—Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloe, *N. F.;* Tinctura Amara, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.;* Tinctura Amara, *N. F.*

ZINCI ACETAS. U. S., Br.

ZINC ACETATE Zinc. Acet.

"Zinc Acetate contains not less than 83.16 per cent. and not more than 87.32 per cent. of $Zn(C_2H_3O_2)_2$, corresponding to not less than 99.5 per cent. of the crystallized salt [$Zn(C_2H_3O_2)_2.2H_2O$]." *U. S.* "Zinc Acetate, $Zn(C_2H_3O_2)_2,2H_2O$, may be obtained by neutralising acetic acid with zinc carbonate." *Br.*

Acetas Zincicus; Acétate de Zinc, *Fr. Cod.;* Zincum Aceticum, *P. G.;* Zinkacetat, Essigsaures Zink, Essigsaures Zinkoxyd, *G.*

A process for this salt is no longer given in the U. S. P. In the U. S. process of 1870 zinc oxide—instead of the carbonate as in the Br. process—is acted upon directly by acetic acid. During the evaporation of the solution of the zinc acetate, a small portion of the acetic acid is lost; and hence the necessity of acidulating with a few drops of acetic acid before crystallizing. Though not economical on the large scale, these processes have the recommendation of being easily performed for supply in an emergency and of yielding a pure product.

Description and Physical Properties.—"Soft, white, six-sided, monoclinic plates, having a pearly luster, a faintly acetous odor, and, in dilute solutions, an astringent, metallic taste. When exposed to air, the salt gradually effloresces and loses some of its acid. One Gm. of Zinc Acetate is soluble in 2.3 cc. of water and in 30 cc. of alcohol, at 25° C. One Gm. is soluble in 1.6 cc. of boiling water and in about 1 cc. of boiling alcohol. When heated, Zinc Acetate is partially fused, losing water and acetic acid. At a higher temperature it is decomposed, with the evolution of inflammable and empyreumatic vapors, and leaves a residue consisting chiefly of zinc oxide.

"An aqueous solution of the salt responds to the reactions for zinc, and for acetates. An aqueous solution of the salt is neutral or slightly acid to litmus paper. A 10 cc. portion of an aqueous solution of the salt (1 in 50), to which 1 cc. of hydrochloric acid has been added, meets the requirements of the test for *heavy metals.* An aqueous solution of the salt meets the requirements of the test for *arsenic.*

"**Assay.**—Dissolve about 1 Gm. of Zinc Acetate, accurately weighed, in 100 cc. of distilled water, render the solution slightly alkaline with ammonia T.S., and warm to 80° C. Completely precipitate the zinc as zinc sulphide by the addition of ammonium sulphide T.S., and warm the liquid on a water bath until the precipitate settles. Collect the latter on a filter, wash it with distilled water containing a few drops of ammonium sulphide T.S., then dissolve it in hot, dilute nitric acid (1 in 3), evaporate the solution to dryness in a tared dish, ignite the residue, and weigh it as zinc oxide. The weight of zinc oxide obtained, multiplied by 2.254, indicates its equivalent in $Zn(C_2H_3O_2)_2$. Each Gm. of Zinc Acetate corresponds to not less than 0.369 Gm. and not more than 0.387 Gm. of ZnO.

"Zinc Acetate may also be assayed by the electrolytic method.

"Preserve in well-closed containers." *U. S.*

"Thin, translucent, colorless, crystalline plates, of a pearly lustre. Taste sharp and unpleasant. Soluble in 2.5 parts of *water.* Yields the *reactions* characteristic of zinc and of acetates. Yields no characteristic *reactions* for lead, copper, cadmium, iron, aluminium, calcium, magnesium, sodium, potassium, ammonium chlorides, or sulphates. *Arsenic limit* 5 parts per million. 0.5 gramme, tested as described under 'Zinci Sulphas,' yields a solution with not more than a faint pink coloration (limit of manganese)." *Br.*

The precipitate thrown down by ammonia from the pure salt is entirely redissolved by an excess of the precipitant, but if ferric oxide be present it will be left undissolved. Zinc acetate is decomposed by the mineral acids, with the escape of acetous vapors.

Uses.—Zinc acetate is used almost exclusively as a local remedy. It is employed principally as an astringent collyrium in *ophthalmia,* and as an injection in *gonorrhea,* after the acute stage in these affections has passed. The strength of the solution usually prescribed is one or two grains to a fluidounce (0.065 or 0.13 Gm. to 30 cc.) of distilled water. Rigney (*M. R.,* 1918, xxvii, 11) recommends a saturated solution for local application in *chilblains.*

ZINCI CARBONAS. Br.

ZINC CARBONATE

" Zinc Carbonate is a hydrated zinc carbonate, and may be obtained by the interaction of zinc sulphate and sodium carbonate." *Br.*

Zinci Carbonas Præcipitatus, *U. S. IX;* Precipitated Zinc Carbonate; Zinci Carbonas Præcipitata, *U. S.* 1870; Carbonate of Zinc; Zincum Carbonicum, Carbonas Zincicus; Carbonate (sous-) de Zinc Hydraté, Hydrocarbonate de Zinc, *Fr. Cod.;* Carbonate de Zinc, *Fr.;* Zinkcarbonat, Kohlensaures Zinkoxyd, *G.*

In the U. S. formula of 1870 a double decomposition takes place between zinc sulphate and sodium carbonate, resulting in the formation of sodium sulphate in solution, and basic zinc carbonate which is precipitated. Sodium carbonate is preferable to potassium carbonate for decomposing the sulphate, since the former gives rise to sodium sulphate, which is more easily washed away than the potassium sulphate derived from the latter. Boiling water is properly used in the process, in order to obtain a pulverulent precipitate, which is readily washed. If cold solutions are used, a gelatinous precipitate is formed, which is washed with difficulty. When a solution of zinc sulphate is precipitated by an excess of acid potassium carbonate, a normal zinc carbonate is obtained. With normal sodium carbonate, on the other hand, taken as a precipitant, a basic salt results.

Description and Physical Properties.— " White amorphous powder. No odor or taste. Insoluble in *water;* entirely soluble in *diluted nitric acid.* Yields the *reactions* characteristic of zinc and of carbonates. Yields no characteristic *reactions* for lead, copper, cadmium, iron, aluminium, calcium, magnesium, sodium, potassium, or ammonium, and not more than the slightest *reactions* for chlorides or sulphates. *Arsenic limit* 10 parts per million. 0.2 gramme, dissolved in *diluted sulphuric acid,* and tested as described under 'Zinci Sulphas,' yields a solution with not more than a faint pink coloration (limit of manganese)." *Br.*

If adulterated with chalk it will be only partly soluble in oxalic acid solution. Precipitated zinc carbonate is often sold under the incorrect name of *flowers of zinc,* a name which properly belongs only to the oxide, as obtained by combustion. When obtained from solutions of zinc sulphate and sodium carbonate it has a variable composition, as different hydrated basic carbonates are formed, according to the temperature used, etc.; the higher the temperature and the larger the quantity of water used, the more basic the carbonate becomes.

Uses.—This was introduced as a substitute for prepared calamine, but, as one of the important virtues of the native product is its pinkish color, the substitution is not a step in advance. It is used locally for much the same purpose as zinc oxide.

ZINCI CHLORIDUM. U. S., Br.

ZINC CHLORIDE Zinc. Chlor.

" Zinc Chloride contains not less than 95 per cent. of $ZnCl_2$." *U. S.* " Zinc Chloride, $ZnCl_2$, may be obtained by the interaction of hydrochloric acid and zinc." *Br.*

Butter of Zinc; Chloruretum Zincicum; Chlorure de Zinc, *Fr. Cod.;* Zincum Chloratum, *P. G.;* Zinkchlorid, Chlorzink, *G.;* Cloruro zincico, *Sp.*

Neither the U. S. nor British Pharmacopœias gives a process for making this salt; that of the Br. Pharm. 1885 follows:

" Take of Granulated Zinc *one pound;* Hydrochloric Acid *forty-four fluid ounces;* Solution of Chlorine *a sufficiency;* Carbonate of Zinc *half an ounce,* or *a sufficiency;* Distilled Water *one pint.* Put the Zinc into a porcelain basin, add by degrees the Hydrochloric Acid previously mixed with the water, and aid the action by gently warming it on a sand-bath until gas is no longer evolved. Boil for half an hour, supplying the water lost by evaporation, and allow it to stand on a cool part of a sand-bath for twenty-four hours, stirring frequently. Test a few drops of the resulting liquid for iron or lead by adding excess of ammonia and then sulphydrate of ammonium, when a black precipitate will be produced if iron or lead be present.

" In the latter case filter the remainder of the product into a gallon bottle, and pour in the solution of chlorine by degrees, with frequent agitation, until the fluid acquires a permanent odor of chlorine. Add the carbonate of zinc, in small quantities at a time, and with renewed agitation, until a brown sediment appears, and the whole of the iron or lead is thus precipitated. Filter through paper into a porcelain basin, and evaporate until a portion of the liquid, withdrawn on the end of a glass rod and cooled, forms an opaque white solid. Pour it out now into proper moulds, and when the salt has solidified, but before it has cooled, place it in closely-stoppered bottles. If no iron or lead be present, filter and evaporate, etc., at once." *Br.* 1885.

Rhighini prepares this chloride by double decomposition between solutions of barium chloride and zinc sulphate. Barium sulphate is precipitated, and zinc chloride remains in solution, from which it is obtained in white flaky crystals by due evaporation. As zinc sulphate is obtainable in considerable quantities as a cheap by-product in the washing of pyrites and other sulphide ores containing zinc, as well as from the so-called "pickle waste" solutions from brass foundries, this is sometimes used as a commercial source for the manufacture of zinc chloride. Finely ground salt is added to the zinc sulphate solution, and the mixture chilled, when the sodium sulphate produced by the reaction crystallizes out, leaving zinc chloride in solution.

Description and Physical Properties.—"A white, or nearly white, odorless, granular powder, or in porcelain-like masses, or moulded into pencils. It is very deliquescent. One Gm. of Zinc Chloride is soluble in 0.25 cc. of water and in about 1.3 cc. of alcohol, at 25° C. It is soluble in 2 parts of glycerin. When heated to about 260° C., Zinc Chloride fuses to a clear liquid. At a higher temperature (about 730° C.), it is partly volatilized in dense, white fumes, and partly decomposed, leaving a residue of zinc oxide. An aqueous solution of the salt (1 in 10) is acid to litmus paper. An aqueous solution of the salt responds to the reactions for zinc, and for chlorides.

"Mix an aqueous solution of Zinc Chloride (1 in 20) with an equal volume of alcohol: a single drop of hydrochloric acid is sufficient to render 10 cc. of the mixture perfectly clear (*oxychloride*). Completely precipitate the zinc from a solution of 1 Gm. of the salt in 50 cc. of distilled water, by means of ammonium sulphide T.S., filter, evaporate the filtrate, and ignite gently: the weight of the residue does not exceed 0.004 Gm. A 10 cc. portion of an aqueous solution of the salt (1 in 50), to which 1 cc. of diluted hydrochloric acid has been added, meets the requirements of the test for *heavy metals.* Add ammonium carbonate T.S., in small portions, to an aqueous solution of Zinc Chloride (1 in 20): the precipitate produced is white, and redissolves completely in an excess of the reagent. Add sufficient sodium hydroxide T.S. to 5 cc. of an aqueous solution of the salt (1 in 10) to redissolve the precipitate which first forms, and then warm the solution: the odor of ammonia is not perceptible (*ammonium salts*). One Gm. of Zinc Chloride shows no more *sulphate* than corresponds to 0.3 cc. of fiftieth-normal sulphuric acid.

"**Assay.**—Proceed as directed under the assay for chlorides, using about 0.3 Gm. of Zinc Chloride, accurately weighed in a stoppered weighing bottle. Each cc. of tenth-normal silver nitrate corresponds to 0.006815 Gm. of $ZnCl_2$. Zinc Chloride may also be assayed by the electrolytic method.

"Preserve in small, glass-stoppered bottles." *U. S.*

"Colorless opaque rods or tablets, or in granules; very deliquescent and caustic. Almost entirely soluble in *water,* in *alcohol* (90 per cent.), and in *ether.* Yields the *reactions* characteristic of zinc and of chlorides. Yields no characteristic *reactions* for lead, copper, cadmium, iron, aluminium, calcium, magnesium, sodium, potassium, ammonium, or sulphates. *Arsenic limit* 5 parts per million. 0.25 gramme, tested as described under 'Zinci Sulphas,' yields a solution with not more than a faint pink coloration (limit of manganese)." *Br.*

When pure, it is wholly soluble in water, alcohol, and ether, but often contains some oxychloride, which is left undissolved by water. There are several of these basic insoluble compounds, the so-called *oxychlorides,* of which Sorel's mass, Zn.OH.Cl, is an example. These are used for cements and as a filling for teeth. Zinc chloride has a strong tendency to combine with organic bases, forming crystallizable compounds, as with strychnine, morphine, quinine, cinchonine, etc., in this respect resembling certain other metallic chlorides, as platinum, palladium, gold, and mercury chlorides. (*J. P. C.,* 4e sér., iii, 56.) When exposed to heat, zinc chloride first melts and then sublimes. It has been obtained in small deliquescent octahedrons of the formula $ZnCl_2 + H_2O$, by evaporating its hydrochloric acid solution to a syrup, and then adding a little concentrated hydrochloric acid. It consists of one atom of zinc and two of chlorine.

Josiah C. and Bertha L. de G. Peacock (*Proc. Pa. Ph. A.,* 1918, xli, 155) conclude "that the separation of zinc oxychloride when zinc chloride is dissolved in water is always accompanied by liberation of free hydrochloric acid which remains in the solution; at the same time a loss of zinc is experienced. Both of these objections may be overcome in solutions up to approximately twenty grains to the ounce by the use of boric acid, weight for weight of zinc chloride taken. For solutions exceeding this strength, or for any strength, ammonium chloride in quantity of not less than one-fifth of the amount of zinc chloride used, will insure complete and permanent solution. Camphor water will dissolve a few grains of zinc chloride per ounce." Broeksmit (*Ph. Wb.,* 1918, lv, 1409) in order to obtain a solution free from zinc oxychloride, one which remains clear on diluting with water, recommends reducing 21.1 grammes of zinc sulphate and 7.9 grammes of barium chloride separately to fine powders, mixing them well and adding to the mixture 100 grammes of water. The mixture is then filtered. The liquid thus obtained contains about 8 per cent. of zinc chloride. (*Pharm. Weekblad.*)

Uses.—Zinc chloride has been used internally in *scrofula, epilepsy, chorea,* and other nervous diseases, but is of little or no value. Its chief use has been as an escharotic in *cancerous affections.* As a caustic it has the advantage of not causing constitutional disorder from absorption. Canquoin prepared zinc chloride as an escharotic by thoroughly and quickly mixing it with wheat flour and water into pastes of four different strengths, containing severally an ounce of the chloride incorporated with two, three, four, and five ounces of flour, fifteen drops of water being added for every ounce of flour, or sufficient to form the paste. According to the French Codex, *Caustique au Chlorure de Zinc* (*Canquoin's Paste*) is prepared by dissolving 8 parts of zinc chloride in 1 part of cold water and incorporating a mixture of 6 parts of flour with 2 parts of zinc oxide.

P. Carles states that the official paste is too hygroscopic; he triturates in a mortar 10 grammes of fused zinc chloride with 2 grammes of 60 per cent. alcohol, and incorporates, with constant trituration, 15 grammes of wheat flour. This mass may be formed into cylinders of suitable size, and when once dry is but little affected by atmospheric humidity.

It is applied in cakes from a twelfth to a third of an inch in thickness, and produces an eschar more or less deep (from a line to an inch and a half), according to the thickness and strength of the paste, the length of the application, and the nature of the part acted on. The surrounding skin should be protected from the caustic by a thickly-spread dressing of simple cerate.

Felix's Caustic Paste (*L. L.*, vol. ii, 1887) is made according to the following formula: Starch, 37 grammes; Wheat Flour, 112 grammes; Mercuric Chloride, 1 gramme; Dry Zinc Chloride, 110 grammes; pure Iodol, 10 grammes; Croton Chloral, 10 grammes; Camphor Bromide 10 grammes; Crystallized Carbolic Acid, 10 grammes; Distilled Water, sufficient to form a stiff homogeneous paste. The hand should be wetted when applying it. The paste is allowed to remain on from six to twenty-four hours, according to the amount of eschar it is desired to form.

Instead of flour, Alex. Ure, of Glasgow, mixes the chloride with pure anhydrous calcium sulphate in impalpable powder. He states that this has the advantages of furnishing a porous medium from which the escharotic gradually exudes into the morbid structure, and of forming afterwards, by acquiring a firmer consistence, an impervious case for the eschar. Cock, of Guy's Hospital, has imitated this mode of preparing the chloride, so as to form a caustic which may be limited in its action and does not run. It may be prepared as a caustic seton by thickly covering a waxed cotton wick with Canquoin's caustic paste, and then rolling it out in the form of a cylinder, according to the plan of Ancrenis, of Lyons. A thread is wound spirally around the cylinder to give it firmness.

Zinc chloride is an active antiseptic. Sternberg found that a 2 per cent. solution destroyed vegetative organisms in two hours, but Koch found that a 5 per cent. solution would not kill anthrax spores in thirty days. Miquel found that in bacteriostatic power it excelled carbolic acid. Its solutions although irritant to the skin are not injurious to iron, brass, wood, or most ordinary fabrics. It has also the advantage of being deodorant, on account of its attraction for hydrogen sulphide, and is widely employed, frequently in mixtures with other substances, as a commercial disinfectant.

It is the principal active constituent in many proprietary forms of astringent mouth wash. About 1 per cent. of zinc chloride is usually present in an aqueous solution flavored with aromatic and antiseptic oils.

In overdoses, zinc chloride acts as a corrosive poison, producing burning pain in the gullet and stomach, nausea and vomiting, cold sweats, depression of the pulse, and cramps of the legs. The antidotes are weak alkalies, or their carbonates, and, if these are not immediately at hand, soap may be used.

ZINCI OLEOSTEARAS. Br.

ZINC OLEOSTEARATE

"Hard Soap, 200 *grammes;* Curd Soap, 100 *grammes;* Zinc Sulphate, 100 *grammes;* Distilled Water, *a sufficient quantity.* Dissolve the Soaps in one thousand five hundred millilitres of the Distilled Water by the aid of heat; add to the solution the Zinc Sulphate previously dissolved in two hundred millilitres of the Distilled Water. Collect the precipitate, wash it with Distilled Water until the washings are free from sulphates, dry it, and reduce it to a fine powder." *Br.*

It is officially described as "a white amorphous powder. Odor faint, resembling that of fat. Insoluble in *water,* in *alcohol* (90 per cent.), and in *ether.* Ash about 13 per cent. The ash, dissolved in *hydrochloric acid* and the solution neutralised, yields the *reactions* characteristic of zinc. When 0.5 gramme is heated with 0.5 millilitre of *hydrochloric acid* diluted with 0.5 millilitre of *water,* a mixture of fatty acids is liberated and floats on the surface of the aqueous liquid; this aqueous liquid, filtered, neutralised with *solution of ammonia,* treated with excess of *solution of ammonium hydrosulphide,* again filtered, evaporated to dryness, and the product gently ignited, leaves no appreciable residue (absence of fixed alkalies and of alkaline earths)." *Br.*

For a process for zinc oleostearate by F. E. Niece in which he uses oleic and stearic acids and solution of zinc acetate, see *Proc. Penna. Pharm. Assoc.,* 1902, 135.

Uses.—Zinc oleostearate is used for the same purposes as zinc stearate.

ZINCI OXIDUM. U. S., Br.

ZINC OXIDE Zinc. Oxid.

"Zinc Oxide, when freshly ignited, contains not less than 99 per cent. of ZnO." *U. S.* "Zinc Oxide, ZnO, may be obtained from metallic zinc by combustion in air." *Br.*

Flores Zinci; Oxydum Zincicum; Oxyde de Zinc, *Fr. Cod.;* Blanc de Zinc, Fleurs de Zinc, *Fr.;* Zincum Oxydatum, *P. G.;* Philosophenwolle, Zinkblumen, Zinkoxyd, *G.;* Oxido zincico, *Sp.*

Preparation.—The British Pharm., 1885, and the U. S. P., 1870, prepared the zinc oxide from the carbonate already formed. By referring to the article on precipitated zinc carbonate, it will be found that it is obtained in the process from zinc sulphate, by the decomposing influence of sodium carbonate. Other methods of obtaining the zinc carbonate are by the mutual decomposition of the sodium chloride and carbonate and the ammonium sulphate and carbonate, but the former official plan is preferred. The zinc carbonate, in whatever way obtained, is exposed to heat to drive off the carbon dioxide and water, in order to obtain the oxide. According to Mohr, a full red heat is not necessary, a temperature between 280° and 300° C. being sufficient. It is probable that an unnecessarily high heat injures the oxide as a therapeutic agent.

Zinc oxide may also be obtained by the combustion of the metal. Zinc melts at 433° C., and immediately becomes covered with a film of gray oxide. When the temperature reaches nearly to redness, it takes fire and burns with an intense white light, generating the oxide in the form of very light and white flocculi, resembling carded wool, which quickly fill the crucible, and are in part driven into the atmosphere by the current of air. This form was at one time called *pompholix, nihil album, lana philosophica,* and *flowers of zinc.* Zinc oxide for use as a pigment has been very largely produced from calamine by the so-called "furnace and bag" process, at Bethlehem, Pa., by the Lehigh Zinc Company. The process consists essentially in calcining a mixture of finely ground calamine and a coal in a specially constructed furnace; the resultant zinc oxide rises, and passes through a huge combustion flue to a large circular tower, 50 feet high, in which the oxide and ashes separate, the latter falling to the bottom while the oxide is forced onward by fans through a "cooling-room," heated to from 204.8° to 371.1° C. into the "bag room" where it is deposited in large muslin bags.

Description and Physical Properties.—"A very fine, odorless, amorphous, white or yellowish-white powder, free from gritty particles. It gradually absorbs carbon dioxide from the air. Zinc Oxide is insoluble in water and in alcohol. It dissolves in dilute acids, in ammonia T.S. and in ammonium carbonate T.S. When strongly heated, it assumes a yellow color which disappears on cooling. A solution of Zinc Oxide in a slight excess of diluted hydrochloric acid responds to the reactions for zinc.

"Mix 1 Gm. of Zinc Oxide in a flask with 10 cc. of boiling, distilled water and add 2 drops of phenolphthalein T.S.: not more than 1 cc. of tenth-normal hydrochloric acid is required to discharge any red color that may be produced (*alkali*). Mix 2 Gm. of Zinc Oxide with 10 cc. of distilled water, add 30 cc. of diluted sulphuric acid, and heat on a water bath with constant stirring: no effervescence occurs (*carbonate*), and the resulting solution is clear and colorless. Five cc. portions of the cooled solution yield white precipitates with potassium ferrocyanide T.S. or with sodium sulphide T.S. (*iron and many other metals*). Add 2 Gm. of Zinc Oxide to 20 cc. of distilled water, and after stirring well, add 5 cc. of glacial acetic acid, and warm upon a water bath until solution is effected: the addition of 5 drops of potassium chromate T.S. produces no turbidity or precipitate (*lead*).

"**Assay.**—Digest about 1.5 Gm. of freshly ignited Zinc Oxide, accurately weighed, with 50 cc. of normal sulphuric acid until solution is complete. Then titrate the excess of sulphuric acid with normal sodium hydroxide, using methyl orange T.S. as indicator. Each cc. of normal sulphuric acid corresponds to 0.04069 Gm. of ZnO. Zinc Oxide may also be assayed by the electrolytic method." *U. S.*

"A soft, white or nearly white, amorphous powder, becoming pale yellow when heated. No odor or taste. Yields the *reactions* characteristic of zinc. Soluble in *diluted hydrochloric acid* without the separation of any black particles. Yields no characteristic *reactions* for copper, cadmium, iron, aluminium, calcium, magnesium, sodium, potassium, ammonium, and only slight *reactions* for lead and carbonates. *Arsenic limit* 10 parts per million. 0.2 gramme, dissolved in *diluted sulphuric acid,* and tested as described under 'Zinci Sulphas,' yields a solution with not more than a faint pink coloration (limit of manganese)." *Br.*

Commercial zinc oxide such as is manufactured for use as a pigment is usually contaminated with cadmium or lead, or both. It should never be employed for medicinal purposes. LaWall (*Proc. N. J. Ph. A.,* 1917, xlvii, 74) states that in many samples of zinc oxide, lead is present to the amount of from 0.1 to 0.5 per cent. and advises the rejection of all samples labelled "U. S. P. in all respects except the heavy metal test." He suggests the following methods for examination: Dissolve 5 grammes of the sample of zinc oxide in a slight excess of diluted sulphuric acid, with gentle heat; collect and wash the precipitate with distilled water; then pour through the filter containing the precipitate a concentrated solution of ammonium acetate (about 25 per cent.) freshly made, and to this filtrate which now contains the lead in a soluble form add a slight excess of solution of potassium chromate which will precipitate insoluble lead chromate which may be collected on counterpoised filters, or on a Gooch crucible mat, washed, dried, weighed and calculated as to its percentage. A more expeditious method which gives good results with the amount of lead usually found at the present time is to simply dissolve 5 or 10 grammes of the sample of an excess of acetic acid and then perform the precipitation with potassium chromate in this solution directly, and collect, wash and weigh the precipitate as before. This latter modification will give low results, however, where part of the lead is present in the form of sulphate as is often the case, as the sulphate will remain behind when the solution is made in acetic acid.

The U. S. P. X has adopted the second test described. The market conditions have improved somewhat and U. S. P. quality zinc oxide is now available to a much greater extent than when the condition described above was reported.

Zinc oxide, prepared by combustion, called commercial zinc oxide, is extensively used in painting as a substitute for white lead, over which it has the advantage of not being discolored by hydrogen sulphide. It is stated that it has greater covering power as a color than white lead, 10 parts being equal to 13 of white lead. It is, however, dearer, so that the pure oxide has not replaced white lead. This form of oxide, even though pure, is often unsuited for medical uses, because of lack of smoothness and the presence of gritty particles. There is an English preparation known as *Griffith's zinc white,* or *lithophone,* made by precipitating zinc sulphate by barium sulphide; it is, therefore, a mixture of zinc sulphide and barium sulphate. If this be roasted in a current of superheated steam the zinc sulphide will be converted into zinc oxide. This process has been patented in Germany by Meissner. (Wagner's *Chem. Technol.,* 11th ed., p. 159.)

Uses.—Zinc oxide has been used as an antispasmodic in *chorea, epilepsy,* and *whooping-cough,* but is probably of little value as a systemic remedy. It is also sometimes employed for its astringent and sedative properties in *diarrhea.* Its most important use, however, is as an application to excoriated surfaces and in various *skin diseases.* It owes its popularity to a combination of four qualities: it is non-toxic, protective, mildly astringent and probably antiseptic. It may be applied as a dusting powder—usually in conjunction with talcum—suspended in aqueous mixtures or in the form of ointment. (See *Unguentum Zinci Oxidi.*) As a cosmetic it has the great advantage over the preparations of lead of not being poisonous.

Dose, two to five grains (0.13–0.32 Gm.), preferably in pill form.

Off. Prep.—Unguentum Zinci Oxidi, *U. S. (Br.)*; Glycerogelatinum Zinci Durum, *N. F.;* Glycerogelatinum Zinci Molle, *N. F.;* Mulla Zinci, *N. F.;* Pasta Resorcinolis Fortis, *N. F.;* Pasta Resorcinolis Mitis, *N. F.;* Pasta Zinci, *N. F.;* Pasta Zinci Mollis, *N. F.;* Pasta Zinci Sulphurata, *N. F.;* Unguentum Picis Compositum, *N. F.;* Unguentum Resorcinolis Compositum, *N. F.;* Lotio Calaminæ, *N. F.*

ZINCI PHENOLSULPHONAS. N. F.

ZINC PHENOLSULPHONATE Zinc. Phenolsulph. [Zinc Sulphocarbolate]

"Zinc Phenolsulphonate contains not less than 73.7 per cent. and not more than 77.4 per cent. of anhydrous zinc phenolsulphonate, corresponding to not less than 99.5 per cent. of the crystallized salt ($(C_6H_5O.SO_3)_2Zn.H_2O$ = 555.76)." *N. F.*

Zinci Sulphocarbolas, *Br.* 1898; Zincum Sulphophenolicum; Zinc Paraphenolsulphonate.

Description and Physical Properties.—"Zinc Phenolsulphonate occurs as colorless, transparent, rhombic prisms or tabular crystals, or in granular form; odorless, and having an astringent, metallic taste. When exposed to the air the salt effloresces, and upon exposure to light and air may become slightly pink. One Gm. of Zinc Phenolsulphonate dissolves in 1.6 cc. of water, and in 1.8 cc. of alcohol at 25° C.; also in 0.4 cc. of boiling water.

"Its aqueous solution (1 in 10) is acid to litmus. When heated to 125° C., the salt loses all of its water of crystallization. At a higher temperature it chars, emitting inflammable vapors having the odor of phenol, and finally leaves an incombustible residue. An aqueous solution of the salt (1 in 20) yields a white, gelatinous precipitate with potassium ferrocyanide T.S., and a white precipitate with ammonium sulphide T.S. Ammonium carbonate T.S., when added in small portions to an aqueous solution of the salt (1 in 20), produces a white precipitate which redissolves completely upon the addition of an excess of the reagent. A dilute solution of the salt (1 in 100) is colored pale violet by ferric chloride T.S.

"The addition of a few drops of barium chloride T.S. to 10 cc. of aqueous solution of the salt (1 in 20), previously acidulated with 3 drops of hydrochloric acid, produces not more than a slight turbidity (*sulphate*). Ten cc. of an aqueous solution of the salt (1 in 50), to which 1 cc. of diluted hydrochloric acid has been added, does not respond to the Test for heavy metals. An aqueous solution of the salt meets the requirements of the Test for arsenic.

"**Assay.**—Dissolve about 1 Gm. of Zinc Phenolsulphonate, accurately weighed, in 100 cc. of distilled water, render the solution slightly alkaline with ammonia water and warm it to 80° C. Completely precipitate the zinc as zinc sulphide by the addition of ammonium sulphide T.S. and warm the liquid on a water-bath until the precipitate settles. Collect the precipitate on a filter, wash it with distilled water containing a few drops of ammonium sulphide T.S., then dissolve it in hot dilute nitric acid (1 in 3), evaporate the solution in a tared porcelain or platinum dish, ignite the residue and weigh it as zinc oxide. The amount of zinc oxide obtained multiplied by 5.059 indicates its equivalent in $Zn(C_6H_5SO_4)_2$. Zinc phenolsulphonate may also be assayed by the electrolytic method (see U. S. P. X).

"Preserve it in small, well-closed containers." *N. F.*

Uses.—Zinc phenolsulphonate has been employed as an antiseptic and astringent application to indolent or foul *ulcers,* and in subacute inflammations of the mucous membrane. The solutions used may be a little stronger than those of zinc sulphate employed for similar purposes. It has also been used as an intestinal antiseptic.

Dose, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Liquor Iodi et Zinci Phenolsulphonatis, *N. F.*

ZINCI STEARAS. U. S.

ZINC STEARATE Zinc. Stear.

"Zinc Stearate is a compound of zinc with stearic acid and variable proportions of palmitic acid, corresponding to not less than 13 per cent. and not more than 15.5 per cent. of ZnO." *U. S.*

Stéarate de Zinc, *Fr.;* Zinkstearat, Stearinsaures Zinkoxyd, Talgsaures Zinkoxyd, *G.*

(See *Zinci Oleostearas,* Br.)

Zinc stearate may be made by mixing a solution of sodium stearate with one of zinc acetate, at a temperature of 50° C., washing, and then drying the precipitate.

Description and Physical Properties.—"A fine, white, bulky powder, free from grittiness, and having a faint characteristic odor. Zinc Stearate is insoluble in water, alcohol, and ether. When heated, the salt fuses. At a higher temperature it is decomposed, giving off inflammable vapors and the odor of burning fat, and finally leaving a residue consisting chiefly of zinc oxide. Heat 1 Gm. of Zinc Stearate with a mixture of 25 cc. of distilled water and 5 cc. of hydrochloric acid: stearic acid is liberated and floats as an oily layer on the surface of the liquid, and the aqueous layer responds to the reactions for zinc.

"The salt is neutral to moistened litmus paper. Boil 1 Gm. of Zinc Stearate with 25 cc. of distilled water and 5 cc. of hydrochloric acid, filter while hot, and wash the filter with 25 cc. of hot distilled water. Render the filtrate alkaline with ammonia T.S., warm to 80° C., and add ammonium sulphide T.S. in excess. Filter, evaporate the filtrate to dryness, and ignite the residue. Dissolve this residue in 10 cc. of hot distilled water, filter, again evaporate, ignite, and weigh. Not more than 1 per cent. of residue remains (*alkalies or alkali earths*). The insoluble residue of fatty acids obtained in the preceding test, when well washed and dried over sulphuric acid, melts at a temperature not below 56° C.

"**Assay.**—Boil about 1 Gm. of Zinc Stearate, accurately weighed, with 50 cc. of tenth-normal sulphuric acid for ten minutes, cool, and filter. Wash the filter and flask thoroughly with distilled water and titrate the excess of sulphuric acid with tenth-normal sodium hydroxide, using methyl orange T.S. as indicator. Each cc. of tenth-normal sulphuric acid corresponds to 0.004069 Gm. of ZnO." *U. S.*

Uses.—Zinc stearate is employed in *eczema, acne* and other cutaneous diseases, in the form of powder, or made into an ointment. It has been largely used in the nursery as a substitute for talcum powder, but according to a special committee of the American Medical Association (*J. A. M. A.,* 1925, lxxxiv, p. 750) possesses no superiority over talcum and a number of fatal cases of pulmonary inflammation have been reported by Heiman and Aschner (*Am. J. Dis. of Children,* 1922, xxiii, p. 503) from inhalation of zinc stearate powder.

Off. Prep.—Unguentum Zinci Stearatis, *N. F.*

ZINCI SULPHAS. U. S., Br.

ZINC SULPHATE Zinc. Sulph.

"Zinc Sulphate contains not less than 55.86 per cent. and not more than 58.63 per cent. of $ZnSO_4$, corresponding to not less than 99.5 per cent. of the crystallized salt [$ZnSO_4.7H_2O$]." *U. S.* "Zinc Sulphate, $ZnSO_4,7H_2O$, may be obtained by the interaction of diluted sulphuric acid and zinc." *Br.*

Sulfas Zincicus, Vitriolum Album; White Vitriol; Sulfate de Zinc officinal, *Fr. Cod.;* Zincum Sulfuricum, *P. G.;* Zinksulfat, Schwefelsaures Zinkoxyd, Weisser Vitriol, Galitzenstein, *G.;* Solfato di zinco, *It.;* Sulfato zincico, *Sp.*

The Pharmacopœias no longer give detailed processes for preparing this salt.

Zinc sulphate is used industrially for the preservation of wood and of hides and for rendering fabrics fire proof. It is also used as a mordant in textile printing.

Preparation on the Large Scale.—Impure zinc sulphate, as it occurs in commerce, is called *white vitriol.* It is manufactured by roasting *blende* (native zinc sulphide) in a reverberatory furnace. This mineral, besides zinc sulphide, contains small quantities of iron, copper, and lead sulphides, and by roasting is converted, in consequence of the oxidation of its constituents, into zinc sulphate, mixed with iron, copper, and lead sulphate. The roasted matter is then lixiviated, and the solution obtained, after having been allowed to settle, is concentrated by evaporation, so that, on cooling, it may concrete into a white crystalline mass. In this state it always contains ferrous sulphate, and sometimes a small proportion of copper sulphate. It may be purified from these metals by dissolving it in water and boiling the solution with zinc oxide, which converts the iron and copper sulphates into zinc sulphate and the respective hydroxides of iron and copper. The purified solution is then decanted or filtered, and, after due evaporation, allowed to crystallize. It has generally been proposed to purify the white vitriol of commerce by digesting its solution with metallic zinc, under the impression that this is capable of precipitating all the foreign metals; but, according to Berzelius, though it will precipitate copper readily, it has no action on iron. F. Stolba recommends a process which has been used successfully for the purification of zinc sulphate by the use of zinc carbonate and zinc permanganate.

The official crystalline zinc sulphate contains seven molecules of water of crystallization; the *white vitriol* of commerce contains but three molecules of water.

The impure commercial variety of zinc sulphate is in the form of irregular white masses having some resemblance to lump sugar. The lumps usually exhibit, here and there on the surface, yellow stains, produced by ferric compounds. It is less soluble than the official salt, on account of its containing less water of crystallization.

Description and Physical Properties.—"Colorless, transparent, rhombic crystals, or a granular, crystalline powder, without odor, and having an astringent, metallic taste. It is efflorescent in dry air. One Gm. of Zinc Sulphate is soluble in 0.6 cc. of water and in 2.5 cc. of glycerin, at 25° C. It is insoluble in alcohol. When rapidly heated, Zinc Sulphate melts. When strongly ignited, it is partly decomposed, losing both water and sulphuric acid. Its aqueous solution (1 in 10) is acid to litmus paper. An aqueous solution of the salt responds to the reactions for zinc, and for sulphates.

"A 10 cc. portion of an aqueous solution of Zinc Sulphate (1 in 50), acidulated with 1 cc. of diluted hydrochloric acid, meets the requirements of the test for *heavy metals.* An aqueous solution of the salt meets the requirements of the test for *arsenic.* An aqueous solution of Zinc Sulphate (1 in 20) is not colored pink by methyl orange T.S. (*free acid*). One Gm. of Zinc Sulphate shows no more *chloride* than corresponds to 0.3 cc. of fiftieth-normal hydrochloric acid. Dissolve 1 Gm. of Zinc Sulphate in 50 cc. of distilled water, precipitate the zinc completely by means of ammonium sulphide T.S., filter, evaporate the filtrate to dryness, and ignite: the weight of the residue does not exceed 0.5 per cent. (*alkalies or alkali earths*).

"**Assay.**—Proceed as directed under *Zinci Acetas,* using 1 Gm. of Zinc Sulphate. The weight of zinc oxide obtained, multiplied by 1.984, indicates its equivalent in $ZnSO_4$. Each Gm. of Zinc Sulphate corresponds to not less than 0.2815 Gm. and not more than 0.2955 Gm. of ZnO. Zinc Sulphate may also be assayed by the electrolytic method.

"Preserve in well-closed containers." *U. S.*

"Colorless, transparent, prismatic crystals. Taste metallic, styptic. Soluble in less than 1 part of *water.* Yields the *reactions* characteristic of zinc and of sulphates. Yields no characteristic *reactions* for lead, copper, cadmium, aluminium, calcium, magnesium, sodium, potassium, ammonium, or acetates, and not more than the slightest *reactions* for iron or chlorides. *Arsenic limit* 5 parts per million. When 0.5 gramme is dissolved in *water,* excess of *solution of ammonia* added, and the mixture allowed to stand, any precipitate that is obtained being filtered off and dissolved in *diluted nitric acid,* then this acid solution, diluted with *water* to about 15 millilitres and heated to boiling, does not acquire more than a faint pink coloration on the addition of 1 millilitre of *N/10 solution of silver nitrate* and 10 millilitres of an aqueous solution (1 in 10) of *ammonium persulphate* (limit of manganese)." *Br.*

Zinc sulphate is incompatible with alkalies and alkaline carbonates, sulphides, lime water, the soluble lead salts, and astringent infusions.

Uses.—Internally, zinc sulphate is, at present, employed only for its emetic action. Because of the promptness and certainty of its effect and its comparative freedom from danger it is one of the most valuable vomitants we possess in various *poisonings.* Schwarz and Alsberg (*J. P. Ex. T.,* 1923, xxi, 1) from experiments on the lower animals conclude that the emetic dose of zinc sulphate depends on the amount of gastric contents rather than on the relation to body weight. They estimate that a dose of thirty grains (2 Gm.) should be sufficient to vomit a man even if the contents of the stomach were 300 cc. There is a wide discrepancy between the fatal doses by mouth and by injection, due to poor absorption; based on their observations on rats, cats and dogs the lethal dose for a man would be about one ounce (30 Gm.).

Externally, it is used as an active astringent, mild caustic, or disinfectant. Its solution constitutes a good styptic to bleeding surfaces, and is frequently resorted to as an injection in *fluor albus* and *gonorrhea,* and as a collyrium in *ophthalmia,* also as a stimulant application to *ulcers* both of the mucous membrane and of the skin. Simpson, of Edinburgh, employed dried zinc sulphate in the form of powder, paste, or ointment, as a powerful, rapid, manageable, and safe caustic in indurated inflammatory ulcers of the cervix uteri, in *lupus,* in *ulcerous forms of skin diseases,* and in removing *urethral caruncles, condylomata, warty excrescences,* etc. The dried salt should be finely levigated. The caustic paste is made by incorporating an ounce of the powder with a drachm of glycerin; and the caustic ointment, by thoroughly mixing the same quantity of the powder with two drachms of lard.

Zinc sulphate, in an overdose, acts as an irritant *poison.* Besides vomiting and incessant retching, it produces anxiety, distressing restlessness, and extreme prostration. Few cases are on record of fatal poisoning by this salt, the patient being generally relieved by its prompt expulsion in vomiting. Death is said to have been caused, however, by an ounce and a half. The treatment consists in the administration of an alkaline carbonate, such as sodium or potassium carbonate, followed by the free use of demulcents as white of egg or mucilage of acacia. Opium is of use to allay excessive vomiting. Other symptoms should be treated as they arise.

Dose, from one-fourth to one-half grain (0.016–0.032 Gm.); as an emetic, from ten to thirty grains (0.65–2.0 Gm.). When used as a collyrium, an injection, or a gargle, or as a wash for indolent ulcers, from one to three grains (0.065–0.2 Gm.) or more may be dissolved in a fluidounce (30 cc.) of water. For medicinal purposes the crystallized salt only should be used.

Off. Prep.—Lotio Alba Veterinaria, *N. F.;* Mistura Adstringens, *N. F.;* Pulvis Antisepticus, *N. F.*

ZINCI VALERIANAS. Br.

ZINC VALERIANATE

"Zinc Valerate, $Zn(C_5H_9O_2)_2,2H_2O$, may be obtained by saturating iso-valerianic acid with zinc carbonate, or by the interaction of zinc sulphate and sodium iso-valerianate." *Br.*

Zinci Valeras, *U. S. IX;* Zinc Valerate, *Br.;* Zincum Valerianicum, *Fr. Cod.;* Valerianas Zincicus; Valérianate de Zinc, Valérate de Zinc, *Fr.;* Zincvalerianat, Baldriansaures Zinkoxyd, *G.;* Valerianato zincico, *Sp.*

This salt has been dropped by the U. S. but is recognized by the Br. No method for preparing this salt is now official; for formulas, see *U. S. Dispensatory,* 19th edition, p. 1359.

Description and Physical Properties.—It is officially described as "white, pearly, tabular crystals. Disagreeable odor; taste metallic. Very slightly soluble in cold *water,* or in *ether;* soluble in hot *water,* and in *alcohol* (90 per cent.). Yields, when heated to redness, after moistening with a small quantity of *nitric acid,* not less than 26 or more than 27 per cent. of zinc oxide. Yields no characteristic *reactions* for lead, copper, cadmium, iron, aluminium, calcium, magnesium, sodium, potassium, ammonium, acetates, or carbonates, and not more than the slightest *reactions* for chlorides or sulphates. *Arsenic limit* 5 parts per million. When heated in a retort with *diluted sulphuric acid* it yields a distillate which, when added to *a solution of copper acetate,* does not immediately become turbid or opalescent, but forms after a short time oily drops, which gradually pass into a bluish-white crystalline deposit (absence of butyrates). 0.2 gramme of the zinc oxide obtained on incineration, dissolved in *diluted sulphuric acid,* and tested as described under 'Zinci Sulphas,' yields a solution with not more than a faint pink coloration (limit of manganese)." *Br.*

"It has the odor of valeric acid, and a sweetish, astringent, and metallic taste. On exposure to the air, it slowly loses valeric acid and becomes partially insoluble in water. One Gm. of Zinc Valerate dissolves in 70 mils of water at 25° C., usually leaving an insoluble residue of basic salt; soluble in 22 mils of alcohol at 25° C. Its aqueous solution (1 in 100) is acid to litmus. When gently heated, the salt melts. At a higher temperature it is decomposed, giving off inflammable vapors, and finally leaving a residue consisting chiefly of zinc oxide." *U. S. IX.*

Assay.—The U. S. IX gave the following process: "Dissolve about 1 Gm. of Zinc Valerate, accurately weighed, in 100 mils of distilled water, with the aid of a few drops of hydrochloric acid, if necessary, and estimate the zinc as zinc oxide by the method given in the assay under *Zinci Acetas.* The salt yields an amount of zinc oxide corresponding to not less than 99 per cent. of $Zn(C_5H_9O_2)_2 + 2H_2O$.

"Each gramme of Zinc Valerate corresponds to not less than 0.265 Gm. of ZnO. Zinc Valerate may also be assayed by the Electrolytic method." *U. S. IX.*

The salt, as obtained by the British, 1885, and U. S. P., 1870, formulas, contained one molecule of water; but when formed by saturating zinc carbonate, made into a paste with water, with valeric acid, it contains six molecules of water, and when dried at 50° C., perfectly resembles the official salt. (Wittstein.) Other authorities (Flückiger, *Pharm. Chem.,* and Roscoe and Schorlemmer's *Chem.,* vol. iii, Part I) gave the formula of the stable crystallized salt as $Zn(C_5H_9O_2)_2 + 2H_2O$.

Uses.—This salt has been used in *neuralgia, epilepsy,* and other nervous diseases, but is probably without therapeutic value. It has also been suggested for *diabetes insipidus.*

Dose, one to two grains (0.065–0.13 Gm.), repeated several times a day, and given in the form of pill.

ZINCUM.

ZINC Zinc.

Speltrum; Zinc pur, *Fr. Cod.;* Speltre, Zinc, *Fr.;* Zink, *G.;* Zinco, *It.;* Zinc, *Sp.*

Metallic zinc is no longer official. It occurs native in two principal states, as a sulphide, called *blende,* and as a carbonate or silicate, to which the name of *calamine* is applied indiscriminately, although the name belongs properly only to the latter. In this country there are two additional ores that are worked for zinc. Both occur at Franklin and Mine Hill, New Jersey, and are characteristic of those localities. They are the native oxide, called *red oxide* or *zincite,* and a mixture of zinc oxide with manganese and iron oxide, known as *franklinite.* Zinc has been detected in the vegetable kingdom in a peculiar violet, *Viola calamina,* growing on the calamine hills of Rhenish Prussia. It is largely produced in Belgium, Germany, and this country, the chief American localities being the southwestern section of Missouri, together with the neighboring counties of Kansas, the New Jersey localities before mentioned, Lehigh County (Pennsylvania), Virginia, Wisconsin and Montana. The metal is extracted generally from blende or calamine. This is roasted and mixed with charcoal powder, and the mixture heated in iron cylinders placed horizontally over a furnace. When the reduction of the zinc commences, iron receivers are adapted to the opening of the cylinder to condense the volatilized metal. The metal is then melted and run into moulds, and forms *spelter,* or the zinc of commerce. In this state it contains iron, and traces of lead, cadmium, arsenic, copper, sulphur, and charcoal. To purify it from these substances, it must be subjected to a second distillation in a crucible, furnished with a tube passing through its bottom and open at both ends, its upper extremity reaching a little more than half-way up the interior of the crucible, and its lower end terminating above a vessel of water. The impure zinc being placed in the crucible, the cover luted on, and the fire applied, the pure zinc is volatilized, and, passing down the tube by a descending distillation, condenses in the water below. In the arts zinc is purified sufficiently for commercial purposes without volatilization.

Zinc was described by the U. S. IX as "a bluish-white metal, showing a crystalline fracture. It occurs in the form of thin sheets, or in irregular, granulated pieces, or moulded into thin pencils, or in powder, and having a specific gravity ranging from 6.9 when it is cast to 7.2 after it is rolled. It is dissolved by diluted sulphuric or hydrochloric acid with the evolution of hydrogen, usually leaving some insoluble residue. When heated above 100° C. and not above 150° C., the metal becomes malleable and ductile; above 200° C., it becomes sufficiently brittle to be powdered in an iron mortar; at from 412° to 415° C. it melts, and at 940° C. it boils and may be readily distilled. Add 1 Gm. of Zinc to 25 mils of diluted sulphuric acid; the liberated hydrogen does not have a disagreeable odor, nor does it color a strip of paper moistened with lead acetate T.S. (*sulphur*), or with silver nitrate T.S. (*arsenic, antimony, and phosphorus*). The filtered solution is colorless, and yields a white gelatinous precipitate with potassium ferrocyanide T.S., and a white precipitate with ammonium sulphide T.S." *U. S. IX.*

Zincum Granulatum, Br. 1885. *Granulated Zinc.*—"Take of Zinc of commerce *one pound.* Heat it in an earthen crucible, and immediately the metal is fused remove the crucible from the fire and pour the fluid in a thin stream into a vessel containing about two gallons of cold water. Drain off the water and dry the granulated zinc." *Br.,* 1885.

Assay.—"Dissolve about 1 Gm. of Zinc, accurately weighed, in a slight excess of hydrochloric acid and add sufficient distilled water to make 100 mils. Dilute 10 mils of the clear solution with distilled water to make 100 mils, render it slightly alkaline with ammonia water and subsequently treat it as directed in the assay for *Zinci Acetas* for the determination of zinc oxide. The metal yields an amount of zinc oxide corresponding to not less than 99 per cent. of Zn.

"Each gramme of Zinc corresponds to not less than 1.232 Gm. of ZnO. Zinc may also be assayed by the Electrolytic method." *U. S. IX.*

Zinc is extensively employed in the arts. It is the best metal that can be used, in conjunction with copper or carbon, for galvanic combinations. Its solution in diluted sulphuric acid furnishes the readiest method for obtaining hydrogen for laboratory experimental purposes. With copper it forms *brass,* and, in the form of *sheet zinc,* it is employed to cover the roofs of houses, to line sinks, put under stoves, and for other purposes. It is also applied to the covering of iron, to protect it from oxidation, in the same manner as tin, forming what is commercially known as *galvanized iron.* A fine powder, known as *zinc dust,* obtained by the condensation of zinc vapor in the distillation of zinc from its ores, is much used in chemical laboratories as a convenient reducing agent in many reactions. Zinc should never be used for culinary vessels, as it is soluble in the weakest acids. The zinc caps on some types of glass fruit jars have been the cause of zinc poisoning when such jars have been employed for putting up pickles and relishes in which vinegar is a constituent. Zinc and its oxide are dissolved to a certain extent by water containing common salt, a double zinc and sodium chloride being produced in solution.

Although Sacher (*In. Dis.,* Dorpat, 1893) has shown that the intravenous injection of blood-soluble zinc salts acts as a depressant to the central nervous system and also to the heart, the metal itself is decidedly less toxic than many of the heavy metals. Workers in zinc factories who are exposed to the fumes of zinc—for it is to be remembered that the metal volatilizes at high temperatures—suffer with a system complex, known as "brass ague" or "zinc fever," which is characterized by cough, muscle cramp, nausea and diarrhea, often accompanied with shivering; the symptoms usually pass off within twenty-four hours. Lehmann (*Arch. f. Hygiene,* lxxii, p. 358) was unable to cause any chronic intoxication in dogs, even with large doses of zinc carbonate continued for months. It is highly improbable that any amount of zinc likely to be absorbed with food-stuffs would exercise a deleterious influence on the health.

Because of the observation of Sacher that zinc salts have a depressant action upon the central nervous system, they have been suggested as remedies for various nervous diseases, especially *epilepsy.* It is to be noted, however, that the official salts being precipitants of protein could not be absorbed into the blood stream. The clinical evidence as to the value of these salts in nervous diseases is as unsatisfactory as the pharmacologic.

ZINGIBER. U. S., Br.

GINGER Zingib.

"Ginger is the dried rhizome of *Zingiber officinale* Roscoe (Fam. *Zingiberaceæ*), known in commerce as Jamaica Ginger, Cochin Ginger, and African Ginger. The outer cortical layers are often either partially or completely removed. Ginger yields not less than 2 per cent. of non-volatile ether-soluble extractive and not less than 12 per cent. of cold water-extractive." *U. S.*

"Ginger is the scraped and dried rhizome of Zingiber officinale, *Roscoe.*" *Br.*

White Ginger; Gingembre blanc, *Fr. Cod.;* Rhizoma Zingiberis, *P. G.;* Ingwer, *G.;* Zenzero, *It.;* Jengibre (Rizoma de), *Sp.*

There are about seventy species of the genus *Zingiber,* the commercial ginger being obtained from *Zingiber officinale.* This species is a native of tropical Asia, but now extensively cultivated in tropical countries of both the Eastern and Western Hemispheres. It has been introduced into southern Florida where it thrives in rich soil and partial shade.

The ginger plant, *Zingiber officinale,* has a biennial or perennial, creeping rhizome, and an annual stem, which rises two or three feet in height, is solid, cylindrical, erect, and enclosed in an imbricated membranous sheath. The leaves are sessile, lanceolate, acute, smooth, up to eight inches long by about three-quarters of an inch in breadth, and stand alternately on the sheaths of the stem. The flower-stalk rises by the side of the stem from six inches to a foot, and, like it, is clothed with oval acuminate sheaths; but it is without foliage leaves, and terminates in an ellipsoidal, obtuse, bracteal, imbricated spike. The flowers are of a greenish-yellow color with a purple lip spotted with yellow and appear two or three at a time between the bracteal scales. The fruit is an oblong capsule. The plants mature in from nine to ten months. The rhizome of the ginger is lifted from the soil by a single thrust of the fork at the time when the stems of the plant turn white, before the rhizome has begun to get tough and fibrous. It is prepared in different ways for the market, which is an important factor in determining the appearance of the several varieties. When simply deprived of roots, and washed, it constitutes the green ginger which is used for condimental purposes. When, in addition, it is scalded in boiling water and rapidly dried, it is known as *black* ginger. There are other varieties, however, which after washing are either peeled and bleached sometimes with chlorine or sulphurous acid or coated with lime or having their cork removed from the flattened sides. But all of the medicinal gingers are dried before marketing.

In Jamaica the so-called *unbleached Jamaica,* or *white ginger,* is produced by carefully peeling the washed fresh rhizomes so that the cork and outer part of the cortex are removed. These are washed again and dried in the sun. The peeled pieces are macerated sometimes in water and sometimes in lime juice, and not rarely the color of the ginger is improved by finally coating it with chalk. (See Kilmer, *A. J. P.*, 1898, p. 65; Harris, *P. J.*, 1909, xxix, p. 379.) An inferior white ginger is produced in the East Indies. The thoroughness of desiccation is a matter of commercial importance. The moisture in ginger should not exceed 10 per cent., but in the poorer specimens may constitute one-fourth of the whole weight. In China the fresh ginger is rasped into a powder and as such dried. Formerly *East Indian ginger* was imported into the United States from Calcutta, while the *Jamaica* or *West Indian ginger* came usually through London. At present the cultivation of ginger is spread almost over the whole sub-tropical world, and the drug is produced in Jamaica, St. Lucia, Dominica and Africa, India, Cochin-China, Japan, etc.

The chief varieties of ginger grown in India are the Cochin and the Calicut, of which the Cochin is reputed to be the better grade. This occurs in two forms, viz., the whitewashed and bleached, cut or scraped and the unbleached. These gingers are sent chiefly from the ports of Cochin and Calicut of Madras to Bombay whence they are exported to England and America.

In Martinique a ginger is said to be obtained by the cultivation of *Zingiber Zerumbet* Rosc. The ginger of Siam is said to be produced by *Alpinia Galanga* Willd. and is the same drug, therefore, as the *Greater* or *Java Galanga Root.* The large, ordinary, *preserved ginger* of China is, according to C. Ford (*Kew Bulletin,* 1891) also the product of *A. Galanga.* It is made by boiling young, tender, carefully selected and decorticated rhizomes in syrup. Preserved ginger from the West Indies is made from the official plant. According to Hartwich and Swanlund, the rhizome of the *Zingiber Mioga* Roscoe, which is cultivated in China and Japan, has a taste less pungent than that of the official ginger, and distinctly recalling bergamot. Its volatile oil differs from Jamaica ginger in physical properties. In commerce the varieties of ginger are known by the place of their production. African and Cochin ginger on an average yield more resin than the other varieties.

The recent rhizome, known in commerce as "green ginger" is from one to four inches long, somewhat flattened on its upper and under surface, knotty, obtusely and irregularly branched or lobed, externally of a light ash color with circular rugæ, internally yellowish-white and fleshy. It sometimes begins to grow when kept in a damp atmosphere. The *black ginger* is of the same general shape, but has a dark ash-colored wrinkled epidermis, which, being removed in some places, exhibits patches of an almost black color, apparently the result of exposure. Beneath the epidermis is a brownish, resinous, almost horny cortical portion. The interior parenchyma is whitish, the cells being filled with starch. The powder is of a light yellowish-brown color. The unbleached *Jamaica ginger* is pale yellowish-buff on the outside. The pieces are rounder and thinner, and afford when pulverized a beautiful yellowish-white powder.

The uncoated ginger of the East Indies resembles the Jamaica, but is darker, being gray rather than whitish. As the Jamaica commands a much higher price than even the uncoated East India production, the latter is occasionally altered to simulate the former. This is sometimes done by coating the exterior with calcium sulphate or carbonate, sometimes by bleaching with the fumes of burning sulphur or in other ways, by which not only the exterior but also the internal parts are rendered whiter than in the unprepared root. Powdered ginger which has been exhausted in the preparation of essence, technically known as "*spent ginger,*" is used to a large extent in the adulteration of powdered ginger. Its detection without assay of some sort is almost impossible, unless so much is present as to sensibly alter the taste of the powder. The factors needed for the detection of spent ginger are the ash and the cold water extract. The latter should not be less than 12 per cent.

Commercial gingers are known as "scraped," "decorticated," and "coated." The "scraped" gingers are those from which the cortex has been removed in whole or in part by peeling, as seen in the Jamaica, and in some Cochin and Japanese varieties. In the "coated" gingers a portion of the outer natural layers are retained as in the African, Calcutta and Calicut varieties. "Bleached" and "unbleached" gingers are also distinguished, the former being lighter in color due to careful washing or special treatment. The U. S. P. X recognizes only the Jamaica, African and Cochin gingers. Of these the Jamaica is the most aromatic and the African the most pungent.

Description and Physical Properties.—"*Unground Jamaica Ginger.*—Rhizome horizontal, laterally compressed, irregularly branched, from 4 to 16 cm. in length and from 4 to 20 mm. in thickness; the cork wholly removed; externally light brown, longitudinally striate, ends of the branches with depressed stem-scars; fracture short, fibrous, starchy and resinous; internally yellowish to light brown; odor agreeably aromatic; taste aromatic and pungent.

"*Unground Cochin Ginger.*—Cork almost or wholly removed on the flattened sides light brown to grayish-yellow, fracture shorter, less fibrous and more starchy than other varieties; internally yellowish-white; oil and resin cells vary from yellowish to brownish-red; odor aromatic, taste pungent.

"*Unground African Ginger.*—Cork partly removed on the flattened sides, leaving light brownish areas; portions with cork, longitudinally or reticulately wrinkled and grayish-brown; internally light yellow to brown; taste aromatic and strongly pungent; otherwise resembling Jamaica Ginger.

"*Structure.*—Chiefly thin-walled, starch-bearing parenchyma cells, numerous scattered secretion cells and small vascular bundles; the latter very numerous, adjacent to the inner face of the narrow endodermis, the latter separating the thin cortex from the central cylinder; secretion cells, similar in size and shape to the parenchyma cells and with yellowish or orange-colored oil or oleoresin or reddish-brown resin; vascular bundles collateral, with few tracheæ, small phloem cells and usually accompanied by fibers lying on the inner face or completely surrounding the vascular tissues; cork of several or many rows of cells in African Ginger and Cochin Ginger.

"*Powdered Ginger.*—Light yellow (Jamaica Ginger), light brown (Cochin Ginger), light brown or brown (African Ginger); starch grains numerous, from 0.005 to 0.040 mm. in diameter, occasionally up to 0.060 mm. in the long axis, nearly spherical, ovoid, ellipsoidal or pear-shaped, frequently with a characteristic beak, slightly lamellated, the hilum excentric and near the smaller end; fibers long, with rounded, pointed or notched ends, thin-walled, non-lignified or only slightly lignified, with oblique pores and, where they join the parenchyma, distinctly undulate; long fiber-like cells with suberized walls and yellowish to dark brownish-red resin-like contents occasionally present; tracheæ spiral, reticulate or scalariform and frequently non-lignified; yellowish or brownish cork cells, thin-walled, occasional in Jamaica Ginger and fairly numerous in Cochin Ginger and African Ginger.

"**Assay.**—Place 4 Gm. of ground Ginger in a 200 cc. flask, fill to the mark with distilled water, and agitate at half-hour intervals during eight hours. Then allow the mixture to stand for sixteen hours and filter. Evaporate 50 cc. of the filtrate, representing 1 Gm. of the drug, on a water bath, dry to constant weight at 100° C., and weigh. It yields not less than 12 per cent. of cold water-extractive. For non-volatile ether-soluble extractive, proceed as directed on page 1552." *U. S.*

"In flattish, irregularly branched pieces, usually from seven to ten centimetres long; each branch marked at its summit by a depressed scar. Fracture short with projecting fibres. Agreeable, aromatic odor; taste pungent. When 5 grammes of powdered Ginger are shaken with 100 millilitres of *alcohol* (90 per cent.) occasionally during twenty-four hours and filtered, 20 millilitres of the filtrate yield on evaporation not less than 0.050 gramme of residue dried at 100° C.; and when 5 grammes are similarly treated with 100 millilitres of *water*, 20 millilitres of the filtrate yield not less than 0.085 gramme of residue dried at 100° C. Ash not more than 6 per cent.; and after deduction of that portion of the ash which is soluble in *water* not more than 1.5 per cent." *Br.*

Those pieces of ginger which are very fibrous, light and friable, or worm eaten, should be rejected. The commercial powder of ginger is very frequently adulterated, rice starch, powdered ginger which has been exhausted in making preparations, and even brick dust and chalk, being used, and the loss of pungency made good by the addition of capsicum or mustard.

The odor of ginger is aromatic and penetrating, the taste spicy, pungent, hot, and biting. These properties gradually diminish, and are ultimately lost, by exposure. The morphology and pharmacognosy of ginger have been studied by Meyer (*Wissenschaftliche Drogenkunde,* vol. ii, p. 64) and Tschirch and Oesterle (*Anatomischer Atlas.,* Lief. vi, p. 109). Kraemer and Sindall have published an article on the "Microscopical and Chemical Examination of the Different Varieties of Commercial Ginger" (*A. J. P.,* 1908, p. 303). Spaeth reports on the adulteration and detection of adulterants of ginger and asserts that the more common adulterants are flour, curcuma, linseed and rapeseed cake, cayenne pepper hulls, and extracted ginger. (*Zeitschr. f. Unters. d. Nahr. u. Genussm.,* x, p. 23.)

The use of capsicum in preparations of ginger is not infrequent. When present, it may be detected by the method described under tincture of ginger.

Garnet and Grier isolated a pungent constituent from ginger which was named *gingerol* by Thresh. This was later investigated by Nomura who identified it as 4-hydroxy-5-methoxy phenylethyl-methyl ketone, and named it *zingerone.* Its composition is $C_{11}H_{14}O_3$ and it melts at 40° to 41° C. It is a crystalline solid forming characteristic combinations with sodium bisulphite, and benzoyl and acetyl derivatives. He also reports the presence of *shogaol* from *shoga,* the Japanese name for ginger. This is an unsaturated ketone and has the formula $C_{17}H_{24}O_3$. (*J. Chem. Soc.,* iii, 1917, 769 and *J. Soc. Chem. Ind.* through *Drug. Circ.,* lxiii 1919, 552.)

Constituents.—The peculiar flavor of the root appears to depend on the volatile oil, its pungency is due to a yellowish liquid called *gingerol.* This is a mixture of homologous phenols of the formula $C_{16}H_{26}O_3.(CH_2O)_n$. *Zingerone,* $C_{11}H_{14}O_3$, is crystalline and has a sweet odor and an extremely pungent taste; it is chemically related to vanillin, and is formed when gingerol is treated with baryta water. The pungency of gingerol, in contrast to that of capsicum, is destroyed by heating with alkaline hydroxides.

The volatile oil is yellow with a sp. gr. of from 0.875 to 0.890 and an optical rotation of about $-25°$ to $-45°$ (the Japanese ginger is said to yield an oil which is dextro-rotatory). It consists largely of a mixture of terpenes, camphene, phellandrene and a new sesquiterpene, which the discoverers, von Soden and Rojahn (*Ph. Ztg.,* 1900, p. 414) call zingiberene. There is also some citral, cineol and borneol in the oil.

There is present in the root a considerable proportion of starch.

Uses.—Ginger is a grateful stimulant and carminative, and is often given in *dyspepsia* and *flatulent colic.* It is an excellent addition to bitter infusions and tonic powders, imparting to them an agreeable, warming, and cordial operation upon the stomach. It is especially valuable in *alcoholic gastritis.* In the serous type of *diarrhea,* when due to a relaxed condition of the bowel, it is a remedy of much service but should not be employed in the presence of inflammatory conditions. The hot infusion is popularly employed under the name of "Ginger Tea" for its diaphoretic effect in *colds,* especially when accompanied with suppression of the menses. Externally it is rubefacient. Under the name of *"Essence of Ginger"* cheap alcoholic preparations of ginger were formerly sold and used as intoxicants. A number of cases of blindness produced by such use have been recorded, the amblyopia having been due to the large use of methyl alcohol in the making of these "essences." The infusion may be prepared by adding half an ounce of the powdered or bruised root to a pint of boiling water, and may be given in the dose of one or two fluidounces (30–60 cc.).

Dose, ten to twenty grains (0.65–1.3 Gm.).

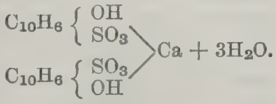
Off. Prep.—Fluidextractum Zingiberis, *U. S.;* Infusum Sennæ, *Br.;* Pilula Scillæ Composita, *Br.;* Pilula Urgineæ Composita, *Br.;* Pulvis Aromaticus, *N. F.* (*Br.*)*;* Pulvis Kaladanæ Compositus, *Br.;* Pulvis Opii Compositus, *Br.;* Pulvis Rhei Compositus, *U. S., Br.;* Pulvis Scammonii Compositus, *Br.;* Syrupus Zingiberis (from Fluidextract), *U. S., Br.;* Tinctura Zingiberis, *U. S., Br.;* Elixir Rubi Compositum, *N. F.;* Pulvis Aromaticus Rubifaciens, *N. F.;* Pulvis Myricæ Compositus, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.;* Tinctura Aromatica, *N. F.*

PART II

UNOFFICIAL DRUGS

In the present section it is proposed to consider remedies which are not recognized in the United States or British Pharmacopœias, but which, on account of their use in domestic or professional medicine, their toxic properties, their history, or the probability that they may prove in the future remedies of power, or valuable products, require notice in an encyclopedic work like the United States Dispensatory. The limit of the present volume forbids an exhaustive description of all these substances, but the attempt is made to give at least the essential information and the key to the literature about almost everything used in medicine.

Abrastol. *Asaprol. Calcium betanaphtholsulphonate. Calcinaphthol.*—*Calcium a-monosulphonate of β-naphthol,*



$$\left.\begin{array}{l} C_{10}H_6\left\{\begin{array}{l}OH\\SO_3\end{array}\right. \\ C_{10}H_6\left\{\begin{array}{l}SO_3\\OH\end{array}\right.\end{array}\right\rangle Ca + 3H_2O.$$

This is a pinkish powder, soluble in water and alcohol, and resembling the salicylates in its taste. It is neutral in reaction, readily soluble in alcohol and water, and not altered by heat. On exposure to light and air it tends to darken and become less soluble. It is incompatible with quinine salts, antipyrine, ferric salts, and potassium iodide, soluble carbonates and oxalates, and when rubbed with some of the synthetic drugs (exalgin, urethane, etc.), it forms a sticky mass. Asaprol was originally brought forward by A. Stackler as a germicide, antipyretic, and antirheumatic in *rheumatism, typhoid fever,* etc. (*B. G. T.*, 1892.) Dujardin-Beaumetz (*B. G. T.*, Jan., 1894) found the fatal dose, by mouth, for rabbits was a little less than 1 Gm. per kilo. In acute *rheumatism,* Dujardin-Beaumetz believed that the remedy is equal to salicylates, and that it has the advantage of not producing tinnitus aurium or eruptions upon the skin. Buck (*Ther. Woch.*, 1897) confirms the value of asaprol in *rheumatism.* Moncorvo (*B. G. T.*, March and April, 1895) recommends it in *chorea* and in *malarial diseases.* He also affirms that, used locally, it is an excellent antiseptic, hemostatic, and cicatrizant. He uses it in aqueous solution, 1 to 4 per cent., or as an ointment with vaseline. He even asserts that a 1 per cent. solution applied to the periglotteal region will rapidly cure *whooping cough.* It has been used to a limited extent as a food preservative, particularly for beverages, and is prohibited by statute in a number of states. It is detected by the yellow coloration produced by mercuric nitrate T.S. when added to the residue obtained by shaking out the acidulated solution, of the substance suspected of containing it, with ether, and evaporating the ether on a watch glass. The *dose* of abrastol is from ten to thirty grains (0.6–1.9 Gm.) three times a day.

Abroma. *Abroma angustum* L. f. (Fam. *Sterculiaceæ.*)—Under the name of *Olutkombul,* the glutinous sap of this plant has long been used in India in *dysmenorrhea.* According to Sircar (*Indian Medical Gazette,* 1900) and other English practitioners, it is an efficient remedy when given in doses of two drachms (7.7 Gm.) at the time of the first premonitory pains and continuing to the end. The fresh root is sometimes used. *Dose,* half a drachm (2 Gm.).

Abrus. *Abri Semina. Jequirity. Prayer Beads. Abrus Seeds. Abrus precatorius* L. (Fam. *Leguminosæ.*)—The seeds of this plant, which grows in India and also in Brazil, are employed in India as a standard weight by druggists and jewelers, and also for criminal poisoning. The seeds are ovoid, from 5 to 8 mm. in length, smooth, shiny and bright scarlet, having a black marking at the lower, or hilum, portion. They are said to be inert when taken whole into the stomach. They contain *abric acid,* $C_{21}H_{24}N_3O$, and according to the researches of Sidney Martin (*P. J.*, Sept., 1887; *Proc. Roy. Soc.*, 1889, vol. xlvi), two proteid poisons, a paraglobulin and an albumose (together called *abrin*), which are almost identical in their physiological properties with principles found in snake venom, although less powerful. According to Flexner, the toxic action of these substances also closely resembles that of true toxins, the most characteristic result being focal necroses in various organs. Flexner suggests that these in turn are due to a lesion in the blood-vessel walls caused by the abrin. (*J. Ex. M.*, 1897, vol. ii.) The ordinary lethal dose of abrin for animals is said to be 0.00001 Gm. per kilo of weight. Both Ehrlich and Calmette succeeded in immunizing rabbits against abrin, and obtained an antitoxic serum. The root of Abrus, known as *Indian liquorice,* possesses toxic properties like the seeds and should not be used in place of licorice. According to David Hooper, it contains *glycyrrhizin.* (*P. J.*, 1894.)

Abrin is used in the treatment of certain chronic diseases of the eye, especially in *corneal opacities,* and *trachomatous pannus.* It excites a purulent inflammation of the conjunctiva, which appears to lead to an increase in the local circulation, provoking thereby an absorption of inflammatory exudates. The remedy is capable of great harm in unsuitable cases, and extreme caution must be employed in its use. The infusion of jequirity, which was formerly employed for this purpose, has been almost abandoned because it was liable to cause an uncontrollable inflammation which in some instances has entirely destroyed vision. According to Ehrlich, the solution of abrin should not be stronger than one part in 500,000; any increase of strength must be made with great care. P. Römer (Graefe's *Archiv. f. Ophthal.*, vol. lii, 1901) has introduced two preparations: *jequiritol*, an abrin solution, sterilized, of four different strengths; *jequiritol serum*, which, as commercially supplied, has such immunizing power that 0.1 cc. suffices to protect a white mouse from the effects of a hundredfold lethal dose of jequiritol when the latter and jequiritol serum are injected conjointly. (For details and methods of use, see *Th. M.*, May, 1902; *M. R.*, 1902; Kattwinkel, *Jequiritol*, Bonn, 1902; Seefelder, *Klinische monatsblätter*, 1905, p. 273; Schoen, *Hospitalstidende*, No. 37, p. 921.)

Absinthium. *Wormwood.*—Absinthium is no longer recognized by either the U. S. P. or N. F. It was defined as: "The dried leaves and flowering tops of *Artemisia Absinthium* Linné (Fam. *Compositæ*), without the presence of more than 5 per cent. of foreign matter." *N. F. IV.*

Wormwood, also known as *Madderwort*, *Wermuth*, *Mugwort*, *Mingwort* and *Warmot*, is a shrubby, more or less herbaceous, finely canescent plant, growing to a height of 2 to 4 feet. The leaves are 1 to 3 pinnately divided, the lobes being lanceolate or obovate, the basal leaves being petiolate while the floral ones are linear and entire; the flowers are all fertile, yellowish, and occur in hemispherical panicled heads. The plant is a native of Europe and is to some extent cultivated in the United States. It is now naturalized and rather common in eastern Canada to Pennsylvania, growing along roadsides and waste places. It should be gathered in July or August, during flowering, for at this time the plant yields the greatest quantity of volatile oil. The yield of oil varies from year to year on account of varying climatic conditions.

The N. F. description was as follows: "Stems and leaves gray-green, finely silky-hairy and glandular throughout; largest leaves reaching 10 or 12 cm. in length, and of nearly equal breadth, on long petioles, two to three times pinnately lobed or divided, the ultimate segments oblong or obovate, obtuse, entire or slightly toothed; upper leaves becoming shorter petioled, small and narrower, the uppermost being only about 2 cm. in length and resembling the ultimate segments of the larger ones; heads racemose-paniculate, drooping on short peduncles, greenish-yellow, from 3 to 4 mm. in breadth, round-ovoid, the outer bracts linear-oblanceolate, obtuse, the inner broader and scarious-margined; receptacle hairy; outer flowers sometimes pistillate. Odor characteristic, aromatic; taste very bitter. The powdered drug is brownish to yellowish-green and, when examined under the microscope, exhibits numerous, characteristic, T-shaped, non-lignified hairs, consisting of a short, one- to four-celled stalk bearing a single apical cell attached near the center and up to 0.8 mm. in length and 0.035 mm. in width. Many of the hairs are more or less collapsed, twisted or broken; glandular hairs, some with one- or two-celled stalk, the glandular portions consisting of from four to eight secreting cells surrounded by a membrane; few simple hairs from the flowers, some of which are very long and up to 0.085 mm. in width; epidermal fragments with elliptical stomata, the latter up to 0.035 mm. in length; fragments of mesophyll and palisade cells containing chloroplastids; tracheæ mostly spiral, up to 0.035 mm. in width; few sclerenchymatous fibers, with thick, usually lignified walls and simple pores, up to 0.02 mm. in width; pollen grains few, somewhat spherical or triangular in outline, up to 0.03 mm. in diameter; calcium oxalate crystals in rosette aggregates about 0.01 mm. in diameter. Absinthium yields not more than 10 per cent. of ash." *N. F. IV.*

The volatile oil (*oleum absinthii*) is usually dark green, sometimes yellow or brownish or even blue, having a strong odor of the plant, an acrid peculiar taste, and the sp. gr. 0.925 to 0.950. It is sometimes adulterated with alcohol, oil of turpentine, etc., which lessen its specific gravity. It is composed of: *thujone* (*absinthol*), which has the specific gravity 0.926, composition $C_{10}H_{16}O$, boiling point 200° C. to 205° C., and when heated with phosphorus pentasulphide or zinc chloride yields cymene ($C_{10}H_{14}$); thujyl alcohol ($C_{10}H_{18}O$), both free and as the esters of acetic, isovaleric, and palmitic acids; phellandrene and possibly pinene; cadinene; and a *blue oil* fraction which is probably azulene. (Gildemeister and Hoffmann, *Aetherische Oele*, 1899.) The *absinthic acid* found by Braconnot is said to be succinic acid. Senger (*A. Pharm.*, ccxxx, p. 94) obtained a yellowish glucoside with an intensely bitter taste which he called *Absinthin.* This he found had a melting point of 55° C. and assigned to it the formula $C_{15}H_{20}O_4$, but Kromayer gives the formula as $C_{40}H_{56}O_8 + H_2O$. Absinthin is soluble in water, alcohol, and ether. *Dose*, one and one-half to three grains (0.1–0.2 Gm.). Adrian and Trillat isolated a new crystalline body ($C_{53}H_{51}O_{20}$) from wormwood by treating an alcoholic extract with amyl alcohol, the absinthin having been previously removed. They also isolated another crystalline principle, *anabsinthin*, $C_{18}H_{24}O_4$ (*P. J.*, 1899, 1, 75). The old *salt of wormwood* (*sal absinthii*) was impure potassium carbonate, made from the ashes of the plant.

Wormwood, which was formerly in vogue as a stomachic tonic, antiperiodic, and anthelmintic, is at present very seldom used. The volatile oil is an active narcotic poison. In dogs and rabbits from thirty to fifty drops (1.5–2.5 cc.) of it will cause trembling, stupor, hebetude, and even insensibility; one to two fluidrachms (3.75–7.5 cc.) of it causes violent epileptiform convulsions, with involuntary evacuations, unconsciousness, and stertorous breathing, which may or may not end in death. (Marcé, *B. G. T.*, Mai, 1864; Amory, *B. M. S. J.*, March, 1868, p. 83.) In man the oil acts similarly; a half ounce (15 cc.) of it caused, in a male adult, insensibility, convulsions, foaming at the mouth, and a tendency to vomit; though the patient recovered under the use of emetics, with stimulants and demulcents. (*L. L.*, Dec. 6, 1862.) According to J. L. Corning, the volatile oil is a powerful local anesthetic, locally useful in *rheumatic pains*. *Dose*, of wormwood in substance, from twenty to forty grains (1.3–2.6 Gm.); of the infusion (one ounce in a pint of boiling water), from one to two fluidounces

(30–60 cc.); of the oil, one to two minims (0.06–0.12 cc.).

Absinthe is a liqueur containing oils of wormwood, angelica, anise, and marjoram. According to Baudrimont, the *absinthe ordinaire* contains 47.66 per cent. of alcohol, the *demi-fine* 50 per cent., the *fine* 68 per cent., and the *absinthe Suisse* 80.66 per cent. The preparation, if manipulated properly, possesses naturally a bright green color, brought to an olive-green by slight addition of caramel coloring; but artificial coloring was formerly often resorted to, and indigo, turmeric, cupric acetate, and aniline green have been used to produce the proper shade. *Absinthism* differs from ordinary alcoholism in its manifestations; its characteristic symptoms are restlessness at night, with disturbing dreams, nausea and vomiting in the morning, with great trembling of the hands and tongue, vertigo, and a tendency to epileptiform convulsions.

Several species of Artemisia have enjoyed some reputation as medicines. The leaves of *A. Abrotanum* L., or *southernwood*, are reported by Craveri to contain a crystallizable alkaloid, *abrotine* $C_{21}H_{22}ON_2$; they were formerly employed as a tonic and anthelmintic. *A. pontica* L. has been substituted for common wormwood, but is weaker. *A. vulgaris* L., or *mugwort*, has been used in Germany in *epilepsy, chorea,* and *amenorrhea. A. ludoviciana* Nutt., a native of the southwestern regions of the United States, has been commended as a stimulant to the hair. (*A. J. P.*, 1872, p. 106.) In China, *moxa* is prepared from *A. chinensis* L. and *A. indica* Willd.

Acalypha. *Br. Add.* 1900.—The fresh and the dried herb, *Acalypha indica* L. This euphorbiaceous plant is said to have expectorant and emetic properties similar to those of ipecac, and also to be employed by the native Indian practitioners in the form of the fresh leaves as a poultice for *ulcers*, and as a suppository for *constipation* in children. The *Succus Acalyphæ*, Br. Add., 1900, was prepared by adding one volume of 90 per cent. alcohol to three volumes of the juice expressed from fresh leaves, with subsequent filtration; *dose*, from one to four fluidrachms (3.75–15 cc.). The *liquid extract* (*Extractum Acalyphæ Liquidum*, Br. Add., 1900), made with a menstruum of 90 per cent. alcohol, is given in doses of from five to thirty minims (0.3–1.8 cc.).

Acetal. *Acetol. Diethylacetal. Diethylaldehyde.* $C_6H_{14}O_2$ or $CH_3CH(OC_2H_5)_2$.—*Ethidene* (*Ethylidene*) *diethylic ether*, a limpid volatile liquid boiling at 103°–104° C., sp. gr. 0.831 at 22° C., and produced by the imperfect oxidation of alcohol. Sparingly soluble in water, readily soluble in alcohol. Used as a hypnotic in *doses* of two or three fluidrachms (8–12 cc.), preferably in emulsion.

Acetonitrile. *Methyl Cyanide.* CH_3CN. (C_2H_3N).—This is a colorless liquid, with a characteristic odor, miscible with both water and alcohol, and prepared from acetamide with glacial acetic acid by heat. Although it is probable that it is partly broken up in the system, methyl cyanide is not highly toxic. According to Lang (*A. E. P. P.*, 1894, xxxiv, p. 24), the fatal dose for rabbits is about one gramme. About one-fifth of the cyanogen which is introduced in the radical may be recovered from the urine in the form of an alkaline sulpho-cyanide. Its chief importance lies in the fact that it has been suggested by Hunt (*A. I. P. T.*, 1904, xii, p. 44) as a means for the biological standardization of the thyroid gland.

Acetophenone. *Hypnone. Phenyl-methyl-ketone. Phenylmethylacetone.* C_8H_8O or C_6H_5CO. CH_3.—A colorless liquid, boiling at 200° C., sp. gr. 1.035, having a very tenacious, persistent odor, suggesting that of bitter almonds and jasmine, not inflammable, made by distilling a mixture of calcium acetate and benzoate. It is insoluble in water or glycerine but soluble in alcohol, ether, etc., and in expressed oil of almonds.

It was originally proposed as a somnifacient but has been shown to be both uncertain as a hypnotic and toxic in its action. *Dose*, from three to ten minims (0.2–0.6 cc.). For further information see *U. S. D.*, 20th ed., p. 1225.

Acetopyrine. *Acopyrin. Pyrosal. Phenazopyrine. Antipyrinæ acetyl-salicylas.*—This occurs as a white, crystalline powder, having an acetous odor; melting point 63°–65° C.; sparingly soluble in cold but freely in warm water; freely soluble in alcohol. It was originally introduced into medicine by Winterberg and Braun (*W. K. W.*, 1900, No. 39) as combining the activities of antipyrine and acetyl-salicylic acid, into which substances, according to W. Meitner (*St. P. M. W.*, xx, 1900), it is broken up in the stomach; the acetyl-salicylic acid undergoing further decomposition in the intestines. Acetopyrine has been used as an analgesic in *migraine, neuritis,* etc., and also as an antipyretic. It has also been employed as an antirheumatic, especially in subacute and chronic cases. Goldmann (*All. W. M. Z.*, April, 1901) claims that it is valuable in *bronchitis;* and Bolognesi (*B. G. T.*, March, 1901) recommends it in *gonorrhea.* It may be given in *doses* of five to ten grains (0.32–0.65 Gm.).

Aceto-Toluid.—Two isomeric compounds, the *ortho-* and *para- Tolyl-acetamid*, $C_6H_4(CH_3)NH.C_2H_3O$, have been used in medicine for their antipyretic effects (see Barbarini, *T. Mod.*, 1892, p. 532). They each occur as colorless crystals, sparingly soluble in water, somewhat more soluble in alcohol. The acet-ortho-toluid is recommended in doses of 8 grains (0.5 Gm.); the acet-para-toluid in doses of 15 grains (1 Gm.).

Acetylene. C_2H_2.—Acetylene was first prepared by Berthelot, who obtained it by passing the electric spark between carbon points in an atmosphere of hydrogen. It is now prepared on a large scale by the decomposition of carbides, like calcium carbide, with water according to the reaction:

$$CaC_2 + 2H_2O = C_2H_2 + Ca(OH)_2.$$

The product so obtained is almost always contaminated with phosphine, and this should always be removed by washing the acetylene with bromine water. It is produced by a number of other methods involving the reduction of higher hydrocarbons and is produced to a limited extent when the flame of a Bunsen burner or gas stove strikes back and burns at the base, giving rise to its characteristic odor, by which the abnormal condition of the flame is frequently detected.

Acetylene is a colorless gas of ethereal odor, slightly soluble in water, more readily in alcohol and ether, and most abundantly in acetone. It burns ordinarily with a very smoky flame, but from a burner with a fine slit gives a clear white flame. It forms an explosive mixture with air, also a series of explosive compounds with copper, silver, and other metals. These compounds are in reality the carbides of the respective metals, the formula of the copper compound being Cu_2C_2.

According to Mosso and Ottolengui (*Rendiconti Della R. Academia dei Lincei.*, 1896) acetylene gas causes death through respiratory failure when more than 20 per cent. is present in the air, but Moissan (*C. R. A. S.*, cxxi) found that from 40 to 79 per cent. could be breathed without toxic manifestations while Oliver (*B. M. J.*, 1898, i) found it practically non-toxic if sufficient oxygen to maintain life was inhaled with it.

Calcium carbide, CaC_2, from which acetylene is made, is prepared by melting a mixture of powdered lime and coke dust in an electrical furnace. It is a grayish-brown, dense substance having a crystalline metallic fracture and the specific gravity of 2.26. It evolves a peculiar odor when exposed to the atmosphere, due to the action of moisture which causes partial decomposition with the production of acetylene. When exposed to the air, it decomposes and becomes coated with a layer of calcium hydroxide, which to a great extent protects the interior of the lumps from further deterioration. Calcium carbide is not inflammable and one pound, if pure, yields 5.9 cubic feet of acetylene gas at 18° C.

Acetylphenylhydrazin. $C_6H_5.(NH)_2C_2H_3O$.—This substance, first introduced into medicine in an impure form, under the name of *pyrodin*, has since been used in an alleged pure condition under the name of *hydracetin*. It is chemically closely allied to acetanilid, which possesses only one imido-group, (NH); it is, as indicated by its name, hydrazin in which hydrogen atoms are replaced by phenyl and acetyl. It forms colorless, inodorous crystals, melting at 128.5° C., soluble in fifty parts of water and readily soluble in alcohol. Guttmann (*Pr. M. W.*, 1889) demonstrated that this substance is a powerful antipyretic, in *doses* of from one and a half to two and a half grains (0.09–0.16 Gm.) but believes it to be a very dangerous remedy on account of its destructive action on the red-blood cells. Externally he considered it to be safe and allied to pyrogallic acid in its influence upon *skin diseases;* but Basch (*L. L.*, 1890) has seen very violent poisoning from the use of a 10 per cent. ointment, without benefit to the *psoriasis*. For fuller information see *U. S. D.*, 20th ed., p. 1226.

Achillea. *U. S.* 1870.—The flowering tops of *Achillea Millefolium* L. *Milfoil*, or *yarrow* is a perennial herb, very common both in Europe and America. It is from a foot to eighteen inches in height, and is specifically distinguished by its doubly pinnate, downy, minutely divided leaves, with linear, dentate, mucronate divisions, from which it derived the name of milfoil, by its furrowed stem and involucre, and by its dense corymbs of whitish flowers, which appear throughout the summer, from June to September. *Achillea nobilis*, L., and *A. moschata* Jacq., or *Iva* of Europe, are sometimes used as substitutes for *A. Millefolium*.

Both the flowers and leaves of *A. Millefolium* have an agreeable, though feeble, aromatic odor, which continues after drying, and a bitterish, astringent, pungent taste. The aromatic properties are strongest in the flowers, the astringency in the leaves. The plant contains volatile oil, tannin, and a peculiar principle, *achillein*, which was discovered by Zanon. (*Ann. Ch. Ph.*, lviii, 21.) As analyzed by von Planta (*Ann. Ch. Ph.*, clv, 1870) its formula is $C_{20}H_{38}N_2O_{15}$. It occurs in a brownish-red mass of a strongly bitter taste, soluble in water, more feebly in alcohol, and not at all in ether. *Achilleic acid*, also discovered by Zanon, is affirmed by Hlasiwetz to be identical with aconitic acid. The oil, which may be obtained separately by distillation with water, has a beautiful azure-blue color, and the peculiar flavor of milfoil. Schimmel & Co. (*B. Chem. G.*, 1894, p. 50) found its most important constituent to be cineol. The high boiling blue portion is probably identical with the *azulein* of chamomile oil. *Ivaïn*, $C_{24}H_{42}O_5$, has also been isolated; it occurs as a dark-yellow resinous mass, insoluble in water, readily soluble in alcohol, and producing an intensely bitter solution. There are a number of other species of achillea which have been distilled for the volatile oil, including *A. coronopifolia* Willd., *A. moschata* Jacq., *A. nobilis*, and *A. ageratum* L. The oils from these plants, while showing certain resemblances, vary greatly in physical properties. The specific gravity of the volatile oil has been variously reported as from 0.869 to 0.927.

Milfoil is a mild aromatic sudorific tonic and divided doses up to from thirty to seventy-five astringent. Pappi states that *achillein* given in grains (2–5 Gm.) causes marked irregularity of the pulse. The infusion is sometimes used in acute *suppression of the menses*. The *dose* of achillea is thirty to sixty grains (1.9–3.9 Gm.); the volatile oil has been used in doses of ten to fifteen minims (0.6–1.0 cc.).

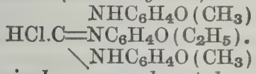
Acocanthera.—The Wa Nyika, the Wa Gyriama, and the Wa Kamba tribes of Eastern Africa, and the natives of Obok on the Gulf of Aden, prepare vegetable arrow poisons probably from different species of plants, although the names *wabayo* and *ouabaïo* seem to have been used as synonyms by missionaries and others sending the extract to Europe.

The botanical sources of these arrow poisons are uncertain. It is certain that several species of the apocynaceous genus *Acocanthera* are used for arrow poisons by the natives of Africa. Of the four principal species, *A. Schimperi* B. and H. is found abundantly in the highlands of Abyssinia and throughout a great portion of Eastern Africa; *A. deflersii* Schwf., which resembles the last-named species closely, but, according to Schweinfurth, differs in that its flowers are larger, sweet-smelling and pure white, has been found in the neighborbood of Yemen; *A. ouabaïo* Arnaud is a native of Somaliland, and *A. venenata* Don. of South Africa. For details, see *A. de S.*, cvii, p. 1162; abs. in *J. P. C.*, 1889, p. 245. From *Acocanthera abyssinica* K. Shum. is prepared the *Shashi-poison* of German Eastern Africa.

In 1882 Arnaud obtained from an unidentified species of the genus *Acocanthera* (which he named provisionally *A. Ouabaïo*), a crystalline glucoside, and in 1893 Lewin separated from the *Acocanthera Deflersii* an amorphous glucoside.

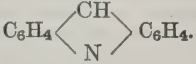
Owing to the imperfect identification of the plants from which the principles have been obtained, there has been much confusion in the names which have been applied to the principles which various investigators have separated from these arrow poisons. According to Lewin (*B. K. W.*, 1906, p. 1583), there are two glucosides found in the various species of *Acocanthera*, one of which is crystalline, and the other amorphous. The amorphous substance, or, as it is generally known, *amorphous ouabain,* corresponds to the *abyssinin* of Briege (*A. I. P. T.*, 1903), and the *carissin* prepared by Bancroft from the *Carissa ovata* R. Br. (Fam. *Apocynaceæ*), an Australian plant. The *acocantherin* of Frazer he regards as identical with the crystalline ouabain of Arnaud, and probably is isomeric with the amorphous variety. It is generally conceded that the crystalline ouabain is chemically identical with the glucoside discovered by Thoms in the *Strophanthus gratus* (see *Strophanthus* Part I). Its action seems to be precisely the same as that of strophanthus. Ouabain was apparently first employed clinically by Stadelmann (*B. K. W.*, 1906, vol. xliii, p. 1586), and has since been used by others with more or less success in the treatment of various forms of *cardiac weakness.* Stadelmann used an amorphous glucoside prepared by Merck from the wood of the *Acocanthera Schimperi,* in *doses* of from one three-hundredth to one two-hundredth of a grain (0.0002–0.0003 Gm.) three times a day.

Crystalline oubain is used in the standardization of digitalis (see *Reagents*).

Acoine. 

$$\mathrm{HCl.C}\begin{matrix}\diagup\mathrm{NHC_6H_4O(CH_3)}\\ =\mathrm{NC_6H_4O(C_2H_5)}.\\ \diagdown\mathrm{NHC_6H_4O(CH_3)}\end{matrix}$$

Di-para-anisyl-mono-phenetyl-guanidine-hydrochloride. Guanicaine.—A white, crystalline powder, melting point 176° C., and soluble in water (six parts to one hundred). It is incompatible with iodine or alkaline iodides. Acoine was introduced as a local anesthetic by Trolldenier. (*Th. M.*, xiii; also *Zeit. T. M.*, 1901.) It has been specially used by ophthalmologists in a 1 per cent. aqueous solution, stronger solutions being very irritant or even corrosive. It is not absorbed through a normal conjunctiva, but when the epithelial covering is destroyed, or when the drug is injected into the sub-conjunctival tissues, it is said to act more powerfully than cocaine, and to be specially efficacious in the relief of deep-seated ocular pains. It is also actively antiseptic, the 1 per cent. solution remaining free from bacteria. Acoine has also been used with asserted excellent results in dentistry and in operations upon the nose. For dental purposes a 2 per cent. solution is preferred.

Acriflavine. *N. N. R.* 1924, *Acriflavine.*—Under the names of Proflavine and Trypaflavine have been introduced two derivatives of *diamino-acridine.* The *acridine* dyes are derivatives of a base found in coal tar,  $C_6H_4\langle{}^{CH}_{N}\rangle C_6H_4$. One of these derivatives—(diamino-methyl acridine chloride) $C_{14}H_{15}N_3Cl_2.H_2O$—was found by Ehrlich to possess valuable properties in trypanosome infections. He called it *trypaflavine.* English investigators later called it *acriflavine.* A closely related substance having similar properties is *proflavine.* Acriflavine is the hydrochloride of 3:6 diamino—10 methyl-acridine chloride $= C_{14}N_{14}N_3Cl.H_2O$. Proflavine is 3:6 diamino—acridine sulphate $= C_{13}H_{11}N_3H_2SO_4.H_2SO_4$. *Neutral Acriflavine* closely resembles acriflavine but is asserted to be less irritating.

These occur as reddish-brown powders, soluble in both water and alcohol, forming dark red solutions which fluoresce when diluted. Abelmann finds that a 1 per cent. solution of flavine is extremely sensitive to sunlight and in a short time turns brown and develops a fungus growth; it, however, keeps perfectly well in the dark. He states that the addition of an organic acid or of hydrogen dioxide produces a similar change to sunlight.

These dye-stuffs appear to be powerfully germicidal. According to Browning and Gulbransen (*Brit. Jour. of Exp. Path.*, 1921, ii, 95) acriflavine exercises a germicidal effect against the staphylococcus in as low a dilution as one in 200,000, although somewhat less powerful against the *B. coli.* There is considerable difference of opinion as to the real value of this compound. Its popularity in England is due largely to the work of Browning and his co-workers (*B. M. J.*, Jan. 29 and July 21, 1917) who assert that it rivals mercury bichloride in its disinfectant powers and against certain organisms, especially the staphylococci, is decidedly more germicidal. Further they assert that its disinfectant powers are enhanced by the presence of serum and that in appropriate concentrations it has no effect on phagocytosis. On the other hand Fleming (*L. L.*, September 1, 1917) finds that it is more injurious in its effects to leukocytes than to bacteria and that a 1 to 500 solution mixed with an equal quantity of pus failed to sterilize the latter within twenty-four hours. Carlslow and Templeton (*L. L.*, April 27, 1918) find that its action in wounds is antiseptic but not germicidal, but that in some way, despite the continuation of living bacteria in the wound, it lessens inflammatory reaction. Bashford, Hartley and Morrison (*B. M. J.*, 1918) state that although there is a marked lessening of suppuration and apparent preservation of the surrounding tissue under the influence of flavine, that it is decidedly inferior to the Carrel-Dakin treatment because it leads to slow epithelial growth and delays all the processes of repair. Flavine has been used as a disinfectant in the treatment of *gonorrhea* and as a surgical *wound* dressing. While many of the reports are favorable there is by no means unanimity as to their precise value (see *J. A. M. A.*, 1919, lxxiii, 1542). It may be used in strengths of 1 to 1,000. Davis (*Journ. Urology*, 1921, v, 215) recommends it by mouth in doses of 0.05 to 0.1 Gm. (three-fourths to one and one-half grains) as a urinary antiseptic in *cystitis,* and Buss has used (*D. M. W.*, 1923, xlix, 476) it intravenously in somewhat smaller doses in *epidemic encephalitis.*

Acrolein. *Acrylic Aldehyde. Allyl aldehyde.* $CH_2 = CH.CHO$.—Acrolein, a decomposition product of glycerin or glycerides, is a fluid which emits an intensely pungent odor, is soluble in two or three parts of water, and boils at 52.5° C. It is asserted by E. Koch and G. Fuchs (*Cb. B.*, 1899, xxvi) to be a valuable bactericide, but its exceedingly disagreeable odor and tendency to undergo decomposition have prevented its coming into use. It is the cause of the irritating vapors given off when glycerin or fats are heated in air to the point of decomposition.

Actæa. *Actœa spicata,* L. *Baneberry. Herb Christopher. Radix Christophorianœ. Racine de Saint Christophe,* Fr. *Christophswurz, Wolfswurz,* G.—This is a perennial herbaceous plant (Fam. *Ranunculaceœ*) growing in the woods of mountainous regions from Japan to Central Europe as well as in Siberia. Its dark-brown, bitterish, somewhat acrid root resembles that of *Helleborus niger,* for which it is said to be occasionally substituted. It is an active emeto-purgative, capable of producing, when in overdose, dangerous effects. There are two American species which probably have medicinal properties similar to those of *A. spicata*—namely, *A. alba* (L.) Mill., or *white cohosh*, and *A. rubra* (Ait.) Willd., or *red cohosh*, distinguished by the color of their berries. *Actæa racemosa* was the former name of the official *Cimicifuga racemosa.* (*Proc. A. Ph. A.*, 1858.)

Actinium.—This was discovered in 1899 in uranium pitch blend by De Bierne, a factory director in the radium plant of the Curies, and is asserted to be identical with the *anemium* of Giesel (De Bierne, *C. R. A. S.*, 1899, cxxix and 1904, cxxxix, p. 538). It is a radioactive element whose spectrum and atomic weight have not yet been definitely determined. It differs from radium in not being spontaneously luminous. Actinium gives out easily absorbable and penetrating deviable rays and a radioactive emanation which loses its activity in a few seconds. It has been used by Czerny and Caan (*M. M. W.*, 1911, p. 1801) in the treatment of various forms of *cancer.* They inject intramuscularly from one-sixth to two grains of actinium suspended in normal salt solution (0.01–0.12 Gm.).

It occurs commercially as a brownish-red powder, insoluble in water, but soluble in strong nitric or hydrochloric acids.

Actinomeris. *Verbesina helianthoides* Michx. (*Actinomeris helianthoides* Nutt.) (Fam. *Compositæ.*)—At one time known as *Gravel Weed, Diabetes Weed,* now known as *Sunflower Crownbeard.* It is a perennial herb growing in the thickets and on dry prairies from Ohio and Missouri to Texas and Georgia. The root was formerly used in Georgia in *dropsy* and *chronic cystitis. Dose* of infusion (one ounce to a pint), one fluidounce (30 cc.).

Adamon.—Adamon is the dibromo-dihydro cinnamic acid ester of borneol. It is used as a sedative in *neurasthenia, hysteria* and other conditions of nervous erethism. According to Oppenheim (*D. M. W.*, 1913, p. 1103), it is especially valuable as an anaphrodisiac in *nymphomania. Dose,* eight to twelve grains (0.5–0.7 Gm.).

Adansonia. *Adansonia digitata*, L. *Baobab.*—A tree of enormous magnitude, belonging to *Bombacaceæ.* It is a native of Africa, extending from Senegal to Abyssinia, and has been introduced into the West Indies. The leaves and bark of this tree abound in mucilage, and have little odor or taste. By the Africans the leaves are used as a diaphoretic, and the subacid pulp of the fruit in *dysentery.* Under the name of *cream-of-tartar tree* various trees have been described. Their fruits contain, or have been supposed to contain, potassium bitartrate. The most important of these is the *Adansonia Gregorii* F. Muell., of North Australia. Another cream-of-tartar fruit is yielded by a tree of South Africa, which, according to E. M. Holmes, is probably the *A. madagascariensis* Baillon. E. J. Millard (*P. J.*, April, 1890), however, could find in this fruit no cream-of-tartar at all.

Heckel and Schlagdenhauffen (*Nouv. Rem.*, xxi, 487) have found in the fruit of the *Adansonia digitata* as much as 2 per cent. of free tartaric acid and 12 per cent. of potassium bitartrate. Duchassaing, of Guadeloupe, West Indies, and Pierre, of France commended the bark of *A. digitata* highly as an antiperiodic. (*A. G. M.*, 3e sér., xxiii, 535.)

Adenanthera. *Adenanthera pavonina* L. (Fam. *Leguminosæ.*) *Zangavara.*—Rochebrune (*Toxicologie Africaine*) obtained from this tree a crystalline principle which resembles in its activity physostigmine, but does not affect the muscles.

Adenia. *Adenia venenata* Troost.—A climbing passion-flower of Africa, said by Schweinfurth to be used as a vesicant. (*P. J.*, March, 1874.) The *Adenia hongkii* is employed by the natives of the Soudan as an ordeal poison. Perrott and LePrince (*P. J.*, 1910, lxxxiv, p. 82) have separated an active principle which is neither glucosidal nor alkaloidal, and which has a strophanthin-like effect.

Adhatoda. *Br. Add.* 1900. (Fam. *Acanthaceæ.*) —The fresh and dried leaves of *Adhatoda vasica* Nees. (*Justicia Adhatoda*, L.) The leaves are four to six inches long and about an inch and a half broad, lanceolate, entire short petiolate, taper-pointed, smooth on both sides. The dried leaves are of a dull brownish-green color which becomes much lighter when the leaves are powdered. They have a strong characteristic tea-like odor and a bitter taste. *Br. Add.*, 1900.

The leaves are stated to contain an alkaloid, *vasicine*, and an organic acid, *adhatodic acid* (see *Pharmacog. Indica*, vol. iii). Vasicine, isolated by Hooper, is soluble in water, sparingly in benzin and carbon disulphide, readily soluble in ether and chloroform. The claim is made for it that it exerts a powerful toxic influence upon lower forms of vegetable and animal life, and is not poisonous to the higher animals. The leaves are considerably used in India as an expectorant and antispasmodic, especially in the treatment of *asthma.* The Br. Add. recognized the *liquid extract* (*Extractum Adhatodæ Liquidum*, Br. Add., 1900), made with alcohol and given in *doses* of from twenty to sixty minims (1.3–3.75 cc.); the freshly *expressed juice* (*Succus Adhatodæ*, Br. Add., 1900), *dose*, from one to four fluidrachms (3.75–15.0 cc.); the *tincture* (*Tinctura Adhatodæ*, Br. Add., 1900), *dose*, from one-half to one fluidrachm (1.8–3.75 cc.).

Adiantum. *Maidenhair.*—Tradition has attributed to various species of this genus of ferns valuable properties in chronic pulmonic *catarrhs. A. pedatum*, L., of America, *A. Capillus-Veneris*, L., of Europe, *A. lunulatum* Burm., of India, are the most important species. The European species is sometimes employed on the Continent as an emmenagogue under the name of *polytrichi, polytrichon*, or *kalliphyllon*, and is given in the form of infusion, sweetened with sugar or honey, and a syrup prepared from it is said to be popular in France under the name of *sirop de capillaire,* and official in the French Codex.

Æsculus. *Horse-chestnut.*—The *Æsculus Hippocastanum*, L. (Fam. *Hippocastanaceæ*) seems to have been originally a native of Asia, but introduced about the middle of the sixteenth century into Europe, whence it has spread to this country. The seed or "nut" abounds in starch, but its bitter, disagreeable taste has prevented its general use as a food, although as long ago as 1856 starch was made from it in France, and recently a pleasant and nutritious article of diet is said to have been improved by removing its bitter principle by means of alcohol. For analysis of the oil it contains, see Stillesen, *Proc. A. Ph. A.*, 1909, lvii, p. 201. In the leaves Rochleder found *quercitrin*, and a bitter principle, *esculin* (*æsculin*); and in the capsules of the fruit a peculiar acid, *capsulæsic acid* (*J. P. C.*, May, 1859; Aug., 1860). (For Rochleder's method of extracting esculin, see *U. S. D.*, 18th ed.; for a second process, see *A. J. P.*, xliv, 400.) Esculin is in shining, white, prismatic crystals, inodorous, bitter, but slightly soluble in cold water, more soluble in boiling water, and very readily so in boiling alcohol and in alkaline solutions. Its solution, which is fluorescent, is precipitated by lead subacetate, and its formula, according to Schiff, is $C_{15}H_{16}O_9 + 1\frac{1}{2}H_2O$. When treated with dilute sulphuric acid, it is converted into grape sugar and a substance called *esculetin*, $C_9H_6O_4$, which is now known to be a dioxycoumarin.

Tannin is found in all parts of the tree, including the leaves as well as the bark and fruit. According to Rochleder, when pure, it is white and soluble in water, alcohol, and ether; becomes red by the absorption of oxygen; colors ferric salts green, but violet on the addition of a little alkali; fluorescent when it is in alkaline solution; in concentrated solution is precipitated, at least partially, by sulphuric, hydrochloric, and metaphosphoric acids, but not by acetic acid, and forms also, with potassium and sodium sulphites and ammonium sulphide, precipitates which are readily dissolved by dilute acetic acid. (*J. P. C.*, Jan., 1868, 72.) Titherly and Coppin have found *allantoin* ($C_4H_6O_3N_4$) in growing shoots of the Horse-chestnut; *leucine* has been reported in the buds and *lecithin* in the seeds.

The powdered kernel of the nut is a sternutatory. The extract of the wood has been used in dyeing silk black. The fixed oil, extracted from the kernels by ether, has been employed in France as a topical remedy in *rheumatism;* and the bark as an antiperiodic in doses of half an ounce (16 Gm.) in the twenty-four hours, given in the form of decoction. The flowers are stated to contain quercitrin. In the United States a decoction of the leaves is popularly employed for *whooping cough*, and to the seeds themselves, when "carried in the pocket of the patient," is attributed the marvellous property of curing *hemorrhoids*, *rheumatism*, etc. Esculin has also been administered in *malarial disorders*, in fifteen-grain (1 Gm.) *doses* repeated once during the intermissions. (*Ann. Thér.*, 1859, 1860.) The glucoside esculin has the property, like other fluorescent substances, of absorbing ultra violet rays which are then gradually given off. Because of these properties, it is used on the one hand, as a protective against the effects of sunlight and on the other as a means of continuing the effect of heliotherapy. Thus Freund has found it useful not only against *sunburn*, but as a prophylactic against *snow blindness* (*Zeit. f. Neuere Physikal. Med.*, 1908, ii), and Graham (*L. L.*, 1905, ii, p. 1769) recommends it in the Finsen light treatment of *lupus vulgaris* and similar conditions. For this purpose he injected five minims (0.3 cc.) of a 2 or 3 per cent. solution immediately beneath the skin in the region to be treated by the light. Under the name of *zeozon* and *ultra-zeozon* there are upon the market pastes whose exact compositions are not stated but which are claimed to contain oxy-derivatives of esculin.

The fruit of the *Æsculus pavia* L., or *Red Buckeye* of the southern United States, is said to be an active convulsant. E. C. Batchelor (*A. J. P.*, xlv, 144) found in the cotyledons of the seeds about 2½ per cent. of a peculiar glucoside.

Æthusa. *Fool's Parsley. Æthusa Cynapium*, L. (Fam. *Umbelliferæ.*)—A fetid annual herb naturalized from Europe and growing in waste places or cultivated grounds in the northern United States and Canada.

The leaves of this plant are reported by Ewing and Clevenger to have been employed as an adulterant of *Conium maculatum* leaves (*Conii Folia*). They may be distinguished by their leaflets which in the case of *Æthusa* are rhomboid oval, deeply lobed, the segments sometimes further lobed, narrow to linear, blunt or abruptly pointed, whereas those of *Conium* are lanceolate-oblong, deeply incised with dentate, quite sharply pointed segments. (*J. A. Ph. A.*, 1919, viii, 385.) In 1859, Walz stated that the fruit of the *Æthusa Cynapium* contains a volatile base similar to coniine. This statement has been confirmed by Power and Tutin (*J. Am. C. S.*, 1905, xxvii) who recovered, besides various inert matters, about one forty-thousandth of 1 per cent. of the volatile alkaloid. This plant has been variously attributed with poisonous properties, but Harley (*P. J.*, 1880, xi, p. 43) denies any noxious quality, and, in the experiments of Power and Tutin, the extract from five hundred grammes of the dry herb caused, in a small dog, vomiting and salivation, but the animal entirely recovered.

Afridol. *Sodium hydroxymercuric toluylate. Mercuretol* $C_6H_3(CH_3)(COONa)HgOH$ 2:3:1.—This is an odorless, tasteless white powder, difficultly soluble in neutral or acid media, but soluble in ammoniacal solution containing ammonium chloride. It is said to be of value for rendering parts of the body antiseptic for surgical operations. It has also been recommended in the treatment of parasitic skin diseases, *acne*, *sycosis*, etc., the afridol soap being proposed for this purpose.

Agathin. $C_6H_5.N(CH_3).N:CH.C_6H_4.OH$. *Salicyl-a-methyl-phenyl-hydrazine. Salizone.*—This is obtained by the reaction of salicylic aldehyde upon *a*-methyl-phenyl-hydrazin. It is a yellowish crystalline substance, without odor or taste, is insoluble in water, soluble in alcohol and ether and melts at 74° C. It was proposed as a remedy by Israel Roos, and is said by E. Rosenbaum to act like salicylic acid. Although excellent results (see *D. M. Ztg.*, 1892, Nos. 50, 93) have been claimed for it in *neuralgia* and *rheumatism*, without unpleasant effects other than headache, in trials by H. C. Wood it did not seem serviceable. *Dose*, from five to ten grains (0.3–0.65 Gm.).

Agave. *Agave americana*, L. *American Agave. American Aloe. Maguey.* (Fam. *Amaryllidaceæ.*)—An evergreen succulent plant, indigenous to Florida, Mexico, and other parts of tropical America, and largely cultivated, chiefly for hedges, in the south of Europe, especially in Spain. Although the *Agave americana* is the best known form, botanists have described fifty species of the genus, which are indigenous to South America and the southern portions of North America, and many of which contribute to the economic products produced in that country from the agave plant. The number of these products is very great. *Sisal grass* or *sisal hemp* and *Tampico hemp*, also known as *Pita hemp* or *Pita fiber*, are the most important of the various fibers obtained from the agave leaves, though a number of other forms are locally known in Mexico. From a number of species of *Agave*, are produced in Mexico, large quantities of fermented liquors, known as *pulque*, and distilled liquors known as *mescal* or *tequila.* All of the pulque agaves have thick leaves. When they are about to bloom the central bud is cut out, leaving a large cavity into which the sap (*aguamiel* or *honey water*) exudes rapidly. At first clear green, yellowish or whitish, this sap soon by fermentation becomes milky and acquires a cider-like taste or, if the process is allowed to go on, is rapidly converted into vinegar. *Pulque* is said to contain about 7 per cent. of alcohol, and is very largely used as a beverage by the Mexicans, but its odor and taste are disagreeable to unaccustomed palates. The juice has in it an optically inactive reducing sugar, *agavose*, $C_{12}H_{22}O_{11}$. The leaves and roots and stocks of the agave contain saponin and are used in Mexico in the place of soap.

The fresh juice is said to be laxative, diuretic, and emmenagogue, and in doses of two fluidounces (60 c.c.) useful in *scurvy.* Under the name of *Matamel*, there has been placed upon the market a preparation, stated to be the concentrated fresh sap of the Agave, and intended for use in *nephritis* and other diseases of the genito-urinary organs. The leaves are said to be used as counter-irritants, and Lenoble has found in them an acrid volatile oil. (*J. P. C.*, xv.) *Agave Gum* has been compared to gum arabic, but differs in containing a much larger proportion of lime, and in being only partially soluble in water, the soluble portions resembling arabin, but the larger insoluble portions having all the characteristics of bassorin.

Agave virginica, L., which grows in our Southern States and is known in South Carolina by the name of *rattlesnake's master*, has a very bitter root, which is used, in the form of tincture, in *colic.*

Agelæa. *Agelæa Lamarckii* Planch.—Under the name of *Cephan-Mahi, Soandrou, Vahé-mainti*, this African plant is used as an antiblenorrhagic. According to Rochebrune (*Toxicologie Africaine*), it contains a poisonous glucoside, *agelætoxine.*

Agrimonia. *Agrimonia Eupatoria*, L. *Common Agrimony. Herba Agrimoniæ. Aigremoine, Eupatoire des Grecs*, Fr. *Odermæning, Leberklette*, G. (Fam. *Rosaceæ.*)—This species of agrimony is a perennial herb, found in both Europe and North America. (Britton, however, maintains that the European species differs from any of ours.) A volatile oil may be obtained from the plant by distillation. Agrimony was at one time used as a folk-remedy in a wide variety of diseases but probably possesses no virtues except some astringent property. *Dose*, one drachm (3.9 Gm.) or more (see 16th ed., *U. S. D.*).

Ailanthus. *Ailanthus glandulosa* Desf. *Tree of Heaven. Chinese Sumach. Tree of the gods. Ailanto. Götterbaum*, G.—This well-known shade-tree, belonging to the Fam. *Simarubaceæ* in its general aspect and the character of its foliage, appears like a gigantic sumach, and was at one time considered to be a Rhus. In France it is cultivated for the sake of its leaves, upon which the Chinese silkworm is fed, and is known by the name of *Japan varnish* (*vernis de Japon*), from its having been mistaken for the true Japan varnish tree, which is a species of sumach. (*P. J.*, vii, 370.) The powdered bark is of a greenish-yellow color, possesses a strong, narcotic, nauseating odor, in the fresh condition, and has a strongly bitter taste. When chewed, it is said to produce a general uneasiness, a sense of increasing weakness, vertigo, cold sweats, with shivering and a sensation of nausea. F. H. Davis detected traces of a crystallizable organic acid, but no alkaloid or glucoside. (*A. J. P.*, 1885, 600.) By the action of alcohol, there is obtained from the bark an *oleo-resin* which has the consistence of tar, a very dark greenish-brown color, and in a high degree the odor and taste of the bark. Hetet found the bark to produce in dogs copious stools and the discharge of worms. The resin purged, but rarely acted as an anthelmintic. The powdered bark has been used successfully against the *tapeworm.* In China the bark is very popular as a remedy in *dysentery* and other *bowel complaints.* (*A. J. P.*, 1874, 276; *P. J.*, vii, 372.) *Dose*, from seven to thirty grains (0.5–2.0 Gm.).

In India the bark of the *Ailanthus excelsa* Roxb. is used as a bitter tonic. It occurs in rough, dirty-green pieces. Narayan Daji found in it a bitter uncrystallizable principle and a bitter nitrogenous acid, *ailanthic acid*, to which he attributes medicinal virtues. (*P. J.*, Aug., 1870, Oct., 1876, June, 1877.) This acid is not used medicinally in this country.

Air. *Liquid Air.*—This substance is produced commercially for the manufacture of oxygen and nitrogen. In its manufacture air is subjected to a pressure of 200 atmospheres, then cooled by a salt and ice mixture, and suddenly allowed to expand to 20 atmospheres. This compression and expansion is repeated until the temperature reaches –189° C., when most of the air liquefies. It is difficult to transport, owing to its tendency to vaporize, and is therefore usually used near the point of manufacture. It is usually a milky liquid, from the presence of solid carbon dioxide, but may be freed from CO_2 and becomes transparent and of a slightly bluish color. Substances such as rubber, meat, eggs, mercury, etc., when plunged into it are frozen solid in a few moments, becoming very brittle. When applied to the skin it freezes the parts and may be utilized as a local anesthetic for minor surgical operations. Taylor and McKenna (*L. L.*, 1909, ii, p. 1774) have used liquid air with good results in the treatment of *lupus erythematosus* and also for the destruction of *nævi.* The method of applying it is to wrap a piece of absorbent cotton around the end of a stick about ten inches long. This is immersed for a moment in liquid air and then pressed firmly against the part to be treated.

Ajowan. *Ajava. Ajwan.*—The ripe fruit of *Carum copticum* Benth. et Hook. (*Carum Ajowan* Benth. et Hook., *Ptychotis Ajowan* DC.), an annual of the Fam. *Umbelliferæ.* It is cultivated in India, Egypt, Persia and Afghanistan. The fruits resemble those of parsley, but are distinguished by their odor. They yield 3 to 4 per cent. of volatile oil which contains from 45 to 55 per cent. of thymol. This oil is official in the B. P. (see *Oleum Ajowan*). The fruits also contain from 25 to 32 per cent. of a fixed oil and from 15 to 17 per cent. of protein, making them a very good cattle food. They are used in the form of an extract and water, viz.: *Extractum Ptychotis Liquidum* P.I. and *Aqua Ptychotis* P.I. The water, known as *Omum water*, is used in India in the treatment of *cholera.* The *dose* of the *Fluidextract of ajowan* is ten to thirty minims (0.6–2.0 cc.).

Ajuga.—Of this genus *A. chamæpitys* L., or *Ground Pine; A. reptans*, L., *Mountain Bugle*, or *Common Bugle;* and *A. pyramidalis*, L., all of them European species, the last naturalized in America, have been used in medicine, and are probably mild astringents and tonics. The ground pine is said to contain a volatile oil, and has been used to some extent in *amenorrhea* and in various forms of *rheumatism*, in *doses* of from one to two drachms (3.9–7.7 Gm.). *Ajuga Iva,* L., of Sardinia, is said to be a depressomotor, an active bactericide, and an antiperiodic. (*A. I. B.*, xxxiv.)

Akazga. *Boundou. Quai. Ikaga. Icaya.*—An ordeal poison, largely used in a district on the west coast of Africa, extending far into the interior, north and south of the equator. The precise botanical character of the plant is unknown, but it is thought to belong to one of the *Loganiaceæ.* Thomas R. Fraser found in the plant an alkaloid, *akazgine.* The alcoholic extract or the alkaloid acts on the system similarly to nux vomica. (For further description, see *U. S. D.*, 19th ed., p. 1373 and also *A. J. P.*, March, 1867.)

Alangine.—This alkaloid, according to Scheriff, occurs in the bark of the stem and root of *Alangium Lamarckii* Thwaites (Fam. *Cornaceæ*), a shrub indigenous to the tropical forest of India and Burma. It is very bitter, soluble in alcohol, chloroform, and acetic ether, but insoluble in water. In small doses it acts as a febrifuge; in *doses* of fifty grains (3.2 Gm.) it is emetic.

Alanin (Alpha). $CH_3CH(NH_2)COOH$. *Propionic Glycocoll. Alpha-aminopropionic acid.*—Prepared from aldehyde ammonia by hydrocyanic and hydrochloric acid and forms white crystals that are soluble in alcohol and water. It is used as the basis for the preparation of alanin compounds.

Alanin Mercury (*Hydrargyri Amidopropionas. Mercury Amidopropionate*) has been used either internally or subcutaneously, in *doses* of from one-twelfth to one-sixth of a grain (0.005–0.01 Gm.).

Alantol. (*Pinguin.*) $C_{10}H_{16}$.—Prepared by distillation from the root of *Inula Helenium* L. (*Elecampane*). It is a yellowish to a brownish-yellow liquid with a taste and odor similar to peppermint. It is insoluble in water and soluble in the immiscible solvents. It has been used in place of turpentine in *pulmonary tuberculosis. Dose,* one-sixth minim (0.01 cc.) 10 times daily.

Alchemilla. *Alchemilla vulgaris,* L. *Lady's Mantle.* (Fam. *Rosaceæ.*)—This astringent, bitter, perennial, European herb was formerly employed in *diarrhea.* By the ancients it was highly esteemed; extraordinary powers were ascribed to it by the alchemists. (*P. J.*, 1885, 791.)

Alcornoque.—For an account of this bark, which has long since fallen into entire neglect, see 16th ed., *U. S. D.*, p. 1545.

Aldehydes.—Aldehyde is a generic term that applies to a class of bodies holding an intermediate position between the alcohols and the acids derived from the former by oxidation. The word itself was coined from the Latin *alcohol dehydrogenatum,* meaning alcohol deprived of hydrogen. They are generally prepared by the oxidation, by chromic acid, of the respective alcohols.

Anisic Aldehyde. Anisaldehyde.—Prepared from anethol by oxidation. Formula $C_6H_4(O.CH_3).CHO$.—A colorless liquid with an aromatic odor. Soluble in alcohol and ether. Insoluble in water. Boiling point 248° C. Sp. gr. 1.126 at 15° C. It is used in admixture with other odorous substances in perfumery, the addition of other odors being necessary to bring out the agreeable hawthorn odor of the aldehyde.

Butylic Aldehyde. (*Iso-butyryl aldehyde.*) $(CH_3)_2CH.CHO$.—A transparent, colorless, highly refractive liquid. Boiling point 63°–64° C. Sp. gr. 0.797. Insoluble in water. Miscible with water and alcohol and possessing a pungent odor. Used in organic synthesis.

Ethyl Aldehyde. CH_3CHO. *Acetic Aldehyde. Ethylic Aldehyde. Aldehyde. Acetaldehyde. Aldéhyde acetique* (*vinique*), Fr.—This substance is commonly given the name "Aldehyde," which, being a generic name, is misleading and indefinite. The following formula for its preparation is given: One part of ethyl alcohol, of sp. gr. 0.842, and 1 part of potassium dichromate are introduced into a large tubulated retort, and 1⅓ parts of sulphuric acid dropped in through the tubulure. Sufficient heat is evolved to start the distillation, but heat must be applied towards the end. The distillate is slightly contaminated with acetic acid. If the aldehyde be desired pure, the distillate is to be mixed with twice its volume of ether, the vessel surrounded with cold water, and dry ammoniacal gas passed in to saturation. Aldehyde-ammonia crystallizes out. This is to be decomposed in a retort by a mixture of 3 parts of sulphuric acid and 4 parts of water, and the distillate rectified and dried by contact with calcium chloride. Aldehyde is a colorless, mobile, inflammable liquid, having a decidedly pungent, ethereal, and suffocating odor. Its sp. gr. is 0.790, and boiling point 22° C. It mixes in all proportions with water, alcohol, and ether, and is rapidly converted into acetic acid on exposure to the air, through absorption of oxygen. It possesses very marked antiputrescent properties, meat being preserved for months by its 2 per cent. aqueous solution. The intoxication caused by it in animals is characterized by a very great loss of sensibility. It appears to paralyze the vagi, although its cardiac action is comparatively feeble. Upon the respiration it exerts a most powerful influence, in small doses quickening it, in large doses depressing it. The temperature is much diminished. Applied locally aldehyde is very irritating. (*M. T. G.*, Sept., 1875.)

A condensation product of Ethyl aldehyde is known as "*Aldol,*" $CH_3CH(OH)CH_2CHO$, and is exploited as a hypnotic and sedative. It boils below 105° C. and is decomposed at 135° C. Like formaldehyde it will, on spontaneous evaporation, leave a solid polymeric residue, *Paradol.*

Heptoic Aldehyde. Oenanthol. Heptanal. $C_6H_{13}CHO$.—A highly refractive liquid, colorless and possessing an agreeable aromatic odor. It is prepared from castor oil by heating and fractional distillation, and is soluble in alcohol and ether and slightly in water. It is used in perfumery and as the basis of the preparation of other odorous aldehyde compounds.

Iodaldehyde may be made by mixing together iodine, iodic acid, and a solution of aldehyde and separating by adding water (see paper by P. Chautard, *P. J.*, 1886, 224).

Paracuminic Aldehyde. Cuminol. Cumyl Hydride. $(C_6H_4)(CH_3)_2.CH.CHO$.—A yellowish oily fluid with a persistent strong odor and an acid burning taste. It is one of the constituents of Roman chamomile. It is soluble in alcohol and ether and has a sp. gr. of .9382 at 0° C.

Propylic Aldehyde. Propionic Aldehyde. $CH_3CH_2.CHO$.—A colorless liquid with a suffocating odor, soluble in water, and boiling at 48° C. Sp. gr. 0.807. It is claimed to be a powerful antiseptic and an effective preservative. It is employed in organic synthesis.

Valeric Aldehyde. Isovaleric Aldehyde. $(CH_3)_2$-

$CH.CH_2.COCO$.—A colorless liquid with a pungent, apple-like odor. It is miscible in all proportions with alcohol and ether, boils at 92° C., and has a specific gravity of 0.804 at 15° C. It is used commercially as an artificial flavoring agent and in perfumery. It was also proposed at one time as a hypnotic and sedative, but was later on abandoned.

Alisma. *Alisma Plantago-aquatica,* L. *Water Plantain. Plantain d'eau. Pain de grenouilles,* Fr. *Froschlöffel, Wasserwegerich,* G. (Fam. *Alismaceæ.*)—A perennial herbaceous plant, common to Asia, Europe, and the United States. The root has, when fresh, an odor like that of Florentine orris, but loses it when dried. Its taste is acrid and nauseous. It contains a pungent volatile oil and an acrid resin, to which all its virtues must be ascribed. The Calmucks in Russia are said to use it for food. The leaves are rubefacient, and will sometimes even blister. They have been recommended in *gravel* and *cystitis. Dose,* a drachm (3.9 Gm.).

Alival. *Iod-dihydroxy-propane,* $CH_2.CH.OH.-CH_2OHI$.—This organic iodine compound occurs as odorless, white crystals, soluble in either water or alcohol, melting between 48° and 49° C. It is used for the effect of the iodine in the treatment of *syphilis* and other conditions, either by inunction or hypodermic injection.

Alkanet. *Alkanna Root, Alkanet Root, Orcanette,* Fr. *Spanish Bugloss. Alkannawurzel,* G.—This is the root of *Alkanna tinctoria* Tausch. or *dyers' alkanet,* an herbaceous perennial plant, of the Fam. *Boraginaceæ,* indigenous to Asia Minor and southeastern Europe. It is not to be confused with the allied bugloss formerly official (see *Anchusa*). (See E. M. Holmes, *P. J.*, 1897, p. 61. *Proc. A. Ph. A.*, 1896, 565.) Alkanet, as found in commerce, is in pieces 10 to 25 cm. long, and from 5 to 15 mm. thick, slightly twisted, one- to few-headed, consisting of a dark-red, easily separable bark, and an internal centrally placed ligneous portion which is reddish externally, whitish near the center, and composed of numerous distinct, slender, cohering fibers. As it comes to us it is usually much decayed internally, very light, and of a loose, almost spongy texture. The fresh root has a faint odor, and a bitterish, astringent taste; but when dried it is nearly inodorous and insipid. Its coloring principle, which abounds mostly in the cortical part, is soluble in alcohol, ether, and the oils, to which it imparts a deep red color, but is insoluble in water. It may be obtained by first exhausting the root with water, and then treating it with a weak solution of potassium or sodium carbonate, from which the coloring principle may be precipitated by an acid. According to Pelletier, by whom it was discovered, it possesses acid properties, forming with the alkalies and earths neutral compounds, which are of a blue color, and soluble in alcohol and ether. Its weak acid character resembles that of alizarin, to which it is chemically related, as when distilled with zinc dust it yields methyl-anthracene. It has also received the names of *anchusin* and *alkannin.* The *anchusin* has been extracted and studied by C. J. S. Thompson. (*A. J. P.*, 1886, 409.) He finds it to vary in amount between 5.25 and 6.02 per cent. It is red, resin-like, insoluble in water, soluble in oils, alcohol, chloroform, and ether, and gives a rich deep blue color in alkali hydroxides, the color changing again to crimson on addition of an acid. According to A. Gawalowski, the red coloring matter of alkanet root consists of two distinct bodies, the one turning blue, the other green by the action of alkalies. The first of these, *alkannic acid,* is extracted by ether and alcohol. The second, *anchusic acid,* is obtained by extraction with benzene. Both form characteristic colored salts. (*Ph. Ztg.*, 1902, 817.) Alkanet is somewhat astringent, and was formerly used in several diseases; but it is now employed exclusively for coloring oils, ointments, and plasters, which are beautifully reddened by one-fortieth of their weight of the root. The best way to use it with this object in view is to suspend the alkanet, after tying it in a piece of suitable fabric, in the melted fat. A fine color is obtained by previously washing the alkanet with water and then thoroughly drying it before suspending it in the fat or oil. It is said also to be used in the preparation of spurious *port wine.* The *Oleum Hypericum,* formerly much used under that title or the name *Red Oil,* consisted of fixed oil colored with alkanet.

Syrian Alkanet is the dried root of *Macrotomia cephalotes* DC., a perennial herb belonging to the same family and indigenous to the same regions as true Alkanet. It differs from true Alkanet in being many-headed, of much larger size, of black-violet color and metallic luster, more twisted and in having laterally placed wood. A similar coloring extract is present in Syrian Alkanet as is found in true Alkanet and in much larger amounts. (For details see Ewing and Clevinger, *J. A. Ph. A.*, 1918, 591–594.)

Allamanda.—*Allamanda cathartica,* L., is a shrub of the Fam. *Apocynaceæ,* growing in Porto Rico, the extract of whose bark is said to be an excellent hydragogue cathartic, in *doses* of from one to two grains (0.065–0.13 Gm.).

Alliaria. *Alliaria officinalis* Andrz. [*Sisymbrium Alliaria,* Scop. *Erysimum Alliaria,* L. *Alliaria Alliaria* (L.) Brit.] *Hedge Garlic.*—A perennial European herb, a native also of Northern Asia, and naturalized from Canada to Virginia, having an alliaceous odor when rubbed, and a bitterish, somewhat acrid taste. When eaten it communicates its odor to the breath. Wertheim obtained from the root a volatile oil, apparently identical with that of mustard. (*Ann. Ch. Ph.*, liii, 52.) The herb and seeds are esteemed diuretic, diaphoretic, and expectorant, and are used as external applications in *gangrenous affections,* and to promote *suppuration.*

Allocain.—In 1909 Professor Nagai of Japan prepared from the alkaloid ephedrine (see *Ephedra*) a synthetic substance which he called *Mydriatine,* which is chemically and physiologically related to epinephrine. By introducing into the molecule of this compound benzoyl and ethyl groups, he has prepared two synthetic substances which are actively local anesthetics; allocain S. contains one ethyl group and forms a soluble hydrochloride, while allocain A., containing two ethyl groups, forms an insoluble chloride.

The mono-ethyl-mydriatine hydrochloride, or allocain S., has been physiologically studied by Kubota (*J. P. Ex. T.*, 1919, xii, p. 361). It occurs as a white odorless crystalline powder freely soluble in either alcohol or water. Because allocain is very feebly basic, the salt has an acid reaction and is easily decomposed even by comparatively weak alkalies. It has a bitter, astringent taste. When applied to the tongue it produces a tingling sensation followed by numbness. He finds it possesses local anesthetic properties midway between those of procain and cocain, but that it is less toxic than either of these drugs. It has also some antiseptic powers.

Allonal.—Under this name has been introduced a sedative which is asserted to be a chemical combination of amidopyrine with *allyl-isopropyl-barbituric acid.* It occurs as a yellowish powder, slightly soluble in water, and represents 37.5 per cent. of allyl isopropyl barbituric acid and 52.5 per cent. of amidopyrine.

Allonal has been used by Burns (*N. Y. M. J.*, April 19, 1922) as an analgesic and hypnotic with marked success. He especially praises it for those cases in which there is *insomnia* caused by *pain.*

It is marketed in the form of tablets each of which represents 0.17 Gm. (2⅔ grains). One to three tablets may be given at a dose.

Allophanic Acid. *Acidum Allophanicum.* $NH_2.CO.NH.CO.OH$.—This is a *urea-carbonic acid,* but occurs only in the form of salts and esters, as at the moment of liberation the acid splits into urea and carbonic acid gas. Its best known derivative is its amide, called *biuret.* Apparently it exercises no influence on the system of itself, but according to Overlach (*B. K. W.*, 1908, p. 1403) is valuable because it has the power of forming compounds with a number of substances of unpleasant taste and penetrating odor, and rendering them much less disagreeable. For instance, santalol unites with allophanic acid to form a tasteless, dry, crystalline powder (having the composition $NH_2.CO.NH.COOC_{15}H_{23}$). The same is true of castor oil and of creosote.

Almatein.—This proprietary article is a condensation product of formaldehyde with hematoxylin and is given the formula $CH_2O_2.(C_{16}H_{12}O_5)_2.CH_2$. It is a bright red, light powder, odorless and tasteless, insoluble in water, but soluble in dilute alkalies, alcohol or glycerin. Astalfoni (*Press. Med.*, 1908) finds that it has a powerful antiseptic action and is non-poisonous. It passes through the system unchanged, and is split up by the alkaline intestinal juices, with the slow liberation of formaldehyde, and is employed as an intestinal disinfectant. It has been used also as a dusting powder on *wounds* (Werndorff, *M. M. W.*, 1909), also dissolved in glycerin as an injection in cold *abscesses.* One drawback to its use is its staining power. The *dose* for internal administration is from five to fifteen grains (0.3–0.9 Gm.).

Alnus. *Alder.*—Of this genus of small trees or bushes, *A. glutinosa* (L.) Medic., or *European Alder, Black Alder; A. rugosa* (Du Roi) K. Koch (*A. serrulata* Willd.), or *American Alder; A. incana* (L.) Willd., or *Speckled Alder,* are tonic and astringent, and have been used in intermittent fever, the bark being the part employed. *A. glutinosa* has been used for dyeing and also for tanning. According to Eitner, the bark contains from 16 to 20 per cent. of tannic acid which, according to F. Dreykorn and E. Reichardt, is resolved by sulphuric acid into *alnine red* and sugar. (*A. J. P.*, xlii, 403.)

Alpha-naphthol. $C_{10}H_7OH$.—This isomer of beta-naphthol is obtained in colorless prisms or powder of a disagreeable taste. It is sparingly soluble in water, but more soluble in alcohol and ether. It melts at 94° C., and boils at 278°–280° C. In antiseptic action it is about equivalent to its isomer, beta-naphthol. It is used internally as an antiferment in five-grain (0.3 Gm.) doses; in *typhoid fever* thirty to sixty grains (2–4 Gm.) a day. Externally it has been used in a 10 to 20 per cent. oily solution in *erysipelas, scarlet fever* and *smallpox,* as well as in various *skin diseases.* According to Maximovitch, alpha-naphthol has the same action upon pathogenic germs as has beta-naphthol, having the superiority over the latter compound, however, of being less poisonous to the higher animals in proportion to its germicidal power. It may be used in the same strength of solution and in the same dose as beta-naphthol.

The substance recommended as a germicide, under the name of *microcidin* is said to be a sodium-naphthol.

Alpha-naphthol has been proposed as a test for sugar in urine. Posner and Epenstein have studied the action of the test, and considered it to be free from many of the objections raised against other tests for sugar. The test depends upon the fact that a solution of sugar, in the presence of pure concentrated sulphuric acid and a solution of alpha-naphthol, gives a violet-colored reaction, due, according to Udransky, to the separation of furfurol. This reaction occurs not only with sugars, but with all carbohydrates and with certain albuminoids; hence *the urine must be free from albumin.* The test is said to be extremely sensitive, showing one-hundredth of one per cent. of sugar. The urine must always be previously diluted. *Winkler's test* for hydrochloric acid in the stomach is performed as follows: 5 Gm. of alpha-naphthol are dissolved in 100 cc. of alcohol, to which is added from 0.5 to 1.0 Gm. of grape sugar. A mixture of the filtered gastric juice is then evaporated with a few drops of the reagent in a porcelain dish on a water bath; if free hydrochloric acid be present, a bluish-violet marginal zone will appear and rapidly become inky black.

Alphol.—*Salicylic Ester of Alpha-naphthol, Alpha-naphthol salicylate,* $C_6H_4\left\{\begin{matrix}OH\\COOC_{10}H_7\end{matrix}\right.$, is obtained by reaction between salicylic acid and alpha-naphthol. It is a white, crystalline powder, melting at 83° C. Soluble in alcohol, ether, and fixed oils; insoluble in water, decomposed in the alkaline secretions of the intestinal tract into alpha-naphthol and salicylic acid. It is incompatible with alkalies and with ferric compounds. Used as an antiseptic and antirheumatic. *Dose,* eight to fifteen grains (0.5–1.0 Gm.).

Alphozone. *Succinic Dioxide.* $(COOH.CH_2CH_2CO)_2O_2$.—This powerful oxidizing agent occurs as a fluffy, white, crystalline powder, the crystals being small, irregular plates. It is fairly soluble in water and alcohol, sparingly so in ether and insoluble in chloroform and benzene. It is devoid of odor and deteriorates slightly on exposure to air. It is employed for the germicidal and antiseptic properties of its nascent oxygen, being used both externally and internally. Unlike hydrogen peroxide it does not effervesce on contact with pus. It is employed in strengths of about 1 to 1000.

Aluminum.—(For description of chemical properties of aluminum, see *Alumen* Part I.) Under the name of *escalin,* a mixture of two parts of the finely powdered metallic aluminum with one part of glycerin has been employed by Klemperer (*Ther. Geg.*, May, 1907) as a substitute for the insoluble salts of bismuth, especially in the treatment of *gastric ulcers.* Sussman (*Ther. Geg.*, May, 1908) has also found this preparation useful in the treatment of *anal fissures.* It is marketed in the form of tablets, which when thrown into water disintegrate and yield on stirring a uniform suspension of the metal. Four of these tablets may be given at a dose, preferably on an empty stomach and repeated daily for three or four days.

Aluminum Acetate as well as the *subacetate* is largely employed in medicine. The deliquescent acetate may be made by the direct combination of hydrated alumina with acetic acid or by reaction between aluminum sulphate and lead acetate,

$$Al_2(SO_4)_3 + 3Pb(C_2H_3O_2)_2 = 3PbSO_4 + Al_2(C_2H_3O_2)_6.$$

The *neutral aluminum acetate* is a valuable astringent and antiseptic in *sore throat* and similar inflammatory conditions. It may be employed in the form of a gargle containing from 1 to 3 per cent. The relatively insoluble *basic acetate* is used as a dusting powder in *sweating feet,* in which it exercises both a desiccating and deodorizing influence, and in chronic *leg ulcers, weeping eczema,* and the like. A solution containing 7.5 to 8 per cent. of *basic aluminum acetate* is official in the N. F. under the title *Liquor Alumini Subacetatis,* which is practically identical with the *Liquor Aluminii Acetici* P. G. This must not be confused with the *Liquor Alumini Acetatis* N. F. or *Burow's Solution,* which is the solution of the neutral acetate also used for much the same purposes (see Part III). Stansburg (*Am. J. Surg.,* 1912, xxvi, p. 82) has found the N. F. solution of aluminum subacetate a valuable local application in *furunculosis, erysipelas* and *ivy poisoning.* He dilutes the solution with from seven to ten parts of water and saturates gauze with this solution and applies it over the diseased area.

Aluminum acetate is used for water-proofing fabrics such as clothing, tents, awnings, etc. A commercial solution of about 10 per cent. strength is diluted with about 40 parts of water. The fabric is completely immersed and after thorough saturation is removed and dried without washing. Metal buttons, fasteners, etc., should be removed before applying the treatment. Aluminum acetate is also used in embalming fluids, in textile dyeing and in the manufacture of lake colors.

Preparations asserted to contain the basic aluminum acetate have been introduced into therapeutics under the names of *lenicet* and *eston.* It seems probable, however, that the latter is a mixture of several aluminum salts (see Friedlander, *Ap. Ztg.,* 1907, p. 819). From eston is prepared two other compounds, one known as *formeston,* in which two of the acetyl radicals are replaced by formic acid, and the other *subeston,* which is a double basic acetate. These appear to be not only astringent, but also germicides of considerable power; Blasius (*Hyg. R.,* 1908, xviii, p. 941) finds that the saturated solution of eston, representing about 2 per cent. of the substance is fatal to most non-sporulating bacteria after thirty minutes' exposure.

Aluminum Acetico-tartrate. *Alsol.*—Under the name of alsol has been employed a 50 per cent. aqueous solution of the acetico-tartrate of aluminum. According to Aufrecht, this solution is a more powerful germicide than phenol. It has been found clinically valuable by Hanau and Pinner (*Med. Klin.,* 1909) wherever an antiseptic astringent is necessary, especially in the treatment of catarrhal conditions of the female genitalia. They applied it by means of gauze soaked in a 5 to 10 per cent. alsol solution. As a gargle or spray in *pharyngitis* and the like, it may be used in from 1 to 3 per cent. solution. A creamy solution of aluminum acetico-tartrate has been highly recommended by Lewitt (*Ther. Geg.,* 1910, p. 95) in the treatment of *pruritus, intertrigo, acne vulgaris,* and other skin diseases. A solution similar to alsol is recognized in the N. F. as *Liquor Alumini Acetico-tartratis* (see Part III).

Aluminum and Iron Sulphate. *Ferroso-Aluminic Sulphate. Sulphate of Aluminum and Iron.* $AlFe(SO_4)_2 + 12H_2O$.—This salt, which is prepared by the action of sulphuric acid on a mixture of recently precipitated aluminum oxide and ferrous carbonate, was formerly used as an internal astringent in chronic *dysentery* and *diarrhea* and externally in *relaxation of the uvula* and as a wash for foul and flabby *ulcers. Dose,* from five to ten grains (0.32–0.65 Gm.), dissolved in some aromatic water.

Aluminum and Potassium Salicylate. *Alkasal. Alkasol.*—It is prepared by the combination of aluminum salicylate and potassium acetate with the use of heat.

Alkasal-Athenstædt is the name of an aluminum potassium acetate. Both of these compounds are used for purposes similar to aluminum acetate.

Aluminum and Sodium Acetate. *Acetonal.* $Al_2(OH)_2.(C_2H_3O_2)_5Na$.—It is used as a 10 per cent. solution, and its equivalent can be prepared by dissolving 82 parts of sodium acetate in 4050 parts of liquor alumini acetatis *N. F.*

Aluminum Boroformate, $Al_2O_3B(OH)_3.H_2CO_2 + 5H_2O$, occurs in lustrous crystals, and may be prepared by introducing freshly precipitated alumina into a mixture of two parts of formic acid, one part of boric acid, and seven parts of water. The solution is evaporated and crystallized. Used as an antiseptic and astringent. (*Ph. Rund.,* 1894, 256.)

Aluminum Boro-tannate. *Cutol, Lutol.*—A brownish powder, insoluble in water, used as an astringent and disinfectant in diseases of the skin. It may be applied as an ointment or as a dusting powder.

Aluminum Boro-tartrate. *Boral.*—This is a crystalline substance, with a sweetish astringent taste, soluble in water. It is used, generally in powder form, as a local astringent in diseases of the nose and throat.

Aluminum Bromide. $Al_2Br_6.12H_2O$.—White or yellowish-white deliquescent crystals, soluble in water and alcohol. Used in organic synthesis.

Aluminum Carbide. Al_4C_3.—Greenish-gray pulverized masses. Sp. gr. 2.36. Used for generating methane extemporaneously.

Aluminum Carbonate. $Al_2(CO_3)_2$.—This occurs in chalky white, easily pulverized, tasteless lumps. It is used as a mild antiseptic astringent in *ocular affections, diarrhea,* etc. It is incompatible with acids, phosphates and lead acetate.

Aluminum Caseinate.—A yellowish-white, tasteless powder containing 5 per cent. of aluminum; insoluble in water, sparingly dissolved when macerated in saliva, and yielding aluminum to dilute acids. It was introduced by Rud. Meyer (*Ap. Ztg.,* Sept. 23, 1899, 566) as a remedy in *intestinal catarrh,* given in doses of four to five grains (0.26–0.32 Gm.). It is prepared as follows: Milk, freed from albumin, by repeated heating to 62° C. and straining, and then sterilized, is precipitated with solution of aluminum subacetate (*Liquor Alumini Subacetatis*); the precipitate is washed completely with water, and after removing the water with alcohol, deprived of fat by means of ether. The product is dried at a moderate temperature, and, while drying, powdered.

Aluminum Chlorate. $Al(ClO_3) + 6H_2O$.—Under the name of *prophylacticum mallebrein* there has been introduced a solution which is stated to contain 25 per cent. of aluminum chlorate. It is claimed to have the property of detoxicating bacterial toxins and hence to be useful in certain infectious diseases, notably *diphtheria* and laryngeal *tuberculosis.* It is applied either as a spray or gargle in strengths of from 0.5 to 1 per cent. See Jarosch (*D. M. W.*, 1912, p. 1979).

Aluminum Iodide. AlI_3.—Brown crystalline masses, soluble in water. Used in organic synthesis.

Aluminum Hydroxide. *Alumini Hydroxidum U. S. IX, Alumini Hydras* (*U. S.*, 1890), *Aluminum Hydrate, Hydrated Alumina; Argilla Pura,* s. *Hydrata; Hydrate de l'Alumine,* Fr.; *Thonerdehydrat,* G.—This salt, which was dismissed at the last revision of the *U. S.*, was defined in the *U. S. IX*, as: "A compound consisting principally of aluminum hydroxide $[Al(OH)_3 = 78.12]$." *U. S. IX.* The official process for its preparation was as follows:

"Alum, *one hundred grammes;* Monohydrated Sodium Carbonate, *forty-five grammes;* Water, *a sufficient quantity.*

"Dissolve each salt separately in *one thousand mils* of Water, filter the solutions and heat them to boiling. Then having poured the hot solution of Monohydrated Sodium Carbonate into a capacious vessel, gradually pour in the hot solution of Alum with constant stirring, and add *two thousand mils* of boiling Water. Allow the precipitate to subside, decant the clear liquid, and pour upon the precipitate *two thousand mils* of hot Water. Again decant, transfer the precipitate to a strainer, and wash it with hot Water, until the washings produce not more than a faint cloudiness with barium chloride T.S. Allow the precipitate to drain, dry it at a temperature not exceeding 40° C., and reduce it to a uniformly fine powder." *U. S. IX.* The alum solution is directed to be added to the sodium carbonate solution, because if the latter is not in excess during the whole period of precipitation a basic sulphate will be produced and contaminate the finished solution.

It was described as "a white, bulky, amorphous powder, odorless and tasteless; permanent in dry air. It is insoluble in water and alcohol; it is dissolved by hydrochloric or sulphuric acid and by the fixed alkali hydroxides. Solutions of Aluminum Hydroxide in hydrochloric or sulphuric acid yield with potassium hydroxide T.S. a white gelatinous precipitate, dissolved by an excess of the reagent but again precipitated by the addition of an excess of ammonium chloride. When heated to redness it loses about 34 per cent. of its weight. Boil 1 Gm. of Aluminum Hydroxide with 20 mils of distilled water, and filter the liquid; the filtrate does not show an alkaline reaction, and, on evaporation, does not leave a residue weighing more than 0.005 Gm. (*alkali salts*). Heat 1 Gm. of Aluminum Hydroxide with 10 mils of hydrochloric acid, evaporate the solution to dryness, and dissolve the residue in 50 mils of distilled water. Ten mils of this solution does not respond to the Test for heavy metals. Heat 1 Gm. of Aluminum Hydroxide with 5 mils of sulphuric acid and 5 mils of distilled water, on a water bath, for fifteen minutes. Then dilute it to 25 mils with distilled water and filter. Five mils of this filtrate meets the requirements of the Test for arsenic." *U. S.*

Aluminum hydroxide is feebly astringent and probably slightly antiseptic. It is used chiefly as a protective and astringent application either in the form of an ointment or suspension, or as a dusting powder in the treatment of various inflammatory *skin diseases.*

Aluminum Lactate.—Perutz (*M. M. W.*, 1913, p. 1261) has used solutions of aluminum lactate in strengths of from 0.1 to 2 per cent. for its astringent effect in *chronic gonorrhea, eczema, mercurial ptyalism,* etc. He was unable to demonstrate any direct antiseptic effect, but found that in suppurative conditions it exercises a beneficial influence. Under the trade name of *Fixin* a proprietary form of this salt has been suggested as a gastro-intestinal disinfectant. Another preparation of aluminum lactate is known as *algal* and is intended as a local astringent. The advantages claimed for this preparation by Kionka (*B. K. W.*, Feb. 25, 1922, 408) are that it has less irritating effect than other preparations of aluminum.

Aluminum Oleate. $Al_2(C_{18}H_{33}O_2)_6$.—A white to a yellowish tenacious mass, soluble in alcohol and ether, and is used as an antiseptic in skin diseases. It is used as a water-proofing compound, and as a dryer in the paint industry. Wiechowski (*M. M. W.*, 1921) has recommended it as a dusting powder and also as a substitute for lead plaster.

Aluminum Phenolsulphonate. *Sozal. Aluminum sulphocarbolate.* $Al_2(C_6H_4HSO_4)_6$.—This forms a reddish-white powder of slight phenol odor and astringent taste. It is soluble in water and alcohol. Merck recommends it as a substitute for iodoform, especially commendable in *cystitis* and suppurating *ulcers.* (*Ph. Ztg.*, 1892.)

Aluminum Salicylate. *Salumin.* $Al(C_6H_4OH\text{-}COO)_3$.—A reddish-white powder, insoluble in water and alcohol, but soluble in dilute alkalies. It is employed in nasal and throat affections by insufflation. *Ammoniated aluminum salicylate,* a yellowish, water-soluble powder, is also used in the same manner, and in solution is employed in *catarrh* and *ozena,* as a spray.

Aluminum-sodium Sulphate. *Sodium Aluminum Sulphate. Soda Alum, S. A. S.,* $Al_2Na_2(SO_4)_4 24H_2O$.—Colorless transparent crystals soluble in water. Used in the textile and paper industry for making dry colors, in water purification and as an ingredient in so-called "alum" baking powders.

Aluminum Subformate. *Aluminum formate.* $Al(HCOO)_2OH$.—Under the name of *alformin,* a solution containing about 16 per cent. of aluminum subformate has been used as an astringent and disinfectant. In *pharyngitis,* five to ten drops of this solution may be added to a glass of water and used as a gargle.

Aluminum Subgallate. *Gallal.* $Al_4(C_7H_2O_5)_3 + 4H_2O$.—Basic aluminum gallate is an amorphous, brownish powder prepared from solutions of alum and sodium gallate. It is insoluble in water, but soluble in diluted acids. It is employed, chiefly in *ozena,* as an antiseptic astringent.

Aluminum Tannotartrate.—Yellowish-white lamellæ or powder, strongly astringent taste, soluble in two parts water. It has been employed as an insufflation or gargle in rhinolaryngological and other catarrhal affections. It is incompatible with iron compounds, phosphates and alkalies.

Alumnol. *Aluminum Beta-naphthol-disulphonate.* $Al_2(C_{10}H_5(OH)(SO_3)_2)_3$. *Alumini Naphthol-sulphonas, N. N. R.* 1924.—A whitish, nonhygroscopic powder darkening slightly on exposure to air, easily soluble in cold water and very soluble in glycerin, slightly soluble in alcohol. Its aqueous solution has a slight bluish fluorescence, feeble acid reaction, and is colored blue by iron chloride. The solution of 40 per cent. is made with hot water and remains clear on cooling. Though it coagulates albumin, it is said to be dissolved in an excess of albumin, and, therefore, to be able to reach deep recesses of wounds.

It has been strongly recommended as an astringent and antiseptic in nasal, urethral, and other catarrhal inflammations. The strength of the solution employed varies from 1 per cent. in *gonorrhea* to 10 per cent. in *abscesses.* (See *B. K. W.*, 1892; *Th. M.*, 1892, 644.) Two to ten parts of alumnol mixed with ten parts of starch has been used by insufflation in cases of *laryngitis.* Alumnol, however, would appear to be very feeble and slowly acting as a germicide, a 1 per cent. solution requiring twenty-four hours to destroy bacilli of anthrax. As a surgical dressing from 1 to 2 per cent. solution may be used. In *infected wounds* the caustic 20 per cent. solution is employed. In diseases of the skin alumnol is used with talc or starch as a powder, or with lanolin as an ointment, the strength varying from 2 to 20 per cent. Its solutions are incompatible with caustic alkalies and alkaline carbonates, with albumen, gelatin solutions, soluble nitrates, silver salts, and other reducible salts. Rubbed with phenol it produces a plastic mass.

Alundum.—A technical name for an artificial form of *aluminum oxide,* Al_2O_3 Made by fusing bauxite in an electric furnace. Used in making porous chemical filters and other apparatus, and as a refractory and an abrasive.

Alypin. *Benzopropyl. Amydricaine. N. N. R.* 1924. $CH_3.CH.C(C_6H_5COO).CH_2N(CH_3)_2.CH_2N(CH_3)_2$. Alypin is 2-benzoxy-2-dimethyl-amino-methyl-l-dimethyl-amino-butane-hydrochloride. It bears a close relation to *Stovaine,* which see. It occurs as a crystalline hygroscopic powder, freely soluble in both water and alcohol, with a melting point of 169° C. Its solution will stand boiling for a period of five minutes. The *nitrate* of this same base has been also introduced, especially for the purpose of using in combination with silver salts.

Alypin has been employed as a substitute for cocaine in the production of surgical anesthesia either by local application or injecting into the subarachnoid space. It differs from cocaine in that it produces relaxation of the blood vessels, when applied locally, instead of constriction. According to Le Brocq (*B. M. J.*, March 27, 1909), alypin is about equally anesthetic to cocaine but is more highly toxic. Sollmann finds (*J. A. M. A.*, 1918, lxx, p. 216) that alypin, when injected into the nerve trunk, is about half as efficient as cocaine and, when applied over mucous membranes about one-fourth as efficient. Several cases of alypin poisoning have been reported of which at least two have ended fatally. The symptoms have been cyanosis, convulsions, stupor and arrest of respiration (see Lichtenstein, *Ther. Geg.*, 1914, xvi). Braun (*D. M. W.*, 1905) reports that it produces pronounced irritation at the point of injection, and this view has been confirmed by other investigators, especially as regards its ophthalmic use. As a local anesthetic it would, therefore, appear to have no advantages over the other preparations of its class. It has also been employed in doses of one-sixth to one-third of a grain (0.01–0.02 Gm.) for the relief of *vomiting.* As a local anesthetic it may be used in strengths of from 2 to 5 per cent. and its solutions in these strengths are stable but become moldy when further diluted. An alkali hydroxide or carbonate gives a precipitate with an aqueous solution of alypin; mixed with calomel and dampened with alcohol alypin gives a black color.

Amapa Milk.—The milky sap of the bitter bark of *Plumeria fallax* Muell. (Fam. *Apocynaceæ*), a Brazilian tree, has been recommended as a vermifuge and antimalarial, having been used and known by the natives of Brazil and South America from time immemorial. It is also used externally in the treatment of *cancerous sores. Dose,* for children, one minim for each year of age.

Amber. *Succinum. Ambre, Succin,* Fr. *Bernstein,* G.—Amber is a fossil resin, occurring generally in small detached masses in alluvial deposits, in different parts of the world. According to Goefert, there are about fifty species of extinct coniferous trees of which amber represents the resinous exudation. It is found chiefly in East Prussia, either on the seashore, where it is thrown up by the Baltic, or underneath the surface. Large deposits occur in some lakes on the eastern coast of Courland, and an extensive bed of yellow amber was discovered in 1854, on sinking a well in the coal mines near Prague. The largest mass of amber yet found weighed thirteen pounds. Amber also occurs in considerable quantities near Catania, in Sicily. It is usually associated with lignite, and sometimes encloses insects and parts of plant tissues. In the United States, it was found at Cape Sable, Maryland, by Troost. In this locality it is associated with lignite and iron pyrites. It has also been discovered in the greensand formation of Martha's Vineyard, at Harrisonville, N. J., and elsewhere. The amber consumed in this country is brought from the ports of the Baltic. A deposit of it is said to have been discovered near Rockwood in Australia.

It is a brittle solid, generally in small irregular masses, permanent in the air, having a homogeneous texture and vitreous fracture, and susceptible of a fine polish. It becomes negatively electric by friction. Its color is generally brownish-yellow, either light or deep, but is occasionally reddish-brown or bluish from staining with ferric phosphate. It has no taste, and is inodorous when cold, but exhales a peculiar, aromatic odor when heated. It is usually translucent, though occasionally transparent or opaque. Its sp. gr. is about 1.07. Water and alcohol scarcely act on it. When heated in the open air, it softens, melts at 286.7° C., swells, and at last inflames, leaving, after combustion, a small amount of ash. Subjected to distillation it yields first a yellow acid liquor, which is a solution of impure *Succinic Acid,* then a thin yellowish oil together with a yellow, waxy substance which is deposited in the neck of the retort. This waxy substance yields the *chrysen* of Laurent and the *idrialin* of Dumas, both of which are hydrocarbons. (Pelletier and Walter, *J. P. C.*, v, 60.) As the distillation proceeds, a considerable quantity of combustible gas is given off, which must be allowed to escape. By continuing the heat, the oil gradually deepens in color, until towards the end of the distillation, it becomes black and of the consistence of pitch.

Tschirch (*Harze und Harzbehälter*) finds the main constituents to be a *Succinoabietic ester of borneol*, which is extracted by prolonged treatment with alcohol, and amounts to 30 per cent. of the amber, and the *succinic ester of succinoresinol*, which is insoluble in alcohol and makes up 70 per cent. of the amber. This latter compound contains a small amount of sulphur (about 0.47 per cent.).

Amber was held in high estimation by the ancients as a medicine, but at present is never so used. The credulous sometimes employ an amber necklace to keep away infantile ills. The *oil of amber* is an empyreumatic product which is prepared by destructive distillation of amber. The heat requisite for the complete decomposition of amber cannot be supported by a glass retort; and, in order that all the oil which it is capable of yielding may be collected, the distillation should be performed in a tubulated iron or earthenware retort, which may be placed immediately upon the fire; sand is added to prevent the amber from swelling too much. The oil may be separated from the acid liquor by means of the separating funnel. As first procured, it is a thick, very dark-colored liquid, of a peculiar, strong, empyreumatic odor. In this state it is occasionally employed as a liniment, but for internal use it should be rectified.

By successive distillations oil of amber becomes thinner and more limpid, till at length, it is obtained colorless. Under the name of *Oleum Succini Rectificatum* the U. S. P. of 1870 recognized the oil of amber purified by redistillation with water. For practical purposes, however, the oil is sufficiently pure when once redistilled. As first distilled it has an amber color, sp. gr. 0.903 at 15.6° C., and a boiling point from 170.5°–186.1° C. (Ebert.) When quite pure it is said to be colorless, as fluid as alcohol, of the sp. gr. 0.758 at 23.8° C., and to boil at 85.5° C. It has a strong, peculiar, unpleasant odor, and a hot acrid taste. It imparts these properties in some degree to water, without being perceptibly dissolved. It is soluble in five parts of 90 per cent. alcohol and in all proportions in absolute alcohol, ether, chloroform, carbon disulphide, and the fixed oils. (Ebert.) It appears to be a hydrocarbon of the terpene class. It was officially described as "a colorless or pale yellow, thin liquid, becoming darker and thicker by age and exposure to air, having an empyreumatic, balsamic odor, a warm, acrid taste, and a neutral or faintly acid reaction. Sp. gr. about 0.920. It is readily soluble in alcohol. When mixed with fuming nitric acid, it acquires a red color, and, after some time, is almost wholly converted into a brown, resinous mass of a peculiar musk-like odor." *U. S.*, 1870.

Rectified oil of amber was employed in *amenorrhea, hysteria,* and *whooping cough.* The *dose* is from five to fifteen minims (0.3–0.9 cc.), diffused in some aromatic water by means of sugar and gum arabic. Externally applied the oil is rubefacient.

Ambergris. *Ambra Grisea (cinerea). Ambre, Ambre gris,* Fr. *Amber, Graue Ambra,* G.—This substance, which is found floating on the sea, particularly in the southern hemisphere, is now generally believed to be produced in the intestines of the *Physeter macrocephalus* L., or *sperm whale.* It is in roundish or amorphous pieces, usually small, but sometimes weighing as much as 50, 100, or even 200 pounds. These pieces are often composed of concentric layers. Ambergris is of various colors, usually gray, with brownish, yellow, and white streaks, often dark brown or blackish on the external surface. It is opaque, lighter than water, and of a consistence like that of wax. Ambergris has a peculiar aromatic agreeable odor, is almost tasteless, softens with the warmth of the hand, melts under 100° C., is almost completely volatilizable by heat, and is inflammable. It is insoluble in water, but is readily dissolved, with the aid of heat, by alcohol, ether, and the volatile and fixed oils. It consists chiefly of a peculiar fatty matter analogous to cholesterin, and denominated by Pelletier and Caventou *ambrein.* When pure this has little or no odor. Beauregard and Gouchet believe that ambergris is a calculus composed of crystals of *ambrene* mixed with black pigment and star-coral débris.

When fresh ambergris is disagreeable in odor. If kept for a year or two in air tight containers it loses its excrementitious odor and acquires the characteristic perfume for which it is valued, although its use in perfumery is more for the purpose of fixing delicate floral odors than for any odor which it contributes to the mixture itself. This change Beauregard believes is due to a microbe (*Spirillum recti physeteris*). (*C. R. A. S.*, cxxv, 254.)

Ambergris was formerly regarded as a cordial and antispasmodic, somewhat analogous to musk, useful in *typhoid fevers,* and various nervous diseases. It is no longer used as a medicament but is employed in perfumery. It is comparatively rare and very expensive, the black variety commanding a price of from $10 to $15 an ounce, while the white or gray variety costs in the neighborhood of twice that figure. *Dose,* five grains to a drachm (0.32–3.9 Gm.)

Ambrine.—The trade name for a French proprietary preparation which has been on the market for many years, but has come into prominence because of its large use during the European war in the treatment of *burns.* Similar preparations are on the market sold under the trade names *ambryl, cerambine, mulene, parresine, thermozine, hyperthermine,* etc. It is essentially solid paraffin with the addition of ingredients which increase its adhesiveness and plasticity. According to Leech, a similar preparation may be made by dissolving 5 drops of asphalt (*asphalt varnish* or *B. asphaltum*) in 1.5 cc. of olive oil with the aid of heat, and incorporating the solution with 97.5 Gm. of melted paraffin (melting point 47.2° C.). (*J. A. M. A.*, lxviii, p. 1498.) A number of other formulas have been proposed, among them paraffin, 96 per cent., and yellow wax, 4 per cent. The essential factor seems to be a melting point between 38° and 53° C., a sterile product, sufficient strength to the film so that it may readily be lifted from the burn and a pliability which will prevent breaking if bent. In applying it to the burn the melted mixture is sprayed or painted over the area, to form a thin layer, absorbent cotton is then applied and afterwards more of the melted mixture. (Sollmann, *J. A. M. A.*, 1917, lxviii, p. 1037 and 1799.)

Ambrosia. *Ambrosia trifida* L. *Ragweed, Roman Wormwood, Hog-weed, Bitter-weed, Ambrosie,* Fr. *Traubenkraut,* G. (Fam. *Compositæ.*)—This and another indigenous annual, *A. artemisiæfolia* L., are deemed by the eclectics astringent and stimulant, and are given in low forms of *fever.*

L. W. Schwab has found in *A. artemisiæfolia* a bitter glucoside (*A. J. P.*, 1890), and Schimmel & Co. have obtained from it about 0.15 per cent. of a green volatile oil (sp. gr. 0.876). (*Schim. Rep.*, 1904, p. 96) The pollen of this plant is one of the causes of hay fever. Sutton (*J. A. M. A.*, 1919, lxxiii, p. 1433) claims that in susceptible persons the ragweed pollen may give rise not only to hay fever but also to dermatitis which may or may not be accompanied with symptoms of nasal irritation. He reports several such cases of dermatitis. It is estimated that there are about 90,000,000 pollen grains in a gramme of ragweed pollen.

Amenyl.—Amenyl is the hydrochloride of *methylhydrastimide.* It occurs as yellowish needles, melting at 227° C., soluble in hot water and alcohol. Amenyl has been used by Falk (*Th. M.*, 1909, p. 581) in the treatment of *amenorrhea.* The *dose* is one grain (0.065 Gm.).

Amidophenols. *Derivatives of p-amidophenol,* $C_6H_4(OH)NH_2$.—In an elaborate series of experiments (*Cb. I. M.*, 1897) Treupel and Hinsberg find that derivatives from amidophenol are active as antipyretics in proportion as they are decomposed in the system, and that the decomposition is to be measured by the amount of indophenol in the urine. Among these substances is *dulcin,* called also *para-phenetolcarbamide* and *sucrol,*

$$CO\begin{cases}NH.C_6H_4.OC_2H_5\\NH_2\end{cases}$$

which occurs in white, glittering, needle-like crystals, melting at from 173°–174° C., soluble in 800 parts of cold and 55 of boiling water, and 25 of alcohol, having a taste which is said to be two hundred times sweeter than sugar. (Dulcitol, the carbohydric alcohol related to gelatose, is sometimes assigned the name of "dulcin," and should not be confused with the amidophenol "dulcin" which possesses distinctly different characteristics.) It has been recommended as a substitute for sugar, in *diabetes,* and, on account of its solubility, to improve the flavor of castor, cod liver, or other oils. According to Treupel and Hinsberg, fifteen grains (1 Gm.) of it will reduce the temperature in fever about one degree Centigrade in the course of about three hours, and no unaltered dulcin is to be found in the urine, but indophenol.

Besides dulcin, Treupel and Hinsberg examined physiologically the following amidophenol derivatives: *Lactylamidophenolethylcarbonate, benzoylacetamidophenol, ethyldiacetamidophenol, oxyphenacetinsalicylate.*

The use of dulcin, saccharin and other artificial sweetening agents as substitutes for cane sugar is prohibited by most food laws.

Ammi. *Ammi visnaga* Lam.—The fruit of this umbelliferous plant, indigenous in the countries around the Mediterranean, contains a crystalline principle, *kellin* (*C. R. A. S.*, August, 1879), which is said (*Union Méd.*, April, 1886) to act upon the heart and spinal cord. Mild antipyretic and antilithic properties have been attributed to the fruit.

Ammonium Arsenate. *Ammonii Arsenas.* $(NH_4)_2HAsO_4$.—This salt is obtained in crystals by saturating a concentrated solution of arsenic acid with ammonia or ammonium carbonate, and allowing it to evaporate spontaneously. The crystals, which belong to the trimetric system, effloresce on exposure to the air, and lose half their ammonia. Its solution is alkaline. It has been used with advantage by Biett in several inveterate *diseases of the skin.* It is administered in solution, one grain of the salt in a fluidounce of distilled water; twenty to twenty-five minims (1.2–1.6 cc.) of this solution may be given in divided portions in the course of the day.

The *ammonium arsenite,* NH_4HAsO_2, a water-soluble, white powder, has also been used after the manner of and for the same purposes as the arsenate.

Ammonium Bicarbonate. *Acid Carbonate of Ammonium.* $H(NH_4)CO_3$.—This salt was brought into notice by Wm. Procter, because of its antacid properties. It is formed by exposure of the ordinary carbonate to the air, and is found in considerable quantities on the sides of casks in which that salt is imported, and less largely even in the bottles in which it is kept in commerce. For further information concerning this salt, see *U. S. D.*, 19th ed.

It is a commercial article occurring as white crystals, sp. gr. 1.59, soluble in water, fairly stable. Used in the manufacture of ammonium salts.

Ammonium Binoxalate. *Acid Ammonium Oxalate.* $NH_4H_2CO_4 + H_2O$.—Colorless trimetric crystals soluble in water and used solely for removing ink stains from fabrics, and ecchymotic spots from the face.

Ammonium Bisulphite. NH_4HSO_3.—White crystals soluble in water and used internally in fermentative *dyspepsia* in ten to thiry grain (0.66–2.0 Gm.) doses and externally as a wash in *sore mouth* and *skin affections.* The *bisulphate,* NH_4HSO_4, colorless water-soluble crystals, has been given in fifteen to sixty grain (0.9–3.9 Gm.) doses in *gastric affections.*

Ammonium Borate. *Ammonium Metaborate.* $(NH_4HB_4O_7) + 3H_2O$.—Only the acid salt is known. By dissolving one part of boric acid in excess, in three parts of heated water of ammonia, sp. gr. 0.960, and allowing the solution to cool slowly, this salt is obtained in crystals. These are rhombic octahedrons, with truncated summits, and often truncated edges, and are semitransparent. The taste of the salt is alkaline, and it has an alkaline reaction. On exposure, it effloresces, losing ammonia, and becoming in time the tetraborate. It is soluble in about twelve parts of water. It is believed by Becker to be the *ludus* of Paracelsus, which had a great reputation in the treatment of *urinary calculi. Dose,* ten to twenty grains (0.65–1.3 Gm.) every hour, in water sweetened with licorice. (*Journ. de Thérap. Méd.-Chir.*, Sept. 1, 1866.)

Ammonium Carbamate. *Ammonium Carbaminate.* $NH_4HCO_3NH_4CO_2$.—A white crystalline powder, exceedingly volatile. It is the anhydride of ammonium carbonate and is used in the manufacture of the latter substance.

Ammonium Camphorate. *Ammonium Bicamphorate.* $NH_4HC_{10}H_{14}O_4 + 3H_2O$.—A white, crystalline powder soluble in water and possessing a sedative action on the nervous system. *Dose,* one to three grains (0.06–0.18 Gm.).

Ammonium Cuprate. Made by precipitation of copper hydroxide from solution of cupric sulphate by molecular proportions of sodium hydroxide solution and the subsequent dissolving of this precipitate in strong ammonia water. Also known as *ammoniated copper oxide* and *cuoxam* used as a cellulose solvent and in waterproofing fabrics.

Ammonium Iodide.—*Ammonii Iodidum,* U. S. IX. *Iodohydrate d'ammoniaque,* Fr. Cod.

This salt has been dismissed from the U. S. P. For process of making it see *U. S. D.,* 20th ed., p. 135. It was officially described as: "minute, colorless, cubical crystals, or as a white, granular powder, odorless and having a sharp saline taste. The salt is very hygroscopic, and soon becomes yellow or yellowish-brown on exposure to air and light, owing to the loss of ammonia and the liberation of iodine. One Gm. of Ammonium Iodide dissolves in 0.6 mil of water, 3.7 mils of alcohol and in 1.5 mils of glycerin at 25° C.; also in 0.5 mil of boiling water. When strongly heated, Ammonium Iodide evolves vapor of iodine, and volatilizes without fusing, leaving not more than 0.1 per cent. of residue. An aqueous solution of the salt (1 in 20) is neutral or not more than slightly acid to litmus. When heated with potassium hydroxide T.S. ammonia is liberated. Add a few drops of ferric chloride T.S. to 5 mils of an aqueous solution of the salt (1 in 20); iodine is liberated which imparts a violet color to chloroform when shaken with the solution. Ten mils of an aqueous solution of Ammonium Iodide (1 in 20), when acidulated with hydrochloric acid, is not rendered turbid by the addition of 1 mil of potassium sulphate T.S. (*barium*). Ten mils of an aqueous solution of the salt (1 in 150) does not at once assume a blue color upon the addition of 3 drops of potassium ferrocyanide T.S. (*iron*). Shake 5 mils of an aqueous solution of the salt (1 in 150) with 1 mil of chloroform; no violet color is imparted to the latter (*free iodine*). An aqueous solution of Ammonium Iodide does not respond to the Test for heavy metals (see Part III, Test No. 3).

"*Assay.*—Proceed as directed under the Assay for iodides, using about 0.5 Gm. of Ammonium Iodide, previously dried to constant weight at 100° C. and accurately weighed in a stoppered weighing-bottle. It shows, in the dried salt, not less than 99 per cent. of NH_4I. Each mil of tenth-normal silver nitrate V.S. corresponds to 0.014496 Gm. of NH_4I. Each gramme of Ammonium Iodide, previously dried, corresponds to not less than 68.3 mils nor more than 70.1 mils of tenth-normal silver nitrate V.S." *U. S. IX.*

Its most serious disadvantage was its instability and the loss of ammonium and liberation of iodine unless most carefully preserved.

Ammonium iodide is employed, both externally and internally, as a resolvent, and does not differ perceptibly from the other iodides (see *Iodum*). It is used in *secondary syphilis, chronic rheumatism,* and in *scrofulous disorders* attended with glandular enlargements. It has been especially recommended in *chronic bronchitis* with fibrinous exudate and in *asthma,* with the thought of combining the resolvent action of the iodide to the expectorant effect of ammonium. Pennock used it in cases of *lepra* and *psoriasis,* in the form of ointment, applied by friction in the quantity of half an ounce, morning and evening. The proportions employed ranged from 4 per cent., in recent cases, to 12 per cent. in the chronic conditions. As the iodide is decomposed by the air, the ointment should be kept in well-stoppered bottles.

Dose, three to ten grains (0.20–0.65 Gm.).

Ammonium Nitrate. *Ammonii Nitras. U. S.* 1890. *Nitrate of Ammonia.* NH_4NO_3.—Ammonium nitrate may be prepared by treating commercial ammonium carbonate with nitric acid so long as effervescence takes place, or to saturation, filtering, and evaporating the solution. It is usually obtained as a by-product in the manufacture of other chemicals.

"Colorless crystals, generally in the form of long, thin, rhombic prisms, or in fused masses, without odor, having a sharp, bitter taste, and somewhat deliquescent. Soluble, at 15° C. in 0.5 part of water, and in 20 parts of alcohol; very soluble in boiling water, and in 3 parts of boiling alcohol. When gradually heated, it melts at 165°–166° C.; at a temperature between 230° and 250° C. it is decomposed into nitrogen monoxide gas and water, leaving no residue. The aqueous solution of the salt is neutral to litmus paper, and when gently heated with potassium or sodium hydrate test-solution, it evolves the odor of ammonia. On heating the salt with sulphuric acid, it emits nitrous vapors." *U. S.,* 1890.

For further information concerning this salt, see *U. S. D.,* 19th ed., p. 1380.

It is used in the manufacture of nitrogen monoxide and of pyrotechnics and explosives.

For the mode of preparing nitrogen monoxide from ammonium nitrate, see *Nitrogenii Monoxidium.*

Ammonium Persulphate, $(NH_4)_2S_2O_8$, is prepared by electrolyzing an acid solution of ammonium sulphate, and is a most efficient oxidizing agent in acid, neutral, or alkaline solutions. It occurs in small, colorless crystals, soluble in water. Its solution evolves oxygen when heated, and is used as an antiseptic and as a cheap and effective mouth wash. Ammonium persulphate is used in photography and in electroplating, and also as a reagent. In medicine it is chiefly valuable as forming the basis of *Klett's test* (*Chem. Ztg.,* 1900, p. 690) for indican in urine. To 10 cc. (160 minims) of urine add 5 cc. (80 minims) of 25 per cent. hydrochloric acid together with a crystal of ammonium persulphate, to which add chloroform and agitate, when a blue color develops in the latter.

Ammonium Phosphomolybdate. $2(NH_4)_3PO_4.24MoO_3.12H_2O$.—A yellow crystalline powder soluble in water and alkaline solutions, used as a reagent for alkaloids.

Ammonium Phosphotungstate. *Ammonium phosphowolframate* $2(NH_4)_3PO_4.24WO_3. + H_2O$.—A white powder soluble in water and alkaline solutions, used as a reagent for alkaloids.

Ammonium Sulphate. *Ammonii Sulphas. U. S.* 1880. $(NH_4)_2SO_4$; 131.21 *Sal Ammonium Secretum Glauberi. Sulfate d'Ammoniaque, Sel secret de Glauber,* Fr. *Schwefelsaures Ammoniak,* G.—Gas liquor is distilled with lime and the gas received in sulphuric acid, which yields a purified product. Most of the ammoniacal liquor is worked up into ammonium sulphate at present. In the United States the production of ammonium sulphate has increased enormously in recent years, owing to the introduction of by-product coke ovens. "Colorless, transparent, rhombic prisms, permanent in the air, odorless, having a sharp, saline taste and a neutral reaction. Soluble in 1.3 parts of water at 15° C. and in 1 part of boiling water; insoluble in absolute alcohol, but slightly soluble in alcohol of sp. gr. 0.817; when heated to about 140° C., the salt fuses, is gradually decomposed, and on ignition is wholly dissipated. The aqueous solution of the salt, when heated with potassa, evolves vapor of ammonia. With test-solution of chloride of barium it yields a white precipitate insoluble in hydrochloric acid. A 1 per cent. solution of the salt should not be blackened by test-solution of sulphide of ammonium (lead and iron), nor, when acidulated with nitric acid, should it be rendered more than opalescent by test-solution of nitrate of silver (limit of chloride)." *U. S.*, 1880. It is not used as a medicine, but enters into the composition of ammonium alum and the iron and ammonium sulphate, and is the principal source of ammonia gas used in chemical manufacturing, refrigeration, etc.

Ammonium Tartrate.—The neutral ammonium tartrate has been used by Clausen for the clearing up of *corneal opacities.* The eye is irrigated with a warm neutralized solution containing 5 per cent. of ammonium tartrate for twenty to thirty minutes two or three times a day.

Ammonium Uranate. *Ammonii Uranas.* $NH_4U_2O_7 + (H_2O)_n$.—This is a reddish-yellow, amorphous powder, insoluble in the usual solvents. It has been used by Weil (*S. M.*, 1907, p. 573) with asserted favorable results in the treatment of *syphilis.* The remedy was administered in doses of five-sixth grain (0.5 Gm.), suspended in a liquid petrolatum, by intra-muscular injection. The strength of the suspension was 5 per cent. and the injections were made once a week. The treatment required on an average of two months. It is used in the arts for painting on porcelain.

Ammonium Urate. *Ammonii Uras.* $C_5H_3(NH_4)N_4O_3$.—This is an acid salt, and may be formed by digesting uric acid in solution of ammonia, or by adding sal ammoniac to the solution of other urates. Ammonium urate is a white, amorphous, very sparingly soluble salt. It is a constituent of some varieties of guano. It has been used with asserted good effects externally in chronic *eczema,* in the form of an ointment (twenty grains to the ounce). (See 16th edition, *U. S. D.*)

Amygdophenin. *Phenetidin Amygdalate.* $C_6H_4.OC_2H_5NH.CO.CH.OH.C_6H_5$. *Phenyl-glycol-phenetidin.*—This is a derivative of *p*-amidophenol, analogous to phenacetin. It is a light, crystalline, grayish-white powder, soluble with difficulty in water. It is obtained by the action of mandelic acid upon *p*-phenetidin in the presence of dehydrating agents. R. Stüve asserts that it is practically free from antipyretic properties; that it is an analgesic which is often useful in *neuralgias* and the pains of *spinal scleroses;* and that it is very useful in *rheumatism,* it having had more effect in some comparative trials than the salicylates. It is best administered in capsules, fifteen grains (1 Gm.), from three to six times a day.

Amyl Alcohol. *Alcohol Amylicum,* $C_5H_{11}OH$. *Isobutylic Alcohol, Isobutylcarbinol. Fousel Oil. Fusel Oil. Hydrate of Amyl. Grain Oil. Potato Spirit Oil. Alcool Amylique, Huile de Grain,* Fr. *Fuselöl,* G.—This alcohol is always present in the products of alcoholic fermentation—particularly when starchy materials are the starting point—and, according to the experiments of L. Perdrix (*J. Chem. S.*, 1892, 90), the bacillus *B. amylozymicus* produces a fermentation in starch resulting in a large production of amyl alcohol. It is an ingredient in the ardent spirit obtained from various grains, but is most abundant in that procured from fermented potatoes. In grain spirit it is present in the proportion of about one part in five hundred by measure. When grain or potato whisky is distilled for the purpose of obtaining alcohol, the pure spirit will continue to come over for a certain time, after which, if the distillation be continued, a milky liquid will be obtained, which, upon standing, will be covered with a stratum of amyl alcohol. Subjected to distillation, the milky liquid will at first boil at a comparatively low temperature, and yield water and a little of the alcohol; but after a time the boiling point will rise to 132° C. when the amyl alcohol will come over pure, and by changing the receiver may be so collected.

Amyl alcohol is an oily, colorless liquid, of a strong, characteristic odor, and an acrid, burning taste. As usually prepared it has a pale yellow color. Its sp. gr. is about 0.810; that of its vapor 3.15. It boils at about 130° C. and congeals at −25° C. in the form of crystalline leaves. It is sparingly soluble in water, but mixes in all proportions with alcohol, ether, and essential oils. It dissolves iodine, sulphur, and phosphorus, and is a good solvent for fats, resins, camphor, and alkaloids. When dropped upon paper it does not leave a permanent greasy stain. It does not take fire like alcohol by the contact of flame, but requires to be heated to a temperature of about 54.5° C. before it begins to burn. Pasteur first observed that the ordinary amyl alcohol of fermentation was a mixture of two distinct alcohols, one present in smaller amount, optically active, levogyrate, and the other, the main portion, optically inactive. Their boiling points are very close, but they may be separated by the difference in solubility of the barium amyl-sulphates, and yield different sets of derivatives. (*C. R. A. S.*, xli, 296.) Heated with phosphoric acid, it loses a molecule of water, and forms a hydrocarbon, C_5H_{10}, homologous with ethylene, called *amylene* or *valerene,* which has been proposed as an anesthetic. According to Long and Linebarger, American fusel oil consists chiefly of active and inactive amyl alcohol, with some isobutyl alcohol, isopropyl and ethyl alcohols, and traces of normal propyl and normal butyl alcohols. (*Chem. News,* lxi, 185–187.) Amyl alcohol should not affect the color of litmus paper, previously moistened with water, should leave no fixed residue upon evaporation, should require to dissolve it about 40 parts of distilled water at 15° C., and should become not more than slightly turbid upon mixture with petroleum benzin (absence of more than a little alcohol, or water). (See *Amylene* below.) When subjected to oxidizing agents, it loses two atoms of hydrogen and gains one of oxygen, and becomes $C_5H_{10}O_2$, or *valeric acid,* the acid found in valerian. Hence the test given in the Br. Pharmacopœia of 1885: "Exposed to the air in contact with platinum-black, it is slowly oxidized, yielding valerianic (valeric) acid." The free amyl, $(C_5H_{11})_2$, has been isolated by E. Frankland. It is a colorless transparent liquid, of the sp. gr. 0.7704. Its hydride, $C_5H_{11}H$, possesses anesthetic powers.

A mixture of amyl alcohol, green soap, phenol (1 per cent.) and water, under the trade name of *Amyl Karbol,* has a wide use in Europe as a disinfecting solution.

Crude fusel oil is found in commerce as a by-product of the distillation and rectification of ethyl alcohol made from grain. Kent, of New York, found in it, as impurities, water, alcohol,

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acetic and valeric acids, oxide of iron, and an amyl compound analogous to *œnanthic ether*. Fusel oil has been used largely by the manufacturers of alkaloids as a solvent and in the preparation of *amyl acetate* (*pear oil, banana oil*), which is used in the manufacture of pyroxylin varnishes and smokeless powder and as a basis for the manufacture of isoprene, lately used in the manufacture of synthetic caoutchouc. This manufacture of amyl acetate for solvent purposes now consumes the great bulk of the fusel oil obtained from the rectifiers.

Fusel oil was formerly recognized by both the United States and the British Pharmacopœias as a source of artificial valeric acid.

Amyl alcohol is an active narcotic, and under the name of *Faints* (*feints*) a strong solution of the substance which is obtained as a by-product in the manufacture of whiskey, is used in England and Northern Europe for the purpose of increasing the activity and prolonging the effects of ordinary liquors. In small doses it is said to be efficacious in controlling the nervous weakness and irritability of confirmed drunkards, while larger doses produce headache, giddiness, double vision, staggering, unconsciousness, fall of temperature, abolition of reflexes, muscular rigidity, followed by complete relaxation, pronounced cyanosis, and a peculiar odor from the breath suggesting that of a Jargonelle pear.

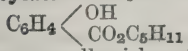
Horand has employed amyl alcohol for its disinfecting and desiccating action in inoperable *cancerous ulcers*. (*R. T.*, 1910.) He asserts that by the local application of from three to ten drops daily there is not only a disappearance of the odors, but often a shrinking in the size of the tumor, and considerable improvement in the general condition.

T. B. Futcher (*Am. Med.*, August, 1901, p. 210) has shown that both in animals and also in man, when taken in toxic doses, fusel oil affects profoundly the blood, causing methemoglobinuria, also glycosuria, attended with the presence of combined glycuronic acid, and in some cases violent nephritis. The size of the fatal dose probably varies very much. It is affirmed that death occurred from the taking of a single fluidounce (30 cc.), but in another case recovery resulted after six fluidounces (180 cc.) had been swallowed.

Amyl Butyrate. *Iso-amylbutyric ester*, $C_4H_7O_2$-C_5H_{11}.—A colorless liquid with pleasant characteristic odor, sp. gr. 0.859, boiling point 154° C. Soluble in alcohol and ether, almost insoluble in water. Used in flavoring and in organic synthesis.

Amyl Formate. *Iso-amyl formate*, $CH_2OC_5H_{11}$.—Colorless, fragrant liquid, sp. gr. 0.902, boiling point 130° C. Soluble in alcohol and ether. Almost insoluble in water. Used in artificial flavoring compounds.

Amyl Salicylate. *Salicylic Amylester. Amylenol.*



$$C_6H_4\left\langle\begin{matrix}OH\\CO_2C_5H_{11}\end{matrix}\right.$$

A colorless or yellowish refractive fluid, possessing an odor resembling that of salol, having the sp. gr. 1.065 at 15° C. Sp. gr. 1.045, boiling point 268°–273° C. It is slightly dextrorotatory. Refractive index (20°) 1.505–1.507. The preparation dissolves in ether, alcohol, and chloroform, but it is almost insoluble in water. This substance has been proposed by B. Lyonnet (*R. T.*, lxviii, No. 2) as a substitute in *rheumatism* for methyl salicylate, over which it has the advantage of less pronounced odor and taste. It is also coming into wide use as a fixing agent for delicate odors in perfumery. As a medicine it is given internally usually in gelatin capsules, three to five minims (0.2–0.3 cc.) each, eight or ten times a day. It has also been found useful as a local application, one-half to one drachm (2.0–3.9 Gm.), being applied to rheumatic joints and covered with wax paper, or other impervious dressing. It is incompatible with acids or acid salts and with iron compounds.

Amyl Valerate. *N. N. R.* 1924. $C_4H_9COOC_5H_4$.—The isovaleric acid ester of iso-amyl alcohol. A colorless liquid having, when diluted with alcohol, in which it is very soluble, an odor of apples. Insoluble in water, sp. gr. 0.881; boiling point 203°. It has been used in the place of valerian in the treatment of various nervous conditions.

Pouchet asserts that amyl valerate (*J. des Pr.*, 1899, 45) has the power of softening, or if present in sufficient quantity, of dissolving cholesterin, and recommends its use in the treatment of *gall-stones*. *Dose*, three to eight minims (0.2–0.5 cc.). It has been used as an artificial apple flavor.

Amylene. *Valerene. Pentene. Pental. Beta-iso-amylene. Tri-methyl-ethylene.* $(CH_3)_2C.CH.$-CH_3.—This name is given to the isomeric hydrocarbons of the olefin series, having the formula C_5H_{10}, of which five are possible. Amylene is prepared by distilling amyl alcohol with a concentrated solution of zinc chloride, which acts by dehydrating, withdrawing a molecule of water. The product is redistilled, and that which comes over first, constituting the more volatile part, is separately collected, and agitated with concentrated sulphuric acid, when the amylene, freed from water, will rise to the surface. Amylene is a colorless, very mobile liquid, having the density 0.666 at 10° C. Its boiling point is 37°–42° C. Its odor is peculiar and disagreeable. It is soluble in alcohol and ether in all proportions, but very sparingly so in water. When pure it does not act on potassium, and is not colored by a prolonged contact with potassium hydroxide. It undergoes polymerization very readily.

In 1857, Snow, of London, proposed amylene as an anesthetic. It was highly commended by W. Lombardino. H. C. Wood and David Cerna have, however, shown that pental acts upon the lower animals as a powerful cardiac depressant, and clinical experience has demonstrated that it is too dangerous for practical use.

Amylene Hydroxide. Amylene Hydrate. Tertiary Amyl Alcohol. Dimethylethylcarbinol ($C_5H_{12}O$ or $(CH_3)_2C.(C_2H_5)OH$) is a clear, colorless liquid, of a strong, penetrating odor, soluble in eight parts of water, and miscible with alcohol, ether, chloroform, petroleum benzin, glycerin, and fixed oils in almost all proportions; sp. gr. 0.814 at 12° C.; boiling point 102° C.

In 1887, von Mering proposed the use of amylene hydroxide as a soporific, stating that it stood midway between hydrated chloral and paraldehyde in power. In cases of poisoning, reported by C. Dietz, by the amylene hydroxide, the symptoms were deep narcosis, dilated pupils, loss of corneal reflexes, slow, deep, irregular breathing, small, slow pulse, and fall of temperature. According to Brackmann, confirmed by W. Niessen, it is valuable in *diabetes insipidus*, lessening thirst and polyuria. Amylene hydrate has also been recommended for the relief of *epileptic* and *eclamptic* *convulsions.* It is also used in artificial fruit flavors and in organic synthesis. *Dose,* fifteen minims (0.9 cc.) morning and evening.

Pentane.—Amyl hydride, $CH_3CH_2CH_2CH_2CH_3$, was discovered by E. Frankland of Manchester. It is a saturated hydrocarbon, and has been proved to be one of the light products in American petroleum, being the portion boiling at from 37°–39° C. (Schorlemmer). Amyl hydride is a colorless, volatile, mobile liquid, possessing a fruity odor, and having no taste. It is one of the lightest liquids known, having the sp. gr. 0.626 at 17° C. It boils at 38° C., and the sp. gr. of its vapor is 2.5. It is very inflammable, and burns with a brilliant white flame. It is readily soluble in alcohol and ether, but insoluble in water. Belonging to the paraffin or saturated series of hydrocarbons, it is a very stable compound, resisting the action of fuming sulphuric acid and the most powerful oxidizing agents. This substance was proposed by Simpson as an anesthetic, but has not sustained the claims made for it. It is used as a solvent in analytical chemistry and as an illuminant in photometric determinations. It is also used for filling low-temperature thermometers and as a lubricant in liquid air machines.

Amylene Carbamate.—Under the name *aponal* amylene carbamate $C(CH_3)_2C_2H_5.COONH_2$ has been introduced as a somnifacient. It seems to be a drug of only moderate power but acting promptly and apparently without injurious after-effects. The *dose* is from eight to thirty grains (0.5–2 Gm.).

Amyloform.—*Formamylum* is a patented chemical compound of formaldehyde and starch, introduced by Claassen as a substitute for iodoform. It is stated to be odorless, innocuous, and nonirritant. *Dextroform* is a similar compound, in which dextrin is used in place of starch. Dextroform is soluble in water and glycerin. Amyloform can be heated to 180° C. without decomposition, and therefore is readily sterilized. It is said to be non-poisonous, and has been used by Langgard, Krabbel, and others as a dusting powder in the treatment of infected *ulcers* and wounds of all kinds. It is said to act more energetically in lessening secretion and as a disinfectant than iodoform.

Amylzyme.—"An extract containing all of the digestive enzymes of the fresh pancreas of the hog." *N. N. R.*, 1924. It occurs as a pale yellowish powder, somewhat hygroscopic and only partially soluble in water with a neutral or slightly acid reaction. Although it possesses the proteolytic and fat-splitting actions of the pancreatic secretions, its power is estimated by its action upon starch. It is stated to digest 110 times its weight of starch in ten minutes. It is used like pancreatin for its enzyme action especially in *starchy indigestion.*

Amytin.—The ammonium salt of a mixture of sulphonated hydrocarbons prepared by the action of sulphuric acid on various hydrocarbons and subsequent treatment with ammonia. Under the name of amytin (*anytin, anysin*), Unna has introduced into medicine a 33 per cent. aqueous solution of *ichthyol-sulphonic acid,* which has the property of dissolving ichthyol, various ethereal oils, phenol, and camphor, forming solutions which are known by Unna as *Amytoles* (*anytoles*). Amytin is more or less irritant to the skin, and is affirmed to be useful in those skin diseases which need stimulation.

Anacardium. *Anacardium occidentale* L. *West Indian Cashew-nut. Acajou à Pommes,* Fr. *Caschunuss,* G.—A small and elegant tree of the Fam. *Anacardiaceæ,* growing in the West Indies and other parts of tropical America. A gum exudes from the bark, which bears some resemblance to gum arabic, but is only in part soluble in water, and consists of true gum and bassorin. It is the *gomme d'acajou* of the French writers. Peckoldt describes *cashew gum* as occurring in hard, fragile pieces which are more or less transparent, yellowish-brown, and stalactite-shaped, and is as soluble in water as acacia. (*Zeit. Oest. Apoth. Ver.*, 1893, 501.) The fruit is a fleshy, pear-shaped receptacle, supporting at its summit a hard, shining, ash-colored, kidney-shaped nut, an inch or more in length and three-quarters of an inch broad, consisting of a pericarp having large balsam canals and of a sweet oily kernel which is now an article of commerce as a food, sold either in the raw state or roasted and salted. The receptacle is red or yellow, and of agreeable subacid flavor with some astringency. It is edible, and affords a juice which has been recommended in *uterine complaints* and *dropsy.* This juice is converted by fermentation into a vinous liquor, which yields by distillation a spirit used in making punch, and said to be powerfully diuretic.

Although the pericarp contains a very acrid oil, the seeds are edible. The black juice contained between the outer and inner shell of the nuts is extremely acrid and corrosive, producing, when applied to the skin, severe inflammation, followed by blisters or desquamation. Staedeler found in it two peculiar principles—*anacardic acid* and a yellow, oleaginous liquid, *cardol* ($C_2.H_{30}O_2$). (See *J. P. C.*, 3e sér., xiii, 459.) At one time it was sometimes applied to the face by women, in order to remove the cuticle, and produce a fresher and more youthful aspect. The juice, or its active oil, has been used in medicine for a discutient. In the West Indies the juice is said to be employed for the removal of *corns* and *warts* and in the treatment of *ringworm* and *elephantiasis.* The oil of cashew-nut hulls has been employed in the treatment of *leprosy.* It is brown in color and has a sp. gr. of 0.9868, a saponification number of 123, and an iodine number of 163. (See *Proc. Penna. Pharm. Asso.*, 1918, xli, 167). The fumes of the roasting nuts have caused violent dermatitis, the exposed parts becoming red and enormously swollen, and very painful. The tincture of iodine has been found useful as a local application. The black juice of the nut and a milky juice which flows from the tree after incision are used for almost indelibly marking linen.

Ammonium Anacardolé has been used as a hair dye. The *Oriental Cashew-nut* or *Anacardium Orientale* is the fruit of *Semecarpus Anacardium,* L., a tree quite common in Southern Asia. It contains principles similar to the West Indian Cashew, and is also said to contain an alkaloid, *chuchunine.*

Anagallis. *Anagallis arvensis,* L. *Scarlet Pimpernel. Red Chickweed. Weather-glass. Mouron rouge,* Fr. *Gauchheil, Rothe Miere,* G. (Fam. *Primulaceæ.*)—An annual plant, growing in Europe and the United States. It has little odor, but a bitterish, somewhat acrid taste. The ancients esteemed it a counter-poison, and Orfila found three drachms of its extract to cause fatal gastroenteritis in a dog. It has been recommended as a local application to old and ill-conditioned *ulcers,* and has been used as a folk-remedy in *visceral* *obstructions, consumption, dropsy,* etc. J. A. Heintzelman obtained from it a volatile oil of a strong, peculiar odor, a pungent and somewhat acrid taste, and the sp. gr. 0.987. Four drops (0.25 cc.) of it produced intense headache and nausea, lasting for twenty-four hours, with pains throughout the body. According to Daccomo and Tommasoli, anagallis contains an active ferment, which rapidly digests raw meat (*Rassegna di Sci. Med.*, 1892, No. 4). *A. cœrulea* (Schreb.) Ledeb., having blue petals, is a variety of *A. arvensis,* and shares its medicinal properties.

Anagyris. *Anagyris fœtida,* L. (Fam. *Leguminosæ.*)—Hardy and Gallois have separated from *Anagyris fœtida* an alkaloid, *anagyrine.* Parthiel and Spasski found that the crude alkaloid could be separated into *cytisine,* $C_{11}H_{14}N_2O$ and *anagyrine,* $C_{15}H_{22}N_2O$; the latter is not obtainable in crystalline form; it forms a brittle, resinous-like mass easily reducible to a yellowish powder, but rapidly absorbs moisture and becomes sticky. It volatilizes at 245° C. (*A. Pharm.*, 1906, ccxliv, 20.) It forms, however, a crystalline hydrobromide.

Anagyrine hydrobromide, which has the formula $C_{14}H_{18}N_2O_2HBr$, occurs in colorless or faintly yellow crystals soluble in water. Anagyrine, according to Loewi (*A. I. P. T.*, vol. vii, p. 66), is physiologically related to lobeline, acting primarily upon the nerve endings as a paralyzant and later upon nerve centers, but having no direct influence upon the muscles. It lessens the cardiac frequency and decreases the force of the systole in the frog, but is said in the mammal to have very little influence upon the blood-pressure, death occurring through respiratory paralysis.

Analgen. *Ortho-ethoxy-monobenzoyl-amidoquinoline. Benzanalgene. Quinalgene. Labordin.* $C_{18}H_{16}N_2O_2$. $C_9H_5.(OC_2H_5)NH(CO.C_6H_5)N$.—The name analgen was first given to the acetyl derivative, but it was found that the benzoyl radical gave a more desirable product, and this is now made exclusively and the name analgen applied to it. It is in colorless crystals, insoluble in water, soluble in hot alcohol, melting point 208° C.

First produced and brought forward by Vis as an antipyretic, analgesic and antirheumatic remedy, it was subsequently investigated by Maass (*Z. K. M.*, xxviii, 1895), who found that in sufficient dose it depresses the heart and the reflexes, finally causing convulsions with loss of power, and death by centric paralysis of respiration. Both it and its derivative, *oxyethylamidoquinoline,* act upon the peripheral nerves as local anesthetics. The fatal dose for the lower animals was found by Maass to be three grammes per kilo. The continuous use of small doses produces emaciation, feebleness, and lessening of the reflexes. In cases of fever it causes active depression of temperature, often with free sweating, and usually decrease in the urinary secretion, and especially of the nitrogenous elimination. After chronic poisoning in the lower animals fatty degeneration was found in the liver and kidneys. The urine of patients taking it is said to become red, owing to the presence of *oxyethylamidoquinoline urate.* In *headaches* and the other nervous disturbances of *neurasthenic* individuals it is said to act well without affecting digestion. It is said also to relieve the pain of organic diseases, and to be distinctly antimalarial. (*B. A. M.*, xxxvi.) *Dose,* eight to fifteen grains (0.5–1.0 Gm.), up to forty-five grains (0.3 Gm.) a day if required; best administered in capsule or in acidulated water.

Anchietea. *Anchietea salutaris* St. Hil. *Cipo Suma. Cipo Carneiro. Pirageia.* (Fam. *Violaceæ.*)—The bark of the root of this Brazilian plant contains *anchietine,* an alkaloid isolated by Peckoldt. (*Ber. d. Chem. Ges.*, 1897, p. 98.) It is used in Brazil in treating *scrofula, erysipelas,* and *eczema.* Given in *doses* of two drachms (7.7 Gm.), it acts as an aperient, while three drachm (11.6 Gm.) doses produce vomiting.

Anchusa. *Anchusa officinalis,* L. *Bugloss. Oxtongue.* (Fam. *Boraginaceæ.*)—The root, leaves, and flowers of this European biennial plant were at one time recognized by the U. S. Pharmacopœia, but probably are devoid of medicinal properties. According to Greimer (*A. Pharm.*, 1900, ccxxxviii, 505) it contains the alkaloids consolidine and cynoglossine (see *Cynoglossum*). It is to be distinguished from Alkanet root, which is also known as Spanish Bugloss.

In France the *Anchusa italica,* which is there known as *buglosse,* is substituted for *A. officinalis* as a diaphoretic and diuretic.

Andrographis. *Br. Add.* 1900. *Andrographis paniculata* Nees. (Fam. *Acanthaceæ.*)—Under the name of *Kiryat* this plant is stated to be used to some extent in India as a bitter tonic, having similar properties to chiretta. It appears scarcely to enter commerce at all, although exposed in the shops of the herbalists. (See *B. P. C.*, p. 122.) The Br. Add., 1900, recognized the *infusion* (*Infusum Andrographidis,* one ounce to a pint), *dose,* one-half to one fluidounce (15–30 cc.); the *concentrated liquor* (*Liquor Andrographidis Concentratus*), *dose,* one-half to one fluidrachm (1.8–3.75 cc.); and the *tincture* (*Tinctura Andrographidis*), *dose,* one-half to one fluidrachm (1.8–3.75 cc.).

Andromeda.—*Oxydendrum arboreum* (L.) DC., (*Andromeda arboreum* L.), *Sour Wood,* or *Sorreltree,* grows in the valleys of the Alleghanies, from Pennsylvania to Florida and west from Indiana to Louisiana. The decoction of the leaves was at one time used as a pleasantly acidulous drink in fevers. The powder of the leaves and buds of *Leucothoë racemosa* (L.) A. Gray (*Andromeda racemosa* L.) is said to be a powerful errhine.

In 1882 Eykman of Japan isolated from the *Andromeda* (*Pieris*) *japonica* Thunb. a poisonous principle which he named *asebo-toxin.* This principle was later found in a number of other ericaceous plants—including several species of Andromeda, as well as the *Azalea indica* L. and *Rhododendron ponticum* L.—by Plugge (*A. Pharm.*, 1883, 1 and 1885, 914) who named it *andromedotoxin.* The same principle has also been found in the *Kalmia latifolia* and *angustifolia* by Lasché (*Ph. Rund.*, Sept., 1889) and in *Monotropa uniflora* L. The chemistry and physiology of this principle has been studied by De Zaayer (*A. G. P.*, 1887, xl, 481) and by Hardikar (*J. P. Ex. T.*, 1922, xx, p. 17).

Andromedotoxin is soluble in cold water and in alcohol, less soluble in hot water, chloroform, ether or amyl alcohol, insoluble in petroleum benzine. De Zaayer gives the melting point as 228° to 229° C., but according to Hardikar it is 258°. It is a neutral, non-nitrogenous principal, precipitated neither by the alkaloidal reagents nor by metallic salts. It does not reduce Fehling Solution and is not decomposed by hot acetic acid. The symptoms of poisoning by andromedotoxin, or the various leaves containing it, are: salivation, vomiting, staggering gait, followed by convulsions, labored respirations, then a progressive paralysis of the extremities until death. The heart is at first slowed, later becomes more rapid but before death becomes slow and weak. Hardikar, from his physiological studies, concludes that the principal has a very complex action: it first stimulates, later paralyzes the peripheral ends of the vagi, which explains the respiratory and cardiac symptoms; it has a narcotic action upon the higher brain centers which is the cause of the staggering gait; it paralyzes the motor end plates in voluntary muscle which is the cause of loss of power in the extremities; in fatal doses it has a depressant action upon the cardiac muscle which explains the late slowing of the pulse; the cause of the salivation and emesis was not determined. The *poisonous honey* of Xenophon, derived from the flowers of *Rhododendron ponticum*, probably owed its toxic properties to andromedotoxin. (See also *Ph. Z. R.*, 1883, xxii,) The oil of *Andromeda Leschenaultii*, of India, was found by J. Broughton to be methyl salicylate. (*P. J.*, Oct., 1871.)

Anemonin. *Pulsatilla Camphor.* $C_{10}H_8O_4$. —From *Anemone Pulsatilla* L. Yellowish-white crystals soluble in hot alcohol and insoluble in water. It is used as an antispasmodic, sedative and anodyne in *asthma* and pulmonary affections. *Dose,* one-fourth to three-fourth grain (0.015–0.05 Gm.), although as high as three grains (0.2 Gm.) has been administered.

Anemopsis. *Yerba Mansa, Apache Beads. Anemopsis californica* Hook. et Arn. (*Houttuynia californica* B. et H.)—This is an erect, aquatic herb belonging to the *Saururaceæ,* which is found growing in the southwestern United States. The root is employed by the natives in *chronic malaria,* and also in *diarrhea* and *dysentery,* and has been used with asserted good results in *gonorrhea* and *rheumatism.* For elaborate histological study, see *D. C.*, May, 1897. *Dose* of the fluidextract, from fifteen to sixty minims (0.9–3.75 cc.). A decoction of this root was used by the Indians as a local application in cuts and ulcers as well as internally in *diarrhea* and *dysentery.* It has also been recommended as a local application in nasal and pharyngeal *catarrhs.* The investigations of Lloyd (*A. J. P.*, 1879) showed a characteristic volatile oil and a tannin together with gum and a fixed oil.

Angræcum. *Angræcum fragans* Thouars.—This is an orchidaceous plant, indigenous to the Isle of Réunion and to Mauritius, where the leaves have been long used, under the name of *faham,* for the same purposes as tea leaves. For description, see *P. J.*, 1881, 913. They have a somewhat pungent aromatic taste, and a strong and highly agreeable odor, scenting the whole apartment with a delicious perfume. Given in infusion, they appear to have an effect on the system somewhat similar to that of tea. (*A. J. P.*, 1866, 441.)

Anhalonium. *Lophophora. Mescal Buttons.*—The dried tops of *Lophophora Williamsii* Coulter (Fam. *Cactaceæ*) and commonly known as *Peyote* or *Mescal Buttons* is a narcotic drug obtained from a small, fleshy, spineless cactus indigenous to northern Mexico and found growing now in Zacatecas, Chihuahua and on both sides of the Rio Grande near Laredo, Texas. It was called "sacred mushroom" by the Aztecs, who, like some of the American Indians of today, used it in their religious rites and attributed to it divine properties. It is probably used also as a habit narcotic although the extent of the habit is doubtful (see Saffow, *J. A. M. A.*, 1921, lxvii, 1278).

The plant is a perennial herb whose main axis is subterranean. From this arise a number of aerial shoots which appear like peltate fungi, the disk or button-like portion being up to 50 mm. in diameter and bearing tufts of yellowish-white hairs among which spring pinkish flowers. This constitutes the "mescal button."

The species was first placed in the genus, *Echinocactus,* by Lemaire in 1845 who described it under the name of *Echinocactus Williamsii.* It was later transferred to the genus, *Anhalonium,* and subsequently made the type of a new genus, *Lophophora,* by Coulter (see "Preliminary Revision of the North American Species of Cactus, Anhalonium and Lophophora," *Contrib. U. S. Natl. Herb.*, 1894, iii, 91–132). The *L. Lewinii* seems to be a variety rather than a distinct species. The mescal button is 6 mm. in thickness, with a convex under surface, a texture which is brittle and hard when dry, but becomes soft when moistened, a very bitter disagreeable taste, and an odor when moist which is peculiar and disagreeable, and is especially marked in the powdered drug. According to C. H. Thompson, the buttons of *L. Lewinii* and *L. Williamsii* are readily distinguished by the fact that the surface of *L. Lewinii* is traversed by thirteen shallow narrow furrows giving the appearance of there being as many irregular or much broken ribs or obtuse ridges, while in *L. Williamsii* the furrows and ridges are eight in number and regular.

In 1888, L. Lewin separated from *L. Lewinii* an alkaloid, *anhalonine,* which has the formula $C_{12}H_{15}O_3N$, and crystallizes in small white prisms, soluble in ether, alcohol, and chloroform. Subsequently, Heffter (*B. Chem. Ges.*, 1896) found in it, besides *anhalonine,* three alkaloids: *mescaline,* $C_{11}H_{17}O_3N$, in white needles melting at 151° C.; *anhalonidine,* $C_{12}H_{17}O_3N$, fusing at 160° C., and *lophophorine,* $C_{13}H_{17}O_3N$. (See also ***A. E. P. P.***, 1898, xl.) Kauder (*A. Pharm.*, 1899, vol. ccxxxvii) has found that in commercial mescal buttons, besides the alkaloids already mentioned, are two other bases, *pellotine,* $C_{13}H_{19}O_3N$, and *anhalamine,* $C_{11}H_{15}O_3N$. E. White (*J. P.*, xxv) obtained *mescaline,* 1.16 per cent.; *anhalonidine,* 1.16 per cent.; *anhalonine,* 0.46 per cent.; *lophophorine,* 0.14 per cent. *Anhaline,* $C_{10}H_{15}ON$, is identical with hordenine found in barley. For further information concerning these alkaloids see Späth (*M. Chem.*, 1919, xl, and 1922, xliii).

From time immemorial the Kiowa Indians of the Rio Grande have used the mescal buttons for the purpose of producing intoxication during their religious ceremonies. Attention was first called to the peculiar cerebral action of the drug by D. W. Prentiss and Francis P. Morgan (*T. G.*, 1895), who found that from two hundred and fifteen to two hundred and thirty grains (14–15 Gm.) (four to five buttons) will produce a peculiar cerebral excitement attended with an extraordinary visual disturbance, characterized by an incessant flow of visions of infinite beauty, grandeur, and variety, of both color and form, often followed after a time by the seeing of monsters, grotesque faces, and gruesome shapes. During the intoxication there are dilatation of the pupil, muscular relaxation, and some slowing of the pulse. Loss of sense of time, partial anesthesia, weakened heart's action, great muscular relaxation, wakefulness, and in some cases nausea and vomiting also have been noted, but no distinct alteration of the respiration. These results have been confirmed by several observers.

A. Mogilewa (*A. E. P. P.*, xlix, 137) found that mescaline, anhalonidine, anhalonine, lophophorine, and pellotine acted similarly in lessening the frequency and force of the isolated frog heart, varying simply in quantitative power. Dixon (*J. P.*, xxv) in an elaborate research, came to the conclusion that the actions of the *Anhalonium* (*Lophophora*) alkaloids are qualitatively indistinguishable although there is some difference in their degree of toxicity. They are not locally anesthetic, the main effects caused in the lower animals being: salivation, slowing of the pulse accompanied with a rise of blood pressure, and increased reflexes due to stimulation of the spinal cord but associated with loss of muscular power due to a paralyzing action upon the motor nerves; in fatal doses it kills by depression of respiration and in human poisoning the most serious result is the rapid, shallow breathing. In man moderate doses produce constipation but toxic doses cause diarrhea with bloody stools. In experiments upon two human subjects, there was wide dilatation of the pupils, with uncertainty of gait like that of alcoholic intoxication, tremors, and heightened reflexes, although sensation was distinctly blunted. The psychical symptoms caused by the largest doses resemble somewhat those from cannabis indica. The *dose* of the alkaloid used by Dixon was three and eight-tenths grains (0.25 Gm.).

Pilcz (*W. K. W.*, ix, 1896) has used pellotine as a calmative in fifty-eight cases of *insanity* in *doses* of from one-third to one grain (0.021–0.065 Gm.) Sleep was produced in about half the cases.

The value of mescal buttons as a remedial agent is doubtful; it has been employed to a slight extent in various forms of *neurasthenia* and *hysteria*, and is asserted by S. F. Landry (*T. G.*, 1888) to be especially valuable in cases of *asthma*. It has also been alleged to be useful in *neuralgic* and *rheumatic affections*. Prentiss and Morgan give the *dose* of the fluidextract, from ten to fifteen minims (0.6–0.9 cc.)

Aniline. *Amidobenzene. Phenylamine.* $C_6H_5NH_2$.—This is an organic base obtained from coal tar or more immediately from nitrobenzene. It was first discovered by Unverdorben, in 1826, among the products of the dry distillation of indigo, and was named by him *Krystallin.* Fritzsche, who obtained it afterwards from indigo by another process, seems to have been the first to give it the name of aniline, from the Portuguese word *anil* (indigo). In 1837, Runge obtained three volatile principles from coal tar, which he named *kyanol, leucol,* and *pyrrhol.* Of these, kyanol was afterwards found by Hoffmann to be identical with aniline, and leucol has been ascertained to be the same as *quinoline* (*chinoline*). Zinn prepared it in 1840 by the reduction of nitrobenzene with hydrogen and called it *benzidam.* The identity of krystallin, aniline, kyanol and benzidam and the true composition of the substance was proved by Hoffmann in 1843. Aniline did not possess any commercial importance until the discovery in 1856, by Perkins, of the first of the so-called aniline colors, Perkins' purple or mauve, when the demand for aniline became so great that it became necessary to find a method for its preparation from one of the other coal tar fractions. (See *Coal Tar Colors.*) Nitrobenzene is now the source whence most of the aniline of commerce is derived. Nitrobenzene, hydrochloric acid, and iron turnings, in equal weights, are introduced into a cast iron vessel, care being taken that the heat does not rise too high, when the following reactions take place:

$$C_6H_5NO_2 + H_6 = C_6H_5NH_2 + 2H_2O$$
$$C_6H_5NH_2 + HCl = C_6H_5NH_2HCl$$

The semi-solid mass which soon forms consists principally of ferrous chloride and aniline hydrochloride. This is distilled, after the addition of milk of lime, in a large cast iron cylinder, and the distillate redistilled, the portion coming over between 175° C. and 190° C. being collected, and considered sufficiently pure for manufacturing purposes.

Properties.—Pure aniline is a thin, colorless, highly refractive fluid, of an oily appearance; but as found in commerce it is generally more or less colored, and sometimes of a deep reddish-brown. It has a peculiar, not disagreeable odor, and a pungent, aromatic, burning taste; its sp. gr. is 1.024. It solidifies at −6° C., if pure, but if impure the freezing point may be below −20° C. It boils at 183°–184° C., and its vapors are condensed unchanged. It is slightly soluble in water, but dissolves in all proportions in ether, alcohol, methyl alcohol, acetone, carbon disulphide, and the oils, fixed and volatile. As a base it is weaker than ammonia in the cold but stronger when hot. Its aqueous solution does not react with litmus or turmeric. With the acids it forms soluble and readily crystallizable salts. It is inflammable, and absorbs oxygen from the air, becoming at first yellowish, afterwards reddish, and ultimately brown. A characteristic property is that it produces instantly a deep blue or purple color when brought into contact with chlorinated lime or other hypochlorite (whence the name kyanol, of Runge). (*P. J.*, Sept., 1862, 128.) It is a derived ammonia, having the group C_6H_5 in place of a hydrogen atom of the NH_3 molecule. It is hence often called *phenylamine.* The chief value of aniline is in the manufacture of numerous derivatives, some of which are used in medicine while others form one group of the numerous so-called coal tar colors of commerce. Beautiful reds, purples, yellows, blues, and various other tints are obtained from it. Certain of the aniline or coal tar dyes possess properties which have led to their employment in medicine. (See under their various names.)

Under the name of *aniline oil* a liquid is to be found in commerce which consists of a mixture of aniline, toluidine, exylidine, cumidine, and varying quantities of by-products found in the "tailings"; it is used as a solvent for rubber, copal, etc.

Medicinal Properties.—The symptoms which are produced by the inhalation or ingestion of aniline are great prostration, heaviness in the head, giddiness, vomiting, violent neuralgic pains, and, if the dose has been large enough, cyanosis, coma with dilatation of the pupils, excessive perspiration, loss of reflexes and of voluntary movement, hurried weak pulse, rapid or irregular respiration, hemoglobinuria, a peculiar discoloration of the skin, and, if the patient survives sufficiently long, jaundice with great increase in the biliary pigment of the urine. At the autopsy reported by Müller (*A. J. P.*, 1887), in a woman killed by the swallowing of about a fluidounce (30 cc.) of aniline, the blood was chocolate brown, and gave the spectrum of methemoglobin. Dehio (*A. J. P.*, 1888) reported a case in which after one hundred and fifty grains (9.8 Gm.) of aniline, the red blood corpuscles fell to 1,400,000 on the eleventh day. Aniline is feebly antiseptic but many of its derivatives are very powerful germicides and have achieved practical importance as disinfectants.

The violent local effects which have been noticed as produced by some aniline dyes have probably been due to the presence of arsenic, which is used in their production and may remain as a contamination.

Aniline Blue. *Triphenyl-rosaniline, Toluidine Blue. Pure Blue. Water Blue.*—This dye-stuff is said to possess anti-malarial properties similar to those of methylene blue. The *dose* is five grains (0.3 Gm.) in capsules three times a day.

Aniline Sulphate, $(C_6H_5NH_2)_2H_2SO_4$, occurs in white crystals, soluble in water and alcohol. It has been used as a nervine in *chorea* and *epilepsy. Dose,* three-quarters to one and one-half grains (0.05–0.1 Gm.) three times daily. Maximum *dose,* three grains (0.2 Gm.) with the daily maximum dose of six grains (0.4 Gm.)

Anisic Acid. *Paramethoxybenzoic Acid. Draconic Acid.* $C_6H_4.OCH_3.COOH$.—It is prepared from anisic aldehyde or by oxidization from *p-kresolmethyl ether.* It forms colorless crystals which are almost insoluble in cold water and slightly soluble in alcohol and ether. As an antiseptic it is alleged to have marked power and it has also been used as an antirheumatic and antipyretic. *Dose,* five to fifteen grains (0.32–1.0 Gm.).

Anisodus. *Anisodus luridus* Link and Otto. (*Scopolia lurida* Dun.)—This is a Himalayan solanaceous plant in which Siebert has found *atropine* and *hyoscyamine.* (*A. Pharm.*, Feb., 1890; *P. J.*, March, 1890.)

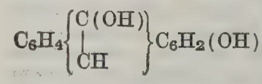
Anisole.—This name has been applied to the *methyl ether of phenol* because of the fact that it was at one time manufactured from anisic acid. It has been found by Professor Fraenkel to be an active agent against *lice* and other body vermin.

Annatto. *Orleana. Annotta. Arnotta. Terre de la Nouvelle-Orléans. Roucou,* Fr. *Orellana, Orlean,* G.—This coloring substance, which is called by the natives *urucu* or *bija,* is the reddish pulp surrounding the seeds in the fruit of *Bixa orellana* L. (Fam. *Bixaceæ*), a middle-sized tree native to northern South America, but widely cultivated in tropical Asia and Africa. The pulp is separated by bruising the fruit, mixing it with water, then straining through a sieve, and allowing the liquid to settle. The mass which remains is dried and formed into flat cakes or cylindrical rolls. Another mode is to bruise the seeds, mix them with water, and allow the mixture to ferment. The coloring matter is deposited during the fermentation, after which it is removed and dried. In commerce there are two kinds of annatto, the Spanish or Brazilian, and the French, the former coming in baskets from Brazil, the latter in casks from French Guiana. The French, which is also called *flag annatto,* has a disagreeable odor, probably from having been prepared by the fermenting process in which urine is sometimes used; but is superior, as a dye stuff, to the Spanish, which is without any disagreeable odor. Annatto is of a brownish-red color, usually rather soft, but hard and brittle when dry, of a dull fracture, of a sweetish peculiar odor and a disagreeable saline, bitterish taste. It is inflammable, but does not melt with heat. It softens in water, to which it imparts a yellow color, but does not dissolve. Alcohol, ether, the oils, and alkaline solutions dissolve the greater part of it. The South American Indians are said to produce directly from the annatto seeds, without fermentation, a color similar to and almost as brilliant as carmine. (*P. J.*, April, 1903.) For a proximate analysis of the leaves see *Ap. Ztg.*, 1899, p. 35. It contains a peculiar coloring principle, to which Preisser, its discoverer, gave the name of *bixin.* This has the formula $C_{28}H_{34}O_5$, and when pure is a dark, red, somewhat crystalline substance. According to Van Hasselt, bixin has the composition $C_{29}H_{34}O_5$, but Heiduschka and Riffart believe that the correct formula is $C_{28}H_{34}O_5$. (*A. Pharm.*, 1911, No. 1, 39.) It is accompanied by a yellow coloring matter, *orellin.* A coloring matter found in the root of *Escobedia scabrifolia* Ruiz et Pavon, a plant growing in tropical America, is used by the Mexicans in coloring fats and butter yellow. (*S. W. P.*, 1912, No. 18, 260.)

The chief uses to which annatto is applied are for dyeing silk and cotton orange-yellow, and for coloring cheese and butter. The color, however, which it imparts to cloth is fugitive. It has been given internally as a medicine; but is not now used, and probably exercises little influence upon the system. In pharmacy it is employed to color ointments and plasters, and has occasionally been substituted for saffron. It is frequently adulterated with red ochre, powdered bricks, colcothar, farinaceous substances, chalk, calcium sulphate, turmeric, etc. The mineral substances, if present, will be left behind when the annatto is burned. *Tincture of annatto* is made by extracting 100 parts of annatto with 100 parts of water containing 1½ per cent. of potassium carbonate, and evaporating to 60 parts, mixing with 12 parts of alcohol and filtering.

Anona.—The seeds of *A. squamosa* L., *Sugar Apple* or *Sweet Sop* of the West and East Indies, are said to be poisonous and to be used to kill lice, while the bark is a drastic cathartic. The seeds of *A. muricata,* L., *A. palustris,* L., and *A. spinescens,* Mart., are employed to poison fish and to exterminate destructive insects. (*Ph. Rev.*, Oct., 1896.)

Anthrarobin. *Anthro-arobin. Leucoalizarin.*



$$C_6H_4\left\{\begin{matrix}C(OH)\\|\\CH\end{matrix}\right\}C_6H_2(OH)_2$$

—This substance, which is produced from commercial alizarin by reduction, was first described by Liebermann (*Ber. d. Chem. Ges.*, 1888), and proposed as a substitute for chrysarobin. It is a yellowish-white granular powder, almost insoluble in water and acidulated solutions, sparingly soluble in chloroform and ether, and readily soluble in alcohol and weak alkaline solutions. It mixes readily with fats to form ointments. It is a powerful reducing agent, and has been used by G. Behrend, (*Th. M.*, 1888), and other clinicians, with asserted advantage in those diseases for which chrysarobin is employed. In alkaline solution anthrarobin readily absorbs oxygen and is reconverted into the blue alizarin. It is incompatible with hydrogen dioxide, potassium permanganate and other oxidizing agents. As a topical application, the ointment or the alcoholic solution (each 10 per cent.) may be used.

Anthrasol. *Colorless Coal Tar.*—Anthrasol is coal tar freed from bases such as pyridin and chinoline by acid treatment and from pitch by distillation. The distillate is purified to remove coloring principles and juniper tar is added to prevent separation of solid constituents. Oil of peppermint is added to correct the odor. It is a thin, mobile, light-yellow oil which stains neither skin nor fabric. Anthrasol is in skin diseases in strengths varying from 5 to 30 per cent.

Anthriscus. *Anthriscus cerefolium* (L.) Hoffm. (*Chærophyllum sativum* Lam. *Scandix cerefolium*, L.), *Chervil.*—An annual European plant of the Fam. *Umbelliferæ*, cultivated in gardens as a pot-herb, and naturalized in Eastern and Southern Pennsylvania. It has a strong agreeable odor, and a pungent, slightly bitterish taste. It contains a volatile oil of very feeble medicinal power, but it has been used as an emmenagogue and diuretic.

Antiaris.—Among the Asiatic arrow poisons one of the most important, which has long been used by the natives of Java and other East Indian Islands under the name of *Upas antiar*, is a gum-resinous exudation obtained from *Antiaris toxicaria* Lesch., a large tree belonging to the *Urticaceæ*, growing in Java, Celebes, and the neighboring islands. This plant is said to exhale a volatile poison which very unpleasantly affects some of those who approach it, causing eruptions upon the skin attended with much swelling; hence the fable of the *deadly upas tree.* The juice is mixed with various substances to give it due consistency. Whether taken internally or introduced into the system through a wound, upas acts with extreme violence, producing vomiting, great prostration, a feeble, irregular pulse, involuntary evacuations, and convulsive movements, which are soon followed by death.

Pelletier and Caventou obtained from it a glucoside, *antiarin*, crystallizable, soluble in water and alcohol, but scarcely so in ether, and of the formula $C_{14}H_{20}O_5$. According to Kiliani (*B. Chem. G.*, 1910, xliii, p. 3574), there are two glucosides, namely, *alpha-* and *beta-antiarin.* For the first of these he suggests the formula $C_{27}H_{42}O_{10} + 4H_2O$, while the formula for the second is uncertain, but may be $C_{22}H_{30}O_8$. Antiarin is a muscle poison, producing first strong fibrillary contractions of the voluntary muscles, followed by a rapid decrease in irritability and finally paralysis, the sarcolemma of the muscles and not the motor nerve endings being the part attacked. It also belongs to the digitalis group of cardiac stimulants, raising the blood pressure at first, and finally arresting the heart in systole. According to Stockman, antiarin diminishes the irritability of the peripheral vagi and stimulates the vasomotor centers. H. W. Bettink claims (*Ned. Tijdschr. v. Pharm.*) that besides antiarin there are present in *Upas antiar* two other active principles, *œpaïn* and *toxicarine.* Headborn (*A. E. P. P.*, 1901, xlv,) states that *antiarigenin*, a derivative of antiarin, is more powerful than antihydropin itself. See also *Arrow Poisons.*

Antiluetin. — *Potassium-ammonium-antimonic bitartrate*, $SbO(C_4H_4O_6)_2K(NH_4)_2.H_2O$, has been used by Tsuzuki (*D. M. W.*, 1913, p. 825) in the treatment of *syphilis.* The beginning dose he used was two-fifths of a grain (0.025 Gm.) increased rapidly to three-fourths of a grain (0.05 Gm.).

Antimony Arsenate.—This is a heavy, snow-white powder, containing 80 per cent. antimonic oxide and 20 per cent, arsenic acid (Merck). *Antimony arsenite*, on the other hand, is said to contain equal parts of the two ingredients, arsenous acid and antimonic oxide. It is stated that antimony arsenate is used in Russia as an alterative in *doses* of one-fiftieth of a grain (0.0013 Gm.) four times a day. (*A. J. P.*, xliv, 301.)

Antimony Colloidal. *Colloidal Antimony* Crookes, is a product containing metallic antimony made by chemical methods, which is remarkably stable. It is not broken down by electrolytes and has been kept unchanged for four years.

Colloidal Antimony Sulphide is made by saturating a 0.5 per cent. solution of tartar emetic with hydrogen sulphide and removing the acid potassium tartrate by dialysis. The reddish turbid liquid which results is adjusted by assay so as to contain 0.2 per cent. antimony sulphide; glucose is then added to make the liquid isotonic, acacia to render physically stable and phenol to preserve. It has been used by Rogers (*L. L.*, 1919, cxcvi, 505) intravenously up to 20 cc. of the 1 to 500 solution in *kala-azar.*

Colloidal Antimony has been used by several investigators in the treatment of *leprosy* with asserted beneficial results. Cawston (*B. M. J.*, December 4, 1920 and March 19, 1921) uses intramuscular injections of a preparation known as *Oscol Stibium.* He gives four injections, beginning with 2.5 cc. (40 minims) and increasing to 5 cc. (80 minims), every day for four days. This treatment, he asserts, leads to a rapid disappearance of at least the external evidence of the disease. Wildish (*B. M. J.*, January 14, 1922) has obtained similar favorable results, not only from Oscol Stibium but also from *Crooke's colloidal antimony* and from ordinary tartar emetic.

Antimony Crocus. *Crocus of Antimony. Saffron of Antimony.*—This compound is formed during the deflagration of a mixture of equal weights of antimony trisulphide and potassium nitrate, to which one-twelfth of hydrochloric acid has been added. Fused crocus of antimony is in masses of a liver-brown color; the unfused is a saffron-brown insoluble powder, containing about four-fifths of trioxide, and one-fifth of trisulphide. It was formerly used in making tartar emetic.

Antimony, diaphoretic. *Antimonium Diaphoreticum. Potassii Biantimonias. Antimoine diaphorétique lavé*, Fr.—This compound may be formed by deflagrating in a crucible, and keeping red hot for fifteen minutes, a mixture of pure antimony with three times its weight of potassium nitrate. The product, washed with water and dried, is *washed diaphoretic antimony.* For improved process, see 14th edition of *U. S. D.*, p. 1640. *Dose*, from one-half to two drachms (1.9–7.7 Gm.). This form of antimony is weak, variable, and rarely used.

Antimony Glass. *Vitrum Antimonii.*—This is prepared from antimony trisulphide by a partial roasting and subsequent fusion. Glass of antimony is an active antimonial; but, owing to its variable composition and unequal operation, it is very seldom used. For further information concerning this substance, see *U. S. D.*, 19th edition, p. 1391.

Antimony Aniline Tartrate. $SbO.C_6H_5NH_2.$-$C_4H_4O_6$.—According to Loweran, this occurs in colorless, yellow crystals, soluble in water, containing 22 per cent. of antimony. Although antimony and potassium tartrate has been used both experimentally and clinically in the treatment of trypanosome infections, its high toxicity has discouraged the hope of its proving a useful therapeutic agent. The antimony and aniline tartrate, which was first prepared by C. S. Evans, was found by Loweran (*C. R. A. S.*, 1909, p. 546) to be much less toxic to the higher animals and to be an efficient trypanocide in guinea-pigs. Thiroux has used it clinically in the treatment of *sleeping sickness*, and, although it is as yet too soon to say definitely concerning its value, his results are at least encouraging. He injected in intravenously in *doses* of one-fourth of a grain (0.015 Gm.).

Antimony Iodide. SbI$_3$. *Antimonii Iodidum. Antimony Triiodide* or *Teriodide.*—According to W. Copney, of London, this iodide may be conveniently prepared by gently heating, in a Florence flask, metallic antimony and iodine, in the proportion of one part to three. The elements combine with sudden heat and liquefaction, and, upon the withdrawal of the heat, the iodide formed solidifies, and is removed by breaking the flask. Antimony iodide, as thus prepared, forms a somewhat crystalline, foliated mass, which, when pulverized, yields a deep orange-red powder. By the action of water it is decomposed. An amorphous variety is prepared by action upon antimony oxide with potassium iodide in the presence of anhydrous acetic acid. It formed a yellow powder which is more stable than the crystalline variety. (*Chem. News*, 1918, cxvii, 306.) It has been tried as an alterative in *doses* varying from one-fourth to one-half grain (0.016–0.03 Gm.), given in pill.

Antimony Sulphide. *Antimonium Nigrum*, Br. 1864. *Black Antimony. Japanese Antimony. Antimony needle. Sulphuret of Antimony. Stibium Sulfuratum Crudum, Antimonium Crudum. Sulfuretum Stibicum. Sulfure d'Antimoine de commerce*, Fr. Cod. *Antimoine sulfuré, Antimoine cru*, Fr. *Stibium sulfuratum nigrum*, P. G. *Schwefelantimon, Schwefelspiessglanz*, G. *Antimoino crudo*, Sp. *Antimonii Sulphidum*, U. S. 1890. *Antimony Trisulphide.* Sb$_2$S$_3$; 334.09.—"Native antimony sulphide, purified by fusion and as nearly free from arsenic as possible." *U. S.*, 1890.

The antimony sulphide which is found in commerce is obtained from the native sulphide, called *antimony ore*, by different processes of purification. Much of the "Black Antimony" of commerce at one time contained no antimony whatever, but was simply powdered coal and marble; it was easily distinguished by its low specific gravity; a dry, tared one-ounce bottle will hold, after shaking down, two and a quarter ounces of powdered black antimony, but only one and a quarter ounces of powdered coal. (*Proc. A. Ph. A.*, 1885, 479.)

Antimony sulphide should never be triturated with a strong oxidizing agent as an explosion is liable to occur. When exposed to the air it is partially converted into the oxide.

Antimony sulphide is mostly prepared in France and Germany. It is called, in commerce, antimony, or *crude antimony*, and occurs in fused conical masses, denominated "loaves." "Steel-gray masses of a metallic luster and a striated crystalline fracture, forming a black or grayish-black, lusterless powder, without odor or taste, and permanent in the air. Insoluble in water or alcohol, but soluble in hydrochloric acid with the evolution of hydrogen sulphide." *U. S.*, 1890.

This preparation is very uncertain in its operation, and ought not to be used in medicine. It has, however, been employed as a diaphoretic and alterative in *scrofula, glandular obstructions, cutaneous diseases*, and *chronic rheumatism.* It is used in the United States solely in veterinary practice. The *dose* for a horse or cow is from ten to thirty grains (0.65–2.0 Gm.), to be given in powder or bolus. For further information concerning antimony sulphide, see *U. S. D.*, 19th edition, p. 1391–1392. See also under *Antimony Colloidal.*

Antimony Sulphide, Purified. *Antimonium Nigrum Purificatum*, Br. 1898. *Antimonous Sulphide. Antimonii Sulphidum Purificatum*, U. S. 1890. *Purified Black Antimony. Sulfure d'Antimoine pur*, Fr. Cod. *Gereinigtes Schwefelantimon*, G. *Trisolfuro di antimonio depurato*, It.—"Native antimonious sulphide, Sb$_2$S$_3$, from which siliceous matter has been removed by fusion, reduced to fine powder, and, if any salt of arsenium be present, purified by digesting with half its weight of solution of ammonia for several days, washing and drying." *Br.* The purpose of washing the antimony sulphide with ammonia is to remove any foreign metals, especially copper and arsenic, which may be present in the native ore.

It is "a heavy, grayish-black, lusterless powder, without odor or taste, and permanent in the air. Insoluble in water or alcohol, but soluble in hydrochloric acid with the evolution of hydrogen sulphide. At a temperature below a red heat it fuses to a dark brown liquid." *U. S.*, 1890. This preparation is not used in medical practice, but is used in the manufacture of sulphurated antimony (see *Antimonium Sulphuratum*, Part I).

Antimony Trichloride. *Butter of Antimony.* SbCl$_3$.—Prepared by subliming antimony sulphide with mercuric chloride, by the action of dry chlorine on the sulphide or metal, or by dissolving the sulphide in hydrochloric acid and concentrating the solution of the chloride; in the latter method the product is usually colored by contamination with iron, but by distillation the pure chloride will finally pass over, the distillate solidifying in a mass of fine white crystals. Antimony trichloride is a deliquescent, soft mass, known as butter of antimony, which melts at 72° C. and boils at 223° C. It is very hygroscopic and corrosive. The addition of water produces the oxychloride known, when dry, as *powder of Algaroth.* A solution was recognized in the Br. Ph., 1885, and is used in medicine as a caustic. McDonald and Hill have improved the formula for *solution of chloride of antimony* by dissolving 132 grains of antimonious chloride in 3 fluidrachms of hydrochloric acid and sufficient distilled water to make 1 fluidounce. If it is desirable to have a tinted solution, add 15 grains of ferric chloride to each fluidounce. (*P. J.*, 1908, 86.) It is extensively used to give a bronze surface to iron and steel ware. For account of fatal poisoning by butter of antimony see Bell, *B. M. J.*, June 10, 1922, 917.

Antimonyl Sodium Tartrate. *Sodium Antimonyl Tartrate.*—This salt is analogous to the official tartar emetic except that it is a compound of sodium instead of potassium.

Napier (*Indian Med. Gaz.*, 1922, lxx, 10) used an especially pure preparation of sodium antimonyl tartrate for intramuscular injections in the treatment of *kala-azar* with asserted advantage over the tartar emetic.

Antinosin. *Sodium tetra-iodophenolphthalein.* $(C_6H_2I_2ONa)_2C.O.C_6H_4O$.—A blue powder, soluble in water and employed as a succedaneum for iodoform or as a surgical antiseptic in 0.1 to 0.5 per cent. wash. (See also *Nosophen.*)

Antipyrin Sulphanilate. *Beta-Sulphopyrin. Sulfopyrine.*—This combination of antipyrin with sulphanilic acid consists of a white powder fairly soluble in warm water and having a pronounced acid taste. It is asserted to be a specific in the treating of *iodism* and is also used in *asthma* and *influenza*, etc. *Dose,* fifteen grains (1 Gm.) three or four times daily.

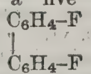
Antipyrine Tannate.—This is described as a yellow powder, insoluble in water, soluble in alcohol, and containing 37 per cent. of antipyrine. It is stated that it may be made by adding concentrated aqueous solutions of its constituents in the proportion of fifty parts of antipyrine to twenty-eight and a half parts of tannic acid. It has been specially recommended on account of its tastelessness, but is probably not an eligible preparation. Its incompatibilities are numerous, including those of both antipyrine and tannin.

Antithermin. *Phenylhydrazin-lævulinic Acid,* $C_6H_5.N_2O = C(CH_3).C_3H_5O_2$.—This substance, occurs in colorless crystals, insoluble in cold water, soluble in ether and hot alcohol, melting point 108° C. It was used as an antipyretic by Drobner (*W. M. P.*, 1892, 540), who finds it active in *doses* of from eight to ten grains (0.5–0.65 Gm.). It produces pallor, excessive sweating, and other evidences of vasomotor depression.

Antithyroidin Moebius. *Serum Antithyroideum. Thyroidectomized Serum.*—This is the blood serum of sheep from which the thyroid gland has been removed, at least six weeks before the blood is drawn, preserved with 0.5 per cent. of phenol. It is an amber-colored fluid, with the faint odor and taste of phenol. It is marketed in vials containing two and a half drachms (10 cc.). With proper precautions it is said to keep indefinitely. It is employed in the treatment of *exophthalmic goitre.* It is administered either hypodermically or by the mouth in *doses* beginning with eight to fifteen minims (0.5–1.0 cc.) three times a day, gradually increasing the dose.

Antituman. *Sodium Chondritin Sulphate.*—Oestreich (*B. K. W.*, 1910) having observed that in carcinoma the arterial walls and cartilaginous tissues were not affected, believed that this immunity of these tissues was due to some substance found in them. On this theory he has employed *sodium chondritin sulphate* in the treatment of *cancers.* According to his observations, the remedy lessens suffering and improves the general health of patients who are suffering with inoperable cancers. Because of the pain which follows the injection of the remedy, it is marketed in combination with eucaine. The beginning *dose* is one and a half grains (0.1 Gm.) once or twice a day subcutaneously, which may be gradually increased.

Antitussin.—*Antitussin* is a five per cent. ointment of *di-fluordiphenyl,*



$$\begin{array}{l} C_6H_4\text{–}F \\ | \\ C_6H_4\text{–}F \end{array}$$

which occurs as colorless crystals melting at 87° C. It is a white aromatic powder, insoluble in water, freely soluble in alcohol, ether, and chloroform, was originally recommended by J. Thimm as a local remedy in the treatment of *syphilitic ulcers* or *wounds,* applied either as a ten per cent. dusting powder or a ten per cent. ointment. (*Derm. Zeit.*, iv, No. 15.) Antitussin has been strongly recommended by Max Heim (*B. K. W.*, Dec., 1899) in the treatment of *whooping cough.* It is an ointment consisting of five parts of di-fluor-di-phenyl, ten parts of vaselin and eighty-five parts of lanolin. For a child a year old, about one-half drachm (2 Gm.) is slowly rubbed into the skin daily on the back, chest, and abdomen, about a drachm (3.9 Gm.) being used for a child five years old. (See also *Merck's Annual Reports,* 1905, 22 and 1907.)

Anusol.—A proprietary suppository, alleged to contain a bismuth compound of *iodo-resorcin-sulphonic acid,* but it is apparently a mixture of zinc oxide, resorcinol, bismuth oxyiodide, balsam of Peru, and cacao butter. (*West. Drug.*, 1898, 75; *J. A. M. A.*, 1911, lvi, 441.) It is used in the treatment of *hemorrhoids.*

Aperitol. *Valothalein.*—Under this name is marketed a palatable form of *iso-valeryl-acetyl phenolphthalein* formed by the combination of esters of isovalerianic acid and acetic acids, in equal proportions.

This substance, which has been introduced as a cathartic, appears to be without any toxic action upon the system, for Hammer and Veith (*Med. Klin.*, 1908, iv) fed fifteen grains (1 Gm.) to a dog daily for ten days without any apparent effect. The same authors report a case in which a man took by mistake twenty-four grains (1.6 Gm.) without any more serious symptom than catharsis. Those who have employed the remedy are almost unanimous in the statement that it causes catharsis without (except in very occasional cases) any griping.

Aphloia theæformis Benn. (Fam. *Bixaceæ*).—This plant is a native of Madagascar and is claimed to possess marked alterative properties and beneficial effects upon hemoglobin. It is administered as an infusion of the leaves, 30 Gm. of the plant being used to make 1 liter of infusion.

Apinol. *N. N. R.*, 1924.—This is a product obtained in the destructive distillation of the wood of *Pinus palustris* Mill. (*Pinus australis* Michx.). It is stated to consist mainly of *lævo-menthone,* $C_{10}H_{13}O$. It is a clear amber-colored oil, of neutral reaction with a pine odor and having a sp. gr. of 0.946 and a boiling point of 182° C. It is used locally as an antiseptic and anesthetic application for *wounds.* It is also employed as an expectorant in chronic catarrhal conditions of the respiratory tract in *doses* of five to ten minims (0.3–0.6 cc.).

Aplopappus. *Aplopappus* (*Haplopappus*) *Baylahuen* Remy.—This composite herb is a native of Chili, where it is said to be relied upon as a stimulant in *flatulent dyspepsia* and *chronic inflammation* with *hemorrhage* of the lower bowels. It has been analyzed by H. H. Rusby (*A. J. P.*, 1890, 488), and later by H. Kahn (*A. J. P.*, 1891, 377). The former found a volatile oil, a fatty oil which had the specific odor of the plant, a brown acid resin of sharp taste, and tannin. The latter determined the percentage of volatile oil as 6.65, and of resin as 21.15. He also considers that this resin is a mixture of four different resins. G. Baille asserts (*B. G. T.*, Feb., 1889) that the remedy is valuable not only in *dysentery,* but in *genito-urinary catarrhs,* and also as a stimulating expectorant. *Dose,* one-half to one tablespoonful (7.5–15 cc.) of a strong decoction, one part to five, may be given every two hours; or the fluidextract, from five to twenty minims (0.3–1.3 cc.).

It has also been used in tincture form as an application to slowly healing *wounds* and *ulcers.*

Apocodeine Hydrochloride. $C_{18}H_{19}NO_2HCl$.—It is a greenish-yellow powder, soluble in water. Apocodeine has been investigated physiologically by W. E. Dixon (*B. M. J.*, 1902) who found that it lowered blood pressure by dilating the blood vessels, increased the intestinal peristalsis and produced a large secretion of saliva. Foy and Combemale (*R. T.*, 1907) have both employed it hypodermically as a laxative with pleasing results. Thirty minims (1.8 cc.) of a 1 per cent. solution may be injected deeply into the muscles.

Apolysin. *Aconitylphenetidin. Monophenetidin Citrate.* $C_6H_4.OC_2H_5.NH(C_6H_7O_6)$.—A compound made by heating together citric acid and phenetidin with one molecule of water. It is a crystalline, yellowish-white powder of peculiar odor and taste. Its melting point is 72° C. It is soluble in cold water (1 in 25), alcohol, and glycerin, and in concentrated sulphuric acid without change of color. The solution in nitric acid turns a pale orange color. The aqueous solution is not clouded by silver nitrate, nor the acid solution by hydrogen sulphide. For tests of purity, see *Zeit. Oest. Apoth. Ver.*, 1910, 301. R. Seifert (*D. M. W.*, xxi, 1895) asserts that in *doses* of from eight to twenty-four grains (0.5–1.6 Gm.), three or four times a day, it is a valuable remedy as an antipyretic in various febrile diseases, and possessed of great power as an analgesic, similar in range of usefulness to acetphenetidin, but free from poisonous properties or disagreeable after effects.

Apomorphine-methylbromide. $C_{17}H_{17}NO_2\text{-}CH_3Br$. *Apomorphine Bromomethylate. Bromophin. Euporphin.*—This occurs in colorless or yellowish crystals soluble in either water or alcohol. It is used as a nauseating expectorant in *acute bronchitis* and is asserted to have the advantage over apomorphine of being more stable and less liable to produce vomiting. The *dose* is from one-twentieth to one-twelfth of a grain (0.003–0.005 Gm.).

Apothesine. $C_6H_5(CH)_2.CO_2.(C_2H_5)_2N(CH_2)_3\text{-}HCl$. *Di-ethylamino-propyl-cinnamate Hydrochloride.*—This occurs as a crystalline powder with a melting point of 137° C. Readily soluble in water or alcohol. It is precipitated from its aqueous solution by alkaloidal reagents.

Apothesine has been introduced as a local anesthetic. According to Sollmann (*J. P. Ex. T.*, 1918, xi, p. 71) its anesthetic efficiency is about one-eighth that of cocaine, and the experiments of Eggleston and Hatcher (*J. P. Ex. T.*, 1919, xiii, p. 433) show that it is slightly less toxic than cocaine.

According to the experiments of Macht, Satani and Swartz (*Journ. of Urology*, Aug., 1920) apothesin has distinct antibacterial powers, 0.5 per cent. solution killing gonococci and staphylococci after 24 hours' exposure.

Aquilegia. *Aquilegia vulgaris*, L. *Columbine.*—A perennial herbaceous plant of the Fam. *Ranunculaceæ*, indigenous to Europe, but cultivated in our gardens. At one time considered diuretic and diaphoretic, columbine is not at present used in practical medicine. For further information concerning this drug, see *U. S. D.*, 19th ed., p. 1394.

Archidendron. *Archidendron Vaillantii* F. Muell.—The bark and black beans of this leguminous plant of New South Wales are said to be an active paralyzant to the motor side of the spinal cord. (Bancroft, *Proc. Roy. Soc. N. S. W.*, 1886.)

Areca Nut. *Semen Arecæ. Betel Nut. Noix d'Arec*, Fr. *Arekanüse, Betelnüse*, G.—The *Areca Catechu*, L., is an East India palm. The fruit, which is ovoid and from 2 to 3 cm. in diameter, and of an orange-yellow color, contains the nut embedded in a fibrous, fleshy envelope, and invested with a brittle shell which adheres to the exterior flesh. The kernel, the betel nut of commerce, is of a rounded-conical shape, rather larger than a chestnut, externally of a deep brown, diversified with a fawn color, so as to present a reticulate appearance, internally brownish-red with whitish veins, very hard, of a feeble odor when broken, and of an astringent, somewhat acrid taste. It abounds in tannin, and contains also gallic acid, a fixed oil, gum, a little volatile oil, lignin and various saline substances. It yields its astringency to water, and in some parts of Hindustan an extract is prepared from it having the appearance and properties of catechu. A red coloring matter known as *Areca red* is extracted, probably resulting from the decomposition of a tannin. It is insoluble in cold water and ether, soluble in boiling water and alkaline liquids, out of which it is precipitated by acids. E. Jahns (*B. Chem. G.*, 1888, xxi, 3404) has found three alkaloids in areca nut: 1. *Arecoline*, $C_8H_{13}NO_2$, identical with the *arekane* of Bombalon. 2. *Arecaine*, (*arecaidine*) $C_7H_{11}NO_2 + H_2O$, which occurs in permanent, colorless crystals, soluble in water, insoluble in absolute alcohol, ether, chloroform, and benzene. 3. An alkaloid which exists in such small quantities that sufficient was not obtainable for close examination. On heating arecoline with strong hydrochloric acid to 150° C. it is decomposed into methyl chloride, CH_3Cl, and *arecaivine.* The third alkaloid of Jahns is probably *guvacine*, $C_6H_9NO_2$, of which the methyl derivative is the base arecaidine before mentioned. In addition to the alkaloids found by Jahns, Emde (*Ap. Ztg.*, 1915, xxx, p. 240) has reported *arecolidine* and Hess (*B. Chem. G.*, 1918, li, p. 1004) *guvacoline.* These alkaloids have been more closely studied by Winterstein and Weinhagen (*Zeit. P. C.*, 1918, civ, p. 48) and by Hess and Liebbrandt (*B. Chem. G.*, 1918, li, p. 1004). From their studies it is apparent that guvacoline and arecoline are the methyl esters respectively of guvacine and arecaine (arecaidine). Meyer (*Monatsh. Chem.*, 1902, xxiii, p. 22) has shown that arecaine is a *methyltetrahydro-nicotinic* acid and it has been prepared synthetically.

Immense quantities of areca nut are consumed in the East, mixed with the leaves of the Betel pepper (*Piper Betle*, L., *Chavica Betle* (L.) Miq.) and with lime, forming the masticatory so well known by the name of *Betel.* The red color which this mixture imparts to the saliva and the excrements is owing to the areca nut, which is also powerfully astringent, and, by its internal use, tends to counteract the relaxation of bowels to which the heat of the climate so strongly predisposes. (See *N. R.*, 1876, 71.) Arecoline resembles pilocarpine in its effects on the system. (Pätz, *Z. E. P. T.*, 1910, vii.) According to Jahns (*B. G. T.*, 1889) arecaine is the active principle of the areca nut, and a powerful tænicide, and is an active poison with an action of the type of muscarine and pilocarpine. Locally applied, or when given internally, it contracts the pupils.

Arecoline hydrobromide, $C_8H_{13}NO_2HBr$, a commercial salt, according to the experiments of Fröhner, is more powerful as a stimulant to the salivary glands than pilocarpine, and more active as a laxative than eserine. It is commended by veterinarians in the colic of horses, given subcutaneously in the *dose* of from one to one and one-half grains (0.065–0.096 Gm.). In human medicine it has been used in the dose of from one-fifteenth to one-tenth grain (0.004–0.006 Gm.) against the *tape worm* and as a myotic. A one-half to one per cent. solution produces a myosis, which reaches its maximum in about ten minutes and begins to subside in half an hour. It is claimed by various ophthalmologists that although in *glaucoma* its action is very transient, it produces a more considerable reduction of the intra-ocular pressure than can be obtained either with pilocarpine or eserine. It may cause considerable irritation but does not injure the continuity of the epithelium.

In India the areca nut has long been used as a vermifuge, the dose being a teaspoonful of the freshly grated nut, and its value against the *tape worm* has been confirmed by various European and American practitioners. The usual *dose* is from one to two drachms (3.9–7.7 Gm.). In this country the nut has also been used for the making of a hard charcoal, employed as a basis of tooth-powder.

Argemone. *Argemone mexicana,* L. *Prickly Poppy. Argémone,* Fr. *Stachelmohn,* G.—An annual plant, belonging to the *Papaveraceæ,* growing in our Southern and Western States, Mexico, the West Indies, Brazil and in many parts of Africa and Southern Asia. For an illustrated paper on the structure of the seed of this plant by Schlotterbeck and Eckler, see *Proc. A. Ph. A.,* 1906, 467. The whole plant abounds in a milky, acrid juice, which becomes yellow on exposure, and has been used as a local application in obstinate *cutaneous diseases,* especially that affection known in Upper India as *dhad,* and also in cases of *warts* and even *chancres.* The alleged presence of morphine in *Argemone mexicana* has been disproven by J. O. Schlotterbeck (*Proc. A. Ph. A.,* 1901, p. 247), who finds that the plant contains berberine, besides an alkaloid, *protopine* ($C_{20}H_{19}O_5N$). This alkaloid, also called *macleyine* and *fumarine* when obtained from other plants, is the *Argemonine* of Peckoldt. The seeds of the plant have been used in *colic,* 8 grains (0.5 Gm.), given in emulsion, and repeated if necessary every half hour until three doses have been taken. (*P. J.,* xiii, 642.) For further information concerning this drug, see *U. S. D.,* 19th ed., p. 1395.

Argulan.—This preparation is stated by Kolle and Rothermundt (*Med. Klin.,* 1913, p. 835) to be an antipyrine sulphamino-mercury, and to represent 46.8 per cent. of mercury. It occurs as white crystalline substance, insoluble in water. It is used in the form of an oily suspension for hypodermic injection in the treatment of *syphilis.* According to Mentberger the injections are quite painful and the antiluetic effect not superior to other preparations of mercury (*Ap. Ztg.,* 1915, p. 580). It is used in *doses* of five one-hundredths to two-tenths gramme (1–3 gr.).

Arhovin. $C_{10}H_{13}C_6H_4(COOC_2H_5)(C_6H_5)_2NH$.—This is asserted to be a mixture of *diphenylamine, thymolbenzoate* and *ethylbenzoate* in molecular proportion. It occurs as a yellowish aromatic liquid with a mentholic taste, and is readily soluble in alcohol, and the fatty oils. It has been used as a urinary antiseptic in *cystitis* and *urethritis* and also as a local application in *vaginitis* and *endometritis.* According to Burchard and Schlockow (*Med. Woch.,* 1903), the ingestion of twelve 4-minim capsules over a period of three days imparted to the urine a marked antiseptic power. Although there have been a large number of favorable reports concerning this preparation, Deutsch (*W. K. W.,* 1906) and others have not had successful results from it. The *dose* for internal administration is from four to eight minims (0.25–0.5 cc.) repeated several times a day. For local application a 5 per cent. solution in olive oil may be employed.

Aristochin. *Aristoquin. Aristoquinine. Diquinine carbonic ester.* $CO(C_{20}H_{23}N_2O_2)_2$.—A white or pinkish amorphous powder, soluble in alcohol, ether, chloroform, glycerin, and dilute acids, but insoluble in water. It is incompatible with alkalies and acids, being decomposed with the liberation of quinine. It is said to contain 96 per cent. of quinine, and probably is an effective antiperiodic, but has been chiefly used in *whooping cough.* It has the advantage over quinine of being practically tasteless. The *dose* for infants is about one grain (0.06 Gm.); for adults eight to fifteen grains (0.5–1.0 Gm.).

Aristolochia.—There are several species of the genus *Aristolochia* which are found in the herbalists' stores of India but do not enter commerce. Of these *A. bracteata* Retz is employed as an emmenagogue. Aristolochia of the Br. Add. was the dried stem and root of *Aristolochia indica* L. As sold in commerce this drug consists chiefly of stems with attached roots and is employed for the cure of *snake bite* and to produce abortion. The possession by it of any distinct medicinal properties is very doubtful. Later investigation has shown *A. rotunda* L. to contain *aristolochine,* $C_{32}H_{22}N_2O_{13}$, which has been used in Europe as a general tonic in febrile debility. The Br. Add. recognized the *concentrated liquor* (1 in 2 of 20 per cent. alcohol) (*Liquor Aristolochiæ Concentratus,* Br. Add.), *dose,* one-half to two fluidrachms (1.8–7.5 cc.); the *tincture* (1 in 5 of 70 per cent. alcohol) (*Tinctura Aristolochiæ,* Br. Add.), *dose,* one-half to one fluidrachm (1.8–3.75 cc.). Among the other species of *Aristolochia* which have been used medicinally *A. Clematitis* L., *A. longa* L., *A. rotunda* L., are still retained in official catalogues of the continent of Europe, where they are indigenous. *A. Pistolochia* L. of Southern Europe appears to have been the aristolochia of Pliny and is still used under the name of *Pistolochia.* The rhizome of *A. Clematitis* is very long, cylindrical, about 5 mm. in diameter, as a goose-quill or thicker, variously contorted, beset with the remains of the stems and roots, of a grayish-brown color, a strong, peculiar odor, and an acrid, bitter taste; that of *A. longa* L. is spindle-shaped, from 5 cm. to 3 dm. in length, about 2 cm. in thickness, fleshy, very brittle, grayish externally, brownish-yellow within, bitter, and of a strong, disagreeable odor when fresh; that of *A. rotunda* L. is tuberous, roundish, heavy, fleshy, brownish on the exterior, grayish-yellow internally, and similar to the preceding in odor and taste; that of *A. Pistolochia* L. consists of numerous slender yellowish or brownish rootlets, attached to a common head, and possessed of an agreeable aromatic odor, with a taste bitter and somewhat acrid.

Aristolochine ($C_{32}H_{22}O_{13}N_2$ or $C_{17}H_{11}O_7N$) is the *aristolochic acid* of Hesse. It was isolated from *A. clematidis* and *A. rotunda* by Pohl (*A. E. P. P.,* 1891, xxix, 282). *Aristinic acid* ($C_{18}H_{13}$-

O_7H) and its isomer *aristidinic acid* as well as *aristolic acid* ($C_{15}H_{11}O_7N$) have been isolated by Hesse (*P. J.*, 1891, li, 551) from *A. argentina.*

Many species of Aristolochia, growing in the West Indies and Southern America, have been used medicinally; *A. cymbifera* Martius, known in Brazil as *milhommen, jarra, jarrinha,* and in Mexico as *guaco,* is said to have medicinal properties similar to those of the official species, but Butte affirms that it is depressant to the sensory nerve centers and is useful in *neuralgia* and *pruritus.* In the Argentine Republic the root of *A. argentina* is used as a diuretic and diaphoretic, especially in *rheumatism.* In the East Indies *A. indica* L. is employed for similar purposes with the European and American species, and the Arabians are said by Forskhal to use the leaves of *A. sempervirens* as a counter-poison. *A. fœtida* Kunth, of Mexico, or *Yerba del Indio,* is used as a local stimulant to foul ulcers. A number of species of aristolochia are employed as a remedy for *snake-bites* in various parts of the world, as *A. Serpentaria* L., in North America; *A. maxima* L. (the rhizome of which is called *Guaco* or *Contra Capitano*), in South America; *A. anguicida* L., in the Antilles; *A. brasiliensis* Mart. et Zucc.; *A. cymbifera* Mart. et Zucc.; *A. macroura* Gom.; *A. trilobata* L., etc. There is no sufficient reason for supposing that any one of them is effective.

Armeria. *Armeria vulgaris* Willd. (*Statice Armeria,* L.) *Maiden Pink.* (Fam. *Plumbaginaceæ.*)—This plant, found in Europe, Asia, and Western North America, is said to be an active diuretic. (*Ph. Post,* May, 1890.)

Arrow Poisons.—Up to the seventh century poisoned arrows were used in Europe in warfare, and they seem not to have disappeared from Spain until the sixteenth century, while poisoned daggers and poisoned swords were used even later for assassinations. The nature of the poisons employed is obscure, though it is stated that *Veratrum album,* L., and snake venom were used. The peregrinations of English and American travellers in Africa, and the various political changes and fomentations which have been the fruit of their discoveries—the war with Spain and the consequent bringing of attention to the Philippine Islands—have developed so much general interest in the wild natives of these various remote regions that we have thought it proper to prepare for our readers a general summary of what is known in regard to the poisons used by these various natives for the killing of game and the destruction of their enemies. In doing this we have thought that a geographical arrangement might well suffice. A number of arrow poisons in various parts of the world have been used to a greater or less extent as therapeutic agents, and are considered elsewhere in this work. Among these may be mentioned strophanthus, acocanthera, antiaris, and curare.

So far as our knowledge goes no poisonous arrows have ever been used in North America or in Northern Asia, unless, indeed, the statements made by Kracheninikow be correct. In the second volume of his *Vogage en Sibérie,* French edition, 1768, this traveller states that the roots of the plant known as *Zgate* are employed by several tribes living in the far north of Asia as an arrow poison, and it has been suggested, probably with insufficient reason, that the plant is an anemone. We have met with no recent author who has seen this poison. Fraser examined a poison used by the Mishmis of northeastern India and concluded it was derived from a species of aconite (*C. D.*, 1915, 40).

The *Upas tieute,* which is used in the East Indies, is said to be obtained from a climbing woody plant growing exclusively in Java, the *Strychnos Tieute* of Leschenault. This author states that a decoction of the bark of the root is concentrated to the consistence of a thin syrup, then mixed with onions, garlic, pepper, etc., and allowed to stand until it becomes clear. The poisonous principles in both *Upas antiar* and *Upas tieute,* according to Pelletier and Caventou, is strychnine combined with igasuric acid. This poison produces death by violent convulsions, the heart stopping before respiration. (Hammond, *Am. J. M. S.*, 1860, p. 363.)

It is very probable that different extracts are employed by different tribes in the islands of the Malay Archipelago. Braidwood (*Ed. M. J.*, 1864) found the arrow poison known as *Dajaksh* to be a cardiac paralyzant. It is not clear whether this is the same as Borneo arrow poison examined by Leubuscher. (*Cb. I. M.*, Bd. xvii, 1896.)

The arrow poisons used by the natives of the Philippine Islands are, according to the researches of P. C. Plugge (*A. J. P.*, 1896, ii), obtained from the *Rabelaisia philippinensis* Planch. Plugge has found in it a non-nitrogenous glucoside, *rabelaisin.* This given in very large doses produced in animals some convulsive movements, followed by profound muscular relaxation, loss of reflexes, and general paralysis, ending in death from asphyxia. On the heart it acted as an energetic stimulant, belonging to the digitalin group. (See also I. Rosenthal, *Sitzungsb. f. Physk. u. Med. Soc.*, Erlangen, 1894.)

An arrow poison is used by the Malays, under the name of *Ipoh;* it is said to be obtained from *Derris* (*Pterocarpus*) *elliptica* Benth. (Fam. *Leguminosæ*), or *tuba root,* which is much used in Java as a fish poison. It contains an active acid resin, to which the name of *derrid* has been given. Derrid appears to be one of the most powerful fish poisons known, as one five-millionth part stupefied gold fish in a few moments, and killed them within half an hour. (*P. J.*, 1890, xxi.) According to the researches of van Hasselt (*A. I. P. T.*, 1911, xxi, p. 242), closely allied, physiologically, to derrid are *pachyrhizid,* from the *Pachyrhizis angulatis,* and *nicoulin,* from the *nekoe* or *stink-wood.* These drugs are powerful poisons to the central nervous system, especially the respiratory center, and in larger doses cause slowing of the pulse by a direct action upon the heart muscle.

The natives of Perak, in the Straits Settlements, use an arrow poison stated to be a combination of aqueous extracts from the root bark of three trees, the individual extracts being known as *ipoh aker, aker lampong,* and *prual.* Ipoh aker and aker lampong are believed to be obtained from undescribed species of *Strychnos;* extracts were prepared from the root bark of these trees by Ralph Stockman (*Lab. Rep. Roy. Soc. Edinburgh,* vol. vi, 1897), and found to be of similar physiological power, each of them having a digitalis-like action and also a well marked curare-like action, causing arrest of the heart in systole and loss of power in the motor nerve endings. *Prual* is said to be made from the root bark of *Coptosapelta flavescens* Korth., now recognized as *C. macrophylla* (Roxb.) K. Sch. (Fam. *Rubiaceæ*); in the experiments of Stockman it was found to be a violent poison, very rapidly killing the muscle at the point of inoculation, and soon involving in a fatal influence the whole muscular system, so that the animal after a large dose collapsed almost at once with diastolic cardiac arrest.

The African arrow poisons are quite numerous. *Exuja* or *Echugin* is a blackish-brown, crumbly, odorless, and intensely bitter arrow poison used by the Ovambos of Southwest Africa. It is said to be yielded by an apocynaceous shrub, *Adenium Boehmianum* Schinz. From it R. Böhm (*Cb. N. W.*, 1889) isolated the crystalline glucoside ($C_5H_8O_2$), *echugin*, and a resinous body, *echugon*. The glucoside crystallizes in small, colorless, satiny, rhombic plates, easily soluble in water and alcohol, and insoluble in ether. It is present to about 10 per cent. in the crude substance, and is said to very closely resemble strophanthin in its physiological properties.

The arrow poison used by the pygmies of Central Africa has been obtained by Surgeon Parke, and is described in the *P. J.*, April, 1891. It has been found to contain two active alkaloids, *erythrophlœine* ($C_{28}H_{43}O_7N$) and *strychnine*.

The Sakayes, the Somangs, and the Wa Kamba tribes in Eastern Africa produce arrow poisons whose relations with one another are still obscure. *Hippo*, according to Laborde, causes in the lower animals vomiting, followed by tetanic convulsions and an almost simultaneous arrest of the respiration and cardiac action. (*P. J.*, July, 1887.) *Vakamba* of Laborde (*Ibid.*) is probably the same as the *ukambin* which has been studied by H. Paschkis, who found its active principle to be a crystalline body belonging to the digitalis group, and causing in the lower animals elevated blood pressure, fibrillary contractions of the muscles, and systolic arrest of the heart. (*Cb. M. W.*, 1862.)

An exceedingly bitter arrow poison, used by the tribes who inhabit the country of Segon in the French Soudan, has been examined by Ferré and Busquet (*A. de P.*, 1895, vii), who find that its active principle is a crystalline glucoside which is a very powerful muscle poison, affecting directly the heart, and producing very rapidly general paralysis, with salivation, exophthalmia, disturbance of respiration and circulation. The first influence is to increase greatly the arterial pressure. The whole action of the poison is very similar to that of strophanthin. For an investigation of South African plants by Juritz, see *P. J.*, 1906, 87.

The Australian natives, according to Lewin, (*A. E. P. P.*, 1912, lxviii, p. 333), derive an arrow poison from the *Buphane disticha* Herb. (*Hæmanthus toxicarius* L.). He found in this an alkaloid to which he gave the name of *hæmanthine*. It somewhat resembles scopolamine in its action, being both a narcotic and mydriatic, and may be the same as that described by Tutin (*Tr. Chem. Soc.*, 1911, xcix) under the name of *buphanine*. Tutin also found several other alkaloids, one of which was identified as *narcissine*.

Animal Poisons.—The use of animal arrow poisons is uncommon, though the Choco Indians, in Columbia, South America, are said to prepare a very deadly extract by holding a tree-frog, the *Hyla chocœnsis*, on a stick near a fire, and scraping off the subsequent exudate from the skin. As it is asserted that an exudate can be obtained from the skin of the ordinary European toad which is a violent heart poison, the extract employed by the Choco Indians is probably a cardiac paralyzant. Again, according to Livingstone, confirmed by Baines, some of the Bushmen prepare a poison from a cream-colored grub or caterpillar, which they term *'Nga*, said to be the first stage of the beetle *Diamphidia locusta*. The grub is gradually squeezed between the forefinger and thumb, and the colorless exudate smeared over the arrowhead. Boehm and his pupil Starcke have found this poison to be similar in its action to the snake poisons, to be dependent for its activity upon a toxic albumose, and to be non-toxic when given by the mouth. As previously stated, it is also probable that snake venom is sometimes mixed with the various vegetable poisons used by barbarians.

Natives along the Amazon River obtain an arrow poison from the venom of a toad, the *Bufo agua*. This has been examined by Abel and Macht (*J. P. Ex. T.*, 1912, iii, p. 319) who found in it 5 per cent. of epinephrine, and a neutral principle to which they gave the name *bufagin*, and assigned the formula of $C_9H_{12}O_2$. It exercises a powerful digitalis-like effect, the fatal dose for the dog being seven-tenths of a milligramme per kilo.

Arsalyt.—*Bismethylaminotetraminoarsenobenzol Hydrochloride*, $As_2(C_6H_2.NH_2.NH_2.NH.CH_3)_2.4HCl$, a yellow, water-soluble powder containing 26.5 per cent. arsenic. It has been used in *syphilis* and *malaria* (*Pharm. Ztg.*, 1915, 180), but there are not yet sufficient reports to establish its value.

Arsacetin. *Sodium Acetyl Arsanilate*, $C_6H_4(NH.CH_3CO)(AsO.OH.ONa) + 4H_2O$.—This is a compound derived from sodium arsanilate by replacing a hydrogen atom of the amino group in sodium arsanilate, with an acetyl radical. It is a white, crystalline substance, odorless and tasteless, soluble to the extent of 10 per cent. in cold and 30 per cent. in warm water. It is free from arsenous or arsenic acid, and solutions are not affected by boiling. An hour's heating in the autoclave has no action on it. One part of arsacetin in ten of water and a few drops of silver nitrate solution added will produce a pure white precipitate. Its solution, clear and colorless, should show at most a faint acid reaction. Its capability of standing thorough sterilization gives it the advantage over compounds of the same nature—like sodium arsanilate, etc.

It has been used for the treatment of *syphilis*, and although some authors have reported favorably, the trend of opinion seems to be that it is inferior, in curative value, to mercury, and that there is danger of producing optic atrophy as is seen after atoxyl. It has also been used in the treatment of *trypanosomiasis* with more or less success, but is less efficient than atoxyl. Arsacetin has been used mostly in *doses* ranging from one-half up to one and a half grains (0.03–0.1 Gm.), although some authors have employed much larger quantities.

Arsenoferratin. *Sodii Arsenoferri Albuminas.*—This is an organic compound of albumen and arsenic with ferratin. A solution of a similar composition is on the market under the name of *arsenferratose*. The latter is a brownish liquid, contains 0.3 per cent. of iron and 0.003 per cent. of arsenic. The solid form of arsenoferratin is marketed in tablets of four grains (0.25 Gm.). They are used in the treatment of *anemias*. Of the solid form 3 to 6 tablets, each containing four grains (0.25 Gm.), may be given in twenty-four hours. Of the liquid arsenferratose the *dose* is one to two teaspoonfuls three times a day.

Arsenophenyl Glycin. *Spirarsyl.*—This combination has been employed especially in the treatment of *sleeping sickness.* Zupitza and Raben (*B. K. W.*, 1910) report favorably upon it, but Scherschmidt (*D. M. W.*, 1911) finds it inferior to atoxyl; it appears to be equally dangerous. The *dose* is from eight to fifteen grains (0.5–1 Gm.) daily, for two or three consecutive days, by intramuscular injection.

Artabotrys. *Artabotrys odoratissima* (Roxb.), R. Br. (Fam. *Anonaceæ*) and *Anona uncinata* Blanco. *Ilag-ilag de China*, Sp.-Fil. *Alag-ilag Sonson*, Tag.—A decoction of the leaves of these plants is used in the Philippine Islands in the treatment of *cholera*; the overdose is said to be capable of producing abortion.

Artar Root.—This is a drug coming from the west coast of Africa, possibly the product of *Fagara Xanthoxyloides* Lam. (Fam. *Rutaceæ*), the leaves of which have been found in commercial specimens. Two alkaloids have been discovered in it by Giacosa and Nionari, one of which is said to resemble somewhat in its action veratrine, but to be a stimulant to the heart. (*Ph. Centralh.*, 1887, No. xxv.)

Artemisia frigida. Willd. *Sierra Salvia. Colorado Mountain Sage.* (Fam. *Compositæ.*)—This Rocky Mountain plant, which is found growing in immense quantities from the Saskatchewan to Western Texas, and westward, is said to be much used in that region as a diaphoretic, antiperiodic, and mild cathartic. F. A. Weiss (*A. J. P.*, 1890) found indications of a glucoside. One or two drachms (3.9 or 7.7 Gm.) of the powdered leaves, or one or two fluidrachms (3.75 or 7.5 cc.) of the *fluidextract*, may be administered in hot infusion every half hour until perspiration has set in. *Artemisia nana* Gaud., one of the North American sage brushes, is reported to yield a volatile oil, which is rich in camphor. (*P. J.*, 1910, xxxiv, 237.)

Arterenol. *Homadrenine.—Aminoethanolpyrocatechin* is a reduction product of *aminoacetopyrocatechin.* Its hydrochloride, $(OH)_2.C_6H_3.CH\text{-}OH.CH_2.NH_2.HCl$, is crystalline and slightly soluble in water. Its therapeutic uses are analogous to those of epinephrine. It is incompatible with alkalies and with ferric chloride and should be kept away from light.

Arum.—The corm of *Arum maculatum* L. (Fam. *Araceæ*), is occasionally used as a medicine in Europe. Its properties closely resemble those of *Arisæma triphyllum.* Its constituents, according to Enz, are a neutral acrid volatile principle soluble in ether, starch, gum, mucilage, sugar, lignin, albumen, saponin, fixed oil, resin, and calcium phosphate, the fresh corm containing 58.4 per cent. of water, 5.2 of lignin, and 27.2 of starch. (*A. J. P.*, xxxi.)

Arisæma triphyllum (L.) Schott. *Gouet à trois feuilles*, Fr. *Dreiblättriger Aron*, G. (Fam. *Araceæ.*) *Dragon-root, Pepper Turnip, Indian Turnip, Jack-in-the-Pulpit, Wake-robin.*—This plant is common in all parts of the United States, growing in moist shady places. The corm was formerly official. It is roundish, flattened, an inch or two in diameter, covered with a brown, loose, wrinkled epidermis, and internally white, fleshy, and solid. In the recent state it has a peculiar odor, and is violently acrid. The acridity has been ascribed to the raphides of calcium oxalate by R. A. Weber (*J. Am. C. S.*, 1891, p. 215). This has been denied, Schneegans proving that *A. maculatum* contains saponin and Spica and Biscaro ascribe the acridity to the same principle. (*Ph. Centralh.*, 1895, p. 731.) The Indian turnip may be preserved fresh for a year, if buried in sand.

From both *Arum maculatum*, L., and *Arum italicum*, Mill., Herbert and Heim (*P. J.*, July 31, 1897) separated a saponin, also a brownish, oily, liquid alkaloid closely resembling coniine in its properties, but less active. They also found a saponin in the arum tubers.

Both the European and American arum are, in their fresh state, violent irritants to the mucous membranes, producing when chewed insupportable burning in the mouth and throat. Taken internally, this plant causes violent gastro-enteritis, which may end in death. The fresh, partially dried root has been used internally as a stimulant to the secretions, especially in *asthma, whooping cough, chronic catarrh,* and *rheumatism.* *Dose*, ten grains (0.65 Gm.), two or three times a day, increased to half a drachm (2 Gm.). The perfectly fresh root should not be used, and the fully dried root is inactive.

The corm of the European arum contains much starch, and a farina is prepared from it, in small quantities, in the Isle of Portland, on the south coast of England, and called *Portland arrow root*, or *Portland sago.* The root of *A. esculentum*, L. (more correctly *Colocasia antiquorum* Schott.), which abounds in starch, is much used by the natives of the Hawaiian and other islands of the Pacific, under the name of *taro*, as an article of food, having been previously deprived of its acridity by heat.

Asarabacca.—*Asarum europæum*, L., is an acrid, herbaceous perennial plant of the Fam. *Aristolochiaceæ*, growing in woods and shady places in Europe, Siberia and the Caucasus. The rhizome is from 2 to 3 inches in thickness, of a grayish color, quadrangular, knotted and twisted, and sometimes furnished with rootlets at each joint. It has an odor similar to that of pepper, and acrid taste, and affords a grayish powder. The leaves, which have long petioles, are kidney-shaped, entire, somewhat hairy, of a shining deep green color when fresh, nearly inodorous, with a taste slightly aromatic, bitter, acrid, and nauseous. According to Feneulle and Lassaigne, the *root* contains a concrete volatile oil (see *Asarum*), a very acrid fixed oil, a yellow substance analogous to *cystin*, starch, albumen, mucilage, citric acid, and saline matters. The root and leaves of asarabacca are powerfully emetic and cathartic, in *doses* of from thirty grains to a drachm (2.0–3.9 Gm.), but are used almost exclusively as an errhine in *headache*, and *rheumatic* affections of the face, mouth, and throat. One or two grains (0.065–0.13 Gm.), snuffed up the nostrils, produce much irritations, and a copious, persistent flow of mucus. For further information concerning this drug, see *U. S. D.*, 19th edition, p. 1400.

Asbestos.—This term is applied to several mineral substances which occur in long capillary crystals placed side by side, the whole producing a fibrous mass capable of being woven into fabrics and which possesses qualities that render asbestos very valuable in the arts. Asbestos is incombustible, insoluble, and a poor conductor of heat. It is either *hydrated magnesium silicate*, when it is known as *chrysotile*, or a compound of silicon, lime, and magnesium known as *amphibole* asbestos (for analysis, see *P. J.*, 1901, p.

575), and is found in Italy, in the Tyrol, Corsica, Savoy, in the Pyrenees, in Cornwall, Scotland, and is largely mined in Canada. For its general properties and uses, see *Ph. Rec.*, 1885, 232. In the laboratory it is used for filtering purposes, for which it is admirably adapted. It is also used as a non-conductor of heat in connection with various forms of apparatus. (See *A. J. P.*, 1883, 37; *Ph. Rund.*, 1885, 252.)

Asimina. *Asimina triloba* (L.) Dunal. (Fam. *Anonaceæ.*) *Papaw; American Papaw; Custard Apple.*—This small tree is found throughout the eastern central and southern United States as far west as Nebraska. It is chiefly notable for its edible fruit. This fruit has a very high nutritive value, weight for weight being approximately equivalent to the banana. Although there have been reported cases of mild poisoning from eating this fruit, Barbour (*J. A. M. A.*, Dec. 30, 1905) believes that these symptoms have been due to personal idiosyncrasies and not to any toxic principle in the fruit. In the fruit are imbedded a number of flat brown seeds. In these J. U. and C. G. Lloyd (*A. J. P.*, 1886) found an alkaloid, *asiminine*, which seems to have emetic properties. The bark was at one time used as a bitter. In it Fletcher could find no alkaloid but gives the principal constituents as fixed oil, 3.53 per cent.; resin, 3.43 per cent.; resin insoluble in ether, 9.5 per cent.; glucose and extractive, 8 per cent. (*A. J. P.*, 1891, 476.)

Asparagus. *Asparagus officinalis*, L. *Asperge*, Fr. *Spargel*, G. *Esparaguera*, Sp. (Fam. *Liliaceæ.*) —This well-known garden vegetable is a native of Europe. It is perennial and herbaceous. The root, which is inodorous, and of a slightly sweet taste, is used in France as a diuretic and aperient in the form of decoction, made in the proportion of one or two ounces of the root to a quart of water. Hayne asserts that, in the dried state, it is wholly inert. In the berries H. Reinsch has found a large proportion of glucose and a yellowish-red coloring matter, *spargin.* (*A. J. P.*, xlii, 371.) From the juice of the young shoots Robiquet and Vauquelin obtained a peculiar crystallizable principle, called asparagin, which has since been found in a number of plants. (See *Althæa.*)

There is at present no sufficient reason for believing that asparagus is of value in practical medicine. The peculiar heavy odor which it imparts to the urine has been the chief foundation for the belief in its diuretic properties; but Nencki (*Provincial Med. Journ.*, March, 1891) appears to have demonstrated that this odor is due to the presence in the urine of *methyl-mercaptan,* a gas which is frequently produced in minute quantities in the intestines by the decomposition of proteids. According to Justin D. Lyle (*N. Y. M. J.*, July, 1892), eating asparagus causes the urine to answer Trommer's, Fehling's, and Böttger's glycosuria tests, although sugar is not present. Tanret found two carbohydrates, *asparagose* and *pseudo-asparagose,* in the roots and green berries of asparagus. (*P. J. Tr.*, 1909, 205.) Certain physiologists have claimed that asparagin has an effect on metabolism, but this view is probably incorrect. (See *Z. B.*, 1892, x.) Asparagus may be administered internally in the form of the syrup produced from the fresh juice or from the tincture. For further information concerning Asparagus, see *U. S. D.*, 19th edition, p. 1401–1402.

Aspirophen. *Phenaspetin Phenocoll Acetyl-salicylate.*—Under this name has been introduced a mixture of thirty-seven parts of free salicylic acid with sixty-three parts monoacetylphenocoll. It is employed as an analgesic and antirheumatic. Fackelmann (*Th. M.*, July, 1907) asserts that it is less prone to produce cinchonism than other salicylates and is more potent in controlling pain and less likely to produce sweating than aspirin. The *dose* is from eight to fifteen grains (0.5–1 Gm.).

Asplenium. *Asplenium Filix-fœmina* (L.) Bern. *Female Fern.*—The rhizome of the female fern has been supposed to possess similar vermifuge properties to that of the male fern. At present, however, it is not used, except as an occasional substitute. The vulgar name of *female fern* is also given to the *Pteris aquilina*, or *common brake,* which is further said by some authors to have the property of destroying the *tape worm.* According to Greshoff it contains a cyanogetic glucoside. The leaves of two species of *Asplenium*, *A. Trichomanes*, L., or *common spleenwort,* and *A. Adiantum-nigrum*, L., or *black spleenwort,* are mucilaginous, and have been used as substitutes for *maidenhair* (*Adiantum Capillus-Veneris* L., and *A. pedatum* L.) as pectorals, though destitute of their aromatic flavor.

Aster. *Aster puniceus*, L. (Fam. *Compositæ.*) —The aromatic astringent rootlets of this indigenous plant have been employed as a stimulating diaphoretic in *rheumatic* and *catarrhal affections.*

Asteracantha. *Asteracantha longifolia* Nees. *Ik Kirit.* (Fam. *Acanthaceæ.*)—This Indian plant is said by A. Jayesingba to be an energetic hydragogue diuretic. (*Ph. Z. R.*, Sept., 1887.)

Astrolin. *Glycopyrin Methyl-ethyl-glycolic antipyrin.* $C_5H_{10}O_3.C_{11}H_{12}ON_2$.—This is a colorless, crystalline powder, with pleasantly acidulous and faintly bitter taste, soluble in water or alcohol. It melts at 64°–65° C. and represents 61.5 per cent. of antipyrin, for which drug it is proposed as a substitute: Winzheimer finds it without deleterious influence upon the lower animals. It is suggested for the treatment of *neuralgic headaches* in *doses* of fifteen grains (1 Gm.).

Asurol. *Hydurol.*—This is asserted to be a double salt of mercuric salicylate and amido-oxy-isobutyric sodium, containing 40.3 per cent. of mercury. It is readily soluble in water. This preparation has been recommended for the hypodermic injection of mercury, especially in the treatment of *syphilis.* According to Neisser (*Th. M.*, 1909, p. 627), however, while it is rapid in its effects, it is not of itself sufficient for the cure of syphilis and should therefore be used in conjunction with some other form of mercurial treatment. The solutions should always be made with boiled distilled water, as the drug is incompatible with both carbonic acid and sodium chloride. It should be freshly prepared because on long standing a turbidity occurs, probably through the action of the carbonic acid of the air. The beginning *dose* is sixteen minims (1 cc.) of a 5 per cent. solution, which would represent one-third of a grain (0.02 Gm.) of mercury.

Atherosperma. *Atherosperma moschatum* Labill. *Australian Sassafras.* (Fam. *Monimiaceæ.*) —The bark of this tree, a native of Southern Australia, is said to have been long used by the aborigines, and later by the settlers, in *rheumatism* and in secondary *syphilis,* and has been highly commended by Greeves (*L. L.*, 1862) in acute *bronchitis.* It has been stated that both the bark and the volatile oil are powerful poisons, and Zeyer (*Vierteljahrschr. f. Pract. Pharm.*, x, 504) obtained from the drug an alkaloid, *atherospermine* ($C_{30}H_{40}O_5N_2$); see also Wittstein's *Organic Constituents of Plants*, 20. The abundant volatile oil is light yellow, and has a pleasant aromatic odor and taste, resembling those of oil of sassafras. Scott obtained from the leaves 1.7 to 2.65 per cent. of volatile oil. (*J. Chem. S.*, 101, 1912, 1612.) Ralph Stockman (*Lab. Rep. Royal Coll. Phys.*, vi, 1897) found it to resemble in its physiological action oil of sassafras and other allied volatile oils. He took repeatedly ten minims (0.6 cc.) without any pronounced effect, and one fluidrachm (3.75 cc.) given to a rabbit caused only temporary stupor, with slowing of the respiration, but not of the pulse. Three fluidrachms (11.25 cc.) caused in the rabbit marked depression of the heart and of the respiration, coma, and death in twelve hours by asphyxia.

Atoquinol. *Allyl-phenyl-cinchonine.*—This ester of phenylcinchoninic acid occurs as odorless, yellowish crystals, insoluble in water, sparingly soluble in alcohol but readily in ether and other fixed oils, with a melting point of 30° C. It appears to possess the characteristic anodyne and eliminant powers of phenylcinchoninic acid and has been used in the treatment of *rheumatism, gout, neuralgia*, etc., in doses of 0.5 to 1 Gm. (8 to 15 grains).

Atoxyl. *Sodium Arsanilate. Sodium p-aminophenylarsonate-arsamin.* $C_6H_4NH_2.(AsO.OH.ONa) + 3H_2O$.—When atoxyl was first introduced into medicine it was supposed to be *metaarsenic anilide* ($C_6H_5NHAsO_2$), but more recent studies have shown it to be sodium arsanilate. It is a white powder soluble in cold water and still more so in warm water. It has a slightly saline taste. On standing the aqueous solution assumes a yellowish tint. It contains 26 per cent. of arsenic.

There is upon the market under the name of *soamin* a substance which appears to be of precisely the same composition as atoxyl, with the exception that it contains five molecules of water instead of three. It therefore contains only 22.8 per cent. of arsenic. The physiological and therapeutic properties of these two substances are the same.

While originally introduced as a means of producing the therapeutic action of arsenic without the toxic disadvantages of that drug, atoxyl owes its notoriety to the results achieved with it by Koch in the treatment of *sleeping sickness* (*D. M. W.*, 1907, p. 200). In this highly fatal disease Koch found that the use of the drug, even in fairly advanced stages, would cause the blood to become free from trypanosomes at least temporarily. Most of the cases, however, eventually relapsed and died of the disease. When the drug was used boldly in the milder cases of the infection, occasionally a permanent cure would result. From the beneficial effects which were produced in *trypanosomiasis*, several clinicians were led to test its efficacy against the biologically allied parasite which is regarded as the causative agent of *syphilis.* While the results in the latter infection were not altogether brilliant, the preparation showed itself to exercise a distinctly toxic action upon the spirochætæ. Blumenthal (*Med. Klin.*, 1907, p. 319) and others have reported more or less favorable results from the internal administration of the drug in *cancers.* It has also been employed against *relapsing fever, malaria, pellagra, leukemia* and *frambesia* with more or less evidence of good effects.

These striking results in some of the most hopeless diseases seemed to foretell for the remedy a most important place among our therapeutic agents. Unfortunately, however, wider experience with the drug showed that it was by no means the innocent remedy which had first been believed. Although the single dose is far less toxic than an equivalent amount of arsenic, when used over long periods of time it produces degenerative changes in various portions of the central nervous system in a large proportion of cases. Igersheimer (*D. M. W.*, 1909, xxv, p. 1142) reports forty-six cases of permanent blindness due to atrophy of the optic nerve following the use of atoxyl. He has also noted in the lower animals histological changes in the brain and in the spinal cord. Schlect (*M. M. W.*, 1909, lvi, p. 971) records fatal results from four injections given on alternate days of 0.6 Gm. each. After death there was found degeneration in the internal organs such as are commonly seen after arsenical poisoning. The number of cases of blindness and even death have been so large that it would seem that the therapeutic use of the drug is scarcely justifiable except in such hopeless infections as the *sleeping sickness.* Bertrand asserts that atoxyl solutions when sterilized by heating at 120° are decomposed into sodium arsenate and aniline and therefore, sterile solutions should be prepared either by tyndalizing or filtering through a suitable clay filter. M. François examined several samples of atoxyl, which had been kept in the tropics for three to four years. Although the appearance of the product was little changed, on mixing with 10 parts of water (atoxyl is soluble in 6 parts) an opaque liquid was obtained from which a white, amorphous precipitate separated, suggesting a decomposition, into arsenous acid and sodium arsenate. Since arsenous acid is considerably more toxic than atoxyl, care should be taken in administering atoxyl which has been kept at high temperatures for any length of time. (*Pharm. Weekblad*, 1918, lv, 1472.)

It has usually been administered hypodermically in *doses* of from one to three grains (0.06–0.2 Gm.), once every other day.

Atropine Salicylate.—This salt is alleged to have advantages over the sulphate, mainly because of its more rapid and efficient action, provided it be pure and perfectly neutral. It may be prepared by Frederici's process, which is to dissolve 23 parts of atropine in pure alcohol by a gentle heat, and to add enough salicylic acid (about 18 parts) to render the solution neutral, which is determined by the use of litmus paper. The solution is carefully evaporated, and finally dried in a drying oven. It is deliquescent, and should be kept in securely stoppered vials. The *dose* is the same as that of the sulphate.

Atropine Sulphuric Acid.—This organic compound of atropine with sulphuric anhydride occurs in colorless crystals sparingly soluble in water, insoluble in most of the organic solvents, but dissolving readily in ammoniacal solutions. It has been recommended by Phillippstal (*B. K. W.*, 1913) in the treatment of *asthma* and *night sweats.* He claims that it has the advantage over atropine that it does not cause drying of the throat nor tachycardia. The *dose* he employed was one sixty-fourth of a grain (0.001 Gm.).

Azadirachta. *Azedarach, U. S.* 1860. *Pride of*

India. Pride of China. Indian Lilac Tree. Ecorce de Margousier, Fr. *Zedrachrinde,* G.—The U. S. P. formerly recognized the bark of the root of *Melia Azedarach* L. (Fam. *Meliaceæ*), a beautiful tree, thirty or forty feet high, with a trunk fifteen or twenty inches in diameter. This species of *Melia* is a native of Syria, Persia, and the north of India, and is widely cultivated. It is abundant in our southern states; north of Virginia it does not flourish. "The bark [root] is in curved pieces or quills of variable size and thickness; outer surface red-brown, with irregular, blackish, longitudinal ridges; inner surface whitish or brownish, longitudinally striate; fracture more or less fibrous; upon transverse section tangentially striate, with yellowish bast fibers; inodorous, sweetish, afterwards bitter and nauseous. If collected from old roots, the bark should be freed from the thick, rust-brown, nearly tasteless, corky layer." *U. S.*, 1880. The Br. Add. recognized under the name *Azadirachta indica* (*Neem Bark, Margosa Bark*) the bark of the stem of *Melia Azadirachta* L., or *Indian Lilac Tree.*—This contains, according to Broughton (*P. J.*, 1873, 992), a bitter amorphous resin, and a crystallizable principle, melting at 175° C. (See also *Ph. Rev.*, 1896, 231.) Cornish (*Ind. Ann. Med. Sci.*, 4, 104) had previously announced the presence of a bitter alkaloid, to which he gave the name *margosine.* It is asserted to possess antiperiodic virtues (*C. D.*, 1919, xci, 551). The bark of the trunk is "externally of a rusty-gray color, internally yellowish, and much foliated; coarsely fibrous; inodorous, bitter and slightly astringent, structure and thickness varying according to age." *Br. Add.* (For a description of the leaves and root bark, see *Ph. Rev.*, 1896, p. 231.)

Oil of Azederach is found of two kinds in Eastern Asia where it is used. One is employed for burning, the other medicinally. The latter oil, according to Lewkowitch (*Oils, Fats, Waxes,* vol. ii, p. 426), is known as *Veepa Oil, Veppam Fat* and *Neem Oil,* and has a specific gravity of 0.914, a saponification value of 196.9, and iodine value of 69.6, a Reichert-Meissel value of 1.1 and a butyro-refractometer reading of 52° at 25° C.

The decoction of azedarach is affirmed to be cathartic and emetic, and in large doses narcotic; but in a number of experiments made by H. C. Wood with extracts from the dried bark and fruit, it was found impossible to poison frogs or rabbits. Robins eating of the sweetish fruit, of which they are very fond, are often rendered so far insensible as to be picked up under the tree; though they usually recover in a few hours. Children are said to eat the fruit without inconvenience, and possibly the robins simply choke themselves with the large berries. The bark is considered, in the Southern States, an efficient anthelmintic. The form of decoction is usually preferred. A quart of water is boiled with four ounces of the fresh bark to a pint, of which the *dose* for a child is a tablespoonful every two or three hours, until it affects the stomach or bowels. Another plan is to give a dose morning and evening for several successive days, and then to administer an active cathartic. The fresh bark and the fruit are said to be superior as vermifuges. The Br. Add. recognized an *infusion* (*Infusum Azadirachtæ Indicæ,* Br. Add.), eighty-eight grains in a pint of cold water, *dose,* one-half to one fluidounce (15–30 cc.); also a *tincture* (*Tinctura Azadirachtæ Indicæ,* Br. Add.), two ounces in a pint of 45 per cent. alcohol, *dose,* one-half to one fluidrachm (1.8–3.75 cc.).

Baccharis. *Baccharis cordifolia* DC. *Mio Mio.*—This composite plant of Southeastern South America is notorious for its deadly effect upon sheep and cattle. Pedro N. Arata has isolated from it an alkaloid *baccharine.* (*P. J.*, x, 6.)

Balanites. *Agialida. Balanites Roxburghii* Planch. (Fam. *Zygophyllaceæ.*)—The fruit of this plant is used medicinally in India. It contains a principle closely resembling saponin. The ripe seed yield about 50 per cent. of a fixed oil (*zachun oil*), which is used for burning. (See *P. J.*, 1913, 905.) The unripe fruit is anthelmintic and purgative.

Balata. *Gum Chicle. Chicle. Tuno Gum. Leche de Popa,* Fr. *Zapota Gum.*—The term "chicle" has been applied to the dried milky juice from two distinct but related trees of the Fam. *Sapotaceæ.* The first of these, known also as *balata,* is the product of *Mimusops globosa* Gaertn., a native of the West Indies, Mexico and Central America. The crude article is solid and somewhat crumbly, of a grayish-white color with reddish-brown spots and veins; the purified article is an amorphous powder. It is an oxidized hydrocarbon, both physically and chemically related to caoutchouc and gutta percha; specific gravity 1.05; tasteless, but emitting a disagreeable odor when warmed. It has the general properties of gutta percha and Mexican chicle, being but slightly extensible, a property which fits it for use in the manufacture of chewing gum. While solid and somewhat crumbly at ordinary temperatures, it softens at 49° C. and can be molded; it is readily soluble in ether, petroleum benzine, carbon disulphide, kerosene and benzol but only slightly soluble in chloroform.

Balata is imported from Mexico, Central America and Africa in the crude form. It is the kind of chicle now most extensively used in the manufacture of the cheaper or "bubble balloon chewing gums." Balata is also used in the manufacture of transmission belts.

The second variety of chicle is that known in commerce as *Mexican Chicle* and represents the dried latex of *Achras Sapota* L. This tree, known also as the *sapodilla* or *sapota plum,* bears a sweet fruit whose flavor resembles that of the quince and is eaten by the natives of tropical America. *Mexican chicle,* also known as *loaf chicle,* occurs in irregular pinkish to reddish-brown pieces to which there is usually found adhering a considerable amount of bark and the bodies of insects. It comes entirely from Mexico. On account of the high cost of this variety of chicle, it is only used at present in the manufacture of the more expensive medicated chewing gums. For this purpose it is first purified by the following method: It is broken up into small pieces which are placed in a revolving screen-drum and washed in strong sodium hydroxide solution to remove extraneous matters. The drum and contents are then lifted out of the revolving machine and placed in a bath of sodium acid phosphate to neutralize the alkalinity.

The material is then washed with water until free from soluble salts, dried and powdered. Purified Mexican chicle occurs as an amorphous, pale pink powder, insoluble in water and the ordinary solvents, soluble in the same solvents as balata. When heated it forms a tenacious mass, which upon cooling is pink in color. On aging, it undergoes partial oxidation, becoming yellowish-brown to brown and very brittle.

Chewing gums averagely contain only about 30 to 35 per cent. of chicle, the other substances present consisting of glucose, powdered sugar, starch and flavoring. The chemical constituents of chicle have been investigated by Tschirch and Scherescheweki who found so-called resins, two of them being crystallizable *a-balaban-* and *b-balaban* and a yellow substance, *balafluavil.* (*A. Pharm.*, 1905, ccxliii, 358; see also Bosz and Cohen's investigations, *A. Pharm.*, 1912, ccl, 52; also *P. J. Tr.*, 1910, 609.) Formerly the chicles were adulterated with paraffin wax but they are now adulterated with sticks, stones and bark. The extraneous matter in Mexican chicle varies from 25 to 40 per cent.

Balsam of Gilead. *Balm of Gilead. Mecca Balsam. Balsamum Meccæ v. Judiacum. Balsamum Gileadense. Baume de la Mecque*, Fr.—The genuine balm of Gilead is the resinous juice of *Commiphora Opobalsamum* (L.) Engl. (Fam. *Burseraceæ*), a small evergreen tree, growing on the Asiatic and African shores of the Red Sea. It was in high repute with the ancients, and is still esteemed by the Eastern nations as a medicine and cosmetic. In Western Europe and in this country it is seldom found in a state of purity, and its use has been entirely abandoned. It is described as a turbid, whitish, thick, gray, odorous liquid, becoming solid by exposure. It possesses no medicinal properties not existing in other balsamic or terebinthinate juices. It was formerly known as *opobalsamum*, while the dried twigs of the tree were called *xylobalsamum*, and the dried fruit, *carpobalsamum.* In this country *Poplar buds* are often, incorrectly, called Balm of Gilead Buds.

Balsam of Cativo. *Cativo Balsam.*—This substance appeared in the London market in 1902 as a substitute for copaiba. It is a balsamic resin, opaque, of a dirty light brown color and slightly bitter taste, and having an extremely adhesive quality. According to Umney, it is not soluble in 90 per cent. alcohol, but is soluble in ether and consists chiefly of acid resins with the addition of an oily substance. According to Weigel's analysis it consists of 80 per cent. of resin acids and 2 per cent. of volatile oil. It is supposed to be a product of *Prioria copaifera* Gris. (Fam. *Leguminosæ*), a large tree indigenous to Panama and Jamaica. (See *P. J.*, vol. lxix; and *Ph. Centralh.*, March, 1903.)

Balsam of Cebur or Tagulaway.—*Cebur* or *Tagulaway Balsam* is prepared in the Philippine Islands by boiling the root and twigs of *Parameria vulneraria* Radl. (Fam. *Apocynaceæ*), in cocoanut oil, so as to form a yellowish-white, oily liquid, which is used with asserted excellent results for *skin diseases* and *wounds.* (*A. Pharm.*, Nov., 1885.)

Balsam of Lagam. *Lagam Balsam.*—A thick, yellowish, fluorescent liquid, of a peculiar aromatic odor, and bitterish, acrid taste, resembling copaiba. (*A. J. P.*, 1883, p. 368.)

Balsam of Riga. *Riga Balsam. Balsamum Carpaticum. Balsamum Libam.*—This is the product of *Pinus Cembra*, L. (Fam. *Pinaceæ*), a large tree growing in the mountainous regions and northern latitudes of Europe and Siberia. The juice exudes from the extremities of the young twigs, and is collected in flasks suspended from them. It is a thin, white fluid, having an odor analogous to that of the juniper, and possessing the ordinary terebinthinate properties. In this country it is very rare; but it is occasionally brought from Riga or Kronstadt in bottles. Keller, of Darmstadt, affirms that Riga Balsam is the product of the ordinary *Pinus palustris* Mill. A similar product, called *Hungarian balsam*, is obtained in the same manner from *Pinus Pumilio* Haenke, growing on the mountains of Switzerland, Austria and Hungary.

Balsam of St. Thome. *Pan Olœo. Belam Pu.*—A balsam obtained from *Santiriopsis balsamifera* (Oliv.) Engl. (Fam. *Burseraceæ*). It is a resinous juice obtained by incisions in the trunk of the tree. It is used as a vulnerary and in diseases of the bladder and bronchi. (*Ap. Ztg.*, 1898.)

Balsam of Sulphur. *Sulphurated Oil of Linseed. Thiolinic Acid. Oleum lini sulfuratum.*—A preparation made by boiling sulphur in linseed oil. A similar preparation made from olive oil and sulphur was known in the old Edinburgh Pharmacopœia as *Oleum Sulphuratum.* It was an extremely fetid, acrid, viscid, reddish-brown fluid, which was formerly used in *pectoral complaints;* but inconvenience arose from its acrid properties, and its internal use was abandoned. It is sometimes applied as a stimulant to *foul ulcers. Haarlem Oil* is a mixture of oil of turpentine with balsam of sulphur. The *dose* is from five to thirty minims (0.3–1.8 cc.).

Balsam Wood. *Palo Balsamo.*—This is a South American wood, derived from an unknown tree, which is believed to contain *guaiacin*, and which yields to distillation nearly six parts of a thick viscous aromatic oil. This contains as its chief constituent a crystalline solid of alcoholic character, melting at 91° C. and corresponding closely to the formula $C_{14}H_{24}O$. It has found employment in perfumery. (*Schim. Rep.*, April and Oct., 1892.)

Balsamorrhiza. *Balsamorrhiza terebinthinacea* Nutt. (Fam. *Compositæ.*)—The root of this plant, obtained from Idaho and Oregon, has a strong, terebinthinate odor, and is used medicinally in the Western States. It contains volatile oil, fixed oil, resin, organic acid, and sugar (Herman T. Kelly, *D. C.*, 1897, 32).

Barbados Nuts. *Purging Nuts. Physic Nuts. Semen Ricini Majoris. Pignon d'Inde* (*des Barbades*), *Semences du Médicinier*, Fr. *Purgirnuss, Schwarze Brechnuss*, G.—These are the seeds of *Jatropha Curcas*, L. (*Curcas purgans*, Adonson) (Fam. *Euphorbiaceæ*), growing in Brazil, the West Indies, and cultivated extensively in all tropical countries. The fruit is a three-locular capsule, containing one seed in each locule, and is about the size of a walnut. The seeds are blackish, oval, 1.5 to 2 cm. long, flat on one side, convex on the other, and the two sides present a slight longitudinal prominence. They yield a fixed oil, an acrid resin, sugar, gum, a fatty acid, glutin, a free acid, and salts. A. Siegel (*Bot. Centralb.*, xlvii, 120) found in the seeds a poisonous principle, *curcin*, which he states is analogous to *ricin*, and places in the class of toxalbumins. The oil, sometimes called *jatropha oil*, may be separated by hot expression, the yield being about 40 per cent. When fresh it is without odor or color, but becomes yellowish and slightly odorous by times. Alcohol does not readily dissolve it. It is colorless, odorless, of sp. gr. 0.91 at 19° C., solidifies to buttery consistence at –8° C. Bouis believed it to be the glyceride of a peculiar acid, *isocetic acid*, but it is now considered to be a mixture of palmitin and myristin. From three to five of the *seeds*, slightly roasted and deprived of their envelopes, operate actively as a cathartic, and not infrequently produce nausea and vomiting, with a sense of burning in the stomach. The *oil* purges in the *dose* of five to ten minims (0.3–0.6 cc.), and is analogous in its action to croton oil, though less powerful. The cake left after the expression of the oil is an acrid emeto-cathartic, operating in the *dose* of a few grains. Either of these substances may produce serious consequences in overdoses. The leaves of the plants are rubifacient, and the juice is said to have been usefully employed as a local remedy in *piles*. (*A. J. P.*, 1893, 335.) The seeds of *Curcas multifidus* (L.) Engl. (*Jatropha multifida* Linn.) have similar properties, and yield a similar oil. This species also grows in Brazil and the West Indies. (See Peckoldt, *A. Pharm.*, 1887, 415.)

Jatropha macrorhiza Benth. popularly called *Jicama*, a shrub which grows in Northern Mexico and the adjoining United States, is a purgative, acting excessively in overdose, and is believed by the Mexicans to be cholagogue. The *dose* of the fluidextract is stated to be from one-half to two fluidrachms (1.8–7.5 cc.).

J. gossypifolia Linn., of South America, is used as a local application in *leprosy* and to indolent *ulcers*, and probably has similar physiological influence to curcas. *J. urens*, L., must be excessively poisonous, as accidental contact of the wrist of a gardener in Kew with a young plant produced such symptoms that for five minutes the man was thought to be dead. (*P. J.*, April, 1872, 863.)

The roots of the *J. cardiophylla* Muell. Arg. are largely employed in Southern Arizona and Mexico for tanning purposes. According to the analysis of Josiah C. Peacock, they contain, when thoroughly dried, over 5 per cent. of tannic acid. (*A. J. P.*, 1900, 432.)

Barium. *Baryum*, Fr., G. $Ba = 137.37$.—This is the metal present in *baryta*. It was first obtained in 1808 by Sir H. Davy, who described it as a difficultly fusible metal, of a silvery-gray color, decomposing water readily; melting point 850° C., specific gravity 3.75. When exposed to the air, it instantly becomes covered with a crust of barium oxide. Barium chloride, barium dioxide, and barium carbonate were formerly official.

Barium Carbonate. $BaCO_3 = 197.37$.—It is the native carbonate, a rare mineral, discovered in 1783 by Withering, in honor of whom it is called *witherite*. It is found in Sweden and Scotland, but most abundantly in the lead mines of Northern England. It occurs usually in grayish or pale yellowish-gray, fibrous masses, but sometimes crystallized. Its sp. gr. varies from 4.2 to 4.4. It is generally translucent, but sometimes opaque. It effervesces with acids, and, before the blow-pipe, melts into a white enamel without losing its carbon dioxide. It is distinguished from strontium carbonate, with which it is most liable to be confounded, by its greater specific gravity, and by its yielding a light greenish tint, instead of red, to the colorless flame. It is used only as a source of barium chloride whose toxic powers it possesses.

Barium Chloride. *Barii Chloridum. U. S.* 1870. *Chlorure de Baryum*, Fr. *Chlorbarium, Chlorbaryum*, G. $BaCl_2 2H_2O$.—For the method of preparing this salt, see *U. S. D.*, 19th, ed., p. 1407 (see also *Reagents*, Part III).

Barium chloride is a permanent white salt, possessing a bitter and disagreeable taste. It crystallizes in rhombic tables with bevelled edges. It dissolves in about two and a half times its weight of cold water, and in a little more than its own weight at 106° C., the boiling point of a saturated solution. It is scarcely soluble in absolute alcohol, but dissolves in rectified spirit. Alcohol impregnated with it burns with a greenish flame. If strontium be present, an alcoholic solution of the salt will burn with a red flame. When exposed to heat, it decrepitates and loses its water of crystallization, and at a red heat fuses. It is decomposed by the sulphates, oxalates and tartrates, and the alkaline phosphates, borates, and carbonates; also by silver nitrate, mercur*ous* salts, and lead acetate. When pure it does not deliquesce. Its solution is not affected by ammonia nor by hydrogen sulphide. Tannic acid will precipitate the barium from a solution of its chloride, as tannate.

Barium chloride is actively poisonous, causing when given in sufficient doses convulsions, dilatation of the pupil, and death from respiratory failure. (For report of fatal cases see Aloy and Cournet, *J. P. C.*, 1918, xvii, 76). According to Laborde (*B. A. M.*, July, 1891), after death the blood remains of a bright red color. In smaller doses it exercises a stimulant effect upon various muscular tissues. Through its action upon the intestinal muscle it gives rise first to diarrhea and later to cramp-like spasm of both gastric and intestinal muscle. Upon the voluntary muscle it exercises an effect like that of veratrine, causing marked prolongation of the contraction; after death from barium poisoning, fibrillary contractions of the voluntary muscles may continue for a considerable period of time. It stimulates both the vascular and cardiac muscles and in sufficient dose throws the heart into permanent contraction like that produced by digitalis. In moderate dose the pulse rate is increased and the blood pressure greatly elevated. Because of its action upon the circulation it has been suggested as a cardiac stimulant in cases of *heart failure*. According to Lauder Brunton (*Practitioner*, June, 1889), the chloride is a rapidly acting heart stimulant steadying the rhythm and increasing the volume and force of the cardiac contractions. Filippi (*Lo Sperimentali*, 1907), however, asserts that the drug has such a profound influence upon metabolism that it is not suitable for medicinal purposes. It has also been used in veterinary medicine in the treatment of wind colic. A solution of barium chloride was formerly official (*Liquor Barii Chloridi, U. S.*, 1870) which contained 1 troy ounce of barium chloride in three fluidounces of water. The dose of this solution is three minims (0.2 cc.). The *dose* of barium chloride is one-half to one and a half grains (0.3–0.1 Gm.).

Barium Dioxide. *Barii Dioxidum. U. S.*, 1890. *Barium Peroxide.* $BaO_2 = 169.37$.—"Commercial, anhydrous barium dioxide. It should be kept in well-closed vessels." *U. S.*, 1890.

It is used chiefly for making hydrogen dioxide. Barium forms two oxides, BaO and BaO_2; the former is produced by the action of oxygen or dry air on barium. Barium dioxide, BaO_2, is made by heating barium oxide to about 450° C., when it takes up another atom of oxygen. It is "a heavy grayish-white or pale yellowish-white, amorphous, coarse powder, odorless and tasteless. When exposed to the air, it slowly attracts moisture and carbon dioxide, and is gradually decomposed. It is almost insoluble in cold water, with which, however, it forms a definite hydrate, and to which it imparts a decidely alkaline reaction. Hydrochloric, phosphoric, and most other mineral acids decompose it, producing the corresponding barium salts, and hydrogen dioxide, which remains in solution for a considerable time, if the reaction has taken place in the cold, and an excess of the acid is present. When heated to a bright red heat, barium dioxide fuses, loses oxygen, and is reduced to barium oxide. Barium dioxide should be dissolved by diluted hydrochloric or phosphoric acid without leaving more than a trace of residue. It should contain at least 80 per cent. BaO_2. It is not used medicinally.

Barium Iodide. *Barii Iodidum. Iodure de Baryum*, Fr. *Jodbarium*, G. BaI_2.—This compound may be formed by double decomposition, by adding native barium carbonate in powder to a boiling solution of ferrous iodide. M. Henry, Jr., obtained it by decomposing a solution of barium sulphide with a concentrated alcoholic solution of iodine, filtering and rapidly evaporating the filtrate to dryness. Barium iodide crystallizes in small, colorless needles, which deliquesce slightly, and are very soluble in water. The solution promptly undergoes decomposition on exposure to the air, barium carbonate being precipitated, and iodine set free, which colors the solution. It has been used by John and Lugol, as an alterative, in *scrofulous affections* and morbid growths. The *dose* is an eighth of a grain (0.008 Gm.) three times a day, gradually increased to three grains (0.2 Gm.).

Barium Oxide or *Baryta* ($BaO = 153.37$) may be obtained from the native carbonate by intense ignition with carbonaceous matter, or from the native sulphate by ignition with charcoal, which converts it into barium sulphide, subsequent solution of the sulphide in nitric acid and strong ignition of the nitrate formed, to dissipate the acid. As thus obtained, it is an anhydrous solid, caustic, alkaline, difficultly fusible, and of a grayish-white color. Recently it has been obtained at Niagara Falls by a reaction in which, at the temperature of the electric arc, a small amount of the sulphide obtained by the reducing action of charcoal is made to react with an excess of unchanged sulphate; $3BaSO_4 + BaS = 4BaO + 4SO_2$.

Its sp. gr. is about 4. When sprinkled with water it slakes like lime, becomes hot, and is reduced to the state of a white pulverulent hydroxide. The same hydroxide is formed in mass when the anhydrous earth is made into a paste with water and exposed to a red heat in a platinum crucible. The excess of water is expelled, and the hydroxide undergoing fusion, may be poured out and allowed to congeal. Barium hydroxide dissolves in water, and forms the reagent called *baryta water*. A boiling saturated solution, as it cools, yields crystals of barium hydroxide containing eight molecules of water of crystallization.

When barium oxide is heated in a current of oxygen or air, it takes up an atom of oxygen and is changed into barium dioxide, BaO_2. When this is heated somewhat higher, it gives off the extra atom of oxygen and becomes BaO again. This power of taking up oxygen from the air and giving it up at a somewhat higher heat is now utilized on a commercial scale in the Brin process for making oxygen, and it is found that this change from BaO to BaO_2 and back again can be effected at one and the same temperature by simply heating first under pressure and then by exhausting and reducing below the normal atmospheric pressure. Barium dioxide is also of importance as the material from which hydrogen dioxide, H_2O_2, is made.

It is poisonous both because of its systemic and its local caustic action.

Barium Sulphide. *Barium Sulphidum.*—An impure form of barium sulphide is found in commerce, containing about 50 per cent. BaS_2. It is used extensively in combination with starch, powdered orris root and other diluents in depilatory mixtures. As it is sometimes abbreviated "Bar. Sulph.," the same as is applied to Barium Sulphate used in X-ray work (which see), care must be taken in dispensing it, as it has on several occasions caused death when taken internally by mistake for barium sulphate. The symptoms of poisoning by barium sulphide are practically the same as those of the chloride (See *Barium Chloride*).

Barringtonia. *Barringtonia speciosa.*—The large Indo-Malayan tree, *Barringtonia speciosa* Forst. (Fam. *Myrtaceæ*) contains, according to Maresuw, 3.3 per cent. of *barringtonin*, a colorless, amorphous glucoside, having the formula $C_{18}H_{28}O_{10}$, and belonging to the saponin group. It is said to be an active cardiac poison. (*S. W. P.*, xli, 1903, pp. 423, 435.)

Basicin. *Corticin.*—This preparation is a compound of quinine hydrochloride and caffeine. The two substances are dissolved in water. The solution is then evaporated to a high concentration and allowed to crystallize. It is employed intravenously for *malaria*, internally for *migraine, neuralgia, influenza* and similar ailments. The *dose* is three to eight grains (0.2–0.5 Gm.).

Bassia latifolia Roxb. (Fam. *Sapotaceæ*) *Mahua, Illipi Butter Tree.*—A large, deciduous tree indigenous to the forests of the central provinces of India. It possesses elliptical or oblong-elliptical leaves, bell-shaped, cream-colored flowers and reddish-yellow or orange-colored, fleshy fruits, one to two inches in length; each containing one to four seeds. Several parts of this plant have been employed in medicine and in the arts. The bark is used as an astringent and tonic and also in tanning as well as an adjunct in dyeing, where dark colors are desired. The succulent corollas of the flowers constitute a well-known Indian food. A decoction of the flowers is employed in the treatment of coughs. An infusion of the flowers is given with sugar, for the relief of thirst, and giddiness.

The greenish-yellow oil expressed from the seeds (*mahwah oil*) is used by the hill tribes in the treatment of skin diseases as well as in the manufacture of candles and soap. The cake left after the expression of the oil is employed as an emetic and detergent.

In the *B. longifolia* L., known as *mowrah* by the natives, there has been found a glucoside which was named *mowrin* by its discoverers, Moore, Baker, Young and Sawton. According to these investigators, mowrin has a digitalis-like action upon the heart and a saponin-like effect of destroying red blood cells.

Spiegel and Meyer find that crude *mowrin* is a mixture of 2 substances, the main, $C_{42}H_{68}O_{25}$, being more soluble in alcohol and yielding upon hydrolysis levulose, arabinose and *mowric* acid. This acid is also a mixture of a crystalline *mowragenic* acid, $C_{19}H_{28}O_5$, and an amorphous mowrageninic acid, $C_{19}H_{30}O_6$. Careful hydrolysis with dilute acetic acid yielded an intermediate pentoside, $C_{29}H_{50}O_{16}$ (*B. P. G.*, 1918, xxviii, 100).

The seeds are also locally known as Illipi, Illipei or Illupi nuts—they also yield about 50 per cent. of a solid fat suitable for candle making and sometimes used for food purposes.

Bassora Gum. *Karaya Gum. Caramania Gum. Hog Gum. Indian Gum. False Tragacanth. Kuteera Gum.*—Bassora gum is a collective term used to indicate a group of high-colored gums somewhat resembling tragacanth. A gum of this class came into commerce originally from the neighborhood of Bassora, on the Gulf of Persia. The soluble portion is *arabin*, and, according to Guérin constitutes 11.2 per cent. The insoluble portion consists of *bassorin*, associated with a small proportion of saline substances, which yield, when the gum is burnt, 5.6 per cent. of ash.

The two chief Bassora gums in commerce today represent pale-colored representatives of the class and are most commonly known as *Indian Gum* and *Gum Kuteera*, respectively. *Indian Gum* is yielded by *Cochlospermum gossypium* DC. (Fam. *Bixaceæ*), a tree indigenous to southern Asia and thriving in India and adjacent countries. It occurs in inodorous rounded or vermiform tears with a rough surface and glassy fracture. If 1 Gm. of this gum be added to 50 cc. of water, an uneven mucilage forms which contains a few reddish-brown to yellowish-brown fragments. Upon stirring the mucilage separates in the form of coarse, uneven strings (distinction from Tragacanth). *Gum Kuteera* is obtained from *Sterculia urens* Roxb. (Fam. *Sterculiaceæ*), a tree indigenous to southern Asia and abundantly found in sub-Himalayan tracts from the Ganges eastward and in Persia. It occurs in inodorous yellowish-brown tears or irregular masses and swells with water. This gum has recently been found admixed with tragacanth and has not been infrequently whitened with carbonate of lead in order to disguise its presence. Bassora gums are frequently used as a filler and thickener in the manufacture of certain food products, as cheap ice creams.

Batiator Root.—The root of the *Vernonia nigritiana* Oliver and Hiern. (Fam. *Compositæ*), a widely distributed plant of West Africa, is said to be largely used in Senegal as a febrifuge, emetic, and antidysenteric, resembling ipecac somewhat in its therapeutic application. The plant is a composite which climbs to the height of a foot and a half, and yields a root composed of numerous fibers from twenty to thirty centimeters long, slender and grayish-yellow externally, a number of which are united to form an irregular knotty rhizome, unequally spherical at the neck or crown, and covered at this point with silky hairs. The active constituent is a glucoside, *vernonin*, $C_{10}H_{24}O_7$. (Heckel and Schlagdenhauffen, *A. de P.*, Aug., 1888; see also *Zeit. An. Chem.*, 1893, p. 364.) This is a hygroscopic whitish powder, forming a pale yellow solution with water, and only slightly soluble in ether and in chloroform. By the absorption of 2 molecules of water it is split into a resinous body and glucose. Physiological experiments made upon frogs show vernonin to be a cardiac poison of the digitalis group; it is also said to act as a paralyzant to the motor nerve trunks. (*P. J.*, June 30, 1888.)

Baume Tranquille. *Balsamum Tranquillans, Huile de Jusquiame Composée. Oleum Hyoscyami Compositum.*—This preparation of the French Codex consists essentially of a fixed oil holding in solution the active matters of certain narcotic and aromatic plants. According to the Codex the fresh narcotic plants, belladonna, henbane, black nightshade, poppy and stramonium, are boiled with poppy seed in a copper kettle until all their water is driven off, and a gentle heat maintained until the oil acquires a fine green color; the oil is then expressed and the essential oils of lavender, peppermint, rosemary and thyme are added. The preparation is used externally by friction as an anodyne in local pains, but especially to relieve *earache*, a few drops being placed in the ear on a pledget of cotton. The National Formulary preparation is approximately the same as the above, although a little less complex. It is known as *Oleum Hyoscyami Compositum* and consists of a solution of oils of lavender, rosemary and thyme in infused oil of hyoscyamus. (See Part III.)

Baycuru Root.—This is the root of a Brazilian plant, probably the *Statice brasiliensis* Boiss. (Fam. *Plumbaginaceæ*), which is used by the natives as a discutient in glandular swellings and as an astringent gargle. F. A. Dalpe (*A. J. P.*, 1884, xiv, 361) believed that he has found in it an alkaloid, *baycurine*, besides volatile oil, gum glucose, etc. It contains about 12.5 per cent. of tannic acid.

Bayer 205.—The composition of this substance has not been made public. It is supposed to be a derivative of amino-napthalene-sulphonic acid. It contains neither mercury nor arsenic.

Bayer 205 is a white powder, soluble in water and apparently not affected by sterilization.

Mayer (*Bull. Instit. Pasteur*, 1922, xx, p. 248), Wenyon (*B. M. J.*, 1921, ii, p. 746) and others have shown that it possesses powerful trypanocidal action. While the reports on its practical effects in human *trypanosomiasis* are not very extensive, they indicate that the drug is likely to prove one of the most efficient agents that we possess against this deadly infection. It is administered intravenously, usually in 5 per cent. solution. The beginning *dose* is 0.5 Gm. (eight grains), gradually increasing at intervals of one or two days. Muhlens and Menk (*M. M. W.*, 1921, lxviii, p. 1488) report transient albuminuria from its use.

Bdellium.—Under this name have been included various gum resins having little or nothing in common. The commercial Bdelliums are naturally divided into the Indian and the African, but E. M. Holmes, in an elaborate study (*P. J.*, lxi), recognizes five commercial varieties of African Bdellium—namely, 1. Perfumed Bdellium, which is believed to be collected in Northeastern Africa; 2. African Bdellium; 3. Opaque Bdellium; 4. Hotai Bdellium from the Somaliland, and 5. A non-aromatic acrid gum resin. *Perfumed Bdellium*, or *Habaghadi* or *bissabol*, closely resembles in appearance *Somali myrrh*, but has a less bitter, more acrid and peculiar taste which distinguishes it at once from myrrh. *African Bdellium*, proper, occurs in hard, translucent roundish pieces of a pale to dark grayish-brown color, red by transmitted light, with a resinous unstreaked fracture, dotted with glistening points. The odor is said to recall that of pepper; the taste is slightly acrid and bitter. *Opaque Bdellium* is of a pale brown color and has a bitter, slightly acrid bitter taste and a faint cedar-like odor; it occurs in tough, roundish pieces about an inch to an inch and a half in diameter. *Hotai Resin* resembles opaque bdellium, but is distinguished by its lack of odor, its slightly soapy taste, and its brittleness. These four bdelliums of Holmes are for the most part collected in Somaliland. They are the product of different species of *Commiphora*, small trees or large shrubs which suggest in appearance the English hawthorn. The species are by Holmes divided into four groups. (See *P. J.*, lxxii.) According to A. Engler, the resin of *Commiphora Roxburghiana* (Stocks) Engl. is the commercial *Gugul*, or *India Bdellium*, which is employed in the East Indies as a remedy for *leprosy*, *rheumatism*, and *syphilis*. Bdellium sometimes comes mixed with gum arabic and gum senegal. It is either in small roundish pieces, of a reddish color, semi-transparent and brittle, with a wax-like fracture, or in large irregular lumps, of a dark brownish-red color, less transparent, somewhat tenacious, and adhering to the teeth when chewed. It has an odor and taste like that of myrrh, but weaker. It is infusible and inflammable, diffusing while it burns a balsamic odor. According to Pelletier, it consists of 59 per cent. of resin, 9.2 of gum, 30.6 of bassorin, and 1.2 of volatile oil, including loss. In medicinal properties it is analogous to myrrh, and was formerly used for the same purposes. In Europe it is still occasionally employed in plasters. The *dose* is from ten to forty grains (0.65-2.6 Gm.).

Bebeeru Bark.—*Nectandræ Cortex*, Br. 1885, is the dried bark of *Nectandra Rodiœi* Hook. (Fam. *Lauraceæ*). The *bebeeru*, *bibiru* or *sipiri*, as it has been variously named, is a tree sixty feet or more in height, growing in British Guiana and the neighboring regions of South America, and yielding the wood known as *greenheart*.

The bark occurs in large, flat, heavy pieces, from 30 to 60 cm. long, from 10 to 15 cm. broad, and about 6 mm. thick, with a short granular fracture, of a grayish-brown color on its outer surface and a dark cinnamon color on the inner. It has an intensely bitter, somewhat astringent taste. On microscopical examination it is seen to be composed chiefly of very thick-walled parenchymatous cells. The inner bark contains peculiar short, sharp-pointed, undulate bast fibers. Within the cells dark brown masses (colored greenish-black by ferrous sulphate) may be seen. Analyzed by Maclagan (1843) of Edinburgh, it was found to contain tannic acid, resin, gum, sugar, albumen, fibrin, various salts, and two alkaloids, *bebeerine* and *sepeerine*. Walz in 1860 showed that bebeerine was identical with *buxine*, obtained from *Buxus sempervirens*. This statement was confirmed by Flückiger, who proved that *pelosine* was identical with both of the above principles. (*P. J.*, *xi*, 1870, 192.) Later Maclagan and Gamgee (*P. J.*, 1869, xi) reported another alkaloid which they called *nectandrine*. Their work, however, has not been confirmed. The studies of Scholz (*A. Pharm.*, 1906, 1911 and 1914) and of Faltis (*M. Chem.*, 1912 and 1921) have demonstrated that commercial "bebeerine sulphate" is a mixture of several alkaloids as follows: *bebeerine*, $C_{18}H_{21}O_3N$, *chondrodine* ($C_{18}H_{24}O_4N$), *isobebeerine* ($C_{18}H_{19}O_3N$), *β-bebeerine* ($C_{21}H_{23}O_4N$) and *bebeerine-b* ($C_{22}H_{23}O_5N$). In the seeds, besides the foregoing principles, Maclagan found 53 per cent. of starch, and a peculiar white, crystalline, volatile acid, which he named *bebeeric acid*. The alkaloids are extracted together from the bark, in the form of impure sulphate, by a process similar to that for preparing quinine sulphate. This preparation was formerly known as the *commercial bebeerine sulphate*.

Pure bebeerine is a white, amorphous powder, whose concentrated aqueous solution is not precipitated by tartar emetic, but affords abundant white precipitates with sodium phosphate, potassium nitrate, iodide, or iodohydrargyrate, mercuric chloride, potassium platinocyanide, and nitric or iodic acid. Its acetate yields yellow amorphous precipitates with potassium ferrocyanide, potassium ferricyanide, potassium chromate, potassium dichromate, or platinum dichloride. For further information concerning these alkaloids see *Pareira*, Part I.

Nectandra is reputed to resemble cinchona in its virtues, although much inferior. It has generally been employed in the form of the impure bebeerine sulphate. In some cases of *intermittent* and *remittent fevers* it has apparently exercised a curative effect but it often fails, and cannot be relied on as a substitute for quinine. Bebeerine sulphate has been given in *dysmenorrhea*, *menorrhagia*, and *leucorrhea*. The *dose* of the commercial salt is from two to five grains (0.13–0.32 Gm.). In *malaria* from ten to thirty grains (0.65–1.9 Gm.) may be given, in divided doses, between the paroxysms.

Bedeguar. *Fungus Rosarum.*—An excrescence upon the *sweetbriar* or *eglantine*, *Rosa rubiginosa* L. and other species of *Rosa*, produced by the puncture of insects, especially by one or more species of *Cynips*. It is of irregular shape, usually roundish, about an inch in diameter, with numerous cells containing larvæ. It is nearly odorless, of slightly astringent taste and was formerly considered a diuretic and anthelmintic. *Dose*, from ten to forty grains (0.65–2.6 Gm.).

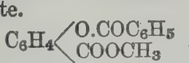
Benzanilid.—*Phenylbenzamide*, $C_6H_5NH(C_7H_5O)$, is closely related to acetanilid, containing the benzoyl radical C_7H_5O instead of the acetyl radical C_2H_3O. White to reddish, crystalline, odorless powder melting at 163° C., practically insoluble in water but soluble in alcohol. This substance has been recommended by Cahn as an antipyretic in diseases of children in *doses* of from one and a half to three grains (0.096–0.2 Gm.) for children one to three years of age; for adults the dose is ten to fifteen grains (0.65–0.9 Gm.). It has been little used.

Benzidine. *Paradiaminodiphenyl* $(C_6H_4)_2(NH_2)_2$.—A grayish-yellow crystalline powder, difficultly soluble in cold water, more readily in boiling water. This substance, especially in the form of its hydrochloride, has attained a considerable use as the means of detecting the presence of occult blood. (See *Diagnostic Tests.*)

The pharmacological properties of benzidine have been investigated by Adler (*A. E. P. P.*, 1908, lviii, p. 167) who found that large doses exercised a paralytic effect upon the central nervous system and caused the appearance of glycosuria and degeneration of the red blood corpuscles. It was oxidized in the body and eliminated as diaminodioxyphenyl.

Benzo-Iodo-Hydrine. $C_3H_5ClC_7H_5O_2$.—Prepared by mixing *benzoyl iodide* and epichlorhydrin. It forms a brown, fatty mass, soluble in ether, alcohol, and petroleum oils, insoluble in glycerin. It is decomposed at 100° C., with separation of iodine. For dispensing, it is usually mixed with powdered sugar, so that the mixture contains 3¼ per cent. of benzo-iodo-hydrine, and a teaspoonful is about the equivalent of sixteen grains of potassium iodide. It is used as a substitute for potassium iodide, because of its freedom from irritating properties and from tendency to produce iodic poisoning.

Benzo-Naphthol. *Betanaphthol Benzoate. Benzoyl-naphthol. Naphthyl Benzoate. β-Naphthyl Benzoate.* $C_6H_5COOC_{10}H_7$.—This compound is made by the action of benzoyl chloride upon β-naphthol. It is a whitish, crystalline powder, without taste or odor, melting at 110° C. and prone to darken with age. It occurs in microscopical crystals, almost odorless and tasteless, nearly insoluble in water at ordinary temperatures, more soluble in alcohol, with solubility rising rapidly with the temperature, but most soluble in chloroform. "A hot alcoholic solution should not give any cherry-red coloration when an equal volume of nitric acid and a few drops of mercuric nitrate solution are added, which would indicate the presence of free β-naphthol." This substance, which was proposed by Yvon and Berlioz (*Pract.*, Dec., 1891) as especially efficacious as an intestinal antiseptic, has been reported upon by Gilbert (*S. M.*, May, 1892), who affirms that it is of little value in *gastric fermentation*, but very valuable in *intestinal fermentation.* It is probably slowly broken up in the intestines into benzoic acid and naphthol, and the experiments made by Ewald (*B. K. W.*, 1892), indicate that it has a positive influence upon intestinal fermentation, a conclusion confirmed by various French clinicians. It appears to be free from irritant properties, and to be a very useful remedy in chronic *diarrhea;* also in *senile pruritus* dependent upon intestinal indigestion. It is best administered in small *doses* of from four to eight grains (0.26–0.5 Gm.), repeated frequently, in capsule; as much as seventy-five grains (5 Gm.) daily may be given to an adult. It is incompatible with antipyrine, camphor, phenol, ferric chloride, menthol, potassium permanganate or ethyl carbonate.

Benzosalin. 
$C_6H_4\left\langle\begin{matrix}O.COC_6H_5\\COOCH_3\end{matrix}\right.$ *Methyl-benzoyl Salicylate.—Benzyl-salicylic Acid Methylester.*—This compound is the methyl ester of benzoyl salicylic acid. It occurs as white, acicular crystals which melt at 85° C., insoluble in water, sparingly soluble in ether, but readily soluble in alcohol and chloroform. It is incompatible with acids or highly acid salts. This compound is asserted to pass through the stomach unchanged and be split up by the intestinal juices into its component parts, salicylic and benzoic acids, which exercise their characteristic anodyne and antirheumatic properties. It has been employed with success in the treatment of *articular* and *muscular rheumatism* and in *neuritis, neuralgia* and similar conditions where the coal tar analgesics are of service. Freund (*D. M. W.*, 1907) believes that the benzoic acid lessens the excessive sweating as well as the local irritant action produced by salicylic acid. The *dose* is eight to fifteen grains (0.5–0.9 Gm.) three or four times a day.

Benzoyl-acetyl-peroxide. *Benzozone. Benzoxate. Acetozone. Acetyl Benzyl Peroxide.* C_6H_5-$CO.O.O.CH_3CO$.—The pure peroxide forms a white, crystalline mass melting at 36.6° C. When gradually heated it slowly decomposes and evaporates; if suddenly heated it almost instantly decomposes and in a tightly-stoppered bottle an explosion will follow. Grinding, compressing, or pounding the undiluted substance will often bring about the same result. In crystalline form, the substance is soluble in oils to the extent of about 5 per cent., slightly soluble in alcohol, moderately soluble in ether, chloroform, and carbon tetrachloride, although gradually decomposed by all the solvents with the exception of neutral petroleum oils. It is decomposed by contact with alkaloids and organic matter of all kinds. It is slowly hydrolyzed and decomposed by water. Acetozone of the markets is benzoyl-acetyl-peroxide diluted with a neutral drying powder so that 50 per cent. of the pure article is represented. Benzoyl-acetyl-peroxide is moderately soluble in water so that fifteen grains of it may be dissolved in one-half gallon of boiled or distilled water; the solution should be used within thirty-six hours after it is made. If the commercial drug be employed, thirty grains may be used in the half gallon; the solution should be allowed to settle and be decanted without filtration. A mixture of acetyl-benzoyl-peroxide and chlorbutanol (chloretone) in liquid petrolatum is known as *acetozone inhalant.*

Benzoyl-acetyl-peroxide is a very active germicide. Experiments in the laboratories of the United States Government in the Philippines show that 1 part of the hydrolyzed substance to 177 of water, and containing only 0.05 per cent. of active oxygen, destroys all germs, including spores, almost instantly; even at a dilution of 1 in 3000, vegetating germs, as a rule, are killed within one minute, but the spores require an appreciable time. It was further shown that 1 part in 1000 absolutely destroys and that 1 in 30,000 distinctly inhibits the growth of the comma bacillus. In the experiments of Ferer and Novy (*Am. Chem. J.*, 1902, xxvii, No. 3), one drachm (3.9 Gm.) of it a day, given for several weeks to a dog weighing eight kilos, produced no sensible effect. Charles L. Bliss has shown that acetozone is eliminated in the form of hippuric acid. In internal medicine benzoyl-acetyl-peroxide has been used in the United States hospitals with most excellent results in the treatment of *cholera*, given in double capsules in *doses* of from three to five grains (0.2–0.32 Gm.) every two to four hours. It was found that when the stomach was full at the time of administration vomiting frequently occurred, probably being due to the decomposition of the peroxide by the organic matter present, since no irritation was produced when the stomach was empty. Benzoyl-acetyl-peroxide has been employed by Wasdin, and subsequently by Harriss and others (*T. G.*, 1902–1903), in *typhoid fever* with alleged most extraordinary results in the reduction of the local and general symptoms—one hundred and thirty to two hundred and ten grains (8.3–13.6 Gm.) being administered in the twenty-four hours. Acetozone has also been employed locally as a germicide in *gonorrhea, malignant edema, tinea tonsurans, infected ulcers,* and similar affections. In surgical cases acetozone may be applied directly to the wound. When used as an intestinal antiseptic in typhoid fever or in conditions similar to those resulting from this disease, a 1 in 1000 solution should be freshly prepared each day, and administered almost *ad libitum.*

Benzoyl-Eugenol.—*Benzeugenol,* $C_{10}H_{11}(C_7H_5O)O_2$, occurs in colorless prisms or crystals, melting at 70.5° C., soluble in alcohol, ether, and chloroform, insoluble in water. It is similar in its properties and medicinal uses to *cinnamyleugenol,*

$C_{19}H_{18}O_3$. Both are used as antiseptics and in the treatment of *tuberculosis.*

Benzoyl Superoxide. *Benzoyl Peroxide. Lucidol.* $C_6H_5.CO.O.O.CO.C_6H_5$.—Sodium peroxide and benzoyl chloride are dissolved in water and heated. The resulting product is filtered and the crystals in the filter are washed with warm alcohol. The crystals of benzoyl superoxide are lustrous, white and prismatic, almost insoluble in water but a little more soluble in alcohol. According to Loevenhart (*Th. M.*, 1905, p. 426), it exercises a more powerful oxidizing effect than even hydrogen peroxide. When locally applied it is non-irritant. He recommends it as an antiseptic and analgesic application, either used pure in the form of a dusting powder, or in the form of a 10 per cent. ointment in *burns* and *skin diseases.*

Benzoyl Tropeine, $C_{15}H_{19}O_2N + 2H_2O$, is formed by heating tropine with benzoic and dilute hydrochloric acids to 100° C., when the benzoyl radical, C_7H_5O, derived from benzoic acid, C_6H_5-CO.OH, replaces a hydrogen atom of the tropine, $C_8H_{15}NO$, and $C_8H_{14}(C_7H_5O)ON$ is produced. It forms silky needles, fusing at 58° C. When deprived of water, the anhydrous base fuses at from 41°–42° C., and can be sublimed without decomposition. It has a strong basic reaction, and its salts are not very stable.

Filehne (*B. K. W.*, vii, 1887) has found that benzoyl tropeine is a powerful local anesthetic, also affecting the pupil and accommodation like other tropeines. He also found other benzoyl compounds to be local anesthetics, *benzoyl methyltriacetonalkamine* being the most powerful, *benzoyl quinine* next, *benzoyl morphine* the least.

Benzyl Alcohol, $C_6H_5CH_2OH$, *Alcohol Benzylicum.*—This has been brought forward by Macht (*J. P. Ex. T.*, 1918, xi, and *J. A. M. A.*, October 30, 1920) as a local anesthetic. The experiments of Sollmann (*J. P. Ex. T.*, 1919, xiii, p. 355) show, however, that although when applied to the cornea it is approximately equal to beta-eucain in power, it has little action upon mucous membranes of the mouth or nose and that it is sufficiently locally irritant to seriously interfere with its usefulness. Solutions even in sealed ampules are likely to undergo decomposition.

Benzyl Benzoate. *N. N. R.*, 1924. *Benzylis Benzoas,* $C_6H_5COO.CH_2C_6H_5$.—Benzyl benzoate is an ester of benzyl alcohol and benzoic acid. It occurs naturally in some of the balsamic resins either alone or in combination with related compounds. Cinnamein is said to consist mainly of this compound. It is a constituent in the delicate fragrant perfumes of hyacinth, gardenia, jasmin, tuberose, and orange blossom.

It may be prepared by fractionation of Peru balsam or synthetically by one of the following methods: 1. By the action of sodium and benzaldehyde. 2. By treating nitroso-benzoyl-benzylamin with alcohol. 3. By acting upon benzaldehyde with sodium hydroxide.

Benzyl benzoate is a colorless oily liquid with a faint odor and a sharp pungent taste, insoluble in water or glycerine, but miscible with alcohol, chloroform or ether. It boils at from 320° to 325° C. with partial decomposition; has a specific gravity of 1.08 to 1.12 at 25° C. and is inflammable. It is neutral to litmus and is decomposed by an alcoholic solution of potassium hydroxide.

The addition of powdered soap to the alcoholic solution of benzyl benzoate makes it miscible with water, the soap acting as an emulsifying agent.

The introduction of this compound into medicine is due to the physiological studies of Macht (*J. P. Ex. T.*, 1918, xi, 419) who found that the benzyl nucleus exercised a paralyzing effect upon unstriped muscle tissue. He experimented with both the benzoate and acetate of benzyl, but the latter was found to produce too much disturbance of the stomach to be clinically useful. Through its influence upon the muscle tissue, benzyl benzoate causes relaxation of the intestines, ureters, bronchi, etc. It also produces a fall in the blood pressure by relaxation of the arterial muscles. Upon the heart itself it exercises practically no effect except in large doses, when it seems to have a slightly stimulant action. It is largely broken up in the system, and appears in the urine as hippuric acid.

Benzyl benzoate has been used clinically for the purpose of lessening spasm of various unstriped muscles, as in *biliary colic, renal colic, intestinal spasms* of various type, *dysmenorrhea, asthma,* etc. It has also been used in cases of high blood pressure, whether due to arterial spasm or secondary to chronic *nephritis.* According to the investigations of Macht, in the latter group of cases it exercises no injurious effects upon the kidneys. Babcock (*J. A. M. A.*, 1924, lxxxii, 193) tried it in *angina pectoris* with complete relief from the pain in a certain proportion of cases, but no benefit in others. Despite the early enthusiastic commendations concerning this drug, it has not justified the high hopes to which it gave rise. Mason and Pieck (*J. Lab. Clin. M.*, 1920, vi, 62) were unable to demonstrate any relaxing effect upon the various unstriped muscles from the intravenous injection into dogs, and Gruber and Shackelford (*J. Lab. Clin. M.*, 1924, ix, 685) found that in doses up to 30 drops it failed to lower the blood pressure in human beings.

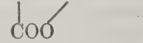
The dose ordinarily recommended for benzyl benzoate is from 3 to 6 minims (0.18 to 0.37 c.c.). It is most commonly exhibited in the form of a 20 per cent. alcoholic solution, of which 15 to 30 minims, well diluted with water, may be given at a dose. In some cases it produces so much disturbance of digestion as to greatly interfere with its use.

Benzyl Mandelate.—This compound was suggested by Macht (*J. P. Ex. T.*, 1923, xxi, p. 443), on the ground that both mandelic acid and benzyl derivatives are depressant to the involuntary muscle. It occurs as colorless crystals practically insoluble in water but soluble in alcohol. His experiments on both the lower animals and human beings show a marked effect in relaxation of the spasms of the involuntary muscles, especially in lowering blood pressure.

Benzyl-Sodium Succinate. *Sodium-benzyl succinate* (*Benzycin*) and *sodium-dibenzyl phosphate* (*Benzyphos*).—Both of these salts occur as white powders freely soluble in water, the former represent 39.5 per cent. of benzyl and benzyphos 60.7 per cent. They are stated to exercise the characteristic physiological effects of the benzyl derivatives on unstriped muscle. (See *Benzyl Benzoate.*) The recommended dose is from five to fifteen grains (0.3 to 1.0 Gm.).

Benzyl Succinate. *Benzylis Succinas. Dibenzyl Succinate N. N. R.*, 1924.—Esterol, $C_6H_5CH_2.OOC.$-$CH_2.CH_2.COO.CH_2C_6H_5 = C_{18}H_{18}O_4$.—This compound occurs in the form of white or pale yellowish crystals, practically tasteless and odorless, insoluble in water but soluble in alcohol and is asserted to be non-irritant to the stomach. It is recommended in the treatment of *dysmenorrhea, asthma, high blood pressure, colic* and similar spasmodic conditions in which benzyl benzoate has been used; the advantage is claimed for it that it does not nauseate. The *dose* is 5 to 10 grains (0.3 to 0.6 Gm.) three or four times a day usually administered in tablet form.

Betaine.—This is an alkaloid of weak basic properties which Scheibler discovered in the juice of the sugar beet. (*A. J. P.*, xli, 559.) Husemann showed it to be identical with *lycine*, and to have the composition $C_5H_{11}NO_2$. (*A. J. P.*, 1875, 209.) Liebreich also obtained it by the oxidation of choline, and called it *oxyneurine*. (*Ber. d. Chem. Ges.*, iv, 735.) It has been made synthetically, and its relation to choline and similar compounds established. It belongs in the series of organic compounds of which choline is the alcohol and muscarine the aldehyde. It is now known to be *trimethyl glycocoll*,



$$\begin{array}{l} CH_2.N(CH_3)_3 \\ | \quad / \\ COO \end{array}$$

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It is prepared by patented processes from beet sugar molasses after the separation of other crystallizable bodies. In plants it is not a nitrogen reserve but is used up by the plant, during its development. It may also be looked upon as the anhydride of hydroxy-trimethyl-amino-acetic acid.

Waller and Plimmer (*P. J.*, lxxi, 517) find that betaine is feebly but distinctly toxic. In dose of 0.1 Gm. per kilo it produced in rabbits fall of blood pressure with final paralysis of the heart. They assert that pure betaine is less poisonous than the commercial. Boger and Josué (*S. M.*, 1898) believe that they have shown that betaine is capable of neutralizing tetanus toxin. Pelicaut (*Press. Med.*, 1904, p. 485) has recorded one case of recovery in which the alkaloid was used in *doses* of eight grains (0.5 Gm.) hypodermically twice a day. Since, however, both chloral and antitoxin were employed in this case, it is doubtful whether the favorable results were due to the betaine.

Betaine Hydrochloride. N. N. R., 1924. *Acidol. Lycine hydrochloride.* $C_5H_{11}NO_2HCl$.—It is prepared by the action of hydrochloric acid on betaine and consists of colorless crystals, freely soluble in water, and contains 23.8 per cent. absolute hydrochloric acid. When dissolved in water it gradually liberates the acid, and has been used by Flatow (*D. M. W.*, 1905) and others as a substitute for hydrochloric acid in *gastric indigestion. Dose*, eight grains (0.5 Gm.).

Beta-Naphtholsulphonic Acid. *Acidum Betanaphtholinsulphonicum.* $C_{10}H_6(OH).SO_3H$.—Betanaphtholinsulphonic acid occurs in white pearly scales, tinged with red. It is readily soluble in water and alcohol, and is of medical interest as a test for albumin in the urine. According to E. Riegler, the reaction is so delicate that it will make plainly visible the presence of one part of albumin in forty thousand of water. Albumoses and peptones are also thrown down, but such precipitates disappear on the application of heat, which does not occur with albumin. *Riegler's test* is best performed by adding from twenty to thirty drops of a 5 per cent. aqueous solution of the reagent to five or six milliliters of the urine.

Betol. *Naphthalol. Naphthosalol. Salinaphthol. Salicylic-naphthyl ester. Betanaphthyl Salicylate. Naphthyl Salicylate. Salicylic Acid Ester of β-Naphthol.* $C_6H_4OH.CO.O.(C_{10}H_7)$.—Betol occurs in white, shining crystals, is odorless and tasteless, melts at 95° C., and is insoluble in cold water or hot water, soluble in cold alcohol with difficulty, but readily dissolves in hot alcohol (1 in 3), in ether, and in benzene. It is not decomposed by acids or alkalies in the cold, but the alkaline pancreatic fluid has the power to decompose it into β-naphthol and salicylic acid.

Betol was proposed by Sahli as a substitute for salol, on the ground of its being less disagreeable and yielding in the intestines naphthol instead of the more poisonous phenol. It contains, however, 10 per cent. less salicylic acid than does salol, and, having a much higher melting point, splits up much less readily in the intestines; a fact which gains importance from the observation that frequently salicylic acid cannot be found in the urine after its ingestion. Sahli has given as much as one hundred and eighty grains (11.6 Gm.) in twenty-four hours. Betol may be used in *rheumatism*, and is especially commended by Kobert in ammoniacal *cystitis*. Butter of cacao will dissolve one-fourth of its weight of betol, so that suppositories or bougies are readily made. *Dose*, four to eight grains (0.26–0.5 Gm.).

The *salicylic ester of a-naphthol*, an isomer of betol, is known as *alphol*. It is also said to resemble salol in therapeutic effect. The *dose* is from eight to fifteen grains (0.5–1.0 Gm.).

Betonica. *Betonica officinalis*, L. *Wood Betony.*—A perennial European labiate herb, feebly aromatic and astringent. Its root has been considered emetic and purgative.

Betula. *Betula alba* L. *Paper*, or *European White Birch. Bouleau*, Fr. *Birke*, G. (Fam. *Betulaceæ.*)—Various parts of this tree have been applied to medicinal uses. The young shoots and leaves secrete a resinous substance, having acid properties, which, combined with alkalies, is said to produce the effects of a tonic laxative. (*J. P. C.*, xxvi, 208.) The *inner bark*, which is bitterish and astringent, has been employed in *intermittent fever*. The epidermis is separable into thin layers, which may be employed as a substitute for paper, and applied to various economical uses. The bark contains *betulin*, or *betula camphor*, which Hausemann (*Ann. Ch. Ph.*, clxxxii, 368) has shown to be a diatomic alcohol, as it forms a diacetate. Its formula is $C_{36}H_{60}O_3$, fusing point 258° C. When oxidized it yields *betulinic acid*, $C_{36}H_{54}O_6$, and *betulinamaric acid*, $C_{36}H_{52}O_{16}$. When the bark is distilled, it yields an empyreumatic oil called *oleum rusci*. (See *Oleum Betulæ Empyreumaticum Rectificatum.*)

The *leaves* of birch, which have a peculiar, aromatic, agreeable odor, and a bitter taste, have been employed, in the form of infusion, in *gout, rheumatism*, and *dropsy*. Active diuretic properties are claimed for birch leaves and attributed to the *betuloretinic acid* in them. An alcoholic extract has been used in daily *doses* of from twenty-five to fifty grains (1.6–3.2 Gm.). When the stem of the tree is wounded a saccharine *juice* flows out which is considered useful in complaints of the kidneys and bladder, and is susceptible, with yeast, of the vinous fermentation. A beer, wine, spirit, and vinegar are prepared from it in some parts of Europe. *Tinctura Rusci* is made, according to Hager, as follows: Ol. Rusci 10, Alcohol, Æther, of each 15, Ol. Lavandule, Ol. Rosmarini, Ol. Rutæ, of each 0.4 part; filter. (*A. J. P.*, 1881.)

Betula lenta L., popularly known as *sweet birch* or *black birch,* is an indigenous tree with a dark brown, close bark with much less tendency to separate into lamina than the other birches. The wood is rose-colored, fine grained, and highly esteemed for cabinet work. The bark of this tree owes its sweet odor to methyl salicylate and is an important commercial source of natural "oil of wintergreen" (see *Oleum Gaultheriæ*).

Bezoar.—This name has been given to concretions formed in the stomach or intestines of animals, which were formerly thought to possess extraordinary medicinal virtues. Many varieties have been noticed; but they were all arranged in two classes, the *oriental bezoar* (*lapis bezoar orientalis*), and the *western bezoar* (*lapis bezoar occidentalis*); the former was most esteemed. The bezoars are essentially impure calcium phosphate, except in the vegetable bezoars where the concretions are made up of plant hairs.

Bidens. *Bidens bipinnata,* L. *Spanish Needles.*—An indigenous composite plant, of which the root and seeds are popularly used as emmenagogues, and by the eclectics in *laryngeal* and *bronchial diseases.*

Bird-Lime. *Bird-glue. Vogelleim,* G.—A viscid substance, existing in various plants, particularly in the bark of *Viscum album* L. (mistletoe), and *Ilex Aquifolium* L., or *European holly,* from the latter of which it is usually procured. Large quantities are made in Japan from *I. crenata* Thunb., *I. othera* Spreng. and *I. latifolia* Thunb. The process for preparing it consists in boiling the middle bark for some hours in water, then separating it from the liquid, and placing the latter in proper vessels in a cool situation, where it is allowed to remain till it thickens, when it is washed to separate impurities. Bird-lime thus prepared is greenish, tenacious, glutinous, bitterish, and of an odor analogous to that of flaxseed oil. Exposed to the air, in thin layers it becomes dry, brown, and pulverizable, but reacquires its viscidity upon the addition of water. It is a complex body, but is thought to owe its characteristic properties to a proximate principle, which is called *glu* by the French chemists. This principle is without odor or taste, extremely adhesive, fusible by heat, inflammable, insoluble in water, nearly insoluble in alcohol, but dissolved freely by ether and oil of turpentine. According to Macaire, it is insoluble in the fixed oils, either hot or cold, a property which distinguishes it from the resins. Macaire proposed for it the name of *viscin* (*J. P. C.*, xx, 18.) Its analysis corresponds to the formula $C_{20}H_{48}O_8$ (or possibly $C_{20}H_{32} + 8H_2O$). After the extraction of the viscin by ether, Reinsch found a substance soluble in oil of turpentine which he called *viscaoutchin,* because of its elastic caoutchouc-like character. He gives it the formula $C_8H_{16}O$. Bird-lime is so tenacious that it may be employed to catch small birds, which, when they alight on a stick thickly covered with it, are unable to escape.

Under the name of *viscum aucuparium verum,* or *viscin,* bird-lime has become a commercial substance which, when dissolved in benzene, gives a syrupy, intensely green solution capable of any degree of concentration, and possesses extraordinary adhesive powers, adapting it for use as the basis of plasters and also as a vehicle for various dermatological remedies. The ordinary base of *viscin plasters,* as proposed by Riehl, consists of a mixture of 1500 Gm. of solution of viscin, 100 Gm. of powdered orris, 400 Gm. of starch, to which are added 280 Gm. of Venice turpentine, and 31 Gm. of Dammar gum, the whole reduced to a paste by evaporation. In the preparation of salicylic viscin plasters the same formula is followed, excepting that the last two substances are replaced by 5 to 10 per cent. of salicylic acid. Various viscin plasters are made with mercury, iodoform, and other active substances. *Zincum viscosum* is a viscin solution of the consistency of linseed oil, containing 10 per cent. of zinc oxide. For medicinal properties of mistletoe, see *Viscum.*

Bismal. $4C_{15}H_{12}O_{10} + 3Bi(OH)_3$.—The bismuth salt of methylene-digallic acid. A grayish-brown powder, insoluble in water or the gastric juice, but soluble in alkaline solutions. It is used as an astringent in *diarrhea,* especially in prolonged cases that are not benefited by opium treatment. The color of this compound becomes darker with age and is found to vary from yellow to dark brown. *Dose,* from one and one-half to five grains (0.096–0.32 Gm.).

Bismon. *Colloidal Bismuth Oxide.*—A substance said to be produced by the reaction between bismuth salts and alkaline solutions of sodium lysalbinate or protalbinate. It occurs as a translucent amorphous mass, containing 22.3 per cent. of bismuth oxide; freely soluble in warm or cold water, the solution up to 25 per cent. being a reddish-yellow and slightly opalescent tasteless fluid; when stronger, syrupy or gelatinous. It has been highly recommended in the treatment of *gastro-intestinal catarrh,* especially in infants. It cannot be used hypodermically on account of its tendency to produce local disturbances and nephritis. Eighty minims (5 cc.) of a 10 per cent. aqueous solution may be given three or four times a day to young children, and *doses* of fifteen grains (1 Gm.) are said to be borne without difficulty by older children; always given in solution and not in powder.

Bismuth Albuminate. *Bismuthi Albuminas. Bismuthum Albuminatum. Wismutalbuminat,* G. *Bismuthose.*—A compound of indefinite composition made by adding a solution of 75 parts of dried egg-albumin to 25 parts of bismuth and ammonium citrate dissolved in a small quantity of water and drying the product at a low temperature.

A pale gray or white powder, not wholly soluble in water, containing from 10 to 12 per cent. of bismuth. It is used in gastric and intestinal cramps in *doses* of from eight to fifteen grains (0.5–1.0 Gm.).

Bismuth and Ammonium Citrate.—*Bismuthi et Ammonii Citras, U. S. IX; Bismuthi Ammoniocitras; Bismuthum Citricum Ammoniatum; Citrate of Bismuth and Ammonium; Citrate de Bismuth et d'Ammoniaque,* Fr.; *Citronensaures Wismutoxyd-Ammonium; Wismutammoncitrat,* G. —"Bismuth citrate rendered soluble by the presence of ammonium citrate; when dried to constant weight in a desiccator over sulphuric acid, it yields, upon ignition, not less than 46 per cent. nor more than 52 per cent. of bismuth oxide [Bi_2O_3]." *U. S. IX.* The process of the *U. S. VIII* was as follows.

"Bismuth Citrate, *one hundred grammes,* Ammonia Water, Distilled Water, each, *a sufficient quantity.* Mix the Bismuth Citrate with *two hundred cc.* of Distilled Water and rub it to a smooth paste, heat the mixture on a water-bath, and gradually add Ammonia Water until the salt is dissolved and the liquid is neutral or has only a faintly alkaline reaction. Then filter the solution, evaporate it on a water-bath to a syrupy consistence, and spread it upon plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in amber-colored, well-stoppered bottles, protected from light." *U. S. VIII.*

The Br. Pharm., 1914, gives a process for a solution in which bismuth citrate is produced. (See *Liquor Bismuthi et Ammoniæ Citratis*, Br.)

The U. S. Pharmacopœia described it as in "shining, pearly or translucent scales, or white powder, becoming opaque with loss of ammonia on exposure to the air; it is odorless and has a metallic taste. Bismuth and Ammonium Citrate is very soluble in water and sparingly soluble in alcohol. When strongly heated, the Bismuth and Ammonium Citrate fuses and finally leaves a blackened residue, having a yellow surface. A solution of this residue in a slight excess of nitric or hydrochloric acid produces a white turbidity when added to 25 volumes of distilled water. An aqueous solution of Bismuth and Ammonium Citrate (1 in 20) is neutral or faintly acid to litmus. Ammonia is evolved when Bismuth and Ammonium Citrate is boiled with a slight excess of sodium hydroxide T.S. An aqueous solution of the Bismuth and Ammonium Citrate, when treated with an excess of hydrogen sulphide, yields a black precipitate. The filtrate from the latter, when deprived by heat of the excess of hydrogen sulphide and boiled with an excess of lime water, yields a white precipitate. Dissolve about 0.05 Gm. of Bismuth and Ammonium Citrate in 1 mil of distilled water, in a test tube, add 5 mils of sulphuric acid (free from nitrous compounds), cool the mixture and carefully pour over it 5 mils of ferrous sulphate T.S without mixing; no red or brown zone appears immediately (*nitrate*). Dissolve 1 Gm. of Bismuth and Ammonium Citrate in 50 mils of distilled water, precipitate the bismuth completely with hydrogen sulphide, filter, evaporate the filtrate to dryness and ignite. The weight of the residue does not exceed 0.005 Gm. (*alkalies or alkali earths*). Ignite 3 Gm. of the Bismuth and Ammonium Citrate, dissolve the residue in just a sufficient quantity of warm nitric acid, and pour the solution into 100 mils of distilled water; a white precipitate is produced. Filter this mixture, evaporate the filtrate on a water-bath to 30 mils, again filter the liquid and divide the new filtrate into portions of 5 mils each. These portions do not respond to the tests for *lead, copper, sulphate, or silver* given under *Bismuthi Subcarbonas.* The residue resulting from the ignition and subsequent treatment of 2 Gm. of Bismuth and Ammonium Citrate, as described in the following test, does not respond to Bettendorf's Test for arsenic.

"*Assay.*—Take about 1 Gm. of Bismuth and Ammonium Citrate, previously dried to constant weight in a desiccator over sulphuric acid, and weigh accurately. Ignite it in a porcelain crucible and, after cooling, add 5 mils of nitric acid to the residue, drop by drop, warming until solution is effected. Evaporate this solution to dryness, and carefully ignite it at red heat. It leaves a residue of bismuth oxide (Bi_2O_3) corresponding to not less than 46 per cent. nor more than 52 per cent. of the original weight of Bismuth and Ammonium Citrate taken." *U. S. IX.*

As frequently seen in commerce it is not entirely soluble in water; this is due to the loss of ammonia through exposure, and a few drops of ammonia water added to the turbid solution are generally sufficient to restore its transparency.

This salt, because of its solubility, lacks the therapeutic virtues of the official preparations of bismuth. It is actively astringent, and more irritant in its action. It is occasionally of service in *serous diarrheas*, but should not be used when there is much inflammation.

Dose, one to three grains (0.065–0.20 Gm.).

Bismuth Benzoate. $Bi(C_7H_5O_2)_3$. *Bismuthi Benzoas.*—It is a white powder, insoluble in water, made by double decomposition between bismuth nitrate and sodium benzoate. It contains about 65 per cent. of bismuth, and may be given as an intestinal antiseptic in *diarrheas*, in *doses* of from eight to fifteen grains (0.5–1.0 Gm.) four to six times a day. It has been commended by Finger as a substitute for iodoform.

Bismuth Betanaphtholate. *Bismuthi Betanaphtholas U. S. IX. Orphol.*—"A compound of bismuth and betanaphthol of somewhat varying composition, yielding not less than 15 per cent. of betanaphthol [$C_{10}H_7OH$] and, upon ignition, not less than 73 per cent. nor more than 78 per cent. of bismuth oxide [Bi_2O_3]." *U. S. IX.*

This compound has been dismissed from the U. S. P. IX. It is obtained by precipitating solution of sodium betanaphtholate with an acetic acid solution of bismuth nitrate with the addition of solution of sodium hydroxide. It was officially described as "a buff-colored to grayish-brown, amorphous powder; odorless or having a faint odor of betanaphthol; tasteless; permanent in the air. Bismuth Betanaphthol is nearly insoluble in water, alcohol, chloroform or ether; partially dissolved by mineral acids with the formation of the corresponding bismuth salts and the liberation of betanaphtol. When strongly heated Bismuth Betanaphthol chars and finally leaves a grayish-yellow residue, which is blackened by hydrogen sulphide T.S. Shake about 1 Gm. of Bismuth Betanaphthol, accurately weighed, with 20 mils of chloroform, filter the mixture, allow the filtrate to evaporate spontaneously and dry the residue in a desiccator over sulphuric acid; the weight of this residue does not exceed 1 per cent. (*free betanaphthol*). Shake about 0.5 Gm. of Bismuth Betanaphthol with 10 mils of distilled water and filter; the filtrate is colorless and neutral to litmus. Heat gently a mixture of about 0.2 Gm. of Bismuth Betanaphthol with 5 mils of potassium hydroxide T.S. and about 0.2 Gm. of aluminum wire; the vapors evolved do not turn red litmus blue (*nitrates*). Incinerate about 2 Gm. of Bismuth Betanaphthol in a porcelain crucible, cool the residue and add just sufficient nitric acid to form a solution with the aid of heat. This solution, when poured into 100 mils of distilled water, produces a white, crystalline precipitate. Now filter the mixture, evaporate the filtrate to 30 mils and again filter if not clear; the clear filtrate does not respond to the tests for *lead, copper, sulphate, or silver* given under *Bismuthi Subcarbonas.* The bismuth oxide obtained in the following assay does not respond to Bettendorf's Test for arsenic.

"*Assay for Betanaphthol.*—Dissolve about 2 Gm. of Bismuth Betanaphthol, accurately weighed, in 20 mils of hydrochloric acid with the aid of heat, cool the liquid and then shake it in a separator with successive portions of chloroform until the extraction of the betanaphthol is complete. Combine the chloroform solutions, allow the liquid to evaporate spontaneously and dry the residue in a desiccator; the weight of the residue corresponds to not less than 15 per cent. of the weight of Bisumth Betanaphthol taken. This residue, crystallized from a solution in boiling distilled water, responds to the tests for identity under *Betanaphthol.*

"*Assay for Bismuth Oxide.*—Incinerate about 2 Gm. of Bismuth Betanaphthol, accurately weighed, in a porcelain crucible, cool the residue and dissolve it in nitric acid. Evaporate the solution to dryness and carefully ignite the residue until of constant weight; the bismuth oxide (Bi_2O_3) so obtained corresponds to not less than 73 per cent. nor more than 78 per cent. of the original weight of the Bismuth Betanaphthol taken." *U. S. IX.*

This salt of bismuth is employed especially in the treatment of *enteritis* on the supposition that when the salt is broken up in the intestinal tract it will liberate betanaphthol, and therefore exercise a more powerful antiseptic action than the other salts of bismuth.

Dose, from five to twenty grains (0.32–1.3 Gm.).

Bismuth Borate.—*Bismuthi Boras*, $BiBO_3$, is a grayish-white powder which has been used as an intestinal antiseptic in *doses* of from seven to fifteen grains (0.45–1.0 Gm.).

Bismuth Borophenate.—*Bismuthi Borophenas, Markasol*, has been recommended as a slightly astringent absorbent powder, to be used in the same way and for the same purposes as iodoform. It is free from odor, and is alleged to be locally antiseptic.

Bismuth Carbolate. *Phenol Bismuth*, $Bi(OH)_2(C_6H_5O)$.—A white, non-irritant, and non-toxic powder, almost odorless and tasteless, which, according to its manufacturer, contains 80 per cent. of bismuth in chemical combination with 19 per cent. of phenol. It is stated by M. F. A. Jasenski to be decomposed in the gastro-intestinal tract, with absorption of the phenol and escape of the bismuth, in great part with the feces. It is also asserted by Jasenski that even the largest doses (seventy-five grains) of it produce no evidences of phenol poisoning, and the probabilities are that but a small portion of the compound suffers decomposition in the intestinal tract. It has been used in all forms of gastro-intestinal catarrhs, fermentative *dyspepsias*, and similar complaints, as an antiseptic; also to some extent locally in various mucous inflammations. *Dose*, eight to thirty grains (0.5–2 Gm.).

Bismuth-Cerium Salicylate is a reddish-white powder, insoluble in water and alcohol. This salt has been highly commended in *diarrhea*, *enteritis* and *dysentery* by Salaya. *Dose*, ten grains (0.65 Gm.). With ferric salts it gives a violet color and is decomposed by acids and acid salts.

Bismuth Chrysophanate. *Bismuthi Chrysophanas. Dermol. Bismuthum Chrysophanicum.* $Bi(C_{15}H_9O_4)2Bi_2O_3$.—This is a yellow, amorphous, insoluble powder, which has been used in the treatment of various diseases of the skin.

Bismuth Citrate. *Bismuthi Citras. U. S. VIII. Bismuthi Citricum, Citrate de Bismuth*, Fr. *Wismut-citrat, Citronensaures Wismutoxyd*, G. $BiC_6H_5O_7$.—This salt, which was formerly official for the purpose of manufacturing bismuth and ammonium citrate, is made by boiling together bismuth subnitrate and citric acid. For details of the process see *U. S. D.*, 19th edition, p. 237.

It is a white, amorphous, microcrystalline powder, odorless and tasteless. It is insoluble in water or alcohol but dissolves in ammonia water or in solutions of the alkali citrates. It is not used in medicine in its natural state.

A combination of bismuth citrate and ferric citrate (*Bismuthi et Ferri Citras*) corresponding to 21 per cent. bismuth and 9 per cent. of iron is marketed as *bismuth and iron citrate* (*soluble*). It occurs in yellowish-green scales and is readily soluble in water. It combines the therapeutic properties of its constituents and is intended for *dyspepsia* associated with *anemia*. *Dose*, five to ten grains (0.32–0.65 Gm.). The same manufacturers have also brought out a similar combination of lithium and bismuth citrate in soluble, colorless scales. It corresponds to 40 to 45 per cent. bismuth and 2.5 to 3 per cent. of lithium. It is incompatible with strongly alcoholic liquids, mineral acids and with some salts of heavy metals. It is recommended for *gouty dyspepsia* and *intestinal catarrh* in *doses* for adults of from five to fifteen grains (0.3–1.0 Gm.).

Bismuth Disalicylate.—Under the name of *Gastrosan* appears in commerce a white powder insoluble in cold water and alcohol which is asserted to be a disalicylate of bismuth. It is claimed for this preparation that it is superior in intestinal fermentation to other preparations of bismuth, because the second molecule of salicylic acid is liberated in the bowel and exercises an antiseptic influence. Witthauer has employed it with beneficial effects in *diarrhea* and in *gastric disturbances.* (*Ph. Centralh.*, 1909, p. 716.) It appeared in the form of lozenges each containing twelve grains (0.75 Gm.) of the salt.

Bismuth Ditannate. *Bismuth Tannate, Bismuth Bi-tannate.*—Under the trade name of *Tannismuth* this salt has been introduced into medicine. It is a light yellow powder, insoluble in water, and represents from 17 per cent. to 21 per cent. of bismuth, one atom of bismuth being combined with two molecules of tannic acid. It has been used in the treatment of *intestinal catarrh*, and by some is believed to be more astringent than the other insoluble salts of bismuth on the supposition that one of the tannic acid molecules will be split off in the intestinal tract. Sollmann (*J. P. Ex. T.*, 1921, xvii, 99) finds that tannismuth is more soluble in acid than in neutral or alkaline media; the portion dissolved by acids acts like free tannin. He believes that it exercises an astringent effect in the stomach and that in the intestines it acts like the insoluble salts of bismuth. The *dose* is five to thirty grains (0.3–2.0 Gm.).

Bismuth Dithiosalicylate. *Bismuthi Dithiosalicylas. Thioform. Deltaform.* $(S.C_6H_3(OH)COO.BiO_2 + Bi_2O_3 + 2H_2O$.—This is a yellowish-gray, odorless and tasteless powder, insoluble in water, alcohol, or ether, containing 72 per cent. bismuth oxide. It has been used externally as a dusting powder in *skin diseases* and in surgery, and probably acts precisely as does dermatol. It has been employed upon the eye to a considerable extent and is not irritant. Internally it has been given in *diarrhea as* an intestinal antiseptic in *doses* of five grains (0.32 Gm.) three or four times a day in capsules.

Bismuth Lactate. *Bismuthi Lactas.* $C_3H_4O_3BiHC_3H_4O_3$.—This salt is a white powder, slightly soluble in water and insoluble in alcohol. For process of manufacture see *U. S. D.*, 20th edition,

p. 1280. It may be used in *diarrhea* in *doses* of one to two grains (0.065–0.13 Gm.).

Bismuth Nucleinate.—*Bismuth paranucleinate* or *parabismuth* is a pale yellow, odorless, insoluble powder, containing about 50 per cent. of bismuth. It has been employed in the treatment of *enteritis* of both the acute and chronic types. *Dose,* fifteen to thirty grains (1–2 Gm.).

Bismuth Oleate. *Bismuthi Oleas.* $Bi(C_{17}H_{33}CO_2)_3$.—A compound resulting from the reaction between sodium oleate and bismuth trinitrate. It forms an insoluble powder or mass and is used as an emollient and astringent.

Bismuth Oxide. *Br.* 1898. *Bismuthi Oxidum. Bismuth Trioxide. Bismuthum Oxydatum, Oxydum Bismuthicum. Oxyde de Bismuth,* Fr. *Wismutoxyd,* G.—"Bismuth Oxide ($Bi_2O_3 = 464.00$), may be prepared by boiling bismuth oxynitrate with solution of sodium hydroxide." *Br.,* 1898. In this process the oxynitrate is decomposed by solution of sodium hydroxide, bismuth hydroxide being precipitated, while sodium nitrate remains in solution.

$$2BiNO_4.H_2O + 2NaOH = Bi_2 6OH \text{ (or } Bi_2O_3.3H_2O) + 2NaNO_3$$

At the temperature of 100° C. the bismuth hydroxide first produced is decomposed, water is liberated, and the anhydrous oxide is left. Bismuth oxide is a powder of a dull lemon-yellow color, insoluble in water, but soluble without effervescence in nitric acid, mixed with half its volume of water. The British Pharmacopœia, 1898, describes it as "a slightly brownish-yellow powder. It should answer to the general characters and tests enumerated under 'Bismuth Oxycarbonate.' Each gramme should yield 1.1 grammes of bismuth sulphide. Heated to incipient redness it is scarcely diminished in weight (absence of bismuth oxycarbonate, bismuth oxynitrate, and moisture)." *Br.,* 1898. It resembles bismuth subnitrate in its medicinal properties, and may be administered in *doses* of from ten to thirty grains (0.65–2.0 Gm.).

Bismuth Oxychloride. *Bismuthi Oxychloridum seu Subchloridum. Bismuth Subchloride. Bismuthyl Chloride. Flake White. Oxychlorure de bismuth,* Fr. *Wismutoxychlorid,* G. BiOCl.—Made by slowly pouring a solution of bismuth trinitrate, in diluted nitric acid, into a solution of sodium chloride, collecting the white precipitate, washing and drying. It is sometimes known as *pearl white,* and in France as *blanc de fard,* or *blanc d'Espagne.* Bismuth oxychloride is insoluble in water, soluble in acids, and is used for the same purposes as bismuth subnitrate and also for cosmetic purposes.

Bismuth Oxyiodide. *Bismuthi Oxyiodidum.* BiOI. *Bismuth Subiodide. Bismuthyl Iodide.*—For F. X. Moerk's process for the preparation of this salt, see *U. S. D.,* 19th ed., p. 1416. The oxyiodide has a light yellowish-red color, and contains no water or crystallization. (*A. J. P.,* 1887, 273.) In 1877 the bismuth oxyiodide was recommended as a local antiseptic and substitute for iodoform, by A. Sidney Reynolds. It has been used to a considerable extent with success in the Philadelphia Hospital, but its high price interferes with its general adoption. It has also been given internally in *gastric ulcer* and other gastric affections for which bismuth is usually employed. The *dose* is from five to ten grains (0.32–0.65 Gm.). Under the name of *bismuth formic iodide* a mixture of formaldehyde-gelatin, thymol iodide, and bismuth sub-iodide is marketed as an antiseptic dusting powder to ulcers and *sores* that require stimulant action.

Bismuth Oxyiodogallate. *Bismuth Iodsubgallate. Airol. Airoform. Airogen.* $C_6H_2(OH)_3COO(BiOHI)$.—This is a basic combination of bismuth, oxygen, iodine, and gallic acid, containing in 100 parts 44.6 parts of bismuth trioxide and 24.3 parts of iodine. It is prepared by heating molecular quantities of bismuth subgallate and hydriodic acid or bismuth oxyiodide and gallic acid in the presence of water until a grayish-green product results which is collected, washed and dried. It is a grayish-green odorless and tasteless powder insoluble in alcohol, ether, chloroform and olive oil, slightly soluble in glycerin. It is decomposed upon contact with water or aqueous solutions, slowly in the cold, more rapidly by heat. Airol is incompatible with water, diluted acids, dilute alkalies, etc., and it should be kept dry, as moist air causes liberation of iodine.

When airol is brought in contact with surgical secretions it becomes red from the liberation of iodine. According to the researches of Carl S. Haegler (Bruns, *B. k. Ch.,* xv, 1896), it is about as feeble an antiseptic as is iodoform, but as in the case of iodoform the substances liberated by its decomposition in wounds are actively germicidal. Von Herrenschwand (*Archiv. fur Ophthalm.,* 1913, lxxxii) finds, however, that one part of airol in a thousand is capable of killing gonococci and that one in ten thousand completely inhibits their growth. It has been largely used as a local remedy in all cases for which iodoform has been employed, having the superiority over that substance of being nearly free from odor. It does not irritate, but rapidly desiccates ulcerated surfaces. In the only case of poisoning by it which we have found recorded, symptoms of bismuth poisoning followed the injection into the cavity of an abscess of nine and a half fluidrachms (35 cc.) of its 10 per cent. solution in glycerin (Nemmer).

Injected into the peritoneal cavities of the lower animals in the dose of from one to two grammes per kilo, airol causes colonic convulsions, with coma, nephritis, and fatty degeneration of the liver.

It may be used as a powder or as a 10 to 20 per cent. salve, which should be prepared with lard or vaseline free from water, since with water, airol undergoes rapid decomposition. Airol is used as an antiseptic dusting powder in the treatment of *wounds.* It has been found of service as a local remedy in various *catarrhs,* as *vaginitis* or *rhinitis.* Bernheimer has used airol successfully in the treatment of gonorrheal *opthalmia.* The eye is first carefully cleansed and the everted lids are then dusted with the finely powdered drug. This procedure is to be repeated several times a day. A 10 per cent. glycerin emulsion has been recommended as an injection into *tubercular abscess* cavities.

Brun's Paste, which has been much used in various skin diseases and ulcerations, is made according to the following formula: Airol, *one part;* Mucilage, *two parts;* Glycerin, *two parts;* Argilla Alba (Kaolin), *sufficient to make a soft paste.* If the paste becomes too dry, use glycerin; if it be too soft, kaolin may be added. No metal instruments should be employed in preparing the paste, since many metals liberate iodine from airol. For the same reason, no water, only glycerin, should be used in the preparation. The paste is preserved in well-stoppered glass or porcelain jars, which are to be kept closed.

Bismuth Oxyiodo-methyl-gallol. *Bismuthi Oxyiodo-methylgallolum. Iodo-gallicin.* $C_6H_2COOCH_3(OH)_2O.BiOH.I$.—Made by acting upon gallicin (methyl gallate) with bismuth oxyiodide. It is in the form of a light, amorphous, dark gray powder, insoluble in ordinary solvents and containing 23.6 per cent. of iodine and 38.4 per cent. of bismuth.

It is used as a siccative and antiseptic powder to replace iodoform.

Bismuth Oxyiodo-pyrogallate. *Bismuthi Oxyiodo-pyrogallas. Pyroform. Gammaform.* $C_6H_2(OH)_2.O.Bi(OH)I$.—Made by digesting bismuth oxyiodide with pyrogallic acid or by precipitating a solution of potassium iodide and pyrogallic acid with bismuth nitrate in acetic acid. A fine, amorphous, yellowish-red powder, permanent in light and air. It is recommended as a surgical antiseptic powder.

Bismuth Oxyiodo-tannate. *Bismuthi Oxyiodotannas. Ibit.*—Bismuth oxyiodo-tannate is a greenish-gray, odorless, tasteless powder, becoming brownish on exposure, insoluble in water, and has been suggested as a surgical substitute for iodoform.

Bismuth Phenolate. *Bismuthi Phenolas. Bismuth Carbolate. Phenol-wismut,* G. $C_6H_5O.Bi(OH)_2$.—Made by a reaction between solutions of bismuth trinitrate and sodium phenolate. A gray, insoluble, inodorous powder, used as an intestinal antiseptic, in *doses* of from eight to fifteen grains (0.5–1.0 Gm.), also as an antiseptic dusting-powder.

Bismuth Phosphate, Soluble. $BiPO_4$. *Bismuthi Phosphas Solubilis. Bisol.*—This is prepared by the melting together of bismuth, sodium hydroxide, and phosphoric acid. It is a white powder easily soluble in water, precipitated by alkalies, acids, or heat, and undergoing spontaneous decomposition when in concentrated solution. It contains 20 per cent. of bismuth, and has been used as an intestinal antiseptic in *choleraic* and other acute *diarrheas* in the *dose* of from three to eight grains (0.2–0.5 Gm.) three times a day.

Bismuth Pyrogallate. *Bismuthi Pyrogallas. Helcosol. Helsosal.* $C_6H_3(OH)_2OBiOH$.—It is a yellowish-green amorphous powder, insoluble in water and alcohol, soluble in acid and alkaline solutions and in the gastro-intestinal juices. According to von Heyden, it represents about 60 per cent. of bismuth oxide. It is said to be non-poisonous, and to be a valuable intestinal antiseptic; if, however, pyrogallic acid should be liberated in the alimentary canal, it might produce disagreeable effects, and the remedy seems to us dangerous. It is asserted that acids liberate pyrogallic acid from this combination, thus contradicting the previous statement. It is incompatible with strong alkalies and alkaline sulphur compounds.

Bismuth Subbenzoate, or *basic bismuth benzoate,* $Bi(C_7H_5O_2)_3Bi(OH)_3$, is a white powder containing 60 to 70 per cent. of Bi_2O_2. It is insoluble in water and used externally as a dry dressing in *syphilitic ulcers.*

Bismuth Tribromphenate. *Bismuthi Tribromphenas, N. N. R.,* 1924. *Tribromphenol-bismuth. Xeroform. Bromphenolis.* $Bi_2O_3(C_6H_2Br_3OH)$.—This is a yellowish-green, insoluble, almost odorless and tasteless powder, which, according to its manufacturer, is a chemical combination of bismuth and tribromphenol, containing about 50 per cent. of bismuth oxide.

It is practically insoluble in water or the ordinary solvents but dissolves readily in diluted hydrochloric acids.

Xeroform has been widely used as a substitute for iodoform in various surgical procedures. The advantages claimed for it are that it is not only practically odorless, but is also non-toxic, and that it exercises a more powerful antiseptic effect. It appears also to possess to a considerable degree the analgesic action, as well as the desiccating and antiseptic effect of iodoform on *wounds.* It has also been employed as a substitute for the salts of bismuth in the treatment of *enteritis, gastric ulcer* and similar conditions. For the latter purpose it is administered in *doses* of from 8 to 15 grains (0.5–1.0 Gm.).

Bismuth Valerate. *Bismuthi Valeras. Valérianate de Bismuth,* Fr. *Wismutvalerianat,* G. $Bi(C_5H_9O_2)_3 2Bi(OH)_3$.—This salt is formed by double decomposition between solutions of bismuth trinitrate and sodium valerate. Bismuth valerate precipitates as a white powder, which is washed with water, and dried with a gentle heat. It has been recommended by Righini in *neuralgia,* and in *gastrodynia.* The *dose* is from half a grain to two grains (0.03–0.13 Gm.), repeated several times a day, and given in the form of pill.

Bistort. *Snakeweed. Bistorte, Couleuvrine,* Fr. *Weissenknöterich, Natterwurz,* G.—This is the rhizome of *Polygonum Bistorta,* L. (Fam. *Polygonaceæ*), a perennial herbaceous plant, growing in Europe and the north of Asia. The rhizome is cylindrical, somewhat flattened, about 1 to 2 cm. in thickness, marked with annular or transverse wrinkles, furnished with numerous rootlets, and folded or bent upon itself, so as to give it the tortuous appearance from which its name was derived. Externally it is dark purplish or blackish-brown. The fracture is nearly smooth, reddish or purple, the taste being astringent. It contains much tannin, some gallic acid and gum, and a large proportion of starch. H. K. Bowman found 21 per cent. of tannin in bistort root. (*A. J. P.,* 1869, 193.) Its medicinal properties are like those of kino, but it is less efficient. It may be employed in powder, decoction, or extract. The *dose* of the powder is twenty to thirty grains (1.3–2.0 Gm.).

Besides the bistort, some other plants belonging to the genus *Polygonum* have been used as medicines. Steenhauer (*Pharm. Weekblad.,* 1919, lvi, 1084) has made careful botanical and chemical examination of several species of *Polygonum,* the most interesting result of which is the finding in a number of them of small amounts of emodin ranging from 0.02 to 0.08 per cent.

Among the species which have been used as medicines are *P. aviculare,* L., or *knot weed,* a mild astringent, formerly employed as a vulnerary and styptic; *P. Persicaria,* L., or *lady's thumb,* of a feebly astringent saline taste, and at one time considered antiseptic; and *P. hydropiper,* L., common *smartweed,* or *water-pepper,* the leaves of which have a burning and biting taste, inflame the skin when rubbed upon it, and are esteemed diuretic, and have been used with asserted success in *amenorrhea* and other *uterine disorders.* Its irritant and also medicinal properties are due to an acid, *polygonic acid,* discovered by C. J. Rademaker. *Polygonum Hydropiper* has been used by Krawkoff (*Russki Vratch,* 1912) in the treatment of *internal hemorrhages*, especially of the uterus. He administered from thirty to forty drops of a fluidextract of the leaves. (*A. J. P.*, xliii, 490.) The *water-pepper* or *smartweed* of this country—*P. acre* H. B. K.—which grows abundantly in moist places, possesses properties similar to those of the European water-pepper, and is occasionally used as a detergent in chronic *ulcers*, and internally in *gravel*. B. Woodward found that the dried plant contains 18 per cent. of tannin, and used a saturated tincture with great advantage in *diarrhea* and *dysentery*, in *doses* of from twenty to sixty minims (1.3–3.75 cc.). Aughey finds that *P. amphibium*, L., is readily cultivated, with a yield of from three to six tons to the acre, that the roots contain 21.75 per cent., the stems 17.1 per cent. of tannic acid, and urges the growth of it for tanning purposes. (*N. R.*, 1876, 75.)

Fagopyrum esculentum Moench (*Polygonum Fagopyrum* L.) is common *buckwheat*. The leaves of this plant have been found by Ed. Schunck to contain a crystallizable coloring principle, identical with the *rutin* or *rutic acid* previously discovered by Weiss in the leaves of the common rue, and probably, with the *ilexanthin* of Moldenhaus, existing in the leaves of *Ilex Aquifolium* L., or the common holly. Buckwheat leaves yielded to Schunck somewhat more than one part of rutin in a thousand.

From *P. cuspidatum* L. has been separated a glucoside, *polygonin*, and also *emodin*. (*P. J.*, Feb., 1896.) The bark of the rhizome has been recommended by Goris and Crète (*Bull. Sci. Pharmacol.*, 1907) as a laxative. The leaves of the *P. dumetorium* are, according to Tunmann (*Ph. Centralh.*, 1906), also practically useful as a laxative.

Various species of the genus *Polygonum* have been used for the production of dye-stuffs; thus indigo is obtained largely in China, Japan, and in some parts of Russia, from the leaves of *P. tinctorium* Ait., and is said also to be yielded by those of *P. aviculare* and *P. barbatum*, L.; while in India, China, and Japan the roots of the *P. cuspidatum* are employed for making a yellow dye. (*J. Chem. S.*, Dec., 1895.)

Bituminol. *Ammonium Sulpho-Bituminolate.*—This substance, manufactured by a German firm, is used as a substitute for ichthyol.

Blennostasine. *Cinchonidine dihydrobromide.*—This forms yellowish, deliquescent crystals and is freely soluble in water. W. F. Campbell (*N. Y. M. J.*, lxiv, 1896) asserted that it is a powerful sedative to the brain and spinal cord, and that in *doses* of from one to four grains (0.065–0.26 Gm.) every hour it is a valuable remedy in nasal and laryngeal hyperesthesia. It has been especially recommended to check excessive secretions in *acute coryza*.

Blood.—As long ago as 1852, Samuel Jackson, of Philadelphia, employed as a tonic the blood of bullocks carefully dried *in vacuo*, giving from five to ten grains (0.32–0.65 Gm.) of it as a *dose*. At one time it was used considerably in Europe, and even drinking fresh bullock's blood was at one time in fashion. Under the name of *Sanguis Bovinus Exsiccatus*, F. E. Stewart introduced defibrinated dried bullock's blood, claiming for it that, by the simple addition of water, bullock's blood can be reproduced minus a small quantity of fibrin. There is no reason for believing that dried blood is more valuable than the more usual ferruginous tonics, if indeed it be of equal value.

The hypodermic injection of blood serum increases the coagulability of the blood and has therefore been used in the treatment of internal *hemorrhages*. There are a number of preparations of blood intended for this use upon the market. *Coagulose* is a desiccated, sterilized horse serum. It is marketed in sealed bulbs each containing 1 grain (0.065 Gm.) of the powder, which is equivalent to 10 cc. of blood serum. This powder is administered by dissolving in sterilized water and injecting the resulting solution hypodermically. *Hemostatic Serum* (*Hemoplastin*) is another preparation of blood intended for use as a coagulant. It occurs as a light, amber-colored liquid. It may be given hypodermically in doses of 1 to 2 cc. (15 to 30 minims). The injection of whole serum is open to the disadvantage that along with the desired coagulating elements there are injected useless and even dangerous protein substances, notably those which give rise to anaphylaxis. In order to obviate this objection there has been placed upon the market under the name of *Coagulen* (introduced by Kocher and Fonio, *K. S. A.*, 1913) an extract which is said to be made from the blood platelets and to contain the thromboplastic substances of the blood mixed with lactose. It occurs as a yellowish, granular powder, freely soluble in water. It is administered generally in the form of a 5 per cent. solution made in physiological salt solution and sterilized by boiling for 2 or 3 minutes. For further information on the subject see under *Thromboplastin*. Curtis (*J. A. M. A.*, 1915, lxiv, p. 332) has found the hypodermic injection of whole human blood to be equally efficacious. He administered subcutaneously from ten to twenty cc.

Blumea. *Blumea lacera* DC. (Fam. *Compositæ.*)—From this plant which is used in India as an insect powder, Dymock has obtained a light yellow volatile oil. It has a sp. gr. of 0.9144 at 26.7° C., and an extraordinary rotating power, 1 mm. turning the ray 66° to the left.

A camphor has been obtained from *Blumea balsamifera* DC. and *B. densiflora* DC., two shrubs indigenous to the Himalayas, by subjecting the entire plants to distillation. That obtained from the last named is known as Ngai camphor (see *Camphora*). *Blumea densiflora* DC., a tall weed, abundant on cut-over forest lands in Savoy, Burma, is claimed to yield a camphor identical with Chinese camphor. (*C. D.*, 1920, p. 425).

Bocconia.—It is probable that various species of this papaveraceous genus have active medicinal properties. *B. arborea* Watson, of Mexico, has been found by Elliott to contain two alkaloids, one of which is probably sanguinarine; and the leaves of other species are used in South America as an abortifacient and purgative. (See Rusby, *Bull. Pharm.*, 1891.) Murrill and Schlotterbeck (*Proc. A. Ph. A.*, 1900, p. 128) examined all parts of *Bocconia cordata*, and isolated protopine, homochelidonine, chelerythrine and sanguinarine.

Bole Armenian. *Bolus Armeniæ. Bolus Rubra. Argilla Ferruginea.*—The term *bolus* or *bole* was formerly applied to various forms of argillaceous earth, differing in color or in place of origin. Such were the *Armenian*, *Lemnian*, and *French boles*, and the *red* and *white boles*. Some of these substances were so highly valued as to be formed into small masses and impressed with a seal, and hence received the name of *terræ sigillatæ*. The only one at present kept in the shops is that called *bole Armenian*, from its resemblance to the substance originally brought from Armenia. It is prepared by trituration and elutriation, from certain native earths existing in different parts of Europe. It is in pieces of various sizes, reddish, soft, and unctuous, adhesive to the tongue, and capable of forming a paste with water. It consists chiefly of a hydrated aluminum silicate with ferric hydrate. The boles were formerly employed as absorbents and astringents in *acidity of the stomach* and in *relaxed bowels*. Bole Armenian is used chiefly as a coloring ingredient in toothpowders.

Bonduc Seeds.—These are seeds derived from *Cæsalpinia Bonducella* Fleming (Fam. *Leguminosæ*), a tree indigenous to India, which are used in India as febrifuge, tonic, and antiperiodic. Heckel and Schlagdenhauffen have discovered in them a bitter principle (*C. R. A. S.*, ciii, 89), probably identical with that previously isolated by Flückiger. (*Pharmacographia*, 2d ed., 212.)

Bone. *Os*, Lat., Fr. *Knochen*, G. *Ossa*, It. *Huesos*, Sp.—Under the name of *Os Ustum*, or *Bone ash*, the Br. Pharmacopœia formerly recognized "the residue of Bones, which have been burned to a white ash in contact with air. Bone ash consists principally of phosphate of calcium, mixed with about 10 per cent. of carbonate of calcium and a little calcium fluoride, silica, and magnesium phosphate." *Br.*, 1867. When bones are subjected to destructive distillation, in closed vessels, they are decomposed without alteration of shape, lose about three-sevenths of their weight, become brittle and are converted into a black substance, containing the inorganic compounds (principally calcium phosphate) of the bone, and constituting the species of animal charcoal called *bone black*. (See *Carbo Animalis.*) The portions which distil over consist of the usual ammoniacal products derived from animal matter, but are especially rich in nitrogenous bases of the pyridine and quinoline series. (See *Ammonii Chloridum.*)

When calcined in open vessels, bones are converted into a white friable substance consisting of the incombustible part, and commonly called *bone earth*, or *bone ash;* and a similar residue is obtained by calcining horns, and is termed *Cornu Ustum*. When bones are treated with boiling water, a small portion of the gelatinous matter is dissolved; but when acted on by water in a Papin's digester, the whole of it is taken up and the inorganic compounds, deprived of their cement, crumble into powder, and become diffused through the solution. When bone is acted on by diluted hydrochloric acid, the inorganic compounds are dissolved, and the bone softens without losing its shape and becomes semitransparent and flexible. The portion remaining unattacked by the acid is the nitrogenous tissue (known as *ossein*), which may be converted into gelatin by boiling with water. The feet of cattle, deprived of the hoofs, boiled with water, furnish a fatty oil, called *neat's-foot oil.*

The bones of different animals, and of the same animal at different ages, vary somewhat in composition. Dry ox bones consist of bone gelatin (cartilage of bone) 33.3, calcium phosphate with a little calcium fluoride 57.35, calcium carbonate 3.85, magnesium phosphate 2.05, and sodium hydroxide with a very little sodium chloride 3.45. Human bones differ somewhat in the proportions of their constituents, and in containing traces of iron and manganese. According to W. Heintz, however, bones exhausted by water, so as to remove the coloring matter of blood, do not contain a trace of iron. Marchand found 1 per cent. of calcium fluoride in human bone. *Calcium bone phosphate* consists of the tribasic phosphate, $Ca_3(PO_4)_2$.

Borago. *Borago officinalis*, L. *Borage. Bourrache*, Fr. *Borasch, Boretsch*, G. (Fam. *Boraginaceæ.*)—A coarse, hairy annual, attaining a height of 1½ to 2 ft., with ovate to oblong leaves and racemes of blue flowers. It is indigenous to Europe and northern Africa. It abounds in mucilage, and the stems and leaves contain potassium nitrate with other salts. To these constituents the plant owes its feeble medicinal properties. An infusion of the leaves and flowers is employed as a demulcent, refrigerant, and gently diaphoretic drink. The expressed juice of the stems and leaves is also given in the *dose* of from two to four fluidounces (60–120 cc.).

Bordisalicylic Acid.—This preparation represents ortho-boric acid in which two hydroxyl groups have been replaced by salicyl radicals, having the formula $OHB(OC_6H_4.COOH)_2$.

It is readily soluble in water, alcohol or glycerin, the solutions being very bitter. It is asserted to be actively germicidal and non-toxic.

Bornyval.—This isovaleric ester of borneol, $CH_3CH(CH_3).CH_2CO.O(C_{10}H_{17})$, $C_{10}H_{17}O.C_5H_9O$, is a limpid fluid with an aromatic odor, suggesting valerian; soluble in alcohol and ether, insoluble in water; boiling under ordinary pressure, at 255° to 260° C., sp. gr. at 20° C. 0.951. Polariscopic rotation: $[a]_D$ 20° = 27° 40′. Bornyval has been highly lauded by a number of physicians in the same class of cases in which valerian is commonly employed, such as *nervous headache, neurasthenia, dysmenorrhea*, and the like. It has also been recommended in the treatment of various forms of *sexual disturbances*, and even in *epilepsy*. The *dose* is four to eight minims (0.25–0.5 cc.) several times a day.

Under the name of *Neo bornyval*, the iso-valerylglycolic ester has been introduced. This is supposed to have the advantage over the older bornyval in that it is less easily affected by the gastric juices and therefore less liable to give rise to disturbances of the stomach. It is used for the same purposes as bornyval and appears in commerce in the form of pearls, each of which contains 0.25 Gm. (3½ gr.). Of these one to three may be given at a *dose*. (See also *Brovalol* and *Gynoval.*)

Borogen.—This is the ethyl ester of boric acid, $B(O.C_2H_5)_3$. It is a liquid, boiling at 120° C., which is decomposed by water into boric acid and alcohol. It is inflammable, burning with a green flame. This substance has been suggested as a local remedy in diseases of the nasal and respiratory mucous membrane, under the belief that it is decomposed into its constituents in the throat and lungs. Borogen is used by inhalation.

Boroglyceride. *Boroglycerinum. Glyceryl borate.*—This substance has been largely employed as a convenient form of obtaining boric acid in a soluble condition. It is made by heating boric acid and glycerin together so as to effect a combination without discoloring the product by overheating. (See *Glyceritum Boroglycerini*, Part I.) James Kennedy (*Nat. Drug.*, 1887, 46) maintained that it is a chemical compound, and not a mere mechanical mixture, as has been supposed;

he gave it the formula $C_3H_5BO_3$, and expressed the reaction in its formation thus:

$$C_3H_5(OH)_3 + H_3BO_3 = C_3H_5BO_3 + 3H_2O$$

The metallic boroglycerides, such as sodium and calcium boroglyceride, are not explained, however, in this case. Aqueous solutions of boroglyceride were formerly used for preserving milk, meat, fruit juices, etc., but are now prohibited by law. Boroglyceride has been largely sold in England under the name of *glacialin*.

Bowdichia. *Bowdichia virgiliodes* H. B. K. (Fam. *Leguminosæ.*)—Under the name of *Alcornoco bark*, or *Sucupira*, the hard, yellow, very bitter bark yielded by this tree is employed in Venezuela and Brazil in *fevers* and *rheumatism*. Petit has found it in a mydriatic alkaloid. (*P. J.*, June, 1885.)

Bragantia. *Bragantia Wallichii* R. Br. (Fam. *Aristolochiaceæ.*)—The roots of this shrub of India contain an alkaloid allied to aristolochine, a soft resin, a resinous acid, and a substance related to dulcite. (*P. J.*, 1894, 231.)

Brassica.—In China the oil of *Brassica sinensis*, or *petsai*, is used for lighting, and is said also to be purgative, and useful in *skin diseases*, while the Japanese employ the yellow oil of *B. Campestris*, L., under the name of *aburana*, for culinary and lighting purposes. (*A. J. P.*, June, 1885.)

Brazil Nuts. *Cream Nuts. Butter Nuts* (not to be confused with the nuts similarly named and obtained from *Juglans cinera* L.). *Para Nuts. Chataigne du Brésil*, Fr. *Paranuss*, G.—These edible nuts imported from Brazil, are the product of *Bertholletia excelsa* Humb. et Bpl. and *B. nobilis* Miers, a large and beautiful tree of the Fam. *Myrtaceæ*, growing over extensive regions in South America. In Brazil an expressed oil is obtained from them, which is said to be used for burning, making ointments, and adulterating copaiba. Cornwinder has found in the kernel of the nut 65.60 per cent. of oil, and 15.31 per cent. of nitrogenous matter. (*P. J.*, Aug., 1873.) Hugo Kühl obtained from the seeds an average fat-content of 62.73 per cent. with 2.59 per cent. of nitrogen, corresponding to 16.20 per cent. of proteins. (*Ph. Ztg.*, 1909, No. 6, 58.)

Brazil Wood.—This is a red-dye wood claimed by Taubert to be derived from *Cæsalpinia Echinata* Lam., a tree indigenous to South America and known to the Brazilians as *Ibira pitanga* or *ymirá pirango*. The part collected represents the heartwood which is gathered in Brazil. It occurs in heavy pieces of variable length and of arm thickness, externally reddish-brown to reddish-black, internally yellowish-red and fine grained. A smaller commercial variety of red-dye wood which has been sold for Brazil wood comes from the West Indies and is yielded chiefly by *C. cristata* L. and *C. bijuga* Sw. The heartwood of *C. Sappan* L., commonly known as *Indian Redwood, Sappan* or *False Sandalwood* is also to be found in commerce as a colorwood. Brazil wood is nearly inodorous, has a slightly sweetish taste, stains the saliva red, and imparts its coloring matter to water. It was formerly used in medicine, but has been abandoned as inert. In pharmacy, it serves to color tinctures, etc., but its chief use is in dyeing. A red lake is prepared from it, and it is an ingredient in a red ink. Its dyeing properties are due to a crystallizable coloring principle, named *brazilin* or *brasilin*, $C_{16}H_{14}O_5$. This, as usually obtained, is of a sulphur-yellow color, which it preserves in the dark, but in the sunlight, to which it is remarkably sensitive, changes to a reddish hue after a few minutes' exposure, and also more slowly in diffused daylight. The principle should, therefore, be kept in perfectly opaque vessels. It is now stated that when absolutely pure it is colorless, and becomes red on exposure to the air. The change is due to the formation of *brasilein*, $C_{16}H_{12}O_5$, which can be prepared from the brasilin by a variety of methods, such as oxidation by nitrous acid, by alcoholic iodine solution, etc. Brasilin is sparingly soluble in water, yielding a sweet and almost colorless solution which is not changed by acids, but is deeply reddened by alkalies. In alcohol and ether it is somewhat more soluble than in water, giving a light yellow solution. Brasilin and hematoxylin (from logwood) are now recognized as related, each being derived from the pyrone nucleus $C_5H_4O_2$, from which the two groups, the xanthone group and the flavone group, are also taken. The coloring principles of most dye-woods are now referred to this source. (Kupe, *Die Chemie der natürlichen Farbstoffe*, Braunschweig, 1900.)

Brea Gum.—This substance, which has been proposed as a substitute for gum arabic, is believed to be derived from *Cæsalpinia præcox* Ruiz et Pavon, a Brazilian tree. It occurs in stalactitic pieces or oval reddish-yellow tears, isolated or agglomerated. It forms with water a viscous, pale reddish-yellow mucilage, of acid reaction, which may be partially decolorized by heating with a few drops of hydrochloric acid. It is said to contain 77 per cent. of arabin.

Algarobilla, the pod of *Cæsalpinia brevifolia*, (Clos.) Benth. which contains over 60 per cent. of tannin and a quantity of *ellagic acid*, is obtained from Chili. (*J. Chem. S.*, 1891, 918.)

Bromal. *Tribromacetaldehyde.* C_2HBr_3O.—This substance is the bromine analogue of chloral which it resembles in its chemical properties, like it existing as an oily, colorless liquid, or, when united with water or alcohol, as a crystalline hydrate or alcoholate. It is prepared by the action of bromine on alcohol; when water is added *bromal hydrate*, $C_2HBr_3O.H_2O$, is formed in rhombic scales fusing at 53.5° C. This was at once suggested as a nerve sedative but did not prove clinically useful. For further information see *U. S. D.*, 20th edition, p. 1286.

Bromalbacid. *Albumen Bromate.*—This substance, whose therapeutic action is said to be identical with that of the bromides, is a *bromated egg albumen*. It is soluble in water and is administered in seven to ten grain (0.5 to 0.6 Gm.) *doses*.

Brometone. *Tribrom Tertiary-Butyl Alcohol. Acetone-Bromoform. N. N. R.* 1924. $CBr_3C(OH)(CH_3).CH_3$.—It is produced by the action of acetone on bromoform in a caustic alkali solution. It occurs in fine, white, prismatic crystals possessing a camphoraceous odor and taste. It is soluble in water and in almost all organic solvents. Brometone is said to have the sedative action of the bromides without the disadvantage of producing bromism. *Dose*, five grains (0.32 Gm.)

Bromine Chloride. *Bromi Chloridum.* BrCl.—This chloride is prepared by passing chlorine gas through bromine, and condensing the vapors which form, by a freezing mixture. It is a reddish-yellow, very mobile and volatile liquid, emitting dark yellow fumes, which have a powerful odor and cause a flow of tears. Its taste is hot and unpleasant. Lebeau doubts the existence of bromine chloride and states that it is a mixture of bromine and chlorine in which the chlorine is simply in solution in bromine. (*Chem. News*, 1906, 241.) Bromine chloride was used by Landolfi, of Naples, internally, in the treatment of *cancer* and as an ingredient in his caustic.

Bromipin. *Brominol. Brominized Sesame Oil. N. N. R.*, 1924.—This preparation, which is the analogue of iodipin, is a bromine addition product of sesame oil containing about ten per cent. of bromine in organic combination. It occurs as a yellow oily liquid with a purely oleaginous taste.

When bromipin is taken by the mouth it passes through the stomach unchanged; but in the intestines a portion of it is broken up by the fat splitting ferments, the bromin, which is liberated, then being absorbed as an inorganic bromide. Apparently, however, a portion of the bromipin is absorbed unchanged and deposited in the fat and lipoid tissues of the body, from which it is slowly given up to the system. Its action, therefore, is slower and more persistent than the ordinary bromides. It may be used as a substitute for the inorganic bromides whenever a prolonged action is desired, as in the treatment of *epilepsy, neurasthenia,* and the like. The dose is ordinarily from one to two fluidrachms (4–8 cc.) which, however, is often exceeded in cases of epilepsy.

Bromochinal. *Bromoquinal. Acid Quinine dibromsalicylate.* $C_{20}H_{24}O_2N_{2}.2(C_6H_2Br_2.OH.COOH)_2$.—Bromochinal occurs in yellow crystals, sparingly soluble in water, alcohol, or ether. According to Von Noorden, in *doses* of nine to twelve grains (0.6–0.78 Gm.) given twice a day, it acts as a feeble antipyretic and is also soporific. (*Ther. Geg.*, v.)

Bromocoll. *Dibromtannin-gelatin.*—This is a yellow, tasteless, odorless powder, composed of 20 per cent. of bromine, 10 per cent. of water, 30 per cent. of gelatin, and 40 per cent. of tannic acid. According to the experiments of Brat (*Th. M.*, 1901, xv, 4), bromocoll is very resistant to gastric juice, but is readily dissolved with decomposition in the intestinal juices. It is claimed that it acts precisely like the bromides, but produces the disagreeable symptoms of bromism only in a very mild degree. Friedländer (*Th. M.*, 1901) determined by experimentation that it depresses the irritability of the psychomotor centers. Meier (*Med. Klin.*, 1906) has found that the subcutaneous injection of bromocoll is useful, at least in the lower animals in strychnine poisoning and in *tetanus.* The *dose* is thirty to seventy-five grains (2–5 Gm.) a day.

Bromoform. *Bromoformum. U. S. IX. Tribrommethane, Formyl Tribromide; Bromo-formium* P. G.; *Bromoform, Tribrommethan,* G.; *Bromoformo,* Sp.—"A liquid consisting of about 96 per cent., by weight, of $CHBr_3$ (252.77) and about 4 per cent. of dehydrated alcohol. Preserve it in glass-stoppered bottles, in a cool place, protected from light." *U. S. IX.*

This compound, the analogue of chloroform, is prepared by methods similar to those used for the manufacture of chloroform.

Bromoform is officially described as "a heavy, transparent, colorless, mobile liquid, with an ethereal odor, and a penetrating, sweet taste, resembling that of chloroform. Bromoform is slightly soluble in water; miscible with alcohol, chloroform, ether, benzene, petroleum benzin or fixed or volatile oils. Specific gravity: 2.595 to 2.620 at 25° C. Bromoform is slightly volatile at ordinary temperatures. Bromoform is not inflammable, but when vaporized by the application of heat, its vapors may be ignited. Evaporate 10 mils of Bromoform from a porcelain dish on a water bath; not more than 0.006 Gm. of residue remains after drying at 100° C. Shake 10 mils of Bromoform with 10 mils of distilled water, and allow the liquids to separate completely. The water removed from the layer of Bromoform is neutral to litmus (*free acid*); 5-mil portions, tested separately, show not more than a slight opalescence on the addition of a few drops of silver nitrate T.S. (*bromides or brominated compounds*), and no blue color on the addition of a few drops each of potassium iodide T.S. and of starch T.S. (*free bromine*). Agitate 10 mils of Bromoform with 10 mils of distilled water, and allow the liquids to separate completely. Remove the aqueous layer from the Bromoform, treat it with an excess of ammonia water, and then with a solution of iodine and ammonium iodide, until the black precipitate of nitrogen iodide, which sometimes forms, slowly disappears; it does not become milky in appearance, due to the separation of iodoform, recognizable by its odor (*acetone*)." *U. S. IX.*

At one time bromoform was suggested as a general anesthetic. Experience has shown, however, that although bromoform produces a rapid narcosis when inhaled, its employment is attended with excessive danger. When taken internally by the mouth it is capable of acting like the older bromides, but it has no advantages and is a much more dangerous remedy. In the recorded cases of poisoning by it the symptoms have been pallor, titubation, dilatation of the pupils, coma, heart failure and collapse.

In the latter part of the last century bromoform was brought forward as a remedy for *whooping-cough.* It enjoyed for some time a considerable popularity but has been largely abandoned because of its dangerous effects. Three drops are said to have produced very serious symptoms in a child of four years, and two drops in one of fifteen months. For cases of poisoning, see *Cb. I. M.*, No. 50, 1902; *B. M. J.*, vol. i, 1900; *T. G.;* 1903; *Ap. Ztg.*, July, 1898, March 24, 1900. A saturated aqueous solution of bromoform (containing about 0.3 per cent.) has been recommended by Desesquell (*B. M.*, 1907) for the relief of *sea-sickness,* in tablespoonful doses.

Dose, one to five minims (0.06 to 0.3 cc.), best administered in capsules, dropped on sugar, or mixed with an equal quantity of olive oil and emulsified.

Bromolein is a compound which contains bromine in combination with the unsaturated fatty oleins of the almond oil for their saturation. This substance, introduced by Coronedi and Marchetti (*Settimana med.*, 1899, liii), is a yellow, clear, oily liquid, containing 20 per cent. of bromine. The *dose* of bromolein is from one-half to one fluidrachm (1.9–3.9 cc.).

Bromophenol.—*Phenol Monobromate. Orthomonobromphenol,* $C_6H_4Br.OH$, is obtained by the combination of bromine and phenol at a temperature of 150°–180° C. It is a dark yellow, oily, strong smelling fluid, soluble in alcohol and ether, slightly in water. It is used as a two per cent. ointment in the treatment of *erysipelas,* also to disinfect the sputum. See also *Tribromphenol.*)

Bromophor.—This preparation, which is stated to be the *dibrom-ricinoleate* is recommended as an external application in *pruritus* and *erysipelas*. According to Linke, however (*Ther. Neuheiten*, March, 1910), its use in *erysipelas* is not to be recommended because of its intense irritation of the skin.

Bromotan.—*Bromotannin-methylene Urea* is a light brown, odorless and tasteless powder, insoluble in water. It has been employed by Rockstroth (*Th. M.*, 1906) as a dusting powder in the treatment of moist *eczema*.

Bromural. *N. N. R.* 1924. *Alpha-monobromisovaleryl Urea.* $(CH_3)_2CH.CH.Br.CO.NH.CO.NH_2$.—This occurs as white, almost tasteless, needle-like crystals, soluble in hot water, ether, and alcohol, but only sparingly in cold water. Its melting point is 147°–149° C. Bromural has been widely employed as a general nerve sedative and as a mild somnifacient. Eeckhout (*A. E. P. P.*, lvii, p. 338) administered to a rabbit 0.1 Gm. daily for two weeks with no apparent disturbance of the health. Sollmann and Hatcher (*J. A. M. A.*, 1908, li, p. 487), however, have found that in cats the relation of the sleep-producing to the fatal dose of bromural was practically the same as that of chloral, and that the effects of bromural come on even more quickly than those of chloral hydrate and last for a comparatively short time. According to Eeckhout, the action is similar to that of the bromides. Takeda (*A. I. P. T.*, 1911, xxi, p. 203) has, however, shown that only a small percentage of the molecule is decomposed in the body, and believes that the drug acts as bromural, not as its constituent parts.

While it is often of service in the milder types of *insomnia*, in severer cases bromural is an uncertain hypnotic. Its most important use is as a general nerve sedative, for which purpose it appears to combine the sedative actions of both the bromides and valerian. Like the bromides it has a certain amount of anodyne power in *neuralgic* pains and like valerian is useful to control the various *hysterical* manifestations. It appears, also, according to the experience of Ferrata and Golinelli (*Gaz. Internaz.*, 1908, No. 13), to exercise the motor sedative effect of the bromides in *epilepsy*. It has also been recommended as a sedative in *asthma*, in *whooping cough*, and for *sea-sickness*. The *dose* of bromural, as a sedative, is from five to ten grains (0.32–0.65 Gm.) several times a day, as may be required, as a hypnotic from ten to twenty grains (0.65–1.3 Gm.) should be administered immediately before retiring. It may be prescribed either in the form of a tablet or as a powder enclosed in a capsule.

Brovalol. *Brom-iso-valeric Acid Borneol Ester. Bornyl Brom-valerate. Valisan.* $CH_3CH(CH_3).CHBr.CO.O.(C_{10}H_{17})$.—A colorless, oily liquid, having a slightly aromatic odor, prepared by esterification of borneol with brom-isovaleric acid or its derivatives. It contains 25.2 per cent. bromine. Brovalol has been used as a nerve sedative in the same type of cases in which valerian is employed. It appears on the market in "pearls," each of which contains four grains (0.25 Gm.). The *dose* is one to three pearls, repeated as required.

Burgundy Pitch. *Pix Burgundica. Poix de Bourgogne, Poix des Vosges, Poix jaune,* Fr. Cod. *Poix blanche,* Fr. *Burgundisches Pech, Burgunder Harz, Wasserharz,* G. *Pece di Borgogna,* It. *Pez de Borgoña,* Sp.—Under the name of *Pix Burgundica* was formerly recognized both by the British (1898) and by the U. S. (1890) Pharmacopœias, "the resinous exudation obtained from the stem of the *Picea excelsa* Link., melted and strained." *Br.*, 1898.

Picea abies (L.) Karst. or *P. excelsa* Link. (Fam. *Pinaceæ*), commonly known as *Norway spruce*, is a lofty tree, rising sometimes one hundred and fifty feet in height, with a trunk from three to five feet in diameter. The leaves, standing thickly upon the branches, are short, obscurely four-cornered, often curved, of a dusky green color, and shining on the upper surface. The male aments are purple and axillary, the female of the same color, but usually terminal. The fruit is in pendent, purple, nearly cylindrical strobiles, the scales of which are oval, pointed, and ragged at the edges. This tree is a native of Europe and Northern Asia, and is cultivated in the United States as a shade tree. Commercially Burgundy pitch is derived not only from the Norway spruce, but also from the *Abies picea* or European silver fir tree. To obtain the *pitch*, portions of the bark are removed so as to lay bare the wood, or perpendicular grooved channels are cut, and the flakes of concrete resinous matter which form upon the surface of the wound, having been detached by iron instruments, are melted with water in large boilers, and then strained through coarse cloths. It is called Burgundy pitch from the province of that name in the east of France, although whether it was ever produced in that province is uncertain. It is chiefly collected in Finland, the Schwarzwald, Austria, and the Bernese Alps. A *factitious Burgundy pitch* is made by melting together common pitch, rosin, and turpentine, and agitating the mixture with water, which gives it the requisite yellow color. Its odor is different from that of the genuine. Hanbury gives as a test of true Burgundy pitch that it is almost entirely soluble in twice its weight of glacial acetic acid while the factitious article similarly treated forms a turbid mixture quickly separating into a thick oily liquid above and a bright solution below.

The resinous exudation from *Pinus sylvestris* is sometimes offered as Burgundy pitch, but Hirschsohn (*Ph. Z. R.*, xxiv) states that it is possible to distinguish the resin of *Picea excelsa* by its being only partially soluble in ether, chloroform, and solutions of salts of ammonium, sodium carbonate, and borax, which dissolve completely the resin of *Pinus sylvestris*. The resin of *Picea excelsa* is also precipitated by the addition of water from its sulphuric acid solution in red violet flakes, while *Pinus sylvestris* resin precipitates white.

As brought to this country, Burgundy pitch is generally mixed with impurities, which require that it should be melted and strained before being used. In its pure state, according to the U. S. P., 1890, it is "hard, yet gradually taking the form of the vessel in which it is kept; brittle, with a shining, conchoidal fracture, opaque or translucent, reddish-brown or yellowish-brown, odor agreeably terebinthinate; taste aromatic, sweetish, not bitter. It is almost entirely soluble in glacial acetic acid, or in boiling alcohol, and partly soluble in cold alcohol." *U. S.*, 1890. It is very fusible, and at the heat of the body softens and becomes adhesive. It differs from turpentine in containing a smaller proportion of volatile oil. Instead of the sylvic acid of ordinary rosin, it contains an isomeric acid, which has been called *pimaric acid*, melting at 148° to 149° C., difficultly soluble in cold but readily soluble in boiling alcohol, and also soluble in ether. According to Perrenoud, its formula is $C_{40}H_{54}O_4$, but Vesterberg (*B. Chem. G.*, 1885, 1886 and 1887) showed it to be a mixture, and prepared from it two isomeric crystalline acids, a *dextropimaric acid,* and a *lævopimaric acid,* both of the formula $C_{20}H_{30}O_2$; with these is mixed a varying amount of an amorphous resin acid known as *pinic acid.*

When applied to the skin, as a plaster, Burgundy pitch acts as a gentle rubefacient, producing a slight inflammation without separating the cuticle. Sometimes it excites a papillary or vesicular eruption, and we have known it to act as a violent irritant, giving rise to severe pain, swelling, and redness, followed by vesication and even ulceration. It is used chiefly in chronic *rheumatic pains,* and in chronic affections of the chest or abdomen, which call for a gentle but long-continued revulsion of the skin.

Burra Gookeroo or *Burra Gokhroo.*—Under this name, in India, the fruit and sometimes the whole plant of *Tribulus terrestris* L., an annual herb belonging to the *Zygophyllaceæ,* is used as a diuretic and aphrodisiac. The carpels have been commended in London as a remedy in *nocturnal emissions; dose* of fluidextract, from twenty minims to one fluidrachm (1.3–3.75 cc.). The fruits of an allied species, *T. alatus* Delile are used for similar purposes.

Butesin. *N. N. R.* 1924. *Normal Butyl-para-aminobenzoate.* $C_6H_4NH_2.COO(C_4H_9)$.—This is a white, odorless, tasteless powder, soluble in alcohol, but almost insoluble in water. It is a local anesthetic, similar in action to benzocaine. It is used chiefly as dusting-powder but also as ointment or troches.

Butesin Picrate has been used for somewhat similar purposes especially in ointments.

Butyn. *N. N. R.* 1924. Paraminobenzoyl-gammadinormalbutyl-aminopropanol sulphate $[NH_2.C_6H_4.COO(CH_2)_3.N(C_4H_9)_2]_2.H_2SO_4$.—This substance, which is chemically related to procaine, occurs as a colorless, odorless, solid hygroscopic soluble in less than its own weight of water. From its aqueous solution the free base is precipitated by alkalies as a colorless oil.

The reports of Bulson (*J. A. M. A.*, 1922, lxxviii, p. 343) and of Schmitz and Loevenhart (*J. P. Ex. T.*, 1924, xxiv, 167) indicate that butyn is a more active local anesthetic than either cocaine or procaine. It is, however, distinctly more toxic than procaine. It is recommended as a local anesthetic for the eye in strengths of about 2 per cent. It does not affect the pupil nor the local circulation.

Buxus. *Buxus sempervirens* L. *Evergreen Box.* (Fam. *Buxaceæ.*)—This evergreen shrub is too well known to require description. Though much cultivated in this country as an ornamental plant, it is a native of Europe and Western Asia. The wood is considered diaphoretic in its native countries, and is used in decoction in *rheumatism, secondary syphilis,* etc. The leaves, which have a peculiar odor and a bitter and disagreeable taste, are said to be purgative in the *dose* of a drachm. A volatile oil distilled from the wood has been given in *epilepsy.* A tincture formerly enjoyed some reputation as an antiperiodic. (Mérat and De Lens.) The alkaloid *buxine,* which has been discovered in the leaves of this tree, is identical with the bebeerine of nectandra bark. (See *Bebeeru.*) Pavia obtained a second alkaloid, which was investigated by Pavesi and Rotondi. (*Jahresberichte,* 1874, 903.) They named it *parabuxine,* and ascribe to it the formula $C_{24}H_{48}N_2O$. Barbaglia (*A. J. P.*, 1885, 145) described still another alkaloid, *parabuxinidine.* It crystallizes in thin, colorless prisms, is insoluble in water, soluble in ether, freely soluble in alcohol, and colors turmeric paper deep red.

Caapi.—According to Rusby the root and rhizome of the *Banisteria Caapi* Spruce (Fam. *Malpighaceæ*), a woody vine growing along the Amazon, is used as a ceremonial drink by the natives to stimulate fortitude during ordeals. The experiences of Gordon MacCreagh indicate that the drug is a powerful mental and motor stimulant. According to Dr. O. E. White the same drug is known in Bolivia under the name of *ayahuasca.* (See Rusby, *J. A. Ph. A.*, 1924, xiii, 98.)

Cabbage-Tree Bark. *Ecorce de Geoffre,* Fr. *Kohlbaumrinde, Wurmrinde,* G.—The bark of *Vouacapoua inermis,* Sw. (*Andria inermis* H. B. K.) This is a leguminous tree, a native of Jamaica, and other West India islands. The bark, which is the part used, is in long pieces, thick, fibrous, externally of a brownish-ash color, scaly, and covered with lichens, internally yellowish, of a resinous fracture, a disagreeable odor, and a sweetish, mucilaginous bitterish taste. The cabbage tree contains an alkaloid which has been variously named *jamaicine, andirine, ratanhine* and *surinamine,* but which appears to be *methyl-tyrosine* (see Johnson and Nicolet, *Am. Chem. J.*, 1912, xlvii, p. 459). Two grains (0.13 Gm.) of it produced violent purging in pigeons.

Cabbage-tree bark is cathartic, and, in large doses, prone to occasion vomiting, fever, and delirium. It is said that these effects are more liable to result if cold water be drunk during its operation, and may be relieved by the use of warm water, castor oil, or a vegetable acid. In the West Indies it is esteemed a powerful vermifuge, and is much employed for expelling *lumbrici;* but it is dangerous if incautiously administered, and instances of death from its use have occurred. It is almost unknown in this country. The usual form of administration is that of decoction, though the medicine is also given in powder, syrup, and extract. The *dose* of the powder is from twenty to thirty grains (1.3–2.0 Gm.); of the extract three grains (0.2 Gm.).

On the continent of Europe the bark of *Vouacapoua retusa* Poir, which grows in Surinam, has also been used. It is considered more powerfully vermifuge and less liable to produce injurious effects. It has a grayish epidermis, beneath which it is reddish-brown, laminated, compact, and very tenacious, and when cut transversely, exhibits a shining and variegated surface. In the dried state it is inodorous, but has an austere bitter taste. The powder is of a pale cinnamon color.

Theodore Peckoldt says of the wood of an allied species, *Vouacapoua Anthelmia* (Vell.) O. Ktze, that the workmen engaged in sawing it are prone to be affected with inflammation of the eyes, constriction of the throat, excessive thirst, a bitter, burning taste, a troublesome itching over the body, and sometimes eruptions on the skin. He obtained a yellowish-brown coloring matter which he called *andirin.* This name has also been given to a glucoside said to have been found in *Vouacapoua inermis,* (see *A. J. P.*, 1885, 558), and a peculiar resin of a bitter, acrid taste, to which is due the irritating properties of the sawdust.

Cacodylic Acid. *Acidum Cacodylicum.* $AsO(CH_3)_2OH$.—Cacodylic Acid is a deliquescent, colorless, crystalline, and odorless solid, which is, however, chemically quite stable. It is very soluble in water with an acid reaction. Cacodylic Acid is *dimethyl-arsenic acid;* that is, arsenic acid in which two hydroxyl radicles have been replaced by two methyl radicles. In the metallic cacodylates the hydrogen in the remaining hydroxyl is replaced by the base; sodium cacodylate is, therefore, $As(CH_3)_2OONa$. The physiological and medicinal properties of Cacodylic Acid are the same as those of sodium cacodylate. (See Part I.) It is, however, rarely used except in the form of one of its salts.

The following preparations have been suggested:

Calcium Cacodylate. Calcii Cacodylas N. N. R. 1924. $[(CH_3)_2AsO_2]_2Ca$ + aq.—A white powder, soluble in water. It contains from 44 to 48 per cent. of arsenic in the form of cacodylic acid and is free from arsenates, arsenites and other arsenic containing compounds. *Dose,* one-half to one grain (0.03–0.06 Gm.).

Guaiacol Cacodylate.—A reddish-white crystalline mass, which dissolves in alcohol and parts with cacodylic acid in the presence of water. Dissolved in oil it has been employed hypodermically in *tuberculosis.* From one to one and a half grains (0.065–0.096 Gm.) may be exhibited every other day.

Ferric Cacodylate. Iron Cacodylate. Ferri Cacodylas. Ferricodil.—Ferric cacodylate is a grayish-brown powder with an apple-like odor, soluble in 16 parts of water, more soluble in hot water but less so in alcohol. It contains from 40 to 45 per cent. of arsenic in the form of cacodylic acid. This salt has been specially recommended by Gilbert and Lereboullet (*R. T.,* 1900, No. 16) for hypodermic use in the treatment of *leukemia, lymphadenoma,* and other serious *anemias.* Montgomery (*J. A. M. A.,* 1916, lxvi, p. 491) calls attention to the fact that iron cacodylate even when given hypodermically may cause the disagreeable garlicky odor of the breath. It is too irritant to be used in concentrated solution, but as much as one grain (0.065 Gm.) dissolved in half a fluidrachm (1.8 cc.) of water may be injected daily. The *dose* by mouth is one to two grains (0.06–0.12 Gm.) several times a day, hypodermically one-sixth to one-half grain (0.01–0.03 Gm.) may be given once a day.

Lithium Cacodylate. Lithii Cacodylas. $(CH_3)_2AsO_2Li$ + aq.—A light, white powder, soluble in water. *Dose,* one-half to two grains (0.032–0.13 Gm.).

Magnesium Cacodylate. Magnesii Cacodylas. $[(CH_3)_2AsO_2]_2Mg$ +aq.—A white powder, soluble in water. *Dose,* one-half to two grains (0.032–0.13 Gm.).

Mercury Cacodylate. Hydrargyri Cacodylas. $[(CH_3)_2AsO_2]_2Hg$.—White crystals freely dissolving in water, but sparingly soluble in alcohol. The solution of pure mercury cacodylate is unstable and locally irritant, and there has been introduced, under the same name, a double salt formed with sodium chloride. Mercury cacodylate is used in the treatment of *syphilis.* Its supposed advantage is in the belief that the cacodylic acid exercises some direct remedial action in syphilis, and will therefore enhance the effects of the mercury. It is generally administered hypodermically in the form of a 5 per cent. solution of which eight to fifteen minims (0.5–0.9 cc.) may be given daily, representing one-third to three-fourths of a grain (0.025–0.05 Gm.).

Potassium Cacodylate. Potassii Cacodylas. $(CH_3)_2AsO_2K$ + aq.—Small, white crystals, soluble in water, but sparingly soluble in alcohol and insoluble in ether.

For description of salts of this acid with quinine and strychnine see *Quinine Cadodylate* and *Strychnine Cacodylate.*

Cacur.—This is a small gourd which, while still unripe, is used by the Kaffirs as an emetic, and which, according to Oliver, is yielded by the *Cucumis myriocarpus* Naud. (Fam. *Cucurbitaceæ.*) G. A. Atkinson (*A. J. P.,* 1887) obtained from it a neutral resinous body, *myriocarpin,* and found that twenty grains (1.3 Gm.) of the fresh pulp produced in man nausea and slight purgation. (*Ed. M. J.,* July, 1886.)

Cadmium. *Kadmium,* G. Cd = 112.4.—This metal is associated with zinc in its ores, occurring principally as *greenockite* (CdS), a yellowish incrustation upon *zinc blende* (ZnS), and, being more volatile than that metal, comes over with the first portions of the zinc in the process for obtaining it. (See *Zincum.*) The cadmium is separated by dissolving the alloy metals in diluted sulphuric acid, precipitating the sulphate by hydrogen sulphide, treating the precipitates with hydrochloric acid, and again precipitating with ammonium carbonate. The cadmium carbonate thus obtained, after being washed and dried, is mixed with charcoal, and exposed to a dull red heat in an earthen retort, when the reduced metal distils over.

Cadmium is a white metal, resembling tin, but somewhat heavier and more tenacious. Like that metal, it crackles when bent. Its sp. gr. is 8.7, melting point from 316° to 320° C. It is little affected by the air, but, when heated, combines with an atom of oxygen to form the oxide, CdO, which forms salts with the acids. The soluble cadmium salts give white precipitates with hydroxides, carbonates or phosphates; and yellow precipitates with soluble sulphides or chromates; with zinc metallic cadmium is precipitated.

Medicinal Uses of Cadmium.—It is probable that the insoluble preparations of cadmium are not actively poisonous, but it is certain that the soluble preparations are corrosive poisons, causing in overdoses giddiness, vomiting, purging, slowing of the pulse and respiration, loss of consciousness, and spasm. In three cases in which the carbonate is said to have been inhaled, the chief symptoms were constriction of the throat, embarrassed respiration, vomiting and purging, giddiness, and painful spasms. (*Ann. Thér.,* 1859.) For a case of poisoning by the *bromide,* see *B. M. S. J.,* 1876.

It has been shown by Athanasius and Langlois (*C. R. S. B.,* 1895, ii,) that the soluble salts of cadmium arrest lactic fermentation. When given hypodermically they produce symptoms similar to those caused by zinc salts, than which, however, they are less powerful; the symptoms are rapid loss of voluntary motion with persistence of the reflexes and pronounced cardiac depression. In the higher animals there is destruction of the red blood corpuscles.

Cadmium Iodide. Cadmii Iodidum. (CdI_2.) *Cadmium Iodatum. Iodidum Cadmicum. Iodure de Cadmium,* Fr. *Jodcadmium, Kadmiumjodür,* G.—Cadmium iodide may be prepared by mixing iodine and filings of cadmium in a moist state, or by dissolving the metal in hydriodic acid, or by double decomposition between potassium iodide and cadmium sulphate. It is soluble in water and alcohol, and may be crystallized from either solution, in large, white, transparent crystals, in the form of six-sided tables, of a pearly luster. These are permanent in the air, melt at 404° C., forming an amber-colored liquid, and give off violet vapors at a dull red heat. The salt is freely soluble in water and in alcohol, and the solution has an acid reaction.

Cadmium iodide was introduced by A. B. Garrod as an external remedy in the treatment of *scrofulous glands, nodes, chronic inflammation of joints,* and various *cutaneous diseases.* The ointment, which was formerly official in the British Pharmacopœia under the name of *Unguentum Cadmii Iodidi* (sixty-two grains to one ounce of simple ointment), is soft, white, and said to readily yield its iodine to absorption when applied by persistent gentle friction.

Cadmium Nitrate.—H. C. Demming recommends a solution of this salt as an insecticide. (*Proc. Penna. Pharm. Assoc.*, 1909, 240.)

Cadmium Salicylate. Cadmii Salicylas. $Cd(C_7H_5O_3)_2 + H_2O$.—Prepared by acting on cadmium oxide with salicylic acid. It is colorless and crystalline, soluble in 24 parts of boiling water, and in alcohol, ether, and glycerin. It is used as an antiseptic.

Cadmium Sulphate. Cadmii Sulphas. Cadmium Sulfuricum. Sulfas Cadmicus. Sulfate de Cadmium, Fr. *Schwefelsaures Cadmiumoxyd, Kadmiumsulfat,* G. $CdSO_4.4H_2O$.—Cadmium sulphate crystallizes in oblique prisms with rhomboidal bases, which are transparent and colorless, and resemble those of zinc sulphate. The ordinary crystals of cadmium sulphate have the formula $CdSO_4.8H_2O$, and, at very low temperature, $CdSO_4.7H_2O$. They have an astringent, slightly acidulous, and harsh taste, effloresce on exposure to the air, and are very soluble in water. The solution, even though acidulated, gives with hydrogen sulphide a yellow precipitate, becoming orange-yellow, of cadmium sulphide, which is dissolved by strong hydrochloric acid, but is insoluble in solutions of potassium hydroxide or ammonia, and is thus readily distinguished from arsenic sulphide. Zinc precipitates cadmium in the metallic state from the solution. Cadmium suspended in a solution of copper sulphate precipitates that metal, leaving cadmium sulphate in solution, and this has been proposed as a method of obtaining the salt. For method of manufacture and tests of purity of cadmium sulphate, see *U. S. D.*, 19th edition, p. 1425.

Cadmium sulphate has been used as a local astringent and stimulant in *diseases of the eye* and in *gonorrhea.* It is employed either in solution, from half a grain to four grains to the fluidounce of distilled water, or in ointment, twelve grains to the ounce of simple ointment.

Cæsium. $Cs = 132.81$.—The physiological effect of cæsium chloride has been investigated by S. Botkin (*In. Dis.*, St. Petersburg, 1888.) He finds that it increases the blood pressure and retards the heart movements to a slight extent. Laufenauer (*Th. M.*, 1889) states that cæsium bromide theoretically ought to, and practically does, control *epilepsy* better than do the ordinary bromides. The physiological and medicinal properties of *rubidium* have also been studied by these investigators and found to resemble those of cæsium.

Cæsium and Ammonium Bromide ($CsBr + 3NH_4Br$).—A white, crystalline powder, readily soluble in water, given in *doses* of fifteen to forty-five grains (1–3 Gm.) in the treatment of *epilepsy.*

Caffeine Arsenate.—A white powder soluble in hot water, used in *neuralgia* and as a cholagogue in certain forms of *jaundice. Dose,* one-sixtieth to one-thirtieth of a grain (0.001–0.002 Gm.).

Caffeine Hydrobromide. *Caffeine Bromide. Caffeinæ Hydrobromidum. Caffeinum Hydrobromicum. Koffeinhydrobromat, Bromwasserstoffsaures Koffein,* G. $C_8H_{10}O_2N_4.HBr + 2H_2O$.—In the form of transparent crystals, readily decomposed but more stable than the hydrochloride. When heated to 110° C. the hydrobromic acid is driven off. Its aqueous solution is very unstable. Used for *nervous headaches* and as a diuretic, injected subcutaneously. *Dose,* one to three grains (0.06–0.2 Gm.).

Caffeine Hydrochloride. *Caffeinæ Hydrochloridum. Caffeinum Hydrochloricum. Koffein-hydrochlorat, Salzsaures Koffein,* G. $C_8H_{10}O_2N_4HCl + 2H_2O$.—Large, colorless, prismatic crystals, readily decomposed by washing with alcohol or water or by long exposure to the air, when water and chlorine are lost. If heated to 110° C. the chlorine is driven off. The normal salt contains about 73 per cent. of caffeine. *Dose,* one to three grains (0.06–0.2 Gm.).

Caffeine Nitrate. *Caffeinæ Nitras. Caffeinum Nitricum. Koffeinnitrat, Salpetersaures Koffein,* G. $C_8H_{10}O_2N_4.HNO_3 + H_2O$.—In the form of yellowish crystals, quickly decomposed by water and alcohol. The salt contains about 70 per cent. of caffeine and all the nitric acid is driven off at a temperature of 100° C. *Dose,* one to three grains (0.06–0.2 Gm.).

Caffeine Salicylate. $C_8H_{10}O_2N_4.C_7H_6O_3$.—White, crystalline masses, soluble in water and alcohol, its solutions, however, undergoing rapid decomposition. It is intended to produce the combined action of its constituents, but the proportion of salicylic acid is too small to exert any perceptible effect. The *dose* is two to four grains (0.12–0.25 Gm.).

Caffeine Sulphate. *Caffeine Sulphas. Caffeinum Sulfuricum. Koffeinsulfat, Schwefelsaures Koffein,* G. $C_8H_{10}O_2N_4.H_2SO_4$.—The sulphate may be made by dissolving caffeine in alcohol, containing more sulphuric acid than is needed to make the salt, and setting the solution aside to crystallize. It is decomposed by alcohol or water alone. The salt contains about 66 per cent. of caffeine. It is used for the same purposes and in the same doses as caffeine. *Dose,* one to three grains (0.06–0.2 Gm.).

Caffeine Triiodide. *Caffeine diodo-hydriodide. Diiodocaffeine.* $(C_8H_{10}O_2N_4.I_2HI)_2 + 3H_2O$.—This occurs in dark green, prismatic crystals soluble in alcohol and water with decomposition. It is used in place of potassium iodide, in the treatment of *rheumatism.* The *dose* is from two to four grains (0.13–0.26 Gm.). It is incompatible with acids.

Cahinca. *David's Root. Radix Caincæ. Cainca,* Fr. *Kainkawurzel,* G.—This medicine attracted at one time considerable attention. The name of *Cahinca* or *cainca* was adopted from the language of the Brazilian Indians. The Portuguese of Brazil call the medicine *raiz pretta,* or *black root.* It is derived from the *Chiococca racemosa* L. (Fam.

Rubiaceæ), and perhaps other species of the genus. The virtues of the root reside almost exclusively in its bark. Four distinct principles were discovered in it by Pelletier and Caventou—(1) a crystallizable, bitter substance, believed to be the active principle and called *cahincic acid*, $C_{40}H_{64}O_{18}$ (also called *caïncic acid* and *caïncin*); (2) a green, fatty matter of a nauseous odor; (3) a yellow coloring matter; and (4) a colored viscid substance. Rochleder and Hlasiwetz found also caffetannic acid. Cahincic acid when treated with diluted hydrochloric acid is decomposed into glucose and other products, of which is obtained at first *chiococcaic acid*, $C_{28}H_{42}O_7$ (thought by some to be identical with *quinovic acid*), and later, by boiling with alcoholic hydrochloric acid, *caïncetin*, $C_{22}H_{34}O_3$.

Cahinca is tonic, diuretic, purgative, emetic, and is capable of producing serious gastro-intestinal irritation. In Brazil it has long been used by the natives as a remedy for the *bites of serpents*, also in *rheumatism* and in *dropsy*. *Dose*, of the powdered bark, from twenty grains to a drachm (1.3–3.9 Gm.); of the aqueous or spirituous extract, from ten to twenty grains (0.65–1.3 Gm.). For further information see *U. S. D.*, 20th ed., p. 1295.

Calamus. *U. S. VIII. Sweet Flag. Radix Calami Aromatici. Radix Acori. Sweet Sedge* (*Cane, Rush, Root* or *Myrtle*). *Myrtle-flag* (*Grass* or *Sedge*). *Acore Vrai*, Fr. Cod. *Acore Odorant*, Fr. *Rhizoma Calami*, P. G. *Kalmus, Kalmuswurzel*, G. *Calamo aromatico*, It., sp.—"The unpeeled, dried rhizome of *Acorus Calamus* Linné (Fam. *Araceæ*)." *U. S. VIII.* The sweet flag, or Calamus, has a perennial, horizontal, jointed, somewhat compressed rhizome, from half an inch to an inch thick, sometimes several feet in length, sending off numerous round and yellowish or whitish roots from its lower surface, and groups of brown fibers resembling coarse hair from its joints, internally white and spongy, externally whitish with a tinge of green, variegated with triangular leaf scars of light brown and rose color. The leaves are all radical, sheathing at the base, very long and sword-shaped. The scape or flower stem resembles the leaves, but is longer, and from one side, near the middle of its length, sends out a cylindrical spadix, tapering at each end, about two inches in length, and crowded with greenish-yellow flowers. The fruit is an oblong capsule, divided into three locules, and containing numerous oval seeds.

This plant grows abundantly in the wet places throughout the United States, Europe, Western and Southern Asia. The leaves as well as the rhizome have an aromatic odor; but the rhizome only is employed. It should be collected late in the autumn, or in the spring. After removal from the ground, the rhizomes are washed, freed from their roots, and dried with a moderate heat. Most of the commercial article has the outer portions of the cortex removed. By drying they lose nearly one-half their diameter, but are improved in odor and taste.

Calamus was officially described as follows: "Rhizome 1 to 2 cm. thick, usually in longitudinally split pieces of various lengths; when entire cylindraceous and somewhat vertically flattened, externally reddish-brown, somewhat annulate from remnants of leaf-sheaths; upper surface with triangular leaf-scars, the lower surface with circular pitted scars of roots; fracture short, showing numerous oil cells and scattered fibrovascular bundles, the latter crowded within the endodermis; odor aromatic; taste pungent and bitter." *U. S. VIII.*

The odor of Calamus is strong and fragrant; its taste warm, bitterish, pungent, and aromatic. From 100 parts of the fresh root of the European plant, Trommsdorf obtained 0.1 of volatile oil. The volatile oil is contained in all portions of the plant, the leaves yielding to distillation, according to the analysis of Schimmel & Co., 0.2 per cent., the fresh root 1.5 to 3.5 per cent., the dried German root 0.8, and the Japan root as much as 5 per cent.

The oil is at first yellow, but ultimately becomes red, and has the odor and taste of Calamus. Kurbatow (*Ann. Ch. Ph.*, vol. clxxiii, p. 4) examined *oil of calamus*, and found that the portion boiling below 170° C. yielded, after treatment with sodium, a terpene, having a sp. gr. .8793 at 0° C., and having a boiling point of 158° C. The extractive matter has an acrid and sweetish taste. H. Thomas (*A. Pharm.*, 1886, p. 465; *P. J.*, 1886, p. 1085) obtained from Calamus rhizomes a bitter glucoside, *acorin*, in the form of a clear, thick, yellow liquid, having a neutral reaction and having the formula $C_{36}H_{60}O_6$, splitting into oil of Calamus and sugar. By oxidation *acoretin*, a neutral resin, is formed, and from the extract remaining after the acorin is removed Thomas obtained an alkaloid which he named *calamine*. Calamus is sometimes attacked by worms, and deteriorates on keeping.

Uses.—Calamus is a feeble aromatic and is used chiefly as a household remedy. The volatile oil is largely used in perfumery, and the powdered root itself is esteemed in Ceylon and India as a vermifuge and an insecticide. *Dose*, in substance, fifteen to thirty grains (0.9–1.9 Gm.).

The *fluidextract*, formerly official, *Fluidextractum Calami U. S. VIII*, was given in *doses*, from fifteen to thirty minims (0.9–1.9 cc.).

Calbroben. *N. N. R.*, 1924. *Calcium Dibrombehenate.* $(C_{22}H_{41}O_2Br_2)_2Ca$.—This is a white powder without taste or odor analagous to calcium iodobehenate. It is insoluble in alcohol, water and acetone, soluble in ether and chloroform, and contains after drying 29 per cent. bromine and 3.8 per cent calcium. *Sabromin* and *Asabromine* are proprietary forms of this compound.

The clinical evidence is indisputable that this preparation is capable of exercising many of the therapeutic properties of the alkaline bromides, but there is considerable contradiction as to the extent to which it may replace the older salts. On the one hand, Von Mering (*Med. Klin.*, iv, p. 1464) has found, despite the fact that it contains only one-half the amount of bromine that potassium bromide does, it is equal in power although slower in action, and Bratz and Schlokow (*D. M. W.*, 1909) assert that weight for weight sabromin is more efficacious than potassium bromide. On the other hand, Ellinger and Kotake (*A. E. P. P.*, 1911, lxv) assert that if administered in large enough doses to obtain the bromide action, sabromin is injurious to the kidney, and Bittner (*Pr. M. W.*, 1910) found it of little use in *epilepsy*. It has been employed by many physicians with mostly favorable results in *hysteria, neurasthenia, insomnia, epilepsy*, and other conditions in which the bromides are habitually employed. The *dose* ordinarily given is from eight to thirty grains (0.5–2.0 Gm.).

Calcium Acetate. *Calcii Acetas. Acétate de Chaux*, Fr. *Essigsaurer Kalk*, G. $Ca(C_2H_3O_2)_2$.

—Made by neutralizing acetic acid with precipitated calcium carbonate, evaporating and crystallizing. Colorless needle-like crystals, soluble in water, less so in alcohol.

Calcium Acetyl-Salicylate. *Calcetal. Tylcalsin. Soluble Aspirin.*—This has been introduced under the trade name of *kalmopyrin.* It is a white powder readily soluble in water, differing from the other salts of acetylsalicylic acid in that it is not hygroscopic and its aqueous solution not so rapidly decomposed. It is used as an antirheumatic and analgesic in *doses* of from eight to fifteen grains (0.5–1 Gm.).

Calcium Benzoate. *Calcii Benzoas.* $Ca(C_7H_5O_2)_2 + 3H_2O$.—This salt may be made by adding calcium carbonate to a hot aqueous solution of benzoic acid, filtering, and evaporating the solution, and collecting and drying the crystals, which usually form in beautiful radiating tufts. It is soluble in 18 parts of cold water and 6 parts of boiling water. *Calcium hippurate,* $Ca(C_9H_8NO_3)_2 + 3H_2O$, is made in a similar manner, and is identical in appearance and uses. Poulet recommends the latter highly in the *uric acid diathesis,* for *scrofula,* incipient *cirrhosis of the liver,* and in *struma. Dose,* ten grain (0.65 Gm.).

Calcium Borate. *Calcii Boras.* $Ca_3(BO_3)_2$.—Calcium Borate is prepared by mixing solutions of sodium borate and calcium chloride. It is a white, inodorous, tasteless powder soluble in hot water. It is given internally in *diarrhea,* and used externally as a deodorant and desiccant. *Dose,* ten to fifteen grains (0.65–1 Gm.).

Calcium Chloride Diglycocoll. *Calciglycin,* $(CaCl_2(2NH_2CH_2COOH) + 4H_2O)$.—It occurs as colorless prismatic needles. It is used as a substitute for calcium chloride over which it has the advantage of being non-hygroscopic and comparatively tasteless.

Calcium Creosotate. *Calcreose N. N. R.,* 1924.—This is a dark brown powder with a creosote-like odor and a sharp taste. It appears to be a mixture of creosotic salts of calcium with free calcium hydroxide and carbonate. When mixed with water a portion of calcreose is dissolved yielding an alkaline solution containing the calcium compounds of the phenols of creosote and the insoluble part consisting of the hydroxide and carbonate of calcium.

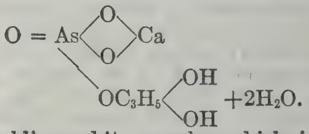
Calcreose is decomposed in the alimentary canal and yields its creosote for absorption and hence may be used for all the therapeutic purposes for which creosote is employed, especially as an expectorant in *tuberculosis, chronic bronchitis,* and the like. It has the advantage over creosote itself of being less irritant to the stomach and may be used in the form of tablets generally without any disturbance of digestion. It represents 50 per cent. of creosote and may be given in doses of from 4 to 16 grains. (0.25–1.0 Gm.).

The term *calcium creosotate* has been also applied to a liquid prepared by mixing creosote with freshly prepared calcium hydroxide in a perculator and then allowing water to run through. It occurs as a reddish-yellow liquid with a creosote-like odor and a sharp, peppery taste, strongly alkaline in reaction. It is asserted to possess the therapeutic properties of creosote and to be much less irritating to the stomach.

Calcium Dithiocarbonate. *Dithio-Calcium Carbonate.* $CaCOS_2$.—An orange-red, crystalline, hygroscopic powder, slightly soluble in water, less so in alcohol. It has been especially employed by Tommasoli and Vicini (*Monatssch. f. Prakt. Dermatol.,* 1892) as a local application in *eczema, psoriasis, lupus, purulent syphilides* and other *skin diseases,* in the form of a 5 per cent. ointment or a somewhat stronger aqueous solution. A 20 per cent. solution produced distinct burning irritation and even pustulation. Sabbatini states that the 1 per cent. solution inhibits, but does not kill pyrogenic micro-organisms. On exposure, its aqueous solution undergoes decomposition with the separation of sulphur and hydrogen sulphide.

Calcium Fluoride. *Calcii Fluoridum.* CaF_2.—A white powder, which is insoluble in water, but becomes soluble in the presence of salts of ammonium. It has been recommended internally by Deninger (*Deutsche Zahnarztliche Wochens.,* 1907, p. 196), during pregnancy, to prevent the loosening of the teeth. It may be given in *doses* of from one-twelfth to one-sixth grain (0.005–0.01 Gm.) twice daily.

Calcium Glycero-arsenate. *Calcii Glycero-arsenas.*



A crumbling white powder which is insoluble in water and alcohol but freely dissolves in mineral and organic acids, especially in a dilute solution of citric acid. According to Schlagdenhauffen and Pagel, the lethal subcutaneous dose of this compound is, for guinea-pigs, 3.10 Gm. per kilo. The preparation is therefore only slightly poisonous and has been employed in daily *dose* of one-sixth grain (0.01 Gm.) internally in *phthisis* by Spillmann and in *diabetes* by Heinrich Stern, in *doses* of 4 to 10 grains (0.26–0.65 Gm.) to be taken three or four times daily.

Calcium Iodate. *Calcii Iodas.* $Ca(IO_3)_2 + 6H_2O$.—This is a white, crystalline powder dissolving in about 400 parts of water. It contains 51 per cent. of iodine and 16 per cent. of available oxygen, which substances are liberated slowly in the presence of putrescent organic matters. It is stated further that in alkaline solution, while the organic matter is being oxidized by the oxygen set free from the decomposing iodate, the iodine slowly reforms iodates by the decomposition of water. The iodate so reformed, in contact with another portion of putrescible matter, yields further proportions of free oxygen and iodine to act as before, and so on. This salt was brought forward by E. Sonstadt as a valuable antiseptic, to be used in the preservation of food. (*Chem. News,* xxviii, 297; confirmed in *Provincial Med. Journ.,* March, 1890.) It is strongly recommended by W. Mackie (*L. L.,* 1900, No. 4035) as a substitute in surgery for iodoform and in internal medicine as a gastro-intestinal antiseptic. The internal *dose* is from three to five grains (0.2–0.32 Gm.) given in capsules after meals.

Calcium Iodide. *Calcii Iodidum. Calcium Iodatum. Iodure de Calcium,* Fr. *Jodcalcium, Calcium Jodid,* G. CaI_2.—According to Malem (*B. G. T.,* April 30, 1868), this salt is preferable to any other iodic compound in *phthisis.* Malem prepares it by treating a solution of ferrous iodide with milk of lime. This liquor thus obtained, being filtered and evaporated, yields crystals of calcium iodide. It may also be made by dissolving lime or calcium carbonate in hydriodic acid.

Pure calcium iodide is white, and crystallizes in large plates of a pearly luster. It is deliquescent, and very soluble in water, and its solution is capable of dissolving iodine added to it. Calcium iodide is much more unstable than potassium iodide. It is incompatible with acids, soluble sulphates, carbonates and tartrates.

Williamson (*B. M. J.*, 1907, p. 909) has found calcium iodide to be especially serviceable in various forms of *ulceration* and *diseases of the skin.* It is also a useful remedy in some cases of *asthma.* The *dose* is from five to ten grains (0.3–0.6 Gm.). The N. F. recognizes a syrup (see *Syrupus Calcii Iodidi,* Part III).

Calcium Permanganate. *Calcii Permanganas. Acerdol.* $CaMn_2O_8$.—This salt probably has the same physiological and medicinal properties as the permanganate of potassium. It has been used in *gastro-enteritis* and *diarrhea* in *doses* of from one-half to one and a half grains (0.032–0.096 Gm.), but has been especially urged for the purification of water. For spring water twenty milligrammes, for river water forty milligrammes, per liter, are recommended. If the color of the water remains red for a short time the permanganate is in excess, as should be the case for effective purification. Calcium Permanganate has also been suggested by Stevens (*K. T. W.*, 1910, p. 166) for the treatment of *lead poisoning.*

Calcium Peroxide. *Calcii Peroxidum.* $CaO_2 + 4H_2O$. *N. N. R.*, 1922.—"A mixture consisting essentially of calcium peroxide and calcium hydroxide and carbonate, containing not less than 60 per cent. of calcium peroxide, equivalent to 13.3 per cent of available oxygen." A yellow, crystalline powder which dissolves but sparingly in water. The solution has an alkaline reaction and possesses a somewhat caustic and astringent taste. In the presence of water Calcium Peroxide splits up into calcium hydroxide and oxygen. It has been brought forward as a powerful oxidizing antizymotic and as an antidote to hydrocyanic acid. In Hornstein's experiments it failed as an antidote unless the cyanide was given in very small quantities and the antidote was administered immediately after the poison. Its germicidal powers appear to be feeble, and its proneness to decomposition is a practical difficulty in its use. It has, however, been highly recommended by Reszkowski (*Gazette Lekarska,* 1899) in the summer *diarrheas* of children, in *doses* of three to ten grains (0.2–0.65 Gm.), administered in milk. It is advised to keep it in parchment capsules in well-stoppered bottles. Under the name of *calcium superoxide* or *gorite* a probably identical oxide has been put on the market. The germicidal influence of gorite was determined by Hornstein (*A. J. P.*, 1901, viii) to be distinctly weaker than that of hydrogen dioxide. Tooth-powders purporting to contain calcium peroxide are upon the market, but in most of them the quantity of the salt present is too small to exercise any therapeutic effect. It is incompatible with acids or acid salts, with soluble phosphates, sulphates and carbonates.

Calcium Phenolsulphonate. *Calcii Sulphophenas. Calcium Sulphocarbolate. Calcium Phenolsulphonate. Karbolsulfosaures Calcium,* G. $[C_6H_4(OH)SO_3]_2Ca + H_2O$.—Made by neutralizing paraphenolsulphonic acid with precipitated calcium carbonate. In the form of a colorless, almost odorless powder, astringent and bitter, readily soluble in water and alcohol. It is incompatible with iron compounds, lead subacetate solution, and peroxides. A 1 per cent. solution is recommended as an intestinal antiseptic, and astringent in *doses* of a fluidrachm (3.75 cc.) every three hours.

Calcium Saccharate.—Under the trade name of *Antacidin* this compound of calcium with cane sugar, $(C_{12}H_{22}O_{11})_3CaO$, has been recommended in the treatment of *dyspepsia* and *flatulency. Dose,* fifteen to sixty grains (1–4 Gm.).

Calcium Salicylate. *Calcii Salicylas.* $CaC_7H_5O_3 + H_2O$.—This compound is the basic calcium salt. It is a sandy, white powder, almost insoluble in water. The neutral salt is also known and is quite soluble in water. Calcium Salicylate has been used in Austria in *doses* of from seven to twenty grains (0.45–1.3 Gm.) for *diarrhea* and *gastro-enteritis.* For method of preparation, see *P. J.*, vol. xxii, 1891.

Calcium Santoninate. *Calcii Santoninas.* $Ca(C_{15}H_{19}O_4)_2$.—This is a white, tasteless, insoluble powder, obtained by saturating hot milk of lime with santonin, and has been brought forward by Bombelen as superior to santonin as a vermifuge on account of its tastelessness, and especially because of its insolubility, which causes it to be absorbed with great slowness. (*Ap. Ztg.*, March, 1899.) *Dose,* one grain (0.065 Gm.).

Calcium Sulph-Ichthyolate.—This preparation, claimed to be more efficient than the ammonium ichthyolate, is made by submitting ammonium sulph-ichthyolate to the action of a solution of calcium chloride in calcium hydroxide solution.

Calcium Sulphate. *Calcii Sulphas Exsiccatus. U. S. VIII. Exsiccated Calcium Sulphate. Dried Calcium Sulphate. Calcii Sulphas,* Br. 1885. *Dried Gypsum. Plaster of Paris. Exsiccated Sulphate of Calcium. Calcis Sulphas. Sulphate of Lime. Gypsum. Calcium sulfuricum ustum,* P. G. *Gebrannter Gyps,* G.—"A powder containing about 95 per cent., by weight, of Calcium Sulphate [$CaSO_4 = 136.14$], and about 5 per cent. of water; prepared from the purer varieties of native gypsum [$CaSO_4 + 2H_2O = 172.17$], by carefully heating until about three-fourths of the water has been expelled. Exsiccated Calcium Sulphate should be kept in well-closed vessels, carefully protected from moisture." *U. S. VIII.* The native sulphate is best known as *gypsum,* and in its massive variety as *alabaster.* Gypsum is an abundant natural product, and the quantity mined in the United States has enormously increased in recent years. It was officially described as "a fine, white powder, without odor or taste. From moist air it attracts water, becomes granular, and then loses the property of hardening with water. When mixed with half its weight of water, exsiccated Calcium Sulphate forms a smooth, cohesive paste, which rapidly hardens. It is soluble in about 378 parts of water at 25° C., and in 451 parts at 100° C. In alcohol it is insoluble. It readily dissolves in diluted nitric or hydrochloric acid; also in saturated solutions of potassium nitrate, sodium thiosulphate, and of various ammonium salts. When heated above 204° C., exsiccated Calcium Sulphate becomes anhydrous and loses the property of forming with water a paste which hardens rapidly. Its saturated solution in water is neutral to litmus paper, and forms white precipitates with barium chloride T.S., with ammonium oxalate T.S., and with alcohol. No effervescence should occur on the addition of diluted acids to exsiccated

Calcium Sulphate (absence of *carbonate*)." *U. S. VIII.*

The solubility of crystallized calcium sulphate, according to Poggiale, varies with the temperature; it is greatest at 35° C. and above or below that temperature gradually diminishes, so that at 100° C., it is very nearly the same as at 5° C. (*J. P. C.*, 4e sér., v, 86.) When deprived of its water by heat, and reduced to the state of a white powder, it rapidly absorbs water added to it, and, from the state of semi-liquid paste into which it is brought with that fluid, hardens without great change of bulk. It is this property which fits plaster-of-Paris so well for all kinds of molding; and to this also it owes its peculiar adaptability to the purpose of a splint. To prepare it for use, the gypsum must first be deprived of the greater part of its water by exposure to a heat of from 100° C. to 121.1° C. It loses both its molecules of water of crystallization at a temperature of about 170° C., and is then known as *burnt gypsum.* If heated above 204° C. it becomes *dead-burnt*, and does not take up water readily and does not harden. When dehydrated, it is reduced to fine powder, and kept in air tight vessels for use. As thus prepared, if mixed with two parts of water, it forms a semi-liquid cream-like mass, which becomes solid and hard in fifteen or twenty minutes, the temperatue rising during the process, as in the slaking of lime. Plaster of Paris sets best when mixed with three-fifths of its weight of water. Colloids retard and crystalline substances hasten the setting; thus, 1 per cent. of salep increases the time of setting from 20 to 50 minutes, while 3 per cent. of alum reduces the time to about five minutes. The hydrated gypsum expands in solidifying, hence its advantages in preparing casts—the expansion causes it to fill accurately all interstices. Cloëz (*Chem. News*, 1903, 58) states that the "setting" of plaster of Paris is due to the succession of three phenomena: (1) Hydration. (2) Partial solution. (3) Solidification of a supersaturated solution.

Gypsum is used, in medicine, chiefly to provide mechanical support or to immobilize various parts of the body. Thus in *fractures* and *sprains* it frequently replaces various forms of splints. Plaster jackets are used to support the thorax in cases of tuberculous diseases of the spine. Ordinarily for surgical purposes it is applied by saturating bandages with the dry powder, these bandages being dipped in tepid water at the time of application. Usually muslin bandages are employed, but, according to T. E. Stark, a medical officer in the British army, flannel is the best material for bandages to be used with gypsum. The bandages should then be rolled up loosely, and kept for use in air tight cases. Dry calcium sulphate has also been recommended as an absorbent dressing in *wounds, foul ulcers* and similar conditions, for which its hygroscopic properties render it valuable.

Cali Nuts.—These nuts, which come from the west coast of Africa, are the seeds of a papilionaceous plant, either a species of *Mucuna* or *Dioclea*, and have a more circular shape than Calabar beans, but otherwise agree with the latter in essential external characters. They contain an alkaloid which is said to be chemically and physiologically closely allied to physostigmine. (Merck, *Chem. Cb.*, 1887.)

Calliandrein.—A glucoside (probably a saponin) obtained from *Calliandra grandiflora* Benth. (Fam. *Leguminosæ*), a Mexican shrub. It is a white, odorless powder soluble in water, the solution forming a heavy froth on shaking. It possesses antipyretic properties, having been administered with asserted good results in *intermittent fever. Dose,* one grain (0.065 Gm.).

Calomelol. *N. N. R.* 1924.—Calomelol is a powder, almost without taste, insoluble in alcohol. It is a colloidal form of calomel containing albuminoids. It is prepared by acting on a solution of sodium chloride in the presence of a proteid with mercurous nitrate, and precipitating the calomel with alcohol. It is asserted to contain 80 per cent. of calomel in the colloidal state and 20 per cent. of albuminoids. It should be guarded from the light and its solution is incompatible with alcohol or alcoholic tinctures and with acids. It is recommended especially for inunction in the treatment of *syphilis.* The advantages over the ordinary mercurial ointment claimed for it are, that it is better absorbed, less likely to cause irritation of the hair follicles, and is almost invisible on the skin. The *calomelol ointment* (*Unguentum Heyden*) contains 45 per cent. of calomelol. The amount applied at one time is ordinarily about ninety grains (5.8 Gm.).

Calotropis. *Mudar. Br. Add.*—The dried root-bark of *Calotropis procera* R. Brown (*Asclepias procera* L.) and of *Calotropis gigantea* R. Brown freed from the outer corky layer. These asclepiadaceous plants are natives of Hindostan, but have become widely naturalized in various parts of the East and West Indies. Their milky juice is a violent local irritant, which, when taken internally, acts as an emeto-cathartic and may produce a fatal gastro-enteritis. In India it has long been used not only for suicidal purposes but to kill newly-born female infants, and is also applied to the womb to cause abortion.

The root-bark occurs in short, more or less quilled pieces having a thickness of from one-tenth to one-fifth of an inch (two to five millimeters) and a width of not more than one and a half inches (thirty-seven millimeters). It is covered with a soft, grayish buff, strongly furrowed and reticulated, easily separated periderm. The fracture is short and mealy; the taste bitter and acrid. According to C. J. H. Warden and L. A. Waddel, calotropis contains an acid resin, a crystalline, colorless substance, *madaralban,* an amber-colored viscid body, *madarfluavil,* and caoutchouc. (*P. J.*, 1885, 165.) Lewin (*A. E. P. P.*, 1913, lxxi, 142) has found a neutral principle (*calotropin*) which is a very active poison of the digitalis type.

Calotropis has been used as a local remedy in Hindostan in *elephantiasis* and *leprosy,* and is asserted by John Morton (*Indian Medical Record,* viii, 1895) to act with extraordinary efficiency upon chronic *eczema.* It has also been employed internally as a remedy in *diarrhea* and *dysentery;* also with less probability of usefulness in *syphilis* and *rheumatism. Dose,* of powder, from three to twelve grains (0.2–0.78 Gm.), three times a day, gradually increased until it affects the system.

Tincture of Calotropis. Tinctura Calotropis. Br. Add., two ounces to a pint (alcohol 6 per cent.), is given in *doses* of one-half to one fluidrachm (1.8–3.75 cc.).

Calycanthus. *Calycanthus floridus* L.—This is a shrub of the Fam. *Calycanthaceæ,* from six to eight feet high, which inhabits the low, shady woods along the mountains of Georgia and North

Carolina, and also Tennessee, where it is known as *sweet shrub* or *Carolina allspice.* The whole plant is aromatic, having, when crushed, the odor of strawberries. According to R. G. Eccles, the seeds contain a fixed oil, and an alkaloid, *calycanthine.* H. W. Wiley (*A. J. P.*, 1890, 96) found in the seeds over 47 per cent. of oil and 4.25 per cent. of alkaloid. H. M. Gordin made an extensive investigation of calycanthine and its salts. (*Proc. A. Ph. A.*, 1905, 224.) According to Cushny (*A. I. P. T.*, 1905, xv, p. 487) calycanthine has the empiric formula of $C_{11}H_{14}N_2$. When injected into the lower animals it causes muscular weakness, by an action upon the peripheral motor nerves, associated with increased reflexes, and, in the higher mammals, with convulsions similar to those seen in picrotoxin poisoning. The alkaloid also exercises a powerfully depressant action upon the heart muscle. Later, a second alkaloid, *isocalycanthine,* was described by Gordin. (*Proc. A. Ph. A.*, 1908 and 1909, 889.) This alkaloid, according to the experiments of MacGuigan and Hess (*J. P. Ex. T.*, 1912, iii), is very similar in its physiological properties to calycanthine. It is asserted that the shrub is important as a source of poisoning to cattle and sheep. Calycanthus has been used as an antiperiodic. The *dose* of the *fluidextract* is thirty to sixty minims (1.9–3.75 cc.).

Calystegia Solandella.—This plant, a member of the fam. *Convolvulaceæ,* has been employed as a cathartic. A compound tincture of solandella has been used with some success, but whether this can be attributed to the calystegia or to other ingredients is not known.

Cam wood.—A red dye-wood, procured from the *Baphia nitida* Lodd., a leguminous tree, growing on the western coast of Africa. The wood is usually kept in the shops in the ground state. When first collected it is white and generally becomes red upon keeping. It yields its coloring matter scarcely at all to cold water, slightly to boiling water, and readily to alcohol and alkaline solutions. The coloring matter is thought to be identical with *santalin,* $C_{15}H_{14}O_5$.

Camellin.—A glucoside obtained from the seeds of *Camellia japonica,* $C_{53}H_{84}O_{19}$. It occurs as a reddish-white, bitter powder, soluble in water. It is used as a cardiac stimulant in *endocarditis* and *pericarditis,* several foreign practitioners preferring it to digitalin.

Camphacollasis. *Camphacol.*—This is the *camphoric acid ester of methylene diguaiacol.* It occurs in crystals, and is used as an expectorant in *phthisis* and as an *antiseptic* in *cystitis. Dose,* five to twenty grains (0.32–1.3 Gm.).

Monobromated camphor. Camphora Monobromata, U. S. IX. Bromated camphor, Bromcamphor, "Ortho-monobromcamphor [$C_{10}H_{15}OBr$ or $C_9H_{15}Br.CO = 231.04$]. Preserve it in well-closed containers, protected from light." *U. S. IX.* This substance may be made by heating together bromine and camphor (for details see *U. S. D.*, 20th ed., p. 275). It "occurs in colorless, prismatic needles or scales, or as a powder having a mild but characteristic, camphoraceous odor and taste; permanent in the air. It is decomposed by prolonged exposure to sun-light. One Gm. of Monobromated Camphor dissolves in 6.5 mils of alcohol, 0.5 mil of chloroform, and in 1.6 mils of ether at 25° C.; almost insoluble in water. It melts between 74° and 76° C. Heat a mixture of about 0.1 Gm. each of Monobromated Camphor and silver nitrate and 2 mils each of nitric acid and sulphuric acid until nitrous vapors are no longer evolved; a yellowish precipitate of silver bromide is obtained. Incinerate about 2 Gm. of Monobromated Camphor; not more than 0.05 per cent. of ash remains. Shake about 0.5 Gm. of powdered Monobromated Camphor with 10 mils of distilled water and filter. The filtrate is neutral to litmus and is not rendered more than slightly opalescent by the addition of a few drops of silver nitrate T.S. (*soluble bromide*)." *U. S.*

The therapeutic action of monobromated camphor resembles, but is not identical with, that of the alkali bromides. It can not be given in large enough dose to obtain a full bromide effect without danger of camphor poisoning; epileptiform convulsions have followed its too free use. It is frequently added to the coal tar analysis for the relief of *headaches.* The *dose* is from two to five grains (0.13–0.3 Gm.).

Camphoric Acid. *Acidum Camphoricum. U. S. VIII. Kamphorsäure, Kamphylsaure,* G. $H_2C_{10}H_{14}O_4 = 198.62$.—"A dibasic organic acid obtained by the oxidation of camphor." *U. S. VIII.* This acid is obtained by the oxidation of camphor by heating it with nitric acid, and purifying the crystals so obtained. On further oxidation it is changed into *camphoronic acid,* $C_9H_{14}O_6$. It has been made synthetically by Komppa. (*P. J.*, 1904, 77.)

It occurs in "colorless, odorless, monoclinic prismatic crystals or plates; melting at 187° C.; at a higher temperature yielding an anhydride, and ultimately decomposing without leaving any weighable residue. Soluble in 125 parts of water at 25° C., and in 10 parts of boiling water; readily soluble in alcohol, less soluble in ether and chloroform; soluble in fatty oils. Camphoric Acid is dextro-rotatory, showing in 10 per cent. alcoholic solution, the value $[\alpha]_D = +47.8°$. The aqueous solution reddens blue litmus paper. If 2 Cc. of a saturated aqueous solution of Camphoric Acid be mixed with 2 Cc. of sulphuric acid in a test tube, and 1 Cc. of a solution made by dissolving 1 Gm. of ferrous sulphate in 2 Cc. of diluted sulphuric acid be poured carefully upon it, no dark-colored zone should develop at the line of contact (absence of *nitric acid*)." *U. S. VIII.*

Camphoric acid was at one time used in the treatment of *night sweats* and to a lesser extent in *cystitis,* but both Tyrode (*A. I. P. T.*, 1908, x, p. 393) and Roth (*J. P. Ex. T.*, 1911, ii, p. 405) find that it has no effect on the secretion of either sweat or salivary glands. According to the latter, it is slightly stimulating to the central nervous system, but Tyrode finds that the neutral salts are entirely inert. The *dose* which has been used is from five to fifteen grains (0.3–1 Gm.).

Canada Pitch. *Pix Canadensis. U. S.* 1880. *Hemlock Pitch.*—This is the resinous exudation from the *Tsuga canadensis* (L.) Carr (*Abies Canadensis,* Michx.), *Hemlock* or *Hemlock Spruce,* of the United States and Canada. This tree, when of full growth, is often seventy or eighty feet high, with a trunk of two or three feet in diameter, and of nearly uniform dimensions for two-thirds of its length. Its leaves are scattered, short, linear, obtuse, from 8 to 13 mm. in length, whitened beneath and appearing as two-ranked. The strobiles are ovate, little longer than the leaves, terminal and pendulous.

The tree is abundant in Canada, Nova Scotia, and northern New England, and is found in the elevated and mountainous regions of the Middle States. Its bark is much used for tanning, an extract being made for the purpose. The tree contains much less juice than some other of the conifers, and very little flows from incisions made into its trunk. But in the trees which have attained their full growth, and are about to, or have begun to decay, the juice exudes spontaneously, and hardens upon the bark, in consequence of the partial evaporation or oxidation of its volatile oil. The bark thus incrusted is stripped from the tree, broken into pieces, and boiled in water. The pitch melts, rises to the surface, is skimmed off, and is still further purified by a second boiling in water. Hemlock pitch is hard, brittle, quite opaque, of a dark reddish-brown color, becoming still darker by exposure to the air, of a weak peculiar odor, and scarcely any taste. It softens and becomes adhesive with a moderate heat, and even at ordinary temperatures takes the form of the vessel containing it, and melts at 92.2° C.

The constituents of this pitch are resin and a minute proportion of volatile oil. It is sometimes known by the incorrect name of *hemlock gum.*

Canada pitch is a gentle rubefacient, closely analogous to Burgundy pitch in its properties, and employed for precisely the same purposes. It is, however, more readily softened by heat, and is sometimes almost too soft for convenient application at the temperature of the body. A volatile oil obtained from this tree, and called *oil of spruce* or *oil of hemlock,* has been employed to a considerable extent in veterinary liniments.

The U. S. Pharmacopœia of 1880 gave the following directions for preparing the *Hemlock* or *Canada Pitch Plaster* (*Emplastrum Picis Canadensis, U. S.,* 1880): "Canada Pitch, *ninety parts;* Yellow Wax, *ten parts,* to make *one hundred parts.* Melt them together, strain the mixture, and stir constantly until it thickens on cooling." *U. S.,* 1880.

W. Zinn (*M. M. W.,* Oct., 1902) reports a case of stupor and involuntary evacuation of urine, and collapse with subsequent psychic disturbance, as produced by the inhalation for many hours of the emanations from branches of *Pseudotsuga tascifolia* (Lamb.) Britton (*P. Douglassi* Car.).

Canary Seed. *Fructus* (*Semen*) *Canariense, Semence de Canarie,* Fr. *Kanariensamen,* G.—The seeds of *Phalaris canariensis* L., an annual grass originally from the Canary Islands, but now growing wild in Europe and the United States. The seeds are ovate, somewhat compressed, about 5 mm. long, shining and of a light yellowish-gray color externally, and light within. Their chief constituent is starch, and they are used chiefly as bird food.

Canchalagua.—This plant, *Erythræa venusta* A. Gray (Fam. *Gentianaceæ*), found on our Pacific coast, has been used as a bitter tonic and stomachic. (*Ph. Rec.,* 1887, 363.) *Erythræa australis* R. Br. is said to be similarly used in Australia. (*P. J.,* xix.)

Candelilla Wax.—Under this name there has been suggested as a substitute for bee's wax a product of the *Pedilanthus pavonis* Boiss, a Mexican shrub. This plant produces stalks which reach a height of from 3 to 5 feet, a large number of stalks springing from a single root without leaves or thorns. From these are obtained 5 per cent. of a hard wax with a melting point of 67° to 80° C. A sp. gr. of 0.98 to 0.99, an acid value of 12.4 and saponification value of 47 to 65. It is soluble in turpentine and chloroform and has been used for a number of purposes in the arts such as shoe polishes, lubricants and phonograph records and suggested as a substitute for bee's wax in pharmaceutical processes. (See *Ph. Era.,* 1919, lii, p. 13.)

Cangoura.—An evergreen creeper, *Bouea oblongifolia* (Fam. *Anacardiaceæ*), from the seeds of which the natives of Salvador are said to produce a paste which is a violent nerve poison, producing in some cases delirium lasting as long as eight days. (*Nouv. Rem.,* April, 1892.)

Capparis. *Capparis spinosa* L. *Caper-bush.* (Fam. *Capparidaceæ.*)—A low, trailing shrub, growing in the south of Europe and north of Africa. The buds of unexpanded flowers, treated with salt and vinegar, form a highly esteemed pickle, which has an acrid, burning taste, and is considered useful in *scurvy.* The dried bark of the root was formerly official. It is in pieces partially or wholly quilled, about one-third of an inch in mean diameter, transversely wrinkled, grayish externally, whitish within, inodorous, and of a bitterish, somewhat acrid, and aromatic taste. It contains *rutic acid* and a volatile substance of garlic-like odor. It is considered diuretic, and was formerly used in *amenorrhea* and *chronic rheumatism.*

Caprokol. (*N. N. R.* 1925) *Hexyl-resorcinol.*—This compound is a resorcinol in which one of the hydrogen atoms of the benzene ring has been replaced by hexyl. It has the formula, therefore, of $C_6H_3(OH)_2C_6H_{13}$. It has been brought forward by Leonard (*J. A. M. A.,* 1924, lxxxiii, p. 2005) as a urinary antiseptic. He finds that it has a phenol co-efficient by the hygienic laboratory method of about 46; that in strengths of one part in 10,000 of urine it kills the *B. coli* in an hour and even in much more dilute solution will destroy the *staphylococcus.* He finds, moreover, that the urine of men taking the drug by the mouth often becomes actively germicidal, and that the effects occur with either acid or alkaline urine. He has employed it in various infections of the urinary tract, such as *cystitis* and *pyelitis* with good results.

The dose advised is from five to fifteen (0.3–1 Gm.) grains three times a day which should be given in enteric-coated capsules to avoid irritation of the stomach.

Capsella. *Capsella Bursa-pastoris* (L.) Medic. *Shepherd's purse. Bourse à Pasteur, Molette,* Fr. *Hirtentäschlein,* G. (Fam. *Cruciferæ.*)—This very common weed in the United States has been naturalized from Europe. Its aerial portion consists of a basal rosette of rarely entire, usually more or less lobed or pinnatifid leaves, from the center of which arises a stem that may attain a length of 20 inches and which bears few lanceolate, auricled or dentate or entire leaves and axillary racemes of white flowers. The fruit is a triangular pod, one-sixth to one-third inch long.

Capsella at one time enjoyed considerable popularity as a uterine stimulant especially in domestic practice. It had disappeared almost from medical notice but in the last few years has been attracting some attention in the treatment of *uterine hemorrhages.* It has been experimentally investigated by Grober (*Ap. Ztg.,* 1915, p. 308) and by Boruttau and Cappenberg (*A. Pharm.,* 1921, cclix,) who both reached the conclusion that it has a stimulating action on the uterine muscles. The latter investigators found that it also produced a lowering of the blood pressure which they attribute to the presence of acetylcholine. In the past the drug has also been used as an antiscorbutic and diuretic. There are several proprietary preparations, ostensibly derived from capsella, upon the market, such as *bursal, thaspan,* etc.

Bombelon, many years ago, asserted the presence of an aklaloid *bursine,* which, however, has been denied by Grimme (*Pharm. Weekblad.,* 1919, lvi, p. 1421) and by Cappenberg (*Ph. Centralh.,* 1921, lxii, p. 751); the former attributes its activity to *bursic acid.* Cappenberg finds in it bases of the choline group and of the nicotine group, also between 0.1 and 0.2 per cent. of tyramine. The plant also yields upon distillation a volatile oil apparently related to oil of mustard. From two to four fluidounces (60–120 cc.) of the freshly expressed juice may be given at a *dose;* or from one-fourth to one-half fluidrachm (0.9–1.8 cc.) of the fluidextract of the dried plant.

Captol. *Chloral Tannin.*—This proprietary preparation is said to be an impure condensation product of tannin and hydrated chloral. It is a brown hygroscopic powder, slightly soluble in cold water, very soluble in hot water and alcohol, not altered by acids but decomposed by alkalies, striking an olive-green color with ferric salts. According to Eichhoff, in *seborrhea capitis* washing the head morning and evening with a 1 to 2 per cent. alcoholic solution of captol is very successful.

Capulincullo.—This drug, derived from the *Rhamnus Humboldtianus* Roem. and Schult. (Fam. *Rhamnaceæ*) of Mexico, is said to be a violent poison, acting like curare. A non-toxic, non-drying fixed oil, tasteless and odorless, is obtained in considerable quantities from the fruit of the tree.

Carana. *Mararo. Gum Carana.*—A resinous substance, in pieces of a blackish-gray color, externally dark brown, internally somewhat shining and translucent, brittle and pulverizable when dry, but, in the recent state, soft and adhesive, like pitch, easily fusible, of an agreeable balsamic odor when heated, and a bitterish resinous taste. (Geiger.) It is said to be derived from *Urotium Carana* (Humb.) L. March (Fam. *Rutaceæ*), a tree growing in Mexico and South America. Geiger refers it also to *Bursera Simaruba* (L.) Sarg. (*Bursera gummifera* L.), of the West India Islands; but the resin of this tree is *résine de Gomari* or *résine de chibou* or *cachibou* of French writers, and is said to bear a close resemblance to the resin *tacamahac.* It is probable that in South America the name *carana* is applied to different products. (*A. J. P.,* xli, 233.)

Carbon Dioxide CO_2.—This gas is used for several purposes in medicine. In solution, it is called carbonic acid, and its popular employment is to improve the taste of disagreeable medicines, especially certain salines, and as a refreshing beverage. *Aqua Acidi Carbonici* (*Carbonic Acid Water,* or *Soda Water* (so-called); *Acidum Carbonicum Solutum, Eau gazeuse simple,* Fr.; *Kohlensaurewasser,* G.), which was formerly official in the U. S. Pharmacopœia, consists of water highly charged with carbon dioxide. It is also used as a mild counter-irritant to the skin in the form of effervescent baths. Certain spas in which there is a supply of naturally carbonated water, such as Nauheim, make these baths a prominent part of the treatment, especialy in cases of circulatory weakness. A formula for preparing these baths is given under *Aqua.*

Another use for carbonic oxide is as an escharotic. Its destructive action depends upon the intense degree of cold produced by the melting of the solidified gas commonly called *carbonic acid snow.* This is prepared by allowing the compressed gas to escape from a cylinder into a cone-shaped felt or woolen receptacle. The rapid expansion of the gas when freed from pressure causes it to solidify in the form of snow which is dished out of the cone with a spoon and pressed into molds of suitable shape. As its melting point is approximately −54° C. when applied to the skin it absorbs an immense amount of heat and almost immediately freezes the area to which it has been applied. The depth and permanency of the results of this freezing depend upon the duration of the application. Superficial freezing of the skin causes complete cessation of all functions and therefore local anesthesia as well as arrest of blood flow. After thorough freezing, as is accomplished with carbonic acid snow, there is probably formed thrombi in the superficial capillaries which lead to a permanent obstruction of the circulation and consequent death of the part. Carbonic acid snow is used with great success for the destruction of various types of neoplasms, as *warts, hairy moles,* and *vascular nevi.* It is also of service in the treatment of *malignant ulcers of the skin* and *epitheliomata.* The duration of single applications is from thirty seconds to one or two minutes, according to the depth of action which is desired. It has long been known that carbon dioxide is a stimulant to the medullary centers causing rise of blood pressure and increased respiration. Henderson and his co-workers (*J. A. M. A.,* 1920, lxxiv, p. 783, and 1921, lxxvii, p. 1065) recommend the inhalations of carbon dioxide as a clinically useful stimulant in the treatment of *surgical shock,* carbon monoxide (*illuminating gas*) poison and similar conditions.

Cardamine. *Cardamine pratensis* L. *Cuckooflower.*—This is a perennial herb of the fam. *Cruciferæ,* with a simple, smooth, erect stem, about a foot in height. The plant grows in Northern Europe and to some extent in wet places and bogs from New Jersey northward to Labrador. Its bitter and slightly pungent leaves are supposed to be antiscorbutic. The seeds are said to contain *myronic acid,* and to yield on decomposition by hydrolysis an oil analogous to oil of mustard. Feist investigated *C. amara* L. and its volatile oil and found *thio-urea.* Kuntze states that two kinds of crystals were isolated, both being forms of thio-urea. (*A. Pharm.,* 1907, 657.) In Europe they are sometimes added to salads. The flowers formerly possessed the reputation of being diuretic, and of being useful in *chorea* and *asthma.*

Carissin.—This is a glucoside which has been isolated from the bark of *Carissa ovata* R. Br. (Fam. *Apocynaceæ*), by J. H. Maiden and H. G. Smith. It is stated to be exceedingly bitter and very poisonous, and in its chemical relations to resemble strophanthin, from which it differs, however, in being precipitated by basic lead acetate and by tannic acid. Its most characteristic reaction is the production of a beautiful emerald-green color on the addition of a minute fragment of potassium dichromate to its solution in concentrated sulphuric acid. (*P. J.,* 1896.)

Carota. *U. S.* 1870. *Carotte,* Fr. *Mohre, Gelbe Rübe,* G. *Daucus Carota* L.—The *wild carrot* (Fam. *Umbelliferæ*) is widely distributed, growing along fences, and in neglected fields and from the beauty of the flowers is often known as *Queen Anne's Lace.* It grows wild also in Europe. The well-known garden carrot is the same plant altered by cultivation. The fruits are very light, of a brownish color, an oval shape, flat on one side and convex on the other, and on their convex surface present four longitudinal ridges, which are beset with stiff whitish hairs or bristles. They have an aromatic odor, and a warm, pungent, and bitterish taste. By distillation they yield about 1.26 per cent. of a yellow to brownish volatile oil, possessing the odor of carrots only to a slight extent. (*Schim. Rep.*, 1907, 31.) Pictet (*B. Soc. Chim.*, 1907, i, 1001) isolated from the leaves of carrots a liquid alkaloid. (*Chem. Ztg.*, 1905, No. 97.) Subsequently two liquid bases, *pyrrolidine* $[(CH_2)_4NH]$ and *daucine* ($C_{11}H_{18}N_2$). Carrot *seeds* are slightly aromatic, moderately excitant and diuretic, and have been employed as a diuretic in chronic *renal diseases* and in *dropsy*. An ounce of them may be given in infusion, in a day. The flowers are sometimes substituted for the seeds, and the scraped root has been used as a local stimulant to sloughing or *indolent ulcers*. For additional information concerning this drug, see *U. S. D.*, 19th edition, p. 1432.

Carthamus. *Carthamus tinctorius* L. *Safflower.*—The *African, false, American,* or *dyers' saffron* is an annual composite, with a smooth, erect stem, somewhat branched at top, and a foot or two in height. The plant is a native of India, the Levant, and Egypt, and is cultivated in those countries, as well as in various parts of Europe and America. The fruit yields 25.82 per cent. of fixed oil, the separated kernels of the seeds 50.37 per cent., according to Fendler. (*Ap. Ztg.*, 1904, 121.) The florets are brought to us chiefly from the ports of the Mediterranean. *Safflower* (*Flores Carthami; Fleurs de carthame, Safran bâtard*, Fr.; *Saflor*, G.; *Cartamo*, It., Sp.) in mass is of a red color, diversified by the yellow of the styles contained within the floret. It has a peculiar, slightly aromatic odor, and a scarcely perceptible bitterness. It contains a fixed oil; also two coloring substances—one red, insoluble in alkaline liquids, and called *carthamin* or *carthamic acid* by Döbereiner, who found it to possess weak acid properties; the other yellow, and soluble in water. Carthamin, $C_{14}H_{16}O_7$, exists to the amount of from 0.3 to 0.6 per cent. only in the safflower, while the safflower-yellow, to which Malin gives the formula $C_{24}H_{30}O_{15}$, is present to the amount of from 24 to 30 per cent. It is the former which renders safflower useful as a dye stuff. Kametaka and Perkins give the formula of carthamin as $C_{25}H_{24}O_{12}$. (*P. J.*, 1910, 299.) The flowers are sometimes fraudulently mixed with Spanish saffron, which they resemble in color, but from which they may be distinguished by their tubular form, and the yellowish style and filaments which they enclose. Unlike Spanish saffron, they do not give a blue color when treated with sulphuric acid.

In large doses carthamus is said to be laxative and, administered in warm infusion, diaphoretic. It is used in domestic practice, as a substitute for saffron, in *measles, scarlatina*, and other *exanthematous diseases*, to promote the eruption. An infusion, two drachms to a pint of boiling water, is usually employed *pro re nata*.

Caruba di Guiden.—Under this name certain gall-like bodies, formed on various species of *Pistacia*, especially *P. Terebinthus* L., as the result of the stings of a hemipterous insect were used for smoking and inhalation in *chronic bronchitis* and *asthma*. They appear to act by exciting free secretion, probably through the turpentine with which they are saturated. For further information, see *U. S. D.*, 20th edition, p. 1306.

Carvacrol. *Isopropyl-o-cresol. Oxycymol.* $C_{10}H_{13}OH$.—A phenol-like body existing in the Trieste and Smyrna *Origanum* oil and some other labiate plants and made artificially from either carvone or camphor. It forms a thick, colorless oil which does not solidify at 25° C., and boils at from 233° to 235° C. For an investigation of *Nitroso-carvacrol*, by Kremers and Brandel, see *Ph. Rev.*, 1904, 248. Cousin and Hérissey prepared from *carvacrol*, *dehydrodicarvacrol* or *dicarvacrol*. (*J. P. C.*, 1910, 2, 49.) Hixson and McKee (*J. Ind. Eng. Chem.*, 1918, x, p. 982) have manufactured carvacrol from spruce turpentine.

According to Martindale, carvacrol is almost as actively germicidal as its isomer, thymol. It has been used in medicine not only for its antibacterial properties, but also as a local anesthetic in *toothache*, cotton saturated with it being inserted into the carious cavity.

The experiments of Sollmann (*J. P. Ex. T.*, 1919, xiv,) and of Livingston (*J. P. Ex. T.*, 1921, xvii, p. 261) have shown that the toxicity of carvacrol on mammals as well as for certain worms is practically the same as that of thymol and the suggestion is made that it would afford a cheap substitute for thymol as an anthelmintic.

Carvacrol Iodide.—*Iodocrol*, $C_{10}H_{13}OI$, is a bulky, grayish-yellow or buff-colored amorphous powder having a faint aromatic odor. It is insoluble in water, slightly soluble in alcohol, soluble in ether, chloroform, petroleum, benzin, carbon disulphide, volatile and fixed oils. From its solution in ether and chloroform it is precipitated on the addition of alcohol, becoming paler in color. This purified product does not show signs of shrinkage until above 170° C., and at 200° C. becomes tarry and black. It is alleged that it combines the antiseptic properties of carvacrol with those of iodine, and possesses the advantage over iodoform in being odorless or nearly so, and in being five times as bulky, It has been used in surgical dressings in *eczema, pruritus, chancres*, and *chancroids*.

Carya. *Hicoria. Hickory.*—Several species of the genus *Carya* Nuttall (*Hicoria* Raf.) grow in the United States of which *Carya illinoënsis* (Wang.) K. Koch bears the *pecan nut*, and grows in the Middle and Southwestern States; *C. ovata* (Mill.) K. Koch, a large and handsome tree known as *shell-bark* or *shag-bark hickory*, is the chief source of the hickory nuts of the market. There are six other common species of *carya* which are indigenous to the United States and Canada, and all yield edible fruits. The leaves of most if not all of these trees are somewhat aromatic and astringent, and the bark astringent and bitter. In the bark of *H. alba* F. R. Smith found a crystalline principle, *caryin*, which he believed to be quercitrin.

Casearia. *Casearia esculenta* Roxb.—This Indian plant (Fam. *Flacourtiaceæ*) whose leaves are used for a food stuff, is said to be a valuable remedy in *hepatic torpor*, and to contain an organic acid allied to cathartic acid. (*P. J.*, xx.)

Casein.—This substance is one of the important constituents of milk and cheese. It is now made on a large scale in the United States from the "skim milk" obtained from creameries; this is conducted into tanks and heated by steam to 49° C., then coagulated by hydrochloric acid and thoroughly agitated; the *casein* separates into a mass, and the remaining liquid is used in the manufacture of sugar of milk. (See *Saccharum Lactis*, also a paper by C. H. LaWall in the *Alumni Report of the Philadelphia College of Pharmacy*, April, 1902, and one by J. W. England, *Proc. A. Ph. A.*, 1902, p. 357.) Commercial casein is used largely in the sizing of paper and in the manufacture of a glue substitute. It has been proposed by Seger as an emulsifying agent in pharmacy. One gallon of milk is treated with two and a half fluidounces of water of ammonia for twenty-four hours, and, after removing the saponaceous matter from the surface of the mixture, the serum is precipitated with acetic acid. The magma of casein, strongly pressed, is treated with sodium bicarbonate, and with a sufficient quantity of sugar to make the dried product contain one-tenth of its weight of casein. The powdered substance dissolves easily in water, and, mixed with an equal weight of gum, may be used for almost all of the emulsions. Resinous matters and balsams previously dissolved in alcohol, essences, and oils, may be mixed with it in the bottle itself without using the mortar. The only defect in this casein saccharate is its slight odor. The casein of milk prepared by a somewhat similar process to the above is largely used in the preparation of many of the so-called "rolling" creams used for cosmetic purposes.

It is commercially used in the manufacture of foodstuffs, as a fixing agent in calico-printing replacing albumin, as a substitute for glue in cements, as a size in paper manufacture, as a basis for cold water paints, and in the manufacture of plastic compounds, hardened with formaldehyde, such as *galalith.* A prepared casein diabetic flour is on the market in which milk casein is modified by a leavening mixture of sodium bicarbonate and acid calcium phosphate.

Pure casein has a sp. gr. of 1.259. It is readily soluble in 1 per cent. solutions of sodium fluoride, ammonium oxalate, and potassium oxalate, and 5 per cent. solutions of ammonium chloride or sulphate, as well as solutions of alkaline hydroxides, carbonates, borates, etc. Iodine compounds of casein are in use as follows: *periodocasein*, containing 17.89 per cent. iodine; *iodocasein*, containing 15.7 per cent. iodine; and *casein iodine*, containing 8.7 per cent. iodine. Bromine compounds are also known. Metallic casein compounds, as *silver caseinate*, are known and referred to under the appropriate heads. Compounds of casein with alkaloids are prepared by suspending casein in alcohol and adding an alcoholic solution of the alkaloid.

Ammonium Caseinate has been put on the market under the trade name of *Eucasin.* It is a grayish-white powder, with an odor like that of buttermilk, soluble in hot water. Feustell (*D. M. W.*, xxii, 1896) has used it as an accessory food.

Calcium Caseinate N. N. R., 1924, contains between 1.4 and 2.1 per cent. of calcium. It is a pale yellowish fluffy powder which when shaken with water yields a turbid suspension. It is used as an accessory food in *diarrheas* of infancy. Proprietary forms of Calcium Caseinate are known as *Caseo, Larosan-Roche,* and *Protolac.*

Sodium Caseinate. Sodii Caseinas. Nutrose. Casein-natrium, G.—A combination of casein and sodium hydroxide, just enough of the alkali being used to dissolve the freshly precipitated casein. The solution is evaporated *in vacuo*, the dry residue powdered, thoroughly washed with alcohol, and then with ether and dried. A white, amorphous powder, with little odor or taste, insoluble in alcohol and ether, slightly so in cold water, but readily soluble in hot water. It is considered to be a valuable food in intestinal and digestive disturbances, also in *anemia* and *scrofula.*

Casimiroa. *Casimiroa edulis* Llav. et Lex. *Zapote blanco. Cochil Sapote. White Sapota.*—This is a large tree belonging to the *Rutaceæ*, a native of Mexico, the leaves are employed in *diarrhea* and as an anthelmintic. Robin and Coyen (*Press. Med.*, 1909, p. 454) and Chevalier (*B. G. T.*, 1909, clviii, p. 96) have asserted that the Casimoroa seeds are narcotic.

Altamirano obtained from the seeds what he believed to be a glucoside which he called *casimirose* and Bickern (*A. Pharm.*, 1903, ccxli, p. 166) an alkaloidal glucoside which he named *casimirin.* Power and Callan (*Tr. Chem. Soc.*, 1911, xcix, 1093) found two alkaloids *casimiroin* and *casimiroedine*, a small quantity of an agreeable aromatic volatile oil and various other organic substances. Neither the alcoholic extract of the kernels nor any of the principles separated from them possess any physiological action beyond a local irritant effect on the stomach confirming the previous conclusion of Esch and Kochmann (*A. I. P. T.*, 1911, xxi, 353.)

Cassia. *Cassia marilandica* L. *Wild Senna. American Senna. Séné Américain,* Fr. *Amerikanische Senna,* G. (Fam. *Leguminosæ.*)—This is an indigenous perennial plant of vigorous growth, sending up annually numerous round, erect, nearly smooth stems, which are usually simple, and rise from three to six feet in height. The leaves are alternate, and composed of from eight to ten pairs of oblong-lanceolate, smooth, mucronate leaflets, green on their upper surface, pale beneath, and connected by short petioles with the common footstalk, which is compressed, channelled above, and furnished near its base with an ovate, stipitate gland. The American senna is common from New England to North Carolina. The leaves, which should be collected in August or the beginning of September, are sometimes brought into the market, compressed into oblong cakes. The leaflets are from an inch and a half to two inches long, from one-fourth to half an inch in breadth, thin, pliable, and of a pale green color. They have a feeble odor, and a nauseous taste, somewhat analogous to that of senna. Water and alcohol extract their virtues. Hermann J. M. Schroeter (*A. J. P.*, 1888, 231) found in them chrysophanic acid; also a principle corresponding in all respects with cathartic acid. American senna is an efficient and safe cathartic, acting like senna but more feebly.

Cassia nictitans L., or *Wild Sensitive Plant,* was investigated by Gallaher (*A. J. P.*, 1888, 280), had failed to find any glucoside or alkaloid. The amount of volatile oil found was very small, and cathartic acid could not be prepared from it, although the powder produced griping. The leaves of *Cassia alta* L. are recommended by Conillebault in *ringworm;* they are moistened and the parts affected rubbed with them. (*A. J. P.*, 1887, 266.)

Under the names of *Cheshmat, Chashmizok, Schischen,* the seeds of *C. Absus* L. are said to be used in India and Africa in the treatment of inflammations of the eye, either in the form of a fine powder or an infusion made from the coarsely ground seeds to which several medicinal substances are added.

The root of the *Cassia bearensis* Miq. is said to be very useful in the so-called *black-water fever* of Africa. (See *P. J.*, vols. xlvii, xlviii.)

Castela. *Castela Nicholsoni texana* Torrey and Gray. (Fam. *Simarubaceæ.*)—This plant, which is known among the Mexicans as *Chaparro amargosa*, that is, *bitter bush*, has been highly recommended by Nixon (*J. A. M. A.*, 1916, lxvi, p. 946) in the treatment of amebic *dysentery*. He found that a detannated fluidextract in the proportion of one part in a million was sufficient to cause the *Entamœba histolytica* to become immobile and to assume a spherical shape, with sharp differentiations of ectoplasm and endoplasm. In ordinary diarrhea or in helminthiasis he found the drug of no value. Putegnat (*N. R.*, 1883, xii, p. 102) has separated a bitter principle, *amargosin*, which, however, is of doubtful importance. The conclusions of Nixon concerning the amebicidal effects of chaparra amargosa have been confirmed by Shepheard and Lillie (*L. L.*, April 6, 1918), Seldards and McIver (*J. P. Ex. T.*, 1918, xi, p. 331). The chemical studies of the latter, while not conclusive, suggested the presence of a glucoside. Nixon preferred a decoction of the drug, but the fluidextract is upon the market and may be given in *doses* of one to three fluidrachms (4.0–12.0 cc.).

Castor. *Castoreum. Castoréum*, Fr. *Bibergeil*, G. *Castoro*, It. *Castoreo*, Sp.—In the beaver, *Castor fiber* L., between the anus and external genitals of both sexes, are two pairs of membranous follicles, of which the lower and larger are pear shaped, and contain an oily, viscid, highly odorous substance, secreted by glands which lie externally to the sac. After death, the follicles containing *castor* are removed, and dried either by smoke or in the sun.

This drug is derived either from the northern and northwestern parts of America, or from Russia, and is called in commerce, according to its source, Canadian or American or Russian castor. It is supposed by some that the American and Russian beavers are distinct species, the former being a building, the latter a burrowing animal, and additional ground for the supposition is afforded by the fact that the products of the two differ considerably. Of the Russian castor only a very small portion is imported into this country.

Castor comes to us in the form of solid unctuous masses, contained in sacs about two inches in length, larger at one end than at the other, much flattened and wrinkled, of a brown or blackish color externally, and united in pairs by the excretory ducts which connect them in the living animal. In each pair one sac is generally larger than the other. They are divided internally into numerous cells, containing the castor, which, when the sacs are cut or torn open, is exhibited of a brown or reddish-brown color, intermingled more or less with the whitish membrane forming the cells. Those brought from Russia are larger, fuller, heavier, and less tenacious than the American; and their contents, which are of a rusty or liver color, have a stronger taste and odor, and are considered more valuable as a medicine. A variety of Russian castor, described by Pereira under the name of *chalky Russian castor*, is in smaller and rounder sacs than the American, has a peculiar empyreumatic odor very different from that of the other varieties, breaks like starch under the teeth, and is characterized by effervescing with diluted hydrochloric acid. Müller found 40.646 per cent. of calcium carbonate. According to Kohli, Canadian castor, treated with distilled water and ammonia, affords an orange precipitate, while the precipitate thrown down from the Russian under similar treatment is white.

Good castor has a strong, fetid, peculiar odor; a bitter, acrid, and nauseous taste, and a color more or less tinged with red. It is of a softer or harder consistence according as it is more or less thoroughly dried. When perfectly desiccated, though still slightly unctuous, it is hard, brittle, and has a resinous fracture. Its chemical constituents, according to Brandes, are volatile oil, 2 per cent.; resinous matter, 14–50 per cent.; albumin; a substance resembling *osmazome;* mucus; salicin; cholesterin; calcium urate, carbonate, benzoate, phosphate, and sulphate; sodium acetate and chloride; potassium chloride, sulphate, and benzoate; ammonium carbonate; membranous matter, and a peculiar proximate principle discovered by Bizio, an Italian chemist, and called by him *castorin*. For additional information concerning castor, see *U. S. D.*, 19th edition, p. 1435.

Castor was at one time much used as a stimulant antispasmodic, also as an emmenagogue, but has passed almost entirely out of vogue except in perfumery where the alcoholic solution is used in the same manner as preparations of musk and civet. It may be given in *hysterical affections* in *doses* of ten to thirty grains (0.65–2.0 Gm.), in capsules or emulsion.

A substance allied to castor is the secretion of the anal glands, used for the purpose of defence by the *Mephitis mephitica*, or common *skunk* of North America. According to T. B. Aldrich, this is a neutral, golden-colored liquid, having an extremely penetrating and disagreeable odor, containing mercaptan, allyl-sulphide, and traces of butyl-mercaptan. (*C. D.*, 1897.)

Catalpa. *Catalpa bignonioides* Walt. *Catalpa-tree*, or *Catawba-tree. Indian Bean.*—This is a beautiful indigenous, flowering tree, of the fam. *Bignoniaceæ*, the seeds of which have been employed in *asthma*. Eugene O. Rau obtained from them tannin and a bitter crystalline principle. (*A. J. P.*, xlii, 204.) F. K. Brown obtained from the seeds resin, fixed oil, tannin, sugar, and two crystalline bodies, their exact nature not being determined. (*A. J. P.*, 1887, 230.) I. Schneck states that large doses cause nausea, vomiting, and slow, weak, intermittent pulse. He gave two fluidrachms (7.5 cc.) of the tincture (1 oz. troy to 1 pint) every one to three hours.

Cataplasms. *Cataplasmata. Poultices. Cataplasmes*, Fr. *Umschläge, Breiumschläge*, G.—*Cataplasms*, or poultices, are moist substances intended for external application, of such a consistence as to accommodate themselves accurately to the surface to which they are applied, without being so liquid as to spread over the neighboring parts, or so tenacious as to adhere firmly to the skin. As they are in this country seldom made by the pharmacist they are not deemed by the compilers of the U. S. Pharmacopœia proper objects for official direction. *Cataplasma Kaolini* is official in the National Formulary. (See Part III.)

Catha. *Catha edulis.*—Under various Arabic names, such as *Kât, Khât, Chaat, Kus es Salahin, Tchaad, Tschut, Tohat, Tohai, Gât,* the leaves of

Catha edulis Forsk. (fam. *Celastraceæ*) (*Abyssinian* or *African tea*) are very largely used as a stimulant in Northern Africa, the plant being extensively cultivated.

The plant is a shrub, reaching the height of nine to twelve feet, with thin coriaceous leaves whose margins are bluntly serrate. The rounded grayish-green twigs are, for commercial purposes, dried with the leaves and tied together in bundles containing about forty twigs; the bundles are commonly from twelve to fourteen inches in length and three to four inches in diameter, but sometimes much smaller. The leaves are chewed both in the green and fresh condition, and are in some places made into a tea. The taste is sweetish and astringent, somewhat suggesting licorice. They are asserted to act as stimulants, overcoming the sense of fatigue in the same way as cocaine, or caffeine. Flückiger and Gerrock found in it an alkaloid, *katine*, $C_{10}H_{18}ON_2$, which has been studied by Chevalier (*B. G. T.*, 1912, xviii), who finds that it is a stimulant to the central nervous system. Stockman (*P. J.*, 1912, lxxxviii) found three alkaloids, *cathine*, *cathinine*, and *cathidine*, and also a fourth alkaloid in too small quantities for study. He found (*J. P. Ex. T.*, 1913, iv) that these alkaloids were stimulating to both the brain and spinal cord, and in large doses produced paralysis through a direct action upon the muscle.

Cayaponia. *Cayaponia globosa. Silva Manso.*—This is a cucurbitaceous plant of Brazil, from which Gubler has extracted the alkaloid *cayaponine*, said to purge without griping. *Dose*, one grain (0.065 Gm.). (*Rép. de Pharm.*, 1879, 193.)

Ceanothus. *Ceanothus americanus* L. *New Jersey Tea. Red-root. Céanothe*, Fr. *Seckelblumen-wurzel*, G.—A small indigenous shrub, of the fam. *Rhamnaceæ*, growing from western Ontario and Maine southward. The *root* is astringent, and imparts a red color to water. F. C. Gerlach (*A. J. P.*, 1891, 332) finds 6.48 per cent. of tannin and 0.52 per cent. of an alkaloid to which he gives the name *ceanothine*. J. A. Buckner (*A. J. P.*, 1891, 428) found 9.45 per cent. of tannin in the leaves. Gordon (*Pharm. Rev.*, 1900, xviii) reported the presence of two crystalline alkaloids melting at 200° C. and 255° C. respectively. *Ceanothus* is said to be useful in *syphilis*. Schoepf states that it is purgative. Ceanothine has also been stated to act as a vasoconstrictor and a preparation of the bark has been put upon the market as a hemostatic. The leaves were used during the Revolutionary War as a substitute for tea. The Mexican *C. cœruleus* Lagasca (*C. azureus* Desf.) is used as a febrifuge.

Cecropia Obtusa Trec. (Fam. *Urticaceæ.*)—An extract of these leaves is used as a diuretic, having an action similar to that of digitalis though less toxic than it. *Dose* of the liquid extract, thirty minims (1.8 cc.).

Cedron.—The seeds of the *Simaba Cedron* Planch., a tree growing in Colombia and Central America, belonging to the *Simarubaceæ*. The fruit is a large solitary drupe, containing a single seed. *Cedron* seed is from 3 to 4.5 cm. long, and 1.5 to 2.5 cm. broad, elongated ovate, convex on one side, flat or slightly concave on the other, and presenting an oval scar near one extremity of the flat surface. It is often yellowish, hard and compact, but readily cut with a knife; is inodorous, but of a pure and intensely bitter taste, not unlike that of quassia. It yields its virtues to water and alcohol. Lowry (*J. P. C.*, xix, p. 365) separated from what he believed to be the seeds of *Simaba Cedron*, a crystalline substance which he named *cedrin*. Tanret, however, in attempting to confirm his work, was unable to obtain a crystalline substance from this plant, but he did from one closely allied to it, namely, the *S. waldivia*, and believed that Lowry was mistaken in the identity of his crude material. (See *P. J.*, 1908, lxxxi, p. 103.) Cedrin is now an article of commerce in the colorless crystals. It is bitter, slowly soluble in water, more readily so in alcohol or ether.

Cedron has been used in Central America as a remedy for snake bite and Purple has recommended it as an antiperiodic. The *dose* of the crude drug is from five to fifteen grains (0.3–0.9 Gm.). The bitter principle cedrin has been given hypodermically in *doses* of one-fifteenth of a grain (0.004 Gm.).

Celastrus.—Various species of the *Celastraceæ* have medicinal properties. In the East Indies the oil obtained from the seeds of *Celastrus paniculatus* Willd. is used as a powerful stimulant and diaphoretic in *rheumatism*, *gout*, and various *fevers*. The oil is said to be deep reddish-yellow, and to become thick and honey-like on keeping. It is sometimes known as *oleum nigrum*. In Abyssinia, according to Dragendorff, the leaves of *C. serratus* Hochst. (*C. obscurus* A. Rich.) are used as an antiperiodic under the name of *Add-add*. Dragendorff found in them tannic acid, a volatile oil, and a bitter principle, *celastrine*. (*A. J. P.*, xxvi.) In North America the bark of *Celastrus scandens* L. (*climbing staff tree, false bittersweet, fever twig*) has been used in chronic affections of the *liver* and in *secondary syphilis*, and is said to be emetic, diaphoretic, and alterative. C. H. Bernhard found in the bark acid and neutral resin, starch, glucose, gum, a caoutchouc-like body, coloring matter, and volatile oil. (*A. J. P.*, 1882, 1.) Wayne stated that he had isolated from *C. scandens* white minute crystals, to which he gave the name of *celastrine*. According to Ugolino Mosso (*Rivista Clinica*, 1891), celastrine arrests the frog's heart in systole; does not affect markedly the blood pressure in mammals, and influences the respiration only through its action on the vagus. The stimulant action is especially manifest on the brain and is not followed by a secondary depression. There is marked, persistent elevation of the temperature.

Celloidin.—A proprietary purified form of pyroxylin. It is supplied in shreds immersed in water. It is much used in microscopical technique.

Cellotropin. *Monobenzoyl Arbutin.* $C_6H_4.O.C_6H_5CO.O.C_6H_{11}O_5$.—This is prepared by acting upon arbutin with benzoyl chloride. It is a white, odorless and tasteless powder, practically insoluble in water or ether, but freely soluble in alcohol. To this substance Kapp (*Med. Rund.*, 1904) attributes the remarkable quality of being a specific curative in *pulmonary tuberculosis*. He asserts that it exercises direct action on the tubercle bacilli which he believes is probably due to an increase of the bodily enzymes. Its influence is generally manifest within a few weeks. It has also been used in *gastro-intestinal catarrh* and digestive disturbances of children. The *dose* for adults is put down as eight to fifteen grains (0.5–1.0 Gm.).

Cellu Flour. *N. N. R.* 1922.—Commercially pure cellulose in the form of flour, used as a means of filling out reduced diets in the Allen treatment for diabetics. A non-nutritive food substitute used to give bulk to foods.

Celluloid. *Zylonite.*—This material, which has been manufactured into so many useful forms, furnishes an excellent substitute for ivory, tortoise shell, amber, and vulcanite. It is a nitrocellulose, which is made capable of molding into any desired form by the admixture of a small amount of camphor. At the temperature at which the camphor melts, it acts as a solvent for the nitro-cellulose and forms a uniform plastic mass with it. This mass may be used directly in the manufacture of various articles, or it may be admixed with mineral coloring matters so as to imitate the various natural stones. The stratified appearance of ivory and the mottled appearance of tortoise shell and amber are obtained by passing between heated rolls plain and colored or clouded celluloid in alternating layers. The material is combustible when ignited, and in thin pieces burns rapidly with a bright light. For this reason it is a dangerous material from which to manufacture articles of wearing apparel, such as collars, combs, etc. Many of these articles are found on the market made of celluloid and some of these are falsely labeled rubber, ivory, tortoise shell, etc.

Within recent years so-called celluloid varnishes have come into extensive use for lacquering on metal; these are often nothing but pyroxylin solutions in which methyl alcohol, petroleum naphtha, and amyl acetate are used as a mixed solvent.

Cephalanthus. *Cephalanthus occidentalis* L. *Button Bush. Button Wood. Crane Willow. Swamp Dogwood.* (Fam. *Rubiaceæ.*)—A common indigenous shrub which grows in moist places, as along streams or on the borders of swamps. Its bark is bitter, is said to be laxative as well as tonic, and has been given in periodical fevers, in decoction or infusion. (See *M. R.*, 1911, 216.) E. M. Hattan found in it crystallizable fluorescent acid, a bitter uncrystallizable principle, a principle resembling saponin, tannin, two resins, fatty matter, gum, glucose, and starch. (*A. J. P.*, xlvi, 314.) According to Claassen (*Ph. Rund.*, Bd. vii, 1889), the fluorescent acid of Hattan is composed of two substances, *cephalin* and *cephaletin.* Carl Mohrberg has separated from the bark a substance which he knows as *cephalanthin*, and also a toxic saponin-like principle which, like its allied poisons, has the power of dissolving the blood corpuscles. Cephalanthin he finds to be a distinct poison to both cold and warm blooded animals, causing destruction of blood corpuscles with conversion of oxyhemoglobin into methemoglobin, violent vomiting, convulsions, and paralysis. (See *Kobert's Arbeiten*, viii, 1892.)

Ceratopetalum.—The New South Wales species of this genus, viz., *C. gummiferum* Sm. and *C. apetalum* Don., of the *saxifragaceæ*, yields considerable quantities of a kino-like gum. The barks contain coumarin. (See *P. J.*, xxi, 742.)

Cerberin.—The original substance described under this name was obtained from the seeds of the *Cerbera Odallam* Gärtn. (*Apocynaceæ*), but the name has been applied to principles from various allied plants. Under the name of *cerberid* there is upon the market a glucoside obtained from the *Thevetia Ycottli* DC. (*Cerbera Thevetia* L.). This is a yellowish, amorphous powder, with a bitter taste and soluble in water. According to Zotos (*In. Dis.*, Dorpat, 1892), it acts upon the heart like digitalis. Wagner (*Russki Vratch*, 1892, 1033) finds that it is too irritant to the intestinal tract to be clinically valuable. The *dose* is, hypodermically, one one-hundredth of a grain (0.0006 Gm.), by mouth, one-sixtieth to one-thirtieth of a grain (0.001–0.002 Gm.).

Cercis. *Cercis canadensis* L. *Judas Tree. Redbud.*—The bark of this beautiful leguminous tree, indigenous and well-known throughout the Eastern and Central United States on account of its brilliant red-purple flowers, which appear before the leaves, has been highly recommended by Wm. R. Smith as a mild but very active astringent in the treatment of *chronic diarrhea* and *dysentery. Dose,* of the fluidextract, from half to one fluidrachm (1.8–3.75 cc.).

Ceresin. *Ozokerite. Earth-wax. Neft-gil.*—Under this name there has been introduced into commerce, as a substitute for wax, a substance which closely resembles white wax, but which is a natural mineral product. It is found most abundantly in Galicia, on the slopes of the Carpathian Mountains, and also on the Wallachian side of the range, in smaller deposits along the Caspian. A valuable deposit has also been discovered in Southern Utah. It consists of a mixture of solid paraffin with some oxygenated bodies. The crude ozokerite is melted to allow earthy impurities to settle out, is treated with sulphuric acid and alkali, as in the treatment of paraffin, and is clarified by bone black, or, better, the black from the manufacture of potassium ferrocyanide. The refined ozokerite or *ceresin* melts between 58° C. and 80° C., is quite odorless and colorless, and has the appearance of bees' wax. It may be distinguished from the latter by its lower specific gravity (0.753 at 98° C. against 0.822) and its absolute resistance to alcoholic potassium hydroxide, no trace of saponifiable matter being present. F. Metz reports the finding of ceresin, colored with coal tar colors. (See *Ph. Ztg.*, 1904, 1031.) The Galician product is worked chiefly in Vienna and in London, where ozokerite candles are manufactured. (See *A. J. P.*, xlv, 11.) In this country ceresin bottles have replaced the gutta-percha bottles formerly used to contain hydrofluoric acid.

Cervitan. *Eldoform.*—This proprietary compound of tannin and yeast has been brought forward as an astringent for the treatment of various types of *diarrhea.* It is a grayish, tasteless powder, sparingly soluble in water or acid solutions but soluble in alkalies. It is marketed in the form of five-grain (0.3 Gm.) tablets of which from 2 to 3 may be given at a dose.

Cereus.—From *Cereus Cæspitosus* Engl. and A. Gray, Heyl separated an alkaloid, *pectenine*, which, according to Heffter (*A. Pharm.*, 1901, ccxxxix, p. 462), produce both in cold and warm blooded animals tetanic convulsions with heightened reflexes. According to the experiments of Mogilewa, the alkaloid acts upon the isolated frog's heart as a depressant.

From *Cereus pilocereus* (?), Heyl separated the alkaloid *pilocerëine*, which Heffter found to produce in frogs central paralysis with great cardiac depression, and in warm blooded animals to kill by cardiac arrest.

Anthelmintic properties have been ascribed to *Cereus flagelliformis* Miller and to *C. divaricatus* (Lam.) DC.

Cerium. (Ce. Atomic Weight 140.25.)—This metal was discovered in 1803 by Berzelius and Hisinger, and named cerium in honor of the goddess Ceres. It was obtained from a Swedish mineral, formerly, from its great weight, called *heavy stone of Bastnas* (*Bastnas Schwerstein*), but now named *cerite*, after the metal extracted from it. Besides cerite, it has been found in several other minerals, as *gadolinite, orthite*, and *monazite*, etc. It is not easy to obtain it pure in the metallic state, as its oxides and salts are difficult of reduction. Berzelius describes cerium as in the form of pulverulent masses, of a deep chocolate-brown color which exhibit, however, under the burnisher a metallic appearance and a dark gray color. Hildebrand and Norton have since prepared it in large quantity by the electrolysis of its chloride. It is a poor conductor of electricity. Sp. gr. 6.92 at 25° C., melting point 645° C. Heated in the air it takes fire before the point of ignition, and burns vividly, passing to the state of peroxide. At ordinary temperatures it is oxidized, in a moist atmosphere, giving out a strong and disagreeable odor. In water, especially when moderately heated, it rapidly oxidizes, with the evolution of hydrogen and the water does not become alkaline. There are two cerium oxides, Ce_2O_3 and CeO_2. Sulphur and phosphorus combine with it.

For methods of isolating metallic cerium see *U. S. D.*, 20th ed., p. 315.

The cerium compounds were formerly obtained chiefly from cerite, which occurs in considerable amounts in Sweden, and affords at least 50 per cent. of *cerium oxide*. The thorium salts were obtained from the mineral *thorite*, which is found in Norway, and contains about 60 to 70 per cent. of its peculiar earth. The supplies of thorite are not sufficient to even approximately meet the demand for thorium salts required for the incandescent gas mantle industry. At present most of it is made from the mineral *monazite*, which occurs in considerable quantities in North Carolina and in the Province of Bahia, in Brazil. Monazite is a *cerous phosphate*, in which a portion of the cerium is replaced by the other cerite earths. The thorium earth is not an integral constituent of the mineral, and, although quite regularly admixed with it, its amount varies within very broad limits.

Metallic cerium has come into prominence recently as an essential constituent of a class of alloys known as *pyrophoric alloys*, of which ferrocerium is the commonest and cheapest. These are used to set fire to inflammable gases, in what are called mechanical or automatic gas lighters, by means of a shower of bright sparks which is emitted when one of these alloys is filed. This property of certain alloys of cerium and other metals was discovered in 1903 by Welsbach, who found the best results to follow the use of a combination carrying about 65 per cent. of cerium earth metals and 35 per cent. of iron. Other alloys have also been experimented with, the one with zinc being used in practice in connection with automatic lighting mine lamps. The greatest pyrophoric power of any alloy yet experimented with was found to be developed in a platinum cerium alloy, but, of course, this is too expensive for practical use. Various theories have been advanced to explain the reason for the spark producing power of these alloys, it being claimed that the property is due to the presence of nitrides, hydrides, etc. None of these theories have been substantiated and the cause remains a mystery.

Cerium Oxalate. *Cerous Oxalate.*—Under the title *Cerii Oxalas*, the U. S. formerly recognized. "A mixture of the oxalates of cerium, didymium, lanthanum, and other associated elements." *U. S. IX.*

From the existing conditions of the thorium industry, the cerium oxalate of commerce, which, although used medicinally, consists of a complex mixture of the oxalates of cerium, lanthanum, and didymium, being more or less a by-product in the manufacture of thorium salts. See Power and Shedden, on the Composition and Determination of Cerium Oxalate. (*J. Soc. Chem. Ind.*, xix, No. 7; also *Ph., Ztg.*, 1902, 297.)

Cerium oxalate was officially described as "a fine white or slightly pink powder, without odor or taste; permanent in the air. It is insoluble in water, alcohol, ether, and in solutions of potassium or sodium hydroxide; insoluble in cold, diluted sulphuric or hydrochloric acid, but dissolved by these acids when heated. When heated to redness it is decomposed, leaving not less than 47 per cent. of a reddish-brown residue. Boil Cerium Oxalate with potassium hydroxide T.S.; an insoluble precipitate of white hydroxides is produced. Filter and supersaturate the filtrate with acetic acid; the addition of calcium chloride T.S. produces a white precipitate, insoluble in acetic acid but soluble in hydrochloric acid. From a solution of Cerium Oxalate in diluted hydrochloric or sulphuric acid, potassium hydroxide T.S., added in slight excess, precipitates white hydroxides, which do not redissolve in a larger excess of the reagent, but gradually turn yellow in contact with air. Ammonium carbonate T.S. added in slight excess to a similar acid solution produces a white precipitate of the mixed carbonates of cerium and associated elements, which is somewhat soluble in a larger excess of the reagent. Dissolve 0.1 Gm. of Cerium Oxalate in 1 mil of sulphuric acid and add 2 mils of potassium sulphate T.S.; small, colorless crystals of double sulphates of potassium and the rare-earth elements in the mixture are deposited after some time. No effervescence occurs when Cerium Oxalate is dissolved in diluted hydrochloric acid (*carbonates*). A solution of Cerium Oxalate (1 in 50) in diluted hydrochloric acid does not respond to the Test for heavy metals (see Part III, Test No. 3). A solution of Cerium Oxalate (1 in 25) in hot dilute sulphuric acid (1 in 3) meets the requirements of the Test for arsenic (see Part III, Test No. 1). Boil 0.3 Gm. of Cerium Oxalate with 15 mils of potassium hydroxide T.S. and filter. No precipitate is produced in 5 mils of the filtrate by boiling with an excess of ammonium chloride T.S. (*aluminum*) or in another 5 mil portion of the filtrate by the addition of sodium sulphide T.S. (*zinc*)." *U. S. IX.*

Bachem (*A. I. P. T.*, xvii, p. 363) has shown that cerium, didymium and lanthanum are all practically non-toxic although some of their salts possess antiseptic virtues. The commercial cerium oxalate being almost insoluble is not absorbed when given by the mouth and escapes wholly through the feces. It was originally brought forward by Sir James Y. Simpson as a remedy for the *vomiting of pregnancy* and has been used extensively in this affection and also in various other gastric disturbances attended with vomiting. Baehr and Wessler (*A. in M.*, 1909) have shown, however, that it has no effect in vomiting which is of central origin. Its value as an antemetic is probably precisely parallel to that of the insoluble salts of bismuth; when used in large quantities it forms a protective coating over the mucous membrane of the stomach.

Dose, one to ten grains (0.065–0.65 Gm.) three or more times a day.

Cetraria. *U. S.* 1890. *Iceland Moss. Iceland Lichen.*—Under this name the U. S. P. formerly recognized the dried plant of *Cetraria islandica* Acharius (*Lichen islandicus* L.) This plant, although known as Iceland moss, is not a moss, but a lichen which grows in most northern latitudes and on elevated mountains further south, including the Northern United States.

The dried plant is of diversified color, grayish white, brown, and red, in different parts, with less of the green tint than in the recent state. It was officially characterized as follows: "From 5 to 10 Cm. long, foliaceous, irregularly branched into fringed and channelled lobes, brownish above, whitish beneath, and marked with small, depressed spots; brittle and inodorous; when softened in water, cartilaginous, and having a slight odor; its taste is mucilaginous and bitter." *U. S.*, 1890. Macerated in water, it absorbs rather more than its own weight of the fluid, and, if the water be warm, renders it bitter. Boiling water extracts all its soluble principles. The decoction thickens upon cooling, and acquires a gelatinous consistence without viscidity. After some time the dissolved matter separates, and when dried forms semi-transparent masses, insoluble in cold water, alcohol, or ether, but soluble in boiling water, and in solution forming a blue compound with iodine. *Lichenin*, or *lichen starch*, $C_{12}H_{20}O_{10}$, resembles starch in its general characters, but differs from it in some respects. Lichenin has been found to consist of two distinct proximate principles, for one of which the name lichenin may be retained, while the other has been called *isolichenin* or *dextrolichenin* or *lichenoid*. According to Th. Berg (*Thèse de Dorpat*, 1872), *cetraria* yields 35.15 per cent. of total lichen-starch. Lichenin is insoluble in cold water, but swells up and easily dissolves in hot water. It is insoluble in alcohol and in ether. It is only tinged by iodine. Isolichenin is, on the contrary, colored blue by that reagent. It is, in part, dissolved in cold water, and the undissolved part is equally colored blue by iodine. It is, like lichenin, insoluble in alcohol and ether. Both substances are hydrolizable with mineral acids, yielding dextrose. For a further account, see *J. P. C.*, 1873.

The name *cetrarin* has been conferred on the bitter principle. Herberger's process for extracting it may be found in the 18th ed., U. S. D. By it one pound of moss yielded to Herberger 133 grains of cetrarin. Schnedermann and Knop have ascertained that cetrarin consists of three distinct substances: (1) *cetraric acid*, $C_{18}H_{16}O_8$, which is the true bitter principle, crystallizable, and intensely bitter; (2) a substance resembling the fatty acids, called *lichen-stearic acid*, $C_{14}H_{34}O_3$, the crystals of which melt at 120° C. and, (3) a green coloring substance, which they name *thallochlor*. These principles are obtained perfectly pure with great difficulty. (*Ann. Ch. Ph.*, lv, 144.) Hilger and Buchner (*Ber. d. Chem. Ges.*, 1890, p. 461) gives to lichen-stearic acid the formula $C_{43}H_{76}O_{13}$, and to cetraric acid the composition $C_{30}H_{30}O_{12}$, and both are shown to be dibasic acids.

The gum and starch amounting to about 80 per cent. in the air dried moss contained in the moss render it sufficiently nutritive to serve as a food for the Lapps and Icelanders, who employ it powdered and made into bread, or boiled with milk, after having partially freed it from the bitter principle by repeated maceration in water. As suggested by Berzelius, the bitterness may be entirely extracted by macerating the powdered moss, for twenty-four hours, in twenty-four times its weight of a solution formed with 1 part of an alkaline carbonate and 375 parts of water, then decanting the liquid, and repeating the process with an equal quantity of the solution. The powder, being now dried, is perfectly sweet, and has been used to some extent in pharmacy as a substitute for acacia, although lacking in adhesiveness. (See *Proc. A. Ph. A.*, 1892, 455.) It has been recommended for emulsion, salve bases, etc., and as a vehicle for disguising the bitter taste of some laxative drugs. This plan which has been proposed of first extracting the bitterness by maceration in water or a very weak solution of an alkaline carbonate, and afterwards preparing the decoction, has been criticized, as the peculiar virtues which distinguish the medicine from the ordinary demulcents are thus entirely lost. A pint (473 cc.) of the decoction may be taken during the day.

Iceland Moss has been much used in chronic *catarrhs*, especially of the pulmonary mucous membrane and even in *phthisis*. It acts chiefly as a mucilaginous drink, but as Kobert has found that *cetrarin* is a stimulant to the gastro-intestinal mucous membrane and to peristalsis, cetraria probably is feebly tonic. A 20 per cent. tincture has been recommended in *doses* of twenty to thirty minims (1.2–2 cc.) by Deying and Brice-Moret as an anti-emetic (*P. J.*, Oct. 30, 1897), which is confirmed by Gigon. (*R. T.*, 1905, p. 610.)

Cetraric acid, $C_{30}H_{30}O_{12}$, the bitter principle, is soluble in solutions of alkalies and their carbonates, in hot water and slowly in cold water. It has been used in the treatment of *anemias* and *digestive disturbances*. *Dose*, one and a half to three grains (0.096–0.2 Gm.).

Decoctum Cetrariæ. U. S., 1890. *Decoction of Cetraria. Decoction of Iceland Moss.*

"Cetraria, *fifty grammes;* Water, *a sufficient quantity*, to make *one thousand cubic centimeters.* Cover the Cetraria, in a suitable vessel, with *four hundred cubic centimeters* of cold Water, express after half an hour, and throw the liquid away. Then boil the Cetraria with *one thousand cubic centimeters* of Water for half an hour, strain, and add enough cold Water, through the strainer, to make the product, when cold, measure *one thousand cubic centimeters.*" *U. S.*, 1890.

Saccharum Cetrariæ.—Cetraria 1, sugar 1, water 100. Wash the cetraria with water to remove bitterness, then boil with 100 cc. of water, strain and express lightly, and in the strained liquid dissolve the sugar and evaporate upon a water bath. When sufficiently firm remove from the bath and dry in an oven to a scale or a powder.

The *Cetraria juniperina* (probably *Cetraria vulpina*) of Europe is said to be sometimes used as a poison for wolves and foxes, while the *wolf's moss* (*Ulfmossa*) of the north of Europe contains *vulpinic acid*, $C_{19}H_{14}O_5$, which has been found by Kobert to be an active protoplasmic poison; in frogs it produces tetanus, convulsions, and paralysis of central origin; in mammals it causes dyspnea, vomiting, trembling, and a slowing of the pulse, with rise of the blood pressure due to stimulation of the respective nerve centers. After death the blood is not coagulable, and the secreting kidney cells are found covered with a crystalline or amorphous mass of a vulpinate. No difference of action exists between vulpinic acid derived from wolf's moss and that synthetically produced. From *Cetraria pinastrin* Zopf has separated *pinastrinic acid,* which seems to be very closely allied to vulpinic acid. (*Sitzungsb. der Dorpat. Naturforsch.-Gesellschaft,* 1892.)

Cetyl Alcohol. *Alcohol Cetylicum.* $C_{16}H_{33}$-OH.—*Cetylic alcohol, ethal, æthol, primary hexadecyl alcohol,* is a tasteless, odorless, waxy powder, which fuses at 49.5° C. and boils at 344° C. It is soluble in alcohol and ether. According to Grimm (*Derm. Zeit.,* 1899, vol. vi), cetyl alcohol is absorbed and obstinately retained by the epidermis, producing a peculiar velvety condition of the skin. It has been found useful in the treatment of *chapped hands,* weeping *eczema,* and *prurigo.* Mixtures of it with boric acid or the borates have been put upon the market as cosmetics under the name of *Borsyl.* Grimm especially recommends equal parts of cetyl alcohol with boric acid or one part with five of powdered talc.

Champaca.—This is the *Michelia Champaca* L. (fam. *Magnoliaceæ*), a Javan tree which is famous for the sweet odor of its blossoms. From it Merck has obtained a camphor ($C_{17}H_{30}O$) to which the name *champacol* has been applied. For a study of the volatile *oil of champaca* flowers, see *Schim. Rep.,* Oct., 1907, p. 32 and Brooks (*J. Am. C. S.,* 1911, xxxiii, p. 1763).

Cheiranthus. *Cheiranthus Cheiri* L. *Wall flower.*—The flowers yield an oil which when highly diluted has the natural pleasant odor, but when concentrated the odor is disagreeable. (*Schim. Rep.,* 1911, 95; also *A. Pharm.,* 1912, 211.) From the leaves of this cruciferous European plant Moritz Reeb (*A. E. P. P.,* 1899, xliii, p. 130) separated a glucoside which exerted a digitalis-like effect on the heart and an alkaloid resembling quinine in its physiological action. These he called, respectively, *cheiranthin* and *cheirinine.* Subsequently Wagner separated another crystalline principle, *cheiroline,* that resembled cheirinine in its effects. Schneider (*Ann. Chem.,* 1912, cccxcii, p. 1) showed that it was a methylthiocarbimido-propylsulphone $C_5H_9O_2NS_2$.

Chelidonium. *U. S.* 1890. *Chelidonium majus* L. (Fam. *Papaveraceæ.*) *Celandine. Tetterwort.* —A perennial herbaceous plant growing wild in both Europe and America, recognized readily by its pinnate leaves, small peduncled yellow flowers and yellow opaque juice. The plant was formerly official and was described as follows: "Root several-headed, branching, reddish-brown; stem about 50 Cm. long, light green, hairy; leaves about 15 Cm. long, thin, petiolate, the upper ones smaller and sessile, light green, on the lower side glaucous, lyrate-pinnatifid, the pinnæ ovate-oblong, obtuse, coarsely crenate or incised and the terminal one often three-lobed; flowers in small, long-peduncled umbels with two sepals and four yellow petals; capsule linear, two-valved and many-seeded. The fresh plant contains a saffron-colored milk-juice, and has an unpleasant odor and acrid taste." *U. S.,* 1890.

Probst, of Heidelberg, found in it a peculiar acid denominated *chelidonic acid;* also the alkaloids chelerythrine, chelidonine and homochelidonine. For description of these see Sanguinaria Part I. There is present also a neutral crystallizable, bitter principle, which from its yellow color he calls *cheliodoxanthin.* Schlotterbeck (*A. J. P.,* 1902) has shown, however, that this is berberine. For an elaborate investigation of chelidonine, see a paper by Schlotterbeck and Knapp in *Proc. A. Ph. A.,* 1905, 217. For color tests for chelidonine, see *Proc. A. Ph. A.,* 1895, 922.

Chelidonine phosphate, chelidonine sulphate, chelidonine tannate, and *chelidonine muriate* have been used medicinally.

Under the name of *Panchelidon* there has been placed upon the market a preparation said to contain all the alkaloids of Chelidonium (see *Ph. Ztg.,* 1915, 539). Hanzlik (*J. A. M. A.,* 1920, lxxv, 1324) has suggested its use in *asthma* and *spasmodic colic.* Ribbing and Rumpf have used chelidonine clinically in *gastralgias* in *doses* of one and one-half to three grains (0.1–0.2 Gm.), but Peronin used from one-twentieth to one-third of a grain (0.003–0.02 Gm.).

Celandine is an irritant purgative to which toxic properties have been ascribed with doubtful correctness; in the fatal case of poisoning reported in the *Zeitsch. f. Medizinalbeamte,* 1898, it was not the cause of death. The irritant juice has long been used locally upon *corns, warts, eczema,* and other diseases of the skin, and even in *cancer.*

The *dose* of the dried root or herb is from thirty grains to a drachm (2.0–3.9 Gm.), that of the fresh root one or two drachms (3.9–7.7 Gm.), and the same quantity may be given in infusion. The *dose* of the aqueous *extract* is from five to ten grains (0.32–0.65 Gm.), of the expressed juice from ten to twenty minims (0.6–1.3 cc.), to be gradually increased.

Chelone. *Chelone glabra* L. *Snake-head. Turtle-head. Balmony. Shellflower. Chelone,* Fr. G.—The leaves of this common indigenous, perennial, herbaceous plant, of the fam. *Scrophulariaceæ,* have a bitter taste, and are said to be tonic and aperient, with a supposed peculiar action on the liver. The decoction (two ounces of the fresh herb to the pint) may be given in the *dose* of one or two fluidounces (30–60 cc.). *Chelonin,* an eclectic medicine prepared from *chelone,* is a brown, bitter powder administered as a tonic laxative in one and two grain *doses* (0.06–0.12 Gm.).

Chemical Food. *Compound Syrup of Phosphate of Iron.*—Under the name of *Chemical Food* several of the older writers have given complex formulæ for syrup containing combined phosphates of calcium, potassium, sodium and iron. Any virtue which resides in these preparations is represented by the compound syrup of the phosphate of the N.F. (See Part III). For Parrish's formula for similar syrup see *U. S. D.,* 20th edition, page 1315. *Compound Syrup of the Phosphates* (see Part III).

Chenopodium. *Chenopodium. American Wormseed.*—The fruit of *C. Ambrosioides* var. *anthelminticum* (L.) Gray (Fam. *Chenopodiaceæ*). This species of *Chenopodium,* known commonly by the names of *wormseed* and *Mexican Tea,* grows in almost all parts of the Eastern United States. By some it is regarded as a distinct species (*C. anthelminticum* L.), by others as only a variety. It is largely cultivated in Maryland (see *Ph. Era.,* 1921, liv, 23). The whole herb has a strong, peculiar, offensive, yet somewhat aromatic odor, which it retains when dry. All parts of the plant are occasionally employed, but the fruit alone was official in the U. S. P., 1890. This should be collected in October.

Wormseed is a utricle, a type of fruit which consists of an achene with a bladdery calyx investment. It is about 2 mm. in diameter, with a membranous pericarp, irregularly spherical, very light, of a dull greenish-yellow or brownish color, a bitterish, somewhat aromatic, pungent taste, and possessed in a high degree of the peculiar odor of the plant. These fruits, when deprived, by rubbing them in the hand, of the membranous calyx covering which invests the achene, exhibit the shining, blackish surface of the obtusely-edged achene. They abound in a volatile oil, upon which their sensible properties and medicinal virtues depend and which is obtained by distillation. (See *Oleum Chenopodii*, Part I.) The same oil impregnates to a greater or less extent the whole plant.

Of the activity of the wormseed as an anthelmintic there can be no question, but it has been entirely displaced by the official oil. The *dose* of the crude drug is from twenty to forty grains (1.3–2.6 Gm.). The seeds of *Chenopodium quinoa* form one of the staple foods of New Granada, Chili and Peru, and were used by Germany to some extent during the war. The protein content is about 20 per cent. and the starch content about 60 per cent. and 5 per cent. of fat is present also.

China Green.—This dye is asserted to have a specific antiseptic action on the *Bacillus coli* and to be useful as a means of distinguishing between that organism and the *B. typhosus.* For method of use, see Werbitzki, *Arch. f. Hyg.*, 1909, p. 191.

China Morada.—Under this name there appear to be used in Bolivia several barks. One of these has been ascertained by Arati and Canzoneri (*L'Orosi*, Feb., 1889) to be the product of a rubiaceous tree, *Pogonopus tubulosus* (Rich.) K. Sch., and to contain an alkaloid *moradeine* besides a fluorescent substance, *moradin*, allied to scolopetin. (See *P. J.*, xix.)

Chinaphenine. $CO\begin{cases}NH.C_6H_4OC_2H_5\\OC_{20}H_{23}N_2O\end{cases}$. *Quinine Carbophenetidide. Phenetidin Quinine Carbonate.*—*Chinaphenine* occurs as a white, tasteless powder, slightly soluble in water, easily in alcohol, ether, and chloroform and benzene, forming salts which are soluble in water. Chinaphenine has been recommended by von Noorden as a mild antipyretic, as an analgesic in *diabetic* and other forms of *neuralgias;* also in *whooping cough.* The analgesic *dose* is twenty to thirty grains (1.3–2.0 Gm.) given in two portions. (*Ther. Geg.*, Jan., 1903.)

Chinaphthol. *Quinaphthol. Quinine-β-naphthol-α-mono-sulphonate.* $C_{20}H_{24}N_2O_2(C_{10}H_6OHSO_3H)_2$.—This substance is a yellow, crystalline powder fusing at 185° C., of a bitter taste, insoluble in cold water, moderately soluble in hot water and alcohol; it has been proposed by E. Riegler (*W. M. Bl.*, xix, 1896) as an antipyretic and intestinal antiseptic. He states that it is decomposed by the alkalies of the intestinal juices into its constituents—namely, quinine and β-naphthol-sulphuric acid—and that he has used it up to forty-five grains (3 Gm.) a day with satisfaction in acute *rheumatism* as well as in *typhoid fever.* It contains about 42 per cent. of quinine.

Chineonal.—This is *quinine diethyl-barbiturate* and represents approximately 63.8 per cent. of quinine and 36.2 per cent. of barbital. It occurs as colorless bitter crystals, sparingly soluble in water, readily so in alcohol. The idea of combining the properties of quinine and diethyl-barbituric acid does not appear to us to be an extraordinarily happy one. Fraenkel and Hauptmann, however (*Med. Klin.*, 1912, p. 1871), believe that the drug is of special value in *whooping cough.* It has also been used as a general nerve sedative. The *dose* is five to ten grains (0.32–0.65 Gm.), preferably in the form of tablets.

Chinoidinum. *U. S.* 1880. *Chinoidine. Quinoidine. Chinoidin. Quinoidin. Precipitated Extract of Bark. Amorphous Quinine. Quinine brute ou amorphe,* Fr.—The term chinoidine was first applied to all of the amorphous alkaloids existing naturally in cinchona bark, but it is now used to define a complex body consisting largely of alkaloidal products which are artificial and accidental, resulting from the application of heat. Evaporation of the mother liquor left after the crystallization of the quinine sulphate in the preparation of that salt, yields a dark colored substance having the appearance of an extract. Sertürner supposed that he had discovered a new alkaloidal principle in this product. Later, by the conjoint labors of the chemists, Winckler, Liebig, and Pasteur, it was proved that ordinary quinoidine consisted of two alkaloids, derivatives from quinine and cinchonine, with which they are respectively isomeric, though differing in being uncrystallizable, and named, in view of their origin, *quinicine* and *cinchonicine.* These alkaloids are decomposition products, caused by the action of heat, from quinine and cinchonine respectively. They differ from their natural alkaloids in being dextrorotatory. The pure amorphous quinine of Liebig was the former of these alkaloids. (*A. J. P.*, xviii, 181.)

The U. S. P. of 1880 described chinoidine as "a brownish-black or almost black solid, breaking, when cold, with a resinous, shining fracture, becoming plastic when warmed; odorless, having a bitter taste and an alkaline reaction. Almost insoluble in water, freely soluble in alcohol, chloroform, and diluted acids; partially soluble in ether and in benzol. The solutions have a very bitter taste. If Chinoidin be triturated with boiling water, the liquid, after filtration, should be clear and colorless, and should remain so on the addition of an alkali (abs. of alkaloidal salts). On ignition, Chinoidin should not leave more than 0.7 per cent. of ash." *U. S.*, 1880.

For formulas for various salts of chinoidine, see *N. R.*, 1882, 11, or *Proc. A. Ph. A.*, 1882, 417.

As an antiperiodic, chinoidine is inferior to the Cinchona alkaloids and more nauseating. From thirty grains to a drachm (2.0–3.9 Gm.) may be given, in divided doses, between the paroxysms of an *intermittent*, and its action closely watched.

Chinol. *Quinoline mono-hypochlorite.* $C_9H_6N.ClO$.—A white crystalline powder, odorless, having a pungent but not disagreeable taste. It is almost insoluble in cold and hot water, but quite soluble in alcohol. This substance is said to be actively antipyretic and analgesic, useful for the purposes for which antipyrin is employed. *Dose*, from three to five grains (0.2–0.32 Gm.).

Chinosol. *Quinosol. N. N. R.* 1924. $(C_9O_7ON)_2H_2SO_4$. *Normal Oxyquinolin Sulphate.*—This is a neutral compound of *oxyquinoline* from which the latter is readily liberated in a nascent condition.

It is a crystalline, yellow powder, very soluble in water, insoluble in alcohol and ether, having a feeble saffron-like odor. Its aqueous solution when very dilute produces with ferric chloride a bright green color.

Chinosol does not precipitate albumin, is affirmed to be very slightly toxic, unirritating, and possessed of an extraordinary power of penetrating tissues. It is incompatible with alkalies, and with iron and mercury compounds. In the report of the Council on Pharmacy and Chemistry of the American Medical Association (*J. A. M. A.*, 1910, liv, p. 1801), it was shown that chinosol is decidedly less efficient in its killing power on bacteria than is phenol; the 1 per cent. solution is not certainly fatal to the bacillus of typhoid fever even after ninety minutes' exposure. On the other hand, its power of restraining development is far superior to that of phenol; one part in ten thousand is sufficient to prevent development of the *Staphylococcus pyogenes* or the *Bacillus typhosus*, while I in 20,000 shows a marked inhibiting effect. Its toxicity is certainly very low; in the report of the Council on Pharmacy and Chemistry, guinea-pigs and rabbits frequently survive the administration of 3 Gm. by the mouth, or 1 Gm. hypodermically. In addition to its antiseptic action it is claimed for chinosol that while its own odor is comparatively little, it is a powerful deodorizer, and also energetic as a styptic.

Although it has been used in surgery for the disinfection of instruments and of the surgeons' hands, the use of chinosol for this purpose is not to be recommended, because of its low germicidal value. On the other hand, as an antiseptic in various conditions, as *vaginitis*, *rhinitis*, and similar *catarrhs*, there is much evidence of its value. It has also been used successfully as an intestinal disinfectant, and Lorch (*Deutsche Ärzte Zeitung*, 1908, p. 406) has even obtained favorable results in the treatment of *Asiatic cholera*.

As a local application to mucous membranes, it may be used in strengths of from 1 to 500 to 1 to 2000. Internally, it has been given in *doses* of five to fifteen grains (0.3–1. Gm.).

Chione. *Chione glabra* DC. *Palo Blanco.*—The bark of this West Indian rubiaceous plant is said to be largely used as an aphrodisiac and tonic. According to B. H. Paul and A. J. Cownley, it yields 1.5 per cent. of a pale yellow volatile oil composed largely of phenols. (*P. J.*, vol. lx.)

Chloral Ammonium. $CCl_3.CH(NH_2)OH$. *Trichloramido-ethylic Alcohol.*—This substance is said by W. B. Nesbit to act like hydrated chloral, but to be a stimulant to the circulation in *doses* of from five to twenty grains (0.32–1.3 Gm.). For method of preparation, see *T. G.*, 1888. The name *chloralamide* is correct as applied to this compound, but it is more frequently, although incorrectly, applied to the substance, Chloralformamide, which see.

Chloral Amylene Hydrate. *Amylene-chloral. Methyl Butanol Chloral. Dormiol.* $CCl_3.CHOH.O(CH_3)_2C_2H_5$.—Made by mixing 10 parts of anhydrous chloral with 6 parts of amylene hydrate. It is a colorless, oily liquid, sp. gr. 1.24, having a pungent, mint- and camphor-like odor and a cooling pungent taste. It is not miscible with cold water and is decomposed by boiling water, but is freely soluble in alcohol, ether, acetone, and the fixed oils. Its incompatibilities are the same as for chloral hydrate. While there is no doubt that dormiol is a powerful somnifacient, the experiments of Mayer (*Th. M.*, 1907, p. 250) indicate that its toxicity is practically the same as that of chloral hydrate. It is at present marketed in the form of a 50 per cent. solution, the *dose* of which is ten to thirty minims (0.6–1.8 cc.).

Chloral Carbol. *Chloral Phenol. Carbolated Chloral.*—According to Boureiz, when hydrated chloral and phenol are rubbed up in the proportion of 10 parts of the former to 14 parts of the latter, a liquid is obtained which has the sp. gr. of about 1.5 and is soluble in all proportions in water, alcohol, and ether. Applied locally it is a counterirritant and local anesthetic.

Chloral Cyanhydrate. *Chloral Hydrocyanate.* $CCl_3.CH(OH)Cn$.—This is a compound first prepared by Pinner and Bischoff, and recommended by Hermes (*Ph. Centralh.*, Aug., 1887) as a substitute for hydrocyanic acid, whose physiological action it is stated to share. *Chloral cyanhydrate* is represented by the formula $CCl_3—CH—\left\{\begin{matrix}OH\\CN\end{matrix}\right.$, and is described as a crystalline powder, consisting partly of colorless prisms and partly of rhombic tables, fusing at 61° C., easily soluble in water, alcohol, and ether. With the vapor of water it volatilizes in small quantity, and breaks up into its components, chloral and hydrocyanic acid. It contains 15.33 per cent. hydrocyanic acid. It is also decomposed by alkalies, with the formation of alkaline cyanides. Its aqueous solutions remain unaltered for a long time. Six and a half parts by weight of chloral cyanhydrate correspond with one part of anhydrous hydrocyanic acid.

Chloralformamide. *N. N. R.* 1924. *Chloralformamidum. U. S. VIII. Chloralamide. Chloralum Formamidatum.* P. G. $CCl_3.CH(OH)NH.CO$.—This compound of chloral and formamide which was formerly official is made by mixing 45 Gm. of formamide with 147 Gm. of anhydrous chloral, when combination ensues; the crystalline mass is purified by recrystallization. Chloralformamide occurs as in "colorless, lustrous crystals, without odor, and having a somewhat bitter taste. Soluble in about 18.7 parts of water, and in 1.3 parts of alcohol at 25° C. It is readily soluble in ether, glycerin, acetone, and acetic ether. When heated with water to 60° C., it is hydrolyzed, hydrated chloral and formamide being produced. When heated to from 114° to 115° C. it melts, but at a higher temperature it is decomposed. It is not affected by diluted acids, but it is decomposed on warming with alkali hydroxides, the solution becoming at first turbid, and then clear, while chloroform separates. If 0.2 Gm. be heated carefully in an open dish, it should not give off inflammable vapors, and should volatilize without leaving a weighable residue (absence of *inorganic impurities* and distinction from *chloral alcoholate* and *ethyl carbonate*). One Gm. of Chloralformamide dissolved in 10 cc. of alcohol should yield a solution which does not redden moistened blue litmus paper (absence of *formic, hydrochloric*, or *other free acids*). If 1 Gm. of Chloralformamide be dissolved in 10 cc. of alcohol, the addition of a few drops of silver nitrate T.S. should not at once produce turbidity (the absence of *decomposition products*)." *U. S. VIII.*

Chloralformamide is rapidly absorbed and after absorption gradually broken up in the system liberating chloral which exercises its characteristic narcotic effects. Apparently the formamide which is liberated at the same time antagonizes the depressant action of the chloral upon the nerve centers, for in the experiments of Wood and Cerna it was found that the action upon the circulation was feeble and the respirations more rapid than normal, which results are in accordance with those of Halasz (*W. M. W.*, 1889). On the other hand Langgaard (*Th. M.*, 1889) maintains that both of these functions are depressed. Clinically the drug is much slower in its action than chloral hydrate and has the advantage of being less irritant to the stomach. It is, however, much less certain in its action and while often of service in the milder types of *insomnia* can not be relied upon for more obstinate cases. The *dose* is from fifteen to thirty grains (1 to 2 Gm.).

Chloralimide. $CCl_3.CH—NH$.—This compound should not be confounded with chloralamide. Chloralimide is in colorless, inodorous, and tasteless long crystalline needles; melting at about 166° C.; insoluble in water; readily soluble in alcohol, in ether, in chloroform, and in oils. Concerning its physiological action we have no certain knowledge; it is asserted to be hypnotic in doses of from fifteen to sixty grains (1 to 3.9 Gm.).

Chloral Menthol. *Mentholated Chloral.*—This is obtained by triturating equal weights of hydrated chloral and menthol, and heating gently in a water bath until liquefied. It is an oily, colorless liquid, with a distinctly mint-like odor and warm taste, having a specific gravity of 1.1984. It is freely soluble in alcohol, chloroform, and petroleum benzin. (*A. J. P.*, 1886, 283.) *Chloral menthol* has been used as a counter-irritant and local anesthetic in facial and other *neuralgias*.

Chloralose. $C_8H_{11}Cl_3O_6$. *Anhydro-gluco-chloral.*—When equal parts of anhydrous chloral and glucose are heated together for an hour at the temperature at which chloral boils, two isomeric substances—*chloralose*, which is soluble, and *parachloralose*, which is insoluble—are formed. *Chloralose* occurs in small crystals having a very bitter and disagreeable but not acrid taste. It is freely soluble in alcohol and in hot water, slightly so in cold water, a little less than five grammes to the liter. Its melting point is 185° C.

Chloralose was introduced by Henriot and Richet (*C. R. S. B.*, 1893) who state that in the lower animals it is an active hypnotic differing from chloral in that it is not depressant to the circulation, has a stimulant rather than a depressant effect upon the motor centers of the brain and spinal cord and has a marked anesthetic power. This statement has been confirmed by Gautrelet (*J. P. C.*, 1918, xvii, 408).

As a practical hypnotic, the action of chloralose is very variable and is often attended by disagreeable results, ten grains frequently failing to cause sleep, although the same amount has produced complete unconsciousness with alarming symptoms. Partial general paralysis, tremors, great slowing of the pulse, and marked evidences of enfeebled heart action have not rarely followed the use of the drug, while involuntary discharges of urine, delirious intoxication, excessive vomiting, and other disagreeable symptoms have been noted. The *dose* is from five to ten grains (0.32–0.65 Gm.), given in capsules.

M. H. Rendu (*B. Hôp. Par.*, xx, 1895) has reported violent collapse, excessively rapid feeble pulse, pronounced disturbance of respiration, epileptiform convulsions, and collapse as produced by four grains (0.26 Gm.) of chloralose.

Chlorarsenol. *Solarson.*—Under this name is furnished a solution which is stated is contain 1 per cent. of *ammonium heptinchlorarsenate*.

This solution is recommended as a substitute for arsenous oxide in the treatment of *anemia, skin diseases, malaria,* etc. The advantages claimed for it are that it is much less irritant and can be given successfully by hypodermic injection and that, therefore, there is more certain absorption and benefit. It is supplied in the form of ampules, each containing 1 cc. and representing approximately 0.004 Gm. (one-fifteenth grain) of arsenous acid.

Chlorcresols.—The combinations of chlorine with the cresols are all of them active germicides.

The alcoholic solution of meta-chlorcresol has been highly recommended by Gottschalk (*D. M. W.*, 1911, p. 928) and others for the disinfection of the surgeon's hands. He used a proprietary preparation, *eusapyl*, which is an aqueous solution of chlorcresol in potassium ricinoleate. He used this solution in 1 per cent. strength in 70 per cent. alcohol. Another similar preparation is on the market under the name of *lysochlor*.

A compound of meta-chlorcresol with an alkali which is sold under the name of *grotan*, according to Schottelius, destroys all vegetative bacteria within five minutes if present in the strength of 0.5 per cent., and even the highly resistant anthrax spores are killed by a 1 per cent. solution in twenty minutes.

Chloretone. *Trichlorbutyl Alcohol. Acetone-chloroform. Chlorbutanol. N. N. R.* 1924. $CCl_3.(CH_3)_2.C.OH + \frac{1}{2}H_2O$.—It forms colorless crystals fusing at 80° to 81° C. It is soluble in approximately 125 parts of water, more readily soluble in alcohol and glycerin. It forms a mass or liquid when triturated with antipyrine, exalgine, menthol and phenol.

Chloretone, in 1894, was introduced as an anesthetic and hypnotic by J. A. Abel. When given in proper *doses* it produces in the lower animals a profound sleep with complete anesthesia without the respiration or blood pressure being seriously affected, although the period of sleep may last some hours or even days. If the dose be sufficient, however, death occurs from asphyxia. Chloretone has no influence upon the blood, very little upon blood pressure, although when brought locally in contact with the heart it acts as a depressant. The bodily temperature is distinctly lowered during anesthesia. The results of Abel in regard to the toxicity of chloretone have been challenged by E. Impens, who finds that chloretone restricts the combustion of oxygen more than 50 per cent. and that it is more dangerous than hydrated chloral.

Chloretone is a very useful anesthetic in the physiological laboratory. For this purpose it is best dissolved in olive oil and administered by intraperitoneal injection. The *dose* should be from 0.1 to 0.2 Gm. (1.5–3 gr.) per kilogramme of body weight.

Chloretone, as a hypnotic and antispasmodic, has failed to achieve the confidence of the profession, possibly because of timidity in dosage. Hutchins (*Annals of Surgery*, July, 1909) and Hobbs (*B. M. J.*, Nov., 1910) found it useful to control the convulsions of *tetanus*. They give from 45 to 60 grains (3–4 Gm.), dissolved in olive oil, per rectum in 24 hours. According to Hamilton chloretone has a phenol coefficient of 1.2. The saturated aqueous solution (containing about 0.8 per cent.) is a complete bacteriostatic and will destroy the *Bacillus typhosus* in two minutes' exposure. Rowe (*J. A. Ph. A.*, 1924, xiii, 22) finds that it has a marked relaxing effect on involuntary muscles. As a local remedy, chloretone is often of value because of its being both antiseptic and anesthetic, although its slight solubility in water interferes with its usefulness.

A dusting powder containing 1 to 2 per cent. has been found a serviceable application in painful ulcerations. Fioca (*Press. Med.*, 1917, p. 460) has reported favorable results from the use of pure chloretone, finely powdered, in painful conditions of the mucous membranes, as in the dysphagia of *laryngeal tuberculosis.* It is also of service for the relief of *gastralgia* and *vomiting;* Wynter (*Lancet*, 1907) and others have reported good results in the treatment of *sea-sickness.* A 1 per cent. solution, with menthol and camphor, in liquid petrolatum, has been used as a spray in inflamed states of the nasal mucosa.

The *dose* of chloretone for internal administration is ordinarily from five to fifteen grains (0.32–1 Gm.), but larger amounts may be given with safety.

According to Aldrich (*J. Biol. Chem.*, 1918) it may be detected in aqueous solutions by distilling with steam and then boiling the distillate in a flask provided with a reflex condenser. Needle-shaped crystals of chloretone will appear in the lower cooled end of the condenser which can be distinguished from chloral, camphor and brometone by physical and chemical tests.

Chlorine. *Chlorine gas.* Cl = 35.46.—The element chlorine is a greenish-yellow gas with an extremely irritating odor and about 2.5 times heavier than the air. It is the active ingredient in several official compounds, such as chlorinated lime and solution of chlorinated soda. In the elemental form it was the first poison gas employed during the World War. It has also recently come into popularity as a treatment for acute respiratory infections such as acute coryza. Vedder and Sawyer (*J. A. M. A.*, 1925, lxxxiv, 361) have reported over 1000 cases of *coryza, acute laryngitis, bronchitis, whooping cough* and *influenza* in which the inhalations of the gas apparently proved of much value. They used a concentration of about 0.015 milligramme per liter of air. Its real value, however, remains to be proven.

Chlorostigma. *Tasi.*—The *C. Stuckertianum* (*Asclepiadaceæ*), a South American plant, is asserted to contain an alkaloid, *chlorostigmine*, which has been used to stimulate the secretion of milk.

Chlorphenols.—By the action of chlorine upon phenol is produced a mixture of ortho- and para-chlorphenol ($C_6H_4Cl.OH.$) and by continued action trichlorphenol ($C_6H_2Cl_3.OH.$). *Orthochlorphenol* is a liquid boiling at 175° C. and solidifying at 7° C.; the *parachlorphenol* forms crystals melting at 37° C. and boiling at 217° C. Both have an unpleasant penetrating odor. *Trichlorphenol* (*omal*), which was discovered by Laurent, crystallizes in needles, which melt at 68° C. and boil at 244° C. It is easily soluble in alcohol and ether.

The introduction of one or more chlorine atoms into the phenol molecule increases very markedly the germicidal power and apparently in proportion to the number of chlorine atoms introduced. Unfortunately, however, the caustic and poisonous actions seem to be increased also. Karpow, working in the laboratory of Nencki, demonstrated that both orthochlor- and parachlorphenol escape with the urine, in combination with sulphuric acid, and probably also with glycouronic acid, the urine becoming rapidly blackish on exposure to air, and confirmed the observations of Külz (*A. G. P.*, Bd. xxx) that the urine of dogs poisoned with the chlorphenols polarizes to the left. It would appear almost certain that the chlorphenols undergo at least partial decomposition in the organism, giving origin to hydroquinone, pyrocatechin, and other educts found after poisoning with phenol. The action of these chlorophenols upon the general system is probably practically that of phenol. According to Bechold and Ehrlich (*Z. P. C.*, 1906, xlvii, p. 173), trichlorphenol in the strength of 1 part in 10,000 prevents the growth of all bacteria and is equivalent to 1 in 800 of phenol. Nencki states that a 2 per cent. solution of monochlorphenol is superior to a 5 per cent. phenol solution.

Spengler (*Arch. des Sci. Biol.*, 1895, iv) states that the parachlorphenol is especially poisonous to the tubercle bacillus and recommends its 10 per cent. solution in the treatment of *tubercular laryngitis.* In dilute solution the chlorphenols have also been used as general surgical disinfectants, but have failed to establish themselves clinically.

The *chlorsalols*, the *salicylic esters of chlorphenols*, were studied by Nencki and found to undergo decomposition in the intestines or system, the salicylic acid or its derivatives appearing in the urine. The antiseptic properties of these chlorsalols were found to be much greater than that of salol. Girard has used them in *doses* of from sixty to ninety grains (3.9–5.8 Gm.) a day in *cystitis* and *diarrhea* with excellent results. Passerini has employed them in *phthisis* and in *bronchitis* by means of an inhaling apparatus in which fifteen minims (0.9 cc.) are placed on a piece of cotton, the patient inhaling with slow and deep inhalations from five to ten minutes daily. Usually at first some pulmonic irritation, and even for a day or two temporary exacerbation, occur, but the final results were said to be remarkable.

Chlorolin is a liquid said to contain about 20 per cent. of a mixture of mono- and tri-chlorphenols. It is used as a disinfectant.

Menthorol, so-called, is a moderately thick liquid, with an agreeable taste and the odor of parachlorphenol, which is said to be a mixture of menthol and parachlorphenol. It may be used as a local remedy in a 5 to 15 per cent. solution in the treatment of *ulcerations of the throat and lungs.*

Chlorpicrin.—This compound which results from the action of nitric acid upon chloroform has been found practically useful for the destruction of insects in rooms. According to Roux (*C. D.*, 1919, xci) 750 Gm. of the gas will kill all insects in a room of 75 cubic meters within four hours.

Cholesterin. *Cholestrin. Cholesterol.* $C_{27}H_{46}O$.—This is a monatomic alcohol and occurs in wool fat, bile, and cod liver oil. When pure it is in the form of white scales, unctuous to the touch, very sparingly soluble in water but readily so in ether or chloroform. It has the property of neutralizing many hemolytic poisons, such as snake venom, saponin, etc., as has been shown by Ranson (*D. M. W.*, 1901) and confirmed by Jahnson-Blohm. (*Z. P. C.*, 1913, lxxxv, p. 59.) Because of this property it has been used in medicine in the treatment of various dyscrasias of the blood; thus it has been employed in *malarial hematuria* and other forms of *hemoglobinuria*, in *purpura*, *chlorosis*, *pernicious anemia*, and other forms of *anemia.*

Pringsheim (*Med. Klin.*, 1913, p. 254) recommends that it be administered intramuscularly, using doses of eight grains (0.5 Gm.) daily in the form of an aqueous emulsion. Reicher (*B. K. W.*, 1908) administers it by mouth dissolved in olive oil. He gives a 3 per cent. solution in tablespoonful *doses.* Under the name of *choleol* there is upon the market an oily solution which is claimed to contain the palmitin and olein esters of cholesterin. Almangea and Mendes (*Il Morgagni,* March 30, 1907) assert that *cholesterin* has the power of fixing the toxin of tetanus, and report two cases of *tetanus* which were cured by daily injections of cholesterin.

Chrome Yellow. *Chromate of Lead. Lemon Yellow. Leipsic Yellow. Paris Yellow.* $PbCrO_4$.—This is the neutral *lead chromate* prepared by precipitating a solution of lead nitrate with potassium chromate. It is of a beautiful lemon-yellow color. The *basic lead chromate* ($PbO,PbCrO_4$) possesses a red color, and is sometimes used as a pigment. *Chrome green* is either *chromium sesquioxide* or a mixture of chrome yellow and Prussian blue. The chromates are often adulterated with lead sulphate. Duviller (*J. P. C.,* Août, 1873, 114) detects this by heating one part of the suspected pigment with a mixture of from two to three parts of nitric acid, sp. gr. 1.420, one to two parts of water, and one-fourth part of alcohol. The chromate is all dissolved, but any sulphate present remains unaffected. Lead chromate has been used by bakers in place of eggs for giving a rich yellow coloring to buns, and there can be no doubt of its having produced fatal poisoning in a number of cases. This dangerous adulteration of food has not been reported for some years, but it was recently reported as being used in a coffee glazing preparation.

Chromium.—Chromium was discovered by Vauquelin in 1797. Its most common ore is *chrome iron,* consisting of ferrous oxide and chromium sesquioxide. This is not an abundant mineral, the principle source of supply being at present Asia Minor. Chromium is obtained by igniting its oxide in contact with charcoal with the aid of the electric arc; or by the more recent methods of reduction of its oxide by finely divided metallic aluminum (Goldschmidt), or by metallic silicon (Gren and Wahl). It is a brittle metal, of a grayish-white color like platinum, with some luster, and very hard, so that it scratches glass. Its sp. gr. is 6.5 to 6.8 at 15° C., atomic weight 15.7, and symbol Cr. It does not change by exposure to the air, and is with difficulty attacked by the acids. It forms with oxygen five compounds: (1) the monoxide (CrO), (2) the sesquioxide (Cr_2O_3), (3) the trioxide or chromic anhydride (CrO_3). (See *Chromii Trioxidum.*) Of the two others, one may be considered as a compound of the monoxide and sesquioxide ($CrO.Cr_2O_3$), and the other, called *perchromic oxide,* consists of two atoms of chromium and seven of oxygen (Cr_2O_7). Chromium combines with chlorine in two proportions, forming the *dichloride* and *sesquichloride.* The chief value of chromium in the arts is as the source of potassium dichromate and of pigments.

Chromium Sulphate.—This salt has been used by Kolipinski (*M. A.,* 1908) in a remarkably wide range of disorders. Thus, he has employed it with asserted success in *prostatic hypertrophy,* in *fibroid tumors* of the *uterus,* in *nervous vomiting,* for the relief of *menopausal symptoms,* but he especially recommends it in the treatment of *locomotor ataxia* and *exophthalmic goiter.* His results do not appear to have been confirmed.

Chrysarobin Oxidized. *Chrysarobini Oxydatum.*—A brownish-black powder, obtained by boiling chrysarobin in water with sodium peroxide; its 5 to 10 per cent. ointment has been highly recommended by Unna in the treatment of facial, genital, and other forms of *eczema* for which chrysarobin is too irritating. It has no influence in dry eruptions.

Cichorium. *Cichorium Intybus* L. *Chicory. Succory. Blue Sailors.*—A perennial herbaceous composite plant, indigenous to Europe, but naturalized in the Northern United States and Canada, where it grows in fields, and in roads along the fences. The whole plant has a bitter taste, without acrimony or any very peculiar flavor. The taste is strongest in the root and weakest in the flowers. The leaves, when young and tender, are eaten as salad. Chicory is a feeble, non-irritating tonic. Nietzki (*A. Pharm.,* 1876) found in the blossoms a glucoside to which the formula $C_{32}H_{34}O_{19}$ has been assigned.

The root is much used as a substitute for, or adulterant of, coffee. In preparing it, Dausse recommends that the dried root should be cut into rather large and equal pieces, which are to be roasted until they lose 140 out of 500 parts. The pieces are then easily ground in a mill, and afford a yellowish-brown powder. (*Ph. Cb.,* 1850, 688.) For methods of detection in ground coffee, see *P. J.,* 1867, 141; also Allen (*Com. Org. Anal.,* 2d ed., vol. iii, part 2, 540), and J. R. Leebody (*Chem. News,* 1874, 243); see also paper by LaWall and Forman (*A. J. P.,* 1913, 535). Chicory root itself is sometimes adulterated with beet root. The latter may be detected according to Collin (*Ann. Falsif.,* 1917) by numerous oral cells filled with calcium oxalate.

The garden *endive* is a variety of *Cichorium, Endivia* L.

Cicuta. *Cicuta virosa* L. *Water Hemlock. Cowbane. Ciguë vireuse,* Fr. *Wasserschierling,* G.—A perennial, umbelliferous European plant, growing on the borders of pools and streams. It is very poisonous to most animals, though said to be eaten with impunity by goats and sheep. A number of the species of *Cicuta* are intensely poisonous; indeed, the statement is made that *C. maculata* L. is the most poisonous plant native in the United States. The *C. vagans* (*Oregon water hemlock*), *C. occidentalis* Dougl. and *C. bulbifera* L., all of which are found in various parts of North America, are actively poisonous, as is also the European species *C. virosa.* From the last named, Van Ankum (*J. P. C.,* 1868) obtained a resinous body which was intensely poisonous, resembling picrotoxin in its physiological action, and to which he gave the name of *cicutoxin.* This has since been shown by Jacobson (*J. Am. Chem. Soc.,* 1915, xxxvii, 1916) to occur in the *C. maculata, C. bulbifera* and *C. occidentalis.* It is a yellowish, viscid liquid which, however, can be obtained as an amorphous solid by dropping a concentrated alcoholic solution in the cold benzin. It has weak alcoholic properties and is very sensitive to heat being decomposed by a temperature of 100° C. Jacobson assigns to it the formula $C_{19}H_{26}O_3$. Böhm (*A. E. P. P.,* v, 281) obtained from the dry root about 3.5 per cent., the fresh 0.2 per cent. of cicutoxin. The presence of a volatile alkaloid resembling coniine, and termed *cicutine,* has been observed by Wittstein and Buignet. According to Jacobson, cicutoxin is fatal to lower animals in doses of 50 mgm. per kilo.

Cicuta maculata L., *American water hemlock, Musquash root, Beaver poison, Spotted cowbane.*

This grows in meadows and on the borders of streams throughout the United States, and is closely analogous, in botanical character and in effects, to the European species. In several instances children have been fatally poisoned by eating its root. This consists of several oblong, fleshy tubers, sometimes as long as the finger, spreading out from the base of the stem, and having an odor and taste not unlike those of parsnip. For microscopic examination of plant, see *A. J. P.*, July, 1891, and *Merck's Report*, 1909, p. 35. Cicuta has been highly lauded as a specific in nervous and sick *headache* (*Proc. A. Ph. A.*, 1858, 253), but is rarely if ever used. J. E. Young found in the seeds an alkaloid supposed to be identical with coniine. (*A. J. P.*, xxvii, 294, confirmed by R. Glenk, *A. J. P.*, 1891, 328.)

Egdhal (*A. I. M.*, 1911, vii, p. 348) has collected the history of 46 cases of poisoning by cicuta, of which twenty-one were fatal. Nausea, vomiting, and convulsions occurred in practically all the cases. In most of them there was also bloody froth at the mouth and in many dilated pupils and unconsciousness. In his own case there was cyanosis apparently from interference with the respiration by the convulsions.

In cicuta poisoning there is generally violent vomiting, followed by vertigo, cold clammy skin, slow, feeble pulse, general convulsions and later paralysis, unconsciousness and dilated pupils. Tannic acid has been suggested as an antidote, but its efficiency has not been proved. The treatment should be evacuation of the stomach, stimulants to combat the collapse, and the cautious use of morphine to control the vomiting and convulsions.

Cignolin. 1–8—*Dioxy-Anthranol.*—This is a yellow powder soluble in fats, alcohol, acetone, etc. It is asserted to have a similar effect to chrysarobin and to be a valuable local remedy in *psoriasis.* (See *Ph. Era.*, 1916, xlix, 193).

Cinchonidine Salicylate. *Cinchonidinæ Salicylas.* $C_{19}H_{22}ON_2.C_7H_6O_3$.—This salt occurs in needles soluble at 18° C. in 766 parts of water. It is capable of producing physiologically the action of the quinine salts, but as an antiperiodic is inferior to other salts of that alkaloid. It has been recommended and considerably used as a specific in *chronic* and *subacute rheumatism*, in *doses* of from fifteen to twenty grains (1–1.3 Gm.) a day, best given in pill or capsule.

Cinchophen Compounds.—A number of compounds of phenyl-cinchoninic acid have been introduced under various trade names as remedies in *rheumatism* and *gout.* The action of these is essentially similar to that of the official cinchophen (see Part 1) although various advantages of lower toxicity and lack of irritant action upon the stomach is claimed for them.

Acitrin is the ethyl ester of phenyl-cinchoninic acid $C_9H_4N.C_6H_5COOC_2H_5$. It occurs as a pale yellow crystalline powder without odor or taste, very slightly soluble in water but soluble in alcohol or ether. The *dose* is eight to fifteen grains (0.5–1.0 Gm.).

Chloroxyl (*Cinchophen Hydrochloride*—$C_{16}H_{11}O_2N.HCl$) is a yellow crystalline powder with an astringent, bitterish taste, insoluble in water, sparingly soluble in alcohol. The *dose* is eight to fifteen grains (0.5–1.0 Gm.).

Paratophan. Methyl-atophan. Homophan $CH_3.C_9H_4N.C_6H_5COOH$.—This is the methyl ester of phenyl-cinchoninic acid. It is a yellow crystalline powder insoluble in water but dissolved by alkalies, also soluble in alcohol or ether. The *dose* is eight to fifteen grains (0.5–1.0 Gm.).

Iriphen is *strontium-alpha-phenylcinchoninate.* It occurs as a yellowish-white crystalline powder and is employed in *doses* of from eight to fifteen grains (0.5–1.0 Gm.).

Neocinchophen. N. N. R. 1924. *Novatophan,* or *Neoquinophan* $CH_3.C_9H_4N.C_6H_5COOC_2H_5$ is the ethyl ester of paratophan. It is a yellowish, odorless and tasteless powder, almost insoluble in water but soluble in alkaline solutions and in alcohol. *Dose,* eight to fifteen grains (0.5–1.0 Gm.).

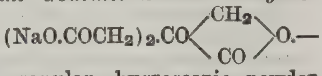
Oxyl-iodide—$C_{16}H_{11}O_2N.HI$.—This is said to be the hydriodide of cinchophen and to represent 67 per cent. of phenylcinchoninic acid and 33 per cent. of iodine. Its effects would seem to be due more to the iodine than to the cinchophen portion. It is recommended in *doses* of three to nine grains (0.2–0.6 Gm.).

Isatophan. Methophan. Methoxy-Atophan. Methoxy-phenyl-cinchoninic acid. $C_9H_5N.C_6H_5COOCH_3O$. *Dose,* eight to fifteen grains (0.5–1.0 Gm.).

Tolysin.—This is an ethyl ester of para-methyl phenyl cinchoninic acid and therefore isomeric with neocinchophen. Barbour, Lozinsky and Clements (*A. J. M. S.*, 1923, clxv, p. 708) find that this compound differs in its effects from cinchophen in that it is so slowly absorbed from the intestines that it is very difficult to give large enough doses to cause toxic manifestations. They find it is a useful drug in *rheumatic fever* and other forms of *arthritis.* They recommend *doses* of fifteen to thirty grains (1–2 Gm.).

Cineraria Maritima L.—This composite plant, known popularly as *Dusty Miller,* is a native of the West Indies, and has been introduced as a house plant into this country. There is upon the market a proprietary preparation which professes to be the expressed juice of this plant, and is recommended in diseases of the eye, especially as an absorbent of *cataracts.* We do not know, however, of any sufficient scientific justification for a belief in this improbable property.

Cinnamic Acid. *Acidum Cinnamicum.* $C_6H_5-CH=CH.COOH$.—This acid occurs naturally in Peru and Tolu balsams and in Styrax, and is made synthetically by the reaction of acetyl chloride upon benzaldehyde, or by the action of a mixture of acetic anhydride and fused sodium acetate upon benzaldehyde. It forms colorless, lustrous plates, melting at 133° C., and is insoluble in cold water, but quite soluble in boiling water and in alcohol. Under the name of *hetol, sodium cinnamate* has been used to a considerable extent in the treatment of *tuberculosis.* For a volumetric method of assay of sodium cinnamate, see *P. J.*, 1910, 365. A. Landerer (*M. M. W.*, xxxv, Nos. 40, 41), put forward most remarkable claims for it; but W. J. Robinson (*M. A.*, 1902), after careful review of all the evidence, reached the conclusion that sodium cinnamate is not a direct curative agent in tuberculosis and is of no more value symptomatically than is creosote. Sodium cinnamate may be given by the mouth in *doses* of from two to three grains (0.13–0.2 Gm.). The initial intravenous *dose* of the intravenous treatment recommended by Landerer, should not exceed one-fiftieth of a grain (0.0013 Gm.); the injection may be made every third day and the amount increased until one-third of a grain (0.021 Gm.) has been reached. A 10 per cent. solution in glycerin affords an excellent method of administration. Sodium cinnamate has also been recommended for the treatment of *keratitis*. Pflüger (*Klin. Monatsbl. für Augenheilkunde*, 1901) instils into the eye a 1 per cent. solution to which is added 1 per cent. of cocaine.

Citarin. *Citromin. Goutine. Sodium Anhydromethylene-citrate.*  $(NaO.COCH_2)_2.CO\left\langle\begin{matrix}CH_2\\CO\end{matrix}\right\rangle O$.—This is a white, granular, hygroscopic powder possessing a slightly acidulous taste. It is soluble in less than 2 parts of water. It readily liberates formaldehyde from its solutions, especially in the presence of alkalies. It is asserted to be a useful remedy in cases of *uric acid gravel*, and in *gout* and *chronic rheumatism*, in *doses* of thirty to forty-five grains (2–3 Gm.) four times a day.

Citrophen. *Paraphenetidin Citrate.* $C_3H_4(OH)(CONH.C_6H_4OC_2H_5)_3. + 3H_2O$.—This compound of citric acid and *p*-phenetidin is a white, crystalline powder, soluble in forty parts of water, with a faint acid taste; its melting point is 181° C. and its ready solubility in water adapts it for hypodermic use. It is used as an antipyretic, also in *migraine* and *neuralgia*. *Dose*, ten to fifteen grains (0.65–1.0 Gm.).

An identifying test for citrophen is the production of a beautiful violet color when its solution is mixed with a solution of potassium dichromate. This reaction is also given by pyramidon which, however, does not give the reaction for the phenetidin group.

Civet. *Zibethum. Civette*, Fr. *Zibeth*, G.—This is an odorous substance, obtained from two animals of the genus *Viverra;* the *V. Civetta* or *civet cat* of Africa, and the *V. Zibetha*, which inhabits the East Indies. It is secreted in a cavity opening between the anus and external genitals, and is collected from animals confined for the purpose. It is semi-liquid, unctuous, yellowish, becoming brown and thicker by exposure to the air, of a very strong, peculiar odor, similar to that of musk, though less agreeable and less diffusible, and of a bitterish, subacrid, disagreeable fatty taste. When heated it becomes quite fluid and at a higher temperature takes fire and burns with a clear flame, leaving little residue. It is insoluble in water, and only slightly soluble in ether and cold alcohol, but heated alcohol dissolves it almost entirely, depositing it again upon cooling. It contains, among other ingredients, a volatile oil, fat, and free ammonia. Sack (*Ap. Ztg.*, 1915, 423) has separated from civet a ketone which he calls *zibethon* which, even in solutions as low as 1 in 1000, shows a fine musk-like odor. E. Charabot and A. Hébert give the following tests for *civet* of normal quality: When dissolved in a mixture of alcohol and ether less than 6 per cent. residue should remain. The saponification number of civet should exceed 100, and the fatty acids which are separated from the saponified civet after acidulation with sulphuric acid should exceed 50 per cent. (*Bull. Soc. Chim.*, 1910, iv, 7, 687.) In medicine it was formerly employed in lieu of castor and musk; it is now used exclusively as a perfume. For analyses of commercial samples, see *P. J.*, 1897, 101.

Clematis. *Clematis recta* L. (*C. erecta* L.) (Fam. *Ranunculaceæ.*) *Upright Virgin's Bower. Waldrebe*, G.—A perennial European plant. The leaves and flowers have an acrid, burning taste. When bruised in a mortar they irritate the eyes and throat, giving rise to a flow of tears and to coughing, and applied to the skin they produce inflammation and vesication; hence their old name of *Flammula Jovis.* The acridity is greatly diminished by drying. Störck found this clematis to be diuretic and diaphoretic, in *doses* of from one to two grains (0.065–0.13 Gm.) of the extract a day, or from thirty to forty grains (2–2.6 Gm.) of the leaves given in infusion three times a day, and to be useful, locally and internally, in *syphilitic, cancerous*, and other *foul ulcers.*

Other species of *clematis* have the same acrid properties; among these *C. flammula* L., or *sweet-scented virgin's bower*, which, though a native of Europe, is cultivated in our gardens, *C. vitalba* L., or *traveller's joy*, also a native of Europe, and several indigenous species, of which *C. virginiana* L., or *common virgin's bower*, *C. viorna* L., or *leather flower*, and *C. crispa* L. have been used as substitutes for *C. recta* L. All these are climbing plants. Rochebrune (*Toxicol. Africaine.* i) affirms that he has found in *C. flammula* L. an alkaloid, *clematine*, two milligrammes of which will produce in the guinea-pig copious and frequent urination, general tremors, great disturbance of respiration, feebleness and intermittency of the heart beat, followed in seven minutes by convulsions ending in coma and death.

From the bruised roots and stems of *C. vitalba* L., boiled for a few moments in water to diminish their acridity, and then digested in sweet oil for a little while, is made a preparation used locally in Europe for the *itch.* Gaube has found in this species an alkaloid. (*J. P. C.*, 1869.)

Clemens's Solution.—*Arsenic bromide* was introduced as a remedy in diabetes by Clemens. This preparation is recognized in the N. F. IV under the name *Liquor Arsenicalis Clemens* (see Part III). It was formerly called *Liquor Potassii Arsenitis et Bromidi* and contains one gramme of arsenic trioxide to the liter (in the form of a complex mixture with bromine and potassium). According to Clemens, the commencing dose of such a solution is one minim three times a day, increased gradually until the equivalent of one-fifth of a grain of the salt is daily exhibited. The clinical reports in regard to this remedy in *diabetes* seem to indicate that along with a restricted diet it is occasionally of distinct service, but in the majority of instances fails to accomplish good.

Clove Bark. *Cortex Caryophyllatus. Cassia Caryophyllata.*—The bark of *Dicypellium caryophyllatum* Nees. (Fam. *Lauraceæ*), a tree indigenous to Brazil but also growing in the West Indies. It is usually in large compound quills, up to 4 cm. thick and 60 cm. in length, composed of numerous separate pieces 1 to 2 mm. thick, rolled around one another and having a chestnut brown color, being more or less flaky on the outer surface and finely striate on the inner surface, with a short fracture showing a whitish line near the outer margin, a pungent taste, and an odor similar to that of cloves (see *A. J. P.*, vol. xv).

Cnidium Officinale.—K. Sakei (*Chem. Abst.*, 1917, xi, 2386) states that native practitioners of China, Japan and Korea use the roots of this plant extensively for various nervous diseases, especially those of the head and brain, and for some female disorders. The chief ingredient of extracts of this drug is a volatile oil—*oil of cnidium*, which is present to the extent of about

0.82 per cent. He finds the volatile oil is a stimulant to the vaso-motor system and to the spinal cord.

Coal Tar Colors.—Many colors used in dyeing and in coloring food-stuffs, beverages and medicines are synthesized from one or the other of the commercially valuable fractions of coal tar. Many of these were formerly known as *aniline colors*, because the earlier colors of coal tar origin came from the fraction known as *aniline*. As many of them are now commercially prepared from other fractions of coal tar, the term *coal tar colors* seems more appropriate. A large number of the coal tar dyes are active anti-bacterial agents. Davis found that 61 out of 204 dyes studied by him had antiseptic properties. Kligler (*J. Ex. M.*, 1918, xxvii, p. 463) has made an elaborate study of the relation between chemical structure and germicidal effect, especially of the triphenylmethane compounds. Most of these which have attained any therapeutic importance, are described under their appropriate titles. (See *Fuchsine, Methyl Violet, Scarlet Red*, etc.)

The use of coal tar colors for artificially imitating the natural color of any food-stuffs is now largely prohibited by law, with the exception of such instances where the color is used principally for æsthetic reasons, as in confectionery, or where proper notice is given to the consumer by plainly printing on the label of the package the words "Artificially colored." Even then such colors are sometimes prohibited, as in the legislation in Pennsylvania concerning fruit syrups (Act of 1905) where all coal tar colors are specifically prohibited in the act.

The feeling against the use of coal tar colors as such, which still largely obtains among the uneducated and less well informed, is undoubtedly due to the indiscriminate use of them in the early days and the fact that many of them were not freed from poisonous mineral constituents like arsenic or mercury, compounds of which were often used in their manufacture. Many of the coal tar colors in former use are now known to be harmful, such as *victora yellow* (*dinitrocresol*). A list of permissible colors has, therefore, been prepared by the U. S. Department of Agriculture, which may be used under such circumstances as permit the use of a harmless color and when not otherwise prohibited. This list has been adopted by a number of the States having food laws in harmony with the National legislation on this subject.

Cobalt. (Co = 58.56.)—This not very abundant metal is usually found associated with arsenic, and is rarely used in its pure condition in medicine or pharmacy. It occurs as *smaltine* or *tin-white cobalt, cobalt glance*, or *sulpharsenide; cobalt bloom, erythrine*, or *arsenate*; *earthy cobalt* or *wad*, a mixture of cobaltous oxide and black manganese oxide, and *spiess cobalt*, $(Co,Ni,Fe)As_2$. It is found chiefly in Bohemia, Pretoria, Sweden, Ontario and Colorado and in smaller amounts in Cornwall and Silesia. Almost the whole of the world's commercial supply now comes from Cobalt City, in the Lake Tamiskaming district, Ontario, Canada. Here the arsenides of cobalt and nickel are associated with silver and constitute a valuable by-product of the silver mining of that district.

Spiess cobalt is frequently employed as the source of cobalt salts, and the substance called in commerce *zaffre* is an impure cobalt arsenate, made by simply roasting the crude cobalt ores or calcining them, with access of air, and is used to give a blue color to glass, enamels, and pottery glaze. The native ore is frequently found in commerce under the name of *flystone*, and is used for poisoning flies, by roughly grinding it and putting a small quantity in a saucer with sweetened water. *Smalt* is the common name used for glass colored by fusing with cobalt oxide, producing a blue pigment, for coloring glass, etc. The soluble salts of cobalt, particularly the *chloride* and *sulphocyanate*, have been used to impregnate paper,* etc., giving it ordinarily a pink tint, indicative of the presence of moisture, while on elevation of temperature and drying the color changes to blue. Advantage has been taken of this fact to produce the so-called *barometer paper*.

A cobalt oxide, prepared by precipitating the chloride with potassium hydroxide, has been employed in *rheumatism*. It is emetic in the *dose* of 10 to 20 grains (0.65–1.3 Gm.). The salts of the metal are irritant poisons. The statement that the cobalt salts and hydrocyanic acid will form in the animal system a potassium or sodium-cobalt-cyanide and are antagonistic poisons and may be used as antidotes one for the other, is probably not correct. (See Hübner, *A. I. P.*, vol. ix.)

Cobalt Blue.—This beautiful pigment is a compound of cobalt oxide and aluminum oxide, obtained by precipitating the mixed solutions of a salt of aluminum and one of cobalt by means of an alkali, and washing, drying, and strongly calcining the precipitate. (Berzelius.) The *cobalt blue* of Thénard is made by heating together the hydrated cobalt sulphosphate and aluminum hydroxide. It is used in painting.

Cobweb. *Spiders' Web. Tela Arachneæ.*—Spiders' webs were formerly much used in *headache, hectic fever, asthmas, hysteria*, and *nervous irritation*, but probably acted solely through the imagination. *Dose*, from ten to twenty grains (0.65–1.3 Gm.) *pro re nata*. Spider's web was formerly used as a styptic, especially after extraction of teeth, the cavity being stuffed full of the web.

Coca. *Cocæ Folia U. S. P. VIII. Br.* 1898. *Coca Leaves. Cuca. Feuilles de Coca*, Fr. *Cocablätter*, G. *Coca del Peru, Ipadu*, Sp.—"The dried leaves of *Erythroxylon Coca* Lamarck (Fam. *Erythroxylaceæ*), known commercially as Huanuco Coca, or of *E. Truxillense* Rusby, known commercially as Truxillo Coca, yielding when assayed by the process given below, not less than 0.5 per cent. of the ether-soluble alkaloids of Coca." *U. S. VIII.* "The dried leaves of *Erythroxylum Coca*, Lam., and its varieties." *Br.*, 1898.

The *coca* plants are shrubs or small trees, some of the species reaching the height of fifteen or twenty feet. It is conjectured that the original habitat was in the Peruvian mountains, from 7° South to 10° North, but either spontaneously or through cultivation the coca shrubs have spread until they are found in the whole Eastern curve of the Andes, from the Straits of Magellan to the borders of the Caribbean Sea, growing on the moist sides of the mountains at the elevation of 1500 to 6000 feet, the climatic requisites being moisture and equable temperature, with a mean of about 17.7° C. The wild coca shrub commonly reaches the height of 12 feet, and some are 18 feet, but the cultivated coca is usually kept down to about 6 feet. The leaves are gathered three times a year; the first harvest, or preliminary picking, is taken at the time of the trimming of the bushes, from the cut-off twigs. Then about the end of June, a scanty crop is gathered, while the last crop of the season is gathered in October or November. Harvesting must always take place in dry weather, so that the fresh leaves when spread out in layers two or three inches thick on the drying pavement can be collected in six or eight hours.

The coca plant, which is propagated from the seed in nurseries, begins to yield in eighteen months, and continues productive for half a century. The leaves, when mature, are carefully picked by hand so as to avoid breaking them or injuring the young buds, are slowly dried in the sun, and are then packed in bags holding from twenty-five to one hundred and fifty pounds each. Coca was in general use among the natives of Peru at the time of the conquest, and has continued to be much employed to the present time. It is affirmed that nearly ten million dollars' worth, or forty million pounds, are annually produced, some plantations yielding three or four harvests a year. For details as to method of cultivation, etc., see *T. G.*, Jan., 1886; also *C. D.*, 1897, 182. Coca leaves are chiefly imported from Peru, where the plant has been under cultivation since prehistoric time. Two varieties of the coca leaf occur in the commerce of the United States, namely, the so-called Huanuco coca and the Truxillo coca, the Huanuco variety being produced in Bolivia, Huanuco, Brazil, Venezuela and Argentina, while the Truxillo coca is produced chiefly in Northern Peru. The great variation in the leaves and other portions of the coca plant, produced by its long-continued cultivation, has produced much doubt and discussion as to the specificity and characteristics of the plant: H. H. Rusby has made an elaborate study of the subject (*D. C.*, Nov., 1900).

Huanuco coca has been for a long time believed to be obtained from *Erythroxylon Coca;* this belief is confirmed by Rusby and was accepted by the Pharmacopœial authorities.

Truxillo coca is the product of the *E. Coca Spruceanum* of Burck; the name "spruceanum" had, however, been used elsewhere before it was suggested by Burck and in obedience to the ordinary rules of botanical nomenclature it was changed by Rusby, who regards it as a distinct species, to *E. Truxillense.*

Coca is cultivated in the British East and West Indies, and in Java, and the product is said to appear, in the London markets, under the names of Truxillo coca and *Java coca.* This coca is entirely distinct from the Truxillo coca of the American market, and does not reach the United States. According to Emma Reens, *E. spruceanum* or *E. novogranatense* are cultivated in Java (*B. Sc. Pharm.*, 1919, xxvi, 497). The coca shrubs of India and Ceylon are the offspring of plants originally sent out from Kew Gardens, which plants were derived from seeds obtained in Huanuco, and were considered by Morris as representing a variety of *E. Coca* to which he gave the name of *E. Nova-Garatense.* According to Rusby, however, this plant is a distinct species, and the same as that previously described by Jacquin, from Colombia, under the name of *E. carthagenense* (the name *E. carthagenense* not being, as it is held in the Kew Index, a synonym of *E. areolatum*).

The leaves of the different varieties of coca do not, on the whole, resemble one another at all closely, but are distinguished from most other leaves by a slightly curved line on each side of the midrib, running from the base to the apex. This line has the appearance of a rib, but is really not of this character, having been produced during development by the peculiar folding of the leaf in the bud. The two commercial varieties were very well described in the *U. S. VIII* as follows:

"*Huanuco Coca.*—Greenish-brown to clear brown, smooth and slightly glossy, thickish and slightly coriaceous, stoutly and very shortly petioled; blade 2.5 to 7.5 Cm. long and nearly elliptical, with a very short and abruptly narrowed basal portion and a short point, the margin entire; midrib marked above by a slight ridge, very prominent underneath, the remaining venation rather obscure, especially above; underneath, a conspicuous line of collenchyma tissue runs longitudinally on either side of the midrib and about one-third of the distance between it and the margin, the enclosed areola being of a slightly different color from the adjacent surface; odor characteristic; taste bitterish, faintly aromatic, followed by a numbness of the tongue, lips and fauces.

"*Truxillo Coca.*—Pale green, thin, brittle and usually much broken, smooth, but not shining, shortly and stoutly petioled; blade 1.6 to 5 Cm. long and one-third to one-half as broad, obovate to oblanceolate, narrowed from near the middle into the petiole, usually with a slight projecting point at the summit, the margin entire; underneath two irregular lines of collenchyma tissue, usually incomplete or obscure, and frequently wanting, run beside the midrib at about one-third the distance from it to the margin; odor more tea-like than that of Huanuco Coca; taste and numbing effect similar." *U. S. VIII.* "The midrib itself is prolonged into a minute horny apiculus, which, however, is frequently broken off. Most of the epidermal cells of the under surface are seen in transverse section to project in the form of small papillæ." *Br.*, 1898.

Coca contains a number of alkaloids (see under *Cocaina* Part I). In addition Hesse (*P. J.*, April, 1903, p. 285) has also extracted four definite compounds not alkaloids, from the leaves of coca obtained from Java. These bodies are 1. *Cocacitrin*, $C_{23}H_{32}O_{17}$, a yellow crystalline compound with three molecules of water, melting at 186° C. This appears to be a glucoside yielding a sugar, *cocaose*, which may be identical with *dextrotalose*, since its osazone melts at 180° C. 2. *Cocacetin*, $C_{16}H_{12}O_7$, forming yellow needles with three molecules of water of crystallization. This melts at 260° to 265° C. 3. *Cocaflavin*, $C_{34}H_{38}O_{19}$, which forms yellow crystals with four molecules of water. It yields dextrose and galactose on hydrolysis with diluted sulphuric acid, and is, therefore, probably a glucoside. 4. *Cocaflavetin*, containing two methoxy groups, forms greenish-yellow needles with three molecules of water and melts at 230° C. The tannin of coca leaves strikes a green-black with ferric salts, and has received the name of *cocatannic acid.* Romburgh detected traces of *methyl salicylate* in the distillate from coca. (*Chem. Ztg.*, 1895, 130.)

Assay. U. S. VIII.—"Coca, in No. 60 powder, *ten grammes;* chloroform, ether, normal sulphuric acid V.S., ammonia water, distilled water, tenth-normal sulphuric acid V.S., fiftieth-normal potassium hydroxide V.S., cochineal or odeosin T.S.,

each, *a sufficient quantity.* Place the *Coca* in an Erlenmeyer flask, add 50 cc. of a mixture of chloroform 1 volume and ether 4 volumes and insert the stopper securely. Allow the flask to stand ten minutes, then add 2 cc. of ammonia water mixed with 3 cc. of distilled water, and shake the flask well, at frequent intervals, during one hour. Then transfer as much as possible of the contents of the flask to a small percolator which has been provided with a pledget of cotton packed firmly in the neck, and inserted in a separator containing 6 cc. of normal sulphuric acid V.S., diluted with 20 cc. of distilled water. When the liquid has passed through the cotton, pack the Coca firmly in the percolator with the aid of a glass rod, and, having rinsed the flask with 10 cc. of chloroform-ether mixture, transfer the remaining contents of the flask to the percolator by the aid of several small portions (5 cc.) of a chloroform-ether mixture, using the same proportions as before, and continue the percolation with successive small portions of the same liquid (in all 50 cc.). Next, shake the separator well for one minute, after securely inserting the stopper, and when the liquids have completely separated, draw off the acid liquor into another separator. Add to the chloroform-ether mixture 10 cc. of a sulphuric acid mixture, using the same proportions as before, agitate well and again draw off the acid liquid. Repeat this operation once more, drawing off the acid solution as before into the second separator, introduce a small piece of red litmus paper, add ammonia water until the liquid is distinctly alkaline, and shake out with three successive portions of ether (25, 20, and 15 cc.). Collect the ether-solutions in a beaker, place it on a water-bath filled with warm water, and allow the ether to evaporate entirely. Dissolve the residue in 3 cc. of ether, and let this also evaporate completely. To the alkaloidal residue add 4 cc. of tenth-normal sulphuric acid V.S. and 5 drops of cochineal or iodeosin T.S., then titrate the excess of acid with fiftieth-normal potassium hydroxide V.S. Divide the number of cubic centimeters of fiftieth-normal potassium hydroxide V.S. used, by 5, subtract this number from 4 (the 4 cc. of tenth-normal sulphuric acid V.S. taken), and multiply the remainder by 0.03 and this product by 10, to obtain the percentage of ether-soluble alkaloids contained in the Coca." *U. S. VIII.* For methods of assaying coca leaves, see Lyons, *Ch. Ph.*, Sept., 1885; Squibb, *Ephem.*, 1887; Dohme, *Proc. A. Ph. A.*, 1893, 159; Prescott, *Organic Analysis; Proc. A. Ph. A.*, 1895, 268; *P. J.*, 1896, 1901, 222, 254; *Ph. Ztg.*, 1901, 965.

In South America many of the Indians habitually chew the leaf of the coca plant, generally mixed with some alkali as ashes or lime. It is stated on good authority that they will go for days performing hard physical labor without any other food. It is, however, clearly proven that these leaves do not take the place of nutriment, but simply put off the sense of fatigue and hunger. Eventually, however, this habit undermines the health and finally the inveterate excessive coca-chewer can be recognized by his uncertain step, general apathy, sunken eyes surrounded by deep purple aureoles, trembling lips, green and crusted teeth, and excessively fetid breath, with peculiar blackness about the corners of the mouth. An incurable insomnia is apt to be developed, emaciation becomes extreme, dropsy appears, and even death results from a condition of general marasmus. It has been believed that the effects of coca chewing are different from those produced by the alkaloid cocaine and hence it has been by some argued that the coca leaf contains other active principles, but there is no difference between the results of the habit as practised by the South American Indian and the use of the alkaloid by depraved Caucasians, which cannot be readily explained on the ground of difference in the mode of taking the stimulant or racial variation. While there are other active substances present in the coca leaf, it is not manifest that they modify the action of the crude drug materially. For a study of the uses and effects of its alkaloids see *Cocaina* Part I and *Tropacocaine* Part II.

Coca has a slight bitter tonic effect as well as a stimulant action upon the central nervous system and has been used as a tonic in *neurasthenia* and other debilitated conditions. The danger of the formation of the habit, however, far outweighs any value the drug may possess, and the use of the crude preparation of coca seems to us hardly justifiable except under the most extraordinary conditions. The *U. S. P., VIII*, recognized a fluidextract, the dose of which was from thirty to sixty minims (2–3.9 cc.), and a wine the dose of which was two to eight fluidrachms (7.5 to 30 cc.).

Cochlearia. *Cochlearia officinalis* L. *Common Scurvy-grass. Herbe au Scorbut*, Fr. *Herba Cochleariæ*, P. G. *Löffelkraut*, G. *Spoonwort.*—This annual or biennial cruciferous plant is a native of northern and middle Europe and grows in Arctic America generally. The whole herb is active. It has, when fresh, a pungent, unpleasant odor if bruised, and a warm, acrid, bitter taste. These properties are lost by drying. They are imparted to water and alcohol by maceration, are retained by the expressed juice, and probably depend on a peculiar volatile oil, which is separable in very small quantity by distillation with water, and is probably produced by reaction between a fixed principle in the plant and water, under the influence of myrosin acting as a ferment. (*Chem. Cb.*, 1856, 124.) According to Hofmann, the oil is a sulphur-containing oil of the butylic series, having the formula $C_5H_9NS = C_4H_9CSN$.

Common scurvy-grass has been much used in *scurvy*, and even in *chronic rheumatism*. The fresh plant may be eaten as a salad, or used in infusion; the expressed juice has also been used.

Codeonal.—Under this name a mixture which is asserted to contain 2 parts of *Codeine-diethyl-barbiturate* with 15 parts of *sodium-diethyl-barbiturate* has been introduced. The purpose of the combination is to obtain the sedative action of codeine and barbital in combination. It is used as a somnifacient, as a cough sedative, and as an analgesic. The *dose* recommended is from two to eight grains (0.13–0.5 Gm.).

Codeine Hydriodide. $C_{18}H_{21}O_3N.HI + 2H_2O$.—A crystalline powder, slightly soluble in cold and very soluble in warm water, is made by the action of hydriodic acid on codeine (alkaloid). It has been used subcutaneously in lung affections and internally in *doses* of one-sixth to one-fourth grain (0.011–0.016 Gm.), several times daily.

Codeine Methyl Bromide. *Codeine Brommethylate.* $C_{18}H_{21}NO_3\ (Br.CH_3)$.—Under the trade name of *Eucodein*, this has been introduced as a cough sedative. The experiments of Jacoby (*Med. Klin.*, 1905, p. 208) indicate that it is a less powerful drug than codeine, but because of its more feeble convulsant effect can be used in larger *doses.* It has been used in doses of one or two grains (0.065–0.12 Gm.) three times a day.

Cœlocline. *Xylopia polycarpa* Oliver. (*Cœlocline polycarpa* DC.). *Berberin Tree. Yellow-dye Tree of Soudan.*—This is a small tree, of the Fam. *Anonaceæ,* growing in Soudan, Sierra Leone, and certain parts of Western Africa. When wounded, the tree exudes a juice which produces a yellow stain upon linen that cannot be washed out. The outer surface of the bark is greenish-gray interrupted by occasional blackish patches; the inner layers are of a golden yellow, and very fibrous, so that they can be separated in ribbon-like bands. The bark is moderately but disagreeably bitter, and stains the saliva yellow. Water extracts its color and bitterness. Stenhouse has ascertained that it contains *berberine.* The bark is much used in Africa for dyeing yellow. In Sierra Leone it is employed topically, in powder or decoction, for *obstinate ulcers.*

Colalin.—A mixture of hyoglycocholic and hyotaurocholic acids obtained from bile, with a little magnesium carbonate to retain the pulverulent condition. *Dose,* one-fourth to one-half grain (0.016–0.032 Gm.).

Collinsonia. *Collinsonia canadensis* L. *Stone-root. Horseweed. Horse-balm. Richweed. Heal-all. Knot-root. Knob-weed. Guérit-tout, Baume de Cheval,* Fr. *Collinsonie,* G.—A labiate plant, which grows in woods from Canada to the Carolinas. The whole plant has a strong disagreeable odor, and a warm pungent taste. C. N. Lochman (*A. J. P.,* 1885, 228) found in the root a resin, tannin, starch, mucilage, and wax; in the leaves resin, tannin, wax, and volatile oil. The alkaloid discovered by H. J. Lohmann in the root of the *Collinsonia canadensis* appears to have been a magnesium salt. (See *D. C.,* 1902.) Collinsonia is tonic, astringent, diaphoretic, and diuretic. It is said to be locally irritant. A decoction of the fresh root has been used in *catarrh of the bladder, leucorrhea, gravel,* and *dropsy.*

Colloids.—The studies of Thomas Graham in 1862 in connection with dialysis, in which he originated the terms "crystalloid" and "colloid," remained without any special industrial or therapeutic application for many years. Recently much work has been done upon this somewhat neglected subject and some wonderful results have been obtained. The *colloids* of Graham's time were mainly organic substances analogous to glue or gelatin, although some inorganic colloids were known, such as the colloidal form of ferric hydroxide formerly known as *dialyzed iron.* As the osmotic pressure observed in colloidal solutions is extremely small we may infer that the colloids possess large molecular weights. They do not form true solutions, but form pseudo-solutions known as *sols,* or *hydrosols* when they are placed in water. The substance separating from a sol or hydrosol is called a *gel* or *hydrogel,* and the phenomenon of separation is called gelatinization. In the case of suspension of a very fine solid in a liquid by means of colloids the sol is called a *suspensoid,* or if globules of liquid are suspended, it is called an *emulsoid.*

Colloids are also known as reversible colloids or non-reversible colloids according to the stability when evaporated or redissolved. As a rule colloidal solutions are decomposed by the presence of ionizable compounds in appreciable amounts. Some colloidal substances as gelatin, casein, etc., promote stability of colloidal forms of other substances and are therefore known as protective colloids. Many colloidal preparations of the metals such as silver, mercury, etc., are prepared in this way and are much more stable than the colloidal form of the pure elements.

Hydrosols have all the external appearance of true solutions because they are homogeneous and may be filtered without leaving any solid residue on the filter and show no visible particles under ordinary microscopic observation. The small suspended particles of hydrosols may be seen clearly with the ultramicroscope (a microscope in which a luminous ray is concentrated by means of a lens and the illumination of the microscopic field produced by directing the ray at right angles to the direction of vision) as shown by the researches of Siedentopf and Zsigmondy in 1903. The particles thus observed are visible as luminous points which are in constant motion, called Brownian movements. The size of the particles varies from one ten-thousandth mm. to one two-hundred thousandth mm. A colloidal solution of gold containing 0.005 Gm. per cc. contains about 1000 million particles of suspended gold per cu. mm., which is equivalent to an immense increase of exposed surface and which accounts for some of the marvellous effects of colloidal metal solutions, particularly as catalysts.

Colloidal metals, gold, silver, iron, etc., are all found in the market at the present time under various designations. They are prepared by either electrical or chemical methods. The electric method comprises the use of the electric arc which, passing between two pieces of a given metal under water, produces the microscopic pulverization of the metal, resulting in a colloidal solution (so called) or hydrosol of that particular metal. The chemical method consists in the application of a powerful chemical reducing agent to a solution of the salt of the desired element. Colloidal suspensoids of metallic salts, as calomel (see calomelol), or bismuth oxide (see bismon), are also coming into use.

In view of the increasing number and importance of colloidal silver preparations, the assay for silver content has been given considerable attention by various authorities (see *Merck's Rep.,* 1914, 69; *Arch. Pharm.,* 2529, 69 and 497).

The colloidal metals in some cases produce catalytic effects similar to those produced by certain enzymes, as, for instance, the inversion of cane sugar by colloidal platinum. The metallic hydrosols are therefore sometimes called metallic ferments.

The colloidal solutions of the metals usually exhibit dichroism to a certain degree, that is, they are clear by transmitted and turbid by reflected light. The coloration of the famed ruby glass is due to a colloidal state of the particles of metallic gold therein contained. The ripening of the silver bromide gelatin plates in photography and of certain clays in ceramics, which require several months' empiric treatment to produce the proper degree of elasticity, is now known to be due to the formation and action of colloids.

In 1905, Robin (*Nouv. Rem.,* 1905) reported the results of some observations of the effects of subcutaneous injections of hydrosols. He found that they produced an increased excretion of urea and uric acid and marked leucocytosis. He likewise reported favorable clinical results in *pneumonia* and *articular rheumatism* from their employment. His results were confirmed by Izar and Hergage, 1909, who also found that it was of no importance which metal was employed. This fact taken together with the statements of Paderi (*Lo Sperimentale*, 1909) that silver hydrosol is without bactericidal or antiseptic properties, and especially in view of the extremely small quantity of metal in solution in many of the preparations used, point strongly toward the conclusion that such benefit as has resulted from the use of colloidal metals is not to be attributed to the influence of the metals themselves. On the other hand, many of those who have assigned beneficial effects to the use of these preparations describe reactions very similar to those which have since been found to be brought about by the parenteral administration of various proteins. (See *Protein therapy*). It seems to justify the hypothesis that the colloidal metals when injected subcutaneously bring about a stimulation of the defensive processes of the body of the same nature as those caused by foreign proteins, in fact, Auld (*B. M. J.*, Feb. 16, 1918) is led to the conclusion that the metals themselves play no part in the clinical benefit but that the favorable results are due to the peptone which has been added as protective.

Among the preparations of colloidal metals which are on the market are: *Electrargol*, a form of colloidal silver (see under *Silver, Colloidal*); *Electraurol*, a form of colloidal gold; *Collaurum*, another form of colloidal gold; *Electrocuprol*, a form of colloidal copper; *Electromercurol*, a form of colloidal mercury (see also *calomelol*); *Electromartiol*, a form of colloidal iron; *Cuprase*, a form of colloidal copper.

Cologne Water. *Spiritus Odoratus. N. F. IV. Perfumed Spirit. Eau de Cologne*, Fr. *Kölnerwasser*, G.—*Cologne water* is official in the N. F. IV (see Part III). A more fragrant spirit, and one more closely resembling the original, would be made if the quantity of oil of orange flowers were doubled.

Colubrina.—*Mabee bark*, yielded by the *Ceanothus reclinatus* L'Herit. (*Colubrina reclinata*, Brongn.) (Fam. *Rhamnaceæ*) of South America, has been analyzed by Elborne and Wilson, who find in it a glucoside. It is used in the West Indies as a stomachic. (See *P. J.*, April 11, 1885.)

Colutea. *Colutea arborescens* L. *Bladder Senna. Baguenaudier, Séné Indigène*, Fr. *Falsche Senna*, G.—A leguminous shrub growing spontaneously in the southern and eastern parts of Europe, and cultivated in gardens. The leaflets are purgative, and in some parts of Europe are used as a substitute for senna, which is said to be sometimes adulterated with them. Barbey (*P. J.*, 1895, 261) isolated *coluteic acid*, which occurs in white crystals, insoluble in water, soluble in alcohol, chloroform, and carbon disulphide. Bladder senna is comparatively very feeble. A decoction made from one to two ounces (30–60 Gm.) of the leaves may be given at a dose.

Combretum. *Jungle-weed.*—The roasted leaves and stalks of the *Combretum sundaicum* (Miquel) have been used in China in the treatment of the *opium habit.* Harrison (*P. J.*, lxxx, 52) was unable to find any alkaloid or glucoside in the plant, and Stanislaus (*J. A. Ph. A.*, 1912) confirmed the absence of active principle, but found a considerable proportion of tannic acid.

Heffner has reported favorably upon its use, but H. C. Wood, Jr., (*J. A. Ph. A.*, 1912), was unable to note any beneficial action from it which might not be justly ascribed to the tannic acid which it contains.

The *Combretum Raimbaultii* is a shrub native of West Africa, where it is known under the name of *Kinkelibah* and is used by the natives in the treatment of *black-water fever* and was introduced a number of years ago into Europe by a missionary, Father Raimbault. Dammermann has reported favorably on its value in this condition (*D. M. W.*, 1906, p. 921), but Heckel was unable to find any active constituent except a tannin. (*Jahresber, d. Pharm.*, 1891 p. 64.) Other species of the combretum appear also to have been used for the same purpose, notably the *C. Altum* Guill. et Perr. (*C. micranthum*, G. Don).

Commelina. *Day-flower.*—Under the name of *Yerba del Pollo, Commelina tuberosa* L. is said to be very largely used in Mexico in the treatment of *internal hemorrhage*, especially from the womb. From thirty to sixty grains (2.0–3.9 Gm.) of the extract may be taken in the course of one day. (See *A. J. P.*, 1897, 290.) The North American species, *Commelina communis* L., has also had hemostatic properties attributed to it. For chemical and microscopical study, see *A. J. P.*, July, 1898.

Comptonia. *Comptonia asplenifolia* Gaertn. (*Comptonia peregrina* (L.) Coulter). *Sweet Fern. Ferngale. Meadow-fern.* (Fam. *Myricaceæ.*)—A shrubby indigenous plant, named from the resemblance of its leaves to the spleenwort fern. It grows in sterile soil, from Nova Scotia to North Carolina and Michigan. All parts of it possess a resinous, spicy odor. R. T. Chiles has found in it tannic and gallic acids, volatile oil, extractive, gum, resin, and a substance resembling saponin. (*A. J. P.*, xlv, 306.) H. K. Bowman found it to contain 8.20 per cent. of tannin. (*A. J. P.*, 1869, 193.) It is said to be tonic and astringent; its decoction is used in *diarrhea.*

Condy's Fluid.—A solution made by dissolving 53 parts of potassium permanganate and 333 parts of crystallized aluminum sulphate in 777 parts of hot water.

The potassium alum, which crystallizes out when the liquid cools, is separated. The liquid is therefore a solution of the permanganate of aluminum with some aluminum sulphate. It is used as a disinfectant.

Condy asserted that in this disinfecting solution all of the available oxygen in the permanganate is utilized, whereas only 60 per cent. of the oxygen is utilized in the simple alkaline permanganate.

Congluten.—A vegetable casein obtained from almonds, containing 18 per cent, nitrogen and 0.6 per cent. sulphur. It is a white powder, soluble in weak alkaline solutions, and used in the form of a 6 per cent. solution in endovenous nutrition.

Conessi Bark. *Holarrhena antidysenterica* (Roxb.) Wall. (Fam. *Apocynaceæ.*)—Under the names of *Conessi bark, Tellicherri bark, Kurchi*, etc., a spongy, rusty-colored, bitter bark of this apocynaceous tree was formerly used in Europe as a remedy in *dysentery* and *diarrhea*, and is said still to be largely employed by the native practitioners of India. Stenhouse in 1864 obtained from the seeds, besides a fixed oil which they contain in large quantity, an alkaloid, called by him *wrightine*, which seems to be the same substance previously described by Haines under the name of *conessine* $C_{24}H_{40}N_2$. The alkaloid conessine is now a commercial product prepared by Merck, and the formula $C_{24}H_{40}N_2$ is given it. It occurs in delicate, white, interlaced masses of crystals, melting at 121° C., sparingly soluble in water, readily so in alcohol. For study of the chemical properties of this alkaloid see Giesma and Halberkann (*A. Pharm.*, 1919, cclvi, 201).

The same alkaloid occurs in the *H. africana* (A.) DC. is stated by German missionaries to be used in parts of tropical Africa in *dysentery*. Pyman (*J. Soc. Chem. Ind.*, 1919, xxxviii, 231) has found conessine and a new alkaloid *holarrhenine* $C_{24}H_{38}ON_2$ in the *H. Congolensis*. Burn (*J. P. Ex. T.*, 1915, vi, p. 305) has found that conessine and holarrhenine have very similar physiological actions. They are only moderately toxic, have a pronounced local anesthetic action, but are of no practical value because of their irritating effects. In small doses they cause a marked rise in the blood pressure due to an action upon the arterial walls, and in large doses lower blood pressure through their disturbing influence on cardiac rhythm. Brown (*B. M. J.*, June 24, 1922) has found that conessine has a powerful amoebicide action approximately equivalent to that of emetine and that it is decidedly less poisonous. When oxidized by iodic acid in sulphuric acid solution, conessine is changed to *oxyconessine* $(C_{12}H_{20}NO.)_2$.

Connarus. *Connarus guianensis* Lamb. *Seribéle.*—The seeds and root bark of this plant (Fam. *Connaraceæ*), from French Guinea, are used as tænifuges; two ounces of the seeds in decoction, without straining. (Maclaud, *P. J.*, 1896, 243.)

Contrayerva. *Contrayerba. Contrayerve*, Fr. *Bezoarwurzel, Giftwurzel*, G.—The root of *Dorstenia Contrajerva* L. (Fam. *Moraceæ*), a native of Mexico, the West Indies, and Peru. The term *contrayerba*, in the language of the Spanish Americans, signifies *counterpoison* or *antidote*, and was applied to this root under the impression that it had the property of counteracting all kinds of poison. The probability is that the root sold as contrayerva is derived from several species of *Dorstenia*, among which, besides *D. Contrajerva*, two others are mentioned by Houston, *D. Houstoni* L. and *D. Drakena* L., the former growing near Campeachy, the latter near Vera Cruz. According to Pereira and Martius, the *contrayerva* of the shops is the product of *D. brasiliensis* Lam., and is brought from Brazil.

The root, as found in commerce, is oblong, an inch or two in length, of varying thickness, very hard, rough, and solid, of a reddish-brown color externally, and pale within; and has numerous, long slender, yellowish rootlets attached to its inferior part. The odor is aromatic; the taste warm, slightly bitterish, and pungent. The rootlets have less taste and odor than the tuberous portion. The sensible properties are extracted by alcohol and boiling water. The decoction is highly mucilaginous. The tincture reddens infusion of litmus, and precipitates on the addition of water. Mussi (*L'Orosi*, 1894, 259) investigated this plant and found two substances, which he called provisionally *cajapine* and *contrayerbine*. Contrayerva is a stimulant tonic and diaphoretic, and has been given in *low fevers, typhoid dysentery*, and *diarrhea*, and other diseases requiring gentle stimulation. *Dose*, of powdered root, half a drachm (2 Gm.). In the root of the *Gabbon ivy* (*Dorstenia klaineans?*) Heckel and Schlagdenhauffen have found a coumarin-like body, *pseudocoumarin*. (*Ph. Cb.*, xliii.)

Copal.—The *copals* are a class of hard resins used principally in varnish manufacture. They are of various origins, both geographically and botanically. Their principal characteristics are their hardness, high melting point and comparative insolubility unless subjected to destructive distillation. There are three chief varieties: (1) *Fossil copal*, found in the ground in localities from which the trees yielding it have entirely disappeared. (2) *Semi-fossil copal*, collected from the ground in the neighborhood of living copal trees. (3) *Fresh copal*, found on living trees, either as the result of natural exudation or from artificial incisions. The fresh copal is of least value and the fossil copal is most highly prized.

The term *animé* (*animi* or *gum animé*) has been applied to a variety of resinous substances, several of them of fossil origin.

East African copals, known in commerce as *Animi gum*, or *resin*, are fossil varieties coming from Zanzibar, Madagascar and along the East African Coast. M. Kahan has investigated *Accra copal* and *Benin copal* (*A. Pharm.*, 1910, ccxlviii, p. 443) and gives the percentages of the various constituents found.

Zanzibar copal is obtained from *Trachylobium Hornemannium* Hayne (Fam. *Leguminosæ*). The trunk and limbs are covered with a clear resinous exudation, portions of which, after solidifying, drop to the ground and are collected, while other portions are broken from the tree. This kind of resin is always smooth, and is exported to India. The variety, known in the English market as *animé* (*gum animi*) is dug from the earth, and, though the product of forests now extinct, originated probably from the same tree. It is in roundish, irregular, or flattish pieces, sometimes several pounds in weight, often rough over the surface, probably from the impression of sand in its soft state, colorless, or brownish-yellow, more or less transparent, very hard, with a shining, conchoidal fracture, inodorous and tasteless. By heat it melts and emits gases, loses from 15 to 20 per cent. of weight, and is altered so as to become more soluble in ether, alcohol, or oil of turpentine, and in this way copal varnishes are usually made. It is not a proximate principle, but consists of various resins united in different proportions. According to Unverdorben and Filhol, some five different resins can be obtained by the successive action of solvents.

Sierra Leone copal or *West Africa copal* is derived from the *Copaifera Guibourtiana* Benth., a large tree growing preferably in mountainous regions. The drug is mostly collected, not from the tree itself, but from the beds and borders of streams, into which it is washed down, during the rains, from the hillsides, in the soil of which it has been deposited.

The Sierra Leone copal is described by Daniell as occurring "in small round tears, or irregular conical and smooth nodulated masses, seldom exceeding in size an ordinary duck egg. They are covered, to a greater or less extent, by a peculiar white efflorescence, which increases by age. Their color graduates from a pale green to a lemon or dull yellow."

Inhambane copal has been shown to be the product of *Copaifera Gorskiana* Benth. and seeds sent to Kew Gardens in 1886 germinated, and the plant has been widely introduced into both the East and West Indies, and into Australia. (*P. J.*, xix, 508.)

American copal is a resin supposed to be derived from the *hymenæa courbaril* L., a leguminous tree of South America, although this origin was denied by Hayne. According to W. Hamilton, the resin exudes from wounds in the bark, and is found also underneath the surface of the ground, between the principal roots. It is in small, irregular pieces of a pale lemon-yellow color, sometimes inclining to reddish, more or less transparent, covered with a whitish powder, brittle and pulverizable, with a shining fracture, a weak but agreeable odor, and a mild, resinous taste. It softens in the mouth, adheres to the fingers when in powder, and readily melts with heat, diffusing its agreeable odor in an increased degree. It consists of two resins, one soluble, the other insoluble, in cold alcohol, and of a small proportion of volatile oil. There is a variety of a darker color, less transparent, and with small cavities in the interior, in other respects resembling the preceding. A study of South American varieties of copal has been made by S. Machenbaum (*A. Pharm.*, ccl, Nos. 1–6 and 13), in which the constituents are stated to be *copalic acid, copalolic acid, copaloresene, copalmic acid,* volatile oil and ash.

Fossil copal from Guiana has been studied by J. C. Essner (*Annal. Chim. Anal.*, xvii, p. 166), who gives the following constants: Sp. gr. 1.089; colorless portion, acid value 118, saponification value 127, iodine value 84.3, yellow portion, acid value 125, saponification value 151, iodine value 81.5.

East Indian copal.—This is supposed to be derived from *Vateria indica*, L. (Fam. *Dipterocarpaceæ*), but never reaches American commerce. According to W. C. Ondaatje, the bark of this plant is in daily use by the natives of Ceylon to arrest the alcoholic fermentation of the juice of the Jaggery palm, *Caryota urens*, L., a favorite beverage. (*P. J.*, 1883, 818.)

The *Dammara* (*Dammar*) resins which come from India and the East Indies are obtained from species of *Hopea, Shovea* and *Balanocarpus.* The dammars are acid resins partly soluble in alcohol and completely soluble in fixed and volatile oils. (See also *Kauri Gum.*) For an account of the present views on the nature of copal resins, see Tschirch, *Die Harze und die Harzbehälter*, Leipzig, 1900.

For descriptions of the so-called Manila copal and Australian copal which are derived from the conifers, see under *Kauri.*

Copal lotion.—Under the trade name *Adhæsol* there appears on the market a lotion containing: Copal, 350 parts; benzoin, 30 parts; tolu, 30 parts; ol. thyme, 20 parts; alpha-naphthol, 3 parts; ether, q. s., 1000 parts. It is used as an antiseptic varnish in *diphtheritic affections* of the throat.

Copper Abietinate. $Cu(C_{19}H_{27}O_2)_2$.—This forms green scales, soluble in oils, imparting to the solutions a rich emerald color. It has been used as an anthelmintic and vermifuge in veterinary practice. It is also used technically for impregnating and preserving wood.

Copper Acetate. *Cupri Acetas. U. S.* 1880. $Cu(C_2H_3O_2)_2.H_2O = 198.14$. *Crystallized verdigris. Crystals of Venus. Verdet, Cristaux de Vénus,* Fr. *Essigsaures Kupfer, Aerugo Crystallisata, Crystallisirter Grünspan,* G.—This salt may be prepared by dissolving verdigris in acetic acid, or by precipitating a concentrated solution of lead acetate with copper sulphate. It is the normal cupric acetate, as distinguished from the basic salt. "Deep green, prismatic crystals, yielding a bright green powder, efflorescent on exposure to air, odorless, having a nauseating, metallic taste and an acid reaction. Soluble in 15 parts of water and in 135 parts of alcohol at 15° C., in 5 parts of boiling water and in 14 parts of boiling alcohol. When heated above 100° C., the salt loses its water of crystallization, and at a temperature above 200° C., it is gradually decomposed. The aqueous solution of the salt has a bluish-green color, which is rendered deep blue by an excess of ammonia. On heating the salt with sulphuric acid, acetous vapors are evolved. If the aqueous solution of the salt be treated with hydrogen sulphide until all the copper is precipitated, the filtrate should leave no residue on evaporation (alkalies, alkaline earths, and iron). If the aqueous solution be heated to boiling with solution of soda in excess, it will yield a filtrate which should not be clouded by hydrogen sulphide (absence of lead, zinc)." *U. S.*, 1880.

Verdigris. Impure Subacetate of Copper. U. S. 1870. *Copper Subacetate. Viride Æris, Ærugo, Cuivre, Vert-de-gris, Verdet,* Fr. *Grünspan, Basisches Essigsaures Kupfer, Kupferoxyd,* G. *Verde Rame,* It. *Cardenillo,* Sp.—It occurs in masses of a *pale green* or *bright blue color,* and composed of a multitude of minute silky crystals.

The *blue variety* has approximately the composition $(C_2H_3O_2)_2Cu_2O$. When treated with water it is generally decomposed. The *green variety* of verdigris has the composition $CuO.2Cu(C_2H_3O_2)_2$. Its taste is coppery. It is insoluble in alcohol, and, by the action of water, a portion of it is resolved into the neutral acetate which dissolves, and the tribasic acetate which remains behind in the form of a dark green powder, gradually becoming black. The green rust, called in popular language verdigris (*vert-de-gris*), with which copper vessels are very frequently coated, when not kept clean, is a copper carbonate, and should not be confounded with true verdigris. Verdigris, apart from its impurities, is a variable mixture of the basic copper acetates.

The local and general action of copper acetate upon the animal economy and the treatment of its poisoning are the same as those of copper sulphate. It is not used internally. Dr. G. Billard (*Presse Medicale,* 1909) uses the fine dust of copper subacetate by inhalation of minute quantities in the treatment of *tuberculosis;* he states that the cough is usually lessened and sometimes disappears completely.

Copper Aluminated. *Lapis Divinus. Divine Stone.*—This copper compound, in the form of a green powder or plates, is a combination of copper and aluminum sulphates and potassium nitrate. It is soluble in water and is used solely as a mild caustic in *ophthalmology.*

Copper Ammonio-sulphate. *Cuprum Ammoniatum. U. S.* 1870. *Ammoniated Copper Sulphate. Cuprum Sulfuricum Ammoniatum. Sulfate de Cuivre ammoniacal, Cuivre ammoniacal,* Fr. *Schwefelsaures Kupferoxyd-Ammoniak, Ammoniakalisches Kupfersulfat,* G.—The character of the salt which results from the interaction between copper sulphate and ammonia varies according to the conditions under which the reaction takes place. The formerly official process was as follows: "Take of Copper Sulphate *half a troyounce;* Ammonium Carbonate *three hundred and sixty grains.* Rub them together in a glass mortar until effervescence ceases. Then wrap the Ammoniated Copper in bibulous paper, dry it with a gentle heat, and keep it in a well stoppered glass bottle." *U. S.*,

1870. The salt which results from this process is probably the same as that which is made by adding copper sulphate to a solution of ammonia and has the composition $CuSO_4.4NH_3 + H_2O$. If this preparation be allowed to remain exposed to the air, it will lose ammonia and water, and be changed into a mixture of basic sulphates. Ammoniated copper sulphate loses two molecules of NH_3 and the one molecule of water at 150° C. and at 260° C. only anhydrous sulphate remains, which frequently, however, contains cuprous oxide.

This salt has a beautiful deep azure-blue color, a strong ammoniacal odor, and a styptic, metallic taste. It is soluble in water, and the solution has an alkaline reaction to vegetable colors; but, unless there is excess of ammonium sesquicarbonate, the solution deposits copper subsulphate if much diluted. When exposed to the air it parts with ammonia, and is said to be ultimately converted into ammonium sulphate and copper carbonate. This change is apt to occur, to a greater or less extent, while it is drying. It should not, therefore, be prepared in large quantities at a time, and should be kept in well-closed bottles. By heat the whole of it is dissipated, except the copper oxide. Arsenic trioxide precipitates a green copper arsenite from its solution. Solutions of potassium and sodium hydroxides, lime water, and the acids are incompatible with it. Ammoniated copper was at one time employed internally in various nervous diseases, especially *epilepsy*, as well as locally for its astringent action, but is at present very seldom exhibited. In overdoses it produces vomiting, and the poisonous effects which result from the other preparations of copper. *Dose*, in pill or solution, a quarter or half a grain (0.016–0.032 Gm.), twice a day, and gradually increased to four or five grains (0.26 or 0.32 Gm.).

Copper Arsenite. *Cupri Arsenis. Copper orthoarsenite.* $Cu_3(AsO_3)_2$. *Scheele's Green.*—This salt was brought forward for the purpose of treating *diarrhea* on the homeopathic principle, in the *Symptomen-Codex* of Jahn, in 1865, and has been greatly lauded by John Aulde and other regular practitioners in the treatment of *diarrhea, enterocolitis, cholera morbus,* and *dysentery.* It is to be given in doses of from one three-thousandth of a grain (0.000022 Gm.), at intervals of from ten to twenty minutes, until some effect is produced. It does not seem to be sustaining its first reputation. According to H. A. Hare, *copper arsenite* is a valuable remedy in *anemia.* The *dose* ordinarily is from one one-hundredth to one-twentieth grain (0.0006–0.003 Gm.).

Copper Citrate. *N. N. R.* 1924. $Cu_2C_6H_4O_7 + 2\frac{1}{2}H_2O$.—*Cupric citrate* contains from 34 to 36 per cent. of copper. It is a bluish-green, finely crystalline powder, without odor or taste. Very slightly soluble in cold water, soluble in acids and alkalies. Used for the same purposes and in the same doses as other salts of copper over which it possesses the advantage of its sparing solubility in water. Proprietary preparations of similar properties are known by the names of *cuprocitrol* and *cusylol.* Copper citrate has been used in the treatment of *conjunctivitis* and *trachoma* in aqueous solutions of from ½ to 5 per cent. An *ointment of copper citrate* in glycerite of boroglycerin has been proposed by Hoffman (*A. J. P.*, 1917, p. 298) for the treatment of *trachoma* and disturbances of the follicles of the ciliæ. It is prepared as follows: Copper citrate, 8 Gm.; glycerite of boroglycerin, 80 Gm.; wool fat, 2 Gm.; white petrolatum, 10 Gm. Heat the glycerite of boroglycerin to 125° C. and slowly add the copper citrate and continue the heat until it dissolves. Then remove the heat, and when it has cooled to 75° C. add the wool fat and white petrolatum and stir constantly until it has cooled to 50° C., and transfer to air tight containers.

Copper Iodide. *Cupri Iodidum. Cuprous Iodide. Kupferjodür,* G. Cu_2I_2.—A white powder, insoluble in diluted acids and in water; soluble in ammonia water and solution of potassium iodide. Made by adding a solution of potassium iodide to a solution of copper and iron sulphates.

Copper Nitrate. *Cupri Nitras. Br.* 1885. *Cupric Nitrate.* $Cu(NO_3)_2,3H_2O$.—"May be obtained by dissolving copper in diluted nitric acid and evaporating the solution until crystallization takes place on cooling to a temperature not lower than 70° F. (21.1° C.)." *Br.*, 1885. This salt, as obtained by the above process, forms prismatic crystals of a deep blue color, and very deliquescent and corrosive. At a temperature below 21.1° C., with one-third of its weight of water it forms tabular crystals which have the composition $Cu(NO_3)_2.6H_2O$. The addition of a very little more water causes the crystals to form a styptic and caustic fluid. The diluted aqueous solution should show only a faintly acid reaction to litmus paper. This salt has the medicinal properties of copper sulphate, and may be used in the same dose.

Copper Nucleinate. *Cuprol.*—This salt is a greenish powder and is said to contain 6 per cent. of the metal and to be readily soluble in hot water and not to be thrown out of its solution by alkalies and not to precipitate with albuminous liquids. It has been highly recommended in the treatment of *trachoma* and other conditions of the conjunctiva. The assertion is made that it has greater penetrating powers and produces less irritation than ordinary salts of copper. (Von Sicherer, *Die Ophthal. Kl.*, 1901.)

Copper Oleate. *Cupric oleate,* $Cu(C_{18}H_{33}O_2)_2$, with excess of oleic acid. A greenish-blue mass, consisting of 10 per cent. copper oxide dissolved in an excess of oleic acid. It is soluble in ether and is used for its antiseptic action as a 10 to 20 per cent. ointment in indolent *ulcers* and unhealthy *granulations.*

Copper Oxide, Black. *Cupri Oxidum Nigrum. Cuprum Oxydatum. Oxyde noir de Cuivre, Safran de Vénus,* Fr. *Kupferoxyd,* G.—*Cupric oxide,* CuO, is obtained most conveniently by heating the nitrate to redness. This oxide, in the form of ointment, made by mixing four parts with thirty of lard, was formerly used locally in chronic *lymphadenitis.* It is also asserted to be an active *tænicide* of very feeble toxic power. It is given by Dörr in *doses* of one and a half grains (0.096 Gm.) four times a day for several days, the last dose followed by castor oil. (See *Ther. Geg.*, 1901.)

Copper Phenolsulphonate. *Cupri Phenolsulphonas. Copper Sulphocarbolate. Paraphenolsulfosaures Kupfer,* G. $(C_6H_4(OH)SO_3)_2Cu + 6H_2O$.—Green prismatic crystals soluble in water and alcohol. Made by reaction between copper sulphate and barium phenolsulphonate. A solution of from ½ to 1 per cent. is applied locally in *gonorrhea,* and also as a styptic, hemostatic and antiseptic under the name of *cupriaseptol.*

Coral. *Corail,* Fr. *Koralle,* G.—The solid mesodermal calcareous skeletons of the coral polyps, *Anthozoa,* were formerly used in medicine, but have passed out of vogue. Their chief constituent is calcium carbonate, colored by ferric oxide, and united with more or less animal matter.

Corallin. *Pæonin. Aurine R.*—A coloring or dyeing material, derived from *rosolic acid* or *aurin* ($C_{19}H_{14}O_3$)—which is made by acting upon phenol with sulphuric and oxalic acids—by exposing together rosolic acid and alcoholic ammonia to a heat of 149° C., and is considered to be an intermediate product between pararosaniline and pararosolic acid. A solid substance is thus obtained, in scales of a peony redness, with reflected green or dull yellow rays, almost insoluble in water, soluble in alcohol and the fixed oils. It has been accused of causing violent toxic symptoms when used as a dye, but it is doubtful whether the effects were due to the dye or to arsenic or other contaminating substances. (See *M. T. G.*, 1869, 421; *P. J.*, 2d ser., xi, 360; also *N. Y. M. J.*, 1870, 599; *N. R.*, i, 228.)

Local poisoning may be caused by *aniline red* (see *Fuchsin*) as well as by corallin. The two colors may be distinguished in tissues. Aniline red disappears very rapidly by contact with ammonia; but the color reappears by the addition of an acid, or by the evaporation of the alkali. Corallin red is not dissolved by cold water, yields a slight color to boiling water, but rapidly disappears from the tissue under the action of boiling alcohol. Alkalies brighten the color without changing it; acids precipitate the coloring matter in yellow flakes.

Corallorhiza. *Corallorhiza odontorhiza* (Willd.) Nutt. *Coral root.* (Fam. *Orchidaceæ.*)—This is a parasitic leafless herb, sending up from a coral-like rhizome a simple scape or flower stem, from six to sixteen inches high, furnished with sheaths instead of leaves, of a light brown or purplish color, and bearing small, greenish-brown flowers in a long spike. The plant grows throughout the United States east of the Mississippi. The rhizome is the part used. It is much branched and toothed, and of a brown color, and its resemblance to coral gave name to the plant. It has a strong peculiar odor, and an astringent bitterish taste. It was much valued by the eclectics as diaphoretic in *fevers; dose,* of powder, thirty grains (2 Gm.) every two hours.

Coramine. *Pyridine-betacarbonic acid diethylamide.*—This substance has been introduced as a circulatory stimulant for use in the treatment of acute depressions such as occur in surgical *shock, pneumonia* and other infectious diseases, poisonings and other forms of *heart failure.* It is marketed in the form of a 25 per cent. solution, of which 1 to 2 cc. (15–30 minims) may be given by mouth or by subcutaneous injection.

Cordol. *Tribromsalol.* $C_6H_4.OHCOO.C_6H_2Br_3$.—A white tasteless, and odorless powder, insoluble in water, ether, and alcohol, freely soluble in chloroform and glacial acetic acid. *Cordyl* or *acetyl tribromsalol* is insoluble in water, and occurs in the form of fine white needles. *Cordeine* or *methyl tribromsalol* occurs in small white crystals, which are insoluble in water, but soluble in alcohol and chloroform. Cordol, cordyl, and cordeine are used as intestinal antiseptics, easily decomposed, giving the combined actions of tribromphenol and salicylic acid when split up in the intestinal canal. The *dose* of either is from eight to fifteen grains (0.5–1.0 Gm.).

Coriaria. *Coriaria myrtifolia* L. *Currier's Sumac. Redoul, Sumac des Corroyeurs,* Fr. *Gerberstrauch,* G. (Fam. *Coriariaceæ*).—This is a shrub growing wild in Southern Europe, which is sometimes cultivated in gardens on account of its handsome foliage. The leaves, which are used for dyeing black, were at one time employed to a considerable extent in France in the adulteration of senna. They have also been reported both in Europe and in America as an adulterant of sweet marjoram, the *coriaria* leaves being finely broken to facilitate admixture. The presence of coriaria in marjoram may be inferred by strewing a specimen of the broken up leaves upon the surface of a dilute ferric chloride solution, which does not affect the fragments of marjoram but which quickly stains the coriaria fragments a deep greenish-black, owing to their high tannin content. The fruit, resembling berries in form, are black, and about the size of a pea. Both these and the leaves are poisonous in large doses, and several instances of death are on record from eating the fruit. Riban, in 1864, found in the fruit a glucoside *coriamyrtin.* It occurs as extremely bitter, white crystals, fusing at 220° C., sparingly soluble in water but freely so in alcohol and other organic solvents. Its empirical formula is $C_{30}H_{36}O_{10}$. Marshall (*J. P. and Ex. T.*, 1912, iv, p. 135) studied the substance supplied by Merck under the name of coriamyrtin which, however, he believed to be different from that described by Reban, because it was soluble in water. The lethal dose was 1 mgm. per kilo. He found that it was a stimulant to the medullary centers, increasing the blood pressure and respiration and slowing the pulse; in large doses it caused cerebral convulsions. Coriamyrtin has been employed as a stimulant in *collapse* in doses of one-sixtieth of a grain (0.001 Gm.).

Tlolocopetale, a Mexican drug, is said to be the product of a Coriaria, probably *C. myrtifolia,* containing *coriarin* and *coriamyrtin,* and to be actively poisonous.

Toot-poison. Tu-tu.—In New Zealand a poisonous plant, known as the *toot-plant,* has proved very destructive to the domestic animals. W. Lauder Lindsay found it to resemble either *Coriaria ruscifolia* of Linnæus or *C. sarmentosa* Forst., and in its action on the system to be an irritant narcotic. It appears that more than one species of *Coriaria* inhabit New Zealand, *C. thymifolia* Humb. et Bonpl. and *C. angustissima* Hook. f., besides the *ruscifolia;* though Lindsay appears to think that the two former may be merely varieties of the third. It is not only cattle that are poisoned by the plant, but not infrequently also children, and occasionally even an adult. W. S. Key attributes poisonous qualities to an oil (*Chem. News,* 1890, xxii), but it has been shown by T. Hill Easterfield and B. C. Aston that the three New Zealand species of coriaria contain a glucoside, *tutin,* $C_{17}H_{20}O_7$, which is not identical with coriamyrtin, and which, according to Marshall, is toxic, especially to the medulla oblongata and the basal ganglia of the brain. (*Proc. Chem. Soc.*, xvi, 213.) It is affirmed by T. H. Hartwick (*P. J.*, vol. xv, 22) that goats are not poisoned by the tu-tu, and that they have even been used to eradicate the plant by browsing, also that the berries when ripe are not only not poisonous to man, but if care is taken to reject the seeds, are a grateful and refreshing fruit. The prominent symptoms of the poisoning in man are giddiness, stupor, and coma, with or without delirium or convulsions. Occasionally the delirium resembles that of alcoholic intoxication, in other instances approaches that of acute mania, and is attended with violent muscular action. Loss of memory is a characteristic of the convalescence. The toxicity of tutin, which was demonstrated by Marshall, has been confirmed by Ford (*J. P. and Ex. T.*, 1910, ii).

Cork. *Suber. Liege,* Fr. *Kork,* G.—The great use made of this substance in pharmacy and the arts justifies a brief notice of it. It is chiefly produced by *Quercus Suber* L. (Fam. *Cupuliferæ*) but is obtained also from the *Q. occidentalis* F. Gay. It consists of the exterior layers of the bark, which acquire in these species an extraordinary development, becoming thick, and of that peculiar spongy consistence which characterizes *cork.* The tree begins to yield cork when fifteen or sixteen years old, and every six or eight years —the interval requisite for the renewal of the suberous layers by the living portions of the bark beneath—furnishes a fresh supply, even for a century and a half, before it perishes. There are three important layers of the bark: the epidermis, the cork, the cellular envelope, and the blast which lies upon the wood. Each of these increases year by year; but the cork thus naturally produced is not valued. The commercial product is the result of an artificial injury to the bark. The exterior layers are removed, and the bast exposed. In the interior of this, at a variable distance from the surface, a layer of the proper cork is now formed by the proliferation of a phellogen. The outer portions of this cork layer perish, while annually a new layer is added to the cork already existing, until it acquires a thickness which will justify its removal. Incisions are made in such a way that the cork is removed in large concave plates, which are then flattened under pressure, and dried. At present cork comes into commerce from Portugal, Spain, France, Italy, Tunis, Algeria, and Morocco.

A cork has recently come into the United States commerce from Nicaragua. It has been found by E. F. D. Baker to be obtained from the roots of the *Anona,* a tree closely resembling in appearance the ordinary cottonwood of the United States.

In selecting cork for use, those parts should be preferred which are soft and of uniform consistence, and in the choice of the larger plates those should be selected which are thick, flexible, elastic, finely porous, and of a reddish color. Boiling hot alcohol extracts from rasped cork tissue some 10 per cent. of soluble principles. From the hot alcohol solution a substance crystallizes which was first noticed by Chevreul under the name of *cerin.* According to Kugler (*Dissertation on Suberin,* Halle, 1884), besides cellulose and lignocellulose, cork contains two constituents, *cerin,* to which he gives the formula $C_{20}H_{32}O$, and *suberin,* which is a fat, and contains stearic acid and *phellonic acid,* $C_{22}H_{42}O_3$. This constituent, suberin, prevents the penetration of liquid into the cork, and is only extracted by alcoholic alkali solutions. When treated with nitric acid, cork yields a peculiar acid, which has been denominated *suberic acid.* This is a dibasic acid homologous with oxalic acid, and has the formula $C_8H_{14}O_4$. It is formed by the oxidation of many other substances, such as the oils from linseed, castor bean, cocoa nut, almond, spermaceti, etc.

Stanislaus Martin has called attention in France to the use of refuse corks in Paris, where they are collected by the scavengers, and sold to persons whose business it is to revive them, recutting such as are of unsuitable shape, filling up the interstices with mastic, and covering them over with some powder which may give them a fresh appearance. Corks are sometimes bleached with sulphurous acid, and the odor of hydrogen sulphide has been noticed in prescriptions which have been compounded, when such corks have been used in the dispensing bottle. (*P. J.*, 1881, 1080.) Mohr has found that old corks may be regenerated by allowing them to soak for twenty-four hours in hot water, washing well several times, allowing to stand for a few hours in a mixture of one part of hydrochloric acid and fifteen parts of hot water, and finally washing well in pure water. It is evident that a cork at one time used to enclose arsenical or other deadly solution may become saturated with the poison, and afterwards impart enough of it to another liquid, if not to produce dangerous effects on the health, at least to give to tests evidence of its presence, and thus lead to serious suspicions. No cork, therefore, which has been used in a bottle containing a poisonous substance should be employed a second time.

In order to overcome the brittleness of corks which are kept in stock they should be kept in a humid atmosphere and they are improved by moistening in clean water just before use and then removing the excess of water by wiping them dry.

Cornutol. *N. N. R.* 1924.—It is a proprietary preparation consisting of a biologically tested liquid extract of ergot containing the water-soluble, alcohol-insoluble constituents of ergot and about 10 per cent. of alcohol. *Dose,* ten to thirty minims (0.65 to 1.8 cc.) hypodermically or double that amount by mouth.

Coronilla. *Coronilla scorpioides* Koch (Fam. *Leguminosæ*).—In 1886 Cardot, in a thesis (Nancy) announced that the *Coronilla scorpioides* (Medic.) Koch, a papilionaceous plant of Southern France, is an active cardiac poison. In 1889 Schlagdenhauffen and Reeb (*Rev. Gen. de Clin. et de Thérap.*, July, 1889) insolated a glucoside, *coronillin,* to which they assigned the formula $C_7H_{12}O_5$. It was a yellowish powder, soluble in water, acetone, and amyl alcohol; slightly soluble in chloroform and ether. Heated with diluted hydrochloric acid an amorphous resin was separated, *coronillein.* This also occurs as a yellow powder, but is not bitter to taste. It is insoluble in water but dissolves in alcohol, acetone, and chloroform. The physiological studies by Gley, by Schlagdenhauffen and Reeb, and by Maramaldi (*R. T.*, cxxxvi) have demonstrated that coronillin acts upon the heart in a manner similar to digitalis. In small doses it slows the pulse through stimulation of inhibition and in larger quantities increases the tonicity of the cardiac muscle and eventually arrests the ventricle in systolic spasm. According to Maramaldi it also depresses the spinal cord and respiration.

Locally, coronillin appears to be actively irritant. In Maramaldi's experiments it failed to assert its physiological action when administered to the dog by the mouth, a result believed by the investigator to be due to its decomposition by the acid in the stomach. As it has been found by various clinicians to be active in man when given by the mouth, it is probable that the comparative feebleness of human gastric juice permits of its absorption unchanged. The *doses* given by various clinicians have diverged greatly, probably because of differences in purity of the various samples used; of the commercial coronillin the *dose* is commonly stated at present to be one and one-half grains (0.096 Gm.) from four to six times a day, but it must be noted that Schlagdenhauffen affirms that three-fourths of a grain (0.048 Gm.) is a toxic dose. *Coronilla varia* of Europe also probably contains coronillin. (V. Poulet, *B. G. T.*, 1891.)

Colmenthol.—*Coryfin. Menthyl ethylglycocolate,* $C_{10}H_{19}O—CO—CH_2—O—C_2H_5$, is a colorless, inodorous fluid, slightly soluble in water and readily soluble in alcohol and ether. Alkalies immediately release the menthol. It is used as a local anesthetic and sedative to mucous membranes of the upper respiratory tract, especially in *catarrhal conditions* of the *nose.* It has the advantage over menthol in these conditions of being much less irritating. It is employed locally by means of a small swab in strengths of from 50 to 100 per cent. Inhalations of its vapors are also recommended in *laryngitis* and even in *bronchitis.*

Corylus. *Corylus rostrata* Ait. *Beaked Hazel.* —This is a small indigenous shrub of the Fam. *Betulaceæ,* growing especially in mountainous districts. The nut is invested with a scaly involucre, projecting beyond it like a beak, and thickly covered with short spicules like those of cowhage (see *Mucuna*). These spicules have been employed by Huebener as an anthelmintic. They operate in the same way as cowhage, and may be administered in the same manner and dose. (See *A. J. P.*, xiv, 280.)

According to Baruttan and Davidson (*M. M. W.*, 1909, p. 2482), the *hazel-nut* contains an alcoholic soluble substance which acts as a stimulant to the uterine muscle. An alcoholic extract has been placed upon the market under the name of *mensan* which these authors have found useful in the treatment of *uterine hemorrhages* due to chronic endometritis. The dose employed was a tablespoonful twice a day.

Coscinium. *Br. Add.*—The dried stem of *Coscinium fenestratum* Colebr. The stem of this menispermaceous plant has long been used in Ceylon and Southern India as a yellow dye and bitter tonic, and has found its way into Europe under the names of *false columba* and *tree turmeric.* It contains berberine and is an efficient stomachic. The Br. Add. recognized an *infusion* (*Infusum Coscinii,* Br. Add.), *dose,* one-half to one fluidounce (15–30 cc.); a concentrated solution (*Liquor Coscinii Concentratus,* Br. Add.), *dose,* one-half to one fluidrachm (1.8–3.75 cc.); and a *tincture* (*Tinctura Coscinii,* Br. Add.), *dose,* one-half to one fluidrachm (1.8–3.75 cc.).

Coto Bark.—In the years 1873 and 1874 a bark bearing this name appeared in the London drug market, coming from Bolivia. During the Mulford Biological Exploration of the Amazon Basin in 1921–22, Dr. O. E. White under direction of Doctor Rusby collected several barks and branchlets of Lauraceous trees, on the mountains south of Huachi, from which barks have been collected for the market under the name of Coto. One of these which is known to the natives as "Coto Piquante" or "Coto Fino" is stated by H. H. Rusby to be a form of genuine coto. He has named the tree yielding it, *Nectandra Coto.* The physical characteristics of this bark are now under investigation. (For a description of *Nectandra Coto* Rusby, Sp. Nov., see *Bull. Torrey Bot. Club,* 1922, xlix, p. 260.)

The *Coto bark* which formerly appeared on the market was described as occurring in pieces 3 dm. or more long, from 3 to 6 cm. wide, and from 5 to 15 mm. thick. The outer surface was irregular, often looking as though it had been shaved or split off, and in other parts covered with a fine adherent corky layer free from lichens; the inner surface also irregular, with numerous rather closely placed, longitudinal projecting bast fibers. The color approached cinnamon-brown; upon fresh cross-section the bark seemed to be filled with yellowish spots, except in the outer portions. The odor was aromatic, and much more apparent if bruised; the taste hot, and somewhat aromatic; the powder very pungent to the nostrils. For microscopic structure, see *P. J.*, vi, 301; also *Ph. Era,* May, 1888.

The true coto bark has disappeared from commerce but under the name of *paracoto* bark a somewhat similar drug has replaced it. This bark was recognized by the N. F. IV which defined it as "the dried bark of an unidentified tree indigenous to Northern Bolivia." *N. F. IV.*

Rusby says that this bark is known by the natives as *Coto ordinario* and he assigns it to a new species *Ocotea Pseudo-coto* Rusby also belonging to the *Lauraceæ.* He further asserts that it is without medicinal value.

The N. F. IV described paracoto as: "In quills, or fragments of quills, of indefinite length, usually from 3 to 6 cm. in breadth, from 5 to 15 mm. in thickness; of a deep brown color throughout, the outer surface nearly smooth, lightly transversely fissured, and often very thinly scaly, the inner surface very coarsely striate; hard and heavy, but splitting and breaking readily, the fracture mealy in the outer layer, with an irregular resinous band, coarse splintery in the inner layer with large, yellowish-brown bast fibers and stone cells and darker resin tissue. Odor strong and characteristic, nutmeg-like; taste strongly aromatic and pungent. Paracoto yields not more than 3 per cent. of ash." *N. F. IV.* It is said that the two barks can be distinguished by their odor, that of the coto recalling cinnamon and that of the paracoto resembling more the odor of nutmeg.

Jobst and Hesse obtained a crystallizable body, *cotoin,* from true coto bark, by making an ethereal extract from the powdered bark, treating this with warm petroleum benzin, decanting and spontaneously evaporating the benzin, and allowing the mixture to stand until clear. Cotoin (methyltrioxy-benzophenone or benzoyl-phloroglucinol-monomethyl ether), $C_{14}H_{12}O_4$, is sparingly soluble in cold water, more soluble in hot water, insoluble in petroleum benzin, very soluble in alcohol, chloroform, benzol, acetone, and carbon disulphide. Nitric acid becomes blood-red in contact with cotoin, sulphuric acid is colored brownish-yellow, and ferric chloride blackens a dilute solution of cotoin. *Hydrocotoin methyl-hydrocotoin, protocotoin* and *methyl-protocotoin* are also present. O. Hesse described a coto bark which did not contain cotoin but *cotellin,* $C_{20}H_{20}O_6$. (*Ph. Ztg.*, 1905, 845.)

The composition of this bark has recently been investigated by H. A. Seil (*J. A. Ph. A.*, 1922, xi, 904) who states it to contain a non-phenolic alkaloid called *parostemine,* a phenolic alkaloid, *parostemine,* and a crystalline substance, cotoin. This bark is undoubtedly a true Coto, since it contains cotoin. Under the name of *coto-coto,* the bark of a rubiaceous plant (*Palicourea densiflora*) is employed in Brazil in *rheumatism.* Whether this be the Bolivian plant or not is uncertain.

Paracotoin, $C_{12}H_8O_4$, is extracted from paracoto bark, in which it exists associated with *hydrocotoin,* $C_{15}H_{14}O_6$, *protocotoin,* $C_{16}H_{14}O_6$, *methylhydrocotoin,* $C_{16}H_{16}O_4$, and *methylprotocotoin,* $C_{17}H_{16}O_6$ and *leucotin* (phenyl coumalin). Paracotoin may be distinguished from cotoin by giving no reaction with ferric chloride. *Piperonylic acid* (*methyleneprotocatechuic* acid), $C_8H_6O_4$, is present in both barks.

Coto bark is decidedly irritating: its powder, rubbed upon the skin, is said to produce heat and redness, and, according to Burkart, fifteen grains (1.0 Gm.) taken into the stomach produce persistent burning pain, followed by repeated vomiting. The remedy was first introduced as serviceable in *diarrhea,* and seems to have established its reputation. Although observers are not explicit upon this point it is evident that when there is a tendency to acute inflammation it must be used with great caution. Inpens (*D. M. W.*, 1913, 1827) from his physiological studies concludes that it acts by lessening intestinal peristalsis. The *paracoto bark* is said to resemble it in its action, but to be much less powerful, which statement is contradicted by Doctor Rusby.

The N. F. IV recognized a *fluidextract of paracoto* (*Fluidextractum Paracoto*) and assigned a dose of five minims (0.3 cc.). Balz (Tokio, Japan) is said to have treated *cholera* successfully by hypodermic injections of three grains (0.2 Gm.) of paracotoin. The value of cotoin in the treatment of *diarrhea* has been confirmed by various clinicians. It has been used in *catarrhal diarrheas* and the *diarrheas* of *tubercular ulceration,* of *typhoid fever,* and of other conditions. (See *B. G. T.*, vol. xi, 167.) It does appear to have some special effect upon the alimentary canal, as, according to Pribram (*Prager Med. Wochens.*, 1880) and Albertoni (*A. E. P. P.*, xvii, 293), it markedly lessens the excretion of indican. Albertoni also believes that it actively dilates the abdominal vessels and thereby hastens absorption, and Bibrana, that it is an antiseptic. It is not probable that cotoin has any general action upon the system, and Jobst found that even fifteen grains (1.0 Gm.) injected hypodermically into the rabbit produced no other than local symptoms. *Dose,* of cotoin, from one to three grains (0.065–0.2 Gm.); of fluidextract of coto, from five to twenty minims (0.3–1.3 cc.), four to six times a day.

Cotula. *U. S.* 1870. *Mayweed. Wild Chamomile. Dog Fennel. Camomille puante, Maroute,* Fr. *Hunds-Kamille, Stinkende Kamille,* G. *Camomilla fetida,* It. *Manzanilla loca,* Sp. *Herba Chamomillæ Fœtidæ. Anthemis Cotula* L.—Mayweed is an annual composite plant, which grows abundantly both in the United States and in Europe. In this country it is found in the vicinity of inhabited places, growing among rubbish, along the sides of roads, and in waste grounds. The flower heads have recently appeared in several commercial samples of Matricaria as an admixture. They may be distinguished from the latter by being conical with a solid receptacle bearing broad and bristly-acuminate scales, pubescent bracts having scarious margins and obtusely three-angled achenes, all of which are entirely devoid of a pappus. W. H. Warner found in the flowers volatile oil, oxalic, valeric, and tannic acids, coloring matter, acrid fatty matter, bitter extractive, and salts of potassium, calcium, magnesium, and iron. (*A. J. P.*, 1858, 390.) Pattone (1859) claimed to have found an alkaloid, *anthemidine,* and a crystallizable bitter acid, *anthemidic acid,* but his results have not been confirmed. The whole plant has a strong, disagreeable odor, and a warm, bitter taste, and imparts these properties to water.

The medicinal properties of this species of *Anthemis* are essentially the same as those of chamomile, for which it may be substituted, but its disagreeable odor is an obstacle to its general use. On the continent of Europe it has been given in *hysteria* as an antispasmodic. It has also been thought to be emmenagogue. It is said to have the property of vesicating, if applied to the surface fresh and bruised. The whole plant is active, but the flowers, being less disagreeable than the leaves, are preferred for internal use. The remedy is best administered in the state of infusion.

Cotyledon Umbilicus L. *Navelwort. Pennywort. Cotylet, Nombril de Vénus,* Fr. *Nabelkraut,* G.—This is a perennial, herbaceous, succulent plant, of the fam. *Crassulaceæ.* The plant is a native of England, where it grows upon old walls and rocks, and dry sandy banks.

According to Flétet, it contains trimethylamine, combined with an unknown acid. When the powder of the plant is exposed to the air, it attracts moisture, and exhales a disagreeable odor strikingly analogous to that of fish, and an extract treated with a fixed alkali disengages, even in the cold, an odor which, at first ammoniacal, soon acquires the fishy character referred to. It has been highly lauded in *epilepsy* (for references, see 16th ed., *U. S. D.*), but it has very uncertain if any therapeutic properties. *Dose,* of fresh juice, from one-half to one fluidounce (15–30 cc.), two or three times a day; of fluidextract, one fluidrachm (3.75 cc.); of dry extract, five grains (0.32 Gm.); to be increased and given steadily for months.

Cow Tree. *Palo de Vaca. Palo de Leche.*—The milky juice of the *Brosimum Galactodendron* D. Don (fam. *Urticaceæ*) is much used in South America instead of cream in tea and coffee, etc. It is obtained by making incisions in the tree, is white and viscous, turns sour on exposure to the air, and deposits a caseous substance. According to the analysis of Boussingault, its composition varies very much, but it always contains a large percentage of fatty matters (32.2 per cent.), and much less casein, albumen, sugar, and phosphates. (*P. J.*, ix, 679.)

Crab's Claws. *Chelæ Cancrorum.*—These, finely powdered, were formerly used in medicine. In 100 parts are 60 parts of calcium carbonate and 14 of calcium phosphate, with 26 of animal matter.

Crabstones. *Lapilli Cancrorum. Crab's Eyes. Oculi* (*Calculi*) *Cancrorum. Yeux* (*Pierres*) *d'Ecrevisses,* Fr. *Krebsaugen, Krebssteine,* G.—Concretions found in the stomach of the European *crawfish* (*Astacus fluvatilis*), at the time the animal is about to change its shell; chiefly procured in the province of Astrakhan, in European Russia. The crawfish are bruised with wooden mallets and laid up in heaps to putrefy. The animal remains are then washed away, and the stones picked out. They are inodorous, insipid bodies, somewhat hemispherical in shape, of a whitish or reddish color, hard and stony consistence, and laminated texture. They are very variable in size, weighing from one to twelve grains each. They consist of calcium carbonate and phosphate, cemented together by animal matter. Crabstones have been used as an absorbent and antacid, given in the same dose as prepared chalk.

Creosote Benzoate.—This is a yellowish liquid, soluble in alcohol and ether. It is used mainly for its antiseptic action as a spray in the treatment of nose and throat diseases.

Creosote Iodide. *Creosotide.*—A product obtained by causing iodine to enter into combination with the cresol constituents of beechwood creosote. It contains approximately 25 per cent. of its weight of iodine. It is an amorphous brownish powder, practically insoluble in water and having a faint characteristic odor and taste. It is prescribed in incipient *tuberculosis* with alleged good results; also in *asthma* and as a gastric and intestinal antiseptic. *Dose,* one-fourth to one-half grain (0.016–0.032 Gm.) three or four times a day.

Creosote - phenyl - propionate. *Proposote.*—This is employed as a stimulating expectorant and is stated to have the advantage over creosote that it does not disturb the stomach as it is not affected by acid media, but passes into the intestine and is broken up by the duodenal juices with the liberation of creosote. It is administered in *doses* of five to ten minims (0.3 to 0.6 cc.).

Creosote Phosphate. *Creosoti Phosphas. Phosote.* $PO_4(C_6H_7)_3$.—A combination of creosote and phosphoric acid, in the form of a syrupy, colorless liquid, with almost no odor or taste of creosote. It contains about 80 per cent. of creosote and 20 per cent. of phosphoric anhydride. The *dose* is fifteen to thirty minims (1–2 cc.). *Creosote Phosphate* and *Creosote Tannophosphate* (*Tophosote*) have also been introduced as antiseptics.

Creosote Phosphite. *Phosphotal.*—This is a reddish-yellow, oily liquid with a faint creosote-like odor, dissolving readily in both water and alcohol. It represents over 90 per cent. of creosote. It is intended as a substitute for that remedy, especially in the treatment of *phthisis.* The *dose* is three to ten minims (0.2 to 0.6 cc.).

Creosote Tannate. *Creosotum Tannicum. Creosal. Tannocreosote. Kreosal. Tannosal.*—The tannic acid ester of creosote. It is obtained by heating equal quantities of beechwood creosote and pure tannin to 80° C. and adding gradually phosphorous oxychloride and purifying the product. It is a brown amorphous powder soluble in water, glycerin and alcohol, and containing 60 per cent. creosote. It passes through the gastric juice undecomposed but in the alkaline intestinal secretion it is split up into its components and acts as an antiseptic astringent in the treatment of *diarrhea.* It is also used for its creosote effect in *phthisis* and may be given in daily *doses* of fifteen grains (1 Gm.), representing 9 grains (0.6 Gm.) of creosote.

Creosote Valerate. *Creosotum Valeras.* (*Eosote.*)—A mixture of the valeric esters of the phenols contained in creosote. It forms a mobile oily liquid, boiling at about 240° C. and soluble in alcohol and ether. This substance as an internal medicine is practically identical in its properties with the creosote carbonate. *Dose,* three to ten minims (0.2–0.6 cc.).

Cresatin. *N. N. R.* 1924. *Metacresylacetate.*—The acetic acid ester of metacresol, $CH_3C_6H_4OCH_3CO$. A colorless oily liquid, insoluble in water, soluble in immiscible solvents. Volatile with steam. Used as an external application, either pure or diluted, as an antiseptic and analgesic.

Cresol Iodide. *Iodocresol. Traumatol.* $C_6H_3I.(CH_3)OH$.—This is formed by the action of potassium iodide solution upon an emulsion of cresol and water. It contains but one atom of iodine, while *losophan* or *cresol triiodide* contains three atoms, and, consequently, a higher percentage of iodine. It is a violet-red, odorless, amorphous powder; insoluble in water, acids, and alcohol; dissolving with difficulty in ether, readily in alkaline solutions, and freely in chloroform. It contains 55 per cent. of iodine, and has been commended as powerfully antiseptic, non-irritant, and having local anesthetic properties. It is used locally in *syphilitic* and other *ulcers, eczema,* especially when attended with much discharge, *intertrigo,* and various other skin diseases. Also as a substitute for iodoform in surgery. In *herpes* a 10 per cent. traumatol collodium has been found very useful, and a 5 to 10 per cent. traumatol zinc ointment has been highly commended. Pure traumatol may also be used as a dusting powder.

Cresol Preparations.—The fact that cresol, which is only sparingly soluble in water, is readily dissolved in saponaceous solutions has led to the introduction of a number of proprietary disinfectants of this nature. There is no reason to believe that any of them has any real advantage over the official compound solution of cresol, but some of them are sufficiently used to justify a few words of description.

Several of these have been bacteriologically tested by the United States Hygienic Laboratory. We give below a table showing the phenol coefficient of these as published in this bulletin (see *Phenol,* Part I).

Preparation	*Phenol Coefficient*	
	Without organic matter	With organic matter
Bacterol	1.58	1.34
Creolin-Pearson	3.25	2.52
Cresoleum	2.90	1.75
Germol	2.12	1.79
Kresolig	2.18	1.48
Kreso	3.92	2.32
Liq. Cresolis Comp. (*U. S. P.*)	3.00	1.87
Lysol	2.12	1.57
Saponified Cresol	1.03	0.57
Trikresol	2.62	2.50

Creolin is said to be an emulsion of cresol, obtained by means of rosin soap. There are in the market at least two sets of preparations, the one of German, the other of English origin. An analysis of creolin-Pearson, published by Pfrenger (*A. Pharm.,* 1890, 701), gives: phenols, 2.67; hydrocarbons, 44.94; organic bases, 2.76; sodium, 1.45; resin, 32.45; sulphur, 0.248; chlorine, 0.14; water (by difference), 5.34. The phenols consisted of ortho- and meta-cresol, with traces of phenol and the oxyleucols; the hydrocarbons, of the higher homologues of benzene, with naphthalene and anthracene; the bases belonged to the quinoline group. Creolin forms a milky emulsion on mixture with water; with chloroform, ether, and absolute alcohol it mixes in all proportions. It is sometimes called *cresoline* or *sanatol.*

The statements made concerning the germicidal powers of creolin have been extraordinarily at variance. Thus, Eisenberg asserted that a 3 per cent. solution of creolin destroyed anthrax spores in forty-eight hours, but Van Ermengen (*B. A. R. B.*, 1889, iii,) failed to kill them by thirteen days' exposure to a 10 per cent. solution. Burgess reached the conclusion that a 20 per cent. solution of creolin was equivalent to a 2.5 per cent. of phenol while Schneyder finds that creolin is from two to four times as strong as pure phenol, according to the species of bacteria on which it is tested. The last conclusion seems to be as near to the truth as it is possible to decide in view of the contradictory reports and corresponds with the findings of the U. S. Hygienic Laboratory. It has been claimed that creolin is non-poisonous, but although its toxicity is certainly much less than that of phenol, it is not entirely innocuous. Mugdan (*V. A. P. A.*, 1890, cxv, p. 131) found that doses of from 5 to 10 Gm. of Pearson's creolin are fatal to rabbits when given by the mouth, and Korach (*D. M. W.*, 1895), Van Ackeren (*B. K. W.*, 1889) and Bitter (*B. M. J.*, 1890) reported serious, although not fatal, poisoning in adults. Fliesburg (*Northwestern Lancet*, 1891, xi, p. 417) reports death in a three-weeks-old baby from 30 drops of creolin. The symptoms of creolin poisoning have resembled those of carbolic acid; namely, nausea, vomiting, frequently convulsions or coma, with albuminous, bloody or smoky urine.

Internally, creolin is probably a useful remedy when it is desired to check fermentation in the alimentary canal. Locally applied, it has been largely used with success in the treatment of *scabies*, in the form of a 5 per cent. ointment with vaseline. Although creolin has been used for various surgical purposes, its most popular employment has been as a disinfectant douche for internal cavities. In *ammoniacal cystitis*, washing out the bladder with a ½ per cent. solution of creolin has yielded excellent results. In the treatment of *acute* and *chronic dysentery* large enemas of a ½ per cent. solution may be used; in the case of infants the strength should be about one-half of this. For washing out the uterus after *labor*, the strength of the creolin solution should be 1 per cent.

Creolin is recommended by Jaksch as a deodorant to iodoform; a mixture of from 1 to 2 per cent. of creolin with iodoform produces a compound *creolin-iodoform* of a faint aromatic odor, soluble in alcohol and ether, and believed to possess the therapeutic properties of iodoform. Water removes from it the creolin and leaves the iodoform.

Ethylenediaminetricresol or *kresamin* is a mixture of tricresol with ethylenediamine. It is a colorless, aqueous liquid, having a phenol-like odor, and after standing in the air becomes of a light-yellow color without losing disinfecting power. According to H. Eckstein, it is an exceedingly powerful antiseptic, especially adapted to the preserving of specimens for microscopic use. As a local application the same author has found it very valuable in those cases of *eczema* in which there was a pronounced secondary infection of the skin, and also in *sycosis* and similar parasitic diseases. Bandages of it wet with a solution of from 1:4000 to 1:400 were kept applied to the part. In *lupus* and some similar conditions local protracted baths of from three to twelve hours' duration, with a concentration of 1:4000, were found efficacious. From 10 to 15 per cent. ointments of it were also employed.

Lysol was introduced by Gerlach (*Z. Hyg.*, 1891) and since then has been very widely used. Fox (*Penna. Health Bulletin*, 1910) has shown that lysol is inferior to the official Compound Solution of Cresol. As regards its toxicity, while it is probably less poisonous than phenol, it is an energetic poison. According to Blumenthal, there are about 100 cases annually of lysol poisoning in Berlin alone. Fries (*M. M. W.*, 1904), from a study of 38 cases of lysol poisoning, of which 17 were fatal, reaches the conclusion that the toxic dose for adults is from 10 to 12 cc. Cramer (*Cb. Gyn.*, 1898) has reported a death from its use as a vaginal douche.

Cresol Salicylates. *Cresalols. Cresol Salols.* $C_6H_4\left\{\begin{array}{l}OH\\COOC_6H_4CH_3\end{array}\right.$.—Salicylates may be prepared from ortho-, meta-, or para-cresol by a process similar to that used in the making of salol. They are insoluble in water, slightly soluble in cold alcohol, and are easily crystallized. The *meta-cresol salicylate* is the cresalol generally referred to by that name. It fuses at 74° C. and is easily soluble in alcohol and ether. Nencki states that the cresalols decompose in the alimentary canal, and are efficient substitutes for phenyl salicylate, and less poisonous. (*C. R. A. S.*, Feb., 1889.)

Cresol Triiodide. *Meta-cresol Tri-iodide. Losophan. Tri-iodo-Cresol* $C_6HI_3(CH_3)OH$.—A fine, yellowish powder, with a rather strong, but not disagreeable odor; insoluble in water, soluble in alcohol, ether, and chloroform, freely so in oil. Merck (*Jahresbericht*, 1892, 77) describes it as obtained in colorless needles, fusing at 121.5° C. It contains 78.39 per cent. of iodine. A specimen prepared by Friedrich Baeyer & Co. was found by Petersen (*M. M. W.*, July, 1891) to yield its iodine with difficulty, passing through the alimentary canal almost without absorption. It is employed externally as an antiseptic and astringent in *various skin diseases*. It is applied in a 2 per cent. solution or as a 10 per cent. ointment.

Cresotinic Acid.—*Cresotic acid. Homosalicylic Acid. Oxytoluic Acid,* $C_6H_3\left\{\begin{array}{l}CH_3\\OH\\COOH\end{array}\right.$.—Although there are ten possible isomeric cresotinic acids, according to the location in the benzyl ring of the hydroxyl and the methyl radicals, the only ones which have been used in medicine are the three methyl derivatives of ortho-oxybenzoic (salicylic) acid. These may be made artificially from cresol by a reaction analogous to that used in making salicylic acid.

Although it was at one time believed that the small amounts of cresotinic acid which were formerly present in the synthetic salicylates had a toxic effect upon the system, the experiments of Demme (*Th. M.*, 1890) and of May (*B. M. J.*, 1909, ii, p. 791) and others show that they are only slightly more toxic than salicylic acid. May has also found that both the meta- and ortho-cresotinic acids were actively germicidal. In 1876 Buss suggested the use of sodium cresotinate—a mixture of the sodium salts of the three isomers—as an antipyretic. The value of cresotinic acid in *rheumatic fever* has been carefully investigated by Stockmann (*J. P. Ex. T.*, 1912, iv, p. 97) who comes to the conclusion that *sodium meta-cresotinate* is capable of entirely replacing the salicylates but has no advantage over it; that the ortho salt is an active antirheumatic but also depressant to the heart; that the para salt is much less efficient.

Crotaline.—Under this name the *venom of the rattlesnake, Crotalus Adamanteus,* was recommended by Mays in the treatment of *phthisis, asthma, neuralgia,* and *epilepsy* several years ago. More recently, Spangler (*N. Y. M. J.*, September 9, 1911) revived this substance as an *antiepileptic.* He gave as a theoretic explanation of its use that the blood of epileptics coagulated with abnormal rapidity and that the venom delayed coagulation. Jenkins and Pendleton (*J. A. M. A.*, 1914, lxiii, p. 1749), in an extended study of 49 patients, found not only that the blood of epileptics was not more coagulable than normal, but that the number of convulsions after the use of crotallin was greater than without the drug. Thom (*B. M. S. J.*, 1915, clxxi), from a study of 203 cases, likewise reached the conclusion that the treatment was of no value. The danger of the injection is not merely from the injurious effects of the venom itself, but, as shown by Anderson (*J. A. M. A.*, 1914, lxii, p. 893), also from the fact that the commercial preparations are not sterile. The beginning *dose* recommended is one two-hundredth of a grain (0.0003 Gm.) hypodermically, which may gradually be increased as the patient forms a tolerance for the drug. The injections are generally followed by severe local irritation and should not be repeated for at least a week.

Crurin. *Quinoline-bismuth sulphocyanide.* $(C_9H_7NHSCN)_3Bi(SCN)_3$.—*Quinoline - bismuth rhodanate,* a reddish-yellow powder with weak odor of quinoline, insoluble in water, alcohol, and ether. *Crurin* of the markets is a preparation containing 25 per cent. of active ingredients with starch. According to the researches of Müller, it is bacteriologically active, and it has been especially recommended in the treatment of ulcers of the leg, by dusting them at intervals in full strength or diluted, *pro re nata.* It has also been highly recommended by E. Jacobi in *gonorrhea,* according to the following formula: Rub fifteen grains (1.0 Gm.) of crurin with seventy-five minims (4.6 cc.) each of distilled water and glycerin and gradually add sufficient distilled water to make six and one-half troyounces (201.5 Gm.).

Cryptocarya. *Cryptocarya australis* Bentham. (Fam. *Lauraceæ.*)—From the bark of this Queensland tree, T. L. Bancroft (*Austral. Journ. Pharm.*, March, 1887) has separated an alkaloid which is said to be a powerful respiratory poison.

Culilawan. *Cortex Culilaban.*—An aromatic bark, produced by *Cinnamomum Culilawan,* Blume (*Laurus Culilawan* L.), (Fam. *Lauraceæ*), a tree of considerable size, growing in the Molucca Islands, Cochin-China, and other parts of the East. It is usually in flat or slightly quilled pieces, 5 to 10 cm. long, 2.5 to 3.5 cm. wide, and 2 to 4 mm. thick. Sometimes the bark is thinner and more quilled, bearing considerable resemblance to cinnamon. The periderm is for the most part removed, but when present is of a light brownish-gray color, soft to the touch, and somewhat spongy. The color of the bark itself is a dull, dark, cinnamon brown, the odor highly fragrant, the taste agreeable, aromatic, and not unlike that of cloves. The active constituent is a volatile oil, smelling like a mixture of the oils of cajuput and cloves. Culilawan has the medicinal properties of the aromatics, but is rarely used. (See *Clove bark.*)

Cumin. *Cummin. Cuminum* Ed. *Cumin,* Fr. *Kreuzkümmel, Mutterkümmel, Römischer (langer, scharfer) Kümmel,* G.—The so-called *cumin seeds* are the fruits of *Cuminum Cyminum* L., an annual umbelliferous plant, which is a native of Egypt, but is cultivated for its fruit in Sicily, Malta, and other Mediterranean countries.

The cumin fruits are oblong cremocarps of a light brown to yellowish-brown color from 5 to 6 mm. long and 1.5 mm. broad, the 2 mericarps of which are coherent. Each mericarp has 5 prominent ribs and 4 broader secondary ones, each beset with fine hairs, as well as 6 oil-tubes (vittæ). Their odor is peculiar, strong, and heavy; their taste warm, bitterish, aromatic, and disagreeable. They contain about 2.5 per cent. of an essential oil, which is yellowish, and has the sensible properties of the fruits. It consists of three distinct oils, one a hydrocarbon, *cymene,* $C_{10}H_{14}$, recognized now as isopropyl-p-methyl-benzene, another *cuminol,* $C_{10}H_{12}O$, which may be regarded as *cuminic aldehyde,* $C_{10}H_{11}OH$, and the third a terpene, $C_{10}H_{16}$. Acymene identical with that of the oil of cummin seed can be prepared by dehydrating camphor or oil of turpentine. (*A. J. P.*, xlvi, 117; see especially *A. J. P.*, xliv, 452.) Cumin aldehyde has also, together with cymene, been obtained from the fruits of *Cicuta virosa* L. Trapp, *Ann. Ch. Ph.*, cviii, 386; see also *Schim. Rept.*, 1909, 49.) In medicinal properties cumin fruits resemble the other aromatic umbelliferous fruits. *Dose,* fifteen to thirty grains (1–2 Gm.).

Cumol. *Cumene. Pseudocumol.* $C_6H_3(CH_3)_3$-(1 :3 :4).—An oily fluid derived from coal tar, boiling at 168° to 178° C. Cumol has been especially recommended by Krönig (*Centralbl. f. Gyn.*, 1894) for the purpose of sterilizing catgut, which is placed in the cumol and slowly heated up to 160° C. After two hours it is removed and freed from the adhering cumol by petroleum benzin.

Cunila. *Cunila Mariana* L. *C. origanoides* (L.) Britt. (Fam. *Labiatæ*), *American or Common Dittany. Sweet Horsemint. Stonemint.*—A small indigenous perennial herb, growing on dry, shady hills, from New York to Georgia, and Illinois and Arkansas westward, and flowering in June and July. This plant has much branched stems bearing opposite, nearly sessile, ovate leaves cordate or rounded at the base and serrate along the margin. Its small flowers are borne in corymbed cymes and vary from white to purple in color. The whole herb has a warm, pungent taste and a fragrant odor, dependent on an essential oil. This was formerly used in the *dose* of five or ten minims (0.3–0.6 cc.) as a carminative, and in *doses* of from fifteen to twenty minims (0.9–1.3 cc.) as a diaphoretic.

Curare. *Woorari. Woorara. Woorali. Urari.*—The term "curare" has no specific meaning, but according to Whiteford is simply the Indian word for poison, and it is evident that there are a considerable variety of arrow poisons used in South America under the same name. As originally described by Waterton, it was in the form of a thick syrup, but as it now occurs in commerce it is a blackish extract, brittle, somewhat resinoid in appearance, encrusting the sides of gourds or little rude earthenware jars, into which it has been poured in a liquid state. The drug varies much in strength. According to the researches of Planchon (*P. J.*, xi, 491), there are really four distinct varieties of *curare.* (1) That from the Upper Amazon, obtained from the *Strychnos Castelnæi* Wedd., and possibly from *S. Yapurensis* G. Planch. (2) That from the Upper Orinoco, extending towards the Rio Negro, yielded by *S.*

Gubleri G. Planch.; this is the variety spoken of by Humboldt. (3) That of British Guiana, obtained from *S. Toxifera* Schomb., associated with *S. pedunculata* Benth. and *S. cogens* Benth. (4) That of French Guiana, made out of *S. Crevauxiana* Baill. (*S. Crevauxii* G. Planch.). These varieties are, however, commercially indistinguishable.

In 1898 Boehm classified the curares of the markets as *Tubocurare,* originating from the Amazon, preserved in hollow bamboo canes, and said to contain about 9 to 11 per cent. of *tubocurarine* as its poisonous constituent; *Gourd curare,* derived from *Strychnos toxifera,* very rarely met with, and having curarine and a second alkaloid soluble in ether for its active principle; *Jar curare,* obtained from *Strychnos castelnœi,* also exceedingly rare in the European markets, containing three alkaloids—*protocurine,* having a feeble curare action; the non-poisonous *protocuridine;* and *protocurarine,* which is more actively poisonous than is curarine. (*Ph. Ztg.*, xlii, 41.) The preparation of woorari has been witnessed by various travellers and variously described. (See *P. J.*, xvi, 502; *B. F. M. R.*, Oct., 1865; *P. J.*, x, 1881.)

Curare now comes into the market in hollow bamboo stems and in small earthen pots, the former being termed "*Bamboo curare*" and the latter "*Pot curare.*" *Bamboo curare* occurs as a dark brown granular extract, the broken fragments of which appear crystalline. *Pot curare* occurs as a dark brown to black mass having the shape of the earthen pot which contained it.

The method followed in the Upper Amazon region is to make a decoction of the bark of *Strychnos Castelnœi,* to which one-tenth of the stem of another liane is added. This is then concentrated by evaporation. To this concentrated juice then is added the leaves of *Petiveria alliacea,* the stems of *Dieffenbachia Seguine,* the root barks of two plants of the *Piperaceæ* and a species of *Marcgravia.* The fluidextract is then evaporated until it is in the condition of an extract, and poured into small vessels. Joubert asserts that the Tecuma Indians use, besides *S. Castelnœi* Weddell, *Cocculus toxiferus* and an arum (*Taya*), which he found to be very poisonous. According to Kobert (*Ph. Ztg.*, June, 1885), *Malouetia nitida* Spruce (fam. *Apocynaceæ*), or *Guachamaca,* a plant which is abundant in the Orinoco and Rio Negro districts, enters largely into the composition of curare. The alkaloid, *guachamacine,* isolated by T. Schiffer in 1883, is very closely allied to, if it be not identical with, curarine, in both its chemical and its physiological activity. It is entirely possible that the varieties of woorari vary in their alkaloid and their physiological properties.

Allied to woorari are the arrow poisons by W. S. W. Ruschenberger from Colombia, and studied by W. A. Hammond and S. Weir Mitchell. (*Am. J. M. S.*, July, 1859.) Corroval was in dark brown lumps, having the appearance of a vegetable extract, and of an intensely bitter and persistent taste. They found its activity to depend upon the presence of a peculiar alkaloid, *corrovaline.* It resembles curare in that it produces general paralysis without previous spasm, but differs, in paralyzing also the heart. *Vao* or *Bao* appears to be a dilute and adulterated form of corroval.

R. Boehm has isolated the two bases, *curarine,* $C_{19}H_{26}ON_2$, and *curine,* $C_{18}H_{19}O_3N$. The free tubocurarine forms an amorphous brown-red mass. Boehm (*Ber. d. Chem. Ges.*, xx, 143) states that curine exists in many specimens of curare; it may also be obtained from the aqueous extract of curare. It is much less poisonous than the accompanying curarine. Curine is a crystalline powder fusing at 161° C., slightly soluble in cold water, freely soluble in alcohol, chloroform, and dilute acids. It forms a voluminous white precipitate with metaphosphoric acid.

Paracurarine (or *tubocurarine*) has the composition $C_{19}H_{21}O_4N$. *Protocuridine* ($C_{19}H_{21}O_3N$) and *protocurarine* ($C_{19}H_{23}O_3N$) are also present in the variety known as *pot curare. Bakankosine* ($C_{16}H_{23}O_8N$) is a nitrogenous glucoside which has been isolated from *Strychnos vacacona.*

Woorari is one of those poisons whose active principle passes through animal membranes with difficulty, and hence when given by the stomach or rectum it acts very slowly, and in some cases elimination may proceed so rapidly that no marked influence is exerted, because not enough of the alkaloid is in the blood at any one time. There is also reason for believing that the alkaloid is destroyed in the liver. When injected into a vein, or introduced by the hypodermic needle or the poisoned arrow into the cellular tissue, it acts with great promptness. The symptoms caused are progressive loss of muscular power, the animal growing weaker and weaker, the respirations becoming more and more feeble, until death by asphyxia results.

The action of curare is to paralyze the peripheral ends of the motor nerves, the muscles, when directly stimulated, retaining their irritability. In mammals, as a result of the paralysis of the phrenic nerves, there is failure of respiration, and consequent death from asphyxia. The heart usually continues beating after cessation of the breathing, only very large doses affecting the arterial pressure directly. If, however, the dose be sufficient, the drug paralyzes the peripheral ganglia, thereby causing a dilation of the blood vessels with consequent fall of pressure, increased rate of the pulse through lack of inhibitory control, loss of irritability in the secretory nerves, and other modifications of functions of less importance. Tillie (*A. E. P. P.*, xxvi,) has brought forward evidence to show that there is a primary excitation of the spinal cord which, however, in ordinary poisoning, is masked by paralysis of the motor nerves. The sensory apparatus does not seem to be affected, unless by enormous doses. Glycosuria has been frequently noticed in animals as the result of curare poisoning. According to Morishima (*A. E. P. P.*, 1889, xlii), this is apparently independent of the amount of glycogen in the liver or muscles.

According to the experiments of Joseph Tillie, *curine* has no influence upon the motor nerves, but acts both in the frog and in the mammal upon the heart, belonging physiologically to the digitalis group. Boehm states that the presence of curine in curare can be recognized by the white precipitate made by metaphosphoric acid.

Voisin and Lionville describe two types of poisoning in human beings. In the milder type the pulse is increased in force and frequency, respirations somewhat rapid, the temperature a little elevated, and the urine contains sugar. After larger quantities symptoms begin with severe chill, tremors, small pulse, and early loss of power in the lower extremities, later the cold skin becomes hot, the pulse rapid and full, there is marked reduction of the body temperature, with redness of the skin, and frequently profuse sweating. In non-fatal cases, the paralysis of the extremities rarely lasts for an hour, but the fever may continue for several days.

In cases of poisoning from the injection of woorari, a ligature around the limb between the place of injection and the heart, the free exhibition of diluents and evacuants, and artificial respiration when required, are the measures recommended. (*Ed. M. J.*, 1867, 667.)

Although curare has in the past been used as an anti-convulsant in *tetanus* and *hydrophobia*, it is a remedy of no practical value, because the phrenic nerve is no less susceptible than the other motor nerves of the body, and if given in sufficient doses to control the spasm, will likely lead to fatal asphyxia. For man the *doses* administered by subcutaneous injection were from one-twelfth to one-third of a grain (0.005–0.02 Gm.) of the crude curare. According to Bernard, curarine is at least twenty times as strong as curare.

Curcuma. *U. S.* 1870. *Turmeric. Safran des Indes, Souchet des Indes*, Fr.; *Kurkuma, Gelbwurzel*, G.; *Curcuma*, It., Sp.; *Zirsood*, Arab.; *Huldie*, Hindoo. *Curcuma longa* L. (Fam. *Zingiberaceæ.*)—The rhizome of this plant is ovate or pear-shaped, and internally of a deep yellow or orange color. The plant is a native of Southern Asia and East Indies, and is cultivated particularly in China, Bengal and Java. The best is said to come from China.

Long turmeric, representing the secondary rhizomes, is in cylindrical or oblong pieces, from 0.5 to 1.5 cm. in thickness, distinctly annulate, tuberculated, somewhat contorted, externally yellowish-brown or greenish-yellow, internally deep orange-yellow, hard, compact, breaking with a fracture like that of wax, and yielding a yellow or orange-yellow powder. *Round turmeric*, representing the main rhizomes, is ovate or pear-shaped, about the size of a pigeon's egg, and marked externally with numerous annular wrinkles. Sometimes it comes cut into two transverse segments. The two varieties are derived from the same plant. The odor of turmeric is peculiar; the taste warm, bitterish, and feebly aromatic. It tinges the saliva yellow. Analyzed by Pelletier and Vogel, it was found to contain lignin, starch, a peculiar yellow coloring matter called *curcumin*, a brown coloring matter, gum, an odorous and very acrid volatile oil, and a small quantity of calcium chloride. Curcumin has been obtained by F. A. Daube, in deep yellow crystals of a high luster, by a process which may be found in the *A. J. P.* (1871, 308). C. L. Jackson and Menke have submitted turmeric root to a thorough examination, and give the following results: The turmeric oil was first removed from the ground root by treatment with ligroine, then the curcumin mixed with a large quantity of resin is extracted with ether, and finally purified by crystallization from alcohol. The oil extracted by ligroine was dark yellow, and amounted to 11 per cent. of the root. The purified curcumin amounted to 0.3 per cent., and melted at 178° C. Analysis of the pure curcumin, of several of its salts, and of derivatives by Daube showed its formula to be $C_{10}H_{10}O_3$. Gajewsky gave the formula as $C_{16}H_{16}O_4$ and Jackson as $C_{28}H_{28}O_8$. Ciamicin and Silber have later given the formula as $C_{19}H_{14}O_4(OCH_3)_2$ or $C_{21}H_{20}O_6$ which has been verified by other investigators. It is brown in mass, but yellow in the state of powder, without odor or taste, insoluble in benzin, scarcely soluble in water, but very soluble in alcohol, ether, and the oils. It is a diatomic monobasic acid. When treated with weak oxidizing agents it yields vanillin. The alkalies rapidly change its color to a reddish-brown, and paper tinged with tincture of turmeric is employed as a test of their presence. The paper is rendered brown also by boric acid, which it thus serves to detect. When treated with a mixture of sulphuric and boric acids it yields a product called *rosocyanin*, because it dissolves in alcohol with a fine red color, and is turned blue by alkalies. Its alcoholic solution produces colored precipitates with lead acetate, silver nitrate, and other salts. Turmeric is used for dyeing yellow, but the color is not permanent.

The rhizomes are dug up at the close of the season's growth, washed and then either scalded or boiled. During this process the starch becomes more or less altered, the contents of many of the cells becoming swollen to form pasty masses which are colored yellow by the curcumin present in the cells. The rhizomes are then quickly dried in the sun.

Statements by some of the older writers as to the presence of an alkaloid in turmeric root have not been recently confirmed.

This root is largely used as a condiment in the tropical East forming the basis of the well-known *curry powder*. In pharmacy it is sometimes employed to impart color to ointments and other preparations. It possesses no medicinal value.

Turmeric, when used as an adulterant, may be detected by means of a mixture of boric and sulphuric acids, but according to A. E. Bell, a much better test is afforded by the use of the reagent made by dissolving 1 gramme of diphenylamine in 20 cc. of 90 per cent. alcohol, carefully adding 25 cc. of pure sulphuric acid. To a little of the suspected powder, placed on a slide, a drop of the reagent is added with a glass rod. Spots of a fine purple color immediately develop, which may be readily recognized with the microscope.

Turmeric paper, used as a test, is prepared by the method described in the appendix of the U. S. P.

The tubers of the *Curcuma angustifolia*, Roxb., and the *C. leucorrhiza*, Roxb., are cultivated in India for the sake of their starch and are sometimes known as *East Indian Arrow Root*.

Curry Leaves. *Currie.*—The leaves of the *Murraya Kœnigii* Spreng. (Fam. *Rubiaceæ*), a tree of India, are very largely used in that country as an aromatic, stomachic stimulant; when powdered and mixed with spices and other substances it forms *curry powder*, which is much used for seasoning food, rice, cooked dishes, etc.; it is also employed in *dyspepsia, diarrhea*, and even *dysentery*. According to J. G. Prebble (*Pharmacographia Indica*, vol. i), curry leaves yield to distillation a small quantity of volatile oil, and also contain a greenish-black resin, and a glucoside, *kœnigin*. The clear oil extracted from the seeds is known as *simabolee oil*.

Curry powder is a term usually applied to a highly seasoned condiment consisting of a mixture of a number of spices. The formulas vary in the identity and proportion of the spices used, but usually include the majority of the following: black pepper, capsicum, nutmeg, cinnamon, cloves, cardamon and turmeric, the latter always predominating. The word "curry" which comes from the Orient, originally signified a stew containing meat, in which a blend of spices was used in preparing the sauce. Curry powder is frequently used with rice and its use is increasing in the western world.

Cusparia Bark. *Cuspariæ Cortex. Br.* 1898. *Angustura, U. S.* 1870. *Angustura (Angostura) Bark. Carony Bark. Cortex Angusturæ. Angusture vraie,* Fr. Cod. *Angusture,* Fr. *Angusturarinde,* G. *Corteccia dell' Angustura,* It. *Corteza de Angostura,* Sp.—This bark was formerly recognized by both the U. S. and British Pharmacopœias but is no longer official in either. It was originally attributed in the *Cusparia febrifuga* Humb. (*C. officinalis,* Hancock, *Galipea cusparia* St. Hilaire) but is now believed to be derived from an allied tree, *Galipea officinalis,* Hancock. *Cusparine* ($C_{19}H_{17}O_3N$), *galipine* ($C_{20}H_{21}O_3N$) and *galipoidine* ($C_{19}H_{15}O_4N$). The tree grows abundantly on the mountains of Venezuela at the height of from six hundred to one thousand feet above the level of the sea.

The bark is generally brought from the West Indies packed in casks; but, according to Brande, the original package as it comes from Angostura consists of the leaves of a species of palm, surrounded by a net-work of sticks.

Cusparia bark "occurs in flattened or curved pieces, or in quills, generally about 10 to 12 Cm. long, 2.5 Cm. wide, and 2 mm. thick. The outer layer usually consists of a gray or yellowish cork which is often soft and easily removed, disclosing a hard, dark brown inner layer; the inner surface is light brown and frequently laminated. The fracture is short and resinous; on the fractured surface many white points are visible. A transverse section exhibits numerous cells filled with acicular crystals of calcium oxalate and small oil glands, but seldom any sclerenchymatous tissue other than small isolated groups of fibers. Odor musty; taste bitter." *Br.,* 1898. Calcium oxalate raphides are abundant in the bark, but the most characteristic peculiarity is the presence of numerous cells a little larger than the other parenchymatous cells and completely filled with oil or a yellowish resin. The odor of Angustura bark is peculiar and disagreeable when fresh, becoming fainter with age; the taste is bitter and slightly aromatic, leaving a sense of pungency at the end of the tongue.

Cusparia bark contains a volatile oil, a neutral bitter principle and several alkaloids. The volatile oil, which may be obtained by distillation with water, is of a pale yellowish color, lighter than water, of an acrid taste, and with the odor of the bark. Of this oil Beckurts and Nehring obtained 1.5 per cent. It had a sp. gr. of 0.956; under a pressure of 35 mm. it commenced to boil at 153° C. and the greater part distilled between 200° and 220° C., the last portions becoming solid when artificially chilled. Beckurts and Froeger (Gildemeister and Hoffman, *Aetherische Oele,* p. 601) found as its essential ingredient a sesquiterpene alcohol, $C_{15}H_{26}O$, to which they give the name *galipol.* This boils between 260° and 270° C., and is optically inactive. They found also a small quantity of an inactive sesquiterpene, *galipene,* as well as traces of a terpene, probably pinene, and cadinene to which the oil owes its laevo-rotatory property.

The bitterness of the bark is due chiefly to a neutral principle *angosturin,* $C_{19}H_{12}O_5$, which melts at 58° C. Beckurts and Nehring (*A. J. P.,* 1892, 410) announced the discovery of four alkaloids in Angustura bark—viz., *galipine,* melting at 115.5° C. and crystallizing in slender lustrous needles of white color; *galipidine,* melting at 111° C. and crystallizing in silky lustrous plates of white color; *cusparine,* melting at 90° C. and readily soluble in alcohol, ether, chloroform, acetone, and benzene, more sparingly in light petroleum; and *cusparidine,* melting at 78° C. and crystallizing in minute slender white needles. Its salts are less soluble than those of galipine and galipidine, but more readily than those of cusparine. The four alkaloids are tertiary bases. The existence of galipidine and cusparidine has, however, been called in question; Troeger and his co-workers (*A. Pharm.,* 1913, ccli, 246 and 1920, cclviii, 250) regarding them as mixtures containing the alkaloids cusparine and galipine. Troeger and Beck find in Angostura bark three alkaloids, cusparine, $C_{19}H_{17}ON_3$, *galopoidine,* $C_{19}H_{15}O_4N$, and a new alkaloid of the formula $C_{16}H_{13}O_2N$. (*A. Pharm.,* 1913, ccli, 246.) A fluorescent glucoside was found by Beckurts and Nehring. For a description of false Angustura barks, see *U. S. D.,* 19th edition, p. 417.

Angustura bark was formerly attributed with febrifuge and antiperiodic powers but probably has no other virtues than that of an aromatic bitter. It is rarely prescribed by physicians, its chief use being in the form of various nostrums advertised directly to the laity. Under the name of *Infusum Angusturæ* the U. S. Pharm., 1870, recognized an infusion made in the proportion of half a troyounce of Angustura bark in a pint of water; *dose,* two fluidounces (60 cc.), repeated every two, three, or four hours. *Dose,* in substance, ten to thirty grains (0.65 to 2.0 Gm.). In larger quantities it is apt to produce nausea.

Cuttlefish Bone. *Os Sepiæ. Cuttle-bone. Os de Sèche (Seiche),* Fr. *Sepie, Weisses Fischbein,* G.—This is a calcareous body, situated underneath the skin, in the muscular mantle of the *Sepia officinalis* L., or *cuttlefish* (Ord. *Dibranchia*), a mollusk abundant in European seas and in the Indian Ocean. It is oblong-oval, from five to ten inches long, and from one and a half to three inches broad, somewhat convex on both sides, with thin edges, of a rather firm consistence upon the upper surface, very friable beneath and composed of numerous layers, loosely connected, so as to give to the mass a porous consistence. It is lighter than water, of a white color, a feeble sea odor, and a saline taste. It contains, according to John, from 80 to 85 per cent. of calcium carbonate, besides animal matter, a little sodium chloride, and traces of magnesia. Its fine powder may be given as an antacid, and it is sometimes used as an ingredient of tooth-powders. Small pieces of it are often put into bird cages that the birds may rub their bills against them, and the powder is employed for polishing. Another product of the cuttlefish is a blackish-brown liquor, secreted by a small gland in an oval pouch, communicating externally near the rectum by a long excretory duct, through which the animal is said to have the power of ejecting it at will. This, when taken from the fish, is dried, and used in making the water-color *sepia* and a writing fluid used by the inhabitants of China, India and Japan. It is not the India ink of commerce, which is made from a specially prepared lampblack.

Cyano-Cuprol.—This liquid is stated to contain copper and cyanogen united chemically with a derivative of tuberculin. It is a colorless, transparent liquid, unstable in the air. It has been used by Koga (*J. Ex. M.*, 1916, xxiv, p. 107) and other Japanese physicians with asserted success in the treatment of *tuberculosis* and also of *leprosy*. Their statements concerning its composition are rather vague and the doses recommended differ widely.

Cyclamen. *Cyclamen europœum* L. *Pain de Porceau, Arthanite.* Fr. *Erdscheibe, Erdbrod, Schweinbrod,* G. *Sowbread.*—This is an herbaceous, perennial, stemless plant, of the subalpine mountainous regions of Europe. Some of the species of *Cyclamen* are among the most popular of winter plants on account of their beautiful foliage and exquisite flowers. The corm is globular, with many branched rootlets, almost black without, and white within, inodorous, and, when fresh, of a bitter, acrid, burning taste. By drying it loses much of its acridity, and is said to be rendered edible by roasting. Hogs are said to root it up from the ground and to eat it with impunity, and hence the common name "Sow Bread." The corm is a drastic cathartic, and is used to cause abortion, but has in such cases produced fatal gastro-enteritis. Its active principle appears to be *arthanitin* of Saladin, the *cyclamin* of S. De Luca. This is a poisonous glucoside, which, when boiled with diluted acids, splits into *cyclamiretin,* $C_{15}H_{22}O_2$, and glucose. It is white, amorphous, inodorous, and, when held a short time in the mouth, intensely acrid, extending its action even to the throat. With cold water it swells and becomes gelatinous, and eventually forms a solution which froths like soap and water, and is coagulated by a heat of about 65.5° C. Its formula, according to an analysis by Klinger, is $C_{20}H_{34}O_{10}$, although Kobert (*Chem. Cb.*, 1893, i, 32) makes it one of the class of saponins, and gives it the formula $C_{20}H_{32}O_{10}$, which is the same as that of sarsaparilsaponin and smilacin. (For further details and method of preparing see *U. S. D.* 20th ed., p. 1356.) *Dose,* of powdered root, is said to be from twenty to forty grains (1.3–2.6 Gm.).

Cyclea Peltata H. and Th.—An East Indian drug, according to Sutterheim, contains an alkaloid, $C_{27}H_{31}O_4N_2$, which he named *cycleine;* it has the effect of a cardiac poison accompanied by action on the respiratory centers. (*Ph. Wb.*, 1906.)

Cycloform. *Isobutyl-para-amino-benzoate.* $C_6H_4(NH_2)COO.CH_2.CH(CH_3).CH_3$.—It occurs as white, crystalline scales, almost insoluble in water. Impens (*Ther. Geg.*, 1910, li, p. 348) asserts, however, that the saturated solution, which contains but 0.02 per cent., will produce complete anesthesia of the cornea of the eye and that even a solution of one-third this strength has a distinct anesthetic influence. According to this author, the salts of *cycloform* are more soluble, but dissociate in solution and are therefore locally irritant. Large doses produce in the lower animals drowsiness, general weakness and collapse with formation of methemaglobin.

Because of its sparing solubility cycloform has not been widely used for surgical purposes, but has received considerable commendation as a dusting powder in painful *ulcers,* especially after *burns,* and in *tuberculous laryngitis.* It appears not only to lessen the pain, but to stimulate the healing processes. Zeller (*Med. Klin.*, 1910) finds that the ointment is useful to relieve the itching of *chronic eczema* and other skin diseases as well as the pain of *anal fissure* and *hemorrhoids.* In making the ointment, Franke (*Aerzt. Rund.*, 1913) recommends that *cycloform* be dissolved in olive oil before it is incorporated with the ointment base. The dusting powder, which may be made with kaolin, should contain from 10 to 20 per cent. of cycloform. The ointment should contain from 5 to 20 per cent.

Cyclosal. *Hexeton. Homocamfin.*—This is stated to be the 3-methyl-5-isopropyl-2-cyclohexonon dissolved in a solution of sodium salicylate. The *methyl-iso-propyl-cyclohexenon,* itself, is a yellowish oily substance sparingly soluble in water. It is recommended as a circulatory and respiratory stimulant in dyspnea, heart failure, asthma, etc. It is marketed in the forms of a 1 per cent. and a 10 per cent. solution in sealed ampules.

Cydonium. *U. S.* 1880. *Quince Seed. Semen Cydoniæ. Semeneces (Pépins) de Coing,* Fr. *Quittenkerne, Quittensamen,* G. *Semi di Cotogno,* It. *Simiente de Membrillo,* Sp. *Pyrus Cydonia* L.—(*Cydonia vulgaris,* Pers.) (Fam. *Rosaceœ*), or common quince tree, has been under cultivation since very remote times. It is a native of Central Asia but grows wild in Austria, on the banks of the Danube, and is extensively cultivated for its fruit throughout the temperate regions of both continents. The fruit is a yellow pome which is covered with wooly hairs in its unripe stage. These, however, loosen and mostly fall off as the fruit matures. There are several varieties, some of which are apple-shaped, others pear-shaped. All, however, have an agreeable odor and an astringent, acidulous taste. Like the apple and pear, each fruit possesses five ripened carpels which constitute its core. Each of these contains from 6 to 15 seeds arranged in 2 rows. Though not eaten raw, it forms a very pleasant confection, and a syrup prepared from it may be used as a grateful addition to drinks in sickness, especially in looseness of the bowels, which it is supposed to restrain by its astringency. The seeds, which were formerly official, are ovate, angled, reddish-brown externally, white within, inodorous, and nearly insipid, being slightly bitter when long chewed. Their coriaceous envelope abounds in mucilage, which is extracted by boiling water. They were officially described as follows: "About 6 mm. in length, oval, or oblong, triangularly compressed, brown, covered with a whitish, mucilaginous epithelium, causing the seeds of each cell to adhere. With water the seeds swell up, and form a mucilaginous mass. The unbroken seeds have an insipid taste." *U. S.*, 1880. The seeds are used in the preparation of *bandoline* and cosmetic lotions. Two drachms of the seeds will render a pint of water thick and ropy. (*A. J. P.*, 1876, 35.) It has been proposed to evaporate the decoction to dryness, and powder the residue. Three grains of this powder form a sufficiently consistent mucilage with an ounce of water. According to Garot, one part communicates to a thousand parts of water a semi-syrupy consistence. (*J. P. C.*, 3e sér., iii, 298.) Pereira considers the mucilage as peculiar, and proposes to call it *cydonin.* It differs from arabin in not yielding a precipitate with potassium silicate, and from bassorin and cerasin in being soluble in water both hot and cold. Tollens and Kirchner (*Ann. Ch. Phys.*, clxxv, 205–226) assign to it the formula $C_{18}H_{28}O_{14}$, regarding it as a compound of gum, $C_{12}H_{20}O_{10}$, and cellulose, $C_6H_{10}O_5$, less one molecule of water. Quince mucilage (*Mucilago Cy-*

donii, U. S., 1880) may be used for the same purposes as other mucilaginous liquids. The U. S. P., 1880, gave the following formula for its preparation. "Cydonium, *two parts;* Distilled Water, *one hundred parts.* Macerate the Cydonium for half an hour, in a covered vessel, with Distilled Water, frequently agitating. Then drain the liquid through muslin, without pressure. This preparation should be freshly made, when required for use." *U. S.,* 1880.

Cynara. *Cynara Scolymus* L. *Artichoke.*—This is a composite plant, indigenous to the south of Europe, and cultivated as a culinary vegetable. The receptacle and the lower portion of the fleshy leaflets of the flower-heads are eaten. When young, the heads are cut up raw and eaten as salad; when older, they are boiled, and variously dressed. The flowers are said to curdle milk, and the plant to yield a good yellow dye. The leaves and their expressed juice are very bitter, and have been thought to be actively diuretic. *Cynara Cardunculus,* the *cardoon* of the garden, very much resembles the artichoke. The stalks of the leaves are used as a vegetable in France. Artichoke leaves have been used in *dropsies* and *rheumatic affections.* The *Jerusalem artichoke, Helianthus tuberosus* L., is another distinct plant belonging to the *Compositæ,* which has been cultivated for its edible tubers. These contain an abundance of inulin and sugar.

Cynoglossum. *Cynoglossum officinale* L. *Hound's-tongue. Langue de Chien,* Fr. *Hundszunge,* G.—A strong-scented biennial plant of the Fam. *Boraginaceæ* indigenous to Europe and naturalized in the U. S. A. Both stems and leaves of this plant are clothed with short, soft hairs. Its leaves are entire and lanceolate, sessile above, petioled below. Its stem terminates in a panicle of reddish-purple, or rarely white, funnel-shaped flowers. The leaves and root have been employed, but the latter has been generally preferred. The fresh plant has a disagreeable narcotic odor, resembling that of mice, which is dissipated by drying. The taste is nauseous, bitterish, and mucilaginous. Although hound's-tongue has been believed by some to be nearly inert, there can be little doubt that it is a dangerous poison. The experiments of Diedülin (*M. S. Rep.,* 1868) many years ago demonstrated that the extract paralyzes motor nerves in vertebrate animals, and K. Greimer has found in it a poisonous alkaloid, *cynoglossine,* which acts upon the animal organism similarly to curare; also a toxic glucoside, *consolidin,* and a notable amount of choline. (*P. J.,* vol. lxv.) *Consolicin,* a derivative of consolidin, like consolidin, paralyzes the central nervous system. Cynoglossum has been used as a demulcent and sedative in *coughs, catarrh, spitting of blood, dysentery,* and *diarrhea.* The *pilulæ de cynoglosso* owe their properties chiefly to opium.

Cystopurin. $(CH_2)_6N_4.2CH_3COONa + 6H_2O$.—A compound obtained by the interaction of formaldehyde, ammonia and sodium acetate. It forms nearly tasteless, colorless, lanciform crystals which are readily soluble in water. It is recommended for the treatment of *cystitis* and *gonorrhea* in *doses* of thirty grains (2 Gm.) dissolved in water. It is also used as a prophylactic.

Cytisus. *Cytisus Laburnum* L. *Golden Chain. Golden Rain.* (Fam. *Leguminosæ.*)—Laburnum is a small hardy tree with pendent racemes of yellow flowers, native to the higher mountains of Europe. Several varieties of this tree varying in foliage and floral color are cultivated in various parts of the world. The roots taste like licorice but have poisonous properties. All parts of the plants are probably poisonous. In fifty-eight boys poisoned simultaneously by the roots, the symptoms were intense sleepiness, vomiting, convulsive movements, coma, slight frothing at the mouth, and unequally dilated pupils. (*M. T. G.,* vol. ii, 875.) In some cases the diarrhea has been severe. The convulsions have at times been markedly tetanic; wide-spread anesthesia has been noted, and also excessive mydriasis, with loss of the pupillary reflex, elevation of temperature, delirium, and cyanosis. After death there have been found erosion of the colonic mucous membrane, extreme hyperemia of the brain, and nephritis. (*D. M. W.,* xxi, 1895.) For reference to cases see *U. S. D.,* 20th ed., p. 1357.

Hausemann and Marmé isolated in 1864 an alkaloid, *cytisine,* a white, crystalline solid, of a bitter, somewhat caustic taste, soluble in water and alcohol, but scarcely at all soluble in ether, chloroform, benzene, or carbon disulphide. A second alkaloid, *laburnine,* was also announced by them. (*Chem. News,* July 16, 1869, 36.) Partheil (*A. Pharm.,* 1892, 448) has since studied cytisine, and gives it the formula $C_{11}H_{14}ON_2$. Ferric chloride colors cytisine and its salts blood-red, which color, however, disappears on diluting with water or on addition of hydrogen dioxide. If after the addition of this latter reagent the mixture is heated gently in the water bath an intense blue color is developed. When cytisine is distilled with soda lime, pyrrol is obtained, besides a base, $C_9H_{13}N$, which is possibly a hydroquinoline. A. Rannerda purified crude cytisine, obtained from the seeds of *Cytisus Laburnum* L., by the well known shaking out process with chloroform, by distilling it in a partial vacuum. Under a pressure of 2 mm. and a temperature of 228° C., the alkaloid distils over as a colorless liquid and congeals in the receiver in the form of fine crystalline needles. It separates from absolute alcohol in the form of small transparent rhombic crystals, which have the sp. gr. 1.0046 (*Ap. Ztg.,* July, 1900, 486).

According to the researches of P. C. Plugge (*A. Pharm.,* 1895), cytisine is a very widely distributed alkaloid. He has found it in eight species of the genus *Cytisus,* two of the genus *Genista,* two of the genus *Sophora,* two of the genus *Baptisia,* and in other plants. He asserts that *ulexine* of Gerrard, from *Ulex europæus* L., *sophorine* of H. C. Wood, from *Sophora secundiflora* (Cav.) DC. (*S. speciosa* Benth.), and *baptitoxine* of von Schroeder, from *Baptisia tinctoria* R. Br., are identical with cytisine. Plugge also believes that the alkaloid of *Euchestra Horsfieldii* Benn. (Fam. *Leguminosæ*), a Javanese pea, whose seeds are used as a contra-poison by the natives, is identical with cytisine. Kobert and Radziwillowicz (*Arb. d. Pharm. Inst. Dorpat.,* 1888, ii) found that cytisine caused in lower animals, spinal convulsions, followed, if the dose were large enough, by paralysis, vomiting of central origin, primary stimulation, and secondary paralysis of respiration and a marked reduction in the ozonizing powers of the red corpuscles. The blood pressure was at first elevated and later depressed and there was a paralysis of the motor nerves similar to that produced by curare. Dale and Laidlaw (*J. P. Ex. T.,* 1912, iii) find that the rise and secondary fall of the blood pressure is due to effects upon the sympathetic ganglia and that cytisine closely resembles nicotine in its physiological action. Gray (*J. P. C.*, 1862) found laburnum to produce in man narcotic effects, and commends it in *vomiting, bronchitis, whooping cough,* and *asthma.*

Of late years several salts of cytisine have made their appearance. The hydrochloride, hydrobromate and nitrate have all been used as diuretics and nervines in one-twentieth to one-tenth grain doses (0.003–0.006 Gm.).

Danais. *Danais fragrans,* Commerc. (Fam. *Rubiaceæ.*)—In this Madagascar plant, the root of which is said to be tonic and antiperiodic, Heckel and Schlagdenhauffen found a glucoside, *danain.* (*A. J. P.*, 1886.)

Daphnandra.—The bark of *Daphnandra micrantha* (Tul.) Benth., an Australian tree (Fam. *Monimiaceæ*), is asserted to be rich in poisonous alkaloid. (*P. J.*, Oct., 1887.) Bancroft states that the active alkaloid is soluble in water, and to some extent is antagonistic to strychnine.

Delpho-curarin.—Under this name an alkaloid obtained from the *Delphinium Scopulorum* A. Gray (Fam. *Ranunculaceæ*) has been placed upon the market as an amorphous white powder. It has the composition $C_{23}H_{33}O_7N$. It has been physiologically studied by Kahn (*A. I. P. T.*, 1909, p. 19) who found that it acts very similarly to curare, paralyzing the peripheral endings of the motor nerves. It has been introduced for use in the physiological laboratory as a substitute for curare, which is becoming somewhat difficult to obtain. According to Kahn, a dose of six milligrammes per kilo of body weight, given intravenously, is sufficient to completely paralyze the motor nerve of the dog. It should not be confounded with delphinine.

Dextroform is a combination of formaldehyde and dextrin, soluble in water and glycerin, but insoluble in alcohol, ether or chloroform; it occurs as a white, almost odorless and tasteless powder; it should be used with caution. It affords, according Bongartz, in from 10 to 20 per cent. solution, a useful injection in *gonorrhea* and for irrigation in half this strength.

Diafor.—This is stated to be *urea acetyl-salicylate* and is intended for use in *neuralgia* and *rheumatism.* The *dose* is 10 to 20 grains (0.6–1.2 Gm.).

Diagnostic Tests.—In addition to the Clinical Tests and Reagents described elsewhere in this volume, the following Diagnostic Tests are of importance.

Complement Fixation Tests.—While tests of this type have been proposed for several diseases, notably tuberculosis, gonorrhea and syphilis, it is only in the last named that the test has proved generally satisfactory. Insofar, also, as the principles obtain alike for all these tests, it will be sufficient here to discuss in brief only the complement fixation reaction for syphilis. This is usually referred to as the *Wassermann Reaction,* and a modified method, known as the *Noguchi Reaction.*

As mentioned elsewhere in this volume (see *Serums*) animals which have been injected with pathogenic bacteria develop certain peculiar properties in their blood. Just so the blood serum of human beings who have been accidentally infected, that is, who have acquired an infectious disease, has similar specific attributes. One of these special attributes is the power of "binding" or "fixing" complement in the presence of a suitable antigen.

Complement is the substance present in all fresh serum, which is necessary to complete certain actions of immune serum, such as the bacteriolytic action of an antibacterial serum. In the same way the serum of an animal which has been treated with red blood cells of an alien species, acting with the complement, acquires the property of destroying these corpuscles—just as if the blood cells had been bacteria—the coloring matter going out into the clear liquid. Now if the serum of a patient suffering with syphilis, for example, were brought in contact with a small amount of complement in the presence of a syphilitic antigen, the three would unite so that the complement would be no longer available for a second reaction, such as the hemolytic one. Thus we test for the presence of the syphilitic antibody by finding whether it will fix complement to itself, and we prove that the complement is fixed only by trying in vain to use it in destroying red blood cells. The antibody in the second part of the test—found in the serum of the animal which has been treated with red blood cells—is called the hemolytic amboceptor, or simply amboceptor. In the complement fixation test for syphilis, the rabbit is commonly used to produce amboceptor. The syphilitic antigen is usually not the microbe causing syphilis, but, strange to say, a heart extract whose only property in common with syphilitic material is in its chemical constitution, that is, it belongs to the class of lipoids.

To perform the test, the suspected blood serum is added to the antigen and a small amount of complement (fresh guinea-pig serum) and kept at 37° C. for an hour. The amboceptor and some red blood cells of the species used in preparing the amboceptor (usually sheep or man) are then mixed in and the five incubated together for a longer time. The tube containing the mixture is then examined and if the blood cells are still intact, forming a red opaque sediment with colorless supernatant fluid, it signifies that the complement was fixed by the first incubation, therefore the patient has syphilitic antibodies in his blood. Other tests must be carried on at the same time to prove that the amboceptor will actually hemolyze the blood cells with the given amount of complement in the presence of a non-syphilitic serum with antigen, and in the presence of the patient's serum alone without antigen. A fourth tube should be arranged to ascertain that the complement will be fixed when a known syphilitic serum is used.

It is obvious that such a reaction requiring at least seven interacting bodies to prove the presence or absence of a characteristic in one of them, is so complicated that only by repeated practice and standardization of methods can reliable data be obtained. Any of the substances concerned may be so subject to change as to have a deleterious effect on the others and destroy the value of the reaction.

It is obvious that the process briefly outlined above is much too complicated for practical demonstration in a work of this character, and in view of the newer modifications which are constantly coming into practice, the reader is referred to the following authorities: Noguchi; *Jour. Am. Med. Assn.*, 1912, lviii, 1163. Kolmer; *Infection, Immunity and Serum Therapy*, Ed. 2, Philadelphia, 1917. Craig; *The Wassermann Test,* Ed. 1, St. Louis, 1918. Boas; *The Wassermann Reaction*, Berlin, 1921.

Epinephrin Test (*Goetsch's Test for Hyperthyroidism*).—This test is conducted as follows: Eight minims of a 1:1000 solution of epinephrin (see *Liquor Epinephrinæ*) are diluted with an equal quantity of sterile water and injected hypodermically into the arm. Immediately there is formed an area of blanching around the point of injection, and about the margin of this usually a red areola gradually shading off into the surrounding tissue. In about half an hour the center of the white area becomes bluish-gray to lavender, and at the end of about one and a half to two hours the red areola takes on the bluish or lavender color, while that in the center disappears. This lavender areola remains for about four hours from the time of injection and is the most characteristic part of the test. Accompanying the local reaction may be increase in pulse rate, with palpitation of the heart and an exaggeration of the tremor and nervous symptoms in general. The test is designed to elicit evidence of hyperthyroidism. (*N. Y. State M. J.*, 18: 259, July, 1918.

Commenting upon this test the *Journal of the Amer. Med. Assn.* (1921, lxxvi, 857) states that the failure of several competent investigators to discover a strict parallelism between the changes in blood pressures and pulse rate and the degree of hyperthyroidism throws into question the diagnostic value of the epinephrin reaction in such conditions.

Tetrachlorphthalein Test for Liver Function.—In 1910 Abel and Rowntree (*J. P. Ex. T.*, i, 231) showed that phenol-tetrachlorphthalein was excreted from the blood entirely by the liver. Based on this fact Rosenthal (*J. A. M. A.*, 1922, lxxix, 2151) has devised a method for using the drug as a test of hepatic function as follows: 5 milligrammes of phenol-tetrachlorphthalein per kilogramme of body weight is injected intravenously, about 8 cc. of blood is withdrawn from a vein after 15 minutes and again in 60 minutes. This blood is allowed to clot and centrifuged and the plasma tested for the dye by adding sodium hydroxide and comparing the depth of color with a standard solution made by dissolving 10 milligrammes of phenol-tetrachlorphthalein in 100 cc. of water. In 8 cases of various indifferent diseases, including severe nephritis, he found at the end of 15 minutes from 2 to 7 per cent. of the dye in the blood and none at the end of one hour. In various diseases of the liver including carcinoma, cirrhosis, abscess of the liver, acute hepatitis, etc., he found that the elimination of the dye from the blood was very greatly prolonged, in several cases there was practically no lessening of the amount in the blood at the end of one hour, and it had not disappeared in 4 or 5 hours. He believes that the method is quantitative and gives an index of the functional capacity of the liver.

Hoxie (*J. A. M. A.*, 1924, lxxxii, 361) quotes Piersol and Bockus (*A. I. M.*, 1923) as having suggested a modification of the Rosenthal phenoltetrachlorphthalein test, the modification being based on the time of appearance of the dye in the bile entering the duodenum after intravenous injection, but Hoxie has found that this time varies so much in the same individual as to be practically useless.

*Agglutination Test for Typhoid Fever. **Widal** Test. Bass Test. Bordet Test.*

The *Widal Test* and its modifications depend upon the presence in the blood of a typhoid patient at a certain stage of the disease of substances termed agglutinins, which when brought in contact with living typhoid bacilli cause the latter to clump together and lose their motility. It is evident, therefore, that the infection must have been present a certain length of time for the Widal test to be positive, that is, until sufficient time has elapsed for the agglutinins of the typhoid germ to have been elaborated in the blood of the patient. Otherwise the test will be negative. We find, therefore, that the test is of no practical value until after the first week or so of the infection. The test is also uncertain because of the fact that the blood of many normal persons, and also persons recently inoculated with the antityphoid vaccine possesses the agglutinating property for typhoid germs. It is less marked, however, than in those infected with typhoid, and, therefore, in making the test the blood-serum is diluted to about 1 to 50, when the agglutinating power (of any but the typhoid blood) is too mild to manifest itself.

Method of Application.—The lobe of the ear having been cleaned with an antiseptic, followed by sterile water, a deep puncture is made with a sterile needle or other pointed instrument. A small amount of blood is collected either in a capillary tube or upon a sterile cover-glass. The blood or, preferably, the serum portion is diluted with normal salt solution or broth to 1 to 25, then a drop of this dilution is mixed with an equal amount of young vigorous typhoid germs from a broth culture, placed in hanging drop beneath the microscope, and observed.

Should the test be positive, in from one-half to two hours the bacilli will be seen to clump together into masses and lose their motility. The test may be made without the use of the microscope by mixing the culture and serum in a testtube, when at the end of the usual time a flocculent precipitate will be observed to form in the mixture.

A carefully heated suspension of killed typhoid bacilli (as supplied by manufacturers of biological reagents) may be used to supplant the suspension of living organisms mentioned in the above test.

Tuberculins.—Tuberculins in the broadest sense are any products of tubercle bacilli used in the treatment, prevention, or diagnosis of tuberculosis. The product to which the name was first applied is now called *Old Tuberculin* (Koch) (*Tuberculin alt, Tuberculin O. T., Concentrated Tuberculin, Crude Tuberculin*), and is prepared by growing tubercle bacilli for weeks on glycerin broth, killing the culture by steaming it for 30 minutes, and evaporating the sterilized broth to one-tenth its volume over a hot bath. The dead bacilli are then filtered out through a bacteriaproof filter and the resulting brown fluid, viscous on account of its high glycerin content and with a characteristic odor, is the tuberculin. *Koch's New Tuberculin T. R.—Tuberkelbacillen Rest, Tuberculin Residue, Tuberculin Ruckstand*—is made by triturating living tubercle bacilli, thoroughly washing in water, and grinding the insoluble residue. By alternate suspension in water, centrifuging and grinding each sediment, a series of very fine suspensions are obtained and combined. Twenty per cent. glycerin solution is added in such amount that 1 cc. of the final product represents the residue of 10 milligrammes of tubercle bacilli; this residue dried weighs about 2 milligrammes.

Tuberculin B. E. (*Bazillenemulsion* (Koch), *Bacilli Emulsion*) was Koch's final effort to find a specific for tuberculosis. This consists of ground tubercle bacilli in a 50 per cent. glycerin suspension. The coarser particles which settle in 24 hours are discarded. The dilution is such that 1 cc. contains 5 milligrammes of bacillary substance.

Tuberculin B. F. (Denys), *Bouillon Filtré, Bouillon Filtrate* is the same product as old tuberculin prepared without heating or concentration. The glycerin broth culture is simply filtered free from bacteria. A similar preparation in Germany is called T. O. A. (*Tuberkulin Original,* O. T.), or if made from bovine tubercle bacilli instead of human, P. T. O. (*Perlsucht Tuberkulin Original*).

Numerous other preparations are to be found, some very closely allied to the four above mentioned, others more variant: *Tuberculol, Tuberculin* A. F. (Albumose free), *Vacuum Tuberculin, Tuberculosis Sero-Vaccine, Tuberculin-Rosenbach, Tuberculin-Beraneck, Tubercle Bacilli Extract* (Dixon), *Suspension of Dead Tubercle Bacilli* (Dixon), *Watery Extract of Tubercle Bacilli* (von Ruck), *Tulose, Oxytuberculin* and others.

For diagnosis, old tuberculin is employed almost exclusively. It has been particularly useful in the diagnosis of tuberculosis in animals, by temperature reaction following subcutaneous injection. This method is also used in human medicine, but in any application of tuberculin, save the most external, extreme care must be used. The multitude of severe reactions and fatalities due to the use of tuberculin in the years immediately following its discovery are not to be forgotten; a dose easily borne by one individual may be highly toxic to another. Careful two-hourly temperature records should be kept for two days preceding and two days following the injection. At first not more than 0.0002 cc. may be given A safer test is the application of the tuberculin to the skin; an abrasion is made through a drop of old tuberculin on the forearm, by means of a small drill twirled between the thumb and forefinger (*von Pirquet test*). A similar abrasion is made without the tuberculin. The appearance of a papule at the former site, but not at the latter, within twenty-four to forty-eight hours, indicates the presence of tuberculosis. By this delicate test it is shown that nearly all adults have, at some time, contracted tuberculosis, even if not showing any clinical manifestations of the disease, so that the test is only applicable to children. A similar test (*Moro test*) is made by the use of a tuberculin ointment. Both of these tests are of greatest value when applied to young children. A large number of apparently healthy adults react positively to these tests, due probably to healed tuberculous processes.

Calmette and *Wolff-Eisner* have devised a conjunctival test—the tuberculin, diluted 10 times or made up to a corresponding strength with glycerin-free dried tuberculin, is dropped in the conjunctival sac. Within 24 hours, if the reaction is positive, the conjunctiva so treated becomes red and often somewhat swollen. On account of reactions which have endangered the eyesight, this test has largely been given up.

In tuberculin treatment, also very great caution should be exercised. It is customary to begin a course of treatment with 0.000,000,1 cc. hypodermically increasing gradually and not giving more than two injections per week.

Accurate records must be maintained of the patient's temperature and general condition, for only thus will the margin of safety in this dangerous product be observed. The success with any of the various tuberculins has not been remarkable, but it is asserted that in certain types of cases, some good may be accomplished. (See under *Serums.*)

Cutaneous and Ophthalmic Allergic Tests.—Some years after the discovery of the phenomenon of anaphylaxis by Richet, American observers experimenting with animals showed that anaphylactic shock induced in animals through injection of foreign proteins simulated the attacks of *hay fever* and *bronchial asthma.* According to their observations, certain persons, apparently normal, become sensitive to pollen from flowers, to animal dandruff and other animal proteins and to foodstuffs. This special sensitization may be inherited, or if acquired, may occur by virtue of defects in the mucous membranes of the nose, bronchioles or intestinal tract.

If a person, sensitive as above stated, breathes air containing pollen or animal protein or eats certain foodstuffs, a typical attack will ensue. Nor are these idiosyncrasies manifested alone in hay fever or asthma, but in many forms of skin diseases as urticaria, eczema, Quincke's edema, etc., and some authors even include migraine and epilepsy in the same group. To all of these diseases the term "Allergic diseases" is applied.

With the purpose of fixing the blame upon a specific protein, diagnostic tests may be made in the case of these *allergic diseases.* Only pollen protein extracts are used in the diagnosis of hay fever, whereas extracts of foodstuffs, and animal proteins, to an almost incredible number are used in the diagnosis of the asthmas and skin diseases. The test is conducted by scarifying, without drawing blood, the skin on the flexor surfaces of the forearm. Into each separate cut (each about an eighth inch long) is placed a small amount of the suspected protein. There is then added a drop of N/10 NaOH solution to dissolve the protein and permit of its rapid absorption. At the end of a half hour the proteins are washed off and the reactions noted, always comparing with a normal control where no protein and only the N/10 NaOH solution is used. A positive reaction consists of a raised white elevation or urticarial wheal surrounding the cut. The smallest reaction, in order to be deemed positive, must measure approximately a fifth of an inch in diameter. Small vials containing material for the application of these tests can be obtained from reliable manufacturers.

Once the diagnosis is made, treatment can be instituted to desensitize the patient by injecting gradually increasing doses of the protein, or proteins, proven by the test to be responsible for the diseased condition. It has been noted, however, that skin reactions may serve to diagnose the allergic state, but not to make a specific diagnosis.

Most recent investigators claim that the instillation of these extremely attenuated proteins upon the conjunctiva serves better as a mode of diagnosis than the cutaneous tests described above.

Dick Test for Scarlet Fever.—While there is still disagreement (1925) as to the causative factor in scarlet fever, Drs. G. and G. Dick, of Chicago, have produced a toxin by the artificial growth of diplococcus scarlatina (a streptococcus) which when injected in specific dilution into persons immune to scarlet fever, shows no reaction, whereas it produces a profound reaction in persons who are not immune to that disease. Thus can be ascertained the susceptibility of an individual to that disease. To date, the test, unlike the Schick reaction, has not been augmented by a curative, toxin antitoxin extract, although at the time of writing a serum has been advanced by Doctor Dochez of the Rockefeller Institute, which it is claimed has specific curative properties. (See under *Serums.*)

Kahn Precipitation Test for Syphilis.—A very valuable specific test and one that is much less complicated than the Wassermann and its modifications is described by Kahn (*Amer. Journ. Pub. Health,* June, 1924). It employs in the test only three ingredients, namely: antigen, serum and physiologic salt solution. The antigen is a cholesterinized beef heart alcoholic extract. Observers have agreed that this new test furnishes a simplified technic and affords results that compare favorably with the complement fixation tests.

Schick Test for Diphtheria.—In 1913, Schick published (*M. M. W.,* 1913, ix, 2608) a method by which the presence of specific antitoxin in the blood and tissue can be determined very easily. A fixed minute quantity of diphtheria toxin is injected intracutaneously and a local reaction occurs if there is less than $^1/_{30}$ of a unit of natural antitoxin per cubic centimeter of blood. This amount is considered sufficient to protect against diphtheria. The explanation of the test is that when no antitoxin is present the toxin acts on the skin; when antitoxin is present it so neutralizes the toxin that no local poisoning occurs. A negative reaction therefore indicates the presence of sufficient protective antitoxin, where a positive reaction occurs inoculation with graded doses of toxin-antitoxin mixtures (see *Antitoxinum Diphthericum*) were demonstrated by Behring to afford protection against diphtheria. This inoculation probably will eventually be as general as vaccination against small-pox.

Dial.—*Diallyl-Barbituric Acid* differs in its structure from barbital in that the two ethyl groups have been replaced by allyl groups introduced into medicine as a somnifacient. It occurs as colorless, shiny, scaly crystals, melting at 170° to 171° C.; readily soluble in alcohol and ether, and difficultly so in water. The aqueous solution gives a slightly acid reaction. It has been recommended as a somnifacient with the statements that it is superior to the allied barbital in that it does not produce unpleasant after-effects, that it requires smaller doses and that it is less toxic. These claims, however, have been brought in question by the Council on Pharmacy and Chemistry (see *J. A. M. A.,* 1920, lxxiv, 266). The dose is from one and a half to four grains (0.1–0.3 Gm.).

Diamine. *Diamidogen.—Hydrazin,* $\left.\begin{matrix}H_2N\\H_2N\end{matrix}\right\}$, is a strong base crystallizing in white crystals at 1.4° C. and boiling at 113° C.; it forms salts with the common acids. The free base mixes with water in all proportions and has a strong alkaline character and powerful reducing action. This substance has been proved by Julius Pohl to be actively poisonous. (*A. E. P. P.,* xli, 1898.)

Dianthus. *Dianthus Caryophyllus* L. *Clove Pink.* (Fam. *Caryophyllaceæ.*)—Of the ordinary garden pink those specimens should be selected for medicinal use which have the deepest red color and the most aromatic odor. The petals should not be collected until the flower is fully blown, and should be employed in the recent state. They have a fragrant odor, said to resemble that of the clove. Their taste is sweetish, slightly bitter, and somewhat astringent. Both water and alcohol extract their sensible properties, and they yield a fragrant essential oil by distillation. The syrup was formerly recognized by the Edinburgh Pharmacopœia as a vehicle.

Diaspirin. *Succinylsalicylic Acid* $(CH_2.COO.C_6H_4.COOH)_2$.—A white, odorless powder, of a somewhat acid taste, readily soluble in alcohol, sparingly soluble in water. *Diaspirin* has been used with asserted benefit in the treatment of various *rheumatic* and *neuralgic* troubles. According to Kaminer (*B. K. W.,* 1909), its value is enhanced by the fact that when given in sufficiently large doses, passing unchanged through the stomach, it not only exercises the effect of the salicylic acid, which is liberated in the intestinal tract, but that it also has a distinct diaphoretic action. Diaspirin is a dibasic acid and reacts with bases, either organic or inorganic, to form corresponding salts.

The *dose* is five to fifteen grains (0.3–1.0 Gm.) from three to six times a day.

Diazyme, Essence and Glycerole. *N. N. R.* 1924.—These are proprietary preparations which are stated to contain the starch-converting enzyme of the pancreas without the protein-converting and fat-splitting enzymes.

Dibromin. *Dibromalonyl-ureide.*—This is cream-colored crystalline solid containing 56 per cent. of bromine. It is soluble in about 33 parts of water but its solutions are not stable; the dry substance is permanent. Dibromin has a powerful germicidal action, probably due to the formation of *hypobromous acid;* it is asserted to be from 50 to 200 times as strong as phenol according to the species of bacteria against which it is tested. It has been used as a surgical disinfectant by Zeinert (*Surgical Journ.,* Nov., 1922) and others in strengths of from 1 in 1000 to 1 in 10,000 and is relatively non-toxic and non-irritant.

Dicentra.—*Dicentra pusilla* Sieb. et Zucc. is a Japanese plant belonging to the *Fumariaceæ* which is used in that country as a folk remedy in dysentery. Asahina (*A. Pharm.,* 1909, ccxlvii) has found it in an alkaloid, $C_{20}H_{21}NO_4$, which is isomeric with papaverine. It has been studied physiologically by K. Iwakawa (*A. E. P. P.,* 1911, lxiv), who finds that it produces in both cold and warm blooded animals a light narcosis, followed, if the dose be large, by convulsions. It also caused a fall in the blood pressure with slowing of the heart and depression of the respiratory center.

Dichlorbenzol. *Para-dichlorbenzene* 1–4, $C_6H_4Cl_2$.—It occurs in colorless crystals and is used as an insecticide. It is said that the vapors are penetrating and kill insects, larvæ and eggs. It is used to combat peach borers by fruit growers.

Dichondra Brevifolia.—An extract of this plant dissolved in glycerin is used as an application in the treatment of *diphtheritic ulcers.* It is applied direct to the mucous membrane and is claimed to possess specific action on the diphtheritic bacilli.

Dichlorethylene.—This is a non-combustible liquid with a specific gravity of 1.29 and a boiling point of 55° C. It has been suggested by Wittgenstein (*A. E. P. P.,* 1918, lxxxiii, 235) as a general anesthetic. He asserts that it exercises no injurious effect upon the circulation. While it has not been used to any large extent in human beings, there have been noticed during the narcosis undesirable muscle contractions; it is asserted, however, that these can be controlled by the use of morphine.

Didymium is now recognized generally as a mixture of *neodymium* and *praseodymium*, freed as far as possible from lanthanum, the salts of the neodymium being in general rose-colored, while those of the praseodymium are of a greenish-yellow. The by-products obtained in the manufacture of gas mantles and certain other chemical manufactures have been utilized in making the salts.

Didymium Chloride. Didymii Chloridum. $Di_2Cl_6 + 12H_2O$.—This salt has been used in the form of a rose-red, odorless and non-irritant solution containing 25 per cent. to 30 per cent. of the salts. It has been affirmed that the chloride is superior to phenol as a germicide, but the experiments of I. Schmidt and of Pflücker (*M. R.*, 1898, 1900) show that it is much inferior, a 5 per cent. solution being required to destroy ordinary germs.

Didymium Nitrate, Didymii Nitras, $Di_2(NO_3)_6.12H_2O$, occurs in rose-colored crystals soluble in water and alcohol. Antiseptic in solution of the strength of 1 in 2000. (*Cb. B.*, xxi.)

Didymium Salicylate. Dymal.—A very fine pinkish powder free from odor. It has been specially recommended by Kopp, Roth, and others as an innocuous, non-irritant, desiccant, and antiseptic dusting powder in various skin diseases, especially in weeping *eczema*, and also *hyperidrosis*, and *burns* of the first and second degree. In *erysipelas* and drier forms of skin disease it failed to be of service. It is especially popular with the veterinarians because of its relatively low cost.

Didymium Sulphate. Didymii Sulphas. $Di_2(SO_4)_3 + 6H_2O$.—This salt has been marketed in the form of a pale rose-red powder to be used for disinfecting closets, etc.

Diervilla. *Diervilla Lonicera* Mill. (*D. trifida* Moench.) *Bush Honeysuckle.*—A low, erect, indigenous shrub belonging to the *Caprifoliaceæ* and found growing in dry woods and rocky places throughout the Eastern Northern States and Canada. The whole plant is supposed to be possessed of diuretic and astringent properties, and is given in infusion by the eclectics in diseases of the urinary passages. L. E. Dawson (*Chem. News*, 1912) examined the fruit of *D. Florida.* The dark-red berries contain fructose, fixed oil, tartaric and citric acids and an alkaloid which he believes to be *narceine.* Charvaux found a glucoside identical with *fraxin* in *D. lutea.* (*J. P. C.*, 1911, 248.)

Diethylketone.—*Propione,* $C_2H_5.CO.C_2H_5$, is obtained by the dry distillation of *calcium propionate* $(C_3H_5O_2)_2Ca$. A transparent liquid, soluble in twenty-four parts of water, mixing with water, alcohol, and ether, boiling at 101° C.; recommended by Albanese and Barabini in 1892, as inducing sleep in animals. It has been used by Giovanni in the treatment of *maniacal* and *hysterical excitement* in *doses* of from eight to twenty grains (0.5–1.3 Gm.). It should be administered in dilute solution.

Digalen.—Under the name of *digalen* there has been introduced into medicine a solution which is asserted to contain *soluble digitoxin.* There is no doubt that this preparation contains a principle which exercises a digitalis effect upon the heart, but that this principle is identical with digitoxin is improbable. The claim for the application of the term digitoxin is based upon the fact that it has the same empirical formula as this glucoside, but since it would appear that its molecular weight is only half of that of crystalline digitoxin it is more probable that it is a polymer of this body. According to Kiliani (*A. J. P.*, 1913, lxxxv, 224), it is identical with digitalein.

Digalen has been used to a large extent in the treatment of chronic cardiac conditions for precisely those cases in which digitalis is useful. It has been used by the mouth and by intramuscular and intravenous injections. Although it appears to be less irritant to the body tissues when injected intramuscularly than are most of the other digitalis preparations, this method of administration is not entirely painless. The *dose* of the remedy is from fifteen to twenty minims (0.9–1.3 Gm.).

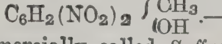
Diiodacetylene, C_2I_2, is made simultaneously with *tetraiodoethylene,* C_2I_4, (*Diiodoform, Ethylene Periodide*), by the action of a solution of iodine in potassium iodide upon calcium carbide. The two are separated by reason of their different solubilities. Tetraiodoethylene is in the form of bright yellow, odorless, needle-like crystals, insoluble in water, only slightly soluble in alcohol but readily soluble in chloroform. It contains 95.3 per cent. of iodine and is recommended in the place of iodoform. It is decomposed by exposure to light. Diiodacetylene has been found by E. Mebert (*A. E. P. P.*, xli, 1898) to be very actively poisonous.

Dimazon. *Diacetylaminoazotoluene.* $CH_3.C_6H_4.N:N.C_6H_3(CH_3)N(CH_3CO)_2$. *N. N. R.* 1924.—This is recommended for the purpose of stimulating epitheliazation over old *ulcers, wounds,* etc. It is asserted to have the advantage over similar preparations that it does not stain. It is used as a 2 per cent. ointment either made with petrolatum or a fatty oil or as a 5 per cent. dusting powder.

Dimethylaminoazobenzene. *Butter Yellow,* $C_6H_5N:N.C_6H_4N(CH_3)_2$.—"It forms yellow plates melting between 115° and 117° C. (239° and 242.6° F.). It is insoluble in water, soluble in alcohol; soluble in hydrochloric acid with a red color from which solution sodium hydroxide T.S. in excess precipitates the orange-yellow base. The solution of this dye in sulphuric acid is yellow and changes to red on dilution with water." *U. S. IX.*

It is used as a test in examining the gastric secretions (see *Diagnostic Reagents*).

Dimethyl Sulphate, $(CH_3)_2SO_4$, is a liquid boiling at 188° C., soluble in alcohol and ether. This substance has come into importance with toxicologists on account of the number of fatal cases of poisoning occurring from it, due to its extended use in chemical factories. It acts locally as a strong caustic and also influences the central nervous system, producing nystagmus, convulsions, and respiratory death during coma. (See S. Weber, *A. E. P. P.*, Bd. xlvii.)



Dinitrocresol. $C_6H_2(NO_2)_2\left\{\begin{matrix}CH_3\\OH\end{matrix}\right.$.—This is a coal tar dye, commercially called *Saffron Substitute* and is a mixture of the potassium salts of dinitro-ortho- and para-cresols. It is said to have been sold for saffron in Berlin, with fatal results. (*Ph. Rund.*, Prague, 1887.)

Dioform. *Acetylene Dichloride.* $CHCl = CHCl$.

—This occurs as a colorless fluid with an odor somewhat like that of chloroform. Sp. gr. 1.29, melting point, 55° C. Villinger (*A. K. C.*, 1907) found that it produced a narcosis with abolition of reflexes without changes in the circulation or in the kidneys. He also employed it as an anesthetic for human beings in doses of from two hundred and fifty to three hundred and fifty grains (15–24 Gm.) and found that it produced a condition suitable for surgical operation in three to five minutes with very slight stage of excitation. It has not been used, however, sufficiently to justify any conclusions as to its practical therapeutic value.

Diogenal. *Dibrompropyl-diethylbarbituric Acid.* $C_{11}H_{16}O_3N_2Br_2$.—This is a white, crystalline powder, almost insoluble in water, but soluble in alkaline solution and alcohol. It is used as a somnifacient and general nerve sedative. According to Heinz (*M. M. W.*, 1913, p. 2618), it is only about one-fourth as toxic as barbital. The *dose* is ten to thirty grains (0.65–2 Gm.).

Dioscorea.—According to Kobert the *Dioscorea Tokoro* contains an extremely toxic saponin, *dioscin.* This is so powerful that one part in 400,000 is sufficient to cause hemolysis. Honda (*A. E. P. P.*, 1904, li, 213) has found in it other saponins. For account of other species of *Dioscorea* see Part 1.

Diospyros. *Persimmon. Date-plum. Possumwood. Fruits de Plaqueminier de Virginie,* Fr. *Persimmonfrüchte, Dattelpflaumen,* G.—*Diospyros virginiana* L., or persimmon (Fam. *Ebenaceæ*), is a small indigenous tree, occurring in woods and old fields from Connecticut to Florida and west to Iowa and Texas. It possesses alternate, simple, oval, entire margined, dark-green leaves and rough bark which is often broken up into quadrangular blocks and cinnamon-red at the base of the fissures. Its greenish-yellow flowers appear about May or June. Its fruit is a spherical, orange-colored, often red-cheeked, 4–8 seeded berry which is surrounded at the base by a thick, 4-parted calyx.

The bark of the persimmon was official in the Secondary List of the first, second and third editions of the *U. S. P.*, while the unripe fruit appeared in the Secondary List of the fourth, fifth and sixth editions. The bark is astringent and very bitter.

While green, the fruit is excessively astringent, but, when perfectly mature, and after being touched by the frost, it is sweet and palatable. The unripe fruit, according to B. R. Smith, contains tannic acid, pectin, sugar, malic acid, coloring matter, and lignin, (*A. J. P.*, xviii, 167.) The persimmon has been used by Mettauer in *diarrhea, chronic dysentery,* and *uterine hemorrhage.* The *dose* of the vinous tincture (an ounce of the fresh green fruit to two fluidounces of dilute alcohol) is half a fluidounce (15 cc.) or more. For further information concerning this drug, see *U. S. D.*, 19th ed., p. 1474.

Diplosal. *Salysal. Salicylo-salicylic acid. Salicyl Salicylate. Salicylic Ester of Salicylic Acid.* $OH.C_6H_4.COO.C_6H_4.COOH$.—On decomposition in the human organism, two molecules of salicylic acid are formed, water being taken up, so that 107 parts of salicylic acid are formed from 100 parts of the ester. It is a white, crystalline powder, insoluble in water.

Diplosal owes its therapeutic virtues to its decomposition in the intestines and the liberation of salicylic acid. Its range of usefulness is precisely similar to that of the other salicylates over which, however, it has the advantage that because of its insolubility in dilute acids it is much less prone to disturb the stomach. It appears, however, to be decomposed in the intestines with comparative slowness, so that its action is less prompt than that of other salicylates and correspondingly more persistent. It has been used by Strauch (*Th. M.*, 1909), Minkowski (*Ther. Geg.*, 1908) and others with success in the treatment of both *acute* and *chronic rheumatism.*

The *dose* is eight to ten grains (0.5–0.7 Gm.) repeated, if necessary, up to a daily maximum of ninety grains (6 Gm.).

Dipropæsin.—A condensation product of 2 molecules of propæsin, $CO.(NH.C_6H_4.COOC_3H_7)_2$. It is a white powder, insoluble in water, soluble in alcohol; melting point, 171°–172° C. It is used as a local anesthetic. Kluger (*Th. M.*, 1909) suggested its employment as a local anesthetic in intestinal conditions, on the theory that its action is only made manifest in the presence of alkaline media and would, therefore, be limited when given by the mouth, to the intestinal tract. The clinical reports, however, are too scanty to justify any conclusion as to its value. The *dose* recommended is eight grains (0.5 Gm.).

Dirca. *Dirca palustris* L. *Leatherwood. Moosewood. Wicopy.* (Fam. *Thymelæaceæ.*)—A shrub growing widely in the Northeastern United States and Canada. The bark is very tough and was formerly used by the Indians for thongs. The wood is soft, white and brittle. The drupes, which are small, ovoid, and of an orange or reddish color, are said to be narcotic and poisonous. The tough bark, in the fresh state, has a peculiar, rather nauseous odor, and an unpleasant acrid taste, and when chewed excites a flow of saliva. It yields its acridity completely to alcohol, but imperfectly to water even by decoction. Six or eight grains of the fresh bark produce violent vomiting, preceded by a sense of heat in the stomach, and often followed by purging. Applied to the skin it slowly excites redness and ultimately vesicates. Lecours reports that this shrub, growing abundantly in Canada, possesses strongly purgative properties. When extracted with 90 per cent. alcohol, an extract on evaporation is obtained which produces a laxative action in doses of 0.3 Gm. The extract contains a small amount of a volatile oil, some fixed oil and a resinous substance, the latter occurring in the form of a soft oleoresin producing a strong laxative effect when administered in doses of 0.05 Gm. (*Chem. and Drug.*, 99, 443.) It is analogous to mezereon in its medicinal characters.

Dolomol.—A white insoluble powder, nearly inodorous and tasteless, consisting mainly of *magnesium stearate* with small amounts of magnesium oleate and palmitate. It is used as a dusting powder in affections of the skin, either alone or in combination with various other remedies.

Doundaké. *Dundaki. Quinquina Africaine. Kina du Rio Nunez.*—*Sarcocephalus esculentus* Afzel (Fam. *Rubiaceæ*) of Africa yields a bark which is said to be an astringent and tonic febrifuge. For a description of the bark and its chemical characteristics, see *P. J.*, vol. xvi, 49. Heckel and Schlagdenhauffen attribute its power to three resinous principles, the first of which is of an orange-yellow color and very bitter, soluble in water, alcohol, and potassium hydroxide; the second light yellow in color, soluble in potassium hydroxide but not in water; the third soluble in potassium hydroxide, insoluble in water or alcohol. (*J. Soc. Chem. Ind.*, 1886, 435.)

The wood of the *Sarcocephalus Diderrichii*, which is used for making shuttles, has been found by Gibson to contain an alkaloid, which is a cumulative cardiac poison. Workers in the wood frequently suffer and even die from cardiac disturbances. (*Bio-Chem. J.*, 1906, i, p. 39).

Dracontium. *Symplocarpus Fœtidus* (L.) Nutt. (*Spathyema fœtida* (L.) Raf. *Dracontium fœtidum* L. *Ictodes fœtidus* Bigelow.) *Skunk Cabbage. Skunk Weed. Polecat Weed. Racine de Pothos fétide*, Fr. *Stinkende Drachenwurzel*, G.—A perennial herb belonging to the *Araceæ* and indigenous to wet places from Nova Scotia to South Carolina west to Minnesota and Iowa. Its spadix, enveloped by a broad spathe beautifully mottled with purple and yellowish-green spots and stripes appears as early as late January in the middle states. The large ovate-cordate leaves appear later. All parts of it have a fetid odor, dependent upon an extremely volatile principle, which is rapidly dissipated by heat. The rhizome should be collected in the autumn, or in the early spring.

The rhizome and roots of Skunk Cabbage have occasionally been found in lots of Veratrum Viride due to the carelessness of collectors. Both of these plants frequently grow together in the same locality.

The rhizome occurs either whole or in transverse slices. When entire, it is cylindrical or in the shape of a truncated cone, 5 to 10 cm. long and 2 to 4 cm. thick, externally dark brown and very rough from the insertion of the radicles, internally white and amylaceous. The rootlets are of various lengths, 2 to 4 mm. thick, coarse, simple, and very strong, very much flattened and wrinkled, white within, and covered by a yellowish or reddish-brown epidermis, considerably lighter colored than the body of the rhizome. The odor is fetid, the taste acrid; both are lessened by drying and progressively diminish with time, so that the dried rhizome should not be kept longer than a single season. This acridity is entirely absent in the decoction. The seeds are very acrid, and, though inodorous when whole, give out, when bruised, the peculiar odor of the plant.

The rhizome is affirmed to be antispasmodic and narcotic; occasioning nausea and vomiting, with headache, vertigo, and dimness of vision. It has been used with alleged success in *asthma, chorea, hysteria*, and *whooping cough. Dose*, of powder, from ten to twenty grains (0.65–1.3 Gm.), increased *pro re nata.*

Dragon's Blood. *Sanguis Draconis. Sang-dragon*, Fr. *Drachenblut*, G. *Sangre de drago*, Sp.—The term dragon's blood has been applied in a number of resinous substances which appear to have nothing in common except a red color. According to Sollmann (*J. A. Ph. A.*, 1920, ix, 141) the term was applied up until the sixteenth century to the exudates from *Dracæna sinnabari* (*African dragon's blood*) and to *D. draco* (*Canary dragon's blood*). Neither of these at present appear in commerce to any extent. The West Indian dragon's blood is derived from the *Pterocarpus draco.* At present the term is usually applied to an exudate from the surface of the fruits of a number of palms and may be designated as "East Indian dragon's blood." Of these there are several commercial varieties, obtained from a number of species of *Dæmonorops*, a genus which was previously ascribed to *Calamus.* Malay dragon's blood is obtained from *Dæmonorops didynophyllos, D. micranthus* and *D. propinquus;* Sumatra dragon's blood from *Dæmonorops Draco* Blume (*Calamus Draco* Willd.). In Borneo a dragon's blood is obtained from *Dæmonorops draconcellus* and other species of *Dæmonorops.* On the surface of the fruit, when ripe, is an exudation, which is separated by rubbing, or shaking in a bag, or by exposure to the vapor of boiling water, or finally by decoction. The finest resin is procured by the two former methods. It comes in two forms: sometimes in small oval masses (*tear dragon's blood*) of a size varying from that of a hazelnut to that of a walnut, covered with the leaves of the plant, and connected in a row like beads in a necklace; sometimes in cylindrical sticks, eighteen inches long and from a quarter to half an inch in diameter, thickly covered with palm leaves, and bound round with slender strips of cane. See paper by E. M. Holmes in *P. J.*, 1905, 933.

Dragon's blood is inodorous and tasteless, insoluble in water, but soluble in alcohol, ether, and the volatile and fixed oils, with which it forms red solutions. According to Herberger, it consists of 90.7 parts of a red resin, which he calls *draconin*, 2.0 of fixed oil, 3.0 of benzoic acid, 1.6 of calcium oxalate, and 3.7 of calcium phosphate. Tschirch (*Harze und Harzbehälter*, 1900, p. 189) has made an elaborate study of dragon's blood, and finds 2.5 per cent. of *draco-alban*, $C_{20}H_4O_4$, a white substance melting with decomposition at about 200° C.; 13.58 per cent. of *draco resen*, a yellow resinous substance of the formula $C_{26}H_{44}O_2$, and 56.86 per cent. of *draco resin*, a resin ester or mixture of esters, *benzoic dracoresinotannol ester* and *benzoylaceticdracoresinotannol ester*, and 18.4 per cent. of insoluble substances. It was formerly employed in medicine as an astringent, but is nearly or quite inert, and is now never given internally. It is sometimes used to impart color to various pharmaceutical preparations. For further information concerning this drug, see *U. S. D.*, 19th ed., p. 1475.

Duboisia.—*D. myoporoides* R. Br. (Fam. *Solanaceæ*) is a tall, glabrous shrub or small tree, which is a native of Australia, New South Wales, New Caledonia, and Queensland. The alkaloid *duboisine* was discovered in the leaves by A. W. Gerrard. (*P. J.*, viii, 787). For his method, see 16th ed., *U. S. D.;* also, for an account of the chemical and medicinal properties of this alkaloid, and its relations to atropine, see *Belladonna.*

According to the researches of Jos. Lanterer (*L. L.*, 1896), the old leaves and twigs of *Duboisia myoporoides*, contain hyoscyamine, the fresh young leaves scopolamine, the dried leaves being stronger than are belladonna leaves, and yielding 0.97 per cent. of alkaloid. *Duboisia Leichhardtii* F. v. Muell. is said to be still richer in alkaloid, which is chiefly amorphous scopolamine; while the leaves of *Datura arborea* L. (*Brugmansia arborea* Steud.) and of *D. cornigera* Hooker (*Brugmansia Knightii* Hort.), natives of South America, acclimatized in Queensland, contain a mixture of hyoscyamine and atropine.

Duboisia Hopwoodii F. v. Muell., *pitury plant*, is the source of *pituri*, a narcotic stimulant largely used by the natives of Central Australia. The drug itself is a fine powder, composed of the leaves and twigs which are gathered during the month of August, while the flower is in bloom, and are put up in various forms of circular mats about 7.5 cm. in diameter. The natives smoke and chew pituri, and it is alleged to have a powerfully stimulating effect, assuaging hunger, and enabling those who are its devotees to perform much labor and go long journeys with but little food. Pituri contains from one to two per cent. of a liquid, acrid alkaloid, *piturine*, $C_{12}H_{16}N_2$, the identity of which with nicotine, although denied by Liversidge (*Proc. Roy. Soc. N. S. W.*, 1880), has been reaffirmed by Rothera (*A. J. P.*, 1918, xc, 34).

Eckaine. — N - Benzoylhydroxypropylnorecgonidine ester. This cocaine substitute is a crystalline base, giving a water-soluble hydrochloride which in neutral solution can be sterilized at 100° C. without decomposition. According to W. Wichura it is only slightly toxic, acts on the respiratory center similarly to cocaine but to a lesser degree, and is a powerful local anesthetic. It causes at first a lowering, often followed by an increase, of the blood pressure. The anesthetic action of other noregonidine derivatives such as *hydroeckaine*, or the corresponding hydroxyethyl and hydroxyamyl compounds, is much weaker than that of eckaine. (*J. Soc. Chem. Ind.*, 1919, xxxviii, 598.)

Elastica. *U. S. VIII* (*Br.*, 1889). *Rubber. Caoutchouc*, Br. *India-Rubber. Resina Elastica, Gummi Elasticum. Caoutchouc*, Fr. Cod. *Kautschuk. Federharz*, G. *Caucho, Cahuchu, Goma elastica*, Sp.—" The prepared milk-juice of several species of *Hevea* Aublet. (Fam. *Euphorbiaceæ*), known in commerce as Para Rubber." *U. S. VIII.* " The prepared milk-juice of Hevea brasiliensis, *Muell. Arg.*, and probably other species; known in commerce as pure Para rubber." *Br.*, 1898.

Rubber was made official in the U. S. P., 1890, because of its use in making mustard paper, and in the Eighth Revision it was used in the formula for belladonna plaster.

Rubber is a mixture of several substances occurring in the coagulated latex or milk-juice of certain tropical plants. It is chiefly composed of caoutchouc, a soft, solid, elastic hydrocarbon. The milk-juice occurs rather in laticiferous vessels which form an anastomosing network, or in latex cells which occur as isolated tubes. Both of these latex-storing devices occur in the middle and inner bark of many stems and roots as well as in the soft parenchymatous regions of numerous leaves, flowers and fruits. Latex is believed by the vast majority of naturalists to be a waste product. It is undoubtedly present as a means of defending plants which possess it against attacks of browsing animals. The yield of pure rubber from the latex varies from 20 to 60 per cent.

The world's supply of rubber to-day is obtained from wild and cultivated plants (India-rubber) as well as prepared synthetically (synthetic rubber). The latex employed in the preparation of India-rubber is collected from plants most of which are trees, shrubs and vines growing chiefly in South America, Mexico, Central America, West Indies, India, Ceylon, the Federated Malay States, East Indies and Africa. Nearly 100 species are known to contain latex from which rubber can be prepared. These are distributed for the greater part in four families, viz.: *Euphorbiaceæ, Apocynaceæ, Moraceæ* and *Asclepiadaceæ.*

The rubber-producing *Euphorbiaceæ* are chiefly members of the genera *Hevea* and *Manihot*, trees, indigenous to Northern South America. *Hevea brasiliensis* and other species of *Hevea* furnish the Pará rubber while *Manihot glaziovii* and allied species furnish the Ceará or Manicoba rubber.

The rubber-producing *Apocynaceæ* are chiefly members of the genera *Landolphia* of West Africa and Madagascar, *Willoughbeia* of India and Australia, *Vahea* of South America, Madagascar and Africa, *Hancornia* of Brazil, *Urceola* of the Malay States and East Indies, *Forsteronia* of Guiana and Jamaica and *Funtumia* of West and Central Africa. The Landolphia species are huge woody vines which yield most of the African rubber. *Willoughbeia firma* yields Borneo rubber. *Hancornia speciosa* is the source of Mangabeira rubber while Penang rubber is the product of species of *Urceola. Funtumia elastica* is the chief source of West African rubber.

The rubber-producing *Moraceæ* are scattered through tropical countries and are chiefly represented by the genera *Castilloa* and *Ficus. Castilloa elastica* and allied species of *Castilloa*, large trees inhabiting Northern South America, Central America, Mexico and the West Indies yield Central American rubber. *Castilloa ulei*, a tree of Peru, yields Cancho rubber. The *Ficus elastica*, native to Southern Asia and the East Indies, is now the chief source of East India rubber. This rubber is collected in Java, Rangoon and Penang.

The cultivation of rubber-producing trees and vines dates back to 1860 when the British government introduced seedlings of *Hevea* into Assam. Successful plantations were established of *Manihot glaziovii* in Ceylon and of *Ficus elastica* and *Castilloa elastica* in the Federated Malay States by British interests. Thousands of acres of *Castilloa elastica* were planted by American interests in Mexico and Central America. All of these species under cultivation yielded an abundance of rubber but could only be tapped at intervals of several months. After some experiments *Hevea brasiliensis* showed that it could be tapped daily and that the year's product from this species surpassed that of all of the other species grown, the cultivation of most of the other rubber plants was abandoned and this species introduced wherever possible to grow it. It is now being successfully grown on plantations in Ceylon, Straits Settlements, Malay States, Burma, the East Indies, Africa and Australia. It is the chief botanical source, to-day, of both plantation and wild rubber.

Of the numerous commercial varieties of crude rubber, that known as " Fine Para " represents the standard of the manufacturer of rubber articles. There are several grades of this variety, the most esteemed being known as " Suarez, Beni Bolivian," a product of trees of *Hevea brasiliensis* which thrive along the upper Amazon river.

Pará rubber is collected from wild plants of the genus *Hevea* growing chiefly in Brazil. It is gathered from June to February by the natives who make small vertical incisions with a machete in each tree to be tapped about six feet from the ground. Below each cut a tin-cup is hung on the tree to catch the milky juice as it flows from the wound. The collector pours the contents of each cup into a large vessel which is carried to his hut. Here a fire is built which furnishes a dense smoke. He takes a wooden paddle, holds it over the smoke, then dips it into the latex, again holding it over the smoke and revolving it slowly, repeating the dipping and rolling maneuver until a " bolacho," or " ham " weighing 50 to 60 pounds is formed. Each bolacho consists of several layers blackened on the surface by oxidation. These are sent down the Amazon by boat to Pará and Rio de Janeiro and boxed for shipment to various parts of the world.

The method of collecting cultivated rubber and preparing it for the market is more scientific than that employed by the natives of South America. In tapping the trees either the herring-bone or the spiral systems are usually employed. In the herring-bone system, vertical channels are cut in the bark with lateral connecting channels about one foot apart at an angle of 45°, the milk-juice being collected in cups at the base of the vertical channels. In the spiral system, a series of spiral grooves are cut around the trunk. The latex is transferred from the cups to rectangular tanks or casks and coagulated by acetic acid. It is then washed, and generally cut up into small pieces which are passed through grooved rollers of a machine coming out as ribbons or "crepe" which are dried. Occasionally the latex is coagulated in shallow dishes and the rubber is then obtained in a block or cake of similar shape to the dish. This is known as "biscuit rubber." The plantation or cultivated rubber is much lighter in color than that coming from South America on account of not being subjected to the natural process of oxidation. The "crepe" variety occurs in sheets of a beautiful amber color. The discovery of a method of preserving the uncoagulated latex has led to its utilization, and shipments of preserved latex are constantly increasing.

The total world's production of wild and plantation rubber in 1922 was 379,920 long tons. Of this amount 354,980 tons represented plantation rubber from Southeastern Asia and neighboring islands.

Synthetic Rubber.—For many years attempts have been made to make rubber substitutes by the vulcanization of fatty oils with either sulphur or sulphur chloride. Linseed oil, cotton seed oil, and the fish oils have all been used for this purpose with varying success. Very successful results have been obtained by the vulcanization of maize oil. These products, known in Germany as *Factis*, may be white or dark colored, the latter color being obtained by the prolonged action of the sulphur. Oxidized or blown oils and sulphonated oils are also used for the vulcanization. In 1894 Nobel patented solutions of nitrocellulose in heavy oil solvents as rubber substitutes for rubber varnishes and coatings. Much reclaimed rubber from old rubber articles is revulcanized and incorporated with pure rubber in the manufacture of new rubber articles. Synthetic caoutchouc, comparable in all respects, both chemically and physically with the natural product, has lately been produced by the polymerization of the hydrocarbon butadiene, C_4H_6, isoprene, C_5H_8, and dipropylene, C_6H_{10}. As isoprene is prepared from amyl alcohol or fusel oil its success commercially depends largely upon the cost of the amyl alcohol.

Properties.—Pará rubber occurs in rounded, cylindrical or flattened masses externally brownish-black and internally of numerous layers of yellowish color separated by dark lines. It possesses a characteristic odor. It contains 40 to 60 per cent. of caoutchouc. Plantation or Ceylon rubber occurs in large thin sheets of an amber or rarely brownish-black color or in yellowish-brown or dark-brown blocks. Rubber was officially described as "in flask-shaped or roundish masses, or in pieces of the same having sharply incised surfaces and exhibiting a laminated structure; floating on water; externally brownish to brownish-black; internally of a lighter tint, mottled; odor creosote-like; nearly tasteless. Pure Para rubber is insoluble in water, dilute acids, or dilute solutions of the alkalies; soluble in chlorofrom, carbon disulphide, oil of turpentine, petroleum benzin, and benzene; when heated to about 125° C. it melts, remaining soft and adhesive after cooling." *U. S. VIII.* "In elastic masses of varying thickness, brownish-black externally and mottled with a pale tint internally; insoluble in water, ethyl alcohol, alkaline solutions, or dilute acids, soluble in chloroform, oil of turpentine, carbon bisulphide. benzol, and petroleum spirit. When heated to about 257° F. it melts, remaining soft and adhesive after cooling. Odor characteristic, somewhat empyreumatic; nearly tasteless." *Br.*, 1898.

Chemical Constitution.—The juice of the rubber trees, when it concretes by exposure to the air, assumes on the outer surface a yellowish-brown color, while the mass remains white or yellowish-white within. It is said that a little alum facilitates the coagulation, while ammonia retards it, so that a little of the latter may be advantageously added, when it is desired to keep the milky juice in the liquid state. The recent juice contains, according to Faraday, 1.9 per cent. of vegetable albumen, traces of wax, 7.13 per cent. of a bitter nitrogenous substance soluble in water and alcohol, 2.9 of a substance soluble in water but insoluble in alcohol, 56.37 soluble in water with a little free acid, and only 31.7 of the pure elastic principle to which chemists have given the name of caoutchouc. Besides these principles, the concrete juice, as it reaches us, generally contains soot, derived from the smoke used in drying it. *Pure caoutchouc*, or rubber, is nearly colorless, and in thin layers transparent. It is highly elastic, lighter than water, without taste and odor, fusible at about 120° C., remaining unctuous and adhesive upon cooling, inflammable at a higher temperature, insoluble in water, alcohol, the weak acids, and alkaline solutions, soluble in ether when entirely freed from alcohol, soluble also in chloroform and most of the fixed and volatile oils, though, in the latter, at the expense of its elasticity. It is said, however, that the oils of lavender and sassafras, dissolve it without change, and that when precipitated by alcohol from its solution in oil of cajuput it is still elastic. But its best solvents, for practical purposes, are petroleum benzin, the empyreumatic oil obtained by distilling caoutchouc itself, carbon disulphide, and pure oil of turpentine. According to Bolley, the best method of effecting its solution, for the preparation of a varnish, is first to digest it, cut in small pieces, in carbon disulphide, which converts it into a jelly, and then to treat this jelly with petroleum benzin. A larger proportion is thus taken up than by any other method. Rubber is not immediately affected by atmospheric air, chlorine, hydrochloric or sulphurous acid gas, or ammonia. Rubber articles usually undergo deterioration upon keeping from oxidation. This may be retarded by storing them in the dark protected from extremes of temperature. Pressure and contact should also be avoided. It is stated that a small amount of naphthalene placed in a confined space with rubber articles will act as a preservative of their elasticity.

Rubber chemically is composed of a mixture of polyterpenes. When destructively distilled, it yields *isoprene*, C_5H_8, and *dipentene*, $C_{10}H_{16}$. When isoprene is treated with concentrated hydrochloric acid, it is polymerized, and a substance obtained which resembles caoutchouc and is probably identical with it. When rubber is vulcanized, it may contain from 2 to 20 per cent, of sulphur, of which, however, not more than the lower amount is chemically combined, the rest being held mechanically, and capable of removal by treatment with caustic alkalies. By the action of sulphur, rubber acquires properties which greatly increase its value in the arts. It either becomes pliable, soft, and tough, or if the amount of sulphur be increased, of a horny consistence, but preserves its elasticity under the influence of moderate heat or cold, is compressible with great difficulty, and resists the ordinary solvents such as petroleum and oil of turpentine. In this state it is said to be vulcanized. The discovery of the process of *vulcanization* is ascribed to Charles Goodyear, of New York. (*Chem. Gaz.*, x, 193.) It consists in submitting rubber in thin sheets to the action of a mixture composed of 40 parts of carbon disulphide and 1 of sulphur chloride. For fuller details the reader is referred to the *J. P. C.* (3e sér., xvii, 205.) The same object may be effected by other methods. When thin layers of rubber are immersed for two or three hours in melted sulphur at the heat of 116° C., they are penetrated by the sulphur, but undergo no change of properties. If now heated in an inert medium to a temperature of from 135° C. to 160° C., a chemical reaction takes place, and the vulcanized product is obtained. The same result takes place if the rubber be first pounded with from 12 to 20 per cent. of finely powdered sulphur, and then heated to the temperature requisite for vulcanization. In either case a portion of uncombined sulphur remains mechanically mixed with the vulcanized rubber, from which it may be separated by various solvents, such as solutions of potassium or sodium hydroxide, carbon disulphide, oil of turpentine, anhydrous ether, etc. The *desulphurated* product thus obtained, while exempt from the disadvantages arising from the reaction of free sulphur, is more porous than before. For details of these two processes—viz., vulcanization by heat with sulphur or metallic sulphides, and cold vulcanization with solutions of sulphur chloride—see Sadtler's *Industrial Organic Chemistry.*

Rubber is so insoluble that it cannot be absorbed in any form into the blood and it is therefore physiologically inert when taken internally. It is used enormously in the arts for an infinite variety of purposes. In medicine it is used as the basis of various adhesive plasters as well as for numerous mechanical purposes.

Egols.—This name has been applied by E. Gautrelet (*C. R. A. S.*, 1899, 11) to a series of substances introduced by him. They are *o-nitroparasulphonates* of phenol, cresol, and thymol, in chemical combination with mercury and potassium. The *egols* are permanent compounds which crystallize with difficulty in rhombohedra, but which occur in commerce as reddish-brown powders, freely soluble in water, forming odorless and tasteless solutions, neutral in reaction, and free from caustic or irritant character. In solutions of 0.4 per cent. they are said to be actively inhibitory to the growth of germs, and in stronger solutions powerfully bactericidal. It is claimed for them also that they are not poisonous to man, although when given in overdoses they sometimes act as an emetic.

Eikonogen.—The sodium salt of amidobetanaphthol-betamonosulphonic acid, $NH_2C_{10}H_5(OH).SO_3Na + 2\frac{1}{2}H_2O$. This is a white powder having a strong reducing action on silver salts. It is soluble in water and is used as a photographic developer. It has also been used in the treatment of *ivy poisoning.* It is decomposed by contact with fumes of ammonia.

Elarson. *Arsoben.*—Under this name *strontium-chlorarsenobehenolate* has been introduced. It is a nearly white, tasteless powder insoluble in water and sparingly soluble in alcohol or ether, and represents about 13 per cent. of arsenium. Its range of usefulness is precisely that of arsenous oxide. The beginning *dose* is about one one-hundredth of a grain (0.0006 Gm.) three times a day, which may gradually be increased up to one-twentieth of a grain (0.003 Gm.) three times a day or more.

Elaterium. *Br.* 1898. *Extractum Elaterii. Elaterium, Elaterion,* Fr. *Elaterium,* G. *Elaterio,* It., Sp.—"A sediment from the juice of the fruit of Ecballium Elaterium, *A. Richard.*" *Br.*, 1898. *Ecballium Elaterium* (L.) A. Rich., commonly known as the *wild* or *squirting cucumber*, is a perennial vine, indigenous to Mediterranean regions. It possesses a large fleshy root, from which rise several round, thick, rough stems, branching and trailing like the common cucumber, but without tendrils. The leaves are petiolate, large, rough, irregularly cordate, and of a grayish-green color. The flowers are yellow and axillary. The fruit has the shape of a small oval cucumber, about an inch and a half long, an inch thick, of a greenish or grayish color, and covered with stiff hairs or prickles. When fully ripe, it separates from the peduncle, and throws out its juice and seeds with considerable force through an opening at the base, where it was attached to the footstalk. The name of squirting cucumber was derived from this circumstance, and the scientific and official title is supposed to have had a similar origin, though some authors maintain that the term *elaterium* was applied to the drug rather from the mode of its operation upon the bowels than from the projectile property of the fruit. It is derived from the Greek *ἐλαύνω*, *I drive,* or *ἐλατήρ*, *driver.* The word *elaterium* was used by Hippocrates to signify any active purge. Dioscorides applied it to the medicine of which we are treating. It is a native of the south of Europe, and is cultivated in Great Britain, where, however, it perishes in the winter. (For description of the culture in England, see *U. S. D.*, 19th edition, p. 432.)

Elaterium is the substance spontaneously deposited by the juice of the fruit, when separated and allowed to stand. Strong expression of the juice injures the product. When the fruit is sliced and placed upon a sieve, a perfectly limpid and colorless juice flows out, which soon becomes turbid, and in the course of a few hours begins to deposit a sediment. This, when collected and carefully dried, is very light and pulverulent, of a yellowish-white color, slightly tinged with green. It is the genuine elaterium, and was found by Clutterbuck to purge violently in the dose of one-eighth of a grain. But the quantity contained in the fruit is very small. Clutterbuck obtained only six grains from forty cucumbers. Commercial elaterium is often a weaker medicine, owing in part, perhaps, to adulteration, but much more to the fact that in order to increase the product, the juice of the fruit is often expressed with great force, and there is reason to believe that it is sometimes evaporated so as to form an extract, instead of being allowed to deposit the active matter.

The best elaterium is in thin flat or slightly curled cakes or fragments, often bearing the impression of the muslin upon which it was dried, of a greenish-gray color becoming yellowish by exposure, of a feeble odor, and a bitter, somewhat acrid taste. It is pulverulent and inflammable, and so light that it floats when thrown upon water. When of inferior quality, it is sometimes dark-colored, much curled, and rather hard, breaking with difficulty, or presenting a resinous fracture. "In light, friable, flat or slightly curved, opaque cakes, about one-tenth of an inch (two and a half millimetres) thick; pale green, grayish-green, or yellowish-gray in color; fracture finely granular; odor faint, tea-like; taste bitter and acrid. It should not give the characteristic reactions with the tests for carbonates or for starch, and should yield half its weight to boiling *alcohol* (90 per cent.). When exhausted with *chloroform*, the solution evaporated, the residue washed with *ether*, and the process of solution, evaporation, and washing repeated, Elaterium should yield 25 per cent., or not less than 20 per cent., of Elaterin." *Br.*, 1898. For an assay of elaterium by Jones and Ransom, see *U. S. Dispensatory*, 19th ed., p. 432.

Maltese elaterium is in larger pieces, of a pale color, sometimes without the least tinge of green, destitute of odor, soft, and friable, and not infrequently gives evidence of having been mixed with chalk or starch. It sinks in water, and usually contains so little elaterin that it should be employed only as a source of that principle. In the analyses of T. A. Elwood, the average yield of English elaterium was 21.5 per cent., of Maltese elaterium 15.3 per cent. (*P. J.*, Nov., 1891.)

Clutterbuck first observed that elaterium resided in the portion of it soluble in alcohol and not in water. The subsequent experiments of Hennell, of London, and Morries, of Edinburgh, which were nearly simultaneous, demonstrated the existence of a crystallizable matter in elaterium which is the active principle, and has been named *elaterin.* (See *Elaterinum.*) According to Hennell, 100 parts of elaterium contain 42 of elaterin, 17 of a green resin (*chlorophyll*); 6 of starch, 27 of lignin, and 6 of saline matters.

Uses.—Elaterium is a powerful hydragogue cathartic, and in a large dose generally excites nausea and vomiting. Two-fifths of a grain (0.025 Gm.) of elaterium proved fatal by purging in an ill and feeble lady of 70 years. (*A. J. P.*, 1868, p. 373.) Because of its variability elaterium should never be employed, preference always being given to the official elaterin.

Elbon. *Cinnamoyl-para-oxyphenyl-urea.*—It occurs as white, tasteless crystals, very slightly soluble in water but readily dissolved by oils and alcohol. It is decomposed in the system and appears in the urine as a derivative of oxyphenyl-urea and hippuric acid. It is used as a stimulating expectorant, especially in *pulmonary tuberculosis* and *pneumonia.* According to Johannessohn (*B. K. W.*, 1913, p. 914), it also has an antipyretic action and increases the leucocytes. The *dose* is fifteen grains (1.0 Gm.).

Elemi. *Gum Elemi. Elemi,* Fr.—The name elemi is applied commercially to a large number of resins. The variety which is mostly used is known as *Manila* or *Philippine Elemi* and is derived from *Canarium commune* L. and probably also from *C. luzonicum* Miq. (Fam. *Burseraceæ.*)

According to Bacon (*Philippine Journal of Science,* 1909, iv, p. 93), the Manila elemi is derived from the *Canarium luzonicum* Miq. When first collected it is soft, but later becomes hard on exposure to the air and light, which has given rise to the belief that there were two varieties of the Manila gum. It is collected by incising the tree at the time when it is developing new leaves, the juice exuding through the bark and collecting in lumps at the point of the incision. This is the variety formerly recognized by the British Pharmacopœia.

There are a number of other commercial varieties of elemi. The so-called carana-elemi is obtained from *Protium Carana* (Humb.) L. March., a tree growing in Venezuela and Northern Brazil. Brazilian Almesseya-elemi is obtained from *Protium heptaphyllum* March., var. *Brasiliense* Engl. East African elemi is probably obtained from *Boswellia Frereana* Birdwood. Yucatan elemi is derived from *Amyris Plumieri* DC. All these plants belong to the *Burseraceæ.* The elemi is obtained by incisions into the trees, through which the juice flows and concretes upon the bark.

Carana-elemi occurs in masses of a greenish-yellow color, externally hard, internally soft, with a peculiar fennel-like aromatic odor. It is insoluble in water, soluble in sulphuric ether, chloroform, and benzene. According to Tschirch and Saal, carana-elemi contains 20 per cent. of exceedingly acrid resin. (*A. Pharm.*, Bd. 241, 1903.)

These are further distinguished as "hard" or "soft" elemi, which are differentiated by the fact that the "soft" elemi contains from 20 to 25 per cent. of volatile oil.

Elemi is in masses of various consistence, sometimes solid and heavy like wax, sometimes light and porous; unctuous to the touch; diaphanous; of diversified colors, generally greenish with intermingled points of white or yellow, sometimes greenish-white with brown stains, sometimes yellow like sulphur; fragile and friable when cold; softening by the heat of the hand; of a terebinthinate somewhat aromatic odor, diminishing with age, and resembling to some extent that of lemon and fennel; of a warm, slightly bitter, disagreeable taste; entirely soluble, with the exception of impurities, in boiling alcohol; and affording a volatile oil by distillation. "Moistened with rectified spirit, it breaks up into small particles, which, when examined by the microscope, are seen partly to consist of acicular crystals." *Br.*, 1885. Elemi is sometimes adulterated with rosin and turpentine.

The two varieties of elemi that have been investigated chemically are the Manila, or soft elemi, and the Brazilian, or hard elemi. The Manila elemi contains 10 per cent. of an ethereal oil (made up of phellandrene and dipentene), *amyrin* (*manamyrin*) $C_{30}H_{50}O$, of which, according to Vesterberg, the isomeric varieties *a-* and *b-amyrin* are present, an amorphous *resin*, small amounts of *a-manelemic acid*, $C_{37}H_{56}O_4$, *β-manelemic acid*, $C_{44}H_{80}O_4$, *bryoidin*, $C_{20}H_{38}O_3$, and a bitter principle. The Brazilian elemi (*protium elemi*) contained *protomyrin*, 30 per cent.; *protolaminic acid*, 25 per cent.; and *protolaresine*, 37.5 per cent The protomyrin has the same melting point and formula as the amyrin from Manila elemi.

Elemi has properties analogous to those of the turpentines, but is exclusively applied to external use. In the United States it is rarely employed even in this way, except as a constituent of plasters prepared upon the large scale. In the pharmacy of Europe it enters into the composition of numerous plasters and ointments. *Unguentum Elemi* (*Br. Ph.*, 1885) was of the strength of about 20 per cent.

Elixir of Iron, Quinine, and Strychnine Phosphates. (*U. S. P. VIII.*) *Elixir Ferri, Quininæ et Strychninæ Phosphatum.*—The U. S. P. VIII process was: " Soluble Ferric Phosphate, *seventeen and one-half grammes;* Quinine, *eight and seventy-five hundredths grammes;* Strychnine, *two hundred and seventy-five milligrammes;* Phosphoric Acid, *two cc.;* Ammonium Carbonate, in translucent pieces, *nine grammes;* Alcohol, *sixty cc.;* Acetic Acid, *twenty-eight and sixty-five hundredths grammes;* Ammonia Water, Distilled Water, Aromatic Elixir, each, a *sufficient quantity,* to make *one thousand cc.* Dissolve the Quinine and Strychnine in the Alcohol, then add the Phosphoric Acid and *three hundred and fifty cc.* of Aromatic Elixir. Add the Acetic Acid to the Ammonium Carbonate, contained in a suitable vessel, and when solution is complete, neutralize with Ammonia Water and add enough Distilled Water to make the product measure *fifty cc.* Mix the solution of Ammonium Acetate with the solution of the alkaloids, and add enough Aromatic Elixir to make the liquid measure *eight hundred and eighty cc.* Dissolve the Ferric Phosphate in *thirty cc.* of Distilled Water, by the aid of a gentle heat, and if the solution be acid to litmus paper, neutralize exactly with Ammonia Water, and add enough Aromatic Elixir to make the product measure *one hundred and twenty cc.* Finally, mix the two solutions and filter, if necessary." *U. S. VIII.*

This elixir was introduced into the U. S. P. VIII because it is largely used and deserved recognition, but because of the darkening of the elixir and frequent precipitation it was omitted from the U. S. P. IX. The difficulty is largely caused by the attempt to produce phosphates of the several ingredients and as this form possesses no special medicinal value it was believed that the use of the more permanent elixir of iron, quinine, and strychnine of the N. F. V (see Part III) should be encouraged. The U. S. P. VIII process is essentially that recommended by Caspari, but as it did not prove satisfactory, Caspari has since recommended the following formula which is less likely to discolor or precipitate: Quinine (alkaloid), 8.75 Gm.; Strychnine (alkaloid), 0.275 Gm.; Ferric Phosphate (U. S. P.), 17.50 Gm.; Phosphoric Acid (U. S. P.), 2 cc.; Alcohol, 60 cc.; Acetic Acid (U. S. P.), 16 Gm.; Ammonium Carbonate, 5.1 Gm.; Distilled Water, Aromatic Elixir, of each, *a sufficient quantity,* to make 1000 cc. Add the ammonium carbonate, in firm translucent pieces, to the acetic acid contained in a beaker and when solution is complete, add 350 cc. of aromatic elixir and the phosphoric acid. Dissolve the quinine and strychnine alkaloids in 40 cc. of alcohol, add this solution to the acid mixture, and rinse the beaker or flask with 20 cc. of alcohol, adding this also to the previous mixture; now add sufficient aromatic elixir to bring the volume of the mixture up to 880 cc. Dissolve the ferric phosphate in 30 cc. of distilled water with the aid of heat, and when cool add sufficient aromatic elixir to bring the volume of the solution up to 120 cc. (If the iron solution shows an acid reaction with litmus paper, it should be neutralized nearly, but not entirely, by the cautious addition of ammonia water.) Finally, mix the two solutions and keep the finished product in dark, amber-colored bottles. The ferric phosphate and the alkaloids are retained in solution in the elixir with the aid of an excess of phosphoric acid, but this makes the elixir unpleasantly acid to the taste; ammonium acetate is used to retain the ferric phosphate in solution with the other ingredients and to make a finished elixir which can be mixed with aqueous solutions without producing turbidity, and remain clear at low temperatures. This elixir should be preserved in amber-colored bottles protected from the light, otherwise the pale greenish color which it has when first made will disappear and be replaced by a brownish tint followed often by precipitation. *Dose,* one to two fluidrachms (3.75–7.5 cc.).

This is one of three preparations which are frequently confused by physicians and pharmacists. The other two are official in the N. F. and are Elixir of Iron Quinine and Strychnine and Elixir of Iron Pyrophosphate, Quinine and Strychnine. Another disconcerting fact is that manufacturers have introduced preparations which are half the strength of the official preparations in Quinine and Strychnine. Pharmacists frequently purchase these substandard preparations and dispense them in ignorance of their character. Investigations of this condition by State Pharmacy Boards has frequently resulted in the penalizing of pharmacists who dispense any other than the official preparations.

Emery. *Lapis Smiridis, s. Smiris. Emeri, Corindon granuleux ferrifère,* Fr. *Smirgel, Schmirgel,* G.—A very hard mineral, the powder of which is capable of wearing down all other substances except the diamond. It is an impure variety of *corundum,* which is *alumina* (Al_2O_3), containing oxide of iron. It was formerly derived almost solely from the island of Naxos, in the Grecian Archipelago. Corundum is found abundantly in Northern Georgia, in North Carolina, and in Chester County, Pennsylvania. *Emery* is pulverized by grinding it in a steel mill, and the powder is kept in commerce of different degrees of fineness. It is used for polishing metals and hard stones. Compact corundum is now ground extensively for the manufacture of emery wheels, etc. Both corundum and emery have been largely replaced in use by the product of the electric furnace, *carborundum,* which is *silicon carbide* (SiC).

Emetine Bismuth Iodide. *Emetinæ Bismutho-Iodidum* (*N. N. R.* 1924) *Emetine Bismuthous Iodide.*—This is an odorless orange red powder sparingly soluble in water with partial decomposition. It is decomposed by strongly alkaline or acid solutions. It represents from 17 to 23 per cent. of emetine and from 15 to 20 per cent. of bismuth. Sollmann (*J. A. M. A.*, 1919, lxxiii, p. 1125) finds that it is freely soluble in a 1 per cent. solution of sodium bicarbonate.

The purpose of this combination is to present emetine in an insoluble form so that irritation of the stomach will be avoided. It is used for the treatment of *amebic dysentery* and it is claimed that the administration by mouth of the emetine bismuth iodide is equally efficacious, if not more so, than the hypodermic use of the soluble salts of the alkaloid. For summary of the literature see the report of the Council of Pharmacy and Chemistry (*J. A. M. A.*, 1918, lxxi, p. 2013).

Some authorities recommend that, in order to further guard against irritation of the stomach, it be given in salol coated pills, or in pills made with suet. The dose employed is about three grains (0.2 Gm.), corresponding to one grain of emetine, daily for three or four days.

Empyroform.—This is a condensation product of formic aldehyde and tar, forming a stable brown powder of a peculiar faint odor quite distinct from that of tar. Upon heating formic aldehyde is split off. It is insoluble in alcohol and water and soluble in acetone, caustic alkalies, and chloroform. It is used in inflammatory *skin diseases*, such as *acute* or *chronic eczema*, in the form of ointment in strengths of from 5 to 15 per cent. Both antipruritic and disinfectant properties are claimed for it. It has the advantage over tar of being less irritant.

Enomorphine.—This is claimed to be the sulphate of *allyl-morphine* $C_{17}H_{17}NO(OH)(OC_3H_5)$. It is asserted by Major and Wiki to possess the advantages of morphine and few of its disadvantages. (*Schweiz. Apoth. Ztg.*, 1915, 119.)

Eosin. *Bromeosin.* $C_{20}H_8Br_4O_5$.—A dye obtained by the action of phthalic anhydride upon phenols and introduction of bromine into the product. When phthalic anhydride acts upon resorcinol, $C_6H_4(OH)_2$, in the presence of a dehydrating agent like sulphuric acid or stannic chloride, at a temperature of 120° C., there is formed a compound resorcinphthalein, $C_{20}H_{12}O_5$, better known as *fluorescein* (see p. 1307). By the action of bromine upon this is formed *tetrabromfluorescein* or *eosin*, $C_{20}H_8Br_4O_5$. Soluble eosin is the potassium salt of this compound, $C_{20}H_6Br_4O_5K_2$. It forms a bronze-colored crystalline powder having a strong green reflection. Its solution in water is a red liquid having a fine green fluorescence. On the addition of hydrochloric acid the fluorescence is destroyed, the liquid becoming yellow. Eosin is largely used at present as a dye; to make a brilliant *red ink*, dissolve 5 grains of eosin and 10 grains of gum arabic in a fluidounce of water. According to Mandach (*K. S. A.*, 1907), eosin affords a most sensitive reagent for the occurrence of bile pigment in the urine. For this purpose a stock solution of 0.1 per cent. is diluted until the yellowish-red color becomes a pale pink showing a slight green fluorescence. In the presence of the bile this pinkish color is changed to a yellowish-brown, and later to a bottle-green. In normal urine no change of color is observed.

There is also sold under the name of *blue eosine* a *sodium iodeosine*, commercially known as *erythrosine*. It is a brown powder, soluble in water and used for dyeing wool, cotton and paper. It is also of use in histology as a stain for cell walls and contents.

Eosin Selenium is the name of a powder which has been used, experimentally, in investigations on the treatment of malignant tumors. The *dose* is one sixty-fourth of a grain (0.001 Gm.), to be increased if necessary.

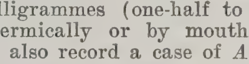
Ephedra. *Ephedra vulgaris* Rich. (Fam. *Gnetaceæ.*)—This gymnospermous plant is a straggling shrub with long-jointed and fluted green stems and scale-like opposite leaves forming at each joint a two-toothed sheath. It grows in Eastern Europe and Western Asia. It has been used as a medicine by the Chinese for thousands of years, being included in the collection made by the Emperor Shen-Nung about 1500 B.C.; in China it is known as *Ma huang*. For pharmacognostic description see Chen (*J. A. Ph. A.*, 1925, xiv, 189).

In 1887 Nagai isolated from this plant an alkaloid *ephedrine*, $C_{10}H_{15}ON$. Subsequently Merck found in the European variety an alkaloid which he called *pseudo-ephedrine*, apparently isomeric with that from the Asiatic variety. Ephedrine occurs as colorless crystals melting at 214° C., while pseudo-ephedrine forms yellowish crystals and melts at 175° C. Spehr (*A. J. P.*, 1892, 234) found in the *E. Monostachya* L. an alkaloid, $C_{13}H_{19}ON$, which was physiologically inert.

Ephedrine has been studied by Miura, Amatsu and Kubota and by Chen and Schmidt (*J. P. Ex. T.*, 1924, xxiv, p. 339) with concordant results. Chemically it is closely related to epinephrin, differing only in that two hydroxyl groups of the latter have been replaced by hydrogen atoms. In physiological action also it resembles epinephrin. It causes a marked rise in the blood pressure with an increase of both the rapidity and excursion of the heartbeat. The rise of blood pressure is also due in part to vasomotor stimulation. It causes dilatation of the pupil, whether injected into the blood stream or applied locally, without loss of the power of accommodation. It relaxes the intestinal muscle and apparently also the bronchial. All these effects seem to be due to stimulation of the sympathetic nervous system. Chen and Schmidt find that it differs from epinephrin chiefly in the persistence of effect and in the fact that it is active when taken by the mouth. A dose of 60 milligrammes in a human being produced a rise of blood pressure of 20 millimeters that lasted for two hours. They have used it clinically as a circulatory stimulant in *doses* of from 40 to 60 milligrammes (one-half to one grain), either hypodermically or by mouth with good effects. They also record a case of *Addison's disease* in which the drug produced a marked alleviation of symptoms. An alkaloid has also been discovered in *Ephedra distachya* L., a shrub whose branches and root are used in Siberia as a remedy in *gout* and *syphilis*. According to Kobert, this alkaloid is essentially different from *ephedrine*, in not being mydriatic or poisonous. *E. monostachya* contains a crystalline base melting at 112° C. and having the formula $C_{13}H_{19}ON$. This latter, as stated by Kobert, is not mydriatic or poisonous. See paper by E. Schmidt, *A. Pharm.*, 1912, ccl, 154, 161.

Ephedra nevadensis S. Wats. and *E. antisyphilitica* C. A. Meyer, which grow abundantly in the extreme Western United States, are used under the names of *caynote*, *canutilo*, *whorehouse tea* as a remedy in *gonorrhea*. Loew thinks that their virtues reside in a peculiar tannin. *Dose*, of fluidextract, from one to two fluidrachms (3.75–7.5 cc.). In Texas *E. trifurca* Torr. is similarly employed.

Epicarin.—A condensation product of creosotinic acid and naphthol which, according to Eichengrün, is *β-oxynaphthyl-o-oxy-metatoluylic acid* thus:



$$C_6H_3\begin{array}{l}/COOH\\—OH\\\backslash CH_2—C_{10}H_6OH\end{array}.$$

Epicarin forms slightly yellowish crystals or powder with a faint odor, melting at 190°–195° C., difficultly soluble in water but freely soluble in alcohol and ether as well as in soaps. It is said to be slightly poisonous, and was primarily introduced into veterinary medicine, especially for the treatment of *mange*, but has been used by Kaposi, Monti, and other dermatologists in *scabies, ringworm, prurigo*, and allied skin diseases as a substitute for naphthol. Its application is sometimes followed by irritation, which, though usually slight, may lead to papular and eczematous eruptions. It is claimed that the remedy is less poisonous than naphthol. In Kaposi's clinic no toxic symptoms followed covering the entire body of children with 10 per cent. ointment. Five to twenty per cent. ointment is used *pro re nata*.

Epichlorhydrin. *Chloropropylene oxide.* C_3H_5ClO.—A colorless liquid of specific gravity of 1.203 at 0° C. and miscible with alcohol and ether. It is used as a general solvent for resins, having a solvent action even on celluloid. It is incompatible with alkaline hydroxides or carbonates, and it should be protected from exposure to air, which turns it red.

Epidermin.—A surgical dressing made by fusing 15 Gm. of white wax, and triturating in a warm mortar with 15 Gm. of powdered acacia until uniform, and adding a boiling mixture of 15 Gm. each of water and glycerin, and stirring until cold. Valentine and Schwartz have given the name *epidermin* to an ointment vehicle said to be composed of fluorxylol and difluordiphenyl.

Epifagus. *Epiphegus. Epifagus virginiana* (L.) Bart. (*Leptamnium virginianum* (L.) Raff.) (Fam. *Orobanchaceæ.*) *Beech-drops. Cancer Root. Orobanche de Virginie*, Fr. *Krebswurz*, G.—This is a parasitic, fleshy plant, found in Northeastern America, growing upon the roots of the beech tree. The plant has a bitter, nauseous, astringent taste, which is said to be diminished by drying. It has been given internally in bowel affections; but its credit depends mainly upon the idea that it is useful in obstinate *ulcers* of a cancerous character, to which it was directly applied. Other species of *Orobanchaceæ*, growing in America and Europe, have also been employed. They are all parasitic, fleshy plants, without verdure, and of a bitter, nauseous taste. In Europe they are called *broom rape.* C. Charaux believes that *chlorogenic acid*, which can be easily converted into *caffeic acid*, exists in plants of the Fam. *Orobanchaceæ* and other families. The allied plants, *Conopholis americana* (L. f.) Wallr. (*Orobanche americana* L. f.) and *Orobanche uniflora* L., growing throughout the United States, are used for the same purposes as the species above noticed, and, like it, are unfortunately called *cancer root.*

Epigaea. *Epigaea repens* L. *Trailing Arbutus. Ground Laurel. Mayflower. Gravel Plant.*—This is a small prostrate or trailing ericaceous plant, having woody stems; evergreen, entire, cordate-ovate leaves, and small very fragrant rose-colored dimorphic, subdioecious flowers, which appear early in the spring. It is found in the sandy woods or rocky soil, and grows on the sides of hills with a northern exposure. Darlington states that the plant has been supposed to be injurious to cattle, when eaten by them. (*Flora Cestrica*, 259.) Jefferson Oxley has found in this plant arbutin, urson, ericolin, (the same constituents as are in uva ursi), tannic and formic acids, and a principle allied to gallic acid. (*A. J. P.*, xliv, 253.) Eli Ives of New Haven, Connecticut, in 1849, highly commended epigaea as a substitute for uva ursi, and we now know that the two drugs contain the same active principles. The decoction of the leaves and stem may be used freely.

Epilobium. *Epilobium angustifolium* L. (*Chamænerion angustifolium* Scop.) *Willow-herb. Fire-weed. Herbe de St. Antoine*, Fr. *Weidenröschen, Antonskraut*, G. (Fam. *Onagraceæ.*)—There are several indigenous species of *Epilobium*, which have the common name of willow-herb, from the resemblance of their leaves to the willow, all of which probably have nearly identical properties. The *E. angustifolium* is the largest of them. Its leaves and roots are said to be demulcent, tonic, and astringent. They are used by the eclectics, generally and locally, in decoction, infusion, or cataplasm, as astringents. Oliver reports (*B. M. J.*, 1897, ii) violent poisoning with epileptiform convulsions caused by *E. hirsutum* L. Under the name of *Kaporie tea*, the leaves of *E. angustifolium* and of *E. hirsutum* are largely used in Russia as a beverage.

Equisetum. *Equisetum hyemale* L. *Horsetail. Scouring Rush. Prêle.* Fr. *Schachtelhalm.* G. (Fam. *Equisetaceæ.*)—A horsetail indigenous to Europe but naturalized in the United States, growing abundantly in wet places. It is characterized by having erect stems which are mostly simple and ridged, attaining a height of 9 dm. and further by showing green parenchyma continuous over the vallecular holes separated by bast fibers beneath the ridges when the stems are examined in cross-sections. The plant derives its name of scouring rush from its use in scouring, for which it is fitted by the silicious character of the stems. Examined by F. J. Young (*A. J. P.*, 1886, 419), it yielded to petroleum benzin as a solvent 1.4 per cent. of a brownish-green, semi-liquid, fixed oil, which was readily saponified. It also contained a green semi-solid resin, sugar, and mucilage. The infusion of the whole plant is used sometimes in *dropsical* and *renal diseases*, but Cow (*A. E. P. P.*, 1912, lxx, p. 393) has shown that the diuretic action is very feeble.

Erechtites. *Erechtites hieracifolia* (L.) Raf. *Fire weed.*—An annual composite, growing in moist woods and recent clearings in lower Canada and the United States. It possesses alternate, lanceolate to oblong, cut-toothed leaves and heads of whitish flowers arranged in panicles or corymbs. Its odor is rank and its taste bitter, and slightly acrid. It yields its virtues to water. It has been recommended in *dysentery.* It is prone to infest the peppermint fields of Michigan, and its oil is said sometimes to deteriorate the oil of peppermint from that region. It has been shown, however, that *Erigeron* (*Leptilon*) *canadensis* L. is far more injurious (see Erigeron).

Erepton.—This preparation, whose use is based upon the discoveries of Abderhalden that the system is capable of synthesizing albumin from the amino-acid, is prepared by digesting lean meat with pancreatic and intestinal secretions. It is a brown hygroscopic powder, readily soluble in water, containing 12 per cent. of nitrogen, and does not give the Biuret reaction. It has been recommended by Jacobson and Rawald (*Ther. Geg.*, 1911, p. 119) for rectal feeding. They administered 250 cc. (8 fluidounces) of a 5 per cent. solution three to six times a day by enemata. They found that 85 per cent. of the nitrogen was absorbed.

Erigeron. *Fleabane. Scabious. Sweet Scabious. Daisy Fleabane. Herbe d'érigeron, Herbe de Vergerette*, Fr. *Berufkraut*, G.—The U. S.

V recognized three species of *Erigeron* (Fam. *Compositæ*), namely, *E. heterophyllum* Muhl., *E. philadelphicum* L. and *E. canadense* L. Under the name of erigeron and under the title of *Erigeron Canadense* it recognized the *E. Canadensis* [*Leptilon canadense* (L.) Britt.]. *Horseweed. Mare's tail. Fire-weed. Butter-weed. Colt's-tail.*

All of these species are abundant weeds in the northern and middle sections of the United States and Canada; fleabane has been reported as very troublesome on the peppermint plantations of the West. All portions of the plants are somewhat aromatic. Whatever virtue they possess is due to their volatile oil, of which they yield 0.2 to 0.4 per cent.

The oil of erigeron remained official in the U. S. VIII but was dropped at the ninth revision.

The U. S. VIII recognized, under the name of *Oleum Erigerontis*, the *oil of Canada fleabane.*

Oil of erigeron is of a light straw color, a peculiar, aromatic, persistent odor, and a characteristic taste. By exposure it becomes darker and thicker and eventually resinifies. Its reaction is neutral. Its sp. gr. is about 0.850, increasing with age (0.855 to 0.890, *Schim. Rep.*). It consists chiefly of dextrogyrate limonene, together with some terpineol. (*A. J. P.*, 1893, 420.) It was officially described as "a pale yellow, limpid liquid rapidly becoming darker and thicker by age and exposure to the air, having a peculiar, aromatic, persistent odor, and an aromatic, slightly pungent taste. Specific gravity, 0.845 to 0.865 at 25° C. (77° F.). Soluble in an equal volume of alcohol (distinction from *oil of fireweed* derived from *Erechtites hieracifolia* Rafinesque (Fam. *Compositæ*) and from *oil of turpentine*). It is dextrogyrate, the angle of rotation being not below +45° in 100 mm. tube, at a temperature of 25° C. (77° F.)." *U. S. VIII.* When distilled without water, it comes over colorless, and a little resinous matter is left behind, probably resulting from the oxidation of one or both of the constituent oils. It is slowly reddened by potassium hydroxide, combines with iodine without explosion, is instantly decomposed by sulphuric acid, and is acted on by strong nitric acid, slowly at ordinary temperatures, but with heat explosively. (Procter, *A. J. P.*, xxvi, 502.) For an account of the difference in properties between this oil and that from *Erechtites hieracifolia*, see Todd, *A. J. P.*, 1887, p. 302; Rabak, *Ph. Rev.*, 1905, 81, and also *Ph. Rev.*, 1906, 326.

It was first brought into notice by the so-called eclectic physicians, who use it in *diarrhea, dysentery*, and the *hemorrhages*, and apparently it is a valuable remedy in *hemoptysis* when there is no fever or other marked evidence of constitutional irritation. It probably acts like the oil of turpentine as a hemostatic, but is much less irritant and stimulating.

Dose, ten minims to half a fluidrachm (0.6–1.8 cc.), repeated every hour or two.

For further information concerning these drugs see *U. S. D.*, 19th ed., p. 1479.

Eriobotrya. *Eriobotrya japonica* Lindl. *Loquat. Japanese Medlar. Bibacier. Néflier du Japon. Nestole di Giappone.* (Fam. *Rosaceæ.*)—A small tree, indigenous to Japan and extensively cultivated. The fruit closely resembles the apricot and has a sweetish acid pulp. The seeds of this tree are said to contain amygdalin and emulsin, and to yield hydrocyanic acid in poisonous quantities. (Hérissey, *A. Pharm.*, ccxlv, 1907.)

Erodium. *Erodium cicutarium* L. *Stork's-bill.*—An annual hairy plant belonging to the *Geraniaceæ.* It grows in Europe, Asia, Northern Africa and is widely cultivated, being found naturalized about cities in the United States. Many years ago it was recommended by W. Abbots Smith (*Am. J. M. S.*, 1865) in *dropsy.* It has been revived by Von Dongen (*C. D.*, 1916, lxxxviii, p. 41) as a substitute for hydrastis in *uterine hemorrhages.*

Eryngium. *Eryngium aquaticum* L. *Button Snakeroot. Corn Snakeroot. Rattlesnake's Master.*—The *button snakeroot* or *water eryngo* is an indigenous umbelliferous plant which grows in low wet places near the coast from New Jersey as far south as Florida and Texas. The root, which is the medicinal portion, has a bitter, pungent aromatic taste, provoking, when chewed, a flow of saliva. It is said to be diaphoretic, expectorant, in large *doses* emetic, and the plant has been used as a substitute for senega.

Erythrina.—The bark of the Australian species *Erythrina Broteroi* (Fam. *Leguminosæ*) is said to contain an alkaloid, *erythrinine*, while the Mexican species, *Erythrina caralloides* DC., bears poisonous seeds in which Altamirano has found *erythroidine*, a powerful paralyzant of the motor system, *erythroresin*, an emetic, *coralin* and *erythric acid.* The *extract* has been suggested as a substitute for curare. (*B. S. Ph. Br.*, 1900.) Langham obtained from the seeds of *E. zeyheri* (which have a scarlet testa), *erythrine*, 15 per cent. (*C. D.*, 1911, 134.)

Erythrina lithosperma Blume. (*Hypaphorus subumbrans* Hassk.)—From the seeds of this beautiful leguminous tree, largely grown for shade in the coffee gardens of Java, P. C. Plugge has obtained *hypaphorine* $C_{14}H_{18}O_2N_2$, a tetanizing alkaloid. (*A. E. P. P.*, xxxii.) (See also Romburgh and Barger, *Tr. Chem. Soc.*, 1911, xcix, 2068.)

Erythrol Tetranitrate. *N. N. R.* 1924. (*Tetranitrol. Butane tetrol.*) $C_4H_6(NO_3)_4$.—*Erythyrol tetranitrate* is solid and crystalline, and melts at 61° C. When pure it is colorless, and if kept in a dark and moderately cool place is fairly stable. If exposed to warmth, and especially sunlight, it rapidly undergoes decomposition, turning yellow and giving off nitrous fumes. It is also capable of rapid decomposition, and death has been caused by the explosion following its trituration in a mortar with glucose. (*B. M. J.*, 1896, i.) Its solubility in water is slight, but it dissolves readily in alcohol and in ether. It is a vasodilator, and belongs to the group of which glyceryl trinitrate (glonoin) or nitroglycerin is the representative. Blood pressure experiments show that the nitrates of erythrol and mannitol have a less marked and more prolonged action than those of glycerol and glycol. In man the effects of the remedy are said not to be apparent in less than half an hour and to last for two or three hours. It may be used in all cases for which glyceryl trinitrate is employed, and has been especially commended in *angina pectoris.* Its alcoholic solution is explosive, so that it should always be used in tablets, in preparing which great care is necessary. *Dose*, from a half to one grain (0.032–0.065 Gm.).

Erythronium. *Erythronium americanum* Ker. *Yellow Adder's Tongue. Dog's Tooth Violet.*

Scrofula Root. Yellow Snowdrop. Rattlesnake Violet.—This is an indigenous, perennial, lilaceous plant found in early spring in valleys of rich woods from New Brunswick to Florida and west to Ontario and Arkansas. Its light yellow, often spotted, and nodding flowers appear the latter part of April or early in May. All parts of it are active. In the *dose* of twenty or thirty grains (1.3 or 2.0 Gm.) the recent bulb is emetic. The leaves are said to be more powerful. The activity of the plant is diminished by drying.

Eschscholtzia. *Eschscholtzia californica. Chamisso. California Poppy.*—Attention has been brought to this California member of the *Papaveraceæ,* as a powerful soporific and analgesic, which is free from the disadvantages of opium. The plant is extensively cultivated and there are now a number of garden varieties. Bardet and Adrain (*G. H. M. C.*, Nov., 1888) assert that they have obtained a glucoside, an alkaloid, and morphine in the proportion of from five to six grains in two pounds of the dried product. According to Fischer and Tweeden, there are seven alkaloids in *Eschscholtzia californica; protopine, β-* and *γ-homochelidonine,* "alkaloid *a*," "alkaloid *b*," *sanguinarine* and *chelerythrine.* As far as could be determined from the small quantities obtained, the alkaloids designated as *a* and *b* differ from any other alkaloids thus far known. (*A. Pharm.*, 1902, No. 7.) Most of these alkaloids are found also in *Sanguinaria* and *Chelidonium* (which see for further information). The narcotic power of the drug seems to be very weak, since, according to Bardet, three drachms were necessary to kill a rabbit. Ter-Zakariant (*G. M. P.*, Feb., 1899) states that the alcoholic extract acts as a respiratory depressant and narcotic, affecting in toxic dose also the spinal cord. Dujardin-Beaumetz has used the extract in commencing *doses* of twelve grains (0.78 Gm.), increasing to one hundred and eighty-five grains (12 Gm.) a day, and affirms that it is a harmless soporific and analgesic.

Escorcin. *Escorcinal, Aescorin.* $C_9H_8O_4$.—This is prepared from *aesculetin* (a decomposition product of aesculin) by the action of sodium amalgam. It is a brown powder, soluble in alkalies, imparting to the solution a green color which quickly changes to red. It is used in discovering defects in the cornea and lesions in the conjunctival epithelium, the red color which it imparts to the lesions being much more distinct on the iris than the green color of fluorescin. *Dose,* one drop of a 10 to 20 per cent. aqueous solution.

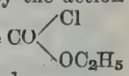
Ethyl Bromide. *N. N. R.* 1924. *Æthylis Bromidum. Bromide of Ethyl. Hydrobromic Ether. Æther Bromatus,* G. P. *Bromure d'éthyle,* Fr. *Bromäthyl,* G. C_2H_5Br.—The hydrobromic acid ester of ethyl alcohol containing approximately one per cent. of ethyl alcohol. This ether was discovered by Sérullas in 1827, who prepared it by acting on alcohol with bromide in the presence of phosphorus. (*Ann. Ch. Phys.*, xxxiv, 99.) Personne suggested the use of amorphous phosphorus, as less dangerous than ordinary phosphorus, and more convenient to manipulate (*C. R. A. S.*, iii, 468.) A process was also recommended by Remington, based upon Personne's suggestion. (*Proc. A. Ph. A.*, 1877.) De Vrij proposed to decompose potassium bromide with sulphuric acid in the presence of alcohol, and a modification of his method is now generally employed. (For description of methods of manufacture, see *U. S. D.*, 19th ed., p. 1480; *A. J. P.*, 1879 and 1880; *Ph. Centralh.*, 1887, xxviii.)

Ethyl bromide is a colorless, strongly refractive, very volatile liquid, not inflammable, having an agreeable odor, and a hot, saccharine taste. Its sp. gr. is 1.453 to 1.457. It boils at from 38°–40° C. It is very sparingly soluble in water, freely soluble in alcohol and ether. When a small portion is evaporated from a porcelain plate by causing it to flow to and fro over the surface, little or no foreign odor is yielded as the last portions pass off, and the plate is covered with a slight deposit of moisture.

Shaken with distilled water, ethyl bromide should not show any acid reaction from hydrobromic acid, nor should it cause any appreciable turbidity with silver nitrate. Shaken with an equal volume of pure concentrated sulphuric acid, no color should develop even after an hour's time; otherwise ethylene bromide may be present. Dropped slowly into potassium iodide solution the drops of the ethyl bromide should settle to the bottom of the vessel without developing any appearance of violet color, which would indicate free bromine. Ethyl bromide should be kept in small, opaque bottles containing not more than 50 cc., completely filled and well stoppered. It must not be confused with ethylene bromide which is a very poisonous compound having a specific gravity of over 2.1. (Fischer, *Die Neueren Arzneimittel,* 6te Aufl., 74.)

Ethyl bromide was introduced some years ago as an anesthetic especially suitable for short operations. Its advantages were the rapidity of its action and the relative absence of nausea. H. C. Wood (*P. M. T.*, 1879 and 1880, x) found that it acted upon the system much like chloroform, but Hamœker (*International Clinics,* Dec. 20, 1891) affirms that in the lower animals death always occurred through arrest of the respiration. It has, however, been found to be a dangerous anesthetic; Gurlt (*A. K. C.*, lv) estimates the mortality at 1 in 5400. A serious practical objection to its use is the ease with which it undergoes decomposition on exposure to light. Its range of usefulness is similar to that of ethyl chloride, but it does not appear to possess any sufficient advantage over the latter to justify its employment. Ethyl bromide has been especially recommended for use in *parturition,* it being stated that it suspends the pain of the uterine contractions without influencing their force.

Ethyl Carbamate.—*Aethylis Carbamas,* U. S. IX. *Ethyl urethane, Urethane; Carbamin-säure-ethylester, Aethyl-urethan,* G.; *Eter Carbamico,* Sp.

"The ethyl ester [$C_3H_7O_2N$ or $CO(OC_2H_5)-NH_2 = 89.07$] of carbamic acid" (*U. S. IX*) is no longer official. It is made by allowing ammonia to act upon ethyl carbonate, when urethane and ethyl alcohol are produced, or by heating urea nitrate with alcohol to from 120° to 130° C., resulting in the formation of ethyl carbamate and ammonium nitrate. It is also made by the action of ammonia upon ethyl chloroformate  $CO\begin{cases}Cl\\OC_2H_5\end{cases}$ which is prepared by the action of phosgene on antipyrine in benzene solution.

Another process is by the interaction of potassium isocyanate and alcohol in the presence of hydrochloric acid. Still another process is by the action of carbamic chloride (produced by the action of phosgene on ammonium chloride) on dehydrated alcohol.

It was officially described as in "colorless, columnar crystals or scales, odorless, and having a cooling, saline taste. One Gm. of Ethyl Carbamate dissolves in 0.45 mil of water, 0.8 mil of alcohol, 2.5 mils of glycerin, 0.9 mil of chloroform, 1.5 mils of ether, and in 32 mils of olive oil, at 25° C. Its aqueous solution (1 in 20) is neutral to litmus. Ethyl Carbamate melts between 48° and 50° C. Add 1 Gm. of Ethyl Carbamate to 5 mils of sulphuric acid and heat it gently; decomposition follows with the evolution of carbon dioxide (alcohol and acid ammonium sulphate remain in solution). Heat 1 Gm. of Ethyl Carbamate with 5 mils of concentrated potassium hydroxide solution; ammonia gas is given off, recognizable by its odor. Dissolve about 0.5 Gm. of Ethyl Carbamate in 5 mils of distilled water with about 1 Gm. of dry sodium carbonate and about 0.01 Gm. of iodine, and warm the solution; yellow crystals of iodoform separate on cooling. Incinerate about 2 Gm. of Ethyl Carbamate; not more than 0.05 per cent. of ash remains. Dissolve about 2 Gm. of Ethyl Carbamate in 2 mils of distilled water and add 5 mils of nitric acid to the solution; no white precipitate is produced (*urea*). Not more than slight opalescence results from the addition of a few drops of silver nitrate T.S. to 10 mils of an aqueous solution of Ethyl Carbamate (1 in 20) (*chloride*). Mix 2 mils of the aqueous solution (1 in 20) with 1 mil of ferrous sulphate T.S. and pour the mixture upon 2 mils of sulphuric acid, so as to form a separate layer; no red or brown zone appears (*nitrate*). When it is heated with ammonia to 180° C. urea is formed." *U. S. IX.*

Uses.—Ethyl carbamate is one of the safest of the somnifacient drugs. In therapeutic doses it has no perceptible effect upon the respiration or circulation, its physiological action being limited almost solely to a depressant influence upon the cerebrum, although large doses also have a depressant influence upon the motor areas in the spinal cord. In ordinary quantities it does not lessen the susceptibility to pain, but toxic doses will produce a condition of anesthesia. In the lower animals, after fatal doses, the respiration becomes slower, there is complete unconsciousness, loss of reflexes, fall of body temperature, and some depression of the circulation, death being due to asphyxia. Although in the milder forms of *insomnia* its freedom from toxicity makes it a very useful remedy, in severe cases its action is uncertain. According to Rappaport (*Z. E. P. T.*, 1911, ix, p. 39) it greatly enhances the narcotic effects of opiates and bromides. It has also been used by Jackman and others (*L. L.*, June, 1886) in various forms of *convulsions*. *Dose*, fifteen to forty-five grains (1–3 Gm.).

Ethyldiiodo-salicylate. *Diiodosalicylic ether.* $C_6H_2I_2(OH).COOC_2H_5$.—White crystals, soluble in alcohol, fixed oils, and slowly soluble in water. Melting point, 132° C. It is used as a succedaneum for iodoform in surgery.

Ethyl Iodide. *Hydriodic Ether. Ethyl-hydriodic Ester. Iodure d'éthyle, Ether hydriodique,* Fr. *Jodäthyl, Jodwasserstoffäther,* G. C_2H_5I.—This liquid may be obtained by gradually and cautiously mixing five parts of alcohol, ten of iodine, and one of phosphorus, and distilling. The residue of the distillation, as ascertained by D. K. Tuttle, is *ethylphosphoric acid.* Personne (*C. R. A. S.*, li, 468) proposed to use amorphous phosphorus instead of the ordinary kind, thus avoiding danger. For description of his process see *U. S. D.*, 19th ed., p. 1481.

Ethyl iodide is a colorless non-inflammable liquid, insoluble in water, with a penetrating ethereal odor and pungent taste. Its density is 1.92, and boiling point from 71°–72° C. Exposed to the air it becomes red from the liberation of iodine; the change in color is said to be prevented by adding to the bottle containing it a globule of mercury but the propriety of such a practice should be questioned unless it can be shown that no mercuric iodide enters solution.

Huette has proposed this ether, placed under a layer of water, as a medicine, to be used by inhalation. Fifteen or twenty inspirations suffice to impregnate the system with iodine. It acts as a powerful anesthetic, when inhaled for a sufficient time. It is said to increase the appetite, render the pulse fuller, and give vivacity to the feelings and activity to the intellect. (See *A. J. P.*, xxiii, 156.) James Turnbull, of Liverpool, and Henry Fischer, of New York, have used this ether by inhalation with satisfactory results in *chronic bronchitis* and *phthisis.* The *dose* is fifteen drops (0.75 cc.) three or four times a day, inhaled from a handkerchief. Ethyl iodide often has an unpleasant odor from the presence of foreign substances which renders it offensive to patients. Phosphorus is a common and injurious impurity.

According to Linosier and Lannois (*S. M.*, 1897), ethyl iodide affords an excellent method of affecting the general system by external application. Absorption of the iodine is rapid; the liquid should be applied with a brush and then covered with paraffined paper; after applying two fluidrachms they recovered thirteen grains of iodine from the urine.

Ethyl Salicylate. $C_6H_4OHCO.O.(C_2H_5)$. *N. N. R.* 1924. *Sal Ethyl.*—This is the salicylic acid ester of ethyl alcohol and is analogous to methyl salicylate. It is a transparent, colorless, volatile liquid, possessing a pleasant characteristic odor and taste. Sp. gr. 1.132 at 20° C. and boiling point 231.5° C.

Ethyl salicylate was suggested by Houghton (*A. J. Phys.*, 1905, p. 331) as a substitute for methyl salicylate in the treatment of *rheumatism.* He asserts that it is only one-half as toxic as the methyl ester and that it is absorbed rapidly from the intestinal tract, although not through the skin. The *dose* is five to twenty minims (0.3 to 1.2 cc.) several times daily.

Ethyl Valerate. $C_7H_{14}O_2$.—This compound is prepared by distilling sodium valerate with alcohol and an acid (HCl or H_2SO_4). It is a liquid having a strong odor with the characteristic valeric taste. It is used in *asthmatic* complaints as an antispasmodic and sedative. *Dose,* one to two drops during attacks.

Ethylene. *N. N. R.* 1925. (C_2H_4).—This is a colorless gas with a characteristic sweetish odor and taste, with a specific gravity of 0.978 as compared with the air. It may be prepared by heating alcohol with sulphuric acid or by passing CO over finely divided platinum at 100° C. It is highly inflammable and may explode from contact with a flame or an electric spark. Brown (*J. A. M. A.*, 1924, lxxxii, p. 1039) has found that mixtures of air and ethylene containing 5 to 10 per cent. of the latter are explosive but that 25 per cent. of ethylene with 75 per cent. of air is not, and that less than 3 per cent. of ethylene in the air is also not explosive, and concludes that it would take six hours of continuous anesthesia to make a sufficient concentration of the gas in a room of 2700 cubic feet to form an explosive mixture. Davis (*J. A. M. A.*, 1924, lxxxii, p. 1607), however, has reported an instance in which the flame of ignited ethylene vapor passed for a considerable distance through the air, eventually exploding the anesthetic mask with painful injuries to the patient.

The introduction of ethylene gas as a surgical anesthetic was the result of experiments by Brown and by Luckhardt and Carter (*J. A. M. A.*, 1923, lxxx, p. 765) on lower animals. Concentrations of 90 per cent. of ethylene with 10 per cent. of oxygen produces anesthesia and abolition of motor reflexes. Trials on human beings indicate that it is more powerful than nitrous oxide gas and that the stage of surgical anesthesia is preceded by one of analgesia. It apparently does not cause irritation of the respiratory tract. It has the advantage over nitrous oxide of producing better muscular relaxation without cyanosis; its disadvantages are the odor, which to some is offensive, and the inflammability. It has not been used enough for its relative danger to be determined.

Ethylene gas is supplied condensed in metallic cylinders and the technic of its administration is similar to that of nitrous oxide.

Ethylene Bromide. *Brom-ethylene. Æthylenum Bromatum.* $C_2H_4Br_2$.—This is a colorless oily liquid smelling like chloroform, with a sweet burning taste. It boils at 131.6° C., and solidifies at 0° C. to a crystalline mass; sp. gr. at 20° C. 2.178. It is insoluble in water, miscible with alcohol in all proportions. In experiments made by Scherbatscheff (*A. E. P. P.*, 1902, xlvii) *ethylene bromide* was found not to act as a true anesthetic in the lower animals, but to produce serious symptoms, usually ending in death. The chief medicinal importance of this agent grows out of its liability to be confounded with the ethyl bromide, death in this way having been produced. Ten fluidrachms of it were inhaled without the production of anesthesia, followed by uncontrollable vomiting and complete suppression of urine. On account of its containing over 85 per cent. of bromine, Donath has used it in *epilepsy.* He gives it in an emulsion with oil, or mixed with almond oil in capsules. Children from eight to ten years begin with ten drops (0.5 cc.) of a 5 per cent. solution; the adult *dose* is two to four minims (0.12–0.25 cc.) of ethylene bromide, three times a day. (See also *P. J.*, xxi, 1068.)

Ethylene Diamine. (*Ethane diamine.*) $CH_2(NH_2).CH_2(NH_2)$.—It is a colorless, thick liquid having the sp. gr. 0.87, boiling at 117° C., having a strong alkaline reaction, an ammoniacal odor and a caustic taste. It is said to be a noncorrosive solvent for false diphtheritic membranes. used in a diluted form. A solution in water of 25 per cent. of *ethylene diamine* and 25 per cent. of trikresol is sold under the proprietary name of *kresamine,* to be used in dilutions of from 2 to 25 per cent. A silver preparation of ethylenediamine used under the name of *Argentamin,* which see under the name of *Euphyllin,* a derivative of ethylene diamine, has been used by Addicks (*D. A. K. M.*, July 25, 1922) to increase the coagulability of the blood in *internal hemorrhages.*

Ethylene Dichloride. *Bichloride of Ethylene. Dutch Liquid. Æthyleni Bichloridum. Æthylenum Chloratum. Elaylum Chloratum. Liquor Hollandicus. Æthylenchlorid, Elaylchlorid,* G. $C_2H_4Cl_2$.—By the mutual action of chlorine and olefiant gas an oily liquid is obtained, discovered by four associated Dutch chemists, and called *Dutch liquid.* Aran found that the monochlorinated Dutch liquid (*monochlorethylene chloride,* $CH_2Cl,CHCl_2$) had a useful anesthetic power, but its cost proved to be too high to allow of its general use at that time as a therapeutic agent. In consequence of this objection to the monochlorinated liquid, Mialhe and Flourens were induced to search for a substitute in the corresponding compound of a parallel series of ethers, formed by the action of successive portions of chlorine on hydrochloric ether, C_2H_5Cl; under these circumstances the hydrogen is replaced by the chlorine, atom for atom, and there are formed the five following compounds: $C_2H_4Cl_2$; $C_2H_3Cl_3$; $C_2H_2Cl_4$; C_2HCl_5; C_2Cl_6. Of this series, the first four members are isomeric with the corresponding Dutch liquid; and the fifth is a chloride of carbon, frequently called *carbon sesquichloride.* The first member, though identical with the Dutch liquid in elementary composition and having a vapor of the same density, has, nevertheless, a lower boiling point, *i.e.*, 60° to 64° C., while the Dutch liquid boils at 84.9° C.; it is also different in chemical properties. The Dutch liquids were chlorides of ethylene while those of Mialhe and Flourens belonged to the ethylidene series.

Mialhe and Flourens proposed the use of the mixed ethers, consisting principally of the tri- and quadrichlorinated compounds, as an anesthetic, under the indefinite name of *chlorinated muriatic ether.* Taube (*A. J. P.*, 1880, 603, and 1881, 119) proved the availability as anesthetics of monochlorethylidene chloride, CH_3,CCl_3, and of monochlorethylene chloride, $CH_2Cl,CHCl_2$.

The precise action of the various esters upon the organism is unknown. The committee of the British Association found (*B. M. J.*, i, 1879) the *ethene dichloride* ("formerly named *ethylene dichloride,* or Dutch liquid, $C_2H_4Cl_2$") to cause convulsions in the lower animals, while E. T. Reichert (*P. M. T.*, xi, 518) found that "ethylene dichloride" produces anesthesia with the usual stages, and that, like chloroform, it depresses the heart and steadily lowers the arterial pressure. His experiments seem to show, however, that its action upon the heart is much less powerful than that of chloroform, and in all of its trials the animal died of centric respiratory paralysis while the heart was still maintaining some degree of circulation. He believes, therefore, that it is a much safer agent than chloroform, ranking it between the latter and ether. It is evident that Reichert was not using the same agent as the English committee were, but exactly what he did have is uncertain. Dr. A. W. Wallace found ethylene dichloride useful in dermatological practice. (*P. J.*, 1910, 787.)

Ethylidene Chloride, *Chlorinated hydrochloric ether, Alphadichlorethane Ethidene bichloride* $CH_3,CHCl_2$), is a colorless, very mobile, neutral liquid, having an aromatic ethereal odor, and a hot, saccharine taste. It is sparingly soluble in water, but readily soluble in alcohol, ether, and most of the fixed and volatile oils. It is not inflammable, is of sp. gr. 1.174 at 17° C., and boiling at 60° C. It can be distinguished from chloroform in that it combines with chlorine even in the dark, liberating hydrochloric acid. The British Association Committee (*B. M. J.*, 1879, i) believed it to be a valuable anesthetic, and it was tried on human beings by Snow and by Binz with satisfaction (*M. T. G.*, 1879, i); but Reeve finds (*N. R.*, 1880, 334) that in animals it lowers the arterial pressure, and it has failed to obtain general recognition.

Eucaine Lactate, *Beta-eucaine Lactate* ($C_{15}H_{21}.NO_2.CH_3.CH(OH).COOH$.—A white, non-hygroscopic powder, melting at 155° C. and soluble in water and alcohol. Its solutions are non-irritating and are employed in the same manner as those of betaeucaine hydrochloride.

Eucalyptus Manna. *Australian Manna.*—This substance exudes during the summer months from punctures made in the bark and leaves of the Australian tree, *Eucalyptus viminalis* Labill. (Fam. *Myrtaceæ*). It occurs in small round opaque masses, and is said medicinally to resemble ordinary manna. It contains melitrose. A similar manna is also formed on *Eucalyptus Gunnii* Hook. The "*blue-grass manna*" of Australia occurs on the stems of *Andropogon annulatus* Forsk. (Fam. *Gramineæ.*) The latter contains 75 per cent. of mannite.

Eucatropine, *Eucatropina, Euphthalmine, N. N. R.* 1924, Phenyl-glycolyl-methyl-vinyl-diacetinalkamine hydrochloride. The 1-2-6-6-tetra-methyl-4-mandeloxy-piperidine hydrochloride.—A white granular, odorless powder, permanent in air, soluble in water, alcohol and chloroform. Insoluble in ether. Melting point above 183° C. It is used in ophthalmoscopic examinations in place of atropine.

When instilled into the eye in strengths of 2 to 5 per cent., euphthalmine hydrochloride causes a marked dilatation of the pupil, which begins in about fifteen minutes, reaches its maximum in about one hour, then slowly disappears and the eye completely recovers in about twenty-four hours. According to Jackson (*Ophthalmic Record*, July, 1899), there is a partial but not complete paralysis of accommodation from the 5 per cent. solution of the drug. It is relatively non-irritant to the conjunctiva, although its repeated use may produce conjunctivitis. It is not locally anesthetic. Its value in ophthalmology depends upon the comparatively short duration of the mydriasis and its relatively low toxicity. Mironescu (*Th. M.*, 1905) found that the lethal dose for the rabbit is about one gramme per kilo subcutaneously. The same author also asserts that it differs markedly from atropine in that it slows the pulse instead of accelerating it.

Eucerin.—This is a mixture of 5 parts of an oxy-cholesterin obtained from wool fat with 95 parts of paraffin. As put upon the market it is usually combined with equal parts of water. It is intended as an ointment base and is said to penetrate the skin with great readiness.

Eucodin. *Eucodeine Codeine Brom-methylate. Methyl-codeine Bromide.* $C_{18}H_{21}O_3N(BrCH_3)$.—A crystalline product, melting point 261° C. and soluble in slight proportions in water. *Eucodin* is asserted to stimulate the respiratory center, but allays bronchial irritation and acts as a general analgesic without narcotic action. Eucodin gives a bluish-green color when added to a solution of formin in sulphuric acid. It is employed in *phthisis* and *coughs* in *doses* of one grain (0.065 Gm.) several times a day.

Eugenia Cheken Hook. et Arn. (*Myrtus Cheken* Spreng.) *Cheken. Chequen Arrayan.* (Fam. *Myrtaceæ.*)—The leaves of this Chilian plant have entered commerce under the name of *Chekan leaves.* Weiss (*A. Pharm.*, 1888, p. 226) has found in them: (1) *chekenon*, $C_{40}H_{44}O_8$, a crystalline body; (2) *chekenin*, $C_{12}H_{11}O_3$, in yellowish rhombic tables; (3) *chekenetin*, $C_{11}H_7O_6 + H_2O$, in olive-colored crystals; (4) *cheken-bitter*, an amorphous, very soluble bitter substance. (See *P. J.*, 1889, 782, and Wein, *A. Pharm.*, 1888, 665.) The leaves are used in their native country as a remedy in *chronic respiratory catarrh*, and have been strongly recommended by Murrell and others in *chronic bronchitis.* Their virtues appear to reside in the tannin, and especially in the volatile oil that they contain. The *dose* of the fluidextract is from one to three fluidrachms (3.9–11.6 cc.).

Eugenia Jambolana Lam. (*Syzygium Jambolana* Lam.) *Jambul. Jambol. Rose Apple. Java Plum.*—This is a large tree belonging to the *Myrtaceæ*, growing in East India and also in Queensland; well known on account of its edible fruit. The bark and seeds are employed in medicine. *Jambul bark* is a dense, hard bark, about 1.5 cm. in thickness, of a pinkish-brown or reddish-brown color, with a whitish-gray mottled cork or thick bark, the inner surface is of a somewhat silky luster, frequently coarsely marked by waving lines or ridges; the fresh fracture varies from pinkish or purplish to fawn color, sometimes distinctly but shortly fibrous, more commonly absolutely abrupt. The taste is somewhat bitter, astringent, after a time distinctly pungent. The bark contains a resin, tannin, and gallic acid. *Jambul seeds* are grayish-black, or blackish-gray, being abruptly truncated at the base, above rounded or dome-shaped. They are from 1 to 2.5 cm. long, and 8 to 12 mm. broad; so hard and dense that they cannot be chewed, and are almost tasteless. The analysis of the seeds by Thomas Christy yielded a trace of volatile oil, but no other characteristic products. Power and Callan (*P. J.*, 1913, 245) found in these seeds a phenolic substance, *jambulol*, $C_{16}H_3O_4(OH)_5$, which is identical with *ellagic acid.* An alkaloid *jambosine*, melting point 77° C., is also present.

In 1886 Binz announced that the exhibition of jambul to dogs who were glycosuric as the result of the administration of phloridzin greatly reduced the excretion of sugar. In 1888 Christy found that jambul increased the activity of the diastasic enzyme. As a result of these studies the drug was at one time used in the treatment of *diabetes* but as it is to-day generally conceded that phloridzin glycosuria is due to the action of the poison upon the kidney and is not allied to true diabetes, the theoretical foundation for the use of jambul falls to the ground, and practically it has failed to establish its value. In India the drug has been used for its astringent and stimulating effect in *diarrhea.* The *dose* of the fluidextract usually recommended is ten minims (0.6 cc.); but according to von Noorden (*Deutsche Praxis*, 1901) half a fluidounce (15 cc.) of the fluidextract should be taken in eight fluidounces (240 cc.) of hot water, one hour before breakfast and late in the evening.

Jamrosin is a proprietary preparation asserted to be the fluidextract of jambul. It is alleged to possess marked remedial qualities in the treatment of *diabetes*.

Euguform.—*Acetylized methylene diguaiacol* is obtained by the action of formaldehyde upon guaiacol and subsequent acetylization. It is a white, almost odorless, dust-like and amorphous powder, insoluble in water. It has been recommended by Ciesielski as a substitute for orthoform, as a dusting powder or in the form of a 2 to 10 per cent. ointment. A 50 per cent. solution of *euguform* in acetone is marketed as *neo-euguform*. (*Derm. Cb.*, 1901, No. 6; see also *M. R.*, 1912.)

Euphorbia. *Spurge. Wild Ipecac. Wild Hippo. Euphorbe*, Fr. *Wolfsmilch*, G.—The genus *Euphorbia* (Fam. *Euphorbiaceæ*) contains numerous species which contain a white milk-juice characterized by containing dumbbell-shaped starch grains. They are herbaceous or shrubby, with or without leaves, and the leafless species, which are chiefly confined to the African deserts, have fleshy, naked, or spiny stems, like those of the cactus. Their flowers are monoecious and placed within a cup-shaped, 4- to 5-lobed involucre. They nearly all afford products which act powerfully as emetics and cathartics, and in overdoses occasion dangerous if not fatal prostration, with symptoms of inflammation of the gastro-intestinal mucous membrane. Their milky juice, which concretes on exposure, usually possesses these properties in a high degree, and, in addition, that of powerfully irritating the skin when applied to it. The U. S. Pharmacopœia formerly recognized the indigenous species *E. corollata* L. (*Flowering Spurge*) and *E. Ipecacuanhæ* L. (*Wild Ipecac*). In a full dose the root of *E. corollata* L. acts as an emetic and cathartic and in smaller doses is a nauseating diaphoretic and expectorant. It is, however, too harsh and uncertain in its action for practical use, and has passed entirely out of vogue. The *dose* of the dried root as an emetic is from ten to twenty grains (0.65–1.3 Gm.), as a cathartic from three to ten grains (0.2–0.65 Gm.). The recent root, bruised and applied to the skin, produces vesication. C. Petzolt (*A. J. P.*, 1873) found in the root of *E. Ipecacuanhæ* a dark resin which in half grain (0.032 Gm.) doses produced watery stools, and in one and a half or two grain (0.096 or 0.13 Gm.) doses nausea and vomiting. It gave no evidence of the presence of an alkaloid. The medicinal properties of *E. Ipecacuanhæ* resemble those of *E. corollata*, though the former is said to be somewhat milder.

The indigenous *E. Preslii* Guss. (*E. hypericifolia* Gray) and *E. maculata* L. according to Zollickoffer is valuable in *dysentery, diarrhea, menorrhagia*, and *leucorrhea*. (See 16th ed., *U. S. D.*, also *A. J. M. S.*, xi.) The juice of *Euphorbia Drummondii* Boiss. is said in Australia to kill annually a great many sheep and cattle, and in 1886 John Reid (*Australasian Med. Gaz.*, No. 61) announced the discovery in it of a new anesthetic alkaloid, *drummine*, which he obtained in colorless crystals almost insoluble in ether, but freely soluble in chloroform and in water. The report of Alexander Ogsden (*B. M. J.*, Feb., 1887) throws, however, very grave doubts upon the anesthetic power of this new alkaloid. *Euphorbia cremocarpus* Auct. of the Pacific Coast is employed for the purpose of poisoning fish in still pools and streams, and is said to contain a volatile oil, besides acid and resins. (See *Proc. California Coll. Pharm.*, 1885.) The oil of *E. Lathyris* L. is stated to physiologically resemble croton oil. (*Proc. A. Ph. A.*, xxvi, 305.)

The *E. heterodoxa* Muell.-Arg., *alveloz* or *aveloz*, a Brazilian species, has been used with asserted extraordinary advantage against *cancerous* and *syphilitic ulcers*. It is a powerful irritant, and even mild caustic. The milky juice, preserved with salicylic acid, or a resin obtained by precipitating with water is employed. The ointment of the resin may be made 3 parts in 100 with vaseline. For further information concerning various euphorbia species which have been used in medicine, see *U. S. D.*, 19th edition, p. 1484.

The concrete resinous milk-juice of *Euphorbia resinifera* Berg, a fleshy cactus-like plant growing in Morocco, was formerly recognized by the German Pharmacopœia under the name of *Euphorbium*, P. G. (*Euphorbiumharz.*) The plant is characterized by having fleshy, quadrangular stems and branches which bear small scale-like leaves supported by two thorny stipules, small flowers and 3-carpelled fruits.

Laticiferous vessels containing a milky-juice occur in cortex and pith. The branches are wounded during the rainy seasons and the milky exudation is collected and dried by Arabs who bring it to Morocco. It is exported from Mogadore. The inspissated juice occurs in the shape of tears, or in oblong or roundish masses, about the size of a pea or larger, often forked, and perforated with one or two small conical apertures, produced by the prickles of the plant, around which the juice has concreted, and which sometimes remain in the mass. The surface is dull and smooth, bearing some resemblance to that of tragacanth; the consistence somewhat friable, the color light yellowish or reddish; the odor scarcely perceptible; the taste at first slight, but afterwards excessively acrid and burning. The color of the powder is yellowish. The sp. gr. of *euphorbium* is 1.124. Triturated with water it renders the liquid milky and is partially dissolved. Alcohol dissolves it about 60 per cent., forming a yellowish tincture, which becomes milky on the addition of water. The most abundant constituent is resin, and the remainder consists chiefly of wax and calcium malate. The resin is excessively acrid, is soluble in alcohol, and, when exposed to heat, melts, takes fire and burns with a brilliant flame, diffusing an agreeable odor. Flückiger (*A. J. P.*, 1868) also found a substance analogous to lactucon, which he named *euphorbon*, $C_{15}H_{24}O$. Tschirch and Paul made an investigation of euphorbium and found *euphorbic acid*, $C_{24}H_{30}O_6$, *euphorbin*, $C_{30}H_{48}O$, malic acid and a bitter, and also an acrid principle. (*A. Pharm.*, 1905, 249.)

Euphorbium taken internally is a very irritant emetic and cathartic, and in large doses acts as a violent gastro-intestinal irritant poison. In consequence of the severity of its action, its internal use has been entirely abandoned. Applied to the mucous membrane of the nostrils, it excites violent irritation, attended by incessant sneezing and sometimes bloody discharges. Persons who powder it are under the necessity of guarding their eyes, nostrils, and mouth against the fine dust which rises. Externally applied it inflames the skin, often producing vesication. It enters into some epispastic preparations, and is especially employed in veterinary practice as a vesicant. See also *Euphorbia pilulifera*, Part I.

Euphorin. *Æthylis Phenylcarbamas. Phenol—Urethane, Phenylcarbamic Acid Ethyl Ester.*

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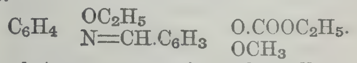
$(C_6H_5NH)CO(OC_2H_5)$.—It is in the form of colorless needles or a white powder, melting at 50° to 51° C., having a faint aromatic odor and taste, almost insoluble in water, readily soluble in diluted alcohol, alcohol or ether. It is used as an anodyne and antipyretic in *doses* of eight to fifteen grains (0.5–1.0 Gm.); also externally in *skin diseases, ulcers,* etc., either as a dusting powder or in an ointment.

Euphrasia. *E. officinalis* L. *Eyebright. Eyewort. Euphraise,* Fr. *Augentrost,* G. (Fam. *Scrophulariaceæ.*)—A small annual plant, native of Europe, without odor, and of a bitter, astringent taste. Enz (*Viertelj. f. Prakt. Pharm.*, viii, 175) obtained a little volatile oil, an acrid and bitter principle, mannite and glucose, and a tannic acid. The name "eyewort" so frequently ascribed to this drug, is derived from the practice of using it in eye affections in older medicine. It is used on the continent to-day as an astringent tonic in the treatment of *jaundice.* G. M. Garland (*A. J. P.*, 1890) states that ten minims (0.6 cc.) of a concentrated tincture every two hours is a specific in acute *nasal catarrh.*

Eupyrine. *Para-phenetidine-vanillin-ethyl-carbonate.*



$$C_6H_4\begin{matrix}OC_2H_5\\ N{=}CH.C_6H_3\end{matrix}\begin{matrix}O.COOC_2H_5.\\ OCH_3\end{matrix}$$

This substance occurs in pale yellow, tasteless needles, with a vanillin odor melting at 87° to 88° C., insoluble in water, sparingly so in cold alcohol, ether, and chloroform, but very soluble in these solvents when warmed. It forms salts by combination with a few acids, and is decomposed by some other acids and by all alkalies. It has been brought forward by Overlach (*Cb. I. M.*, xxi, 1900) as an antipyretic, who found that half an ounce of it causes no serious symptoms in dogs. He claims that it produces a gradual but marked fall of the temperature, accompanied by a sense of euphoria rather than of depression. In neuralgia he found that it was without influence. Porges has confirmed the statements of Overlach. The remedy is stated to be of special value in the young and the aged. *Dose,* twenty to thirty grains (1.3–2.0 Gm.).

Euresol. *N. N. R.* 1924. *Resorcin monoacetate. Monoacetyl Resorcinol.* $C_6H_4(OH)OCOCH_3$.—A viscid honey-like liquid, boiling at 283° C. It is made by heating resorcinol with glacial acetic acid. It is used as a substitute for resorcinol in the treatment of *seborrhea, sycosis* and other diseases of the skin. According to Joseph and Vieth (*Derm. Cb.*, 1905), it has the advantage over resorcinol in exercising a deeper influence, and being less irritant. It may be employed in strengths of from 5 to 10 per cent.

Eurobin. *Chrysarobin Triacetate.*—This is a yellowish-red powder, *triacetyl chrysarobin,* used as a substitute for chrysarobin; it is soluble in chloroform, acetone, and ether, insoluble in water. It acts like chrysarobin on the skin, but is more powerful. Kromayer commends it applied as a paint, according to the following formula: Saligallol, 5 to 10 parts; eurobin, 1 to 20 parts; acetone, to make 100 parts. *Lenirobin,* the tetracetyl derivative, *chrysarobin tetra-acetate,* is less irritant than chrysarobin, and has the special advantage of not staining the linen.

Neorobin is made by dissolving chrysarobin in glacial acetic acid and subsequent reduction with metallic tin. It is stated, however, that it is neither a complex acetate nor a tin compound but a primary reduction product. It dissolves in acetone with a golden yellow solution instead of dark red as does chrysarobin. According to Masucci and Slothower (*J. A. Ph. A.*, 1923, xii, 335) it is a more active reducing agent than chrysarobin.

All these preparations are used as local applications in *skin diseases,* especially *psoriasis.*

Europhen. *Di-isobutyl-ortho-cresol-iodide.* $C_6H_3(C_4H_9)\ (CH_3)\ (OI)C_6H_2(CH_3){:}O\ (.C_4H_9)$.—This is a yellow amorphous powder, of a specific aromatic odor, which has been proposed as a substitute for iodoform. It is asserted that it is five times lighter than iodoform, and can be used in much larger bulk; that it is equally efficacious with iodoform; also that it is decomposed more slowly than iodoform, and is, therefore, less poisonous. (See *Ph. Ztg.*, July, 1891; also *Th. M.*, July, 1891.) *Europhen* is made by the action of iodine upon isobutylorthocresol in alkaline solution. It occurs as a fine, soft, amorphous powder, light yellow, tasteless, and having but a faint odor. It is soluble in ether, chloroform, collodion, alcohol, and fixed oils; insoluble in water and glycerin; melting at 110° C. Its solution undergoes decomposition when exposed to light or heat.

Europhen contains about 28.1 per cent. of iodine, which element is slowly liberated from its alcoholic and ethereal solutions. It is incompatible with metallic oxides and mercurial salts, and undergoes slight change in the presence of organic matter. Taken internally it is said to pass out in great part from the alimentary canal with the feces unchanged, though some absorption takes place. It is asserted that it is non-toxic, two or three drachms (7.7–11.6 Gm.) having been given to dogs and fifteen grains (1 Gm.) to human beings without effect. As an antibacterial it is affirmed to be about equivalent to iodoform. (*Revue Méd. de l'Est,* Feb., 1892.)

It has been used by a number of clinicians with asserted good results as a local application in *chancres, syphilitic ulcers, burns, psoriasis, eczema, lupus,* and various *skin diseases.* It may be applied either as a dusting powder or in an ointment varying in strength from 1 to 10 per cent. It has also been employed in *rhinitis, laryngeal tuberculosis,* and other inflammatory disorders of the preliminary air-passages. Internally it has been used, especially hypodermically, dissolved in oil, in *constitutional syphilis,* with not very encouraging results. *Dose,* one-half to one and one-half grains (0.032–0.096 Gm.).

Euscopol. $C_{17}H_{21}O_4N.HBr$.—An optically inactive scopolamine hydrobromide. (See *Scopolaminæ Hydrobromidum,* Part I.)

Evodia.—Several species of this rutaceous genus are stated to have medicinal properties. *Evodia febrifuga* St. Hil. (*Esenbechia febrifuga* A. Juss.) of Brazil is astringent and tonic, *E. meliæfolia* Benth. of Japan contains berberine, while *E. longifolia* A. Rich. of the Fiji Islands is used to prevent abortion. The allied plant *E. Rutaecarpa* yielded to Asahina (*J. P. C.*, 1916, xiv, p. 54) two alkaloids—*evodiamine* and *rutaecarpine.*

Exalgine. *Methylacetanilide.* $C_6H_5N(CH_3)$-$COCH_3$ or $C_9H_{11}NO$.—This substance, which was discovered by Brigonnet, is one of the three isomeric methyl derivatives of acetanilide (*C. R. A. S.*, cviii, 571), and is made by warming together monomethylaniline and acetylchloride. It occurs in needles, or in long tablet-like crystals, sparingly soluble in cold water, quite soluble in hot water, and readily soluble in very dilute alcohol; it fuses at 101° C. and boils between 240° and 250° C. without decomposition. The hot aqueous solution is said by Upton to retain most of its exalgine on cooling.

According to Brigonnet, hypodermic injections of exalgine produce in the lower animals violent epileptiform convulsions, profuse salivation, cyanosis, disturbance of breathing, fall of temperature, and methemoglobinemia. When given to man in full, non-poisonous doses, it produces some slight amblyopia, vertigo accompanied in some patients by vomiting, tinnitus aurium, headache, drowsiness, and vasomotor disturbances, such as sweating. After toxic doses, dyspnea, cyanosis, dilated pupils, paresis, heart weakness, and convulsions have been noted, but we know of no fatal result; in a boy fourteen years old two doses of three grains each produced most alarming symptoms.

Therapeutically, exalgine has been used as an analgesic and antispasmodic. According to Moncorvo, it is very well borne in children; he has used it extensively in *chorea*, *polyuria*, and for the relief of *pain*. He believes that its analgesic effect is at least five times as strong as that of antipyrine. *Dose*, for an adult, three to five grains (0.2 to 0.32 Gm.), not more than twelve grains to be given in twenty-four hours.

Exodin.—This is stated to be a hexamethylester of rufigallic acid. *Rufigallic acid* or *rufigallol*, which is manufactured by heating gallic acid with five times its weight of strong sulphuric acid, is a hexahydroxy-anthraquinone. Exodin, therefore, bears some chemical relation to the principles found in the vegetable cathartics. It occurs as a yellow, odorless, tasteless powder, insoluble in water. It has been used with satisfactory results by a number of clinicians as a cathartic, especially in chronic constipation. It is claimed for it that it is non-irritant and does not produce after constipation. The *dose* is from fifteen to thirty grains (1 to 2 Gm.), usually given in the form of tablets.

Fabiana. *Fabiana imbricata* Ruiz and Pavon. *Pichi.* (Fam. *Solanaceæ.*)—This is a small shrub growing in Bolivia, Peru, Chili and the Argentine Republic. The plant somewhat resembles a juniper. The branches are brownish-gray and about 5 mm. in diameter; the wood is yellowish and tough; leaves scale-like, about 1 mm. in length, closely imbricated and bluish-green; the flowers are about 12 mm. in length and possess a white or purplish corolla; the fruit is a capsule containing a few sub-globular seeds. The odor of the drug is aromatic and the taste bitter and terebinthinate. For microscopic structure, see *Ph. Ztschr. f. Russland*, 1891, No. 44; *Apoth. Ztg.*, 1892, p. 22.

A. B. Lyons obtained from it a fluorescent body resembling æsculin, a neutral crystalline principle, some volatile oil, resin, and apparently traces of an alkaloid. (*A. J. P.*, 1886, 65.) Henry Trimble and J. M. Schroeter (*A. J. P.*, 1889, 407) considered the crystalline principle to be a resin, and gave it the formula $(C_{18}H_{31}O_2)x$. H. Kunz-Krause (*A. J. P.*, 1900, p. 80) made a full study of pichi and found a tannin which he named *fabiana-tannoid*, a fluorescent substance proven to be *chrysatropic acid* (*β-methyl æsculetin*), $C_9H_5(CH_3)O_4$, while no alkaloids are present, the sole basic principle being choline. The volatile oil he names *fabianol* and gives it the formula $C_{54}H_{90}O_2$. The resin he calls *fabiana resin* and gives to it the formula $(C_{18}H_{30}O_2)_3$. The resin appears in microscopical crystals, melting at 280° C. The tannin proved to be like caffetannic acid.

Pichi appears to belong with the terebinthinate diuretics and has been used to a considerable extent in the treatment of both acute and chronic *cystitis* and in gonorrheal *prostatitis*. It was formerly attributed with cholagogue properties. It is somewhat irritating and must be used very cautiously in cases of inflammatory conditions of the kidney. The solid extract may be used in the *dose* of from two to ten grains (0.13–0.65 Gm.); the fluidextract, in the *dose* of from ten to forty minims (0.6–2.5 cc.).

Fanghi di Sclofani.—This is a light yellowish fine powder of volcanic origin, consisting chiefly of sulphur and small quantities of iron, manganese, calcium, etc., the sulphur being in an exceedingly fine powder. It is highly praised by Otto v. Fleischl as a remedy in *acne rosacea*. Two or three grains (0.13 or 0.2 Gm.) of the powder are mixed with a teaspoonful (4 cc.) of water and the opaque mixture applied with the finger on going to bed and allowed to dry on the part.

Ferioben. *Ferro-sajodin. N. N. R.* 1924. *Basic ferric iodo behenate* (approximately $(C_{21}H_{42}I\text{-}COO)_2(OH)Fe$) representing at least 5 per cent. of iron and 25 per cent. of iodine. It exhibits the action of iodide and of iron and is claimed to be more stable and palatable than ferrous iodide. *Dose*, eight to fifteen grains (0.5–1 Gm.).

Ferment Diagnosticum. *N. N. R.* 1924. *Solution of Glycyltryptophan.*—This solution is used in determining the presence of a proteolytic ferment on account of its being split up by such ferments with the liberation of *tryptophan*, which may readily be detected.

Ferratin. *Sodii Ferri Albumas.*—This is a light brown powder containing from 6 to 8 per cent. of iron in a form soluble in alkaline liquids. It is an albuminous compound, originally prepared by Schmiedeberg from the liver of the hog, and believed to be the natural compound of iron as it exists in the system. It is now made by the reaction of the albumin with a double tartrate of iron and an alkali. It is almost insoluble in water, soluble in alkalies, and contains 7 per cent. of iron in organic compounds. The iron is firmly united to the albumen molecule so that ammonium sulphide does not react at once. A solution of ferratin has also been put upon the market under the name of *ferratose*.

Ferratin may be given in *doses* of from three to five grains (0.2–0.32 Gm.) three times a day. It appears to be capable of acting as a chalybeate, but there is no sufficient reason for believing it to be superior to the older preparations of iron.

Ferratogen. *Ferri Nucleinas.*—This substance is obtained by the cultivation of yeast on a ferruginous nutritive medium and subsequent extraction. It occurs as a grayish-white or yellow powder, insoluble in water or gastric juice, but believed to be dissolved by pancreatic fluids. The content of iron is claimed to be slightly over 1 per cent. It has been recommended by Cloetta in *chlorosis* when the stomach is delicate. *Dose*, five to ten grains (0.32–0.65 Gm.).

Ferric Albuminate. *Ferri Albuminas.*—This preparation has come into some prominence, more particularly in Europe, on account of its asserted advantages over various other compounds of iron, Démarquay, Chrisnard, and others recommending its employment in *chlorosis* and *anemia*, as being very readily absorbed. Various methods have been proposed for preparing either the solution or dry salt. C. L. Diehl, after a careful review of these processes, offers the following: 4 troyounces of white of eggs are diluted with 8 fluidounces of water; 65 minims of official solution of ferric chloride diluted with 4 fluidounces of water are added, and the solution filtered. The filtrate is now mixed with 10 fluidounces of a saturated solution of sodium chloride, the precipitate collected on a wet muslin strainer, washed with a mixture of 1 volume of the saturated solution of sodium chloride and 3 volumes of water, until the washings give but a faint reaction for iron. The washed ferric albuminate is, after draining, powerfully pressed to get it as dry as possible, and then exposed to a dry atmosphere, and finally powdered. This salt contains the equivalent of 5 per cent. of ferric oxide, or 10 per cent. of ferric chloride. (For other processes, see *A. J. P.*, 1880, 177.) As thus obtained, ferric albuminate is a cinnamon-brown powder, having a slight saline taste, soluble in water, particularly if slightly acidulated with hydrochloric acid. It is best administered in *doses* of from twenty to thirty grains (1.3–2.0 Gm.) in simple aqueous solution, which should be freshly prepared. See *Liquor Ferri Albuminati, N. F.* (Part III). For method of preparing *iron and potassium albuminate*, and *iron and sodium albuminate*, see 16th ed., *U. S. D.*

Ferric Ammonium Chloride. *Iron Ammoniated. Ammoniated Iron. Ferrum Ammoniatum. Ammonio-chloride of Iron. Ammonii et Ferri Chloridum. Ammonium Chloratum Ferratum. Sel Ammoniac Martial*, Fr. *Eisensalmiak*, G.—This drug was formerly recognized both by the U. S. and London Pharmacopœias, which contained formulas for its preparation. (See *U. S. D.*, 15th edition, 1568.) There is no reason to believe that the ferric chloride and ammonium chloride are chemically combined in the preparation. According to Phillips, they are in the proportion of 15 parts of the iron to 85 of the ammonium salt.

Ammoniated iron is in crystalline grains of a fine reddish-orange color, and a sharp, styptic, saline taste. It is entirely soluble in water and diluted alcohol, is deliquescent, and should be kept in well-stoppered bottles. As procured by sublimation (*Flores martiales, Ens martis*), it is of a yellow color and feeble odor. It unites aperient with chalybeate properties, and is said to have been used with advantage in *amenorrhea, epilepsy, scrofula, rickets*, etc.; but it is at best uncertain, and is now very seldom prescribed. *Dose*, from four to twelve grains (0.26–0.78 Gm.).

Ferric Ammonium Sulphate. *Ferri et Ammonii Sulphas. U. S. VIII. Iron and Ammonium Sulphate. Ammonio-Ferric Alum. Iron Ammonium Alum. Ferrum Sulfuricum Oxydatum Ammoniatum. Ferrum Ammonio-Sulphuricum. Ferri Ammonio-Sulphas. Alumen Ammoniacale ferricum. Iron Alum. Sulfate de Fer et d'Ammoniaque. Alun de Fer ammoniacal.* Fr. *Schwefelsaures Eisenoxyd-Ammonium. Ammoniakalischer Eisenalaun*, G. $FeNH_4(SO_4)_2 + 12H_2O = 482.21$.—The *U. S.*, 1870, gave the following process for this salt: "Take of Solution of Tersulphate of Iron *two pints;* Sulphate of Ammonium *four troy-ounces and a half.* Heat the Solution of Tersulphate of Iron to the boiling point, add the Sulphate of Ammonium, stirring until it is dissolved, and set the liquid aside to crystallize. Wash the crystals quickly with very cold water, wrap them in bibulous paper, and dry them in the open air." *U. S.*, 1870.

Ammonio-ferric alum is in "pale violet, octahedral crystals, without odor, and having an acid, styptic taste; efflorescent on exposure to the air. Soluble in 2.7 parts of water at 25° C. and in 0.8 part of boiling water; insoluble in alcohol. When strongly heated, the crystals fuse, lose their water of crystallization, expand, and finally leave a pale brown residue. The aqueous solution of the salt has an acid reaction upon blue litmus paper, and yields with potassium ferrocyanide T.S. a blue precipitate, and with barium chloride T.S. a white precipitate insoluble in hydrochloric acid." *U. S. VIII.* According to H. Rose, the pure salt is white, and gives a colored solution with water, in consequence of the formation of a basic ferruginous salt. This decomposition is prevented by dissolving it in diluted sulphuric acid, when the solution is colorless. Instead of ammonium sulphate, potassium sulphate may be employed with the solution of ferric tersulphate, in which case a potassium iron-alum is produced, called *potassio-ferric alum*, which has all the properties, physical and remedial, of the ammonio-ferric salt, and the two appear to have been indiscriminately used.

The iron-alum is an active astringent and was used chiefly as a local application in passive *leucorrheas*, and as a styptic.

Dose, from five to ten grains (0.32 to 0.65 Gm.).

Ferric Ammonium Tartrate—*Iron and Ammonium Tartrate. Ferri et Ammonii Tartras. U. S. VIII. Ferrum Tartaricum Ammoniatum. Ammonio-Tartrate of Iron. Tartrate Ferrico-ammonique*, Fr. Cod., Fr. *Weinsaures Eisenoxyd-Ammonium*, G.—This iron scale-salt should contain Iron and Ammonium Tartrate corresponding in amount to not less than 13 per cent. of metallic iron.

The process of the U. S. P., 1890, for preparing iron and ammonium tartrate was: "Solution of Ferric Sulphate, *one hundred cc.;* Tartaric Acid, *twenty-nine grammes;* Distilled Water, *two hundred cc.;* Ammonia Water, Water, each, *a sufficient quantity.* To *one hundred and ten cc.* of Ammonia Water, previously diluted with *two hundred and fifty cc.* of cold Water, add with constant stirring, the Solution of Ferric Sulphate, previously diluted with *thirteen hundred cc.* of cold Water. When the precipitate has subsided, draw off the clear, supernatant liquid by means of a siphon, then mix the precipitate intimately with about *fifteen hundred cc.* of cold Water, again draw off the clear liquid, and repeat the washing with Water in the same manner until the decanted liquid gives not more than a slight cloudiness with barium chloride test-solution. Then transfer the precipitate to a wet muslin strainer, allow it to drain, and express the water as completely as possible. Dissolve one-half of the Tartaric Acid in the Distilled Water, neutralize the solution exactly with Ammonia Water, then add the other half of the Tartaric Acid, and dissolve it by the application of a gentle heat. Now add the moist ferric hydrate, in successive portions, stirring constantly, and continue the heat, which should not exceed 60° C., until the hydrate is dissolved. Filter the solution while hot, evaporate it in a porcelain vessel, at or below the above-mentioned temperature, to the consistence of syrup, and spread it on plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in well-stoppered bottles, protected from light." *U. S.*, 1890.

Theoretically this process should yield a double salt consisting of one molecule of tartaric acid and two molecules of base, one of ammonia and the other of ferric oxide $2(FeO)NH_4.C_4H_4O_6.3H_2O$. It is hardly probable that the salt has exactly this chemical composition, as the scaled salts cannot be said to be definite compounds.

This compound is in "thin, transparent scales, varying in color from garnet-red to reddish-brown, without odor, and having a sweetish, slightly ferruginous taste; slightly deliquescent in the air. Very soluble in water; insoluble in alcohol." *U. S. VIII.* For further tests for this salt see *U. S. D.*, 20th edition, p. 1445. *Dose*, as a mild chalybeate, from five to ten grains (0.32–0.65 Gm.).

Ferric Arsenate. $Fe_3(AsO_4)_2 + 6H_2O$.—*Iron arsenate* is a green, amorphous powder, insoluble in water, but soluble in the presence of dilute mineral acids. It is used as an insecticide especially for agricultural purposes, and may be employed in strengths of from 0.1 to 0.2 per cent.

Ferric Arsenite. *Arsenite of Iron. Iron Arsenite.* $4Fe_2O_3As_2O_3 + 5H_2O$.—This is a brownish-yellow powder soluble in acids and insoluble in water, but the combination with ammonium citrate is soluble and has been put upon the market under the name of *ammoniated citro-arsenite* of iron. *Ferr-arseno-citras Ammoniatus.* This represents about 16 per cent. of iron and 1.4 per cent. of arsenous acid. It is used in the treatment of various forms of *anemia* but is especially commended in *pellagra.* It has been highly commended by Valvassori and Peroni (see *M. R.*, 1900) for the hypodermic treatment of *malaria*, especially in children. It may be given either by the mouth or hypodermically. The *dose* for the latter purpose is from one-half to one grain (0.032 to 0.065 Gm.) every second or third day.

Ferric Benzoate. *Ferri Benzoas. Ferrum Benzoicum. Eisenbenzoat, Ferribenzoat,* G.—$Fe_2(C_7H_5O_2)_6 + nH_2O$.—This is made by precipitating a solution of ammonium benzoate with a diluted solution of ferric chloride. The precipitate, after being washed, is dried at a temperature not above 30° C., protected from light. A brownish-red, odorless, tasteless powder, insoluble in water. When freshly prepared it is soluble in cod liver oil.

Ferric Citrate. *Ferri Citras. U. S. VIII. Iron Citrate. Citras Ferricus. Citrate Ferrique,* Fr. *Ferrum Citricum Oxydatum,* P. G. *Citronensaures Eisenoxyd, Eisencitrat,* G. *Citrato di ferro,* It. *Citrato ferrico,* Sp.—"It should contain Ferric Citrate corresponding in amount to not less than 16 per cent. of metallic iron, and should be kept in well-stoppered bottles, protected from light." *U. S. VIII.* This preparation is made by evaporating a solution of ferric citrate. The latter was dropped from the U. S. P., but is now official in the National Formulary IV (see Part III).

Ferric Citrate is not a definite chemical salt, but a compound containing ferric citrate, to which the following formula has been assigned: $Fe_2(C_6H_5O_7)_2.6H_2O$. The U. S. P. required not less than 16 per cent. of metallic iron. It is important, in making it, that an excess of citric acid be avoided, and the ferric hydroxide be thoroughly washed to free it from sulphates, otherwise brilliant scales will not be formed.

Ferric citrate is in "thin, transparent, garnet-red scales, without odor, and having a slightly ferruginous taste. Slowly but completely soluble in water at 5° C., and readily soluble in hot water, but diminishing in solubility with age; insoluble in alcohol." *U. S. VIII.* For further tests of this salt see *U. S. D.*, 20th ed., p. 1387.

Ferric citrate is an excellent chalybeate, nearly free from astringency and is preferably given in solution. Bullock (*J. A. M. A.*, 1911, lvii, p. 1428) has had most excellent results in the *anemia* of *tuberculosis* from the hypodermic use of this salt. He injected one grain (0.065 Gm.) directly into the muscle substance daily. (See also *Ferri et Ammonii Citras*, Part I.)

Dose, by mouth, three to ten grains (0.2–0.65 Gm.).

Ferric Hydroxide. *Ferri Hydroxidum. Ferri Oxidum Hydratum. Ferric Hydrate. Hydrated Oxide of Iron.* $Fe(OH)_3 = 106.86$. *Ferri Peroxidum. Ferri Sesquioxidum. Ferri Oxidum Rubrum. Hydrous Peroxide of Iron. Ferric Oxyhydrate. Ferrugo. Hydrated Peroxide of Iron. Hydrated Sesquioxide of Iron. Moist Peroxide of Iron. Hydras Ferricus. Oxyde (sesqui) de fer Bihydraté,* Fr. Cod. *Sesquioxide (Péroxide) de Fer hydraté humide, Hydrate de Péroxyde de Fer gélatineux,* Fr. *Eisenoxydhydrat, Gegengift der Arsenigensaure,* G. *Ossido ferrico idrato,* It. *Hidrato ferrico gelatinoso,* Sp.—Under the name of *Magma Ferri Hydroxidi* the N. F. recognizes a mixture containing the washed precipitate formed by mixing a solution of ferric sulphate with ammonia water, which is essentially the same as the preparation recognized by the U. S. VIII under the name of *Ferri Hydroxidum.* "This is a brownish-red magma wholly soluble in hydrochloric acid without effervescence." *U. S. VIII.* In preparing this it is important that the solution of ferrous sulphate be poured into the ammonia solution and not vice versa as when the ammonia water is added to the iron solution there is formed a clotty precipitate of uncertain composition.

As prepared by the old process of the Dublin Pharmacopœia, in which it was heated to redness, it lost the second molecule of water, and became the anhydrous sesquioxide (Fe_2O_3), identical with the *colcothar* of commerce. This is less easily soluble in acids, and altogether without effect as an antidote. Kept for some time in the moist state, it loses half its combined water, and becomes less soluble in acids and less efficient as an antidote. Hirsch has given some useful details in making precipitated ferric oxide upon a comparatively large scale, in *Am. Drug.*, 1884, 66.

The *monohydrated sesquioxide* is a reddish-brown, tasteless, insoluble powder, differing from colcothar in containing a molecule of water. Hence, "heated to dull redness in a test-tube it yields about 10 per cent. of moisture." *Br.*, 1885. It should not be deliquescent, and should dissolve entirely in hydrochloric acid without effervescence. Its solution in diluted hydrochloric acid yields a copious blue precipitate with potassium ferrocyanide, but none with the ferricyanide, showing that it contains ferric oxide but no ferrous oxide. Dawies states that if the hydrated oxide recently prepared be kept for four days in boiling water it loses a large proportion of its water, containing at the end of that time only 5.77 per cent.; the larger portion of the oxide has, therefore, become dehydrated, and the same thing happens at a lower temperature, 41.1° C., as in two or three months it becomes of a brick-red color, and is but slightly soluble in nitric acid. (*J. P. C.*, 4e sér., iv, 400.) Ferric Hydroxide is not an eligible ferruginous medicine; its sole therapeutic use is as an antidote to arsenic and for this purpose it is inferior to the pharmacopœial *Ferri hydroxidum cum magnesii oxido.* It was an ingredient in the *Emplastrum Ferri* (*iron plaster*) and the *Trochisci Ferri, U. S.*, 1890. The former Dublin *rubigo ferri*, or *rust of iron*, formed by exposing moistened iron wire to the air until converted into rust, is essentially the sesquioxide, containing a little ferric carbonate, and does not differ materially from the iron subcarbonate formerly official.

Ferric Oxide, Magnetic. *Ferri Oxidum Magneticum. Magnetic Iron Oxide. Martial Ethiops. Ferrum Oxydatum Magneticum. Oxydum Ferroso-Ferricum. Black Iron Oxide. Oxyde de Fer noir* (*magnétique*), *Oxyde ferroso-ferrique*, Fr. *Magneteisen, Eisenoxyd-Oxydul*, G. $Fe_3O_3(OH)_2$.—The artificial magnetic iron oxide is a brownish-black powder, without taste, and strongly magnetic. It dissolves without effervescence in hydrochloric acid diluted with half its bulk of water, and the solution gives a blue precipitate both with the potassium ferrocyanide and the potassium ferricyanide, showing the presence of ferrous and ferric oxide. *Dose*, from five to twenty grains (0.32–1.3 Gm.).

Scales of iron (*ferri squamæ*) were formerly official with the Dublin College under the name of black oxide. They were prepared from the scales found at the blacksmith's anvil, by washing them with water, separating them from impurities by means of a magnet, and reducing them to a fine powder. They are of variable composition, being mixtures of the two oxides of iron with metallic iron.

The magnetic iron stone has been introduced as a substitute for bismuth salts in röntgenological examination of the intestinal tract. Alexander (*D. M. W.*, 1909, p. 877) especially recommends a mixture of iron oxide with cocoa and milk sugar, known as *diaphanit.*

Ferric Salicylate. *Ferri Salicylas. Ferrum Salicylicum. Ferrisalicylat*, G.—Made by adding sodium salicylate to a concentrated solution of ferric chloride. The violet-colored precipitate, when washed and dried, forms a brown mass or powder insoluble in water. It is sometimes used as a tonic and antirheumatic in *doses* of from three to ten grains (0.2–0.65 Gm.). The N. F. recognizes a solution containing iron salicylate (see *Liquor Ferri Salicylatis*).

Ferric Subcarbonate. *Ferri Subcarbonas. U. S.* 1870. *Iron Subcarbonate. Red Oxide of Iron. Precipitated Carbonate of Iron. Aperitive Saffron of Mars.*—Ferric carbonate is a reddish-brown powder, of a disagreeable slightly styptic taste, insoluble in water, and not readily dissolved by any acid except hydrochloric, with which it effervesces slightly. When of a bright red color it should be rejected, as this color shows that it has been injured by exposure to heat. After precipitation from its hydrochloric solution by ammonia or potassium hydroxide, either of which throws down ferric oxide, the supernatant liquor should give no indications of containing any metal in solution by the test of hydrogen sulphide or potassium ferrocyanide. It is incompatible with acids and acidulous salts. In composition it is a hydrated ferric oxide containing a little ferrous carbonate. By exposure to a red heat, it absorbs oxygen and loses water and carbon dioxide, being converted into the *astringent saffron of Mars* of the French Codex.

Ferric carbonate is a rather feeble ferruginous tonic, nearly free from astringency. It has been especially commended in *neuralgia* in doses of a teaspoonful. *Dose*, five grains (0.32 Gm.).

Ferric Magnesium Citrate. *Iron and Magnesium Citrate. Ferri et Magnesii Citras.*—This double salt, introduced by Van der Corput, is made by dissolving two ounces of freshly precipitated ferric hydroxide in a moderately heated solution of three ounces of citric acid, and saturating the liquor with magnesium carbonate. The solution, after filtration, is evaporated by means of a water bath to a syrupy consistence, and spread on glass to dry in scales. Three and a quarter ounces of ferrous sulphate will furnish by decomposition the necessary hydroxide for three ounces of the acid. This salt is in transparent, greenish-yellow scales, having a slightly ferruginous, somewhat acid taste. It is very soluble in water, but insoluble in alcohol and ether. *Dose*, from five to ten grains (0.32–0.65 Gm.).

Ferric Strychnine Citrate, Iron and Strychnine Citrate. *Ferri et Strychninæ Citras. U. S. VIII. Citrate de Fer et de Strychnine*, Fr. *Citronensaures Eisen-Strychnin*, G.—"It should contain not less than 0.9 nor more than 1 per cent. of strychnine, and ferric citrate corresponding in amount to not less than 16 per cent. of metallic iron. It should be kept in well-stoppered bottles, protected from light." *U. S. VIII.*

The process for this preparation of the U. S. P., 1890, is as follows: "Iron and Ammonium Citrate, *ninety-eight grammes;* Strychnine, *one gramme;* Citric Acid, *one gramme;* Distilled Water, *one hundred and twenty cubic centimeters*, to make *one hundred grammes.* Dissolve the Iron Ammonium Citrate in *one hundred cubic centimeters* of Distilled Water, and the Strychnine, together with the Citric Acid, in *twenty cubic centimeters* of Distilled Water. Mix the two solutions, evaporate the mixture by means of a water-bath, at a temperature not exceeding 60° C., to the consistence of syrup, and spread it on plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in well-stoppered bottles, protected from light." *U. S.*, 1890.

This salt should never be prescribed in solution. E. R. Squibb has shown that it gradually deposits strychnine. When ammonia water or ammonium citrate was added, the precipitate was redissolved, but later the precipitate reappears. There might be dangerous or alarming symptoms if this solution were dispensed without shaking, and the last dose containing an undue proportion of the strychnine were administered. (*Ephem.*, June, 1888, p. 1128.)

It was officially described as in "thin, transparent scales, varying in color from garnet-red to yellowish-brown, without odor, and having a bitter, slightly ferruginous taste; deliquescent in moist air. Readily and completely soluble in water, partially soluble in alcohol." *U. S. VIII.* For method of assay see *U. S. D.*, 20th edition, p. 1446.

This combination has no advantages over the two active substances it contains when given conjointly in an uncombined state, and has the great disadvantage that the dose of one principle cannot be varied independently of that of the other.

Dose, from three to five grains (0.20 to 0.32 Gm.), in pill.

Ferric Peptonate. *Iron Peptonate. Peptonized*

Iron. Ferri Peptonas. Ferrum Peptonatum. Peptonate de Fer, Fr. *Eisen Peptonat,* G.—To a solution of 2 parts of dried peptone in 200 parts of water add a mixture of 24 parts of solution of dialyzed iron (See p. 1484) and 200 parts of water, in a thin stream while stirring constantly. A solution of caustic soda (1.5 per cent.) is added until there is produced a very weak alkaline reaction. The precipitated iron peptonate is washed rapidly with water until no reaction with silver nitrate is shown. The precipitate is drained on a wet strainer and dissolved in 3 parts of 25 per cent. hydrochloric acid. The solution is evaporated on a water bath and spread on plates to dry at a temperature not exceeding 50° to 60° C. Iron peptonate, thus prepared, is in the form of shining brown scales, and contains about 17 per cent. of iron. It is slowly soluble in cold water, more quickly in hot water, and the solution is not clouded by boiling nor by the addition of alcohol. Iron peptonate, its solution, and a syrup prepared from it are used in preference to inorganic salts of iron because of the absence of injurious effects upon the teeth and mucous membrane and its deficiency in astringency. The *dose* is from three to ten grains (0.2–0.65 Gm.).

Liquor Ferri Peptonati.—Solution of iron peptonate is now included in the N. F. and while made by a process somewhat different from that given above yields an essentially similar product.

Ferric Succinate. *Ferri Succinas. Iron Succinate.*—The precipitate obtained by adding ferric chloride to a solution of a succinate is a basic salt $(C_4H_4O_4)_2Fe_2(OH)_2$. This is yellowish in color, becoming darker on standing. Ferric succinate has been introduced as a remedy for *jaundice* resulting from obstruction of the biliary duct; also as a chalybeate. *Dose,* five grains (0.32 Gm.).

Ferric Tannate. *Ferri Tannas.* $Fe_2(C_{14}H_7O_9)(OH_3)$.—This salt is prepared by dissolving 44 parts of precipitated ferric subcarbonate, moderately dried, in a boiling solution of 9 parts of pure tannic acid, evaporating the solution at the temperature of 80° C., in a porcelain vessel, until it becomes thick, pouring it out on a glass or porcelain plate, and drying it with a gentle heat. As thus obtained, ferric tannate is in flat pieces, of a crimson color, without taste, and insoluble in water. It is not a definite chemical compound. *Ink* is an aqueous solution of the ferric gallotannate, and probably possesses similar medicinal properties. It is a popular application for *ringworm. Dose,* of ferric tannate, from eight to thirty grains (0.5–2.0 Gm.), in the course of the day.

Ferric Valerate. *Ferri Valerianas. U. S.* 1890. *Iron Valerianate.* $Fe_2(C_5H_9O_2)_2(OH)_4$.—This salt was at one time official in the U. S. Pharmacopœia, but was dismissed from the 8th revision. It may be prepared by precipitating a dilute solution of ferric sulphate with a solution of sodium valerate and collecting and washing the precipitate. When so made it forms a dark brick-red powder of somewhat varying composition with the characteristic odor of the valerates. It is insoluble in water, but readily soluble in alcohol. It is decomposed by boiling water with the liberation of valeric acid and the formation of ferric hydrate.

Ferric valerate has been used as a chalybeate, especially in *nervous exhaustion* associated with *anemia.* It has also been alleged to have almost specific properties in *diabetes insipidus.* The *dose* is from two to five grains (0.13 to 0.32 Gm.).

Ferrichthyol.—This compound occurs as an amorphous, dry powder of brownish-black color, devoid of taste and containing 3.5 per cent. of iron combined with ichthyol. It is employed as a hematinic in daily *doses* of thirty grains (2.0 Gm.).

Ferripyrine. *Ferropyrine. Antipyrina cum Ferro.*—This compound is prepared by adding 5 parts of crystallized ferric chloride, dissolved in 10 parts of 96 per cent. alcohol, to a solution of 5 parts of antipyrine in 10 parts of alcohol and 50 parts of ether. It is in the form of a fine, orange-red powder, containing about 64 parts of antipyrine, 24 parts of chlorine and 12 parts of iron. Soluble in 5 parts of water at 15° C., less soluble (9 parts) in boiling water, very soluble in alcohol but insoluble in ether. Alkalies or alkaline carbonates added to an aqueous solution precipitate ferric hydroxide. It combines the properties of both antipyrine and ferric chloride and is given in *anemic conditions* accompanied by *headache.* It has been used in *chlorosis* as a chalybeate; is strongly astringent, and affirmed to be often useful in chronic *diarrheas.* In strong solution (1 to 5) it is said to be a powerful non-irritant styptic. *Dose,* from three to six grains (0.2 to 0.4 Gm.).

Ferrivine.—Ferrivine is claimed to be ferric tri-para-amino-benzene sulphonate. It has been introduced by McDonagh as a cure for *syphilis* by intramuscular injection. Harrison and Mills (*L. L.,* June 17, 1916), however, from clinical trials, reached the conclusion that not only did the drug fail to show any curative action but that its use was distinctly dangerous because of the violence of the reactions following its injection. It was intended to be used with a sulphur compound called *Intramine.*

Ferromangan. *N. N. R.* 1924. *Liquor Ferro Mangani Peptonati,* "Dieterich."—This is a proprietary solution containing 0.6 per cent. of iron, 0.1 per cent. of manganese and 1.5 per cent. of peptone. It is a clear liquid of a dark brown color and a pleasant odor and taste. The N. F. *Liquor Ferri Peptonati et Mangani* is of similar composition. It is used in *anemia, chlorosis* and as a general tonic in a *dose* of from one to four fluidrachms (3.75 to 15 cc.).

Ferro-silicon.—This is a mixture made by heating quartz, steel turnings and coal in an electric furnace and is used in the arts for increasing the tensile strength of steel. Its interest to medicine depends upon the fact that in the presence of moisture it evolves hydrogen phosphide and also hydrogen arsenide and has caused several deaths upon ships in which it was being transported. As a result of an investigation under the direction of the British Government, it was recommended that *ferro-silicon* should be exposed to the air for at least a month before being sold, that its carriage on passenger vessels should be forbidden and that when carried on cargo boats it should, if possible, be carried on the deck, or at least in well-ventilated places, cut off by air-tight bulkheads from the quarters of the crew.

Ferrous Arsenate. *Ferri Arsenas. Br.* 1898. *Iron Arsenate. Arsenate of Iron, Br.* 1885. *Ferrum Arsenicum. Arséniate Ferreux,* Fr. Cod. *Arsensaures Eisenoxydul,* G. *Arseniato ferroso-ferrico,* It. *Arseniato de hierro,* Sp.—" Ferrous arsenate,

$Fe_3(AsO_4)_2,6H_2O$, with ferric arsenate and some iron oxide." *Br.*, 1898.

Ferrous arsenate is white when first formed, but quickly turns green on exposure to the air during the process of washing and drying, and finally becomes a *ferroso-ferric arsenate* of the probable composition $3Fe(FeO)AsO_4.16H_2O$. It is an amorphous powder, without odor or taste, insoluble in water, but readily dissolved by hydrochloric acid. The British Pharmacopœia gave the following characters of the salt: "A tasteless amorphous powder of a greenish color, insoluble in water, but readily dissolved by hydrochloric acid. It affords the reactions characteristic of ferrous and ferric salts and of arsenates." For further tests for this salt see *U. S. D.*, 20th edition, p. 1392.

Ferrous arsenate is supposed to unite the virtues of the two metals which enter into its composition, but the quantity of iron in any permissible dose is so small as to be nearly or quite insignificant, and the activity of the medicine is in fact due to the arsenic alone. The complaints in which it has been found efficient are those in which arsenic in other forms has proved to be a valuable remedy, and it ought undoubtedly to be so ranked rather than with the chalybeates. Should the coexistence of an anemic state of the system with any disease requiring the use of arsenic indicate the joint use of iron, it would be unsafe to depend on ferrous arsenate alone. This remedy is useful in chronic affections of the skin, especially those of a scaly character, as *lepra, psoriasis*, and the advanced stage of *eczema* and *impetigo*.

Dose, from one-tenth to one-eighth of a grain (0.006 to 0.008 Gm.).

Ferrous Bromide. *Iron Bromide. Ferri Bromidum. Ferrum Bromatum. Bromure ferreux, Bromure de fer*, Fr. *Eisenbromid*, $FeBr_2$.—*Ferrous bromide* is a yellowish, deliquescent salt, very soluble, and extremely styptic. For medicinal employment it should be in aqueous solution, protected by sugar. This solution has been used with alleged success as an alterative tonic in *chorea*, and in various *scrofulous* and *erysipelatous affections.* (See 16th ed., *U. S. D.*) The *dose* of ferrous bromide is from one to three grains (0.065–0.2 Gm.), three times a day, gradually increased until its effects are manifested.

Ferrous Iodide. *Ferri Iodidum. Iron Iodide. Iodure de Fer*, Fr. *Ferrum Jodatum. Eisenjodür, Jodeisen*, G. $FeI_2 + 3H_2O$.

The solid ferrous iodide in its unprotected state is omitted in the present editions of the U. S. and Br. Pharmacopœias. The former directs it in pills and syrup prepared immediately from the materials. The iodide is extremely liable to spontaneous change.

Ferrous iodide is a crystalline substance, exceedingly deliquescent, of a greenish-black color, and styptic, chalybeate taste. Its solution, by evaporation with as little contact of air as possible, affords transparent, green, tabular crystals. When heated moderately it fuses, and, on cooling, becomes an opaque crystalline mass, having an iron-gray color and metallic luster. At a higher temperature it emits violet colored vapors, and the iron is left in the state of sesquioxide. It is very soluble both in water and in alcohol. When recently prepared it is wholly soluble in water, forming a pale green solution; but, if made for some time, it almost unavoidably contains some ferric oxide, from a partial decomposition, and will not entirely dissolve. The aqueous solution is very liable to spontaneous decomposition, becoming at last orange-red from the generation of free iodine, and depositing ferric oxide. According to Richard Phillips, Jr., the first step in this change is the formation of ferrous oxide and hydriodic acid, from the decomposition of water. As the ferrous oxide immediately begins to be converted into ferric oxide by absorbing oxygen from the air, and in this state is precipitated, the hydriodic acid is set free, and hence is explained the acidity of the solution from the first moment the ferric oxide is deposited. Afterwards, the hydriodic acid is decomposed by the air, and iodine liberated. (*P. J.*, iv, 19.) The plan of Squire of placing in it a coil of iron wire does not prevent the deposition of ferric oxide, and has, therefore, been superseded by the use of saccharine matter, which affords a better protection to the solution. (See *Syrupus Ferri Iodidi.*) Ferrous iodide is incompatible with alkalies and their carbonates, with lime water, and with all other substances by which ferrous sulphate is decomposed.

Ferrous iodide was first employed in medicine by Pierquin in 1824. For uses of this preparation, see *Syrupus Ferri Iodidi*, Part I. The *dose* is a grain (0.065 Gm.), gradually increased to eight grains (0.5 Gm.).

This salt, on account of its deliquescent property and proneness to decomposition, should not be given in pill, unless protected from change by saccharine matter by coating or other means. (See *Pilulæ Ferri Iodidi*, p. 864.) The most convenient form of exhibition is that of a syrup, but it has no advantage over the official syrup. For a process for making *Glycerite of Ferrous Iodide*, see *U. S. D.*, 19th ed., p. 1491. *Iron Iodates* have been used to some extent as therapeutic agents in Dublin. For formulas, see *P. J.*, i, 624.

Ferrous Malate. *Ferri Malas Crudus.*—Under the name of *extractum ferri pomatum* (*ferrated extract of apples*) the N. F. recognizes an impure form of ferrous malate made by digesting fresh apple juice with reduced iron and evaporating to the consistency of a pilular extract. It is of a dark green color and contains varying quantities of iron. *Dose*, five to fifteen grains.

Ferrous Oxalate. *Ferri Oxalas. U. S.* 1880. *Iron Oxalate.* $FeC_2O_4H_2O$. *Ferrum Oxalicum. Oxalas Ferrosus. Oxalate de Fer*, Fr. *Oxalsaures Eisenoxydul*, G.—For description of this salt which was recognized by the U. S. P. 1870 and 1880, see *U. S. D.*, 19th ed., p. 1491. It is a very feeble, inefficient chalybeate. *Dose*, from two to three grains (0.13–0.20 Gm.).

Filicon.—A tænicide consisting of an extract of the rhizome of *Aspidium spinulosum* (Mill.) Sw. (Fam. *Filices*) combined with an aromatized castor oil. The *dose* is stated to be one tablespoonful.

Flindersia. *Flindersia maculosa* (Lindl.) F. Muell. *Leopard Tree.*—This is a tree of New South Wales, belonging to the *Meliaceæ.* During the summer it yields large masses of a clear amber-colored gum, which has a pleasant taste and is eaten by the aborigines; it has been used as a remedy for *diarrhea.* *Leopard tree gum* occurs in pieces as large as pigeons' eggs, dissolves rapidly in cold water, and has been found by J. H. Maiden to contain 80 per cent. of arabin but no metarabin. (*P. J.*, vol. xxi, 1890.)

Flour. *Farina tritici. Wheat flour.*—According to the official standards of the U. S. Department of Agriculture (see Circular 19, Bureau of

Chemistry), "Flour is the clean, sound product made by bolting wheat meal and contains not more than 13.5 per cent. of moisture, not less than 1.25 per cent. of nitrogen, not more than 1 per cent. of ash, and not more than 0.5 per cent. of fiber." The same circular states that "Graham flour is unbolted wheat meal" and "Gluten flour is the clean, sound product made from flour by the removal of starch and contains not less than 5.6 per cent. of nitrogen and not more than 10 per cent. of moisture."

The farina or flour produced by grinding other grains is designated by the appropriate prefix in each case, as maize or corn meal, rice flour, oatmeal, rye flour, buckwheat flour, etc.

The highest grade of wheat flour is known as "patent"; other grades are known as "bakers' flour" or "low grade flour." A barrel of flour weighs 196 pounds and requires about 258 pounds of wheat for its manufacture.

There are many trade designations for grades of flour, such as, "family," "blended," "gluten," etc., some of which (especially the last) are frequently misleading, if not actually illegal.

The nutritive value of flour depends upon a number of factors and the average composition of good flour is as follows: Moisture, 12.5 per cent.; proteids (N. x 5.70), 9.6 per cent.; dry gluten (including proteids), 10 per cent.; fat, 1.0 per cent.; ash, 0.5 per cent.; starch, 75 per cent.; crude fiber, 0.2 per cent.

The character of a wheat flour is measured largely by the quantity of gluten which it may contain. The separation of the gluten is accomplished by making a sticky, doughy mass with the flour by adding a small quantity of water, after which it may be washed with water accompanied with constant kneading until the gluten alone remains, which can be determined by the washings being no longer milky in appearance. The excess of moisture may then be removed from the gluten by squeezing and rolling it, after which it may be weighed as moist gluten (varying in amount from 25 to 35 per cent.), or dried to constant weight at 100° C. and calculated as dry gluten (which runs from 9 per cent. to 12 per cent. in ordinary flours).

The modern demand for a pure white flour has led to processes of grinding wheat which lead to the complete rejection of the outside layers of the grain. This highly-milled flour is deficient in phosphates and other mineral salts but especially in vitamin content. Although on a mixed diet this is not a matter of great importance, Little (*J. A. M. A.*, 1912, lviii, 2029) has reported an outbreak of beri-beri among the fishermen of Newfoundland who live mainly on white bread.

As flour is usually valued in proportion to its whiteness it has been extensively bleached in the past by the use of ozone or of oxides of nitrogen or by nitrosyl chloride. The question of the effect of bleaching upon the digestibility or harmlessness of bleached flour has never been satisfactorily settled. It is a practice which is very prevalent at present because of the foregoing fact and the unwillingness of the authorities to antagonize the milling trade.

Adulteration of flour, which was formerly very common, has not been practised to any extent for years in the United States. Occasionally samples are seen in which foreign seeds, smut, etc., have been ground with the grain, owing to insufficient cleaning of the grain preparatory to grinding. Such gross adulterants as terra alba or soapstone, which were formerly reported are unheard of at the present time and even the practice of the addition of copper sulphate or alum in small proportions to flour, which was formerly made by bakers who were thus enabled to bake white bread from inferior grades of flour, seems to have been altogether abandoned. (For methods of testing flour see any modern work on food analysis.)

The proteids of wheat, usually included in the term "gluten," are several in number and, according to Osborne and Vorhees (*Am. Chem. J.*, xv, 392; xvi, 524) are as follows: Globulin, 0.6 to 0.7 per cent.; albumen, 0.3 to 0.4 per cent.; proteose, 0.3 per cent.; *gliadin*, 4.25 per cent.; *glutenin*, 4 to 4.5 per cent.

The last two are the only ones present in gluten as determined by the washing out process previously described, as the first three are soluble in water.

"*Gluten*" is a term popularly known in connection with the names "gluten flour" and "gluten bread," used and recommended especially in connection with the dietary of diabetics when starchy foods are to be administered in small amounts or altogether prohibited. These preparations are legion and in many instances are sold under claims which are as false and misleading as they are cruel in the hope which they hold out to the sufferer from the disease. For a complete discussion of these products with analyses of hundreds of commercial samples, see *Bull. Conn. Ag. Exp. Sta.*, 1913, on Diabetic Foods.

Pure Gluten prepared by the mechanical method described above for its estimation is sometimes used in combination with medicating agents, some of which, like certain salts of the metals, form insoluble and tasteless compounds with it.

It is scarcely necessary to state that *bread* is formed by making flour into a paste with water, with the addition of yeast, setting it aside to ferment, and then exposing it to the heat of an oven. The fermentation excited by the yeast is accompanied by the extrication of carbon dioxide, which, being retained by the tenacity of the gluten, forms innumerable little cells or bubbles throughout the mass, and thus renders the bread light.

Wheaten flour is no longer used in its unaltered state in medicine. It was at one time employed as a desiccant dusting powder but has been completely replaced by powdered starch. A poultice is often made by boiling bread with milk. The effects of this poultice are similar to those of a flaxseed poultice although it does not hold the heat so well. The crumb (*mica panis*) is, moreover, frequently used to give bulk to minute doses of very active medicines administered in the form of pill. It should be recollected that it always contains common salt, which is incompatible with various substances.

Bran is laxative, and may be used with advantage to prevent *costiveness*. Bran bread, made from the unsifted flour, is an excellent laxative article of diet in some dyspeptic cases. The action of the bran is probably mechanical, consisting in the irritation produced upon the mucous membrane of the bowels by its coarse particles.

Flumerin. *Di-sodium-hydroxy-mercuric-fluorescein.*—This is a dark red powder with a greenish iridescence, slightly hygroscopic but otherwise permanent in the air. It is soluble in about ten parts of water, the solutions generally being permanent, although on long standing they sometimes show a slight precipitate of metallic mercury. The salt represents 32.5 per cent. of mercury so combined that it is not precipitated by either hydroxids or blood serum.

Flumerin has been brought forward by Hill and Young (*J. A. M. A.*, 1923, lxxx, p. 1365) for the treatment of *syphilis.* They gave it intravenously in doses of 0.5 milligramme per kilo of body weight; this for a man of 150 pounds would be equivalent to about one-half of a grain (0.03 Gm.) every other day.

Fluorescein. *N. N. R.* 1924. *Fluoresceinum. Resorcinolphthalein. Dioxyfluoran.* $O:(C_6H_3OH)_2:C.C_6H_4.COO$.—This may be prepared by heating phthalic anhydride (5 parts) with resorcinol (7 parts) to 200° C. The mass is treated with water and the residue dissolved in solution of potassium hydroxide, after filtration the *fluorescein* is precipitated by an acid. It is a yellowish-red or dark red powder, soluble in alcohol with yellow-red color and green fluorescence. The sodium salt, *uranin* (*sodio-fluorescein*), $C_{20}H_{10}O_5Na_2$, and the potassium salt (*potassio-fluorescein*) are marketed. They differ in that the first is a brownish-yellow and the second a yellowish-red powder; both of them yield aqueous solutions which are red by transmitted light and exhibit an intense yellow-green fluorescence.

An aqueous solution containing ten grains (0.65 Gm.) of fluorescein with fifteen grains (1 Gm.) of sodium bicarbonate to the ounce (30 cc.) is used as a diagnostic agent in various ophthalmic conditions. In lesions of the cornea two per cent. solution is dropped into the eye, and those portions which are deprived of the epithelium will show a green discoloration, while the healthy parts of the cornea remain unaffected. The eye should be cocainized before applying the fluorescein. According to Hamberger (*All. M. C. Z.*, 1909, p. 368), if thirty to forty-five grains (2–3 Gm.) be given by the mouth, while the body becomes yellow as in jaundice, in the healthy eye there is no change of color. When there is intra-ocular disease, however, the aqueous humor assumes a bright green color. In diseases of the conjunctiva, the eye reacts as though healthy.

Fluorescein sodium has been recommended by Strauss (*B. K. W.*, 1913, p. 2226) as a test for renal function. He administers fourteen grains (1.0 Gm.) on an empty stomach. In healthy individuals the urine shows fluorescence within ten to twenty minutes and continues for thirty-five to forty hours; the continuation of the dye in the urine for a longer time is indicative of kidney disease.

It is also used as a test for death. It is stated that if 15 grains be injected into the human body the whites of the eyes will become a greenish color provided life remains, within one hour. After death there is no coloration. It is also used for the purpose of tracing the course of underground streams and the connection between cess-pools and wells. One part in two billion can be recognized in water.

Fluorescein-Zinc is a reddish-yellow, difficultly soluble powder of the composition $ZnC_{20}H_{10}O_5$. Its zinc content is 16.4 per cent. It has been used by Wolff (*Ph. Ztg.*, 1915, 181) with asserted benefit as an antiseptic in *conjunctivitis.*

Owing to the close similarity in name between fluorescein and its derivative *fluorescin* much confusion has arisen, leading to the general belief that the two substances are identical. Fluorescin, however, is a reduction product of fluorescein, made by acting on the latter with sodium hydrate and zinc dust. It occurs as a yellow powder readily oxidizable to fluorescein. It is used like fluorescein as a diagnostic agent in ophthalmic practice. It has also been recommended by Fleig (*Press. Med. d'Egypte*, 1910, p. 281) as a test for the presence of blood in the urine. The test depends upon the fact that the non-fluorescent fluorescin-sodium shows an intense fluorescence in the presence of blood when treated with hydrogen peroxide.

Fluorides.—*Hydrofluoric acid* is a pungent, fuming, acid gas, very corrosive, attacking glass and porcelain and etching its surface. It is very soluble in water, the specific gravity of the solution rising to 1.25. The concentrated aqueous acid becomes weaker on boiling until, when boiling at 120° C., it attains a constant composition of from 36 to 38 per cent. of the anhydrous acid. Anhydrous hydrofluoric acid has been prepared and concentrations of all degrees may be obtained by the dilution of this acid. The concentrated acids are kept in containers of lead or platinum while more dilute acids are kept in gutta percha or ceresin bottles.

A 60 per cent. acid is employed in the cut glass industry for polishing lead, potash, soda and lime glass. Spent hydrofluoric acid, after use in the industry, is made use of by adding an equal volume of the 60 per cent. acid and about 10 per cent. of strong sulphuric acid. Stamping or etching upon glass for the purpose of putting trade marks, etc., upon glassware is accomplished by means of a rubber stamp using, in place of ink, a paste made of 2 parts of 50 per cent. hydrofluoric acid and 1 part of ammonium carbonate with enough barium sulphate to form a thick paste which may then be spread on a pad. Concentrated hydrofluoric acid is a powerful corrosive, having the peculiar property of hardening the skin or tissue with which it comes in contact and continuing its action underneath the hardened tissue, with an extraordinary amount and persistency of pain. For case, see *B. M. S. J.*, Jan., 1882; also *B. M. J.*, 1880, i. According to L. A. Waddell (*Indian Med. Gaz.*, 1883), the dilute 8 per cent. acid applied to the skin causes stinging sensation and pallor, followed by redness and desquamation. From 15 to 20 per cent. acid destroys the epithelium and produces severe burning and aching pain. The vapor of the acid is exceedingly irritant to the lungs, causing, even when very dilute, spasm of the glottis and other symptoms of irritation. According to Husemann, death has been produced by it. Nevertheless, L. Olivieri and F. Mergoni affirmed that in solution of 33 per cent. the daily inhalation of hydrofluoric acid from half an hour to an hour is a valuable adjuvant to quinine in chronic *malaria.*

Alkaline Fluorides.—According to the studies of Tappeiner (*A. E. P. P.*, xxvii), the fluorides are powerfully depressant to the blood pressure through an action upon the vasomotor centers and also produce lowering of the bodily temperature. Death occurs, amid symptoms of collapse, from respiratory failure. Waddell found in his studies a marked decrease in the number of red blood cells which he believed, but does not prove, to be the result of a direct action upon the spleen. Schwyzer (*Biochem. Zeit.*, 1914, lx, p. 932) finds that the continued intake of sodium fluoride in doses of 1 to 2 milligrammes per kilo causes increased coagulability of the blood and irritation of the bone marrow with a loss of chlorine and calcium. He believes that these symptoms are due to the affinity of hydrofluoric acid for calcium with which it forms insoluble salts.

Sodium fluoride has been used by various authors in the treatment of *goiter*, *rheumatism*, *epilepsy*, and *phthisis*. Its value, however, is extremely questionable and it is certainly toxic. McNally (*J. A. M. A.*, 1923, lxxxi, 811) reports 4 cases of fatal poisoning by sodium fluoride with extensive references to the literature. The fatal dose for a man is between 5 and 10 Gm. (75 to 150 grains). The most common symptoms are epigastric pain, nausea, vomiting, diarrhea with frequently local paralysis either in the legs or face. Necropsy shows congested and edematous mucous membrane of the stomach and upper bowel with often scattered hemorrhages. Most of the cases resulted from the mistake of roach powder for baking powder. The *dose* which has been recommended is from one-sixth to one grain (0.01–0.065 Gm.).

The fluorides are active antibacterials. (*M. R.*, 1908.)

Ammonium Fluoride.—Under the name of *bifluoride of ammonium* a solution containing 20 per cent. of hydrogen-ammonium fluoride, and 10 per cent. of hydrofluoric acid has been used by Dr. Joseph Head in the treatment of *pyorrhea alveolaris*. This solution is actively germicidal, having a phenol coefficient of 5.82. According to Head it is not caustic to wet mucous membranes, although on dry it produces a burn like that of carbolic acid. It is applied by flowing it into the pus pockets; it should never be injected into the tissues and care should be taken to prevent it coming in contact with the mucous membranes in other parts of the mouth. Dr. Head claims for this solution that it aids in loosening the tartar as well as in destroying infective micro-organisms and that it is not injurious to the tooth.

A technical form of ammonium fluoride is used in cleaning granite and stonework and sometimes as an ingredient in roach poisons.

Silver Fluoride. AgF. *Tachiol.*—This salt, which occurs in deliquescent crystals acquiring a yellow color in the air and finally being converted into a black crystalline mass, making stable solutions in water, has been brought forward by Durante and Perez as a valuable antiseptic for surgical use. It is a feeble coagulant of albumin, and great penetrating power is claimed for its solution. It is employed in the proportion of one to a thousand; the one per cent. solution is said not to be distinctly irritant to the skin. It blackens linen and other organic substances. Zappuli has destroyed *malignant pustules* by injecting into them silver fluoride solution.

Organic Fluorides.—A number of organic fluoric compounds have been proposed and put upon the market. According to Tischer and Beddies (*Aerzt. Rund.*, 1898), they are antispasmodic, bactericidal, and are primarily stimulant, secondarily depressant to the motor nerve.

Difluor-diphenyl is described elsewhere under its trade name, *Antitussin.*

Formalbumin.—A condensation product of formaldehyde and casein is a yellowish, odorless powder, soluble in diluted acids. It is used as an external antiseptic. A similar combination is sold under the name of *galalith* and is used as a plastic for making toilet articles, etc., similar in appearance to celluloid.

Forman. *Chlormethylmenthyl-ether*, $C_{10}H_{19}$—$O.CH_2Cl$, a product formed by the action of formaldehyde upon menthol in the presence of hydrochloric acid. It is a colorless oil, emitting dense fumes and boiling at 160° to 162° C. under a pressure of 16 mm. In the presence of water or merely moist air the ether splits up into its original constituents, formaldehyde, menthol, and hydrochloric acid. It has been used locally in the treatment of various conditions of the nasal and even bronchial mucous membrane.

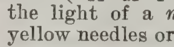
Formasal.—Under this name has been introduced a condensation product of formaldehyde and salicylic acid which is claimed to be a *methylene disalicylic acid.* Several salts of this acid are upon the market, including those of caffeine (*cafformasal*), bismuth (*bisformasal*) and sodium (*sodiformasal*).

It is claimed for *formasal* that it is decomposed in the system, liberating both salicylic acid and formaldehyde. Its sodium salt is used as an anti-rheumatic and anti-neuralgic in doses of five to fifteen grains (0.32–1.0 Gm.). The bismuth salt is used as an intestinal antiseptic. The dose is ten to twenty grains (0.65–1.3 Gm.). The caffeine salt is very soluble in water, and has been suggested as a means for the hypodermic administration of caffeine. It is used as a diuretic and in *rheumatism* in *doses* of five to fifteen grains (0.32–1.0 Gm.).

Formicin. (*Formaldehyde Acetamid.*) $CH_3.CO.NH.CH_2.OH$.—This product is prepared by a patented process involving the action of a formalin polymer on acetamid.

Because of its hygroscopic qualities, *formicin* is marketed only in concentrated solution. It is a colorless, syrupy liquid, specific gravity, 1.25, of a characteristic odor, miscible in all proportions of water, alcohol or chloroform. The addition of either acids or alkalies causes the liberation of formaldehyde. With Mayer's reagent it gives a reddish-violet color. According to Koch (*Ph. Ztg.*, 1905) this agent exercises at body temperatures a powerful bactericidal effect probably due to the liberation of formaldehyde. It has been used in strengths of from 2 to 5 per cent. for disinfecting internal cavities, as the bladder, and also as an injection in suppurative infection of the joints. Bartholdy (*D. M. W.*, 1906, p. 1601) has injected as high as 2 cc. of the 5 per cent. solution daily into a child of eight years without causing any systemic symptoms. According to this author it has the great advantage over formaldehyde of causing practically no pain.

Fortoin.—This is obtained by the action of formaldehyde upon *cotoin*, the active principle of the true coto-bark. Its composition is



$$CH_2\left\langle\begin{matrix}C_{14}H_{11}O_4\\C_{14}H_{11}O_4\end{matrix}\right.$$

and it is therefore to be viewed in the light of a *methylenedicotoin.* ***Fortoin*** forms yellow needles or a yellow powder emitting a feeble cinnamon-like odor; it is freely soluble in chloroform, acetone, glacial acetic acid, and dilute alkalies, but dissolves sparingly in alcohol and ether, while in water it absolutely insoluble; melting point, 211° to 213° C. It is claimed for *fortoin* that it has the peculiar action of cotoin upon the intestinal mucous membrane, united with the antiseptic and disinfecting properties of formaldehyde. It is used in those cases of *chronic intestinal catarrh* in which there is no active inflammatory process. It has been also recommended by Overlach as a local application in badly *ulcerated sore throats* and in *gonorrhea.* In making local applications from one to six grains may be dissolved in a fluidounce of ten per cent. alcohol. *Dose,* four to seven grains (0.26–0.45 Gm.) three to five times a day.

Frankenia. *Frankenia grandifolia* Cham. and Schlecht. *Yerba Reuma.* (Fam. *Frankeniaceæ.*)—This herb, which grows in California, Nevada, Arizona and Northern Mexico, contains about 6 per cent. of tannin and is employed as a topical remedy in *catarrhal affections,* especially of the nose and genito-urinary tract; also internally in *doses* of from ten to twenty minims (0.6–1.3 cc.) of the fluidextract. For local application the fluidextract may be diluted with from two to five times its volume of water.

Frasera. *American Columbo. Radix Fraseræ. Radix Columbo Americanæ. Racine de Colombo de Mariette (d'Amérique),* Fr. *Frazerawurzel, Amerikanische Colombowurzel,* G.—*American Colombo* is yielded by *Frasera caroliniensis* Walt. (Fam. *Gentianaceæ*), a smooth biennial or triennial herb which flourishes in rich dry soil from New York and Wisconsin southward. The plant attains a height of up to 2.5 m. Its roots are thick and fleshy; its leaves are oblong-lanceolate and arranged 4 at each node; its pale greenish-yellow and brown-purple dotted flowers are borne in a loosely flowered, pyramidal panicle, appearing from May to late June. The roots, which were formerly included in the Secondary List U. S. P., should be collected in the autumn of the second or the spring of the third year. Before being dried, they should be cut into transverse slices.

As formerly in the market, Frasera was in disc-like pieces resembling calumba, but are easily distinguishable by the greater uniformity of their internal structure, the absence of concentric and radiating lines, and their purer yellow color, without a greenish tinge. The root sliced longitudinally, so as to imitate gentian, has been offered in the market as *American gentian.* The taste of frasera is bitterish and sweetish. It contains gum, pectin, glucose, wax, resin, fatty matter, yellow coloring matter, bitter extractive, and an acid which is probably peculiar. (*A. J. P.,* Jan., 1862, 23.)

Frasera is a feeble, simple bitter. *Dose,* of powder, one drachm (3.9 Gm.); of infusion (1 fl. oz. to 1 pint boiling water), two fluidounces (60 cc.) a day. The fresh root is said to be emetic and cathartic.

Fruit Essences, Artificial.—Several of the esters of alkyl radicals with organic acids have been found to possess the odor and flavor of certain fruits, a property which has led to their employment as flavoring materials under the name of fruit essences. They are esters, which, according to the older nomenclature, were improperly called "ethers" or "compound ethers."

Ethyl Butyrate. Ethyl-butyric Ester. $C_3H_7COOC_2H_5$.—Butyric ether, as it is sometimes erroneously called, is sparingly soluble in water, but very soluble in alcohol, and boils at 121° C. It is used to communicate a pineapple flavor. Dissolved in 8 to 10 parts of alcohol, it formerly was sold under the name of *pineapple essence. Butyric acid,* $C_4H_8O_2$, is formed during what is called the butyric fermentation, which usually consumes two or three months before it is completed, and which is preceded by the lactic fermentation. Butyric acid is a colorless liquid, of disagreeable odor and taste resembling rancid butter. It dissolves in all proportions in water and alcohol, boils at 163° C.; density, 0.973.

Ethyl Pelargonate. Ethyl-pelargonic Ester. Œnanthic Ether. $C_8H_{17}COOC_2H_5$.—This compound has the agreeable odor of quince, and when dissolved in alcohol in due proportion, was formerly sold as *quince essence.* It may be obtained from wine lees, by adding sulphuric acid and water, and distilling in a current of steam. Pure pelargonic ethyl ester (œnanthic ether) is a colorless liquid, having a peculiar, vinous, stupefying odor, and a taste at first slight but afterwards acrid. Its sp. gr. is 0.8635 at 17.5° C. and its boiling point from 227° to 228° C. It is insoluble in water, but dissolves readily in alcohol and ether. It has been much used in the production of factitious or imitation brandy. *Pelargonic acid,* first obtained from *Pelargonium capitatum* (L.) Ait., or *rose geranium,* belongs to the fatty acid series and has the formula $C_8H_{17}COOH$. Delff's analysis of *œnanthic acid* gives it the same composition, and he considers the two acids identical. This ester is one of those naturally found in grape brandy and the artificial ester is much used in preparing artificial brandies.

Amyl Acetate. Amyl-acetic Ester. Pentyl Acetate. $CH_3COOC_5H_{11}$.—It is a colorless, limpid liquid, lighter than water, boiling at 137° C., insoluble in water, but soluble in alcohol. It is manufactured on a large scale as a solvent for lacquers and varnishes under the name of *banana oil* on account of the resemblance of the odor of the ester to that of ripe bananas. An alcoholic solution of this ether also has been sold under the name of *Jargonelle pear essence.* This ester is commercially sold under the name of "banana oil," and is the solvent used largely in lacquering, the film, as a rule, consisting of pyroxylin which is quite soluble in amyl acetate.

Amyl Valerate. $C_4H_9COOC_5H_{11}$. *Amyl Valerianate. Amyl-valeric Ester. Apple Oil.*—It boils at 188° C., and has a sp. gr. of 0.879 at 0° C. An alcoholic solution of this ester, in the proportion of one part to six or eight of alcohol, has been used as a flavoring liquid under the name of *apple essence.* (See *Valeric Acid.*)

Besides the essence here described, there are found in commerce the strawberry, raspberry, apricot, greengage, mulberry, and black currant essences, all of which may be viewed as various mixtures of the esters of the ethyl and amyl series, modified by the addition of pure nitrous ether, tincture of orris, vanilla, volatile oils, etc., to bring about a resemblance to the fruit the odor and taste of which it is the object to imitate.

The fruit essences have been extensively employed in the past for flavoring ices, jellies, lozenges, and drops and for making fruit syrups and effervescent beverages. They are, however, vastly inferior to the concentrated juices and extracts from the real fruits, and their use is largely being abandoned on account of the necessity of labeling the products thus made as artificial or imitation under existing federal and state food laws.

Kletzinsky prepared a table giving the ingredients, and their proportions, of a large number of fruit essences. (See *U. S. D.,* 19th ed., p. 1497; also a paper by George R. Pancoast and Willard Graham, *Proc. Penn. Phar. Assoc.,* June, 1906.)

Fuchsine. *Magenta Red, Aniline Red, Azaleine, Solferino, Harmaline, Erythrol-benzin, Rosein,* *Rubin.*—This compound is now included among the U. S. P. reagents (see Part III). It is a mixture of salts of *rosaniline* and *pararosaniline.* One of the earliest coal-tar colors discovered, it has had an extended use for many years. The poisonous results which have been alleged to follow the use of fuchsine as a coloring for foods and as a dyestuff for fabrics, have been undoubtedly due to arsenical impurities remaining in the dye from its manufacture. There is still some doubt, however, as to its properties in this respect, and it is not included in the seven permitted colors under the ruling of the U. S. Dept. of Agriculture.

Fuchsine and *safranine,* $C_{21}H_{20}N_4$, were formerly largely employed in France for coloring wines red. In the experiments of Cazeneuve and Lépine (*G. H. M. C.*, Nov., 1885) fuchsine was found to be free from toxic properties, but safranine proved itself a violent poison, causing marked dyspnea, acceleration of the heart's beat, violent diarrhea and albuminuria, and death from respiratory paralysis. It stains animal tissue directly violet-red while vegetable fiber must first be mordanted.

Reiss (*G. H. M. C.*, 1888) recommends fuchsine as a specific in *acute* and *chronic Bright's disease.* Fuchsine, according to Weber and Krause (*B. K. W.*, 1907, p. 192) surpasses trypan red in its destructive action upon trypanosomes. It does not appear, however, to have been as yet tried in human trypanomiasis. According to May (*J. A. M. A.*, 1912, lviii, and 1913, lx) it is a powerful germicide rivalling phenol in its efficiency, and like many of the other dyestuffs stimulates granulation and epitheliazation. A number of other authors have reported favorable results in *varicose ulcers, burns,* and granulating *wounds* of various kinds. Triboulet also reports pleasing results in various *skin diseases,* especially *impetigo.* These conclusions have been confirmed by Gismondi (*Pediatria,* 1917, xxv, 718). It is used generally in strengths of about 1 per cent. either as an ointment or as an aqueous solution. *Dose,* of rosaniline, one-tenth to one-sixth grain (0.006–0.010 Gm.).

Fumaria. *Fumaria officinalis* L. *Fumitory. Beggary. Fumeterre,* Fr. *Erdrauch, Feldraute,* G. (Fam. *Fumariaceæ.*)—A small annual European plant, naturalized in this country, growing in waste places, and flowering from May to August. It was formerly considerably employed as a medicine, and is still used in Europe. The leaves are the official part. They are dissected, compound, inodorous, have a bitter, saline taste, and are very succulent, yielding by expression a juice which has the sensible and medicinal properties of the plant. An extract, prepared by evaporating the expressed juice or a decoction of the leaves, throws out upon its surface a copious saline efflorescence. *Fumaric acid,* $C_4H_4O_4$, was early identified as present, and its isomerism with *maleic acid,* the acid obtained from malic acid by heat, was established later. The alkaloid *fumarine* first discovered by Peschier was at one time believed to be identical with corydaline, but according to Dankwortt (*A. Pharm.*, ccl, p. 590) is protopine. (See also Adermann, *A. J. P.*, 1890, 396.) Fumitory has been considered gently tonic, alterative, and, in large doses, laxative and diuretic. It has been used in *scurvy* and various hepatic disorders. Cullen gave two fluidounces (60 cc.) of the expressed juice twice a day. Others have prescribed it in much larger quantities. The leaves, either fresh or dried, may be used in decoction or extract, in almost indefinite dose. The inspissated juice has also been employed.

Furfural. *a-Furol. Pyromucicaldehyde. Furfuraldehyde,* improperly called *furfurol. Artificial Oil of Ants.* $C_4H_3(CHO)O$.—A decomposition product of certain proteids, occurs in beer and brandy and is produced in the distillation of bran, pentoses, etc., with diluted sulphuric acid. It is a limpid, colorless liquid, soluble in 11 parts of water and freely in alcohol and ether.

A number of years ago Lauter Brunton suggested that the toxic effects of certain raw spirits might be due to action of furfural. McGuigan (*J. P. Ex. T.*, 1923, xxi, p. 65) finds that in doses of about 0.6 cc. per kilo by the mouth it produces marked symptoms and occasionally death in the lower animals; that it is a primary stimulant and secondary paralyzant of the central nervous system; that it causes formation of methemoglobin. He also finds that it possesses some local anesthetic and germicidal actions. The *dose* of one and a half grains (0.096 Gm.) of furfural produces in man a persistent headache. Ammonia is said to be antidotal to furfural, hence its value in "pick-me-ups." Furfural occurs as a by-product in the inversion of sugar by acids, and its presence in commercial invert sugar makes it possible to detect that substance when used to adulterate honey. (See test for invert sugar under honey.)

Fustic.—A yellow dye-wood, obtained from *Chlorophora tinctoria* (L.) Gaud. (*Maclura tinctoria* D. Don.), a tree of the Fam. *Moraceæ,* growing in the West Indies and South America. It is not used in medicine or pharmacy. The wood of *C. tinctoria* owes its coloring properties to two principles, which have been isolated by R. Wagner; one denominated *morin,* or *morindon,* $C_{15}H_{10}O_5$, and the other *moritannic acid,* $C_{13}H_8O_6$, from its resemblance to tannin. The former, when distilled with zinc dust, yields methyl-anthracene, whence the conclusion has been drawn that it is a *trioxymethylanthraquinone,* $C_{15}H_7O_2(OH)_3$. (See *Chem. Gaz.*, ix, 1, 21, and 241.) It has long been known in the Southwest that the wood of the *Osage orange tree, Maclura pomifera* (Raf.) Schneider, contains a dyestuff that would give a more or less fast yellow color. An examination of the wood from Texas by Kressmann showed that it not only contains *moric acid* and *morintannic acid,* the same as fustic wood, but also that the dyeing principles are present in amount to be commercially valuable. A comparative series of dyeing experiments made with fustic and Osage orange wood and extracts showed the latter to be of equal value with fustic in regard to depth of colors produced, the amount of extract, the character of the dyeing, and fastness to light, weather, washing, etc. (*Science,* 1914, 37.) Under the names of *Hungarian Fustic* or *Young Fustic* the wood of the *Rhus cotinus* L. (Fam. *Anacardiaceæ*), or *Venice Sumach* has also been used as a yellow dye. From it Chevreul extracted a yellow coloring matter, in small crystalline needles when pure, which he called *fisetin.* J. Schmidt (*B. Chem. G.*, xix) states that it occurs in the wood as a tannic acid compound of the glucoside of fisetin, which he calls *fustin.* The *fisetin* has the formula $C_{15}H_{10}O_6$, and is probably a *tetroxymethylanthraquinone,* $C_{15}H_6O_2(OH)_4$. It is obtained by recrystallization from dilute alcohol or acetic acid; it forms fine yellow needles or yellow prisms. It is very slightly soluble in hot water, easily soluble in alcohol and acetic ether, sparingly in ether and benzene.

Galactose. $C_6H_{12}O_6$.—*Dextro-galactose* has been used by Bower as a test for functional activity of the liver. (*W. M. W.*, 1906.) He found that in healthy persons after the administration of six hundred and twenty grains (40 Gm.) of *galactose* none appeared in the urine, but that in cases of cirrhosis of the liver after the same quantity the presence of galactose could be recognized in the urine.

Galbanum. *Gummi-resina Galbanum. Galban, Mutterharz,* G. *Galbano,* It., Sp.—This gum-resin was formerly official in both the U. S. and British Pharmacopœias. It is mentioned by the earliest medical writers and was an ingredient of the incense used in the worship of the ancient Israelites. At present it is only used to a small extent in medicine. Some confusion exists as to the botanical source of *Galbanum.* Buhse, during his travels in 1848, saw the gum-resin spontaneously exuding from a plant growing near the southern coast of the Caspian. He was informed by the natives that the drug was obtained from it. This plant is the *Ferula galbaniflua* Bassier and Buhse. Buhse also stated that the Persian galbanum is yielded by a second plant, the *F. rubricaulis* Boissier but Schumann considers this identical with *F. galbaniflua.* Holmes is of the opinion (*P. J.*, 1891, 194) that "Levant" galbanum is yielded by *Ferula galbaniflua*, and its variety *β-Ancheri;* that solid "Persian" comes possibly from *F. Schair* Borsez, while the *liquid* "Persian," judging from the fruits found in it, derived from an undescribed species allied to *F. galbaniflua.* All of the *Ferula* species mentioned are tall, umbelliferous herbs indigenous to Persia. These contain in their axes many schizogenous secretion reservoirs that secrete a milky fluid, the gum-resin. A portion of the drug is obtained by collecting the natural exudation from the stem, but most by cutting the stem off near the crown of the root and collecting the exuded juice after it hardens. Slices of the crown are taken off at intervals of several days as long as exudation continues. There are two commercial varieties of the drug, Persian and Levant. The Persian variety is soft, contains fragments of stems and fruits and at present is not on the American market. The Levant variety is in dry tears or lumps and contains transverse slices of roots. This variety has alone appeared on the American market within recent years. Most of the drug is exported from Persian Gulf ports.

Galbanum rarely appears in the form of masses composed of whitish, reddish, or yellowish tears, from the size of a pin's head to that of a pea and larger, irregularly agglutinated by a darker colored yellowish-brown or greenish substance, more or less translucent, and generally mixed with pieces of stems, seeds, or other foreign matters. (Persian Galbanum). It is usually found, in our markets, in the state of distinct roundish tears, about as large as a pea, or in lumps a yellowish-white, an orange brown or brownish-yellow color, shining externally as if varnished, translucent, and often adhering together. Internally the tears are soft, opaque and yellowish-white. Occasionally the tears are bluish-green in color. Galbanum has in cool weather the consistence of firm wax, but softens in summer, and by the heat of the hand is rendered ductile and adhesive. At 100° C. it is sufficiently liquid to admit of straining, and it generally requires to be strained before it can be used. It is of a dark-brown or blackish color, and of a soft consistence.

According to Ludewig, a gum-resin, designated as *Persian galbanum,* had been received in Russia by the way of Astrakhan or Orenburg, and is the kind used in that country. It came enclosed in skins, and was in masses of a reddish-brown color with whitish streaks, of a disagreeable odor, somewhat like that of asafetida, and of an unpleasant bitter, resinous taste. It was so soft as to melt with a slight elevation of temperature. It differed from common galbanum in its odor, in its color, which is never greenish, and in the absence of tears, and is probably derived from a different plant. It abounds in impurities. This variety of galbanum is probably the same as that obtained by Aitchison in Afghanistan, which on chemical examination yielded—volatile oil, 3.108 per cent.; resin (ether extractive, 61.2, alcohol extractive, 7.576), 68.776; water extractive (gum), 17.028; insoluble matter, 1056. (*P. J.*, Dec. 11, 1886.)

The odor of galbanum is characteristically aromatic; its taste bitterish, warm and acrid; its sp. gr. 1.212. Triturated with water, it forms an imperfect milky solution, which on standing deposits the greater portion of what was taken up. Alcohol dissolves a considerable proportion, forming a yellow tincture, which has the odor and taste of galbanum, and becomes milky with water, but affords no precipitate. In diluted alcohol it is wholly soluble, with the exception of impurities. Ether dissolves the greater portion. "When moistened with alcohol, galbanum acquires a purple color on the addition of a little hydrochloric acid." *U. S.*, 1880. According to Conrady (*A. Pharm.*, 1894, ccxxxii, 98) the composition of galbanum is as follows: ethereal oil, 9.5 per cent.; resin, soluble in alcohol, 63.5 per cent.; gum and impurities, 27 per cent. The purified resin was found by Conrady to contain about 20 per cent. of combined umbelliferone, about 0.25 per cent. of free umbelliferone, and about 50 per cent. of *galbaresinotannol.* This latter representative of the class of resino-tannols, first established by Tschirch, was proved to have the alcohol character by forming the acetyl and benzoyl derivatives. Conrady also considers that the umbelliferone is combined with this galbaresino-tannol in the form of an ester. The volatile oil which is obtained from galbanum to the extent of about 10 per cent. he found to consist essentially of a d-pinene hydrocarbon of the formula $C_{10}H_{16}$, with small amounts of a sesquiterpene, which, according to Wallach, is *cadinene* (Gildemeister and Hoffman, *Aetherische Oele*, p. 753.) The resin, constituting about 60 per cent., is very soft, and dissolves in ether or in alkaline liquids, even in milk of lime, but only partially in carbon disulphide. When heated with hydrochloric acid for some time, it yields umbelliferone. If a small fragment of galbanum be immersed in water, a fluorescence will be produced by a drop of ammonia. Asafetida shows the same reaction, but ammoniac does not.

Galbanum submitted to dry distillation yields a thick oil of brilliant blue color. This oil on rectification yields a greenish portion, and then a superb blue oil. Kachler (*B. Chem. G.*, 1871) found a colorless oil, $C_{10}H_{16}$, and a blue oil, $C_{10}H_{16}O$, which agreed with the blue oil of the flowers of

Matricaria Chamomilla. By fusing galbanum resin with potassium hydroxide, Hlasiwetz and Barth (*Ann. Ch. Ph.*, cxxx, p. 354) obtained resorcinol, together with acetic and volatile fatty acids.

Galbanum was known to the ancients. It is stimulant, expectorant, and antispasmodic, and is considered as intermediate in power between ammoniac and asafetida. It was formerly used in chronic affections of the bronchial mucous membrane, *amenorrhea*, and *chronic rheumatism*, but is now used chiefly in the form of plasters as an external stimulant.

Compound pills of galbanum were official in the British Pharmacopœia, 1898, under the name of *Pilula Galbani Composita* (formerly *Pilula Asafœtida Composita*) consisting of equal parts of galbanum, asafetida and myrrh, syrup of glucose being used as excipient.

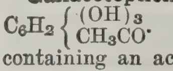
Dose, from ten to twenty grains (0.65 to 1.3 Gm.), given in pill, or triturated with gum arabic, sugar and water, so as to form an emulsion.

Under the name of *Zalou root* there appears in the Bayrout markets the root of the *Ferula Hermonii* Boiss. This contains, according to Guiges (*P. J.*, 1906, p. 65) a resin which differs from Galbanum in that it gives with hydrochloric acid a green color, which disappears on heating. It is used by the people of that section as an aphrodisiac.

Galium. *Galium Aparine* L. *Cleavers. Goosegrass. Grateron. Rièble*, Fr. *Klebkraut*, G.—This is a delicate annual, succulent, rubiaceous plant, indigenous to Europe and Asia and naturalized in the United States, growing along the seashore and in shaded ground inland. It possesses quadrangular, reclining stems that are hairy at the nodes and bristle-prickly, lanceolate leaves that are arranged 8 in a whorl, and small white flowers on axillary stalks. It is inodorous, and has a bitterish, herbaceous, somewhat acrid taste. Schwartz found in it a variety of tannic acid, which he named *galitannic acid*, citric acid, and a peculiar acid, previously discovered by Schwartz and Rochleder, and named *ribichloric acid*, $C_{14}H_8O_9$. (*P. J.*, xii, 190.) The expressed juice is said to be aperient, diuretic, and antiscorbutic, and has been used in *dropsy, congestion of the spleen, scrofula, scorbutic eruptions*, and *lepra.* Orwin (*T. G.*, vol. i, 767) commends it highly in *psoriasis.* Three ounces (90 cc.) may be given twice a day.

Galium verum L. *Yellow Ladies' Bedstraw. Cheese Rennet. Caille-lait jaune*, Fr. *Megerkraut, Liebfrauenstroh*, G.—This is a perennial species of Galium (Fam. *Rubiaceæ*) which is indigenous to Europe but found in northeastern United States and lower Canada. It differs from the former species in having erect, smooth stems, linear leaves and yellow flowers, the latter arranged in dense panicles. It is inodorous, but has an astringent, acidulous, bitterish taste. The bruised plant is sometimes used to color cheese yellow, being introduced into milk before coagulation. It is also used for dyeing yellow. The roots of this and of most other species dye red, and the plant, eaten by animals, colors the bones like madder. Schwartz found the same principles in it as in *G. Aparine.* It was formerly highly esteemed as a remedy in *epilepsy* and *hysteria*, and was applied externally in *cutaneous eruptions*, in the form either of the recently expressed juice or of a decoction from the fresh plant. Of the American species, *G. tinctorium* L. is closely allied in properties to *G. verum.* It is said to be useful in *cutaneous diseases*, and the root is employed by the Indians for staining their feathers and other ornaments red. *G. triflorum* Michx. contains coumarin, as pointed out by L. von Cotzhausen. (*A. J. P.*, 1876, 405.)

Gallacetophenone. *Alizarine Yellow. C.*—



$C_6H_2\begin{cases}(OH)_3\\ CH_3CO\end{cases}$. This is a derivative of pyrogallol, containing an acetyl group replacing an H atom of the benzene nucleus. Forms a pale yellow powder, crystallizing from hot water, in which, as well as in alcohol and ether, it is readily soluble. It is also soluble in glycerin. This substance has been proposed as a substitute for pyrogallic acid in the local treatment of *psoriasis*, it being claimed that it does not stain, and is not so poisonous as the acid.

Gallic Acid.—*Acidum Gallicum. U. S. IX. Trioxybenzoic Acid. Dioxysalicylic Acid. Trihydroxybenzoic Acid. Acide gallique*, Fr. Cod.; *Gallussäure*, G. *Acido gallico*, It. *Acido agallico*, Sp. $C_6H_2(OH)_3.COOH$. Gallic acid was dropped from the Br. at the 1914 revision and from the X revision of the U. S. It was first prepared by Scheele in 1786. Gallic acid is made by the decomposition of tannic acid either through the effect of living ferments or by the action of strong acids. The method of the U. S. P. of 1870 was based upon the spontaneous decomposition of tannic acid when exposed to the air. The British Pharmacopœia of 1885 employed a process based upon the decomposition of tannic acid by sulphuric acid. Fernbach (*C. R. A. S.*, 1900, cxxxi, 1214) found that a tannin splitting ferment *tannase* is present in *Pencillium*, and Pottevin (*C. R. A. S.*, 1900, cxxxi, 1215) isolated a similar ferment from *aspergillus.* This accounts for the conversion of the tannic acid into gallic acid when galls are moistened and allowed to stand, for they always become moldy during the process, and explains the sweated gallic fermentation of Robiquet and LaRoque.

Gallic acid is *trioxybenzoic acid* or, more properly speaking, 3:4:5 *trihydroxybenzenecarboxylic acid.* It is monobasic. Unlike tannin it does not precipitate alkaloids from their solutions.

Gallic acid is in "white, or pale fawn-colored, silky, interlaced needles, or triclinic prisms; odorless; having an astringent and slightly acidulous taste; permanent in the air. One Gm. of Gallic Acid dissolves in 87 mils of water, 4.6 mils of alcohol, 10 mils of glycerin, and in about 100 mils of ether at 25° C.; also in about 3 mils of boiling water; almost insoluble in chloroform. A saturated aqueous solution of Gallic Acid is acid to litmus. Add 6 drops of sodium hydroxide T.S. to 5 mils of a cold, saturated aqueous solution of the Acid; a deep green color gradually develops, which is changed to reddish or brownish-red by acids. Gallic Acid neither colors nor precipitates solutions of pure ferrous salts, but it forms a bluish-black precipitate with ferric salts. When dried to constant weight at 100° C., the Acid loses not more than 12 per cent. of its weight. Incinerate about 1 Gm. of Gallic Acid; not more than 0.1 per cent. of ash remains. A cold saturated aqueous solution of Gallic Acid yields no precipitate with gelatin T.S. or starch T.S. (*tannic acid*)." *U. S. IX.*

It produces a deep bluish-black color with solutions of ferric salts, which disappears when the solution is heated, a result which Mahla has shown to depend on the conversion of the gallic into *pyrogallic* or *metagallic acid* (pyrogallol) by the loss of carbon dioxide. Gallic acid does not precipitate gelatin, or a solution of ferrous sulphate.

By the action of arsenic it is converted almost entirely into tannic acid without the production of arsenous acid. (Schiff, *Chem. News*, xxix, 73.) Young's test, potassium cyanide, gives a reddish color with gallic acid and none with tannic acid. A mixture of ammonium chloride and ammonia produces a red coloration, but no precipitate, in gallic acid solution; while in tannic acid solution it produces a whitish precipitate rapidly turning reddish-brown. (*A. J. P.*, April, 1889.) A test proposed by Flückiger consists in adding to the solution of gallic acid a diluted (1 to 100) solution of pure ferrous sulphate. To the colorless solution a little sodium acetate is to be added, when a deep violet color will appear, due to the formation of ferrous gallate. Heated to 216° C., gallic acid gives off carbon dioxide, and is changed into *pyrogallic acid.*

Uses.—Gallic acid differs essentially from tannic acid in that it does not coagulate albumen. It is readily absorbed from the intestinal tract and eliminated through the kidneys. Its presence in the urine can be demonstrated by the addition of a soluble ferric salt after acidulation of the urine with hydrochloric acid. The older writers attributed astringent properties to gallic acid, although less active than those of tannic acid, but as the modern conception of the action of astringent drugs is that their effects depend upon the precipitation of albuminous matters this view must be regarded with doubt. Nevertheless it is used to a considerable extent by many physicians as an internal styptic, for example, in *hematuria* or *hemoptysis.* It is also asserted that it will lessen the quantity of albumen in the urine in cases of *nephritis.* Gallic acid is incompatible with solutions of alkali hydroxides and carbonates with which it combines to produce colors ranging from green to yellow, red, and brown. With lime water it gives even more marked color changes and produces a blue precipitate. With ferrous salts no change occurs, but as soon as oxidation begins or with ferric salts direct, an inky color is produced. It acts as a reducing agent with salts of silver and gold, and with iodine, arsenates, permanganates, etc. With lead salts and some other metallic salts it produces precipitates.

Dose, five to twenty grains (0.32–1.3 Gm.).

Gallicin. *Methyl Gallate. Methyl Ester of Gallic Acid.* $C_6H_2(OH)_3.COO.CH_3$.—This product is made by the interaction between warm solution of tannin in methyl alcohol and hydrochloric acid gas. It forms rhombic prisms or fine needles melting at 202° C., soluble in hot water, ether and alcohol. It is a non-toxic antiseptic and is used in *conjunctivitis, keratitis,* and other ocular inflammations, as an antiseptic dusting powder.

Gallinol. *Gallanol. Gallanilide.* $C_6H_2\text{-}\left\{\begin{matrix}CO.NH.C_6H_5\\(OH)_3+2H_2O\end{matrix}\right.$.—This anilide of gallic acid is formed by boiling tannin with aniline, and was brought forward by Cazeneuve and Rollet as a local remedy to replace chrysarobin in the treatment of skin diseases. (*C. R. A. S.*, 1893.) It occurs in colorless crystals melting at 205° C., of a bitter taste, soluble in hot water, ether, and alcohol, insoluble in benzene and chloroform. It has been especially commended by Gonon, Bayet, Max Joseph, and others, not only in *psoriasis,* but also in chronic *eczema,* to be used in a 10 per cent. solution or ointment, or sometimes in very advanced cases as high as 20 per cent.; it is affirmed never to produce irritation. The removal of the hair is not necessary, provided the skin be thoroughly cleansed with alkaline soap solutions.

Gallobromol. *Dibromgallic Acid.* $C_6Br_2(OH)_3COOH$.—A light brown powder composed of fine needles melting at 205° C.; soluble with difficulty in cold water, easily soluble in hot water, alcohol, and ether, and having a strong acid reaction and a slightly bitter taste. It has been used by Lépine in *neurasthenia* and *epilepsy* to replace potassium bromide, but it would seem to be a somewhat dangerous remedy, as in Lépine's experiments a dog weighing 11 kilogrammes was killed in two hours by 11 Gm. According to Stein, it is to dogs more poisonous than the sodium bromide, less than the potassium bromide. In the dog small doses produce a primary moderate rise of the blood pressure, followed by fall of pressure, with cardiac arythmia. It has also been used as a local application in *cystitis* and *skin diseases.* It is incompatible with alkalies or alkaline salts, and iron compounds. *Dose* (Lépine), as a sleeping potion, forty-five grains (3 Gm.); in *epilepsy,* from thirty to forty-five grains (2–3 Gm.) a day. (See *Cb. G. T.*, xiii, 1895.)

Gallogen. *Ellagic Acid.* $C_{14}H_6O_8$.—This is a yellowish powder devoid of odor and taste, insoluble in an acid or neutral fluid, but soluble in alkaline fluids. In solution it shows the characteristic tannic acid reactions. With nitric acid containing nitrous acid it gives a characteristic dark red color. It is employed as an intestinal astringent in all forms of *diarrhea. Dose,* adults fifteen grains (1 Gm.) several times a day; for children, five to eight grains (0.32–0.5 Gm.) several times a day.

Gallols.—E. Kromayer (*Monatshefte für Prakt. Dermatologie,* vii) has tested as remedies for diseases of the skin a number of chemical combinations of pyrogallol, chrysarobin, and resorcinol, with various acids. Of these a few give promise of therapeutic usefulness.

Lenigallol. Pyrogallol Triacetate. $C_6H_3(CH_3CO_2)_3$.—This is a white powder, insoluble in water, and is used in paste form. This derivative of pyrogallic acid has been highly commended as a local remedy in acute and moist *eczema,* and in *pityriasis rosea.* It is said not to act well in the dry desquamating eczemas. It is generally applied in the form of a paste containing from 2 to 5 per cent. of *lenigallol.* In the strength of 30 to 50 per cent. it is also useful as a keratolytic. It is slowly soluble on warming with aqueous solutions of alkalies, with decomposition.

Eugallol, pyrogallol monoacetate, is a very thick, syrupy, transparent, dark yellow mass, readily soluble in water. Marketed only in a 66 per cent. solution in acetone.

These substances are stated not to be affected by contact with healthy skin, but to be slowly decomposed by the diseased skin with the liberation of pyrogallol. Strong ointments of lenigallol are to be employed in *psoriasis,* 1 or 2 parts of lenigallol to 200 parts of zinc paste in *eczemas.* Even the most acute eczemas, as well as those with impetiginous crusty exudations, are reached by the ointment.

Eugallol produces great local excitement, and is only to be employed in the most obstinate cases of *psoriasis.* Under such circumstances, however, the direct local application as a paint, daily or every other day, produces a marked inflammation, under which the most stubborn patches are said to disappear. Dusting the painted parts with zinc oxide before drying makes the action more vigorous. The value of eugallol has been strongly confirmed by Paul Gruneberg (*Derm. Zeit.*, vi, 1899), who uses in *lupus* a zinc paste with from 11 to 12 per cent. of eugallol continuously applied after free curetting, and in *psoriasis* a 33½ per cent. acetone solution followed by zinc oxide dressing.

Galyl.—This arsenic compound is said to be *tetroxy-diphospho-amino-diarseno-benzene* with the empiric formula $C_{24}H_{22}O_8N_4P_2As_4$. It is asserted to possess curative properties in *syphilis* similar to those of salvarsan (see Dudley, *L. L.*, July 8, 1916) and to be decidedly less toxic (Pearce and Brown, *J. Ex. M.*, 1915, p. 517). It has also been recommended by Falconer and Anderson (*L. L.*, 1917, ii, 486) as an adjuvant to quinine in obstinate *malarial fevers.* It is given in *doses* of from three to six grains (0.2–0.4 Gm.) injected intravenously or intramuscularly, at intervals of from three to seven days until a total of about thirty-two grains (2.0 Gm.) has been administered.

Gardenia. *Gardenia grandiflora* Lour. (Fam. *Rubiaceæ.*)—A Chinese tree, the fruit of which is employed in dyeing the yellow robes of the mandarins, and according to Lorenz Mayer, contains *crocin* (see *Crocus*). The fruit of another species, *G. campanulata* Roxb., growing in the forests of Chittagong, in India, is said to be used by the natives as a cathartic and anthelmintic. (Lindley, *Flor. Med.*, 434.)

Garrya Fremontii Torr. *California Fever Bush. Skunk Bush.*—A shrub belonging to the *Cornaceæ,* indigenous to California and Oregon. Its leaves are ovate or oblong, acute, yellowish-green. Its flowers are borne in dense axillary spikes and its fruit is a 1–2 seeded berry. The leaves are intensely bitter, and were formerly esteemed tonic and antiperiodic. D. W. Ross (*A. J. P.*, 1877) states that he found in them a new alkaloid, *garryine.* The *dose* of the fluidextract of the leaves is from ten to thirty minims (0.6–1.8 cc.).

Gaultheria. *Wintergreen. Boxberry. Teaberry. Checker-berry. Gaulthérie couché, Paloninier, Thé du Canada, Thé de Terreneuve,* Fr. *Canadischer Thee, Bergthee,* G.—*Gaultheria procumbens* L. (Fam. *Ericaceæ*) is a small indigenous, woody, evergreen plant. The leaves, which were formerly official in the U. S. Pharmacopœia, are short-petiolate, obovate or oval, about 4 cm. in length and 2 cm. in breadth, acute, revolute, obscurely serrate at the edges, coriaceous, shining, bright green above, paler beneath, of unequal size, and supported irregularly on short red petioles.

The plant extends from Newfoundland and Manitoba southward, growing in large beds in mountainous tracts, or in dry barrens and sandy plains, beneath the shade of shrubs and trees. The white, nodding flowers appear from July to August, singly in the leaf axilla and the red, baccate fruit ripens at corresponding periods. To the very peculiar aromatic odor and taste which belong to the whole plant the leaves add a marked astringency. The aromatic and medicinal properties of wintergreen reside exclusively in their volatile oil. (See *Methylis Salicylas.*)

Gelanth. *Gelanthum.*—*Gelanth* is a combination of equal weights of tragacanth and gelatin, prepared by Unna as a basis for various pastes for the skin. It is stated to be superior to the older pastes in drying more quickly and leaving a smoother coating upon the skin, as well as in holding more uniformly and in tighter suspense the drug used with it, and in not spoiling readily. It is made by allowing tragacanth to soften with twenty times its mass of water for four weeks, then warming the mass to fluidity with steam and pressing it through a mill. In the meanwhile gelatin has been softened in the water and then for some time exposed to a high pressure of steam in Unna's boiler, which exposure lessens its capability of gelatinization. The mixture of the two masses is allowed for two days to soften in the steam, then passed through a mill and mixed with 5 per cent. of glycerin, a little rosewater, and 2 per cent. of thymol. The finished gelanth contains about 2½ per cent. each of dry gelatin and tragacanth. In using it as a vehicle, fatty matters must first be emulsified and insoluble substances rubbed up with water to a soft paste before they are mixed with gelanth.

Genista. *Genista tinctoria* L. *Dyers' Broom. Dyers' Weed. Green Weed. Woad-Waxen. Genet des Teinturiers,* Fr. *Färberginster,* G. (Fam. *Leguminosæ.*)—A low shrub, growing wild in Europe, and established on sterile hills and roadsides from Maine to New York, cultivated in greenhouses in this country on account of its profusion of yellow leguminous flowers. The flowering tops of the plant are employed to dye yellow, whence its name was derived. Both these and the seeds have been used in medicine. They are said to be purgative and even emetic, especially the seeds, which were formerly given as a cathartic in the *dose* of a drachm and a half (5.8 Gm.). By some authors they are said to be diuretic and to be useful in *dropsy.*

Gentian Violet.—*N. N. R.* 1925. This is a trade name of *methyl violet* which is a mixture of the hydrochlorides of penta- and hexamethyl-pararosaniline, $C_{19}H_{12}(CH_3)_5N_3HCl$ and $C_{19}H_{11}(CH_3)_6N_3HCl$. A proprietary form of the same chemical is known under the name of *Pyoktanin.* It is a green crystalline powder, soluble in about 20 parts of water, alcohol or glycerin. It is insoluble in petroleum fractions.

Boer called attention many years ago to the extraordinary difference in the susceptibility of various species of bacteria to the disinfectant action of this dye. In 1912 Churchman (*J. Ex. M.*, 1912, xvi, and *J. Ex. M.*, 1921, xxxiii, p. 569) showed that in very dilute solution (1 to 100,000) it inhibits the growth of "Gram-positive" organisms (that is, bacteria which are not decolorized by Gram's iodine solution), but does not affect "Gram-negative" bacteria nor human tissue cells. The "Gram-positive" group of bacteria includes the diphtheria bacillus, the staphylococcus pyogenes, the gonococcus, etc. On the basis of these effects he injected a saturated aqueous solution into the joint cavity in cases of gonorrheal and staphylococcic *arthritides* with great benefit (see *J. A. M. A.*, 1920, lxxv, 1921, lxxvii, p. 24). Smith and Casparis (*J. A. M. A.*, 1923, lxxxi, p. 2184) and later Young and Hill (*J. A. M. A.*, 1924, lxxxii, 672) have employed it with brilliant results in cases of staphylococcus *septicemia.* They used *doses* of from 2 to 5 milligrammes per kilo of body weight. It has been used to a considerable extent in veterinary practice; Klein (*Berlin. Tierartz. Wochens.*, 1911) and others have reported favorably on the value of pyoktanin in *foot and mouth disease.* It is also used in *doses* of one to eight grains (0.065–0.5 Gm.) in the treatment of *cholera* and *carcinoma.*

According to Fühner (*A. E. P. P.*, 1908, lix, p. 161), methyl violet has an effect upon the heart similar in kind to that of digitalis, and *methyl green*, which is prepared from methyl violet, has no effect upon the heart, but acts upon the peripheral motor nerves as does curara.

Germanium. (Ge–72.5.)—This element was discovered in 1886 by Winkler in the silver-containing mineral argyrodite which contains germanium to the extent of 6 or 7 per cent. He named it for his native country as argyrodite had just been discovered near Freiburg in 1885. Germanium has since been found in several other rare minerals including Canfieldite and Euxenite. The element germanium is a grayish white metal having a fine luster and crystallizing in octahedra. It melts at about 900° C. and has a specific gravity of 5.46. It forms two classes of salts corresponding to the oxides GeO and GeO_2.

Germanium dioxide is a white powder soluble in alkalies but almost completely insoluble in acids.

Hammett and Nowrey (*J. Ex. M.*, 1922, xxxv, p. 507 and *J. P. Ex. T.*, 1922, xix, p. 337) have shown that *germanium dioxide* has remarkable power of stimulating the formation of red blood cells. The histological examination of animals which had received the drug led to the inference that the increase in the number of corpuscles was due to a stimulating influence upon the bone marrow; there was no evidence of any destruction of red blood cells nor any action upon the spleen. They found also that the agent is of very low toxicity, rats surviving doses up to 180 milligrammes per kilo. These results naturally suggest the use of this agent in *anemia.* It has been used clinically by Lenker (*Penna. Med. J.*, 1922, xxvi, p. 86) and by Kast (*J. Lab. Clin. M.*, 1922, vii, p. 643) and others in the treatment of various types of *anemia.* Lenker concludes that in secondary anemia its beneficial effects are very positive; in *pernicious anemia* it caused more or less temporary improvement and he classes its effect in this disease with that of arsenic. Alexander (*A. J. M. S.*, 1923, clxvi, p. 256) found the results in pernicious anemia less satisfactory than those of iron cacodylate.

Although Kast administered the drug by mouth, most of those who have used it employed it hypodermically. Lenker recommends that the aqueous solution be neutralized with sodium hydroxide for hypodermic injection. In this case it is manifest that sodium germanate will be formed. Nowrey (*J. H. H. B.*, 1922, xxxiii, p. 341) has experimentally found that solutions of *sodium germanate* are efficacious. The solutions are injured by boiling.

The *dose* of germanium dioxide recommended is from one-third to two-thirds of a grain (0.02 to 0.04 Gm.) daily. Kast gave by mouth from one and one-half to three grains (0.1 to 0.2 Gm.) daily for two or three days.

Geum. *Water Avens. Radix Caryophyllatæ Aquaticæ. Radix Benedictæ Sylvestris. Racine de Benoîte aquatique* (*de Benoîte des Ruisseaux*), Fr. *Sumpfnelkenwurzel, Wasser-Benedikten-Wurzel*, G.—Several species belonging to this rosaceous genus have been medicinally employed, but three or four are deserving of particular notice—*Geum rivale* L., which once had a place in the U. S. Secondary List, *G. urbanum* L., formerly recognized by the Dublin College, *G. virginianum* L., an indigenous species, the root of which has been recommended in *dysentery* by W. A. Gibson (*Med. Rec.*, 1868), and *G. canadense* Jacq. (*G. album* Gmel.), recommended by W. A. Spurgeon in *gastric irritation* and *headache.* (*A. J. P.*, 1883.)

The rhizome of *Geum urbanum* L. is from 3 to 7 cm. in length and about 8 mm. in thickness. It is more or less branching, having on the upper surface the remains of the short stems and petiole-bases and on the lower surface numerous fibrous roots. Externally it varies from a brownish to a brownish-yellow and internally it is dark brown. The fracture is short. When quite dry it is nearly inodorous, but in the recent state has an odor like that of cloves, whence it is sometimes called *radix caryophyllatæ.* The taste is bitterish and astringent. It imparts its virtues to water and alcohol, which it tinges red. Buchner obtained a yellow, amorphous, neutral, bitter-tasting mass, which he calls *geum-bitter.* Distilled with water it yields 0.04 per cent. of a thick, greenish-yellow volatile oil, consisting chiefly of eugenol, a tasteless resin, gum, bassorin, and starch. It has been much used in Europe as a tonic and astringent, in chronic and passive *hemorrhages, chronic dysentery* and *diarrhea, leucorrhea, intermittent fever,* etc. The *dose* is from thirty grains to a drachm (2.0–3.9 Gm.) of the powder three or four times a day, or an equivalent quantity in decoction.

Geum rivale L.—*Water* or *purple avens,* a plant growing in bogs and wet places in the northern United States, has a perennial, horizontal, jointed, scaly, tapering root, about 15 cm. long, of a reddish-brown color externally, white internally, and furnished with numerous descending yellowish fibers. The dried root is hard, brittle, easily pulverized, reddish or purplish, without odor, and of an astringent, bitterish taste. Boiling water extracts its virtues.

Water avens possesses similar therapeutic properties to avens, for which it is sometimes substituted, but is less esteemed. The *dose* of the powdered root is from twenty grains to a drachm (1.3–3.9 Gm.), to be repeated three times a day. A weak decoction is sometimes used by invalids in New England as a substitute for tea and coffee.

Gillenia. *Racine de Gillénie,* Fr. *Gillenienwurzel,* G.—Under this name the U. S. P. formerly included in its Secondary List the roots of two species of *Gillenia.* (Fam. *Rosaceæ.*)

Gillenia trifoliata (L.) Moench. or *Bowman's Root* is a perennial herb whose underground portion consists of a rhizome having numerous long slender roots. The leaves are trifoliate with ovate-oblong, cut-serrate leaflets and small awl-shaped stipules. It grows throughout the United States, east of the Mississippi. The root should be gathered in September. (See *A. J. P.*, 1898, 501.)

G. stipulata (Muhl.) Trel., commonly known as *Indian-Physic* or *American Ipecac,* also a perennial herb, differing from the preceding species in possessing lanceolate, deeply cleft leaves with large leaf-like, doubly incised stipules. It grows as far north as the state of New York, and extends as far west as Kansas. Its root is precisely similar to that of the eastern species, and is reputed to possess the same properties.

The roots of *G. stipulata* resemble those of

Ipecac, the bark being thinner and enclosing in the inner layers numerous reddish resin cells. The roots of *G. trifoliata* are smaller and indistinctly annulate, exhibiting few or no distinct fissures. For microscopic characters, see G. L. Curry. (*Am. Pract. and News*, May, 1892.) The bark, which is easily separable, has a bitter, not disagreeable taste; the wood is nearly insipid and comparatively inert, and should be rejected. The powder is of a light brownish color, and possesses a feeble odor, which is scarcely perceptible in the root. The bitterness is extracted by boiling water, which acquires a red color. The root yields its bitterness also to alcohol. *Gillenin* of W. B. Stanhope was a whitish substance, very bitter, slightly odorous, permanent in the air, soluble in water, alcohol, ether, and the dilute acids, and neutral to test paper. Nitric acid rendered it blood-red, chromic acid green. Tannic acid produced no effect. It gave white precipitates with potassium hydroxide, lead subacetate, and tartar emetic. Half a grain (0.032 Gm.) of it produced nausea and retching. (*A. J. P.*, xxviii, 202.) G. L. Curry (*A. J. P.*, 1892, 513) has found two glucosides: the first, *gillein*, obtained from the ethereal extract, formed white feathery crystals, was colored red by sulphuric acid, yellow by nitric acid, and deepened the color of chromic acid; the second, *gilléenin*, obtained from the aqueous infusion, was amorphous, of yellowish color, of faint taste at first but becoming very bitter, and giving no color reactions with the acids.

Gillenia is a mild and efficient emetic, and, like most substances belonging to the same class, occasionally acts upon the bowels. In very small doses it has been thought to be tonic, and has been used as a substitute for ipecacuanha, which it is said to resemble in its mode of operation. It was employed by the Indians, and became known as an emetic to the colonists at an early period. Linnæus was aware of its reputed virtues. *Dose* of the powdered root, as an emetic, from twenty to thirty grains (1.3–2.0 Gm.).

Ginseng. *Panax quinquefolium* L. *Panax. U. S.* 1870. *Ginseng*, Fr. G., Sp. *Ginsen*, It.—*American ginseng* is a perennial herb belonging to the *Araliaceæ.* It is indigenous to eastern North America and grows in rich, cool woods, especially along the mountains, from Quebec and Ontario, south to Georgia. The plant is characterized by its large, aromatic, spindle-shaped, often forked root, its solitary stem bearing a single whorl of 3 palmate leaves, each of which usually has 5 ovate-oblong leaflets, its terminal umbel of greenish-white flowers and its red berry fruits. The root is the part employed. It is not used in America, but is exported to China. While supplied with *ginseng* exclusively from their own country, which furnished the root only in small quantities, the Chinese entertained the most extravagant notions of its virtues, considering it a remedy for all diseases, and as possessing almost miraculous powers in preserving health, invigorating the system, and prolonging life. It is said to have been worth its weight in gold at Pekin, and the first shipment from North America to Canton yielded enormous profits. John Henry Wilson (*P. J.*, July, 1888) states that there are in the Chinese market five ginsengs, four of them of Asiatic origin, derived from *Panax Ginseng* C. A. Meyer, the fifth, the American ginseng, from *Panax quinquefolium.* According to E. M. Holmes, *T'angshên,* which is used by the poor of China as a substitute for the costly ginseng, is a root of a campanulaceous plant, *Codonopsis Tangshen,* and is exported from Hankow and Oo-chang to the extent of five hundred tons annually. (*P. J.*, xxi.) For an account of the Chinese methods of using ginseng, see *P. J.*, vi, 86.

On account of the growing scarcity of the American ginseng plant, it is now cultivated quite extensively, but many precautions are necessary for success. The cultivated roots were larger than those of the wild plant. For an account of the ginseng cultivation in Corea, see *P. J.*, 1885, 732; and of its collection in the United States, see *D. C.*, 1884, 33. (For details of culture and preparation, see *Bulletin 62, Pennsylvania State Agricultural Experiment Station; Bulletin No. 16, Division of Botany, U. S. Department of Agriculture; Proc. A. Ph. A.*, 1901, p. 90; *Ph. Era*, 1900, p. 581; 1903, p. 497; *P. J.*, 1904, p. 652.)

The root is fleshy, somewhat spindle-shaped, from 5 to 12 cm. long, and 1 to 2.5 cm. thick, often bifid or trifid, occasionally having a remote resemblance to the human figure, from which circumstance it is said the Chinese name *ginseng* originated. Externally it is yellowish-white to yellowish-brown, annulate and longitudinally wrinkled. Its fracture is short, exhibiting a soft, thick, mealy bark containing many reddish oil and resin cells and a central yellowish wood with narrow wedges and broad medullary-rays.

Ginseng has a feeble odor, and a sweet, slightly aromatic taste, somewhat analogous to that of licorice root. It contains a glucosidal principle, *panaquilon,* besides saponin, a bitter principle, a volatile oil, resin, sugar, mucilage and starch. S. S. Garrigues gives the formula for panaquilon as $C_{12}H_{25}O_9$. It is an amorphous, yellow powder, soluble in water and alcohol, but not in ether, of a sweet bitterish taste, and has the characteristic property that, when treated with strong acids, it is converted into a white substance, insoluble in water, with the escape of carbon dioxide and water. Garrigues proposed for this white substance the name of *panacon,* $C_{11}H_{19}O_4$. (*A. J. P.*, xxvi, 511.) Davydow (*A. J. P.*, 1890, 338) investigated these principles discovered by Garrigues, but adds nothing new to our information concerning them. W. Sakai states that the ether soluble fraction of ginseng contains the active principle, and that the volatile oil has a density of 0.925 and consists mainly of *panacen* $(C_5H_8)n$, which increases the blood pressure and the rate of respiration. An unsaturated acid of high molecular weight is also present both in the free state and as an ester. He states that the resin is physiologically inert. Kondo and Yamaguchi obtained 10 Gm. of this same volatile oil from 18 kilos of Japanese ginseng. They also isolated a phytosterol and several fatty acids.

The extraordinary medicinal virtues formerly ascribed to ginseng had no other existence than in the imagination of the Chinese. It is little more than a demulcent, and in this country is rarely employed as a medicine. Sakai (*Sei-I-Kwai*, 1917, xxxvi, p. 113) from physiological experiments concludes that ginseng has a sedative effect upon the cerebrum and a mildly stimulating action upon the vital centers. Some persons are in the habit of chewing it, having acquired a relish for its taste, and it is sold chiefly to supply the wants of these.

Glaucium. *Glaucium flavum* Crantz. (*G. luteum; G. Glaucium* Karst.) *Yellow Horned*

Poppy. Sea Poppy. Bruiswort. Pavot cornu, Fr. *Hornmohn,* G. (Fam. *Papaveraceæ.*)—An annual or biennial plant with clasping cauline leaves and solitary yellow or orange flowers indigenous to Europe and sparingly naturalized in waste places from New England to Virginia. In contains a saffron-colored, milky juice. The stems and leaves, according to Fischer (*A. Pharm.*, 1901, ccxxxix, p. 426), contain two alkaloids—*glaucine* and *protopine*—while the root contains besides protopine traces of chelerythrine and sanguinarine (see under *Sanguinaria*). Glaucine has also been studied by Gadamer (*A. Pharm.*, 1911, ccxlix, 680); it has the formula $C_{21}H_{25}O_4N$, and forms yellow crystals. Maepmann and Helt recommended the plant in the treatment of *diabetes* (*Med. Neuigkeiten d. Pharm-Post.*, 1899, 346).

Glechoma. *Nepeta hederacea* (L.) Trevisan (*N. Glechona* Benth.). *Herba Hederæ Terrestris. Lierre terrestre,* Fr. *Gundermann, Gundelrebe,* G. *Ground-ivy. Gill-over-the-ground.*—A small perennial creeping herb (Fam. *Labiatæ*), with roundish kidney-shaped leaves and light blue flowers indigenous to Europe and widely naturalized in the United States, and growing in damp, shady, grassy places, as in orchards and along fences and hedges. The herb was formerly official, and still enjoys some credit as a domestic remedy. It has a peculiar, disagreeable odor, and a bitter, somewhat aromatic taste, and imparts its properties to boiling water. It was formerly used in chronic *pulmonary* and *urinary catarrhs.* From a half drachm to a drachm (2–3.9 Gm.) was usually given in infusion as a dose.

Gleditschine.—*Gleditschia triacanthos* L., or *Honey Locust,* and *G. Macracantha* Desf. (Fam. *Leguminosæ*), are small, thorny trees having pinnate leaves, small spikes of inconspicuous, green flowers, and elongated pods containing flat seeds and a sweet pulp. The former grows in rich woods in the eastern and central United States and is common in cultivation; *G. Macracantha* is indigenous to China. These trees were chemically studied by B. F. Lautenbach (*P. M. T.*, 1878), who abstracted from them an alkaloid, which he found to produce in the frog stupor and loss of reflex activity, due to an action upon the spinal cord. To this alkaloid Lautenbach gave the name of *gleditschine.* In 1887 a solution asserted to contain an alkaloid *stenocarpine,* which was asserted to be obtained from the *Gleditschia triacanthos,* was brought forward as a local anesthetic. This solution was shown by Marshall (*Phila. Med. News,* 1888) and others to contain 6 per cent. of cocaine, besides some atropine or other mydriatic alkaloid. (See also *A. J. P.*, 1887, 589.)

Glidin.—Glidin is an albuminous preparation made from wheat flour and is asserted by Loeb (*Med. Klin.*, 1905–1906, p. 625) to represent 98 per cent. of albumin and 1 per cent. of lecithin. While it has been used to a slight extent as a nutrient, its greatest interest lies in the fact that it forms chemical combinations with various irritant drugs. An examination of glidin by Coblentz showed 30 per cent. albumin, 2 per cent. nutritive salts and 68 per cent. carbohydrates, varying greatly from Loeb's analysis.

Arsen-glidin (*Arsan*) is a yellowish-gray powder insoluble in water but dissolving with a yellow color in alkalies. It represents about 4 per cent. of arsenous acid. It is generally administered in the form of tablets, each of which represents one thirty-second of a grain (0.002 Gm.) of arsenic.

Bromo-glidin is a brownish, odorless, almost tasteless powder, sparingly soluble in water and is used in the same manner as the inorganic bromides. The *dose* is eight to fifteen grains (0.5–1.0 Gm.). Another of these compounds is *iodoglidin* which is recommended in *doses* of fifteen to forty-five grains (1.0–3.0 Gm.) per diem in the various conditions in which iodine has been employed. It is a dark, yellow powder, said to contain 10 per cent. of iodine, and according to Boruttan (*D. M. W.*, 1907, p. 1490) it is much more slowly absorbed than the inorganic iodides.

Globularia. *Globularia Alypum* L. *Wild Senna* of Europe. (Fam. *Globulariaceæ.*)—This is a small shrub indigenous to the European shores of the Mediterranean. Its leaves have been occasionally used as a cathartic since the Middle Ages. Heckel and Schlagdenhauffen obtained from the leaves *globularin,* $C_{15}H_{20}O_8$, an amorphous glucoside which splits by treatment with mineral acids into glucose and *globularetin,* C_9H_6O. *Globularia vulgaris* L. was found to contain the same substances. (*J. P. C.*, 1883, 361.) It is asserted that globularin is a vasomotor constrictor which acts especially upon the renal arteries. Jaksch (*R. T.*, 1910, p. 596) has observed diminution of the quantity of urine in *diabetes insipidus,* also of *diabetes mellitus,* after the administration of the glucoside. The *dose* of globularin is one-half to one grain (0.03–0.065 Gm.) daily. It does not diminish the excretion of sugar. Globularetin, a brownish-yellow powder, has also been used in medicine as a diuretic and purgative, although no definite information can be found regarding either its efficiency or its manner of use. *Dose,* of Globularia, according to Planchon, one ounce (31 Gm.), in decoction.

Gloriosa. *Gloriosa superba* L.—This plant, commonly known as *Climbing Lily* (Fam. *Liliaceæ*) is found in the forests of tropical Africa and Asia. It possesses ovate-lanceolate leaves, and its flowers, while opening yellow, later become yellowish-red and deep scarlet. The roots, stalk, and leaves are said to be an acrid narcotic poison, and not infrequently used for suicidal purposes in India. Gloriosa contains according to Warden a poisonous alkaloid *superbine* (*P. J.*, xi, 496) and two resins. Clewer, Green and Tutin (*Tr. Chem. Soc.*, 1915, cvii, p. 835) report also the presence of colchicine and another base—possibly methylcolchicine—and choline.

Glue.—An impure form of gelatin, obtained from various animal substances by boiling them in water, straining the solution, and evaporating it until, upon cooling, it assumes the consistence of jelly. The soft mass which results is then divided into thin slices, which are dried in the open air. It differs from gelatin in containing a larger proportion of glutin and a smaller amount of chondrin. Glue, when of good quality, is hard and brittle, of a color varying from light yellow to brown, and equally transparent throughout. It softens and swells very much in cold water, without dissolving, but is readily dissolved by hot water. It is soluble in large proportion of glycerin, and with heat forms with it in smaller proportion a jelly. It is employed chiefly for cementing wood.

An elastic and imputrescible preparation of glue may be made by dissolving glue in water by means of a water bath, concentrating the solution, then adding a weight of glycerin nearly equal to that of the glue employed, thoroughly mixing, evaporating the excess of the water, and finally pouring into molds, or on a marble slab. It has been used for the preparation of artificial anatomical specimens. The various *hectograph compositions* introduced for copying purposes are similar mixtures. One of the best copying masses is made by dissolving one part of glue or gelatin in a mixture of two parts of water and four parts of glycerin, with a few drops of phenol, heating, straining, and adding three parts of sifted whiting or terra alba. (See *N. R.*, 1879, 338, 364.) A good *liquid glue* may be made by mixing two pints of distilled water, sixteen ounces of the best white glue and four ounces of dry white lead, heating upon a water bath until homogeneous, then adding four fluidounces of alcohol, and continuing the heat and the agitation for a few minutes. The mixture is to be poured into bottles while still hot. A liquid glue may also be prepared by mixing in a stoppered bottle 38 parts of glue properly divided, and 100 parts of 36 per cent. acetic acid. On exposure the acid evaporates, leaving the glue unchanged. (*J. P. C.*, 3e sér., xlvi, 35.) Knaff prepares *strong liquid glue* by covering three parts of good glue, in small pieces, with eight parts of water, and, after it has stood for some hours, adding half a part of hydrochloric acid and three-fourths of a part of zinc sulphate, and exposing the whole for ten or twelve hours to a heat from 81.1° to 87.2° C. This does not gelatinize, and keeps well. For a *waterproof glue* add potassium dichromate to the solution of glue just before using, in the proportion of one part to fifty. (*A. J. P.*, xliii, 420.) *Chromatized gelatin*, obtained by the addition of one part of potassium dichromate to five parts of a solution (5 or 10 per cent.) of gelatin, forms an excellent cement for glass. The surfaces to be united, after being smeared with the cement, are placed upon each other and exposed to the sun. After a few hours the adhesion is perfect and almost invisible, and boiling water itself has no action on the cement. (*L. L.*, Nov. 11, 1876.) For other formulas for liquid glue, see *A. J. P.*, xliii, 421.

Glutaric Acid. *Acidum Glutaricum.* COOH.-CH_2.CH_2.COOH.—*Glutaric acid*, also called normal *pyro-tartaric acid*, forms colorless crystals, soluble in water and alcohol. It melts at 97° C. and boils above 290° under decomposition.

Wilenko (*D. M. W.*, 1908) found that glutaric acid diminished or caused a complete disappearance of the glycosuria caused by phloridzin. In a later communication (*Ther. Geg.*, 1909, 277) he reaches the conclusion that this action is due to an effect upon the kidneys, for he found acute parenchymatous nephritis and does not believe that the substance has any effect upon the metabolism. The *dose* which was employed ranged from one-half to one grain (0.03–0.065 Gm.) per kilo, body weight.

Glutoid Capsules.—Gelatin capsules which have been hardened by exposure to formaldehyde are recommended by Sahli in several grades, the weak capsule capable of withstanding the action of the gastric juices for from one and a half to seven hours, the strong for twelve hours. They appear to have great applicability for the purpose of conveying intestinal antiseptics, medicinal substances which are destroyed by the peptic secretions, and irritating drugs, through the stomach into the intestines. They have been used by Sahli (*D. A. K. M.*, lxi) for diagnostic purposes. By their means he asserts that he is able to determine the condition of the pancreatic secretion and the closure of the pancreatic duct, the varieties of jaundice, etc. (See also under *Gelatinum.*)

Glutol. *Glutoform.*—This is made by the action of the solution of formaldehyde upon gelatin. It is a hard, clear, transparent mass, which may be pulverized. It is claimed to be a non-irritating and non-toxic antiseptic, exerting its action only when in contact with living cells in consequence of the liberation of nascent formaldehyde, employed in the undiluted form as a dusting powder, etc.

Glycerinophosphoric Acid. *Acidum Glycerino-Phosphoricum. Glycerophosphoric Acid.* $H_2C_3H_5(OH)_2PO_4$.—This is an oily liquid whose salts have been commended as powerful nerve tonics in *neurasthenia* and allied conditions. Several of the salts are official, see *Calcii Glycerophosphas* and *Sodii Glycerophosphas* in Part I.

Glycosal. *Monosalicylic Glycerinester.* C_6H_4-OH.COO.$C_3H_5(OH)_2$.—This substance, originally prepared by E. Tauber, is a white crystalline powder, soluble (one per cent.) in cold water and freely in hot water, very soluble in alcohol, decomposed by alkalies and alkali carbonates, and also, it is said, by the intestinal juices with the separation of salicylic acid. Under the name of *antirheumol* a 20 per cent. solution of the glycerin esters of salicylic acid in glycerin and alcohol is claimed to have marked remedial effects in the treatment of *rheumatism*. A concentrated solution, 50 per cent. strength, is also marketed as "antirheumol concentrated." It is used externally with thorough friction. It is not to be confused with Glysal (see below).

Glycosal has been especially recommended as affording means of treating *rheumatism* by external application. Zeigan (*B. K. W.*, 1903) found that from 50 to 100 grammes of its twenty per cent. alcoholic solution, to which a little glycerin had been added, placed upon the rheumatic part and covered with waterproof wadding, was sufficient to produce in four or five hours strong sweating lasting from a half to two hours, and in from six to eight hours a notable elimination of salicylic acid with the urine with the relief of the local symptoms. Ratz, however, has been unable to secure absorption either by means of the alcoholic solution or yet by inunctions made with an indifferent fatty basis; although when ether, oil of turpentine, or chloroform was added in the proportion of fifteen per cent. to the ointment, a notable proportion of salicylic acid appears in the urine after the local application. R. Block (*Th. M.*, Sept., 1903) found that the best method of using glycosal is a twenty per cent. collodion, which he applied every two to four hours to swollen rheumatic joints with asserted most extraordinary results. He claimed that if no relief is afforded the inflammation may be positively considered not to be of rheumatic origin.

Glycosal is also used internally as an antirheumatic in *doses* of one hundred and fifty to one hundred and eighty grains (9.8–11.6 Gm.) a day, usually without the production of salicylism; eight to ten grains (0.5 to 0.65 Gm.) may be given every half to three hours until sweating is induced. The remedy is probably uncertain and feeble in its influence.

Glycotauro. *N. N. R.* 1924.—This is a proprietary preparation of bile salts freed from bile pigment and standardized to contain 50 per cent.

of the natural mixture of sodium glycocholate and sodium taurocholate. Each gramme represents about 10 cc. of fresh ox bile. (See *Extractum Fellis Bovis*, Part I.)

Glycozone.—A proprietary preparation claiming to possess antiseptic properties which has been found to consist essentially of 5 per cent. glyceric acid, 90 per cent. glycerin with a small proportion of water, and to contain no hydrogen or other peroxides or any ozones.

Glysal. *Spirosal. N. N. R.* 1924. *Mono-glycol Salicylate.* $C_6H_4OH.CO.O(CH_2.CH_2.OH)$.—It occurs as an almost colorless and odorless liquid, freely miscible with alcohol, and with eight parts of olive oil. It has been brought forward as a means of administering salicylic acid endermically. According to Schoenheim (*Med. Klin.*, 1907) it is more rapidly absorbed through the skin than the other preparations of salicylic acid intended for percutaneous absorption, and a number of clinicians have reported favorably upon its application in various forms of *rheumatism.* It has also been suggested for the treatment of *furunculosis* of the external auditory canal. It is applied either undiluted, or mixed with equal parts of alcohol, about a drachm at a dose, well rubbed into the skin, and then covered with impermeable dressing.

Gnaphalium. *Gnaphalium margaritaceum* L. (More correctly *Anaphalis margaritacea* (L.) Benth. and Hook.) *Pearl Everlasting. Cudweed. Life-everlasting. Pied de Chat, Immortelle,* Fr. *Katzenpfötchen, Immerschön,* G. (Fam. *Compositæ.*)—An indigenous herbaceous perennial, which with *G. obtusifolium* L. (*G. polycephalum* Michx.), or *sweet-scented life-everlasting,* is sometimes used in the form of tea in intestinal and pulmonary *catarrhs,* and, externally, in the way of fomentation, in *bruises,* but it probably possesses little medicinal virtue. In Europe different species of *Gnaphalium* are occasionally employed for similar purposes.

Gold.—The chief preparations of gold which have been employed in medicine are metallic gold in a finely divided state, the oxide (trioxide, incorrectly called *auric acid*), the chloride (trichloride), the iodide, the double gold and sodium chloride formerly official, the ammonium chloraurate (a compound of gold trichloride and ammonium chloride), and gold cyanide. Aqueous solutions of gold in the *colloidal* state have been prepared by Bredig by forming an electric arc under water with gold wires. The sparking between gold electrodes liberates finely divided gold which dissolves with bluish-red color. The addition of acids and certain salts coagulates this colloidal gold solution; the addition of gelatine prevents this coagulation. *Gold in powder* may be obtained by rubbing up gold leaf with ten or twelve times its weight of potassium sulphate until brilliant particles are no longer visible, and then dissolving away the sulphate with boiling water.

The soluble salts of gold are active disinfectants. Miquel found that 1 part in 4000 of the chloride would inhibit the growth of bacteria and according to Boer it is germicidal in strengths of from 1 part in 500 to 1 part in 8000 according to the species of bacteria. Behring asserts that the *gold and potassium cyanide* is an extraordinarily acting antibacterial, 1 part in 1,000,000 being sufficient to inhibit multiplication of these microorganisms.

Various preparations of gold have been highly lauded in the treatment of various forms of *tuberculosis* and *syphilis.* The cyanide and chloride were used many years ago in *scrofula.* Bruck and Glück (*M. M. W.*, 1913, p. 57) assert that the intravenous injection of the gold and potassium cyanide, through a systemic antiseptic influence, is a value in the treatment of *lupus.* They employed doses of from one-half to three-quarters of a grain (0.03 to 0.05 Gm.) two or three times a week. In a similar way it has also been used in *syphilis* and in *pulmonary tuberculosis.* Hauck (*M. M. W.*, 1913, p. 1824), however, reports a fatal case from the treatment which he attributed to gold poisoning.

The preparations of gold are decidedly poisonous, though in different degrees. The chloride is most virulent, and, according to Chrestien, is even more active than corrosive sublimate. In an overdose, it produces pain, inflammation, and even ulceration of the stomach and bowels and otherwise acts as a corrosive poison. It is said that these preparations, in moderate doses, produce increased fulness and frequency of the pulse, and augment the urine and insensible perspiration, without interfering with the appetite or the regular action of the bowels, but, if the dose be pushed too far, general irritation is apt to be produced, inflammation seizes upon some organ, according to the predisposition of the individual, and fever is developed.

Under the name of *Crysolgan* (*Krysolgan*) the sodium salt of *amino-auro-thio-phenolcarbonic acid* was used by Lowy (*D. M. W.*, 1922, xlviii, 223) in *lupus* and various forms of local *tuberculosis.* The rapidity of recession of local lesions rivals the effects of the arsenicals in syphilis. He also noted marked improvement in cases of pulmonary and osseous *tuberculosis.* He administers intravenously 0.01 to 0.1 Gm. (⅙ to 1.5 grains) at weekly intervals.

Sanocrysin, a *sodium auric thiosulphate* which has been used by Molgard of Denmark, has acquired considerable notoriety and been attributed with an almost specific effect in *tuberculosis.* The drug is not free from danger and although it contains elements of hopefulness cannot be considered as of established value (see *J. A. M. A.*, 1925, lxxxiv, p. 287).

In 1889 Goubert asserted before the French Academy that *gold bromide,* administered in a weak solution, is more efficacious and durable in its action in *epilepsy* than are any of the other bromides, and is also better tolerated. This statement led Shtcherbak to study the effect of the gold bromide upon the motor area of the cerebral cortex, according to the method of Albertoni. He found that in the dose of from one-half to three grains per kilogramme of weight it so depressed the cortical motor centers that even the strongest electric stimulation failed to bring about any epileptic seizures. It is further asserted that the gold bromide never causes in man general depression, languor, emaciation, or other pronounced symptoms of bromism. The amount of bromine in the bromide, 55 per cent. by weight, would seem too small to make it probable that the bromine is the active ingredient of the salt. The *dose* of the bromide for the adult is from one-eighth to one-fifth grain (0.008–0.012 Gm.); for children, one-twentieth to one-tenth grain (0.003–0.006 Gm.). As a substitute for this preparation, E. Merck has proposed *gold* and *potassium bromide* (*Aurum-Kalium bromatum,* $AuBr_3.KBr + 2H_2O$), which has been tested by I. Jankura and Laufenauer (*Pest. Med. Chirurg. Presse,* 1892), and found to be a valuable anti-epileptic. It may be used hypodermically, by dissolving 2 parts of the salt in 100 parts of distilled water, and injecting of this eight minims (0.5 cc.) and increasing the dose to thirty-two minims (2 cc.). Solutions of gold pentabromide or pentachloride, recognized by their deep red color, are offered by several manufacturers under proprietary names, and advertised to produce remarkable effects in *anemia, diabetes,* and in various dyscrasias. *Solution of gold and arsenic bromide* is official in the National Formulary V under the name of *Liquor Auri et Arseni Bromidi,* the dose is given as three minims (0.2 cc.).

Ammonium chloraurate has been recommended by Bouchardat in *amenorrhea* and *dysmenorrhea* in debilitated subjects, in the *dose* of about the tenth of a grain (0.006 Gm.). A grain may be dissolved in five teaspoonfuls of alcohol and five of water, and a teaspoonful given morning and evening, mixed with sweetened water.

Gold monocyanide (*aurous cyanide*) is a yellow insoluble powder, unstable in the sunlight. It has been used as an antitubercular.

The usual *dose* of either the chloride, cyanide, iodide or oxide of gold is from one-fifteenth to one-tenth of a grain (0.004–0.006 Gm.), most frequently given in pills. Gold cyanide has been found useful in the treatment of *syphilis* and *scrofula* by Pourché and is said to be less irritating than the double chloride.

The different medicinal compounds of gold should not be prepared in pill, powder, or otherwise until they are wanted for use, as they are liable to undergo decomposition when kept. They should be carefully secluded from the light.

Gold salts of various alkaloids have been prepared by Jowett. (*Tr. Chem. Soc.,* 1897.)

Gold and Sodium Chloride. *Auri et Sodii Chloridum U. S. IX. Chloride of Gold and Sodium.*—The U. S. P. formerly recognized, "A mixture of equal parts of anhydrous gold chloride [$AuCl_3$ = 303.58] and anhydrous sodium chloride, representing, when dried to constant weight in a desiccator over sulphuric acid, not less than 30 per cent. of metallic gold." *U. S. IX.*

Gold and sodium chloride may be prepared by dissolving gold in nitrohydrochloric acid, evaporating the solution to dryness, weighing and dissolving the dry mass in eight times its weight of distilled water. To this solution a weight of pure decrepitated common salt equalling that of the dry gold chloride is added, previously dissolved in four parts of water. The mixed solutions are then evaporated to dryness, being in the meantime constantly stirred with a glass rod. A process for making this salt from gold coin without requiring the preliminary purification necessary in the above process may be found in *Proc. A. Ph. A.,* 1882, p. 311. (See Kebler, *A. J. P.,* 1900, 325; and Averkief, *Chem. News,* 1903, 84.)

The pure crystallized salt, $AuCl_3NaCl.2H_2O$, is of a golden-yellow color, and is in the form of prismatic crystals. The mixture of the U. S. P. is described as "an orange-yellow powder, odorless, having a saline and metallic taste, and deliquescent when exposed to damp air. Gold and Sodium Chloride is very soluble in water; alcohol or ether dissolves the gold chloride leaving the sodium chloride. A fragment imparts a persistent, intensely yellow color to a non-luminous flame. An aqueous solution (1 in 100) shows a slightly acid reaction, and yields with silver nitrate T.S. a white precipitate insoluble in nitric acid but readily soluble in ammonia water. Hold a glass rod, moistened with ammonia water, close to a portion of Gold and Sodium Chloride; no white fumes appear (*free hydrochloric* acid). The filtrate from the precipitated gold in the following assay process, after acidulation with hydrochloric acid, is not affected by hydrogen sulphide T.S. (*metallic impurities*).

"Assay.—Dissolve about 0.5 Gm. of Gold and Sodium Chloride, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed in a stoppered flask, in 10 mils of distilled water in a porcelain dish. Render the solution alkaline by the addition of 10 mils of potassium hydroxide T.S., heat it for five minutes on a water bath, add 25 mils or an excess of solution of hydrogen dioxide and continue the heating for an hour on a water bath, or until the addition of a few drops of solution of hydrogen dioxide produces no further precipitation in the clear liquid. (During the heating on the water bath occasionally replace the liquid lost by evaporation by the addition of hot distilled water.) Wash the precipitate of metallic gold with distilled water slightly acidulated with hydrochloric acid, dry and ignite it. Its weight corresponds to not less than 30 per cent. of the weight of the dried Gold and Sodium Chloride taken." *U. S.*

This salt, like the other soluble salts of gold, was formerly used in the treatment of various chronic nervous diseases as *locomotor ataxia, neurasthenia,* etc. By many gynæcologists it is believed to have a specific direction to the genital organs, and it is used in *hysteria, ovarian irritation,* and even *chronic uterine inflammation.* It has also been commended in *syphilis, chronic rheumatism, diabetes mellitus,* and other chronic disorders affecting nutrition. Its greatest fame, however, was as the basis of the so-called "gold cure" treatment of the *alcoholic habit.* It would seem certain that no medication can suffice for moral reformation and any benefit from the drug must be by toning up the nervous system and bringing about a general increase of nutritive tone. *Dose,* one-twelfth to one-quarter of a grain (0.005–0.016 Gm.).

Gomabrea.—This is an exudation from a Chilian tree, which has been offered in large quantities in France as a substitute for gum arabic, and is said to be of practical value.

Gourd. *Bottle gourd. False calabash. East Indian calabash.*—The pulp of the root of the *Lagenaria leucantha* Rusby (*Lagenaria vulgaris* Ser., *Cucurbita Lagenaria* L.), a tender annual, probably native to tropical Africa and Asia (Fam. *Cucurbitaceæ*), was used by the natives of the Sandwich Islands in the treatment of *dropsy.* The fruit of certain varieties is edible but the pulp of the root possesses purgative powers.

Gratiola. *Gratiola officinalis* L. *Hedge-hyssop. Gratiole,* Fr. *Gnadenkraut, Gottesgnadenkraut,* G. (Fam. *Scrophulariaceæ.*)—This is a perennial herb, indigenous in the south of Europe, in meadows and other moist grounds. The whole herb is used. It is nearly inodorous, but has a bitter nauseous taste. The indigenous *G. virginiana* L. closely resembles the European plant and indeed was regarded by Michaux as identical with it. Both water and alcohol extract its active properties. F. G. Walz found in it two glucosides, *gratiolin* and *gratiosolin; gratioloic acid;* a fat and a brown resin. For chemistry, see *P. J.*, lxix, 295, and lxx, 385. Hedge-hyssop is a drastic cathartic and emetic, possessing also diuretic properties, and has been used in Europe for the relief of *dropsy, jaundice, worms, chronic hepatic affections,* and *scrofula.* The *dose* of the powdered herb is from fifteen to thirty grains (1.0–2.0 Gm.); of the infusion (half an ounce to the pint of boiling water), half a fluidounce (15 cc.).

Ground Nuts. *Peanuts. Earth nuts. Goober-nuts.*—The fruit of *Arachis hypogœa* L., a leguminous, annual plant, probably native to Brazil and abundantly cultivated in our Southern States, China, etc. Although this fruit is universally known as a nut it bears neither botanical, chemical nor nutritional relations to the true nuts.

A remarkable property of the plant is that its fruit ripens under the surface of the ground, into which the pods penetrate after flowering, until the young fruit is completely buried under the soil in the progress of their growth. The kernels or seeds contain about 45 per cent. of a fixed oil. (See *Oleum Arachis*, Part I.)

Guaco.—Although the guacos of South America seem to be entirely distinct drugs they appear to be indiscriminately used by the natives for the cure of the *bites of poisonous serpents.* The most important of these belong to the genus *Aristolochia.* Guaco is also used in South America as a febrifuge, anthelmintic, antirheumatic and antisyphilitic. Some years ago it attracted considerable attention on the continent of Europe on account of its alleged power in *epidemic cholera* and *chronic diarrhea.* The *Aristolochia cymbifera* Mart. and Zucc. has been the subject of a careful study by L. Butte. (*Annales de la Policlin. de Paris*, Sept., 1890.) The root of this plant as it occurs in commerce is cylindrical, from three to four centimeters in diameter, much broken up into long rootlets, yellowish, with a strong odor, especially in the bark. The plant itself is a vine, growing in great abundance in the province of Tabasco in Mexico. Butte was not able to find in it either an alkaloid or a glucoside. In the physiological experiments made with the aqueous extract it was found that massive doses produced cries and excitement, followed after a time by sleep, with muscular relaxation and symptoms of gastro-intestinal irritation. There was also depression of the nerve centers, both sensory and motor. If the dose were sufficient death was produced by an arrest of the respiration. The heart continued to beat after the cessation of respiration; nevertheless there was depression of the arterial pressure, apparently due to the action of the drug upon the heart. After death marked signs of irritation of the gastro-intestinal tract and kidneys were found. Butte believes that guaco has valuable therapeutic properties in the treatment of skin affections, especially *eczema* and *pruriginous maladies,* in which he used it both locally and internally. He gives the *dose* of the aqueous extract of guaco as three grains (0.2 Gm.) three times a day. In the external application the following formula was used. Guaco (bruised), 30 parts; sodium bicarbonate, 5 parts; water, 1000 parts; boil for a quarter of an hour, allow to macerate one hour, decant, and use the liquid as a lotion. Another form of guaco, sometimes known as *guaco de San Cristobal,* is derived from species of *Aristolochia* (Fam. *Aristolochaceæ*). This is probably derived from *Aristolochia fragrantissima* Ruiz., *A. grandiflora* Sw., and *A. pentandra* Jacq. Apparently the *Comocladia integrifolia* Jacq. of the *Anacardiaceæ* also furnishes a variety of guaco.

Species of the genus *Mikania* (*Willugbœya*), composite plants related to the Eupatoriums, are also used in Brazil under the name of Guaco against snake and scorpion bites. The species most frequently employed are *M. amara* Willd. and *M. Gauco* H. B. K.

M. amara is described as having twining stems, with round, sulcate, and hairy branches; ovate subacuminate, remotely dentate leaves, somewhat narrowed at the base, rough above and hairy beneath, and flowers in opposite axillary corymbs. The plant is a native of tropical America, and has been introduced into the West Indian Islands from the continent. The leaves are the part used. The result of a long and close investigation into the natural history of guaco by Guibourt is, that the guaco from this source, instead of possessing, as has been asserted, a strong, penetrating, and nauseous odor, is in fact inodorous, and destitute of all active properties, and that the strongly aromatic plants which have been employed under the name of guaco all belong to the genus *Aristolochia,* especially *A. cymbifera* Mart. and Zucc., growing in Brazil, after this *A. maxima* (DC.), and in less degree *A. maxima* Jacq. (*A. geminiflora* H. B. K.). (*J. P. C.*, 1867, 99.)

Guaiacol Compounds and Derivatives.—A very large number of these compounds have been produced by pharmaceutical chemists and put upon the market as substitutes for and improvements on ordinary guaiacol. The advantages claimed for these compounds are lower toxicity; especially lack of irritant effects on the mucous membrane of the stomach. In regard to their manufacture we refer the reader to elaborate papers by F. G. Ehlert (*Ph. Rev.*, 1901 and 1902).

Guaiacol Albuminate. Histosan.—According to Huhs (*Ther. Geg.*, 1907, 313), while of service it is not superior to other creosote preparations. The *dose* is eight to twelve grains (0.5–0.75 Gm.) three times a day.

Guacamphol. Guaiacol Camphorate. $C_8H_{14}.(COOC_6H_4O.CH_3)_2$.—This *camphoric ester of guaiacol* is a white, tasteless, insoluble powder, which is asserted to be broken up in the intestines into camphoric acid and guaiacol. It has been especially recommended as a remedy of great value in the treatment of the *night sweats of phthisis.* In some cases it is necessary to be administered for one or even two weeks for the desired effect. *Dose,* three to fifteen grains (0.2–1.0 Gm.) exhibited two hours before bed time.

Guaiacol Acetate. Eucol. Eucolo. Guaiacol Ester of Acetic Acid. $C_6H_4\left\langle\begin{matrix}OCH_3\\OCH_3CO\end{matrix}\right.$.—This product forms a colorless fluid with a specific gravity 1.138, and boiling at 238° C. with partial decomposition. It can be mixed in any proportion with ether or alcohol and may be dissolved to the extent of 20 per cent. in olive oil. It is used for the same purposes as guaiacol.

Guaiacol Benzoate. Benzosol, N. N. R. 1924. $C_6H_5COO.C_6H_4.OCH_3$.—This occurs as colorless crystals with a faint aromatic odor almost insoluble in water. It is slowly decomposed in the intestines and appears to exert the characteristic effects of its two constituents. Benzosol was highly commended by Walzer and Hughes (*D. M.*

W., 1891) as a substitute for creosote in *phthisis*, and has been used to a considerable extent by clinicians as an intestinal antiseptic in *intestinal indigestion, diarrhea*, and other conditions. It has also been used successfully in *cystitis*, and is affirmed by Piatokowski, J. Blake White, and others to be valuable in the treatment of *diabetes*. *Dose*, five to ten grains (0.3–0.6 Gm.) several times a day.

Guaiacol Benzyl Ester. Pyrocain. Brenzcain. $OCH_3.C_6H_4.OCH_2.C_6H_5$.—This is in colorless crystals, soluble in ether and melting at 62° C. It possesses the general therapeutic properties of guaiacol, but is less caustic. It is not to be confused with Benzosol (guaiacol benzoate).

Guaiacol Cinnamate or *Styracol*, $C_6H_5CH{:}CH.COO(C_6H_4OCH_3)$, the cinnamic acid ester of guaiacol, occurs in white, odorless, tasteless, stable needles, almost insoluble in water, readily soluble in alcohol, chloroform, acetone and benzene. They fuse at 130° C. It is said when taken internally to be broken up in the intestines into cinnamic acid and guaiacol and to be useful not only in *phthisis* but in various chronic *gastro-intestinal* and *genito-urinary catarrhs*. *Dose*, fifteen grains (1 Gm.), three or four times a day.

Guaiacol Ethyl, $C_6H_4OC_2H_5OH$, *Pyrocatechin Monoethyl Ether. Guethol. Thanatol.*—This is an oily liquid of an agreeable aromatic odor, soluble in water, which was brought forward as a remedy in *tuberculosis*, with the statement that it acts upon the human system like guaiacol, but more quickly and energetically. The researches of De Buck (*Belg. Méd.*, 1897) indicate, however, that it is not more effective than is guaiacol in tubercular diseases. It is affirmed, however, to be a pronounced analgesic, which when applied to the skin by means of a brush is rapidly absorbed, and in cases of *neuralgia* or *neuritis* produces great relief. It may also be used subcutaneously in 10 per cent. emulsions with sterilized glycerin, and has been so applied; the glycerin solution has also been used in *cystitis*.

Guaiacol Methylglycolate. Monotal. Methylglycolic Acid Ester of Guaiacol. $CH_2(OCH_3)COO(C_6H_4OCH_3)$.—This is a colorless, oily liquid, slightly aromatic, almost insoluble in water, soluble in alcohol and immiscible solvents. It is readily absorbed through the skin and is employed not only for its local anesthetic properties in various painful conditions, but to obtain the systemic effects of guaiacol through endermic administration. It is said to produce the effects of guaiacol without its toxic properties. Externally applied in *doses* of one-half to one fluidrachm (2–4 cc.).

Guaiacol Phosphate. Phosphoric Guaiacol-ether. Biogaicol. $(C_6H_4O.CH_3O)_3PO$.—A white, crystalline powder has been shown by A. Gilbert (*S. M.*, 1897) to be split up in the intestines, with the liberation of its constitutents, and to afford, therefore, a method of administering guaiacol, over which it has the advantage of being innocuous to the mucous membrane of the stomach. It would appear, however, much less active and much more uncertain in its influence than is guaiacol. *Dose*, one to three grains (0.06–0.2 Gm.).

Guaiacol Phosphite. Phoso-Guaiacol. $P(OC_6H_4OCH_3)_3$. *Phospho-guaiacol. Guaiacophosphal.*—*Phosphite of Guaiacyl-ether* is a white, crystalline powder, possessing a sharp taste and indifferent odor. It is soluble in water, dissolves very freely in alcohol, ether, chloroform, acetone, benzene, toluol, and the fatty oils, but it is sparingly soluble in oil of turpentine and in glycerin. Melting point 77.5° C. It contains 92.25 per cent. of guaiacol, and was introduced in 1897 by Ballard. (*Rép. de Pharm.*, 1897.) *Dose*, three to fifteen grains (0.2–1.0 Gm.).

Guaiacol Salol. Guaiacol Salicylate. $C_6H_4OHCOO(C_6H_4OCH_3)$.—A compound closely related to phenyl salicylate (salol) which occurs in small odorless, tasteless, colorless crystals, readily soluble in alcohol, ether, chloroform or benzene, melting at 65° C. It is said to be split up into its constituents in the intestines and has been used in *phthisis* and as an *intestinal antiseptic*. *Dose*, ten to fifteen grains (0.65–1.0 Gm.).

Guaiacol Succinate. $(C_6H_4OCH_3)_2C_4H_4O_4$.—This drug occurs in fine, silky, white crystals insoluble in water, slightly so in alcohol and ether, very soluble in chloroform or acetone, and melting at 136° C. It is said to act medicinally like guaiacol.

Guaiacol Valerate. Geosote. $C_6H_4OCH_3O.COC_4H_9$.—This occurs as a pale yellow, oily, mobile liquid, insoluble in water, freely soluble in alcohol, ether, and benzene. Sp. gr. 1.038, boiling point variously given from 240° to 260° C. Geosote is used in *phthisis* and as a gastro-intestinal antiseptic in fermentative *dyspepsia* and *diarrhea*. *Dose*, five to ten grains (0.32–0.65 Gm.).

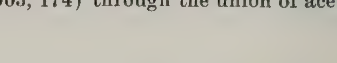
Guaiacose.—This is stated to be a combination of *calcium guaicol-sulphonate* with somatose which is a partially digested protein. Guaiacose occurs as a dark brown fluid with a not unpleasant taste and miscible with water. The dose recommended is about 1 teaspoonful 3 or 4 times a day.

Guaiacyl. Gajacyl. Calcium Ortho-guaiacol Sulphonate. $(C_6H_3(OH).(OCH_3)SO_3)_2.Ca$.—This is a powder of a bluish-gray color, soluble in water and in alcohol. The aqueous five per cent. solution has a violet-red color and may be used hypodermically in quantities of eight to twenty minims (0.5–1.3 cc.). *Guaiacyl* has also been used as a local anesthetic in 5 to 10 per cent. solution.

Guaiaform. Geoform. Methylenediguaiacol. Pulmoform.—The drug is a tasteless yellow powder, odorless at first but acquiring a vanilla-like odor, soluble in alcohol or ether but insoluble in water. It is affirmed to contain 95.38 per cent. of guaiacol and to be non-irritating and non-toxic. *Dose*, five to fifteen grains (0.3–1.0 Gm.).

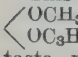
Guaiaquin. Quinine Guaiacol Bisulphonate. $C_6H_4O_2CH_3HSO_3\ \ C_{20}H_{24}N_2O_2$.—This substance occurs as a yellowish crystalline bitter powder, very soluble in water, alcohol and diluted acids. It represents about 45 per cent. of quinine and 34 per cent. of guaiacol. It has been used to some extent in internal medicine as a tonic, but especially as an antiperiodic in various *malarial diseases* with asserted good results. It is stated that the sterilized 10 per cent. solution may be given hypodermically with the production of little pain. This solution has also been used locally with alleged good results in *gonorrhea* and other infected conditions. *Dose*, three to ten grains (0.2–0.65 Gm.); sixty grains (3.9 Gm.) may be given in a day.

Guaiasanol. Gujasanol. Diethyl-glycocollguaiacol Hydrochloride.



$$C_6H_4\begin{matrix}\diagup OCH_3\\ \diagdown O.CO.CH_2N.(C_2H_5)_2.HCl\end{matrix}$$

This substance occurs in very soluble white prisms fusing at 184° C., emitting an odor faintly suggestive of guaiacol and possessing an acrid taste. It was first produced by Einhorn and Hutz (*J. P. C.*, 1903, 174) through the union of aceticomonochlorguaiacol and diethylamine. In the presence of alkalies it breaks up, liberating guaiacol, which has been found in the urine of animals to which it had been given. Guaiasanol was introduced as a substitute for guaiacol, especially in the treatment of *pulmonary catarrhs.* Rahn (*M. M. W.*, 1905, p. 783) has also found the injection of a 2 to 4 per cent. solution a valuable treatment for *seat worms.* It has been given in *doses* of forty-five to one hundred and eighty-five grains (3–12 Gm.) daily.

Guajamar. Guaiamar. Guaiacolglyceryl Ester.—This is a white crystalline powder,  $C_6H_4\left\langle\begin{matrix}OCH_3\\OC_3H_7O_2\end{matrix}\right.$, which possesses a bitter aromatic taste, melts at 75° C. and dissolves in alcohol, ether, glycerin or 20 parts of water at the ordinary temperature. According to G. Buttler, it splits up in the intestines into guaiacol and glycerin and affords an excellent method of intestinal antisepsis in *typhoid fever, diarrhea,* etc. Great relief has been obtained in *acute* and *articular rheumatism* by the local application of the remedy in the form of an ointment consisting of two parts of guajamar and one of lanolin. *Dose,* three to fifteen grains (0.2–1.0 Gm.).

Guano. *Bird-manure.*—A fertilizing excrement formerly found on many small islands in the southern ocean on the western coast of Africa and also near the Peruvian Coast of South America, but exhausted many years ago for agricultural purposes. These islands were the resorts of large flocks of sea birds and formerly the beds of deposited excrement were sometimes 50 or 60 feet in depth. It constituted an excellent manure and was used for upward of a century for that purpose. It consisted of phosphates together with much ammonium urate and ammonium oxalate, and some peculiar nitrogenous bases. At present small amounts are obtained from the Peruvian islands. Guano is a powerful local irritant, and was sometimes employed as an external stimulating application. For further information see 16th ed., *U. S. D.*

Gum Cebil.—This gum is a product of the Brazilian leguminous tree, *Piptademia Cebil* Griseb. It occurs in reddish-yellow tears, or in dark-colored angular masses, and forms a reddish-yellow, odorless, viscous mucilage of acid reaction. It is said to contain 80.78 per cent. of arabin.

Gum, Cedar.—This, the product from *Cedrela Toona* Roxb. (*Toona ciliata* Roem.), or *Red Cedar,* a tree native of the Himalayas but growing in Queensland (Fam. *Meliaceæ*), is a very pale yellow or brownish gum, occurring in tears about 2.5 cm. long, having an astringent taste, swelling and, finally, almost dissolving in water. It contains about 68 per cent. of arabin, and 6 per cent. of metarabin, but no resin. (*P. J.*, vol. xx, 1890.)

Gum, Indian.—Under the name of *Gummi Indicum* the Br. recognizes the gummy exudation from the wood of *Anogeissus latifolia* Wallich. (Fam. *Combretaceæ*), a tree native to India and Ceylon. (See Part I.) The forests of India produce large quantities of other gums, a number of which have found their way in commerce and are used to a considerable extent as substitutes for gum arabic and gum tragacanth. Several of these are known colloquially as "Indian Gum." Among them that yielded by *Prosopis spicigera* L. (Fam. *Leguminosæ*) occurs in small, angular, yellowish fragments, or sometimes in large ovoid tears 5 cm. long, of an amber color, frosted externally with fissures. It forms with water a dark-colored tasteless mucilage and resembles in its behavior to reagents the *Mesquite gum.* The gum of *Feronia Limonia* Swingle (Fam. *Rutaceæ*) is in small, irregular tears varying from reddish-brown to pale yellow and forms a thick, tasteless, colorless mucilage which resembles gum arabic, but is precipitated by neutralized lead acetate and gelatinized by ferric chloride, although unaffected by borax. (See also *Gum Sterculia* and *Bassora.*)

Gum Mango.—This gum, which is obtained from the mango tree, *Mangifera indica* L. (Fam. *Anacardiaceæ*), occurs in the Indian bazaars in amber-colored or reddish-yellow lumps, almost transparent, with a brilliant conchoidal fracture, 39.4 per cent. of which is soluble in water. (See *J. P. C.*, xix, 584.)

Gum Mesquite. *Mesquite Gum. Mezquite Gum.*—This is the product of *Prosopis juliflora* DC., and perhaps other species of the same genus. Mesquite is a small, thorny, acacia-like tree or shrub belonging to the Fam. *Leguminosæ,* and growing in New Mexico, Texas, and other neighboring regions, where it covers vast extents of country. The fruit is a long, compressed pod, filled with a sweet pulp, which is said to contain 30 per cent. of grape sugar, and to be used by the Indians as a food. A gum exudes from the stem and branches. It occurs in irregular, roundish pieces, of various sizes and usually of a dark amber-brown color, though sometimes, especially when gathered from young trees, it is nearly colorless. Procter found it to resemble gum arabic in its solubilities, but to differ essentially in not being precipitated by lead subacetate, and in its strong solution not being coagulated by borax. (*A. J. P.*, xxvii, 224.)

The saccharine pods of *Prosopis odorata* Torr. and Frem. (*P. pubescens* Benth.) are largely employed as food by the Indians, and those of all the species form valuable fodder for cattle.

Gum Sassa. *Sassa Gum.*—This name has been applied by Guibourt to a gum, occasionally brought into commerce from the East. It is produced by a tree growing in Abyssinia, *Albizzia fastigiata* Oliv. (Fam. *Leguminosæ*). According to Guibourt's description, it is in mammillary masses, or in convoluted pieces resembling an ammonite, of a reddish color and somewhat shining surface, and more transparent than tragacanth. Its taste is like that of tragacanth, but slightly acrid. When introduced into water it becomes white, softens, and swells to four or five times its original bulk; but it preserves its shape, neither, like tragacanth, forming a mucilage, nor, like Bassora gum, separating into distinct flocculi. It is rendered blue by iodine.

Gum Sonora. *Sonora Gum.*—According to Krewson, the exudation from *Covillea tridentata* (DC.) Vaill. (*Larrea mexicana* Moric.) contains 17.27 per cent. of resin, and 11.71 per cent. of mucilage and allied substances. (For details, see *P. J.*, xvi, 128; also *A. J. P.*, May, 1898.) This plant is known in Southwestern United States and Mexico as *Creosote bush,* because of the odor of the oleoresin which covers the herbage.

Gum Sterculia. *Sterculia Gum. Indian Tragacanth. Indian Gum. Karaya Gum.*—A number of trees belonging to the genus *Sterculia* in India—particularly *Sterculia urens* Roxb., and *Cochlospermum gossypium* DC.—Africa, and Australia yield gums in considerable quantity, most of which resemble in their appearance tragacanth, some of which have remarkable adhesive properties and in some of which the adhesive power is lacking but the swelling power when moistened with water is enormous. These gums have been much used of recent years, frequently under the unqualified name of tragacanth. They are employed frequently as fillers in the manufacture of ice cream and even desserts where vegetable gums are found to be of service in preventing the product from losing its form as it melts. The difference between the sterculia gums and true tragacanth can be readily proved by a distillation test with water and the determination of the acidity which is due to acetic acid. (See *A. J. P.*, Jan., 1900; 1912, pp. 155 and 393; *Drug. Circ.*, 1909, p. 116; *J. A. Ph. A.*, 1917, vi, 88.)

Gutta-Percha. *N. F. IV. Gutta Pertscha. Gutta Gettania. Gutta Taban. Getah Pertscha. Getah Taban. Guetah* or *Gueutta-pertcha* Malay (from *gueutta*, gum and *pertcha*, rags or scraps). *Gummi plasticum.*—This is a hydrocarbon defined by the N. F. as "the purified, coagulated, milky exudate of various trees of the genus *Palaquium* Blanco (Fam. *Sapotaceæ*)." Nevertheless, it is also obtained from trees belonging to the genus *Payena* (Fam. *Sapotaceæ*). These plants are all tropical trees, which are characterized by possessing rows of latex cells in the cortex, pith and leaves. Their leaves are alternate, evergreen and leathery in texture and they possess large, perfect axillary clusters of flowers and berry fruits. It is somewhat like India rubber, but less elastic, so that when changed in form by mechanical force it preserves its new shape. At a temperature of boiling water it becomes highly plastic and, on cooling, of preserves the shapes in which it has been molded, while India rubber, treated by heat, preserves its elasticity until the temperature becomes excessive, when it changes in its physical and chemical properties. Perhaps the most important difference between the two substances is in their reaction with sulphur, rubber readily vulcanizing, gutta-percha being practically incapable of so doing.

The plants which are capable of yielding gutta-percha are quite numerous, but those yielding the commercial substance inhabit the limited region of South America between the third degree of south and the fifth degree of north latitude, and the limited portion of Asia between longitude 102° and 112°. It is probable that other equatorial or sub-equatorial regions do, however, produce gutta-percha.

Formerly the most important of the gutta-percha yielding trees was *Palaquium Gutta* Burck (Fam. *Sapotaceæ*). This furnished the article known commercially as *Gutta Taban* or *Getah Taban.* Most of the gutta-percha of commerce is now obtained from *P. oblongifolium* Burck; *P. borneense* Burck; *P. Treubii* Burck and *Payena Leerii* Benth. et Hook. All of these are natives of Malaya. At the present time some of these species are being cultivated, viz., *Palaquium Gutta* and *Palaquium oblongifolium* are being cultivated in sumatra—the latter being said to yield the best of all the gutta-perchas, and it is stated that *P. pustulatum* is cultivated in Ceylon and *Payena Leerii* in its native Sumatra. At the present time most of the guatta-percha is obtained from Sumatra.

Gutta-percha is also obtained in considerable quantities in the Philippine Islands, whence it is sent to Singapore. In obtaining gutta-percha, after the tree has been cut down, incisions are made through the bark into the latex, and the milk, after having been collected in gourds, is coagulated by heat, the resulting masses washed by kneading with water, increased in weight by additions of wood, dirt, pebbles, etc., and finally sent into trade worked into masses with a fair exterior.

It has been proven by the researches of Jungfleisch that the leaves of the gutta-percha trees contain, even after drying, nine per cent. of gutta-percha, as extracted by toluene. Hitherto the leaves have been simply lost in the forest. It is further stated that the year's product of leaves of the thirty year old tree will yield as much gutta-percha as does the tree when cut down, and efforts are being made to induce the Malays to collect the leaves instead of destroying the trees. Patents have been taken out for at least four different processes, in which carbon disulphide, toluene, rosin oil and light petroleum are used as solvents.

In Singapore the gutta-perchas of various sources are mixed, and three commercial articles are sold—viz., (1) first quality, (2) medium quality, (3) white gutta-percha.

Small quantities of commercial gutta-percha may be freed from impurities and obtained perfectly white by dissolving one part of gutta-percha in twenty of boiling benzene, shaking the solution frequently with calcium sulphate, which upon standing two or three days carries down with it the coloring matter, then decanting the clear liquid, and adding it, in small portions at a time, to alcohol, agitating continually. The deposited gutta-percha is then dried by exposure to the air.

It was described as "in masses, sticks or sheets of irregular size and shape, tough, yellowish-white in color and usually with reddish, marbling streaks. Insoluble in water; partly soluble in chloroform, carbon disulphide, petroleum benzin, or oil of turpentine, leaving not more than 10 per cent. of undissolved residue. Slightly elastic at ordinary temperatures, becoming pliable at from 25° to 30° C. It gradually softens on further heating, becoming quite plastic at 60° C. One Gm. of Gutta Percha when boiled for one hour with 20 cc. of dehydrated alcohol in a flask, connected with a reflex condenser, leaves not less than 0.5 Gm. of undissolved residue. When exposed to air and sunlight, Gutta Percha absorbs oxygen and becomes brittle. Gutta Percha yields not more than 5 per cent. of ash." *N. F.* Its sp. gr. is 0.9791. (Soubeiran.) At about 49° C. it becomes softer and more flexible, but is still elastic, resisting, and tenacious. At from 66° to 71° C. it is soft, very plastic, and capable of being welded and molded into any form. It can be softened either by means of hot water or by dry heat. On cooling, it reassumes its former state, and retains any form which may have been given to it. In the softened state it is readily cut with a knife, though with some difficulty when cold. Exposed to a heat of 166° C., it loses a portion of water, and on hardening becomes translucent and gray; but it recovers its original characters if immersed in water. Subjected to destructive distillation, it yields volatile products resembling closely the volatile oil obtained from caoutchouc by the same process. Heated in an open vessel, it melts, foams up, and takes fire, burning with a brilliant flame and much smoke. A portion thus melted retains the state of a viscid fluid on cooling. Gutta-percha is a non-conductor of electricity. It is insoluble in water, alcohol, alkaline solutions, and the weak acids. Ether and the volatile oils soften it in the cold, and imperfectly dissolve it with the aid of heat. It is partly soluble in carbon disulphide, chloroform, petroleum benzin, and oil of turpentine, leaving not more than 10 per cent. of undissolved residue. It does not yield more than 3 per cent. of ash.

Its composition is closely analogous to, if not identical with, that of caoutchouc. According to Bamhauer, pure gutta-percha, as it issues from the tree, is a hydrocarbon, with the formula $(C_{10}H_{16})_2$, which he calls *gutta*, and by the oxidation of which, in various degrees, the different bodies constituting gutta-percha are produced. This hydrocarbon can be separated by treating gutta-percha with diluted hydrochloric acid, and boiling the residue with ether, which deposits the gutta on cooling, but the ethereal treatment must be frequently repeated to obtain it quite pure. (*J. Pr. Chem.*, lxxviii, 279.) Arpe considers gutta-percha as a mixture of six different resins which may have been formed from a hydrocarbon, $C_{10}H_{16}$. (See *Chem. Gaz.*, ix, 471.) Oudemans (*Jahresb.*, 1859, 517) finds two resinous products in gutta-percha: *fluavil*, fusing at 42° C. with the formula $C_{20}H_{32}O$, and soluble in cold alcohol, and *albane*, fusing at 140° C., with the formula $(C_{10}H_{16}O)_2$, and soluble in chloroform, carbon disulphide, and ether, from which last it crystallizes out on cooling. Payen has shown that three proximate principles exist in the natural gutta-percha—viz., *gutta* (insoluble in cold alcohol and in boiling alcohol), 78 to 82 per cent.; *fluavile* (insoluble in cold alcohol), 4 to 6 per cent.; *albane* (soluble in boiling alcohol), 14 to 16 per cent. Gutta-percha resists putrefaction strongly; but in certain situations, as when employed to protect underground telegraph wires passing near the roots of the oak, it has been observed to undergo speedy decomposition, in consequence, it is supposed, of the action of fungi. (*P. J.*, xvii, 193.)

Gutta-percha is employed very largely in the arts for various purposes, especially as an insulating material. In medicine it is used simply for mechanical purposes, as in the formation of splints and the manufacture of surgical instruments. For details of its use the reader is referred to works on surgery.

Gymnema. *Gymnema silvestre* (Willd.) R. Br.—This is a woody climber, belonging to the *Asclepiadaceæ*, which grows in Australia, India and also in Africa. The root has for a long time been employed by the natives as a remedy in *snake bite*, and it is affirmed by T. Dyer (*Nature*, 1887) that directly after the eating of one or two leaves it is impossible to taste sugar, though other tastes are not obscured; thus, pungency alone is detected in gingerbread, and a sweet orange tastes like a lime. The active principle is *gymnemic acid*, $C_{32}H_{55}O_{12}$ (see *J. Chem. S.*, 1904, lxxxv, 624), and has been used with considerable success as a remedy for *parageusia* and *hallucinations of taste*. The 1 per cent. aqueous solution is to be applied with a brush to the inside of the mouth, or a hot infusion (15 per cent.) of the crude drug may be used. (See *Th. M.*, ix.)

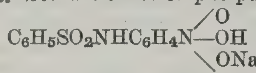
Gymnocladus. *Gymnocladus dioica* (L.) Koch. (*G. Canadensis* Lam.) *Kentucky Coffee-tree. Kentucky Mahogany.* (Fam. *Leguminosæ.*)—A tall tree with bipinnate leaves, terminal panicles of greenish-white flowers, growing in the woods from New York southward and west as far as Oklahoma. The fruit is an oblong, flattened pod, persisting through the winter; it contains several seeds in a fleshy pulp. The seeds are flattish and about 1 cm. in diameter. According to Bartholow, the aqueous extract of the seeds is toxic. (*Am. Drug.*, April, 1886.) Mell (*A. J. P.*, 1887, 230) obtained from them about 10 per cent. of fixed oil which is yellowish, saponifiable, and of sp. gr. 0.919, tannin, and a small quantity of glucoside. This latter had a peculiar odor and an acid burning taste. James H. Martin (*A. J. P.*, 1892, 558) obtained a yellow, saponifiable oil from the bean and the bark and a glucoside from the pulp. Sayre and Watson found in the seeds saponin and a toxalbumin similar to if not identical with that of ricin, the poisonous principle of castor bean. (*J. A. Ph. A.*, 1917, vi, 601.) They state that while the raw seeds are poisonous after roasting they may be eaten with impunity. In Colonial times they were used, west of the Alleghanies, as a substitute for coffee.

Gynoval. *Ferminal.*—Gynoval is the iso-valeric ester of iso-borneol, $(CH_3)_2CH.CH_2.COOC_{10}H_{17}$. It occurs as a colorless, neutral fluid with a peculiar aromatic odor and a slightly oily taste, very sparingly soluble in water, but readily soluble in alcohol and ether. Gynoval is asserted to have the advantage over other preparations of valeric acid that it does not irritate the stomach. It is employed in *hysteria* and the various functional neuroses for which valerian is commonly recommended. It is administered generally in capsules containing four minims (0.25 cc.) of which one or two may be given at a *dose*.

Halozone. *Para-sulphon-dichloramido-benzoic acid.* $C_6H_4(SO_2NCl_2)COOH$.—This compound which is formed as a by-product in the manufacture of glusidum occurs as a white crystalline powder with a pronounced chlorinous odor, sparingly soluble in water but forming soluble salts with the alkalies. Its melting point is 213° C.

Halozone was introduced by Dakin and Dunham as a means of purifying water by chlorination. (*B. M. J.*, Jan. 29, 1916 and May 26, 1917.) They state that 1 part in 300,000 will sterilize ordinary water in about 30 minutes without destroying its palatability and that in the amounts required it is completely innocuous. These conclusions have been confirmed by Fantus (*J. A. Ph. A.*, 1918, vii, 1034 and *J. Inf. D.*, 1919, xxiv, 200) who fed to kittens and rabbits doses which would be equivalent to 7 Gm. daily for a man (enough to disinfect more than 400 gallons of water), for 4 months without observable effect. He also found that tablets of halozone showed no change in the proportion of available chlorine after 4 months, while similar tablets of chlorinated lime had lost 30 per cent. of their available chlorine in the same period. While for disinfecting large masses of water, as in municipal plants, the chlorinated lime is cheaper and equally efficient he concludes that halozone is of great practical value because of the practicability of tablet form. While the slowness of its action is a drawback Fantus finds that this may be greatly accelerated by the simultaneous use of small amounts of citric or other organic acid.

Because of the greater solubility of its salts the tablets of halozone usually contain sodium bicarbonate or sodium borate, sodium chloride is also added to give bulk.

Hectine. *Sodium-benzo-sulpho-paramino-phenyl-arsenate.*  $C_6H_5SO_2NHC_6H_4N\begin{smallmatrix}/O\\ -OH\\ \backslash ONa\end{smallmatrix}$.—It occurs as colorless needles, freely soluble in water, the solution not being decomposed by boiling. It has been brought forward as an organic arsenical, especially for the treatment of *syphilis* and *filariasis* and a number of practitioners have used it with good effects. Whether or not it will give rise to optic neuritis, as does atoxyl, is uncertain, but Ballet and Hirschmann (*Press. Med.*, 1911) have reported temporary disturbance of vision from its use. The *dose* recommended is from one and one-half to three grains (0.096–0.2 Gm.) daily, injected deeply into the muscle; by mouth, one grain (0.065 Gm.) several times a day. This treatment is kept up for two weeks and then discontinued for two weeks and this method is repeated as long as necessary.

Hedeoma. *Pennyroyal. American or Mock Pennyroyal. Squawmint. Mosquito Plant. Herbe de Pouliot Américaine,* Fr. *Amerikanischer Polei,* G.—The U. S. VIII recognized "The dried leaves and flowering tops of *Hedeoma pulegioides* (Linné) Persoon (Fam. *Labiatæ*)." *U. S. VIII.*

This plant is entirely distinct from *Mentha Pulegium* or European pennyroyal. It is probable that various other species of the genus are used in the localities in which they grow. Thus, *H. piperita* Bentham is said to be used in Mexico as a substitute for peppermint, and *H. thymoides* Gray, in Texas as an aromatic diaphoretic.

Hedeoma pulegioides (L.) Pers. [*Cunila pulegioides* L.; *Melissa pulegioides* L.] is an indigenous annual plant, from nine to fifteen inches high, with a small, branching, fibrous, yellowish root, and a pubescent, quadrangular stem, which sends off numerous slender erect branches. The plant is common in the Eastern and Middle Western United States, preferring dry grounds. Hedeoma was officially described as "branchlets quadrangular, with numerous spreading hairs; leaves opposite, short-petioled, oblong, 15 to 35 Mm. long, thin, obtuse, obscurely serrate, glandular-hairy beneath; flowers in axillary fascicles, with a tubular-ovoid, bilabiate and 5-toothed calyx, and a pale blue, spotted, bilabiate corolla containing two sterile and two fertile, exserted stamens; odor strong, somewhat mint-like; taste aromatic and pungent." *U. S. VIII.* The activity of hedeoma depends upon a volatile oil. The oil of hedeoma (*Oleum Hedeomæ, U. S. VIII, Oil of Pennyroyal*), is "A pale yellow, limpid liquid, having a characteristic, pungent, mint-like odor and taste. Specific gravity: 0.920 to 0.935 at 25° C. It should form a clear solution with 2 volumes or more of 70 per cent. alcohol. It is dextrogyrate, the angle of rotation varying from about $+ 18°$ to $+ 22°$ in a 100 Mm. tube, at a temperature of 25° C." *U. S. VIII.* Its chemical composition was investigated by E. Kremers (*A. J. P.*, 1887, p. 535) and F. W. Franz (*A. J. P.*, 1888, p. 161). Each of them found a body of the composition $C_{10}H_{18}O$, boiling at 217° to 218° C. (constituting, according to Franz, about 33 per cent. of the oil). For this the name *hedeomol* was proposed. Franz also found a body of the composition $C_{10}H_{17}O$, boiling at 220° to 225° C., and constituting 12 per cent. of the oil; likewise a body of the composition $C_6H_{12}O$, boiling at 165° to 170° C., and constituting about 0.7 per cent. of the oil. Both investigators found formic and acetic acids, and Kremers considers *isoheptoic acid* also to be present. Beckmann and Pleissner (*Ann. Ch. Ph.*, cclxii, p. 1) found in American as well as in Spanish and Algerian pennyroyal oil the ketone, *pulegone.* This compound forms with hydroxylamine an oxime, $C_{10}H_{16}NOH.H_2O$, crystallizing in beautiful needles melting at 157° C., and with hydrogen bromide a crystalline compound melting at 40.5° C. The two compounds of the formula $C_{10}H_{18}O$, discovered by Kremers (*Ph. Rund.*, ix, p. 130), are also ketones and yield corresponding oximes.

American pennyroyal is a gently stimulant aromatic, and may be given in flatulent *colic* and *sick stomach,* or to qualify the action of other medicines. Like most of the aromatic herbs, it possesses the property, when administered in warm infusion, of promoting perspiration, and of exciting the menstrual flow when the system is predisposed to the effort. A large draught of the warm tea is in popular practice often given at bedtime, in recent cases of *suppression* of the *menses,* the feet having been previously bathed in warm water. The drug may be given in *doses* of two drachms (7.7 Gm.). The oil in *doses* of two to ten minims (0.12–0.6 cc.).

Hediosit. $C_7H_{12}O_7$.—It is the lactone or inner anhydride of *alpha-glucoheptonic acid,* $CH_2OH.(CHOH)_5COOH$. It occurs as white crystalline powder without odor, but with a sweet taste, but inferior to that of saccharin. It is readily soluble in both water and alcohol, its solution reacting to litmus as an acid. It has been brought forward as a substitute for sugar in the management of *diabetes.* It is asserted that that it has a food value equal to that of glucose, but does not increase the amount of sugar in the urine. According to the investigations of Lenel (*A. E. P. P.*, 1914, lxxvii, p. 335), only a very small proportion of the food value of hediosit, however, is utilized by the system. He found that from 25 to 75 per cent. might escape unchanged with the feces and of the remainder a very large proportion could be recovered unaltered in the urine.

Hedonal. *Methyl-propyl-carbinol-urethane.* $CH_3CH_2CH_2CH(CH_3)O.CO.NH_2$.—This is a white, crystalline powder of weak aromatic odor, fusing at 76° C., sparingly soluble in cold water, somewhat more so in boiling water, soluble in alcohol, ether, and other organic solvents. Decomposed by boiling with alkalies. It forms colorless crystals melting at 76° C. The solutions have a powerful menthol-like taste. Hedonal is believed to split up in the system into carbon dioxide, ammonia, and urea. Probably owing to the presence of the urea, it sometimes acts as a diuretic, but more usually it has no other effect than that of an hypnotic. It is claimed by de Moor that its diuretic action is much increased by its administration in solution. According to Dreser, in the dog it acts very feebly upon respiration and blood pressure. As an hypnotic it is mild in its action and but rarely produces disagreeable aftereffects. In severe cases of *insomnia,* or when the patient is kept awake by pain, it is of little service. No case of poisoning by it have been reported, and so far its prolonged use has not been followed by disagreeable symptoms. The *dose* is fifteen to forty-five grains (1.0–3.0 Gm.), given preferably in capsules half an hour before the desired effect.

Hedera. *Hedera Helix* L. *Ivy. English Ivy* (Fam. *Araliaceæ.*)—This well-known evergreen creeper and climber is a native of Europe, Asia and north Africa, climbing by aerial rootlets, with alternate, long-petioled, usually 3–5 lobed leaves, dark-green above and paler beneath. The fresh leaves have a balsamic odor, especially when rubbed, and a bitterish, harsh, unpleasant taste. They were formerly used for dressing issues, and, in the form of decoction have been recommended in *sanious ulcers* and *cutaneous eruptions*, particularly *tetter* and the *itch.* The berries, which have an acidulous, resinous, somewhat pungent taste, are said to be purgative and even emetic. Posselt, in 1849, separated a principle which he called hederic acid but which Kingzetl (*P. J.*, 3rd s., viii, 205) showed to be a glucoside. J. Vernet (*Ber. d. Chem. Ges.*, xiv, 685) obtained a glucoside, which separated from solution in boiling acetone, in silky needles, melting at 233° C. This glucoside appears to be the substance studied by Moore (*J. P. Ex. T.*, 1913, iv) and which he called *hederin.* He assigned to it the formula $C_{32}H_{52}O_{10}$. Moore found that this principle belonged physiologically among the saponins; it has a strongly hemolytic action and although actively poisonous when injected subcutaneously appears to be harmless when taken through the stomach. Van der Haar isolated two glucosides, *hederin*, $C_{42}H_{66}O_{11}$, and *hederagenin*, $C_{31}H_{50}O_4$. (*A. Pharm.*, 1912, 424.) From the trunks of old ivy plants, growing in the south of Europe and the north of Africa, a resinous substance exudes through incisions in the bark, which has been employed in medicine under the name of *ivy gum.* It is in pieces of various sizes, of a dark yellowish-brown color internally, of a vitreous fracture, pulverizable, yielding an orange-yellow powder, of a peculiar not disagreeable odor when heated or inflamed, and of a bitterish resinous taste. Its chief constituent is resin, though some pieces contain a considerable proportion of bassorin, and other large quantities of ligneous matter. It was formerly used as a stimulant and emmenagogue, but is now scarcely employed. Placed in the cavities of carious teeth, it is said to relieve *toothache.*

Hedychium. *Hedychium spicatum* Sm. (Fam. *Zingiberaceæ.*)—The root of this perennial herb, which is used in perfumery in India, has been found by J. C. Thresh to contain *ethylmethyl paracoumarate.* (*P. J.*, Nov. 8, 1884.)

Hegonon. *Silver Nitrate-ammonia-albumose.*—This is a light brown powder obtained by treating silver-ammonium-nitrate with albumose. It is readily soluble in water and contains approximately 7 per cent. of silver. It is used locally in the treatment of various forms of *gonorrhea* in concentrations of from 1 in 200 to 1 in 3000.

Helenium. *Helenium autumnale* L. (*H. grandiflorum* Nutt.) (Fam. *Compositæ.*) *Sneezeweed. False Sunflower.*—A tall, perennial herb indigenous to North America and usually found growing in moist situations. It has a rough, branching stem bearing alternate, lanceolate, mostly toothed leaves and terminal heads of yellow florets. The leaves and flowers snuffed up in the state of powder produce violent sneezing, and have been used as an errhine. Reeb found a crystalline bitter principle, *helenin,* with the formula $C_{20}H_{25}O_5$. This has been physiologically studied by Lamson (*J. P. Ex. T.*, 1913, iv) who found that it is an intense irritant to the mucous membranes, capable of causing a fatal gastro-enteritis, and that it acts as a paralysant to the heart and voluntary muscles. (This principle must not be confounded with "helenin" from Inula, which see in Part I.) *Helenium nudiflorum* Nutt. has similar properties; *H. tenuifolium* Nutt., a common roadside weed of Mississippi and Louisiana, is stated by Gallaway to produce in animals muscular twitchings, passing into violent convulsions, terminating in death. In four negroes *helenium* caused spasms with delirium and loss of consciousness. (*A. J. P.*, 1872, 309; D.C., 1907, 459.)

Helianthemum. *Rock-rose. Frostweed. Herbe de Hélianthème de Canada,* Fr. *Canadisches Sonnenröschen,* G.—"The dried herb of *Helianthemum canadense* (Linné) Michaux (Fam. *Cistaceæ.*" *N. F. IV.* *Frostwort* grows in all parts of the Eastern United States, preferring dry sandy soils. It has been omitted from the National Formulary V. The dried herb is employed in medicine and was described as follows: "Stems mostly less than 5 cm. in length, branched above, terete, frequently reddish, canescent, the slender branches mostly erect; leaves very short-petioled, from 1 to 3 cm. in length, and from 4 to 8 mm. in width, oblong to oblanceolate, with entire, revolute margins, green and somewhat rough on the upper surface, canescent underneath; flowers of two kinds, rarely present at the same time, the early ones mostly solitary, pedicelled, with bright yellow corolla, from 2 to 3 cm. in breadth, hairy calyx, about thirty stamens and a single three-carpelled pistil, producing an ovoid capsule, about 7 mm. in length; later flowers apetalous, clustered in the leaf-axils, nearly sessile, having but four stamens and producing a capsule about 4 mm. in length. Odor slightly aromatic; taste astringent and bitter." *N. F. IV.* William Crutcher (*A. J. P.*, 1888, 390) found in it volatile oil, wax, fatty oil, tannin, and apparently a glucoside crystallizing in white needles. Frostwort has an astringent, slightly aromatic, and bitterish taste, and appears to possess tonic and astringent properties; it was formerly employed in *scrofula, diarrhea,* and *secondary syphilis,* and locally as a gargle in *scarlatina,* and as a wash in *prurigo.* The *Fluidextractum Helianthemi* was recognized by the N. F. IV. and may be given in *doses* of one fluidrachm (4 cc.).

Helianthus. *Helianthus annuus* L. (Fam. *Compositæ*) *Common Sunflower. Hélianthe, Grand Soleil,* Fr. *Sonnenblume,* G.—The *Sunflower* has long been under cultivation in this and other countries both as an ornamental and economic plant. Its stems yield a fine textile fiber; its flowers furnish a yellow dye; its leaves are used for fodder, and its "seeds" (akenes) yield a fixed oil and are used for food.

The plant is a rough-hairy annual possessing a stem 3 to 12 feet high, broadly ovate to cordate, long-stalked, acute, coarsely serrate and 3-nerved leaves, large flower heads with yellow-ray and disk florets and 4-sided, laterally compressed akenes. The oil has a sp. gr. of from 0.924 to 0.926, solidifies at –15° C., is colorless or yellowish, limpid, nearly tasteless and odorless, and dries slowly. It is said to make an excellent salad dressing, and to be one of the best burning oils known. The increase in cultivation is stated to be nearly a thousandfold, 275 pounds of oil being a fair yield per acre. For particulars as to cultivation, see *A. J. P.*, 1875, 460; also *N. R.*, 1876, 165. Ludwig and Kromayer (*A. Pharm.* (2), 99, 1 and 285) obtained a tannin which they called *helianthitannic acid,* and gave it the formula $C_{14}H_9O_8$. On boiling with moderately diluted hydrochloric acid they obtained a fermentable sugar and a violet coloring matter. Buschmann obtained from the flowers of Russian helianthus, betaine and choline, he believed that their presence accounts for the observed activity of the extract. The stalk, when treated as is flax, yields a long, fine fiber, which is said to be used in China for the adulteration of silk.

Kazatchkoff states (*B. G. T.*, Oct., 1889) that in the Caucasus the inhabitants employ the sunflower in *malarial fevers* (see also C. D., 1919, xci, 1181). A tincture of the flowers and the leaves of the sunflower has been recommended by Beldau, in combination with balsamics, in the treatment of *bronchiectasis.* The Pah Ute Indians are said to use very freely as food the seeds of two indigenous sunflowers, *H. petiolaris* Nutt. and *H. lenticularis.* (*Proc. A. Ph. A.*, xxvii, 178.)

Helium. He–3.99.—This gaseous element was discovered in a gas yielded by deveite, a variety of uraninite, in 1895 by Ramsay. The spectrum showed it to be identical with the substance discovered in the solar chromosphere by Lockyer in 1868 which had been named by him helium, from the sun. A few months after Ramsay's discovery Kayser found the element as one of the rare gases of the atmosphere. It was later found as a constituent in natural gas from certain wells in Western America, and on account of its combination of qualities of lightness and non-inflammability it was collected for use in dirigible balloons. It is now collected for this purpose and stored for future use.

Helleborus. *Helleborus niger* L. *Black Hellebore. Hellébore noir,* Fr. *Schwarze Niesswurzel, Weihnachtswurzel, Winterrose,* G. *Elleboro nero,* It. *Eléboro negro,* Sp. (Fam. *Ranunculaceæ*).—*Black Hellebore* is a native of the mountainous regions of southern and temperate Europe, and is sometimes cultivated on account of the early opening and beauty of its flowers, whose expansion in midwinter has given to the plant the name of *Christmas rose.* Black hellebore is sometimes called *melampodium,* in honor of Melampus, an ancient shepherd or physician, who is said to have cured the daughters of King Prætus by giving them the milk of goats fed on hellebore. For a history of the use of hellebore by the ancients, see 15th edition, *U. S. D.*

The plant is a perennial, acaulescent evergreen herb possessing a short, black rhizome which gives rise each year to a single, palmately-divided leaf and a flower stalk bearing one or two large white flowers that occasionally are flushed with purple.

The formerly official rhizome is irregular, tortuous, often branched and knotty in appearance, about 3 to 5 cm. long and 6 mm. thick; externally black; upper and lateral surfaces marked by short, erect branches possessing annulations from leaf scars and terminal buds or stem scars; lower surface exhibiting numerous root scars and short stumps of roots; fracture short; inner surface yellowish-white to yellowish, showing thick bark, radially-elongated narrow-wood wedges and large pith; odor slight; taste bitter and acrid. The rhizomes of various other plants, some not belonging to the same genus, are substituted for true hellebore. These have been examined by Tschirch and Neuber, who state their results as follows: The rhizome of *H. niger* exhibits a small pith and comparatively large acutely wedge-shaped, radially-elongated wood-bundles. The odor of the rhizome and roots is slight but rather pleasant, especially in the fresh drug. The rhizome of *H. viridis* L. has a large pith and tangentially extended, bluntly wedge-shaped or almost square wood-bundles; older roots exhibit a wood with from five- to seven-angular wedges. In both rhizome and root of *H. fœtidus* L., the wood is more strongly developed and radiate in appearance; it contains abundance of wood-fibers and encloses little or no pith. The rhizome of *Actœa spicata* L. is flattened and bears cushion-like protuberances, due to the remains of the aerial stems. The wood-bundles are thickened at either extremity and rounded by wood-fibers, so that in transverse section the wood-ring has a scalariform appearance. The root exhibits a regular three- to five-rayed wood, the rays being broader toward the outside. (*S. W. P.*, xl, 410.)

William Bastick discovered in black hellebore a crystalline principle, *helleborin,* $C_{36}H_{42}O_6$, of a bitter taste with a tingling effect on the tongue, not volatilizable, slightly soluble in water, more so in ether and alcohol, and more readily in these liquids hot than cold. (*P. J.*, xii, 274.) Marmé and Husemann obtained from the black and from the green hellebore (*H. viridis* L.) a glucoside, *helleborein,* $C_{26}H_{44}O_{15}$, by precipitating a solution of an extract of the root with solution of lead subacetate, freeing from lead by hydrogen sulphide, and again precipitating with phospho-molybdic acid; by boiling with acid it separated into glucose and *helleboretin,* $C_{14}H_{20}O_3$, a compound of a fine violet color. The helleboreïn exists both in the root and leaves. It has a taste at once sweet and bitter, is soluble in water and weak alcohol, much less so in ether and absolute alcohol, and is crystallizable in yellowish rhomboidal prisms. It is precipitable by tannic acid and mercurous acetate. (*J. P. C.*, 4e sér., ii, 258.) Husemann and Marmé (*Ann. Chem.*, cxxxv, 61) examined more thoroughly the *helleborin* of Bastick. They found that when boiled with diluted sulphuric acid, or, better, zinc chloride, it is converted into sugar and *helleboresin,* $C_{30}H_{38}O_4$. They obtain this glucoside by treating with hot water the green fatty matter which is dissolved out of the root by boiling alcohol. Though both helleborin and helleboreïn are poisonous, the products of their decomposition are said to be harmless.

Helleboreïn is strongly irritant to the mucous membranes, causing, when applied to the conjunctiva, redness, swelling, and increased secretion, with indirect enlargement of the pupil, and when applied to the nasal membrane, sneezing, though less than veratrine. Small doses produce little effect on the stomach; but, repeated and accumulated, they cause anorexia, nausea even to vomiting, pain, increased secretion, and inflammation both of the stomach and bowels. The experiments of Van der Haide (*A. E. P. P.*, 1885, xix), Trendelenburg (*A. E. P. P.*, 1909, lxi, p. 262) and others demonstrate that physiologically helleboreïn belongs to the digitalis group of drugs. In small doses it diminishes the rate of the pulse, increases the force and out-put of the heart, and causes a rise in the blood pressure. In toxic doses, the pulse becomes rapid, and small in volume, and the heart is finally arrested in systole. According to Cushny, the action of helleboreïn on cardiac inhibition is less than most of the other members of the digitalis group. The *helleborin* of Marmé and Husemann is a more active poison, though less irritant to the mucous membrane. It acts on the tongue like aconite. Its influence appears to be directed especially to the nervous system. In the lower animals it causes quickened breathing, restlessness, tension and trembling of the muscles, uncertainty of movement; then retardation of the breathing and pulse, irritability of the peripheral nerves, dilatation of the pupil, loss of hearing, and finally almost complete anesthesia, with cerebral and spinal congestion, even to apoplexy.

Hellebore was formerly used as a drastic purge in *doses* of from ten to twenty grains (0.65–1.3 Gm.). This employment has, however, justly passed out of vogue. It was highly esteemed by the ancients in *mania, dropsy,* and *epilepsy. Bacher's pills,* celebrated for the cure of *dropsy,* consisted chiefly of black hellebore. The glucoside helleboreïn has been used internally as a cardiac tonic in *doses* of from one-sixth to one-third of a grain (0.010–0.021 Gm.) several times a day, but its irritant action on the stomach militates against its practical usefulness. Ischistowitsch (*Cb. M. W.*, 1887) has used an aqueous extract of hellebore with apparent benefit in *heart diseases.* Venturini and Gaspairini (*B. G. T.*, June, 1888) states that helleboreïn is a local anesthetic, which, in affections of the eye, is preferable to cocaine, because of the great permanency of the anesthesia, and because neither the pupil nor the intra-ocular pressure is affected. They use from three to four drops of a solution, each drop of which represents one one-hundred and sixty-fourth of a grain (0.0004 Gm.). In overdoses hellebore produces inflammation of the gastric and intestinal mucous membrane, with violent vomiting, hypercatharsis, vertigo, cramp, and convulsions, which sometimes end in death. The fresh root applied to the skin produces inflammation and even vesication. The *dose* of the powdered root is two or three grains (0.13–0.2 Gm.).

Hemidesmus Root. *Br.* 1898. *Hemidesmi Radix. Indian Sarsaparilla. Nunnari. Racine de Hemidesmus,* Fr. *Hemidesmus-Wurzel,* G.—"The dried root of *Hemidesmus indicus* R. Br." *Br.*, 1898. *Hemidesmus indicus* (Fam. *Asclepiadaceæ*) is a climbing shrub native to India and Ceylon. It has twining, woody, slender stems, and opposite, petiolate leaves, which are entire, smooth, shining, and of a firm consistence. The leaves vary much in size and shape, some being linear and acute, others broad-lanceolate, and others again oval or ovate. The flowers are small, green on the outside, purple within, and disposed in axillary racemes. The fruit consists of two long, slender, spreading follicles. This plant is common over the whole peninsula of Hindostan. The official portion was the root, which has long been used in India as a substitute for sarsaparilla. It is 30 cm. or more long and from 3 to 6 mm. thick, rigid, tortuous, cylindrical, and little branched, consisting of a large yellow ligneous center, and a brownish, corky bark, marked with longitudinal furrows and transverse fissures. The odor is aromatic, recalling that of tonka bean, the taste is aromatic and sweetish. On one side of the root the cork is frequently separated from and raised above the cortex, and is transversely fissured. The transverse section exhibits numerous laticiferous cells in the cortex. For details of microscopic structure, see *P. J.*, 1872, 62. Garden obtained from hemidesmus a peculiar, volatilizable acid principle, which he named *smilasperic acid,* under the erroneous impression that the root was derived from *Smilax aspera.* Pereira proposed to call it *hemidesmic acid.* Scott also obtained a stearopten by distillation with water, presumably the same material. It has not been further investigated.

Hemidesmus root is said to be tonic, diuretic, and alterative. It was introduced into Great Britain from India, and was employed for some time under the name of *Smilax aspera.* It is used for the same purposes as sarsaparilla. The native practitioners in India are said to employ it in nephritic complaints, and in the sore mouth of children. It is used in the form of infusion or decoction, made in the proportion of two ounces of the root to a pint of water. A pint (500 cc.) may be given in wineglassful doses in the course of the day. A *syrup* was official in the Br., 1898.

Hemoglobin. *Hæmoglobin.*—A constituent of venous blood, passing in the arterial blood into *oxyhemoglobin.* Its molecular formula is very complex. It is a conjugated protein, consisting of the protein, *globin,* in combination with the chromatogenic substance, *hematin.* It is readily obtained in a crystalline state and the crystals are said to vary in form according to the kind of animal from whose blood they are prepared. The principle property of hemoglobin is its power of combining with gases, especially oxygen and carbon monoxide. Whereas the oxygen compound readily dissociates, the carbon monoxide compound is very stable and cases of poisoning from illuminating gas where much carbon monoxide is present, as in the instances where it consists partly of water gas, are therefore often fatal. Various preparations of *desiccated blood* containing hemoglobin have been put upon the market. Crystals of hemoglobin may be obtained from the blood of certain animals (guinea-pigs, rats, etc.) with ease by simply adding water to the blood. The hemoglobin dissolves in the water, the corpuscles separating, and the crystals form in a few minutes. Another method consists in adding to defibrinated blood 6 per cent. of its volume of ether, or a mixture of alcohol and ether; on shaking the mixture, the corpuscles dissolve, and a thick magma of crystals forms sooner or later; these may be purified by washing with 25 per cent. alcohol and by recrystallization. Freezing has been resorted to for the purpose of separating the crystals.

Ferrohemol is a brown, almost tasteless powder containing 3 per cent. of iron, which is made by the precipitation of blood by a dilute solution of iron and neutralization with soda. *Fer cremol* is a similar substance.

Hemol and *Hemogallol* are made, as suggested by Kobert, by the action of reducing agents upon the blood coloring matter. (See *E. Merck's Jahresber.*, 1891.) With the hemol, zinc dust is used as the reducing agent; with the hemogallol, pyrogallol is used. The former is a dark brown, the latter is a reddish-brown, tasteless powder.

Either of these blood derivatives may be employed instead of the older preparations of iron. There is sufficient clinical evidence to show that they are effective ferruginous tonics which may be, as is claimed for them, less constipating and less disagreeable to the stomach than are the older preparations of iron; but there is no sufficient reason for believing that they have any real superiority. *Dose*, five to ten grains (0.32–0.65 Gm.).

A number of hemol preparations have also been recommended by Kobert and prepared by Merck & Co., such as *arsenhemol, bromhemol, iodohemol, iodomercuryhemol*, and *copperhemol*.

Heracleum. *Heracleum lanatum* Michx. *Common Cow-parsnip.*—This is a coarse, pubescent, perennial umbelliferous herb growing on moist, low grounds in northern North America as far south as North Carolina. Its grooved stem attains a height of 6–8 feet and bears ternate leaves with irregularly toothed leaflets and large umbels of white flowers.

The root, which is the part used, bears some resemblance to that of common parsley. It has a strong disagreeable odor and a very acrid taste. Both the leaves and root excite redness and inflammation when applied to the skin. Bigelow considers the plant poisonous. It appears to be somewhat stimulant and carminative, and has been used in *epilepsy*. (See 16th edition, *U. S. D.*)

Heretine.—An ether-soluble alkaloid obtained from *Heritiera javanica* (Fam. *Sterculiaceæ*), is said to be effective in the treatment of *epilepsy, chorea* and *migraine*.

Hermodactyls. *Hermodactyli.*—Under this name are sold in European commerce the roots or bulbs of an uncertain plant, growing in the countries about the eastern extremity of the Mediterranean. By some botanists the plant is thought to be a *Colchicum*, and *C. variegatum* L., a native of the south of Europe and the Levant, is particularly indicated by Fée, Geiger, and others, while by authors, no less eminent, the roots are confidently referred to *Iris tuberosa* L. They certainly bear a considerable resemblance to the corm of *Colchicum autumnale* L., being heart-shaped, channelled on one side, convex on the other, and from 12 to 25 mm. in length by nearly as much in breadth. As found in commerce, they are destitute of the outer coat, are of a dirty yellowish or brownish color externally, white and amylaceous within, inodorous and nearly tasteless, though sometimes slightly acrid. They are often wormeaten. Their chief constituent is starch, and they contain no veratrine or colchicine. From this latter circumstance, and from their insipidity, it has been inferred that they are probably not derived from a species of Colchicum. They are in fact almost without action upon the system. It is doubted whether they are the *hermodactyli* of the ancients, which acted like colchicum and were useful in *gout* and *rheumatism*. Pereira describes a bitter variety of hermodactyls, which was brought from India by Royle. The bulbs are smaller and darker than the others, and have externally a striped or reticulated appearance.

Hermophenyl. *Sodio-mercuric Phenoldisulphonate. Mercurio-sodic Phenol-disulphonate.*—This substance, which contains 40 per cent. of metallic mercury, occurs as a white amorphous powder, freely dissolving in cold water (up to 22 per cent.). According to Lumiere and Chevrotier (*B. M. J.*, 1901, 690), it possesses very feeble toxic properties, while it is actively bactericidal. Its hypodermic injections are said to cause but little pain. Hermophenyl is used in the treatment of *syphilis*. It may be exhibited either by intramuscular injection or, in pill form, by the mouth. The *dose* is ordinarily from one-eighth to one-third of a grain (0.008 to 0.021 Gm.) which, when administered by the mouth is given several times a day, by injection, once a day. Bernard claims that it may be made into a 1 per cent. soap without decomposition, affording an excellent preparation for rendering the hands aseptic. The 2 per cent. aqueous solution may be used for surgical purposes.

Herniaria. *Herniaria glabra* L. (Fam. *Caryophyllaceæ*) *Herniary. Rupture-wort. Knot-weed. Breastwort. Bruchkraut, Tausendkorn, G.*—A small perennial European herb about 2 inches high and producing, when a number of plants are grown together, a dense carpet of moss-like leaves which turn bronze-red in winter. Its flowers are inconspicuous and greenish. Goblez has obtained from this plant a crystalline principle, *herniarine* (*J. P. C.*, 4e sér., xx, 270), which proved to be *methylumbelliferone*, $C_{10}H_8O_3$. Schneegans has also discovered an alkaloid, *paronychine*. (*A. J. P.*, 1890, 488.) Besides these it contains a saponin which was discovered by Schulz in 1896. This saponin is strongly hemolytic, 1 part in 40,000 being sufficient to dissolve the coloring matter from the red blood cells. It appears to be absorbed unchanged and after its absorption to stimulate the kidneys. According to Kobert this plant, as well as the allied *Herniaria hirsuta* L., contains an acid and a neutral saponin both of which are diuretic.

Herniaria is recommended by Zeissl in *catarrh of the bladder*. Very active diuretic properties have been attributed to it by Kuhn (*Med. Klin.*, 1908) and others, who have found that it was successful in the treatment of *dropsy*, whether of cardiac or nephritic origin.

Heteromeles. *Heteromeles arbutifolia* (Poir.) Roem. (Now ascribed to *Photinia arbutifolia* Lindl.) (Fam. *Rosaceæ.*) D. D. Lustig has found in this California plant (*toyon* of the Indians) tannic, gallic, and hydrocyanic acids. (*A. J. P.*, April, 1882.)

Hetocresol. *Metacresol Cinnamate. Cinnamometacresol.* $C_6H_5CH = CH.COOC_6H_4CH_3$.—Forms crystals melting at 65° C., insoluble in water, but soluble in alcohol, ether, benzene, chloroform, and glacial acetic acid. It is claimed that this substance is especially valuable as a local remedy in external *tuberculosis*. In tuberculosis of the bladder Landerer uses, after cocainization, 1.4 per cent. solutions containing 0.7 per cent. of common salt. Fistulous tracts he injected with hetocresol, 1 part; iodoform, 2 parts; water, 1 to 8 parts. In *scrophuloderma*, after scraping, hetocresol has been found to be very useful.

Heuchera. *Heuchera americana* L. *Alum Root. American Sanicle. Racine d'Heuchère d'Amérique*, Fr. *Amerikanische Sanikelwurzel*, G. (Fam. *Saxifragaceæ.*)—This is a perennial, herbaceous plant which grows in shady, rocky situations from New England to Carolina and westward to eastern Kansas. The rhizome, which was formerly official, is horizontal, somewhat compressed, knotty, irregular, yellowish, and of a strongly styptic taste. Alum-root is powerfully astringent, and may be employed in similar cases with other medicines belonging to the same class. J. Peacock (*A. J. P.*, 1891, 174) found a percentage of tannin ranging from 9.33 to 19.66 reckoned on the dry drug, according to the season of the year when collected; also a percentage of starch, calculated the same way, ranging from 5.17 to 16.32. Frederick Stearns (*Proc. A. Ph. A.*, 1858, 263) speaks of two other indigenous species, *H. villosa* Michx. (*H. caulescens* Pursh.) and *H. pubescens* Pursh., as having similar properties; and F. W. Anderson reports (*Botan. Gaz.*, 1887, 65) that the roots of *H. hispida* Pursh., *H. cylindrica* Douglas, and *H. parvifolia* Nuttall are much used by hunters of Montana and others as astringents, particularly in *diarrhea* caused by the drinking of alkali water.

Hexamethylene-tetramine Compounds.—There have been introduced an extraordinary number of combinations of hexamethylenamine. Some of the more important of these are considered below.

Hexamethylene-tetramine Bromethylate. Bromalin. Bromethylformin. $(CH_2)_6N_4C_2H_5Br$.—Formed by the action of ethyl bromide upon hexamethylene tetramine. It occurs in colorless scales or white powder, melting at 200° C. with decomposition; nearly tasteless, readily soluble in water. Bromalin has been used by a number of neurologists as a substitute for the alkaline bromides in the treatment of *epilepsy.* It is asserted that it exercises all of the beneficial effects of the bromides in this disease, but does not give rise to symptoms of bromism. These statements, however, are hard to credit, as Bermann and Bilinski (*Th. M.*, 1910) have found that the compound is broken up in the body, and the entire content of bromine appears in the urine as an alkaline bromide. Broma represents 32 per cent. of bromine and is ordinarily administered in *doses* of thirty to sixty grains (2–4 Gm.).

Hexamethylene-tetramine Camphorate. Amphotropin. N. N. R. 1924. $((CH_2)_6N_4)_2.C_8H_{14}(COOH)_2$.—A molecular combination of camphoric acid and hexamethylene-tetramine. This is a white, crystalline powder easily soluble in both water and alcohol. It is used as a urinary disinfectant. *Dose,* eight to fifteen grains (0.5–1 Gm.).

Hexamethylene-tetramine Methylene Citrate. Uropurgol. Helmitol. Citramine. $C_7H_6O_7.(CH_2)_6N_4$.—This substance is a white acidulous, odorless powder, soluble in water, but almost insoluble in alcohol. It is said to be a combination of anhydromethylene-citric acid and hexamethylene-tetramine, 2 Gm. representing 0.85 Gm. of the latter constituent. Theoretically, helmitol should undergo decomposition in the human system with the formation and subsequent elimination of formaldehyde, and S. Goldschmidt (*Th. M.*, Jan., 1903) states that after the administration of helmitol formaldehyde is present in the urine when freshly voided. Helmitol has been highly recommended by P. Rosenthal (*Ther. Geg.*, Dec., 1902) in chronic *gonorrhea* and other infective diseases of the genito-urinary tract. Its value has been confirmed by S. Goldschmidt. It may be given in *doses* of fifteen to twenty-three grains (1.0–1.5 Gm.) up to forty-five to sixty grains (3–3.9 Gm.) a day.

Hexamethylene-tetramine Resorcinol. Hetralin. Dioxybenzene-hexamethylenetetramine. $C_6H_6O_2C_6H_{12}N_4$.—Soluble in four parts of hot water and in fourteen of cold water. Contains 60 per cent. of *hexamethylenetetramine.* It has been used as a urinary antiseptic in precisely the same class of cases in which hexamethylenamine has been employed. Fries (*All. M. C. Z.*, 1906) asserts that it has an advantage over the latter, in that it exercises an antiseptic influence even in alkaline fluids. Birnbaum (*W. K. R.*, 1906) asserts that it is also a valuable remedy in *spermatorrhea* and allied complaints. The *dose* is from eight to fifteen grains (0.5–1.0 Gm.) three times a day.

Hexamethylene-tetramine Salicylate. Saliformin. $C_8H_{12}N_4.C_6H_4OH.COOH$.—A white crystalline powder of a pleasant acidulous taste. Easily soluble in alcohol and water. It is employed as a uric acid solvent and genito-urinary antiseptic. *Dose,* eight to thirty grains (0.5–2.0 Gm.).

Hexamethylene-tetramine Quinate. Quinotropin. Urotropin Quinate. Chinotropin.—This quinine compound is furnished commercially in two forms, Quinotropin I, containing 73 per cent. quinic acid and 27 per cent. urotropin, Quinotropin II, containing 80 per cent. quinic acid and 20 per cent. urotropin. These compounds yield aqueous solutions of an acid, agreeable taste. According to Nicolaier and Hagenberg (see also De la Camp, *M. M. W.*, 1901, No. 30), quinotropin does not decrease the excretion of uric acid but aids in its solution in the urine. *Dose,* Quinotropin I, twenty-five to fifty grains (1.6–3.2 Gm.) per day; Quinotropin II, fifty to seventy-five grains (3.2–5.0 Gm.) per day.

Hexamethylene-tetramine Sulphosalicylate. Hexalet. Sulphosalicylate Hexamethylenamine. Hexal. Sulphexine. Sulphexet. $(CH_2)_6N_4.SO_3H.C_6H_3(OH)COOH$, occurs as white crystals soluble in water with a pleasant acid taste. It is claimed for it that it is broken up in the system, and that the sulphosalicylic acid exercises an astringent action upon the mucous membrane of the bladder as well as enhances the antiseptic action of the hexamethylenamine portion of the molecule. The *dose* is from ten to twenty grains (0.65–1.3 Gm.) three times a day.

Hexamethylene-tetramine Sodium Acetate, Cystopurin.—A double salt of hexamethylenamine and sodium acetate in the molecular proportion of 1:2 which, according to Bergell (*Apoth. Zeit.*, xxii), has the following formula: $(CH_2)_6N_42CH_3COONa + 6H_2O$. This salt forms long, acicular crystals which are soluble in cold or warm water. This compound has been employed as a urinary antiseptic in *cystitis, pyelitis,* and similar conditions. It is asserted by one authority that its advantage over hexamethylenamnie is that the formaldehyde is more slowly liberated and by another because the sodium acetate hastens the liberation of formaldehyde.

Hexamethylene-tetramine Tannin. Tannopin.—A light brown, odorless and tasteless powder, insoluble in alcohol, water and ether, and soluble in alkalinated liquid. It contains 87 parts of tannic acid and 13 parts of hexamethylamine-tetramine. It is employed as an intestinal astringent and antiseptic. *Dose,* eight to fifteen grains (0.5–1 Gm.).

Hexamethylene-tetramine Tetraiodide. Siomine.—This compound is insoluble in water and contains 78.5 per cent. of iodine. It is said to be decomposed in the intestines with the liberation of its two constituents. It is used in medicine chiefly for its iodide action.

Hexamethylene-tetramine Triborate. Borovertin. $(CH_2)_6N_4.3HBO_2$.—It is prepared by the direct combination of boric acid and formin. A white powder, slightly acid in its reaction, it is soluble in eleven parts of water and almost insoluble in alcohol and ether. On heating with acids formaldehyde is developed; on saturation with alkalies ammonia.

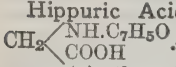
It is asserted to have the advantage over hexamethylenamine that it of itself renders the urine acid and therefore leads to the splitting up of the hexamethylenamine molecule and the liberation of formaldehyde, so that it is useful as an urinary antiseptic, when the urine is alkaline as well as when it is acid.

The *dose* is five to ten grains (0.32–0.65 Gm.) three or four times a day.

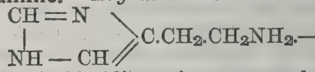
Hibiscus. *Hibiscus Abelmoschus* L. (*Abelmoschus moschatus* Mœnch.) (Fam. *Malvaceæ.*)—An annual or biennial plant indigenous to India but cultivated in many tropical countries. It yields the seeds known under the names of *Semen Abelmoschi* (*grana moschata, Musk seed, Graine d'Ambrette, Ambrettekörner, Bisornkörner*). These are of about the same size as flaxseed, kidney-shaped, striated, of a grayish-brown color, of an odor like that of musk and of a warm somewhat spicy taste. They were formerly considered stimulant and antispasmodic, but are now used only in perfumery. The Arabs flavor their coffee with them. They are said to be employed in the adulteration of musk. Another species, *Hibiscus esculentus* L. (*Abelmoschus esculentus* Moench.), is cultivated under the name of *okra, bendee,* or *gumbo* in various parts of the world, for the sake of its capsular fruit, which abounds in mucilage (*gombine*), and is used for thickening soup. The leaves are sometimes employed for preparing emollient poultices. The roots, which are a foot or two long, are said also to abound in mucilage free from any unpleasant odor. Their powder is perfectly white, and superior to the marshmallow. The plant is sold, in some parts of the United States, in the vegetable markets. The bark is also used in making paper and cordage.

Hieracium. *Hieracium venosum* L. (Fam. *Compositæ.*) *Rattlesnake Weed. Poor Robin's Plantain. Eperviere,* Fr. *Habichtskraut,* G.—The plant is a common perennial herb, growing in dry places and open woods from Maine to Georgia and westward. It is characterized by having a rosette of radical leaves which are elliptic-oblong, smooth and often purple veined or mottled above and glaucous beneath. It bears bright yellow ligulate flowers in heads. The leaves and roots are thought to possess medicinal virtues, and, being deemed astringent, have been used in *hemorrhagic diseases.* The juice is supposed by some to have the power of removing *warts. Dose* of infusion (two ounces to the pint), a wineglassful (60 cc.).

An allied species, *Hieracium pilosella* (*Mouse-ear Hawk-weed*), was used in the Middle Ages to cure hernia and dissolve calculi. Leclerc (*B. Sc. Pharm.*, 1922, xxix, p. 30) has found that it possesses diuretic properties and has used a fluid extract in doses of 2 cc. (30 minims) in various types of *edema* with asserted benefit.

Hippuric Acid. $C_6H_9NO_3$. *Benzoylglycocoll,*  $CH_2<\begin{matrix}NH.C_7H_5O\\COOH\end{matrix}$.—This occurs in considerable amount in the urine of herbivorous animals, sometimes in that of man. Benzoic and cinnamic acids, toluol, and other aromatic substances, when taken internally, are eliminated as hippuric acid. It crystallizes in rhombic prisms, melting at 187° C. and at about 240° C. decomposes into benzoic acid, benzonitrile, and prussic acid. Boiling acids, alkalies, or high temperatures decompose it into benzoic acid and glycocoll. According to the experiments of Meissner and Shepard, hippuric acid injected into the blood of animals acts as a very decided poison, but the hippurates have been suggested by Garrod as a remedy in the *uric acid diathesis.* He affirms that if outside of the body the sodium hippurate be added to blood serum that shows the presence of a urate, the latter is soon removed. *Sodium hippurate* may be combined with lithium or potassium salts; the *dose* is ten grains (0.65 Gm.) three times a day.

Hirudin. *Hirudine.*—A principle obtained from the heads of leeches which prevents the coagulation of blood. It occurs as brownish scales easily soluble in water. One-sixtieth of a grain is said to permanently prevent two fluidrachms of blood from coagulating without changing its property in any other way. Its use in gynecology is based on this property. See *Hirudo,* Part I. Marshall (*J. P. Ex. T.*, 1915, vii, p. 157) finds that some commercial samples of *hirudin* are highly toxic. He believes that these effects are due to the presence of decomposition products.

Histamine. *Ergamine. Betaiminazolylethylamine.* .—Histamine chemically is histidine minus one molecule of carbon dioxide. Histamine hydrochloride is used as a reagent for standardizing pituitary preparations. Histamine occurs in various putrefying proteins and also in ergot. The commercial supply, however, is obtained synthetically. It is a general stimulant to unstriped muscle, including the uterus, but through some action upon the blood vessels not clearly understood, it produces a fall of blood pressure. It also produces, in rodents, a spasm of the bronchial muscles, giving rise to symptoms very analogous to those of the so-called anaphylactic shock. (See Abel and Kubota, *J. P. Ex. T.*, 1919, xiii, 243.) It has been suggested as a uterine stimulant in *postpartum hemorrhage.* The *dose* of histamine is one-sixtieth of a grain (0.001 Gm.).

Histogenol.—Monneyrat (*Prog. M.*, April, 1902), finding that *sodium methylarsenate* ($OAsCH_3O_2Na_2$) was not poisonous, has combined it with nucleinic acid to form this preparation, which he claims to be of great value in the treatment of *tuberculosis.*

Hoang-Nan.—This is the bark of *Strychnos malaccensis* Benth. (Fam. *Loganiaceæ*), a climbing plant, which grows in Malacca and surrounding countries. Brucine and strychnine are stated to have been found in it, brucine being the more abundant of the two. It has been found to produce in animals general tetanic spasms similar to those caused by strychnine. It probably has the same range of medicinal application as has nux vomica, although special virtues have been claimed for it in the treatment of *chronic skin diseases. Dose* of powdered bark, three grains (0.2 Gm.).

Holadin. *N. N. R.* 1924. *Extractum Pancreaticum Integrum.*—A dried extract of the entire pancreas containing all the constituents of the glands and having power to digest starch and proteids and to curdle milk, also aiding in the splitting up of fats. *Dose,* three to ten grains (0.2–0.6 Gm.).

Holigarna. *Holigarna longifolia* Roxb. Now *Senecarpus longifolia* Blume. (Fam. *Anacardiaceæ.*)—According to David Hooper (*P. J.*, xxv, 1895), the black juice of this tree, which is used in India as the basis of a varnish, is actively vesicant, and contains a body closely allied to, if not identical with, cardol.

Homorenone. *Ethylamino-acetopyrocatechin.* $C_6H_3(OH)_2CO.CH_2NH_2.C_2H_5$.—The hydrochloride occurs as bitter white crystals, readily soluble in water with a melting point of 260° C. It is asserted to resemble closely the physiological action of epinephrine except that it requires solutions of greater concentration to produce the same result. A 5 per cent. solution is asserted to be equivalent to one per thousand of epinephrine. (See *P. J.*, 1908, lxxx, p. 784.)

Honthin.—This is a grayish-brown odorless and tasteless powder, insoluble in water but yielding a light-brown solution in alcohol and in aqueous alkali, in which it is partly soluble. It is said to be chemically a *keratinized albumin tannate.* It is given in *doses* of from ten to twenty grains (0.65–1.3 Gm.) three to five times daily, as an astringent, in all forms of *diarrhea* without great irritation.

Hoochinoo.—This is an alcoholic drink which is clandestinely distilled by the Alaskan Indians, and has been supposed, on account of the frenzy which it produces in them, to contain some poisonous substance other than alcohol. John Marshall found it, however, to be simply an alcoholic liquor of about the strength of sherry, *i. e.*, between 20 and 25 per cent.

Hordenine. *Para-oxyphenyl-dimethyl-ethylamine.* $C_{10}H_{15}ON$.—It was isolated by Léger from malted barley. The sulphate, crystallizes in prismatic needles giving a violet-blue color with ferric chloride.

Hordenine has been used by Sbrazes and Guerive (*C. R. A. S.*, 1908, cxlvii) and other authors, in the treatment of various forms of *diarrhea* and *dysentery* and in gastric hyper-secretion. According to the researches of Camus (*A. I. P. T.*, 1906, xvi), which are reported by the authors quoted, it would appear that it acts by paralyzing the peripheral ends of the secretory nerves, as does atropine. It appears to affect also the pneumogastric and motor nerves and is asserted to have a tonic action upon the heart. Jackson (*J. P. Ex. T.*, 1914, iv, p. 491) finds that hordenine has a powerful effect in overcoming bronchial spasm and suggests its use in *asthma.* We know, however, of no clinical trials of it in this condition. The *dose* is three to eight grains (0.2–0.5 Gm.) three or four times a day.

Hordeum. *Barley. Orge,* Fr. *Gerste,* G.—The grains of cultivated varieties of *Hordeum vulgare* L. and *H. distichon* L. (Fam. *Gramineæ*). The original country of the cultivated barley is unknown. The plants have been found growing wild in Sicily and in various parts of the interior of Asia. *Hordeum vulgare* yields the six- and four-rowed barleys and *H. distichon*, the two-rowed barleys. There are several forms of each of these under cultivation. A form of four-rowed barley, *Hordeum vulgare pallidum,* is the common barley in Northern America, Europe and Asia.

Clifford Richardson (*Bulletin No. 9, Department of Agriculture,* 1886) gives the following as the average composition of American barley: water, 6.47 per cent.; ash, 2.87; oil, 2.67; sugar, etc., 7.02; dextrin and soluble starch, 3.55; starch, 62.09; albuminoids soluble in 80 per cent. alcohol, 3.66; albuminoids insoluble in 80 per cent. alcohol, 7.86; fiber, 3.81; total, 100.00. He finds, moreover, that on an average the grain makes up 84.78 per cent. and the hull 15.22 per cent. of the barley. Kühnemann (*B. Chem. G.*, 1875 and 1876), found a crystallized dextrogyrate sugar which did not reduce alkaline copper solution, and an amorphous lævogyrate mucilaginous substance called *sinistrin.* According to Kühnemann, barley does not contain dextrin.

Barley contains *hordein,* a proteid substance somewhat related to *gliadin* which is derived from the kernels of wheat and rye. Hordein is soluble in alcohol. The name was formerly given to a pulverulent mixture obtained from barley which was believed to be a definite substance.

Hulled barley is merely the grain deprived of its husk, which, according to Einhoff, amounts to 18.75 parts in the hundred.

Barley meal is formed by grinding the seeds, previously deprived of their husk. It has a grayish-white color; the constituents are the same as described above for barley. It may be made into a coarse, heavy, hard bread, which in some countries is much used for food.

Pearl barley (*Hordeum decorticatum,* Br., 1885) is the seed deprived of all its investments and afterwards rounded and polished in a mill. It is in small round or oval grains, having the remains of the longitudinal furrow of the seeds, and of a pearly whiteness. It is wholly destitute of hordein, and abounds in starch, with some gluten, sugar, and gum. This is the proper form of barley for medicinal use.

Barley in the form of the decoction, popularly known as *barley water,* affords a mucilaginous drink much employed from the time of Hippocrates to the present. Pearl barley is the form usually preferred for the preparation of the decoction, made by pouring four pints of boiling water on two troyounces of pearl barley and boiling away to two pints, and straining. It is especially used in infant feeding, as it seems to prevent the formation of large milk curds by its colloidal character.

Hormonal. *Peristaltic Hormone.*—It has been demonstrated that certain substances are formed in the body which, being absorbed into the blood, act as stimulants to secretion in distant glands. The presence of these metabolic products, which are known to physiologists as *hormones,* is generally presumed to be essential for normal function. Zuelzer (*B. K. W.*, 1908) claimed to have demonstrated that there is formed in the cells of the mucous membrane of the stomach, a hormone which is an excitant to intestinal peristalsis, and that this hormone is stored in the spleen. He has accordingly brought forward as a remedy for *constipation,* under the name of *hormonal,* a preparation, made from the spleen of an animal at the height of digestion, which is intended for intravenous injection. A number of authors have reported favorably on its effects, but there have been several cases of serious and even fatal collapse following its application. Zuelzer (*D. M. W.*, xxxviii) asserts that these mishaps have been due to errors in the manufacture by which the substance was contaminated with an albumose, and that since the discovery and correction of these there has been no further trouble. On the other hand, Dittler and Mohr (*Z. K. M.*, 1911, lxxv) from both laboratory and clinical observations, conclude that the remedy is of doubtful utility, and too dangerous for practical use.

Huamanripa.—This is a Chilian drug, the plant growing on the slope of the Cordilleras at considerable heights. Lapater found it to be stimulating, emetic, sialagogue, and diaphoretic. (*West. Drug.*, 1886, 410.)

Hura. *Hura crepitans* L. *Sandbox tree. As-*

sacou. Sablier, Fr. *Sandbüchsenbaum*, G.—This tree, belonging to the *Euphorbiaceæ*, is indigenous to tropical America and is extensively cultivated in the tropics. It is characterized by the tendency of its capsular fruit when ripe to break with violence into several pieces, and thus scatter the seeds. It is an acrid emeto-cathartic; in large doses acting as a violent poison. The fresh juice, the seeds, and a decoction of the bark all have these properties; an oil expressed from the seeds is actively purgative. According to Richet, the toxicity is due to the presence of a toxalbumin to which he gave the name of *crepitin*. (*P. J.*, 1910, lxxxiv, p. 571.) The juice of *Hura crepitans*, according to J. J. Surie (*Nederl. Tijdscgvoor Pharm.*, 1900, 107), contains a volatile, colorless liquid, *hurin*, closely allied to cardol, and is stated by Martius to be used to intoxicate fish. It has been employed to a considerable extent with alleged favorable results in the treatment of the *elephantiasis*, or *leprosy*, in Brazil. (For a method of using it, see *J. P. C.*, xiv, 424.) The juice is extremely acrid, producing on the skin, when applied to it, an erysipelatous redness and a pustular eruption; the natives are said to employ it in the preparation of a poison.

Hychlorite. *N. N. R.* 1924.—A solution of chlorinated soda each 100 Gm. of which is said to contain sodium hypochlorite 4.05 Gm., sodium chloride 3.20 Gm., and calcium hydroxide 0.17 Gm.

This solution represents 3.85 per cent. of available chlorine, being, therefore, of approximately the strength of liquor sodi chlorinata. Its chief importance lies in the comparative slowness of its deterioration; the available chlorine content decreases at the rate of about 12 per cent. per annum. It is also of very much lower alkalinity and for this reason it is used as a surgical disinfectant.

Hydracetin. *Pyrodine.*—The *hydracetin* of commerce is stated to be a varying compound, whose active principle is *acetylphenylhydrazin* (C_6H_5,-NH–NH.C_2H_3O). It is soluble in alcohol and in water in proportion to 1 to 50. According to Guttmann (*Ph. Centralh.*, May 16, 1889, 311), hydracetin is a powerful antipyretic and antirheumatic remedy. It occurs as a white, odorless, almost tasteless crystalline powder, melting at from 128°–129° C. It is stated that it cannot be continuously used without danger. Externally, hydracetin is used in place of chrysarobin in *psoriasis* and similar disorders, in an ointment of from 5 to 15 per cent. *Dose*, three-quarters of a grain (0.048 Gm.) two or three times a day.

Hydrastinine Hydrochloride. *Hydrastininæ Hydrochloridum*, U. S. IX.—This salt, which was formerly official was defined as "The hydrochloride $[C_{11}H_{11}O_2N.HCL = 225.57]$ of hydrastinine, an alkaloid obtained by the oxidation of hydrastine. Preserve it in well-closed containers, protected from light." *U. S.*

It is an artificial alkaloid, produced by acting on hydrastine, the alkaloid from hydrastis, with oxidizing agents. When manganese dioxide and sulphuric acid are used together, or when platinic chloride is employed, hydrastinine and *opianic acid* are the products. Hydrastinine is also manufactured synthetically from narcotine by first producing cotarnine, which is reduced to *hydrohydrastinine* and the latter subsequently oxidized to hydrastinine.

It can also be made from berberine, from piperonal or from *homopiperonylamine.*

Hydrastinine hydrochloride was officially described as in "light yellowish needles, or as a yellowish-white, crystalline powder without odor. One Gm. of Hydrastinine Hydrochloride dissolves in 195 cc. of chloroform, and in 1820 cc. of ether at 25° C.; very soluble in water and alcohol. Its aqueous solution (1 in 20) is neutral to litmus and shows a blue fluorescence, especially when highly diluted. It melts at about 210° C. with partial decomposition. In an aqueous solution of the salt (1 in 20), potassium dichromate T.S. produces a precipitate which redissolves if gently heated, but on cooling the solution it separates again in glistening needles. Silver nitrate T.S. produces in an aqueous solution of the salt a white precipitate, insoluble in nitric acid. No weighable ash remains on incinerating 0.1 Gm. of Hydrastinine Hydrochloride. In an aqueous solution of the salt (1 in 20) bromine T.S. produces a yellow precipitate, which is completely soluble in ammonia water, producing an almost colorless solution (*hydrastine*). Add a few drops of ammonia water to 1 cc. of an aqueous solution of Hydrastinine Hydrochloride (1 in 20); no turbidity is produced (*foreign alkaloids*). Add slowly 4 or 5 drops of a solution of sodium hydroxide (1 in 7) to a solution of 0.2 Gm. of the salt in 3 cc. of distilled water; each drop causes a milky turbidity, which disappears again on shaking (*foreign alkaloids*). From this solution, after standing for some time, pure white hydrastinine separates, and the supernatant fluid is almost colorless." *U. S.*

Uses.—Hydrastinine is, when given in large enough amount, a powerful depressant to the whole motor tract, affecting the psycho-motor centers of the cerebral cortex, the motor nerve, and the muscle itself. In the present state of our knowledge it is uncertain whether the depression is or is not preceded by a brief period of excitation, but it is almost certain that there is a primary stimulation of the muscles. The alkaloids slows the action of the heart but increases the force of the beat, and markedly augments the blood pressure, contracting actively the blood vessels by stimulating both the vaso-motor centers and the muscles in the walls of the arterioles. In the toxic dose it finally paralyzes respiration, although there is reason for believing that in the beginning it stimulates the function. Death occurs from asphyxia, to which it usualy ascribed the final fall of the arterial pressure.

It has a direct stimulant action upon the uterus. According to Kehrer (*Monatsschr. Geburtsh. u. Gynäk.*, 1907, xvi, p. 709), it rivals in the certainty of its effect the best preparations of ergot. It would seem that it is a universal muscle poison, primarily stimulant in its action, and that in this way it affects the heart, the arterioles, and the uterus. According to von Bunge, it markedly increases peristalsis, so that even the intestines do not escape its muscular action.

Hydrastinine was originally recommended by Falck in the treatment of *menorrhagia, metrorrhagia, dysmenorrhea*, and even *endometritis.* The testimony as to its value in all forms of uterine hemorrhage seems to be conclusive, and it is affirmed by many gynæcologists that it has a pronounced alterative influence upon the mucous membrane of the uterus. From our own experience we are convinced that it has value as a cardiac tonic, not equal in power or certainty of action to digitalis, but often useful as a substitute for that drug, especially in minor cases of heart failure. Its sedative action on the central nervous system, conjoined with its stimulating influence upon the circulation and its pronounced effects upon the genital system, make it a very valuable remedy in the treatment of feeble women of hysterical temperament, with tendency to uterine fluxes.

Dose, usually employed, from three-fourths of a grain to one and a half grains (0.048–0.096 Gm.) every three to six hours, but probably larger doses might often be used with advantage, since no ill effects have been as yet recorded as being produced by it. The salt may be given hypodermically.

Hydrogen Ion Concentration.—The transformation of electrical into chemical energy is illustrated by the phenomena of *electrolysis.* An electric current passed through certain substances, capable of conducting a current of electricity, called *electrolytes,* which are in a state of fusion or solution, causes dissociation of the compound, and electropositive elements or groups (*ions*) are liberated at the negative electrode or cathode, while electronegative elements or groups are set free at the positive electrode or anode. The negative elements or groups are known as *anions* while the positive elements or groups are called *cations.*

Even when a current of electricity does not pass through a solution of an electrolyte a certain amount of dissociation takes place which is frequently in inverse proportion to the dilution. Thus strong sulphuric acid undergoes very little dissociation and is almost devoid of chemical action upon pure iron while a dilution with about ten volumes of water brings about a marked dissociation with an intensifying of the reaction upon iron. Sometimes the elements or groups set free undergo secondary changes through reaction with the solvent which is usually water. Why certain solvents such as water should favor the ionic dissociation is not thoroughly understood.

Ionic dissociation as applied to acids and alkalies may be interpreted as an intensity factor rather than a concentration factor. This factor is capable of being measured either by electrical or colorimetric methods. The former method being first employed, the symbol pH was adopted for this factor, signifying "Hydrogen Potential." The expression of this factor as applied to acids or alkalies is expressed in H ions on the acid side of neutrality and in OH ions on the alkaline side. The following table gives the pH values in whole numbers, in the first column, the equivalent in H ions and OH ions per given volume of the solvent in the second column and the equivalence in normality of acid and alkali respectively in the third column. (See also Clark's *Determination of Hydrogen Ions* for complete details of this important subject.)

ACID RANGE

pH* value	1 Gm. H ions in	Equivalent in acid volumetric solution
0.0	1 Liter	Normal acid
1.0	10 "	0.1 Normal acid V.S.
2.0	100 "	0.01 " " "
6.0	1,000,000 "	0.000001 " " "
7.0	10,000,000 "	Perfect Neutrality

ALKALINE RANGE

pH* value	17 Gm. (OH) ions in	Equivalent in alkaline volumetric solution
8.0	1,000,000 Liters	0.000001 Normal Alkali V.S.
9.0	100,000 "	0.00001 " " "
13.0	10 "	0.1 " " "
14.0	1 "	Normal Alkali

*The pH figure is the logarithm of the reciprocal of the H ion concentration expressed in relation to a certain volume of the solvent. The pH of neutral water is 7, since water contains 0.0000001 Gm. of hydrogen per liter, or 10^{-7}.

The measurement by means of an electrical apparatus is much more accurate than the colorimetric method, but the apparatus is quite costly and requires technical knowledge and skill to use. A hydrogen electrode consisting of one of the noble metals such as platinum, coated with platinum black, or an electrode of mercury coated with calomel will serve. A potentiometer is needed to measure the electromotive force.

The colorimetric method of determining hydrogen ion concentration is much more frequently employed. It takes advantage of the fact that certain indicators have a range of color change which is directly indicative in each case of a certain limited range of hydrogen ion concentration (acidity or alkalinity) and by carefully selecting a number of these indicators whose values have been carefully studied and checked by the potentiometer method almost the entire range may be covered. The indicators given in Clark's list are as follows:

The following list has been compiled from those given by Clark and by F. X. Moerk (*Proc. Pa. Ph. A.*, 1924):

Indicator	pH Range
Thymol Blue	1.2–2.8
Methyl Orange	2.9–4.0
Bromphenol Blue	3.0–4.6
Tetrabromphthalein	3.0–5.0
Methyl Red	4.4–6.0
Bromcresol Purple	5.4–7.0
Bromthymol Blue	6.0–7.6
Phenol Red	6.6–8.2

Indicator	pH Range
Phenolsulphonphthalein	6.8– 8.4
Alphanaphtholphthalein	7.0– 9.0
Cresol Red	7.2– 8.8
Orthocresolphthalein	8.0–10.0
Thymol Blue	8.2– 9.8
Tetranitrophthalein	9.0–10.0
Thymolphthalein	10.0–11.0
Sodium Indigodisulphonate	12.0–14.0

Slightly different values are given by some authorities for a few of the indicators in both of these lists. The use of these indicators require the use of certain buffer solutions or stabilizers, and for the intelligent application of this method of determining pH values either the details as described in Clark's book must be accurately followed, or one of the ready to use "Hydrogen Ion Testing Sets" which are now available may be employed.

The practical applications of the determination of pH value are increasing rapidly. Culture media are now brought to a very fine degree of uniformity. The action of germicides and disinfectants has been developed along more scientific lines. The fermentation and baking industries have been benefited. The determination of the pH value of the blood has thrown new light upon certain diseases. Soil productiveness and plant growth have been found to depend upon certain narrow limits in this connection. The action of enzymes is more intelligently controlled. These are a few of the more important fields when a knowledge of pH values has been of service.

Hydrogen Sulphide. *Hydrosulphuric acid. Sulphuretted Hydrogen.* H_2S.—A colorless gas of unpleasant odor, soluble in water, to which it imparts an acid reaction. 3.23 volumes of gas are absorbed by one volume of water at 15° C. Also soluble in alcohol. Has been liquefied at ordinary temperatures under a pressure of 17 atmospheres, or at ordinary pressures by a cold of −74° C., and at −85° C. becomes an ice-like solid. *Liquefied hydrogen sulphide* is a colorless, transparent, very mobile fluid with strong solvent properties. (*Chem. Ztg.*, 1904, No. 70.)

The symptoms of poisoning by hydrogen sulphide vary with the amount taken. Its inhalation in a concentrated form is followed by giddiness, nausea, excessive weakness, and rapid or immediate loss of consciousness. The very diluted gas produces nausea, pain in the head, and great general weakness; followed, if sufficient be taken, by coma, or stupor with delirium, and in some cases by general convulsions. The blood becomes of a brownish-black color, and after death remains fluid. The general appearances at the autopsy are not to be distinguished from those produced by the absorption of carbon dioxide, but the diagnosis is readily made by the odor which pervades the whole corpse.

Bruère (*J. A. P.*, Oct., 1891) showed that hydrogen sulphide formed with hemoglobin a greenish-brown compound, *sulphmethemoglobin* or *sulphemoglobin,* and it has been shown by Paul Binet (*Rev. Méd. de la Suisse Rom.*, xvi, 1896) that this sulpho-methemoglobin is produced in the blood during life, especially when the gas is in very large amount. It is worthy of remark that Bruère found *hydrogen selenide* and *hydrogen telluride* to act the same as the hydrogen sulphide.

In 1886 Bergeon proposed to the French Academy a method of treating *tuberculosis* by injecting hydrogen sulphide, diluted with pure carbon dioxide, into the large intestine, but the method has fallen into desuetude. Hydrogen sulphide is, however, a useful remedy in *pulmonary catarrh,* chronic or acute, as well as in *chronic rheumatism* and in *gout.* It is for this reason that sulphur springs are so frequently resorted to. Sulphuretted natural waters must be taken at the spring as they quickly decompose after issuing from the ground. Water saturated with hydrogen sulphide and carbon dioxide is usually not objected to by patients after the first day or two of its taking, and does not disagree with the stomach. *Dose,* from two to four fluidounces (60–120 cc.) three or four times a day.

Hydroquinone. *Hydrochinone. Quinol. Paradioxybenzene.* 1–4 $C_6H_4(OH)_2$.—This is one of the three isomeric diatomic phenols, of which resorcin is the meta variety. It was first prepared by the dry distillation of quinic acid, but is now made from quinone by reduction with sulphurous acid, the quinone being made by oxidizing aniline with dichromate mixture ($K_2Cr_2O_7 + H_2SO_4$). It is in shining white leaflets melting at 169° C., soluble in water, alcohol, and ether, and is used largely in photography as a developing agent. In 1877 Brieger found that *hydroquinone* produces in man giddiness, tinnitus aurium, and a lessening of the force and frequency of the pulse. The experiments of P. J. Martin have shown that in the frog hydroquinone causes violent convulsions, followed by paralysis. In the mammal small doses produce a rise in the arterial pressure, followed by a depression; both of these phenomena are apparently the result of an action of the drug upon the arterial vaso-motor system, although it is probable, from the experiments of Beyer, that the toxic dose of hydroquinone paralyzes both the heart muscle and the muscle fibers in the coat of the arterioles. The bodily temperature is lowered by large doses of hydroquinone, and, according to the experiments of Martin, this is chiefly due to an increase of heat dissipation and is, therefore, probably the result of a vasomotor paralysis.

Hydroquinone is also antiseptic, but inferior in power to phenol. The influence of hydroquinone upon the human being has been especially studied by Silvestrini and Picchini, and by Gaetano Traversa. (*France Méd.*, May, 1890.) According to these authorities, it is a prompt antipyretic, producing depression of temperature in *fever,* the reduction beginning in half an hour, and reaching its maximum in an hour and a half. Usually the antipyretic action is not accompanied by disagreeable symptoms, although after the larger dose excessive sweating chills, and some nervous disturbances have been noted. Hydroquinone has been used in *infectious fevers,* and in *acute articular rheumatism;* also as a gastro-intestinal disinfectant. *Dose,* three to eleven grains (0.2–0.71 Gm.).

Hydroxylamine Hydrochloride. $NH_2.OH.HCl$.—The free base is known only in solution, and is unstable. The crystalline hydrochloride forms colorless hygroscopic crystals similar to ammonium chloride in appearance, soluble in an equal weight of water, also in glycerin and in fifteen parts of alcohol. In 1888 Binz found that this substance caused in the lower animals stupor, convulsions, and a destruction of the red blood corpuscles, of such character that their hemoglobin was reduced to methemoglobin or even to hematin. In 1899 L. Lewin of Berlin, further investigated the subject, confirming in part the results obtained by Binz, and showing that the poison acts both upon the dead and living blood, and that its action upon the corpuscle is probably due to its decomposition, and the liberation of nitric or nitrous acid. In 1889 John Fabry (*Arch. de Derm. et de Sph.*, tome ii, 1889) found that a 10 per cent. solution is exceedingly irritating to most human skins, producing intense redness, violent burning, sweating, and not rarely vesication. Some skins will not bear a 1 per cent. solution, so that it is not safe in any new case to use a solution stronger than this. The substance was employed by Fabry, and since then by other clinicians, as an agent to replace pyrogallol and chrysarobin in the treatment of skin diseases, offering at the same time the advantage of being colorless, and not staining the skin, linen, etc. It has been used in *chronic psoriasis,* in *scabies,* in *lupus, herpes tonsurans, parasitic sycosis,* etc., with asserted excellent results, though Groddeck condemns it as being too irritating and liable to produce constitutional symptoms, and inferior in its healing powers to chrysarobin and pyrogallol. The solution of *hydroxylamine hydrochloride* may be prepared with alcohol or water, but should always be rubbed up with prepared chalk to neutralize any excess of acid.

Hydroxylamine Sulphate. *Oxy-ammonium Sulphate.* $(NH_2OH).H_2SO_4$.—It has been suggested by Bang (*B. K. W.,* 1907, p. 216) for the quantitative estimation of sugar in the urine with Fehling's solution. The method consists in boiling definite quantities of the urine to be tested with an excess of the copper solution, and then determining the amount of hydroxylamine necessary to decolorize the copper. It is also used as a reducing agent in the quantitative determination of chlorates, bromates and iodates. (Schimpf, *Volumetric Analysis,* 5th edition.)

Hygrophila. *Br. Add.* 1900.—The dried herb including the root of *Hygrophila spinosa* T. And. (*Asteracantha longifolia* Nees). (Fam. *Acanthaceæ.*) This species of *hygrophila* has long been used in India as a diuretic in the treatment of *dropsies,* especially where there is hepatic obstruction, and also as a popular *aphrodisiac.* In Southern India the root is an article of commerce, but in Bombay the seeds are commonly employed. By means of petroleum benzin C. H. Warden obtained from the roots a crystalline principle (*Phg. Ind.,* vol. 3). The *decoction of hygrophila* (*Decoctum hygrophilæ,* Br. Add., 1900), two ounces of the root with three pints of water boiled to a pint, is given in *doses* of one-half to two fluidounces (15–60 cc.).

The seeds of the *H. salicifolia* of Java are called by the natives "Telor kodok" (that is, frog's eggs), from their peculiar property of forming a gelatinous shiny mass when added to water. They are used for the preparation of poultices (Leudner, *Ph. Era,* 1918, ii, 181).

Hypericum. *Hypericum perforatum* L. *St. John's Wort. Millepertuis, Casse-diable,* Fr. *Johanniskraut, Harthen,* G. (Fam. *Hypericaceæ.*)—A perennial herb, with a very acrid juice, 1 to 2 ft. in height, with 2-edged stems, opposite, sessile, oblong to linear, obtuse, black-dotted leaves, bright yellow flowers arranged in terminal cymes and ovoid, capsular fruits. It is indigenous to Europe but naturalized in fields in the United States. It has a peculiar balsamic odor, which is rendered more sensible by rubbing or bruising the plant. Its taste is bitter, resinous, and somewhat astringent. It imparts a yellow color to cold water, and reddens alcohol and the fixed oils. Its chief constituents are volatile oil, a resinous substance, tannin, and coloring matter. This latter, known as *hypericum red,* is a reddish resin, smelling like the flowers, soluble in alcohol, ether, ethereal and hot fatty oils, coloring the solution from wine red to blood red. It is soluble in alkalies with green color, and gives yellow precipitates with the alkaline earths and metallic salts. As a medicine it was in high repute among the ancients in an extraordinary variety of complaints but it was, perhaps, most highly esteemed as a remedy in *wounds* and *bruises,* for which it was employed both internally and externally. It probably has somewhat analogous power to the turpentines. It formerly enjoyed great reputation for the cure of demoniacs, and the superstition still lingers among the vulgar in some countries. At present the plant is scarcely used except as a domestic remedy. The summits were given in the *dose* of two drachms or more. A preparation, *oleum hyperici* or *red oil,* made by macerating four ounces of the tops in a pint of olive oil, is still used as a home remedy for *bruises.*

Hypnal.—*Chlorpyrine. Chloralhydrate antipyrine,* $C_{11}H_{12}N_2O.CCl_3.CH.(OH)_2$, results by rubbing together 188 parts of antipyrine and 165.5 parts of hydrated chloral and crystallizing out the product. It forms colorless crystals melting at 67° C. It is supposed to combine the somnifacient action of chloral with the anodyne effect of antipyrine, and is used not only in the treatment of *insomnias* of nervous origin, but also in those caused by pain. The *dose* is from fifteen to thirty grains (1.0–2.0 Gm.).

Hypnone.—*Phenyl-methyl-ketone. Benzoylmethide. Acetophenone,* $C_6H_5.CO.CH_3$, is obtained by the dry distillation of a mixture of calcium acetate and calcium benzoate; colorless or yellow liquid of oily consistency, boiling at 198° C. It has a pleasant odor suggesting that of orange flowers. It has been used as a somnifacient. *Dose,* three to eight minims (0.2–0.5 cc.).

Hyssopus. *Hyssopus officinalis* L. (Fam. *Labiatæ*) *Hyssop. Hysope,* Fr. *Isop, Ysop,* G.—Hyssop is a perennial herb indigenous to Europe but naturalized in the U. S., occurring in gardens and along roadsides. The flowering summits and leaves have been used in medicine. They have an agreeable aromatic odor, and a warm, pungent, bitterish taste, due to the presence of a volatile oil. This oil is colorless or greenish-yellow, of peculiar odor, sharp camphor-like taste, and neutral reaction. It has a sp. gr. from 0.88 to 0.98, distils between 142° and 162° C., and is soluble in its own bulk of alcohol of 0.85 sp. gr. The acid found in the oil has been identified as *l-pinonic acid,* and the ketone *l-pinocamphene.* Hyssop is a warm, gently stimulant aromatic, applicable to the same cases as the other labiate plants.

Iatrevin.—This is a condensation product of menthol and isobutyl-phenol. It is a clear fluid of an aromatic odor, miscible with alcohol in all proportions. It has been used by Munter (*Med. Klin.,* 1906, p. 1097) as an internal antiseptic in the treatment of *pulmonary tuberculosis.* His conclusions, as far as we know, have not been confirmed.

Iberis. *Iberis amara* L. (Fam. *Cruciferæ*) *Bitter Candytuft.*—A small European bitter, annual herb with alternate, lanceolate leaves, white flowers and orbicular fruits. The leaves, stem, and root are said to possess medicinal properties, but the seeds are more efficacious. The plant appears to have been employed by the ancients in *rheumatism, gout,* and other diseases. In large doses it is said to produce giddiness, nausea, and diarrhea, and to be useful in *cardiac hypertrophy, asthma,* and *bronchitis,* in *doses* of from one to three grains (0.065–0.2 Gm.) of the seed.

Ibogaine. $(C_{52}H_{66}O_2N_6)$.—This alkaloid was separated by Dybouski and Landrim (*Nouv. Rem.,*

1905) from the roots of the *Tabernanthe Iboga*, a plant found in the Congo. In overdose it causes hallucination and general paralysis, with death due to failure of the respiratory muscles. In *dose* of one-third to one-half grain it is said to act as a stimulant to the nervous system somewhat similar to caffeine. Haller and Heckel (*C. R. A. S.*, 1901, cxxxiii) have found another alkaloid, ibogine, in the same plant.

Ichthoform.—This is said to be obtained by the action of formaldehyde upon the products of sulphonization of ichthyol hydrocarbons, and to be superior to iodoform as an antiseptic. Externally it has been used by Unna, and in skin diseases is superior to the ordinary formaldehyde preparations. He asserts that it softens rather than hardens the skin. It has also been employed as an intestinal antiseptic in *doses* of fifteen to thirty grains (1–2 Gm.) three to four times a day.

Ichthyocolla. *U. S.* 1890. *Isinglass. Colla Piscium*, P. G. *Fish-glue. Ichthyocolle, Colle de Poisson*, Fr. *Hausenblase, Fischleim*, G. *Colla di Pesce*, It. *Colla de Pescado*, Sp.—Isinglass is a gelatinous substance prepared from the sounds or swimming bladders of many species of fish in various parts of the world. The best known variety is chiefly procured from the Volga and other streams of Southern Russia. It is prepared from several species of sturgeon including the *Acipenser Huso* L., or *beluga*, the *A. ruthenus* L., or *sterlet*, the *A. Sturio* L, or common *sturgeon*, and the *A. stellatus* Pallas or *starred sturgeon*. The air bags, having been split open, cleansed, and dried, are known in commerce by the name of *staple isinglass*, which is divided into the *long* and the *short staple*. Sometimes the membranes are dried in a flat state, or simply folded, and then receive the name of *leaf* or *book isinglass*. The scraps or fragments of these varieties, with various other parts of the fish, are boiled in water, which dissolves the gelatin, and upon evaporation leaves it in a solid state. This is called *cake isinglass*, from the shape which it is made to assume. It is sometimes, however, in globular masses. Of these varieties, the long staple and the finest book isinglass are the best. That in cakes is brownish, of an unpleasant odor, and employed only in the arts. Inferior kinds, with the same commercial titles, are said to be prepared from the peritoneum and intestines of the fish. An inferior Russian product, known in English commerce by the name of *Samovey isinglass*, is procured, according to Pereira, from the *Silurius glanis* L. It comes, like the better kind, in the shape of leaf, book, and the short staple. Isinglass, little inferior to the Russian, is made in Iceland from the sounds of the cod and ling. It is said also to be prepared by the fishermen of Newfoundland. We receive from Brazil the air-bladders of a large fish, prepared by drying them in their distended state. They are oblong, tapering, and pointed at one end, bifid with the remains of their pneumatic duct at the other, and of a firm consistence. The *Brazilian isinglass* is inferior to the Russian. Considerable quantities of isinglass are manufactured in New York and New England from the sounds of the *hake* (*Gadus merluccius*) and of the weak-fish (*Otolithus regalis*). This *American isinglass* is in thin ribbons 6 dm. in length, and from 2.5 to 6 cm. in width. It has a fishy taste and odor, which render it unfit for culinary or medicinal purposes. The sounds are dried whole, or merely split open, and vary much in size and texture, weighing from a drachm to an ounce. An article called *refined* or *transparent isinglass* is made by dissolving the New England isinglass in hot water, and spreading the solution to dry on oiled muslin. It is in very thin, transparent plates, and is an excellent glue, but retains a strong fishy odor. In India and China the swimming bladders of various species of fish furnish the so-called Indian and Chinese isinglass. At the present writing the various forms of isinglass are comparatively little used, their place being supplied by various brands of gelatin produced from fresh bones. (See *Gelatinum*, p. 509.)

In its purest form it is "in separate sheets, sometimes rolled, of a horny or pearly appearance; whitish or yellowish, semitransparent, iridescent, inodorous, insipid; almost entirely soluble in boiling water and in boiling diluted alcohol. A solution of isinglass in 24 parts of boiling water forms, on cooling, a transparent jelly." *U. S.* 1890. The inferior kinds are yellowish and more opaque. In cold water it softens, swells up, and becomes opalescent. Boiling water entirely dissolves it, with the exception of a minute proportion of impurities, amounting, according to Hatchet, to less than 2 per cent. The solution on cooling assumes the form of a jelly, which consists of pure gelatin and water. Isinglass is composed of *collagen* which on boiling hydrolizes to gelatin. It is insoluble in alcohol, but is dissolved readily by most of the diluted acids, and by alkaline solutions. It has a strong affinity for tannin, with which it forms an insoluble compound. Boiled with sulphuric acid, it is converted into a peculiar substance, called *glycocoll* or *sugar gelatin*, which is in reality *amidoacetic acid*, $CH_2.NH_2.COOH$. Its aqueous solution speedily putrefies. An ingenious adulteration has been practised by rolling a layer of gelatin between two layers of genuine isinglass. This may be detected by the disagreeable odor and taste of the adulterated drug, and the effects of water upon it. Genuine isinglass, cut into shreds and treated with water, becomes opalescent and more opaque than before; while the shreds, though they soften and swell, remain unbroken, and when examined by the microscope are seen to be decidedly fibrous. Gelatin, on the contrary, when similarly treated, becomes more transparent than before; the shreds are disintegrated, and the structure appears amorphous under the microscope. In the adulterated article both these characters are presented in layers more or less distinct. (*P. J.*, ix, 505.) Moreover, Redwood and Letheby observed that the ash of true isinglass does not exceed 0.9 per cent., while glue contains from 2 to 4 per cent. of ash. An adulterated isinglass would therefore yield more ash than the normal. A *false isinglass* has been imported into England from Para, in Brazil, consisting of the dried ovary of a large fish. It has somewhat the form of a bunch of grapes, consisting of ovoid or roundish masses attached by a footstalk to a central axis. It is not gelatinous, and is unfit for the purposes to which isinglass is applied. (*A. J. P.*, xxv, 144.) For table showing value of different kinds of European isinglass, see *P. J.*, 1884, p. 900.

Isinglass has been strongly recommended by Wm. T. Wenzell instead of hide powder in the estimation of tannin. (*A. J. P.*, 1894, 447.)

Isinglass plaster or *court plaster* (*Emplastrum Ichthyocollæ*, U. S., 1890), a very popular adhesive for closing small wounds, may be made as follows: "Isinglass, *ten grammes;* Alcohol, *forty grammes;* Glycerin, *one gramme;* Water, Tincture of Benzoin, each, *a sufficient quantity.* Dissolve the Isinglass in a sufficient quantity of hot Water to make the solution weigh *one hundred and twenty grammes.* Spread one-half of this, in successive layers, upon taffeta (stretched on a frame), by means of a brush, waiting after each application until the layer is dry. Mix the second half of the Isinglass solution with the Alcohol and Glycerin, and apply it in the same manner. Then reverse the taffeta, coat it on the back with Tincture of Benzoin, and allow it to become perfectly dry. Cut the plaster in pieces of suitable length, and preserve them in well-closed vessels. The above-directed quantities are sufficient to cover a piece of taffeta *thirty-eight centimeters* square." *U. S.*, 1890.

Ichthyol Substitutes.—There have been placed on the market a large number of compounds intended for the same uses as ammonium sulphichthyolate (See Part I). Among these may be mentioned in addition to those described below, *ichtammon, ichthium, ichtolithum, ichden, ichthyopon, isarol, petrosulpho, piscarol, pisciol, subitol, petrosulfol, sulfogenol, thilaven, thiolin, thiozin,* etc. Beckurts and Freerichs (*J. A. Ph. A.*, 1913, ii, p. 335) finds that there is great difference in the chemical composition of these various preparations.

Ammonium Ichthynatum, N. N. R. 1924.—This is an aqueous solution of sulphonated ammonium compounds resulting from the action of sulphur upon distillates from certain bituminous shales. It is a dark brown, syrupy liquid with a characteristic odor and a burning taste. It is completely soluble in water, partially soluble in alcohol and miscible with glycerin in all proportions. Its aqueous solution is slightly acid to litmus. It is incompatible with acids, carbonates and hydroxides, alkaloids and mercuric chloride. It is used internally in doses of 5 to 15 minims (0.3 to 1 cc.) and locally in varying strengths ranging from 3 to 40 per cent.

Hirathiol, N. N. R. 1924.—This synthetic compound is manufactured in Japan and is an aqueous solution containing sulphones, sulphonates and sulphides in combination with ammonium. It is a brownish-black, syrupy liquid with a characteristic empyreumatic odor, soluble in water, glycerin and alcohol and miscible with fats. The aqueous solution is faintly acid to litmus.

Isarol. Ichthyodin.—This is a proprietary form of ammonium sulphichthyolate of Swiss origin. It occurs as a brownish-red thick liquid, having an odor like that of ichthyol; containing about 9 per cent. or, when dried, 17 to 19 per cent. of sulphur of which 5 to 7 per cent. is in the "sulphidic" form. It makes a clear solution in water, and is also soluble in ten parts of 95 per cent. alcohol.

Saurol.—An oily substance obtained by the distillation of bituminous rock in Switzerland. It contains from 6 to 7 per cent. of sulphur in organic combination.

Thigenol.—This is prepared by dissolving sulphur in boiling glyceride of oleic acid and subsequent treatment with sodium hydroxide whereby is formed sodium sulpho oleate, and evaporating the solution *in vacuo* to a specific gravity of 1.05. Thigenol is a dark brown liquid freely soluble in water, dilute alcohol and glycerin. With hard water it throws down a precipitate.

Thigenol is asserted to possess the local therapeutic virtues of sulphur and is used chiefly in the treatment of *skin diseases* in the form of a 20 per cent. ointment. It is occasionally prescribed internally in *doses* of 3 to 10 grains (0.2 to 0.6 Gm.).

Thiol.—This is a thin, dark-brown, neutral liquid, with an odor somewhat like that of Russia leather, having a specific gravity of from 1.082 to 1.089; its aqueous solution is transparent, froths when shaken, and is not precipitated by strong alcohol; it is also feebly soluble in glycerin. On evaporation, liquid thiol yields about 40 per cent. of dried thiol. It is prepared from paraffin oils of from 0.89 to 0.90 sp. gr., which are treated with sulphur at high temperatures. The unsaturated hydrocarbons (olefins, etc.) are alone attacked, and these are then extracted by suitable solvents from the saturated hydrocarbons. They are then acted upon by concentrated sulphuric acid at low temperatures, and the thiol separated out by the addition of ice. It may then be evaporated *in vacuo* to either *thiolum liquidum* or *thiolum siccum.*

It is asserted that thiol possesses the remedial properties of ichthyol, to which it is superior on account of its being odorless. It has been used in the treatment of superficial and deep inflammations, as in *eczema* and *syphilitic ulcers* and in various joint conditions as *sprains, rheumatism* and the like. Kretzomer states that painted along the nerve in cases of *acute sciatica,* it produces immediate relief. (*All. M. C. Z.*, 1909.)

The liquid is used in the form of a solution or ointment; the dried thiol is sometimes employed as a powder. In *rheumatism* thiol has been given internally in *doses* of from five to ten minims (0.3–0.6 cc.), or the dried preparation in *doses* of from one to two grains (0.065–0.13 Gm.).

Tumenol.—A dark brown or brownish-black liquid, of a syrupy consistence, which is made from bituminous shale oils. These are agitated with sodium hydroxide solution to remove phenols and then with sulphuric acid to remove pyridine and other bases. The oil is then treated with fuming sulphuric acid. The dark syrupy liquid which separates is washed with water and dissolved in sodium hydroxide. From this solution ether extracts *tumenol oil.* Hydrochloric acid, on the other hand, if added to the sodium hydroxide solution, throws down *tumenol-sulphonic acid.* A mixture of these two substances constitutes *tumenol venale,* a soft, resinous, odorless mass. A. Neisser (*D. M. W.*, 1891) highly commends tumenol as a local application in *eczema* and as having extraordinary powers over the itching of *prurigo, parasitic dermatitis* and other *skin affections.* He uses a lotion made with equal parts of ether, rectified spirit and water or glycerin and 10 per cent. of tumenol.

Ichthyol Albuminate. *Ichthalbin.*—This is a greenish-brown powder, insoluble in water and acid solutions, soluble in alkaline solutions, odorless, almost tasteless. It is prepared by precipitating *egg albumin* with ichthyol and prolonged washing of the precipitate until the ichthyol odor and taste are removed. It is stated to contain about 75 per cent. of ichthyol. It is not toxic, and when given internally, even in large doses, produces little or no irritation of the gastro-intestinal tract. It is affirmed that as an internal remedy it is practically the same as ichthyol, and as such is useful in various conditions connected with wide-spread vascular dilatation, in *syphilis*, in *struma*, and in other states of lowered nutrition. It has also been used in the treatment of various inflammatory conditions of the intestinal tract, especially in chronic *colitis* and *enteritis*. *Dose*, from fifteen to thirty grains (1–2 Gm.) three times a day, best taken in capsules; or in the case of young children it should be mixed with chocolate.

Ilex. *Holly.* *Houx*, Fr. *Stechpalme, Christdorn*, G.—Several species of *Ilex* (Fam. *Aquifoliaceæ*) are employed in different parts of the world. *I. Aquifolium* L., or *European Holly*, is an evergreen tree growing to the height of 40 feet, but under cultivation is often shrubby. It has a pyramidal crown of short spreading branches which bear alternate, ovate or oblong-ovate, sinuate, spiny toothed, shining coriaceous leaves and globular, scarlet fruits. It is the most beautiful of all evergreens, but is unsuited to our climate, being too tender to withstand the winters in the northern States and equally affected by the hot, dry summers in the southern States. A viscid substance called *birdlime* is prepared from the inner bark (see *Viscum*). The leaves, which are of a bitter, somewhat acrid taste, were formerly much esteemed as a diaphoretic, and in the form of infusion were employed in *catarrh, pleurisy, small-pox, gout*, etc. At one time they enjoyed a brief reputation in France as a cure for *intermittents.* They were used in powder, in the *dose* of a drachm two hours before the paroxysm, and this dose was sometimes repeated frequently during the apyrexia. Labourdais obtained an amorphous bitter principle which he called *ilicin* from the leaves. (See *A. J. P.*, xxi, 89.) Moldenhauer in 1857 separated a yellow coloring substance called *ilixanthin*, and a peculiar acid called *ilicic acid. Ilicic alcohol*, $C_{30}H_{50}O$, was separated by Personne from birdlime and found to be identical with α-amyrin. (*C. R. S. B.*, 1908, 862.) Ilixanthin is $C_{17}H_{22}O_{11}$. It crystallizes in yellow needles, which change color at 185° C., melt at 198° C., and at 214° C. boil with decomposition, and are not sublimable. It is insoluble in ether, but soluble in alcohol. In cold water it is almost insoluble; but hot water dissolves it freely, and deposits it in crystals on cooling. The *berries* are about the size of a pea, red and bitter, and are said to be purgative, emetic, and diuretic. Ten or twelve of them will usually act on the bowels, and sometimes excite vomiting. Their expressed juice has been used in *jaundice.*

Ilex opaca Ait., or *American holly*, is a middling evergreen tree attaining a height of 50 feet, growing throughout the Atlantic section of the United States, and especially abundant in New Jersey. It resembles European holly in many details but has less glossy leaves and fruits. The berries, examined by D. P. Pancoast, were found to contain tannin, pectin, two crystallizable organic principles, and salts of potassium, calcium, and magnesium. One of the crystallizable principles was inodorous and tasteless, the other inodorous but intensely bitter. The latter is probably pure *ilicin.* (*A. J. P.*, xxviii, 314.) Walter A. Smith (*A. J. P.*, 1887, 1668) obtained a resin soluble in alcohol by the ether extraction, and in the portion of this soluble in water he obtained evidences of a glucoside. This species is said to possess the same medicinal properties as *I. aquifolium* L.

Ilex paraguayensis St. Hil. (*I. Maté* St. Hilaire) yields the celebrated *Paraguay tea*, or *Maté*, so extensively consumed as a beverage in the interior of South America. It is a small tree or shrub growing wild along streams in Paraguay, Brazil and other South American countries, and also cultivated for the sake of its leaves, which are the part used. They vary in outline from obovate, obovate-oblong to elliptic-oblong, possess an obtuse or obtusely acuminate apex, tapering base and crenate-serrate margin and are short-petioled. These are stripped from each plant every two or three years. The period of their collection extends from December to August, sometimes beginning earlier but never continuing later. Companies are formed who penetrate far into the forest at a distance from the settlements, and devote a long time to the collection and preparation of the leaves. These are first dried by exposure to heat, and are then reduced to powder more or less fine, which is kept for several months protected from moisture, and then packed in sacks and delivered to commerce. (See *Ph. Rec.*, 1891.) They have a balsamic odor and bitter taste, and are usually at first disagreeable to the palate. They have a pleasant and corroborant effect upon the stomach, but, when largely taken, cause purging and vomiting. They are used in the form of infusion, which is prepared from the entire leaves as we prepare tea; or, under the name of *cha maté*, a fine powder is put in a cup of hot water by the drinker, and after a moment's stirring, the fluid is sucked up by means of a tube expanded below, and pierced with fine holes, so as to strain out the powder. They contain, besides other substances, a peculiar tannin and the alkaloid caffeine in variable amount. Some fresh leaves of *Ilex paraguayensis* grown in the Cambridge Botanical Gardens were found by A. H. Allen, after drying, to contain 15.6 per cent. of tannin and 1.13 per cent. of caffeine. (*Com. Org. Anal.*, 2d ed., iii, Part II, 527.) The consumption of *maté*, or *yerba*, in South America is enormous. Although largely produced in the Argentine Republic, tons are annually shipped to countries in South America.

Ilex vomitoria Ait. (*I. Cassine* Walt.) is a handsome evergreen shrub or small tree growing in our Southern States, and especially abundant along the southern coast of Florida. It possesses oval, oblong or elliptic glossy leaves, deep green on upper surface and pale green beneath. These are obtuse at the apex and crenate-serrate along the margin. Those of the upper branches are 1 to 2.5 cm. long while those on the lower branches are frequently larger and oblong-lanceolate in outline. The flowers are small and white and occur in axillary clusters on branches of the previous year. The fruit is a red globose drupe which usually contains 4 nutlets. This species has often been confused with *Ilex Cassine* L. which differs from it in having larger leaves and acute calyx teeth. The calyx teeth of *I. vomitoria* are obtuse. Analysis of its leaves by Venable (*A. J. P.*, 1885, 390) gave 7.39 per cent. of tannic acid and 0.27 per cent. of caffeine. Smith (*A. J. P.*, xliv, 217) found 0.011 per cent. of volatile oil and 0.122 per cent. of caffeine. It is the *Cassena* or *Yaupon* of the North Carolina and Florida Indians, who formerly employed a decoction made from the toasted leaves, called *black drink*, both as a medicine and as a drink of etiquette at their councils. It acts as an emetic. The leaves of the *Ilex Dahoon* Walt. (*I. Cassine* L.) or *Dahoon holly*, have similar properties, and are also said to have entered into the composition of the black drink.

Illicium. *U. S.* 1890. *Star-Anise. Chinese Star Anise. Fructus Anisi Stellati. Semen Badiani. Sternanis*, G. *Badine*, Fr.—"The fruit of *Illicium verum* Hooker filius (Fam. *Magnoliaceæ*)" *U. S.*, 1890. Of the genus *Illicium*, seven species are recognized, of which two are found on the Atlantic coast of southern North America, two in Hindostan, and three in China and Japan. Many of the species are possessed of aromatic properties.

The plant yielding star-anise is indigenous to Southeastern Asia and extensively cultivated in subtropical countries. It is an evergreen tree with entire, elliptic to oblanceolate, glandular-punctate leaves and greenish-yellow axillary flowers each with about 10 petals. The fruit which is chiefly used in the manufacture of oil of anise consists of usually 8 boat-shaped follicles or carpels arranged around a central axis. The carpels have an acute summit and taper to a nearly straight beak; externally, they are reddish-brown and somewhat wrinkled; the inner surface is smooth and shiny and encloses a single, smooth, compressed ovoid, brown seed. The odor and taste is aromatic, resembling anise, and this serves to distinguish them from the fruits of the Japanese star-anise which are also known as "*Shikimmi fruits*" or "*Skimmi fruits.*" The latter have an odor resembling Cajuput or Sassafras and are obtained from *Illicium religiosum* Sieb. et Zucc., a tree which is extensively cultivated in the groves of the Buddhist Temples in Japan.

I. religiosum Sieb. *et Zucc.* of India, is very poisonous, causing vomiting and epileptiform convulsions, with dilated pupil and exceedingly cyanosed countenance (see Guerrero, *Philippine J. of Sci.*, 1916, xi, 203); in it has been found by J. F. Eykman (*P. J.*, xi, 1046) a crystalline principle, for which the name of *shikimine* or *sikimin* has been proposed. Its seeds are sometimes sold for those of star-anise with baneful results.

Eykman (*P. J.*, 1885, p. 985) has shown that in the essential oil of the fruit of *Illicium religiosum*, safrol is found, accompanied by eugenol. On the other hand, the chief constituent of the oil of *I. verum* is anethol. See table by Eykman showing constituents of oil of *Illicium religiosum* compared with those from allied oils in *U. S. D.*, 19th ed., p. 1526.

The fruits of star-anise are gathered from wild and cultivated plants. Most of the drug is used for the production of volatile oil. The commercial supplies come chiefly from China.

Star-anise was examined by C. E. Schlegel (*A. J. P.*, 1885, p. 426), who found a saponin in the aqueous extract; in the alcoholic extract, a crystalline principle of a strong musk-like odor, which did not show alkaloid or glucosidal reactions, and *oil of star-anise.*

I. floridanum Ell., *poison bay, sweet laurel*, a small evergreen tree or shrub with oblong-lanceolate, acuminate leaves, which grows westward from Florida along the coast bounding the Gulf of Mexico, has its bark, leaves, and probably also seed vessels endowed with a spicy odor and taste, analogous to those of anise. Another species, *I. parviflorum* Vent. (*I. anisatum* Bartr., not L.) a shrub found by Michaux in the hilly regions of Georgia and Carolina, has a flavor closely resembling that of sassafras root. A decoction of the seeds is said to produce violent gastro-intestinal irritation, followed by motor and sensory paralysis, with convulsions and death if the dose has been sufficient. E. Barral (*Revue Gén. de Clin.*, Oct., 1889) states that he has obtained a poisonous glucoside from the kernel. H. C. C. Maisch (*A. J. P.*, 1885, 280) obtained from the leaves a crystalline alkaloid to which the bitter taste is due, tannin, and a resin. In the root bark and capsules he found volatile oil and a crystalline principle, melting at 100° C., insoluble in alcohol and ether, but soluble in chloroform, and neutral to test paper.

The constituents of low boiling-point in star-anise oil, consisting of terpenes essentially, have been reported upon by the chemists of Schimmel & Co. (*Schim. Rep.*, April, 1893.) They find dextro-pinene, boiling at 157° to 163° C., and lævophellandrene, boiling at from 170° to 175° C.

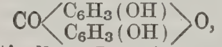
The medicinal properties of the oil of star-anise are similar to those of oil of anise. Sikimin is not used in medicine. It is violently poisonous, belonging to the group of convulsants of which picrotoxin is the type. (See Plugge and Schutte, *A. I. P. T.*, iv, 1897.)

Impatiens. *Impatiens biflora* Walt. and *I. pallida* Nutt. *Touch-me-not. Jewel-weed. Balsam-weed.*—These two species of *Impatiens* (Fam. *Balsaminaceæ*), the former of which is better known commonly as *Spotted Touch-me-not* and the latter as *Pale Touch-me-not*, are indigenous, annual, succulent plants growing in low, moist, shaded grounds, and flowering from July to September. They may be known by their tender, juicy, almost transparent stems; by their yellowish flowers, which in *I. pallida* are pale and sparingly punctate, and in *I. biflora* are orange-colored and spotted with reddish-brown and by their capsules, which burst elastically, and curl up with the slightest pressure. They probably possess properties similar to those of *I. nolitangere* L., of Europe and Asia, which has an acrid burning taste, and, when taken internally, acts as an emetic, cathartic, and diuretic, though considered dangerous, and therefore little used. Ruan of Philadelphia, employed with great advantage, in piles, an ointment made by boiling the American plants, in their recent state, in lard. The flowers may be used for dyeing yellow. The fresh juice is reputed to be efficacious in the treatment of rhus poisoning. The *I. Balsamina* L., or *balsam-weed, touch-me-not*, etc., of the gardens resembles the other species in its effects.

Imperatoria. *Imperatoria Ostruthium* (L.) Kch. *Masterwort. Rhizoma Imperatoriæ*, P. G. *Impératoire*, Fr. *Meisterwurz, Kaiserwurz*, G.—An umbelliferous plant, indigenous in Southern Europe. The root has a strong odor, similar to that of angelica, and a pungent, aromatic taste, attended by a flow of saliva, and followed by a growing warmth which remains long in the mouth. A crystallizable, tasteless principle, called *imperatorin*, was extracted from the root by Wackenroder, and Gorup-Besanez found in the root another principle, to which he gave the name of *ostruthin*. Besides these two crystalline compounds, masterwort contains a volatile oil, composed of a hydrocarbon and an oxygenated compound, probably the aldehyde of angelic acid. (Wagner, *J. P. C.*, lxii, 283.) Jassoy (*Ap. Ztg.*, v, 150) has since investigated the substance ostruthin and gives it the formula $C_{18}H_{20}O_3$. He states that it does not contain a methoxyl group but a phenol-like hydroxyl. By the action of bromine in chloroform solution it is changed in the presence of acid sodium carbonate into *tribromostruthin*, $C_{18}H_{19}Br_3O_3$. (Schmidt, *Pharm. Chem.*, Bd. ii, 3te Auf., 1510.) Herzog subsequently examined the rhizomes and found a substance identical with oxy-peucedanin. (*A. Pharm.*, 1908, 414.) The root of masterwort was formerly used in a wide circle of complaints with so much supposed success as to have gained for it the title of *divinum remedium.* It is, however, merely a stimulant aromatic, which in this country is unknown as a remedy. Its leaves are used as a potherb and to flavor cheese.

Incassa Poison.—This is an African ordeal bark, which has been studied by Liebreich, who found in it a very violent cardiac poison.

Indian Red.—A purplish-red pigment, brought from the island of Ormus in the Persian Gulf. It is *red ochre,* and owes its color to *ferric oxide.*

Indian Yellow.—This is a pigment manufactured from a yellow substance from India, called *purree.* Purree occurs in commerce in balls, from three to four ounces in weight, which are dark brown externally and deep orange within. It has a peculiar odor, closely resembling that of castor. This circumstance gave rise to the belief that it was of animal origin, but Stenhouse found it to consist of magnesia, united with a peculiar acid, which he names purreic (*euxanthic acid* of Erdmann), and which forms nearly one-half of the crude substance. *Purreic acid* is in small crystals of a light yellow color, dissolving sparingly in cold water, quite readily in boiling water, and abundantly in hot alcohol and ether. It has at first a sweetish and then a slightly bitter taste, and possesses, in appearance, considerable resemblance to berberine. When acted upon by boiling nitric acid, it is finally converted into trinitroresorcinol, $C_6H(NO_2)_3(OH)_2$. Heated with diluted sulphuric acid (3 per cent.) to 140° C., it decomposes into *euxanthon* and *glycuronic anhydride.* The euxanthon is recognized as *dioxydiphenyleneketone oxide,*  $CO\langle{}^{C_6H_3(OH)}_{C_6H_3(OH)}\rangle O$, and has been made synthetically. Purreic or euxanthic acid is monobasic, and has the formula $C_{19}H_{16}O_{10} + 3H_2O$. Stenhouse concludes that purree is probably the juice of some plant, saturated with magnesia, and boiled down to a solid consistence.

The term "Indian yellow" is sometimes applied to the *cobalt and potassium nitrite* and to an aniline derivative, *Azoflavin-Z,* which is a mixture of nitrated diphenylamine orange and nitrodiphenylamine. These should not be confused with the foregoing drug.

Indigo. *Indicum. Pigmentum Indicum. Indigo,* Fr., G.—This well-known and highly important dye-stuff is obtained from various species of *Indigofera* (Fam. *Leguminosæ*), especially *I. tinctoria* L. and *I. Anil* L., and is accorded also by other plants, such as *Wrightia tinctoria* R. Br. (Fam. *Apocynaceæ*), *Polygonum tinctorium* Ait. (Fam. *Polygonaceæ*), *Tephrosia tinctoria* Pers., *Galega tinctoria* L., and *Tephrosia Apollinea* Link. (Fam. *Leguminosæ*), etc. For an interesting account of the manufacture in Manchuria of indigo from *Polygonum chinense,* see *Am. Drug.*, Aug., 1888. It does not exist ready formed, but is generated, during fermentation, from another principle existing in the plant. This principle appears to have been isolated from *Isatis tinctoria* L. (Fam. *Cruciferæ*), by Ed. Schunck, who has named it *indican.* Through the agency of the mineral acids, it is resolved into indigo and sugar, and perhaps the same result may take place in fermentation. Indican is yellow, amorphous, of a nauseous bitter taste, with an acid reaction, and readily soluble in water, alcohol, and ether. In the process of preparing indigo, the plant is macerated in water; fermentation takes place; the liquor becomes of a greenish color, and in due time is decanted; the coloring principle dissolved by the water absorbs oxygen from the air, and assumes a blue color, becoming at the same time insoluble; a gradual precipitation takes place, favored by the addition of lime water or an alkaline solution, and finally the precipitated matter, having been washed upon linen filters, is dried, shaped usually into cubical masses, and sent into market. It is of an intensely blue color, but assumes a coppery or bronze hue when rubbed by a smooth hard body, as the finger nail. Heated to 287.7° C., it emits a reddish-violet vapor, which condenses in minute crystals. It is insoluble in water or alcohol, but is readily dissolved by concentrated or fuming sulphuric acid, because of the formation of *monosulphindigotic* and *disulphindigotic acids,* of which the first is difficultly soluble in water and the second easily soluble. The sodium salt of this latter is the *indigo-carmine* of commerce (see below). Indigo is soluble in chloroform, aniline, oil of turpentine, paraffin, phenol, and benzene. By deoxidizing agents such as the acid sulphites, and in a less degree with sulphurous acid, it is deprived of its blue color, which it recovers by exposure to the air, in consequence of the absorption of oxygen. Certain volatile oils have a reducing effect when boiled with tincture of indigo, as the oils of turpentine, peppermint, lavender, etc. The reduction and decolorization of indigo solutions by glucose is the basis of one of the most delicate qualitative tests for diabetic sugar in urine. Chlorine also destroys the blue color. For modes of testing the value of a specimen of indigo, see Sadtler's *Industrial Organic Chemistry,* 443. The most important of the methods for the determination of the indigo blue may be summarized under three heads,—viz., oxidation methods, reduction methods, and sublimation of the pure indigo blue from the commercial product. A table of analyses of commercial samples with results according to the several methods above referred to will be found in Allen, *Com. Org. Anal.*, 2d edition, iii, 311.

The artificial production of indigo was successfully solved by A. von Baeyer of Munich, who proposed several methods capable of commercial utilization. One method starts with cinnamic acid, $C_9H_8O_2$, made artificially from benzaldehyde, which is changed into *ortho-nitro-cinnamic acid,* $C_9H_7NO_4$, and this by the intervention of the di-bromine derivative into *ortho-nitro-phenylpropiolic acid,* $C_9H_5NO_4$, and this by the action of alkalies in the presence of reducing agents, like grape sugar or xanthogenates, is converted directly into *indigo blue* $(C_8H_5NO)_2$.

A second method was by the action of dilute alkalies upon a solution of *o-nitro-benzaldehyde* in acetone according to the reaction:

$$2C_6H_4(NO_2)CHO + 2C_3H_6O = C_{16}H_{10}O_2N_2 + 2C_2H_4O_2 + 2H_2O$$

A method of Heumann, also successfully carried out on a large scale, is to treat *phenylglycin,* $C_6H_5.NH.CH_2.COOH$, with alkalies, and then oxidize the resulting alkaline solution, when *indigotine,* $C_{16}H_{10}N_2O_2$, is formed. These methods were found to be to expensive, but it has finally been made commercially, and on a scale which is fast displacing natural indigo, by the following method. *Anthranilic acid,* $C_6H_4(NH_2)COOH$, (which can be prepared cheaply from naphthalene), combines with monochloracetic acid to form *phenyl-glycocollcarboxylic acid,* $C_6H_4\begin{matrix}\diagdown NH.CH_2COOH\\ \diagdown COOH\end{matrix}$, and this on fusion with caustic soda yields *indoxyl,* $C_6H_4\begin{matrix}\diagup NH \diagdown\\ \diagdown C(OH) \diagup\end{matrix} CH$, which, in alkaline solution, is converted by atmospheric oxidation into indigo.

The synthetically prepared indigotine caused the almost complete extinction of indigo culture of India. At one time the importations from India to the United States averaged about 2,000,000 lbs. a year; in 1902, less than 250,000 lbs. entered during the first six months and after June ceased entirely. During the Great War, however, the interference with the chemical industry caused a return to natural sources. In 1917 there was four times the total acreage in India devoted to the culture of the indigo plant that there was in 1914. (*C. D.*, 1917, lxxxix, 460.)

Schunck first showed that all urines, whether pathological or not, contain an indigo-producing body in minute quantities. This body is commonly spoken of as *indican* in medical books. Its true chemical nature was first ascertained by Baumann, who showed that it was not a glucoside, like the indican of plants, but the potassium salt of a peculiar acid, *indoxylsulphonic acid.*

Indigo carmine, $C_{16}H_8N_2O_2(SO_3Na)_2$, has been used as a test of the functional power of the kidneys, especially in surgical affections of these organs. The method consists essentially of the injection of 4 cc. of the 4 per cent. solution intravenously, the urine being collected separately from each kidney from 20 to 30 minutes after the injection. Healthy kidneys should excrete the drug within eight or twelve minutes, while if the kidneys are seriously affected the functional incapacity is shown by either the absence or the paleness of the urine.

Indigo was at one time considerably used in medicine, but at present is very rarely if ever employed. It is said to produce, when taken in sufficient quantity, nausea, vomiting, purging with bluish, dark stools, a dark violet or dark green color of the urine, and sometimes to cause menstrual flux. It was formerly used in *epilepsy, infantile convulsions, chorea, hysteria,* and *amenorrhea. Dose,* from twenty grains to an ounce (1.3–31 Gm.) three times a day. For further details, see 16th ed., *U. S. D.*

Indium. In.=114.8.—A rare metal named from the indigo blue line given by the spectrum of the metal. It is a shining white ductile metal, softer than lead. Some of its salts have been prepared and are asserted to be of value as external antiseptics. They are the sulphate, $In_2(SO_4)_3+nH_2O$, and the trichloride, $InCl_3$, a yellow hygroscopic powder. Both of these salts are active poisons.

Insect Powder. *Pyrethri Flores. Camomille de Perse,* Fr. *Persische Bertramblumen,* G.—The insecticide and Fungicide Board of the United States Department of Agriculture recognizes as insect powder an insecticide made from the powdered flower heads of *Chrysanthemum cinerariæfolium* (Trev.) Bocc., *C. roseum* Web. et Mohr and *C. Marschallii* Aschers, unexpanded or partly expanded flower-heads of several species of *Chrysanthemum* (Fam. *Compositæ*). There are two principal commercial varieties: (1) the Dalmatian insect powder which is obtained from *Chrysanthemun cinerariæfolium* (Trev.) Bocc., a perennial herb indigenous to Dalmatia and cultivated in the United States; (2) the Persian insect powder, obtained from *C. roseum* Web. et Mohr and *C. Marschallii* Aschers, perennial herbs indigenous to the Caucasus, Armenia and northern Persia and cultivated in Japan. The flower-heads are collected from plants that are from two to six years old, carefully dried and preserved. The most powerful insect powder is obtained from the closed or only partly expanded flower-heads providing they are properly dried and preserved. Insect powder containing more than 5 per cent. of naturally adherent flower-stems and 2 per cent. of acid-insoluble ash is held to be adulterated. No foreign matter is permissible under the ruling of the U. S. insecticide Bureau.

Dalmatian Flowers.—The heads are hemispherical, about 12 mm. in diameter, and consist of a conical torus subtended by a straw-colored campanulate and imbricate involucre, the bracts of which are slightly thickened or keeled; the torus bearing numerous yellow tubular flowers and a circle of cream- or pale straw-colored ray flowers. The latter are pistillate, the corolla being from 1 to 2 cm. in length, having about 15 delicately veined and 3 short, obtuse or rounded teeth. The achenes are 5-ribbed.

Persian Flowers.—The heads are flattened top-shaped; the involucral scales are greenish-brown and bordered by a reddish-brown edge; the ray florets are reddish-brown or reddish-purple, attaining a length of 15 mm., being somewhat plicate and having 7 veins. The disc florets are tubular, yellow, and 5-toothed. The achenes are usually 10-ribbed.

For details as to the special anatomical character of these flowers see *Bull. 824, U. S. Dept. Agri.*, 1920.

C. cinerariæfolium is now being cultivated on a large scale in California, and as more care is given to the preservation during drying of the color and of the volatile oil than in Dalmatia, the California product, which is known by the name of *buhach* is said to be superior to the foreign drug. (*C. D.*, August, 1889; see also for method of cultivation, *Reports of the Fourth U. S. Entomological Commission*, 1885, and papers by Seidler, *Riedel's Berichte*, 1913, and Jüttner, *Ph. Ztg.*, 1912, 817. At present *insect flowers* are cultivated commercially in Dalmatia, Australia, Japan, Montenegro, Algeria and California. Dalmatia, Montenegro, and Japan produce nearly all the flowers entering international commerce.

The insect powder of commerce varies in color from greenish-yellow to brown, the finer qualities verging towards brown and the poorer towards green. Brilliant yellow powder should be viewed with suspicion. On microscopical examination of an insect powder, it will be found to consist of fragments of involucral scales composed of sclerenchyma, perhaps bits of stems composed of collenchymatous cells, pollen grains, fragments of the corolla and of its epidermis and papillæ. The absence or scarcity of pollen in the powder shows the absence or scarcity of the flowers in the drug, while the proportion of collenchymatous tissue indicates the proportion of stems. As the activity of the insect powder resides in the flower, specimens containing little of the flowers or much of the stems should be rejected. The powder yielded by the Dalmatian plant can usually be distinguished from Persian insect powder by the following characters. The presence of somewhat rectangular patches of sclerenchyma tissue from the achene or ovary containing many diamond-shaped crystals. The outer surface and edges of the scales of the Dalmatian flowers contain numerous hairs, consisting of a long cell with attenuated ends placed horizontally upon a one- to three-celled stalk. The Persian flowers are almost entirely glabrous, a white hoariness being found only at and near the base of the scales, and very few hairs near the apex; the hairs are of the same structure as the preceding, only the terminal cell being much longer. Fragments of bracts with reddish-brown scarious margins are more striking in the Persian than in the Dalmatian powder. Sclerenchymatous cells are much more numerous in the Persian than in the Dalmatian.

The ground flower heads of *Chrysanthemum Leucanthemum* L. (Fam. *Compositæ*), a common weed in the United States and Europe (*daisy, ox-eye daisy, Hungarian* or *Russian daisy,* or *Marguerite*), have been employed for years as an adulterant of Dalmatian and Persian insect powder. The presence of this adulterant can be positively detected microscopically by the irregular dark red to reddish-brown, often angular, amorphous masses, from the resin canals of the daisy ovary or achene, as well as by the narrow, thick-walled palisade cells of the ribs of the achene. No such structures are present in insect flowers. According to George R. Durrant, the Hungarian daisy powder yields 10 per cent. of ash, whereas true insect powder yields but 6.5 per cent. F. Dietze, after careful study, found that the best chemical method of valuation of insect powder is based on the amount, appearance and odor of the extract obtainable by the use of petroleum spirits boiling under 55° C. With such menstruum true insect powder affords a bright yellow percolate possessing the odor peculiar to the drug. (See *P. J.*, 1905, 902; also 1906, 891; *Ph. Ztg.*, 1905, 871.)

The toxicity may be determined experimentally by injecting a weak alkali solution of the ether extract into the lymph sac of frogs; quantitative results may be obtained.

E. H. Gane, 1910, reports that insect powder is adulterated with ground stems and not ground from flowers only, as it should be. One sample from one of the largest pharmaceutical manufacturing houses was composed wholly of ground stems.

Insect powder does not appear to be actively poisonous to man, though it is said to cause some confusion of mind in those who sleep in close apartments where much of it is used and workers in factories where the powder is ground suffer with dermatitis. Upon the insects, however, which are apt to infest the person of man and animals, as well as bedding and sleeping apartments, it acts very destructively, first stupefying and then killing them. It is scattered over the person, upon the beds, about apartments, etc., and is even employed as a dressing for ulcers and wounds to prevent the formation of maggots. It also answers for preserving dried insects and plants in cabinet collections. The powder, exhausted by alcohol, is harmless to insects. The active principle is not definitely known. Fujitani (*A. E. P. P.*, 1909, lxi, 47) believed it to be a neutral ester which he called *pyrethron;* this is a non-volatile substance of syrupy consistence. Gamamoto states that it is a mixture of esters. Reeb (*J. Pharm. Elsass-Lothringen*, 1909, xxxv, 267) attributed the activity to an acid which he called *pyrethrotoxic acid.* The presence of both of these substances has been confirmed by McDonnell (*Bulletin 824, U. S. Dept. of Agriculture,* 1920). In addition to these principles there is present *pyrethrum camphor* ($C_{10}H_{16}O$), an acrid resin, a volatile oil, an alkaloid (*chrysanthemine*), etc. The experiments of Zeigler (*J. A. Ph. A.*, 1923, xii, 19) seem to demonstrate that the active principle is of a resinous character and but very feebly toxic to mammals. The ash content varies from 5 per cent. to 8.3 per cent.

In a series of experiments, Riley has found that the fumes of the burning powder are very poisonous to insects, and for certain purposes afford a ready mode of application, but that generally an aqueous infusion is the best and cheapest preparation. It is also used now in the form of cones made by making a mass with mucilage of gum arabic, with the addition of a small quantity of potassium nitrate. After drying these are ignited like a fumigating pastile. Twenty-five grains stirred up in two quarts of water were sufficient to kill young cotton worms. The infusion soon spoils. The tincture and the alcoholic extract are both efficient preparations. The tincture (one part to four) has been especially recommended, diluted with ten times its bulk of water, by F. Jager, to keep off vermin from the human body. The commercial preparations known as "fly-sprays," to be used in the destruction of flies and other insects by the use of an atomizer, are made by extracting pyrethrum flowers with kerosene and adding volatile oils for masking the odor of the solvent.

Insindiyandiya.—This substance, a remedy of the Kaffir doctors of South Africa, is a violent poison, and has been shown by E. M. Holmes to be derived from a *Bersama,* apparently *B. abyssinica* Fresen. (*P. J.*, lxxiii, 893.)

Insipin. *Quinine Di-glycol Sulphate.* $O(CH_2.CO[C_{20}H_{23}O_2N_2])_2.H_2SO_4.3H_2O$.—This compound is very sparingly soluble in either water or alcohol, and is asserted to be practically tasteless. It was brought forward as a substitute for quinine. Werner (*D. M. W.*, 1911) has employed it in *malaria* in *doses* of from three to six grains (0.2–0.4 Gm.) given every three or four hours.

Intarvin.—Intarvin occurs in white greasy lumps having an odor resembling that of tallow. It consists approximately of 82 per cent. of *glyceryl margarate,* 12 per cent. of liquid petrolatum and 6 per cent. of water. It is intended as a food stuff for diabetics. The excessive amount of fatty foods which are necessary to maintain nutrition in cases of *diabetes* sometimes leads to the formation of large amounts of oxybutyric and diacetic acids, which are generally regarded as the immediate cause of the dreaded diabetic coma. On the theory that a fat containing an uneven number of carbon atoms could not split up into butyric acid, Kahn prepared this fat. Its present price, however, is so high as to practically preclude its use as a food except by millionaires. Its food value is said to be 6 calories per Gm.

Iodalbacid. *Albumen Iodate.*—An iodine-albumen compound which contains 10 per cent. of iodine in intramolecular combination. It is a cream-colored powder, inodorous, tasteless, and soluble in water. Iodalbacid is used in all cases where iodine is indicated, especially in *syphilis,* possessing the advantage of being less irritant to the stomach. It is especially recommended where protracted iodine action is desired. *Dose*, fifteen grains (1.0 Gm.) three to six times a day.

Iodalbin. *N. N. R.* 1924.—This is another iodine albumen product being soluble only in alkaline solutions. It is a reddish powder made by acting upon blood albumen with iodine and containing 21.5 per cent. iodine. It is used in preference to the alkali iodides due to its tastelessness, its freedom from harmful action on the stomach and to its ready assimilability. *Dose*, eight to fifteen grains (0.5–1.0 Gm.) several times daily.

Iodic Acid and its Salts. *Acidum Iodicum.* HIO_3.—*Iodic acid* occurs as a white, crystalline powder, soluble in its own weight of water. In concentrated solution it is caustic, and in solutions of 0.1 to 0.5 per cent. it is astringent and disinfectant. It has been employed as an astringent gargle and application to inflamed mucous membranes. Iodine acid is astringent and disinfectant and, like the other mineral acids, in concentrated solution caustic. In 1 to 3 per cent. solution it has been employed as a local application in *trachoma* and indolent *corneal ulcers*. Pencils made by adding iodic acid to powdered acacia have been used by Rudas in the treatment of *trachoma*.

The salts of iodic acid are physiologically more nearly related to the chlorates than to the iodides. They are more toxic than the chlorates, giving rise to a slow intoxication accompanied with inflammatory changes in the bowels and fatty degeneration of the liver.

The Br. formerly included a solution of *potassium iodate* among its test solutions. It was made by the mutual decomposition between iodine and potassium chlorate in the presence of nitric acid (see *U. S. D.*, 20th ed., p. 1561).

The iodates have been used chiefly as local remedies in the same manner as the chlorates.

The salts of iodic acid are actively disinfectant. According to Griffiths a 0.5 per cent. solution of potassium iodate is capable of destroying many forms of bacteria. Both potassium and *sodium iodate*, a white, odorless, crystalline substance, very soluble in water, have been used locally in inflammatory conditions of the mucous membranes for much the same purposes as sodium chlorate. As a local remedy it may be useful in tubercular and other inflammations of the nose and larynx, either pure or diluted. Ruhemann (*B. K. W.*, 1905) has employed sodium iodate in epidemic *cerebrospinal meningitis*. He administered four grains (0.25 Gm.) in water twice a day. Mackie (*L. L.*, 1905) recommends *zinc iodate* and *calcium iodate* as local applications in various suppurating *wounds*, *eczema*, *cystitis*, and similar conditions.

Iodine Trichloride. ICl_3.—This compound occurs in reddish-yellow crystals; very soluble in water and alcohol; rapidly decomposed with liberation of iodine and chlorine when brought in contact with organic matter. It has been especially recommended by Belfield (*B. M. J.*, Aug., 1892) as a powerful local antiseptic. A solution is prepared for medicinal use by suspending 5.5 Gm. of iodine in 22 Gm. of water, and passing in chlorine as long as it is absorbed by the well-cooled mixture; the resultant solution contains 10 Gm. of *iodine trichloride*. The strength of the solution used is 1 to 5 per cent. Gauze sterilized by boiling and immersing in 1 to 10 per cent. solution and dried is said to retain iodine trichloride indefinitely. Iodine trichloride is a very powerful germicide, at least four or five times as active as phenol. According to Rideal five parts in a hundred thousand will kill the bacillus typhosus after half an hour's exposure. The five per cent. solution is fairly permanent if protected from the light, but dilute solutions rapidly deteriorate. It has been used locally in infectious conditions of the various mucous membranes in strengths of from 1 in 1000 to 1 in 2000. For disinfecting the hands a one per cent. solution is recommended. It has also been used internally as a gastro-intestinal disinfectant in *doses* of one and one-half grains (0.096 Gm.) a day. Fourneau and Donard have suggested the use of *iodine monochloride* which they claim forms more stable solutions than the trichloride. A solution containing 1.5 parts per thousand is asserted not only to be an excellent antiseptic but completely devoid of caustic action.

Iodipin. *Iodized sesame oil. N. N. R.* 1924.—This is an iodine addition product of sesame oil containing between 9.8 and 11.2 per cent. of iodine. It is a yellowish oily liquid with a purely oleaginous taste.

Iodipin is used as a substitute for the alkaline iodides in the treatment of *asthma*, *arterial sclerosis*, etc. It is allied in its therapeutic effects to calioben (see *Calcii Iodobehenas*) and like this compound has the advantage of being less irritating to the stomach and more persistent in its action than the inorganic forms of iodine. For summary of the literature on this compound see McLean, *A. In. M.*, 1912, x, p. 505 and Jan., 1915.

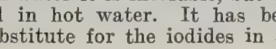
The *dose* of iodipin is from 1 to 2 drachms (4 to 8 Gm.) three times a day. It should be protected from light. A stronger form of iodipin intended for veterinary use was formerly manufactured.

Under the name of *iodipinum solidum*, tablets of an emulsified iodipin have been put upon the market. Each of these corresponds to five-sixths of a grain (0.05 Gm.) of iodine. Three or four tablets may be given at a *dose*, and repeated several times a day.

Iodized Starch. *Amylum Iodatum. U. S.* 1880. *Iodide of Starch; Iodure d'Amidon*, Fr. *Jodstärke*, G.—"Starch, *ninety-five parts;* Iodine, *five parts;* Distilled Water, *a sufficient quantity*, to make *one hundred parts.* Triturate the Iodine with a little Distilled Water; add the Starch gradually, and continue triturating until the compound assumes a uniform blue color, approaching black. Dry it at a temperature not exceeding 40° C., and rub it to a fine powder. Iodide of Starch should be preserved in glass-stoppered vials." *U. S.*, 1880.

This preparation has been highly recommended as a means of obtaining the effect of iodine on the system free from local irritant properties. Dalton, of New York, found that nearly all the animal fluids decompose starch iodide and destroy its blue color. (*Am. J. M. S.*, April, 1856, p. 327.) This result is owing, no doubt, to the alkaline nature of most of the animal fluids, especially those of the duodenum, alkaline iodides being formed at the expense of the starch.

Lumière (*C. R. A. S.*, 1917, clxv, 376) has successfully employed an iodized starch, containing 1 per cent. of iodine as a *wound* disinfectant. The internal dose of the formerly official iodized starch is from 1 to 2 drachms (4–8 Gm.).

Iodival. *Iodisovaleryl Urea. Mono-iodo-isovaleryl Urea.*  $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!HC\text{–}CHI\text{–}CO\text{–}HN\text{–}NH_2$.—This is a white powder representing 47 per cent. of iodine. In cold water it is insoluble, but dissolves in alcohol and in hot water. It has been suggested as a substitute for the iodides in *syphilis*, *asthma, scrofula* and other conditions in which the iodides are employed. According to the investigations of Menne (*In. Dis.*, Bonn, 1909), it passes through the stomach unchanged but is dissolved and absorbed in the intestinal tract. Iodine appears in the urine in about an hour after its ingestion and the elimination is complete within two or three days. It is marketed in the form of tablets each containing five grains (0.32 Gm.). Of these tablets one may be taken from two to six times in the twenty-four hours.

Iodocasein. *Casein-iodine. N. N. R.* 1924.—A compound of iodine and casein obtained by precipitation of sodium casein solution by means of a potassium iodide and iodine solution. It is a yellowish-brown powder practically odorless and tasteless, insoluble in water and representing approximately 18 per cent. of iodine. It is used as a substitute for the inorganic iodides over which the advantage is claimed of being less prone to disturb digestion. *Dose*, five to twenty grains (0.32–1.3 Gm.). Another combination of casein and iodine is known as *Lactoiod* or *Proiodine*. This is asserted to contain 8 per cent. of iodine, but according to Stanieck (*Ther. Geg.*, 1909, p. 134) it contains only 5 per cent. He used it in *doses* of about one drachm (4 Gm.).

Iodoformin. *Iodoformolin. Iodoform Hexamethylentetramine.* $CHI_3(CH_2)_6N_4$.—Iodoformin is obtained through the action of an alcoholic iodoform solution on *methenamine*. It is a white crystalline powder of faint iodoform odor, fusing at 178° C. and insoluble in water. In boiling water or in wound secretions it is split up into its component parts yielding 75 per cent. iodoform. This compound not only is free from odor but appears to have direct antibacterial properties far in excess of that of iodoform. It is asserted to have especial toxicity for the gonococcus. It is used in medicine as a dusting powder to *wounds* and also as a local application in *urethritis*. For the latter purpose bougies containing 10 to 20 per cent. of iodoformin have been recommended.

The *iodoformin-ethyl-iodide*, $C_6H_{12}NC_2H_6ICHI_3$, known as *iodoformal*, is stated to be still more actively antiseptic. This is obtained through the action of iodoformin on ethyl iodide. It forms yellow needle-like crystals or a heavy powder. It dissolves in boiling water and fuses at 128° C. It is used for the same purposes as iodoformin.

Iodoformogen. *Iodoformalbumen.*—According to K. Gaab (*Ph. Centralh.*, 1898, xi, 189), *iodoformogen* is a chemical combination of iodoform and albumin. It occurs as a fine, loose, dry, nonconglutinating powder, having a faint aciduloethereal odor, and being two and one-half times as voluminous as powdered iodoform. According to Kromayer (*B. K. W.*, xxxv, 1898) and to Aspegren (*Festschrift des Prof. Kaposi*, Vienna, 1901), iodoformogen is more slow and continuous and certain in its local action than is iodoform. It bears sterilization at 100° C. without change.

Iodol. *Iodolum. U. S. VIII.* $C_4I_4.NH$. *Tetraiodopyrrol. Iodopyrrol. Pyrrol Tetraiodide. Jodol, Tetrajodpyrrol,* G. *Jodolo,* It. *Yodol,* Sp.—*Iodol* was discovered by Silber and Ciamician, and is made from the pyrrol obtained in Dippel's oil (bone oil), which, after purifying, is treated with a solution of iodine in potassium iodide, when the tetraiodide (iodol) precipitates. It is purified by redissolving in hot alcohol, and again precipitated by the addition of water. It contains nearly 89 per cent. of iodine. It should be protected from the light.

Iodol was official in the United States Pharmacopœia VIII. It was officially described as "a odor or taste. It is soluble in about 4900 parts light grayish-brown, crystalline powder, without of water, 9 parts of alcohol, 1.5 parts of ether, and 105 parts of chloroform at 25° C.; soluble in fixed oils. It is soluble in concentrated sulphuric acid, producing a green solution gradually changing to brown. When heated to 100° C. it remains unchanged, but at a temperature of 140° to 150° C. it is decomposed with the liberation of violet iodine vapors. When ignited it should leave not more than 0.1 per cent. of residue (limit of *inorganic impurities*). If 0.5 Gm. of Iodol be shaken with 100 cc. of water and filtered, the filtrate should not be made more than slightly opalescent by silver nitrate T.S. (absence of *hydriodic acid* or soluble metallic *iodides*). If 0.5 Gm. of Iodol be shaken with 100 cc. of water and filtered, the filtrate should not communicate more than a light yellowish tinge to chloroform (absence of appreciable amount of *free iodine*)." *U. S. VIII.*

When given in sufficient dose to animals, iodol causes emaciation, albuminous urine, fall of temperature, general loss of muscular power, and finally death from fatty degeneration of the liver and kidneys and other tissues. That iodol applied externally is capable of producing constitutional symptoms is shown by C. Lauenstein (*T. G.*, 1887, 768), in a case in which the surgical use of the drug caused dizziness, marked rise in the temperature, vomiting, small, rapid, irregular pulse, albuminous urine, and apathy which did not subside for four days, iodine was found in the urine for twelve days. It is, however, a less dangerous topical application than iodoform due to its slower absorption. Iodol may be employed for all purposes for which iodoform has been used. It has been found valuable in the treatment of *tuberculous laryngitis*, and may be blown into the larynx directly upon the ulcers without causing irritation. It has been used with asserted great success in the treatment of blennorrhagic and simple *vaginitis*, in *chancres* and other *ulcers*, in suppurative *adenitis*, and as an antiseptic dressing to *wounds*. Mazzoni's solution was: iodol, one part; alcohol, sixteen parts; glycerin, thirty-four parts. Iodol has also been used as an internal remedy in *tertiary syphilis* and in *scrofula*. Good effects have also been claimed for it in *diabetes*. Assaky and Reck have given thirty grains (1.9 Gm.) a day with asserted good results. *Dose*, two to four grains (0.13–0.26 Gm.). Under the name of *iodolen*, a compound of iodol with albumin has been used as a surgical dusting powder.

Iodolein. *Dubois's Iodolein. Iodized Poppy Seed Oil. N. N. R.* 1924.—This compound is an oily brownish liquid containing about 33 per cent. of iodine. It is used as a substitute for the inorganic iodides in *doses* of from 2 to 10 minims (0.13 to 0.6 cc.) taken in capsules after meals.

Iodolin. *Quinoline chlormethylate iodochlorid.* $C_9H_7NCH_3Cl.ICl$.—This is a yellow insoluble powder used as an iodoform succedaneum. It is the product of the action of a chloride on quinoline and methyl iodide.

Iodopyrine. $C_{11}H_{11}IN_2O$. *Antipyrine Iodide, Iodantipyrine.*—This substance contains 60 per cent. antipyrine and 40 per cent. of iodine. It forms colorless crystals melting at 160° C., and has been recommended as a substitute for the iodides in *muscular rheumatism* and in *asthma* and *syphilis.* It is capable of producing iodism. It has also been used as an analgesic in *neuralgia* and *herpes zoster* and as a local application in *syphilitic sores* and *psoriasis.* The *dose* given by Junkers was fifteen grains (1 Gm.) for adults every three or four hours. For children from 1 to 10 years old he gave one and a half to eight grains (0.096–0.5 Gm.). To those over 10 years he gave eight to twelve grains (0.5–0.78 Gm.). (*Th. M.*, vol. xiii, 604.)

Iodostarin. *Diiodo-tariric Acid. N. N. R.* 1924.—This is an addition product with a fatty acid, tariric, derived from a species of *Picramnia* (formerly *Tariri*), see *Cascara amarga.* It has the chemical formula $CH_3.(CH_2)_{10}CI = CI.(CH_2)_4CO\text{-}OH$. It forms white, shining, crystalline scales, which are odorless and tasteless, containing 47.5 per cent. of iodine. It is insoluble in water, slightly soluble in cold alcohol, readily soluble in hot alcohol, in ether, chloroform and benzol. Iodostarin itself is not affected by light, but its solutions, after short exposure to light, turn brown with separation of iodine. Bachem (*M. M. W.*, 1911) has shown that the iodine is much more slowly eliminated after the exhibition of iodostarin than after alkaline iodides. Its action is similar to that of calioben. It is marketed only in the form of tablets each containing 4 grains (0.25 Gm.).

Iodosyl $C_6H_3I.OI.COOH$.—A bulky, amorphous powder of a deep red color, nearly odorless, and having only a faint taste suggestive of that of iodine. Insoluble in water and in oils and only sparingly soluble in chloroform and ether. It is used as a substitute for iodoform, over which it has the advantage that it is odorless, as a dressing for *wounds* and *ulcers,* Also as a local application in *nasal catarrh* and *ozena,* in *ringworm* of the scalp, in various *cutaneous affections,* being especially recommended in the treatment of *corneal ulcers.* It is employed either as a dusting powder, in the form of an ointment, 2 to 10 per cent., or in that of a medicated gauze.

Iodylin. *Iodiline. Bismuth-iodo-salicylate.*—It is a fine, yellowish-green powder with an odor suggestive of that of iodoform. According to Israel (*Med. Wochens.*, 1902, p. 139), this substance is efficient as a substitute for iodoform.

Iogen.—Iogen is produced by the action of iodine upon the anhydride of phthalic acid. It is a lustrous crystalline compound of dark green color, liberating 52 per cent. of iodine in the presence of moisture. It is claimed to be antiseptic and germicidal, and is used, in about 4 per cent. strength, in oil for the treatment of nose and throat affections, in ointment for application to the skin or to wounds, or as an antiseptic dusting powder.

Ionidium.—A species of *Ionidium* growing in Ecuador, in the neighborhood of Mount Chimborazo, was used by the South American Indians in the treatment of *elephantiasis,* under the name of *cuichunchulli.* It was probably derived from the *Ionidium glutinosum,* Vent. It is said to be diaphoretic, diuretic, occasionally sialagogue, and in large doses emetic and cathartic. The root is the part used. For further information, see *A. J. P.*, iii, 125.

Iopropane. *Iothion. N. N. R.* 1924. *Di-iodohydroxypropane,* $C_3H_5I_2(OH)$.—It is a thick, yellowish liquid, soluble in alcohol, ether, and the fixed oils, but almost insoluble in water. It contains from 77 to 80 per cent. of iodine.

Iothion is intended as a means of endermic administration of iodine. It is asserted that after its external application, iodine appears in the saliva within an hour, and that from 30 to 50 per cent. of the amount of the substance employed can be eventually recovered from the excretions. It has been used to a considerable extent in the treatment of *tertiary syphilis, asthma, chronic arthritis,* and other conditions in which iodine is indicated. (See Richter, *B. K. W.*, 1909.) It is applied generally in the form of an ointment containing from ten to fifty per cent. of iothion, of which a quantity equivalent to fifteen to thirty grains (1–2 Gm.) may be well rubbed into the skin once a day.

According to Herzfeld and Makler (*Med. Klin.*, 1912), a portion of the iodine is retained in the organism. It is used in the treatment of *syphilis* and other conditions in which a continued iodine effect is desired. Herzfeld and Elin (*Med. Klin.*, 1912) found 50 per cent. of the iodine in the urine after application of a 10 per cent. iothion ointment.

Iridium. *Ir.*—This metal, discovered in 1804, and named after Iris, the goddess of the rainbow, is a white lusterless, steel-like metal of the platinum group. It has a sp. gr. of 22.7 and is the heaviest of all metals. Several of its salts and compounds of its salts with other salts, usually of the alkali group, are prepared and marketed. Of these but one, the bromide, is used in medicine, and even this has failed to show any decided therapeutic value.

Iotriferrin.—This is a reddish powder with metallic taste and a faint odor of iodine. It is said to contain 15 per cent. of iron, 8 per cent. of iodine and 2 per cent. of phosphorus. It is insoluble in water or acid media but readily soluble in alkaline solutions. It is intended for the treatment of *anemia* and *scrofula.*

Iron-Wood. *Ostrya virginiana* (Mill.) Willd. (*O. virginica* Willd. *Carpinus virginiana* Mill.) (Fam. *Betulaceæ.*)—The wood of the *hop-hornbean* is said to be tonic, antiperiodic, and alterative, and the fluidextract has been used in *doses* of from a half to one fluidrachm (1.8–3.75 cc.) in *ague.*

Isatis. *Isatis tinctoria* L. *Woad. Dyer's Woad. Pastel.* (Fam. *Cruciferæ.*)—A glabrous and glaucous biennial plant, indigenous to and cultivated in southern and central Europe to central Asia, as well as in the United States. *Dyer's woad* is mentioned in the writings of Dioscorides and Pliny. It produced the chief blue coloring-matter for woolen fabrics in Europe before indigo became common. The first year's growth consists of a rosette of lanceolate leaves. During the second year a stem rises to the height of 2 to 4 ft. bearing alternate, lanceolate, entire, sessile leaves, panicled racemes of yellow flowers and 1-celled samara fruits. The leaves have a fugitive, pungent odor, and an acrid, very persistent taste; they have been used in *scorbutic affections, jaundice,* and other complaints, but are of no value. They were formerly of importance as a source of indigo. (See *Indigo.*) The leaves are prepared by grinding them to a paste, which is made into balls placed in heaps, and allowed to ferment. When the fermentation is at an end, the mass falls into a coarse powder, which is woad.

Isocain. This name has been applied to the para-amino-benzoyl-di-iso-propyl-amino-ethanol hydrochloride. Schmitz and Loevenhart (*J. P. Ex. T.*, 1924, xxiv, p. 167) find that it is approximately equal to cocaine in its anæsthetic effects on mucous membranes, is six times as powerful in its nerve blocking action and less than one-third as poisonous. We do not, however, know of any clinical reports.

Isoform. *Para-iodoanisol.* $C_6H_4(OCH_3)IO_2$.—It is a white powder having an odor feebly suggestive of aniseed. It is sparingly soluble in cold water, but dissolves more freely in hot water. In alcohol and ether it is insoluble. When heated to about 225° C. it decomposes explosively.

Because of its explosive properties it is marketed only mixed with equal parts of calcium phosphate—if intended for a dusting powder—or as a paste with equal parts of glycerin.

According to Winterberg (*Med. Klin.*, 1906), *isoform* in 1 per cent. strength has a distinct, and in 3 per cent. strength, a well marked antiseptic action. It has been used to a considerable extent as a surgical dressing, especially for suppurating *wounds.* It is applied either in the form of a dusting powder or by saturating gauze with it, or in paste or emulsion, as the conditions may indicate. It has also been employed as an antiseptic in purulent *otitis media,* various *skin diseases, urethritis,* and in tooth paste. Although Heile has stated that isoform is non-toxic, Hoffman (*B. K. W.*, 1905) has reported violent dermatitis from its use, and Urbantschitch (*W. K. R.*, 1907) asserts that it has a depressant action upon the central nervous system.

Isopropyl Alcohol. $(CH_3)_2CHOH$. *Dimethylcarbinol.*—It is a by-product of the petroleum and natural gas industries. The anhydrous alcohol has a specific gravity of 0.789 and boils at 82.4° C. The commercial product contains 91 per cent. by volume of the alcohol with 9 per cent. of water. It is a colorless liquid with a somewhat bitter taste and a characteristic odor, miscible in all proportions with water. (For further details see paper by Grant and Johns, *A. J. P.*, 1922, xciv, p. 418). Its solvent properties are similar, but not identical with those of ethyl alcohol. *Isopropyl acetate* has been prepared by Grant and Johns and is a useful solvent for nitrocellulose.

Macht (*J. P. Ex. T.*, 1920, xvi, p. 1) found that isopropyl is about twice as poisonous as ethyl alcohol but that it does not produce the permanent, injurious effects characteristic of methanol. It has been suggested for various purposes in the arts and pharmacy, especially for the extraction of resins and in the preparation of substances intended for external application. In medicine it has been used to a limited extent as a solvent for phenol, as a wound dressing in the place of grain alcohol and for the preparation of various lotions intended for external use.

Isopral. *Trichlorisopropylalkohol,* $CCl_3.CHOH.CH_3$.—This substance, which has been proposed as a hypnotic, occurs in microscopic prisms, melting at 49° C., readily soluble in water, alcohol, or ether, readily subliming and having a camphor-like odor and aromatic taste. Heated for a long time with alkalies it loses chlorine without the formation of chloroform. According to Impens, it is readily absorbed through the skin, subcutaneous tissue, and the digestive tract, the impression, when taken internally being manifested in from three to five minutes. It is said, also, that the inhalation of a stream of air directed over warmed isopral will produce marked narcosis in the lower animals in ten or twelve minutes. It is eliminated through the kidneys chiefly as a compound with glycuronic acid (*trichlorisopropylglycuronic acid*) although it is believed also to escape to some extent through the respiratory tract.

The experiments of Hatcher (*J. A. M. A.*, 1907) have shown that, although weight for weight it is somewhat more powerfully somnifacient than is chloral hydrate, it is correspondingly more toxic, so that in its therapeutic efficiency it is about the same. The *dose* is ten to twenty grains (0.65–1.3 Gm.).

Isopyrum. *Isopyrum thalictroides* L. (Fam. *Ranunculaceæ.*)—F. A. Harsten believes he has found two alkaloids, *isopyrine* and *pseudo-isopyrine,* in the root of this plant, which grows in the forests of middle and southern Europe. (*A. J. P.*, xliv, 453. See also *J. Soc. Chem. Ind.*, 1919, xxxviii, 197A.)

Issue Peas.—These were globular beads, of the size of a pea, made of woody substances of spongy structure, intended to be introduced into issues, abscesses, etc., for the purpose of promoting suppuration. They are not used by modern surgeons.

Istizine.—Under this name a synthetic dioxyanthraquinone has been introduced as a purgative. It occurs as an orange-yellow crystalline powder, difficultly soluble in water or the ordinary organic solvents, but an alkaline solution dissolves it with the formation of a cherry-red color. Ebstein (*Med. Klin.*, 1913) has used it as a laxative in *doses* of two to eight grains (0.13 to 0.5 Gm.).

Iwarancusa.—The roots of *Andropogon Iwarancusa* Boiss., now considered to be in large part *A. Schoenanthus* L. (Fam. *Gramineæ*), a native of Central India (see *Oil of Citronella*). It contains a volatile oil, resin, and a bitter substance, and is stated to be used on the continent as a diaphoretic drug. It is also used in perfumery. In India it has been reputed to be of service in *cholera.*

Ixora.—The *Ixora coccinea* L. (Fam. *Rubiaceæ*), a smooth shrub with oblong leaves and corymbs of red flowers and indigenous to the East Indies, is used in India in the treatment of *dysentery.* According to Ghosh it is second in value only to ipecac. (*P. J.*, 1916, xcvii, 369.)

Izal. *N. N. R.* 1924.—This is an albuminous emulsion containing not less than 50 per cent. of "izal oil," a coal tar fraction of monatomic phenols exclusive of cresols and phenol. It is used as a germicide and disinfectant. It is stated to be twelve times as efficient as phenol, with a lower degree of toxicity. It is not intended for internal use but is employed externally or as a household disinfectant in dilutions of from one-third to one per cent.

Jacaranda.—Several species of this genus (Fam. *Bignoniaceæ*) are employed in *syphilis* in Brazil and other portions of South America under the names of *caroba, carobinha,* etc. Peckolt (*A. J. P.*, 1882, 134) has found in them a crystalline substance, *carobin,* besides resins and acids, such as *carobic* and *steocarobic acids,* and *carobon, caroborelinic acid,* and *caroba balsam.* Hesse (*Ann. Chem.*, cclii, 150) found only an aromatic resin, but no alkaloid. The value of the remedy has been asserted in the *B. M. J.*, vol. i, 1885. For further information, consult *P. J.*, 3d series, vols. v, xii, and xiv, and also *A. J. P.*, 1882.

Jambosa Root.—This is the root of *Eugenia Jambos* L. (*Myrtus Jambos*) (*Jambosa vulgaris* DC.), a tree, with lanceolate leaves and greenish-white flowers belonging to the *Myrtaceæ,* which is widely cultivated in the tropics under the name of the *rose-apple.* It has been found by A. W.

Gerrard to contain an oleoresin, besides a crystalline principle, *jambosin*, $C_{10}H_{15}O_3N$. Lyons has also found in it minute quantities of an alkaloid. The decoction of the bark of the root is used as an astringent in *dysentery*, *gonorrhea*, and *leucorrhea*. (*P. J.*, March, 1884.)

Jambu Assu.—The root of *Piper Jaborandi* Vell. (Fam. *Piperaceæ*) of Brazil, is used by the natives as a sudorific, a diuretic, and a febrifuge. It is said to contain an alkaloid and a pungent oleoresin. It has no botanical, and probably no medicinal, relation with pilocarpus.

Jeffersonia. *Twinleaf. Rheumatism Root. Jeffersonia diphylla* (L.) Pers. (Fam. *Berberidaceæ.*)—This is a low perennial herb found in woods from New York to Wisconsin and Iowa extending southward. It possesses long-petioled, 2-lobed or parted radical leaves and a naked scape bearing a single terminal white flower. The rhizome, which, with the matted fibrous rootlets attached, is the part used, has a brownish-yellow color, and a bitter, acrid taste, which resides in its cortical part, the inner portion being nearly tasteless. E. S. Wayne, of Cincinnati, found it to contain albumen, gum, tannic acid, starch, pectin, a fatty resin, hard resin, sugar, lignin and a peculiar acrid principle having acid properties and resembling polygalic acid. The root is said to be emetic in large doses, tonic and expectorant in smaller doses and not unlike senega, as a substitute for which it is sometimes used. (*A. J. P.*, xxvii, 1.) According to Mayer, of New York, the rhizome of this plant contains a small quantity of berberine and a second white alkaloid. The pectin of Wayne he considers to be saponin. (*A. J. P.*, 1863, 99.) A. W. Flexor proved the absence of berberine from the root. (*Am. Drug.*, 1884.) Gordin has since confirmed this view (1902).

Job's Tears. *Coix Lacryma. Semen Lacrymæ Jobi.*—This seed is from *Coix Lachryma-Jobi*, a graminaceous plant growing, under favorable conditions, to a height of seven or eight feet. It is a native of the East Indies but is extensively cultivated not only in the Orient but in parts of Europe and America. The seeds are about one-quarter inch in length, round at one end and pointed at the other, and with a very hard siliceous coat of a pearly gray appearance. They have been used in medicine either as a tincture or decoction in catarrhal affections of the air passages and in inflammation of the urinary passages. They are very frequently strung and used as beads to make necklaces, in the superstitious belief that they protected the infants from the ills incident to teething.

The continued search for food products by the U. S. Department of Agriculture has brought attention to the fact that these seeds are used extensively as food in some parts of the world under the name of *adlay*.

The outer hard shell of the individual grains constitutes 75 per cent. of the total weight of the seed. The varieties raised for food purposes are numerous and a species has been developed which has a softer outer coat, and the milling expert of the U. S. Department of Agriculture has found that good flour can be made with ordinary milling equipment.

Seven distinct varieties of the plant have been found in the Philippines and still other varieties grow in Burmah and other Oriental countries. The high yield per acre, which averages over 2000 pounds or about three times that of wheat, makes it a lucrative crop from an economic standpoint. The chemical analysis shows the following composition: (in parts per hundred).

Water, 8.49; protein, 17.58; fat, 7.15; crude fiber, 2.04; soluble carbohydrates, 6.24; ash, 2.33; starch, 51.58. The protein is similar to gliadin. Its distinctive character has led the Japanese investigators, Yoshimura and Sagara, to name it *coicin*. (*Jour. Tokio Chem. Soc.*, 1919, p. 483.)

Juniperus Virginiana L. (Fam. *Coniferæ*) *Red Cedar. Cèdre de Virginie*, Fr. *Virginische Ceder, Rothe Ceder*, G.—The *Red Cedar* is a slow growing, evergreen tree with shreddy bark and a crown which is usually narrow, dense and pyramidal but which occasionally, in old plants, becomes spreading and round-topped. It grows on dry hills or in swamps from Nova Scotia to Florida and west to the Rocky Mountains. In northern latitudes it usually attains a height of 25 to 40 feet but, in the south, specimens attaining 100 to 120 feet in height are recorded. Its leaves vary from acicular to scale-shaped. The acicular type, occurring on young trees and vigorous shoots are opposite and scattered, the scale-shaped type which are the more common are bluish-green, about $^1/_{16}$ inch long, glandular on back and 4-ranked, giving the twigs an angular appearance. Both staminate and pistillate flowers occur, either on the same tree or on different trees, in catkins. The staminate flowers are yellow, each with numerous anthers attached to several scales that are united into an ovoid catkin; the pistillate flowers are greenish, minutely globular with about 6 bluish scales. Upon ripening these scales become fleshy and connate producing a dark-blue berry-like fruit, termed a galbulus, which is often covered with a bloom.

The tops of this plant were formerly included in the Secondary List of the U. S. Pharmacopœia. The wood, which is characterized by its red duramen and nearly white alburnum, yields valuable oil which is used as a clearing agent in microscopic technique. When evaporated to a thick consistency, it furnishes the *immersion-oil* for use with oil-immersion objectives. The wood itself is extensively used for moth-proof chests, lead-pencils, fence posts and furniture. Small excrescences, which are sometimes found on the branches of the tree, are popularly known as *cedar apples* and used as an anthelmintic in the *dose* of from ten to twenty grains (0.65–1.3 Gm.) three times a day. The tops have a pleasant odor, and a strong, bitterish, somewhat pungent taste. These properties reside chiefly in a volatile oil, and are readily imparted to alcohol. The leaves bear a close resemblance to the leaves of *Juniperus Sabina* L., an European shrub, from which they can be readily distinguished by the strong, disagreeable odor of the latter, after bruising. I. W. Brandel obtained from the leaves of *J. Virginiana* 0.47 per cent. of volatile oil, sp. gr. 0.913 at 15° C. It had a very pleasant odor. (*Proc. A. Ph. A.*, 1906, 459.) *Cedrene camphor*, $C_{10}H_{26}O = C_{16}H_{24} + H_2O$, may be obtained by cooling the oil until coagulated, and separating the crystalline portion by expression; the expressed liquid is *cedrene*, $C_{15}H_{24}$, which, after rectification and distillation, has the sp. gr. 0.984 at 15° C., boiling at 237° C. Cedrene may also be prepared from the cedrene camphor by the dehydrating action of phosphoric anhydride, P_2O_5. *Oil of cedar wood* and *oil of cedar leaves* are both articles of commerce. Schimmel describes a volatile oil from Haitian cedar wood which differs from our domestic oil of cedar, only in having a higher specific gravity. (*Schim. Rep.*, 1905, 17.)

The volatile oil, which resembles oil of savin in its medicinal properties, has been used for the purpose of producing abortion, and in some cases has caused death. The symptoms have been burning in the stomach, vomiting, convulsions, coma. and a slow pulse, with evidences of gastro-intestinal inflammation after death. (See S. C. Watt, *B. M. S. J.*, vol. xl.) A counterirritant ointment was formerly made from the leaves.

Under the name of *cedar* are known in commerce various trees, some of which do not belong to the genus *Juniperus.* The wood of *Juniperus bermudiana* L. is said to be largely used in making pencils. The cedar of Lebanon, *Cedrus Libani* Loud. and two allied species, the *African cedar*, *C. atlantica* Manetti, and the *Indian cedar* or *deodar*, *C. Deodara* Loud., are sometimes distilled for oil. Under the name of *libanol*, an oil obtained from *Cedrus atlantica* Manetti, or *satin-wood*, has appeared in commerce and is said to be useful in the treatment of *blennorrhagia*, *phthisis*, *bronchitis*, and *eruptions* upon the skin, having properties very similar to those of the oil of santal. It may be given in capsules up to forty-five grains (3 Gm.) per day. In skin eruptions the 25 per cent. ointment made with vaseline has been used. Other trees known as cedars are the *white cedar*, *Cupressus thyoides* L. (*Chamæcyparis thyroides* (L.) Brit); the American white cedar, *Thuja occidentalis* Linn.; the Californian white cedar, *Libocedrus decurrens* Torr.; the New Zealand cedar, *Libocedrus Bidwillii* Hook. The Australian red cedar, *Cedrela Toona* Roxb., and the West India cedar, *Cedrela odorata* L., belong to an entirely different family, the *meliaceæ* (*Cedrelaceæ*). The wood of the latter species is used in making cigar boxes, and, according to Schimmel, yields 3 per cent. of a volatile oil, which has a specific gravity of 0.915, boils between 265° and 270° C., and has an optical rotation of 0.053° in a 100 mm. tube. It is said to be a powerful insecticide. (*P. J.*, Aug. 29, 1896, 179.)

Kairine.—The hydrochloride of methyloxytetrahydroquinoline, $C_{10}H_{13}ON.HCl + H_2O$), is the commercial kairine (*kairine M*). *Kairine A* is the corresponding ethyl compound, and has similar properties. Kairine, as brought into commerce, is readily soluble in water and alcohol, and forms a grayish-white crystalline powder, with bitter, salty taste. Ferric chloride produces a dark brown color, which upon the addition of sulphuric acid turns purple.

Kairine belongs to the antipyretic remedies, and is without doubt capable of producing pronounced fall of temperature in *fever*, accompanied by copious sweating. It is, however, a cardiac depressant, which is said to act directly upon the cardiac muscles, and is very prone to produce cyanosis and collapse. The reports have been so unfavorable that, in the absence of advantage over antipyrine and antifebrine, kairine is no longer used in practical medicine. *Dose*, five to ten grains (0.32–0.65 Gm.).

Kalagua.—A study of this South American plant, which has been put upon the market as a specific for *tuberculosis*, made upon the lower animals by D. H. Bergey, shows that it has no specific influence upon the tubercle bacillus.

Kalmia. *K. latifolia* L. (Fam. *Ericaceæ*) *Laurel. Mountain* or *American Laurel. Broad-leafed Laurel. Calico-bush. Spoonwood. Kalmie*, Fr., G.—This is an evergreen shrub with a round-topped head from 4 to 10 feet in height, rarely tree-like. It is indigenous to rocky hills and mountains as well as pine barrens from New Brunswick and Ontario south to Florida and Tennessee. Its leaves are mostly alternate, entire, elliptic-lanceolate, dark green on upper and yellowish to bright-green on lower surface. Its flowers are pink, rose-colored or white with purple markings, have a cup-shaped corolla with 10 stamens, and are arranged in terminal compound corymbs. Its fruit is a small capsule. The leaves and tops are poisonous. In the leaves George W. Kennedy detected the glucoside arbutin. (*A. J. P.*, xlvii, 5.)

Kalmia angustifolia L. (Fam. *Ericaceæ*) *Sheep Laurel. Lamb Kill. Wicky.*—This is a low undershrub usually attaining a height of 1½ to 2 feet with opposite or whorled, entire, oblong leaves that are dark-green on upper surface and pale-green beneath. Its flowers are smaller than those of *K. latifolia;* crimson to light purple in color and are borne in lateral, many-flowered corymbs. Its fruit is a small capsule. This species is indigenous to pastures, hillsides and peat bogs from Newfoundland and Hudson Bay to Georgia.

Both the *Kalmia latifolia* and the *K. angustifolia* are not infrequently the source of serious and even fatal poisoning to sheep although it is said that they are eaten with impunity by deer and goats. According to Crawford (*Bulletin 121, Bureau of Plant Industry*, U. S. Dept. of Agriculture), laurel causes either when fed to, or injected into, the lower animals, great salivation, lachrymation and emesis, convulsions, and later paralysis of the extremities, with greatly labored respiration. The toxicity of these plants is due, according to De Zaayer (*Chem. Ztg.*, July, 1887), to andromedotoxin (see *Andromeda*). The leaves have been used internally in *diarrhea* and in *syphilis*, and externally in skin diseases. (See 16th edition, *U. S. D.*)

A decoction of the leaves of *K. angustifolia* is used by the negroes as a wash for ulcerations between the toes.

Kamala. *U. S.* 1890. *Kamala. Glandulæ Rottleræ.*—The U. S. Pharmacopœia, under the name of *Rottlera*, U. S., 1870, *Kameela*, formerly recognized the glands and hairs from the capsules of *Mallotus philippinensis* (Lamarck) Muell.-Arg. (Fam. *Euphorbiaceæ.*) This tree grows in Abyssinia, Southern Arabia, Hindostan, the East India Islands, China, and Australia, reaching a height of from fifteen to twenty feet, and yielding a roundish, three-valved, three-locular capsule about the size of a small cherry, thickly covered with a red powder, which is collected in Hindostan by rolling the berries about in large baskets until the free powder sifts through the open wickerwork. This powder has been used for many centuries in Asia as a dyestuff under the name of *wars*, although this term is more properly applied to the product of the *Flemingia.* (See *Wurrus.*)

Kamala, as brought to our market, is a light, finely granular, very mobile powder, of a brownish-red or madder color, with little odor or taste, but producing a slight sense of acridity in the mouth, and feeling gritty under the teeth. (When the grittiness is excessive, the drug has probably been adulterated with earthy matters.) It is inflammable, and flashes almost like gunpowder when dropped into the flame of a candle. It is insoluble in cold and but very slightly soluble in boiling water; but alkaline solutions, alcohol, and ether dissolve a large proportion of it, forming a deep red solution, from which water precipitates resinous matter, "imparting a deep red color to alkaline liquids, alcohol, ether, or chloroform, and a pale yellow tinge to boiling water." *U. S.*, 1890. Under the microscope it consists of garnet-red, semi-transparent, roundish, glandular hairs from 0.040 to 0.100 mm. in diameter, containing numerous red, club-shaped cells admixed with minute aggregate hairs, and the remains of stalks and leaves, the latter of which are easily removed by careful sifting. It has been examined chemically by Thomas Anderson, of Glasgow, and by G. Leube, in Germany. As given by the former, the constituents are, in 100 parts, 78.19 of resinous coloring matter, 7.34 of albumin, 7.14 of cellulose, etc., a trace of volatile oil and volatile coloring matters, 3.84 of ash, and 3.49 of water. The amount of earthy impurities, chiefly sand, in commercial kamala, varies greatly, sometimes amounting to fifty or even sixty per cent. It can readily be detected by a high ash percentage. The U. S. P., 1890, permitted the presence of "not more than 8 per cent. of ash." Rusby found one shipment loaded with sand, one with olive stems, one olive stems and sand, and one ground bark. Two samples, 40.8 per cent. acid, 43.4 per cent. ash, were mostly sand. (See also *Ph. Rev.*, 1907, 129; *P. J.*, 1906, 258.) Of the resinous coloring substances, Anderson obtained one in a pure state by allowing a concentrated ethereal solution to stand for two days, draining and pressing in bibulous paper the resulting mass of granular crystals, and purifying them from adhering resin by repeated solution in ether and recrystallization. To this substance he gave the name of *rottlerin.* It is in the form of minute crystalline plates, of a yellow color and a satin-like luster, insoluble in water, sparingly soluble in cold but more so in boiling alcohol, and readily dissolved by ether, and by alkaline solutions, which assume a dark red color. Perkins (*Chem. Soc. Trans.*, lxiii, p. 975) shows rottlerin to consist of six distinct substances, *i. e.*, rottlerin, isorottlerin, wax, two resins and a coloring substance. The pure rottlerin has the chemical composition $C_{33}H_{30}O_9$. (See also *Ph. Ztg.*, 1906.) Crude rottlerin, sometimes known as *kamalin,* melts when heated moderately, and at a higher heat is decomposed, giving off pungent vapors. A. and W. Perkin (*B. Chem. G.*, xix, 3109) and Jawein (*B. Chem. G.*, xx, 182) both stated that rottlerin can be extracted from kamala by the action of carbon disulphide. Jawein gave its fusing point as 200° C., and said that it was easily soluble in hot alcohol and acetic acid. In a later communication, A. G. Perkin (*P. J.*, 1893, 159, 236) stated that there is also present a trace of a yellow crystalline coloring matter melting at from 192° to 193° C. Perkin also found in kamala a small quantity of a sugar soluble in water. Potassium permanganate oxidizes it to oxalic and benzoic acids; nitric acid of 1.5 sp. gr., on the other hand, oxidizes it to oxalic acid, ortho- and para-nitrocinnamic acids, and para-nitrobenzoic acid.

Kamala is actively or even violently purgative in full doses, occasionally causing nausea, but seldom vomiting. Kamala has long been used in India against the *tape worm.* Semper (*A. E. P. P.*, 1910, lxiii, p. 10) has found that kamala has a paralyzing effect on motor nerves and muscles, to which action he believes it owes its tænifuge powers. It is given, without previous preparation of the patient, in the *dose* of from one to three drachms (3.9–11.6 Gm.), suspended in water, mucilage, or syrup. In the latter dose it sometimes acts violently. The worm is usually expelled at the third or fourth stool. If the first dose fails to operate on the bowels, it may be repeated in four hours, or followed by a dose of castor oil. The tincture (four ounces to eight fluidounces of diluted alcohol) is also said to be efficient in *doses* of from one to four fluidrachms (3.75–15 cc.). As an external remedy, kamala is used by the people of India in various affections of the skin, particularly *scabies* and *ringworm.* A tænifuge composed of kamala and koussin and known as *kamakosin,* is in use on the continent.

Kauri. *Cowrie. Gum Kauri. Australian Copal.* —This is an amber-like substance, varying from a soft cream-white to an amber color, dug in large quantities from the soil of Australia and New Zealand. It is a resinous exudation from the Kauri Spruce, *Agathis australis* Salisb. (*Dammaris australis* Lamb.), of the Fam. *Coniferæ,* but, as it first exudes and is found on the surface of the ground, it is not esteemed. The useful resin is a fossil deposit found especially in New Zealand swamps at depths of from 2 to 14 feet. The production of kauri is largely carried on under governmental supervision. The resin appears in pieces ranging in size from that of a hen's egg to a man's head, of a pale greenish-yellow color and with a balsamic odor. Large quantities are used in the arts, especially in the manufacture of linoleum. According to Tschirch and Niederstadt, it contains *kaurinic acid,* $C_{10}H_{16}O_2$, 1.5 per cent.; *a-* and *β-kaurolic acids,* $C_{12}H_{20}O_2$, 48 to 50 per cent.; *kaurinolic acid,* $C_{17}H_{34}O_2$, and *kauronolic acid,* $C_{12}H_{24}O_2$, together, 20 to 22 per cent. All these resin acids are soluble in solution of sodium hydroxide. *Baume Calédonien* consists of a solution of kauri gum in an equal weight of 90 per cent. alcohol. It has been used with alleged great success in the treatment of *wounds* and *ulcers,* of *eczema* and other skin affections, and as a substitute for collodion and the soluble sodium silicate. When applied to a well cleansed and dried wound it leaves a slight deposit of resin as a varnish, which is not affected by friction or contact with water.

The commercial product known as *Manila copal,* according to Tschirch and Koch, is derived from *Agathis Dammara* Rich. (*Dammora orientalis* Lamb.), a conifer. It consists chiefly of free amorphous resin acids, namely, *alpha-* and *beta-mancophalolic acid,* $C_{10}H_{18}O_2$ (about eighty per cent.), and contains besides about 12 per cent. of a resin, $C_{20}H_{32}O_2$, and about five per cent. of essential oil. The latter, when fresh, forms a liquid as clear as water, very mobile, having a pleasant odor, and the sp. gr. 0.840; it boils at from 165° to 170° C., and mixes in all proportions with alcohol, ether, chloroform and fatty oils. See also the article on *Copal.*

Kefir. *Kephyr. N. N. R.* 1924. (See also *Lactic Acid Therapy* and *Lac Fermentatum.*)—From time immemorial the Tartars and the Balkan peoples have employed as a food and beverage one or another form of fermented milk. The Tartars prepared from mare's milk a drink known as *koumiss* or *kumys.* This is prepared by the action of a peculiar ferment known as *kephir* (*kepir*) and called also by the Mohammedans "*the prophet's millet.*" In Western Europe mare's milk not being available, an imitation of kumys has been made from cow's milk, to which the term "*Kephir milk*" should be applied, limiting the word kumys to the genuine Tartar drink. The Armenians employed a fermented milk, *madzonn* or *matzoon*. *Giaourdi* is a fermented milk prepared in Greece from sheep and goat's milk with an enzyme obtained from fermented figs. The Bulgarians use a fermented milk known as *yoghourt* (*yaowite*). The Arabians have a fermented milk called *leben.*

The *kefir grains* (or seeds) are white, irregular, roundish bodies about the size of a walnut with a rough, ferruled surface, of gelatinous or, when dried, cartilaginous consistency. Despite considerable investigation, their composition is not yet definitely settled. They probably contain several micro-organisms as follows: (1) a yeast fungus which Spivak (*N. Y. M. J.*, 1896) believes identical with the ordinary yeast, *Saccharomyces cerevisiæ*, but which Beyerinck believes to be a distinct species, *S. kefir*, (2) *Bacillus Dispora Caucasica* (Kern) or *Bacillus Kephir* (Sorokin), (3) *Bacillus acidi lactici*, (4) other bacteria which are probably of little importance to the process of fermentation.

There are a number of directions for preparing kephir milk, varying more or less in the details. The following is a simple one: About 120 grains of kephir grains are softened by soaking over night in a pint bottle full of water. The following morning the water is poured off and the bottle is three-quarters filled with unboiled milk and tightly stoppered. This is kept at a temperature of 20° C. for from one to three days. The milk is strained through cheese-cloth immediately before use and the residue recovered may be used for fermenting other milk. For various other processes see Kobert (*Zeitsch. f. Krankenpflege*, 1904, p. 377; *Ph. Ztg.*, 1904, 819 and 1912, 277), Drasler (*Med. Klin.*, 1908), and Spivak (*N. Y. M. J.*, 1896). According to Spivak, the changes in milk during kephirization are as follows: 1. Fat, salts, and water remain unchanged; quantity of lactose is lessened and lactic acid is increased. A part of the casein—namely, about 10 per cent.—is transformed into acid albumin and peptone, 10 per cent. into hemialbumose, and the rest loses its lime, and therefore becomes more easily digestible. Alcohol, in amounts of from 0.5 to 1.0 per cent., and carbon dioxide to about 1 per cent. are also produced.

There is largely sold, under the name of kumys, a spurious drink which is made by fermenting sweetened milk with ordinary yeast. It is a pleasant beverage, but differs in important regards from the true kephir milk. The following formula has been suggested by L. Wolff (*A. J. P.*, 1880, 291): "Grape sugar, half an ounce. Dissolve it in four ounces of water. Dissolve twenty grains of compressed yeast, or well-washed and pressed out brewer's yeast, in two ounces of milk. Mix the two solutions in a quart champagne bottle, which is to be filled with good cow's milk to within two inches of the top. Cork well, secure the cork with wire and place in a cellar or ice chest, where a temperature of 10° C. or less can be maintained, and agitate three times a day. In three or four days the koumys is ready for use, and should not be kept longer than four or five days; it should be drawn only with a champagne tap." A beer bottle with patent stopper may be substituted for the champagne bottle.

The composition of true koumys, according to Stalberg, is given below; other analysis may be found in the *J. P. C.*, 1875, 62. *Koumys of June.* In 100 parts, alcohol 1.65, fat 2.05, sugar of milk 2.20, lactic acid 1.15, casein 1.12, salts 0.28, carbonic acid 0.75. *Koumys of September.* Carbonic acid 1.86, alcohol 3.23, fat 1.05, lactic acid 2.92, casein and salts 1.21. These fermented milks vary in composition with the milk they are prepared from. Warnikiewicz found in koumys from cow's milk casein 3.08, butter 2.2, milk sugar 1.77, salts 0.33, lactic acid 0.62, alcohol 1.23 parts per hundred. (See also König's *Nahrungs- und Genussmittel*, 416–419.)

Gordon Sharp (*P. J.*, 1892, 512) stated that the composition of koumys is complex, and that the decomposition which its proteids undergo is closely allied to putrefaction.

Kephir milk is useful either as an accessory or sole food in various conditions of malnutrition. Not only does it offer the nutritive elements of milk in a partially digested form, but it is claimed that the living ferments which are contained in it have an influence in aiding digestion in the alimentary canal, and that it also stimulates the appetite. It first came into Europe as a remedy in *pulmonary tuberculosis*, but has also been recommended in various forms of *dyspepsia*, whether functional or organic, in *anemia*, *rachitis*, and other conditions of impaired nutrition. It has also been employed as an infants' food with asserted remarkable results. Its value in *phthisis* has been extraordinarily lauded by Uroganski. (*Wiener Med. Wochens.*, 1907.)

Keratin.—The outer skin surface, the material of horns, hoofs, tortoise shell, the finger nails, all show a similar chemical composition, the empirical formula of which is said to be $C_{41}H_{71}N_{12}SO_{14}$. The percentage of sulphur varies, however, considerably.

Gissmann boils the quills of feathers in glacial acetic acid for from twenty-four to thirty-six hours in a retort furnished with a return condenser. A thick yellow-brown liquid is thus obtained, which is filtered through glass wool, evaporated on a water bath to the consistence of an extract, and afterwards dried. Dietrich recommends that before the treatment with acetic acid the feathers be digested in water for ten hours and then for eight days macerated in a mixture of equal weights of ether and alcohol, to eliminate fatty matters and cholesterin. The *keratin* obtained by the foregoing process is dissolved with the aid of a gentle heat either in acetic acid or ammonia, and the solution is allowed to clear by standing. Fischer recommends the employment of seven parts of keratin with either one hundred parts of acetic acid, or a mixture of equal parts of ammonia and diluted alcohol. Another method of preparing keratin is by macerating horn shavings, first with a mixture of ether and alcohol, then with a pepsin solution and finally dissolving in glacial acetic acid, filtering and evaporating.

According to Unna and Golodetz (*Monatshefte f. prakt. Dermatol.*, 1907, p. 109), when a horny material is treated with nitric acid, three sorts of keratin may be distinguished. Keratin A, not digested by either pepsin or hydrochloric acid, does not give xanthoproteic reaction; keratin B, not digested by pepsin nor hydrochloric acid but dissolved by nitric acid, gives a xanthoproteic reaction; keratin C, not affected by digestive mixture nor dissolved by nitric acid, gives the xanthoproteic reaction. The various horny substances may contain any one or two of these forms.

Keratin is insoluble in water, alcohol, ether, and diluted acetic acid, or acidulated pepsin solution. Diluted sulphuric acid on boiling changes it into leucin, tyrosin, and other products. It is soluble in concentrated acetic acid, alkalies, and ammonia.

Keratin is used sometimes for the purpose of coating pills, so as to enable them to pass through the acid juices of the stomach unchanged, and be dissolved in the alkaline intestinal fluids. While it has been suggested to protect in this manner the stomach against the effects of irritant drugs, the method is much more frequently used to protect drugs, such as the alkalies, bile-salts, calcium sulphide, pancreatin, tannin, etc., whose activity would be injured by the gastric secretions.

For the preparation of a solution of keratin suitable for the coating of pills several formulas have been proposed in all of which either acetic acid or ammonia is used as a solvent. The acetic solution is suitable for coating pills containing salts of mercury, gold, or iron, arsenic, creosote, salicylic acid, tannin, alum, etc. On the other hand, an ammoniacal solution is preferred for pills containing pancreatin, trypsin, bile-salts, alkalies, iron sulphide, etc. The pill mass must not contain water, for pills will shrink and fissures be produced in the keratin coating. It is, therefore, recommended to use in the making of such pills a mixture of yellow wax, one part, and suet or cacao butter ten parts. It is also necessary to avoid the use of vegetable powders as fillers and to employ in their place kaolin or charcoal powder.

When the pills are ready for coating they should first be dipped in cacao butter and rolled in charcoal powder. To coat with keratin, the pills, placed in a porcelain capsule, are moistened with a suitable quantity of keratin solution and then agitated in the presence of a current of air until the evaporation of the solvent takes place. This moistening and drying require to be repeated many times (sometimes ten) before the layer of keratin is sufficiently thick. The process employed for coating pills with gelatin, which consists in dipping into the solution the pill fixed on the point of a needle, is not suitable here, for it leaves a hole through the keratin coating that can never be completely closed.

In order to insure that the keratin used is insoluble in the stomach, Unna recommends that a preliminary experiment should be made with calcium sulphide pills coated with it. If in the course of some hours after such pills are taken eructations of hydrogen sulphide are observed, it would indicate that the pills have been dissolved in the stomach. Finally, the pills when placed in water should not liquefy or crack. This method of producing what are commonly called *enteric pills* has been largely replaced by the simpler one of hardening a gelatin capsule or gelatin-coated pill by means of formaldehyde solution or vapor, or by coating with salol which gives the same result as regards insolubility in the stomach, but ease of solubility in the intestinal tract. (See *Glutoid*, p. 1411.)

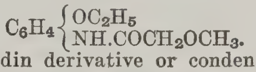
Zypkin (*W. K. W.*, 1907, p. 727) believes that keratin has the property of inhibiting the growth of connective tissue and has used it with asserted benefit in the treatment of various sclerotic diseases, such as *locomotor ataxia* and *cirrhosis of the liver.* He gives from sixty to two hundred and forty grains (3.9–15.5 Gm.) by the mouth, or injects subcutaneously a solution containing 2 Gm. of keratin with 0.1 Gm. of sodium bicarbonate and 10 cc. of water.

Kinkeliba. *Combretum album.* (Fam. *Combretaceæ.*)—The leaf of this plant, growing in Western Africa, is affirmed to be of great value in the treatment of bilious *hematuric malarial fevers.* Heckel and Schlagdenhauffen found in the leaves nothing more active than tannin and potassium nitrate. (See Perrot and Lefevre, *Travaux du Laboratoire de Mat. Méd.*, p. 67.) (See also *Combretum.*)

Kosam Seeds. *Fructus Bruceæ*, Pharm. Nederland.—The seeds of *Brucea sumatrana* Roxb. (Fam. *Simarubaceæ*), indigenous in China and Southern Asia. Schlagdenhauffen found in them a saponin, and Physalis and Bertrand a glucoside, *kosamin.* They are asserted to be useful in *menorrhagia*, also in *dysentery* and *diarrhea.* (*P. J.*, lxiv, p. 463.) According to Power and Salway (*Year-book of Pharmacy*, 1907), the *B. antidysenterica* has similar properties and is largely used in Abyssinia.

Kossala.—An Abyssinian remedy against *tapeworm.* (*Proc. A. Ph. A.*, xxvi.) It is said, however, to produce gastric irritation.

Kryofine. *Cryofine. Methoxyacet-p-phenetidin. Methyl-glycollic Phenetidin.*



$$C_6H_4\begin{cases}OC_2H_5\\NH.COCH_2OCH_3.\end{cases}$$

This phenetidin derivative or condensation product is made by heating paraphenetidin and methylacetic acid together; the acid replaces the acetic acid in the phenetidin derivative and the product is thus closely allied to acetphenetidin. Kryofine crystallizes from aqueous solutions in needles, with a melting point of from 98°–99° C. These crystals are white, at first tasteless, but becoming bitterish when chewed for a few moments. Kryofine is soluble in boiling water 1 in 52, in cold water 1 in 600, soluble also in alcohol, ether, chloroform, and the oils. The physiological action of kryofine has not been worked out, but in a medium-sized dog two hundred and one grains caused general paralysis and extreme slowing of respiration and pulse, ending fatally. Seventy-five grains (5 Gm.) given to man have produced no more serious effect than cyanosis with some lessened frequency of respiration. Kryofine can be detected in the urine from fifteen to twenty minutes after taking, disappearing in from six to eight hours. (Ebstein.) In doses of from two and one-half to twenty-five grains it has been strongly commended as an analgesic for *pains* of purely nervous origin and antipyretic in various *fevers*, as less dangerous, though acting more slowly, than other allied drugs.

The range of action of kryofine appears to be that of acetphenetidin. The assertion that it is less dangerous than that drug seems hardly to be sustained by the facts; depression and cyanosis have been produced by it in various cases. The usual *dose* is eight to fifteen grains (0.5–1.0 Gm.). In the feeble, great caution is necessary in its employment.

Kryogenin. *Meta-benzamino-semicarbazide.* $C_6H_4(CO.NH_2)(NH.NH.CO.NH_2)$.—This is a colorless, odorless, slightly bitter powder, soluble in forty parts of water, more freely in alcohol. It is asserted by Lumière (*Ph. Post*, 1903, 7) to be an antipyretic of value, especially used in *tuberculosis*, producing, it is said, a rapid fall of temperature without unpleasant symptoms. *Dose*, ten to twenty grains (0.6–1.2 Gm.) in capsules.

Labdanum. *Ladanum.*—A resinous substance, obtained from various species of *Cistus* (Fam. *Cistaceæ*), especially *C. creticus* L., *C. ladaniferus* L., *C. cyprius* Lam., and *C. laurifolius* L., small evergreen shrubs, inhabiting the islands of the Grecian Archipelago, and the different countries bordering on the Mediterranean. Upon the leaves and branches of these shrubs a juice exudes, which is collected by means of an instrument resembling a rake, with leather thongs instead of teeth, which is drawn over the plant. The juice adheres to the pieces of leather, and is afterwards separated. It is said that labdanum was formerly collected by combing the beards of goats which had been browsing upon the leaves of the cistus, and Landerer states that it is still gathered in Cyprus from sheep and goats whose fleeces become loaded with it while they are pasturing. (See *P. J.*, xi, 6; xv, 301; xvi, 386, 779.) It comes chiefly from the Grecian Islands. Two varieties exist in commerce. The purest labdanum is in masses of various sizes, sometimes weighing several pounds, enclosed in bladders, dark red, almost black externally, grayish internally when first broken, of the consistence of a plaster, softening in the hand and becoming adhesive, of an agreeable balsamic odor like that of amber, and of a bitter, balsamic, somewhat acrid taste. It is very inflammable, burning with a clear flame. On exposure it becomes dry, porous, and brittle. Little of this variety is found in the markets. Common labdanum is in contorted or spiral pieces, light, porous, blackish-gray, hard and brittle, not softening between the fingers, similar in odor and taste to the preceding variety, but less inflammable, and mixed with sand and other earthy matters, which are obvious to the sight. Guibourt found in 100 parts of the labdanum in masses, 86 parts of resin with a little volatile oil, 7 of wax, 1 of aqueous extract, and 6 of earthy substances and hair. In the contorted variety, Pelletier found 20 per cent. of resin, 3.6 of gum with calcium malate, 0.6 of malic acid, 1.9 of wax, 1.9 of volatile oil, including loss, and 72 of a ferruginous sand. Schimmel & Co. (*Schim. Rep.*, April, 1893) state that they obtained from labdanum resin 0.91 per cent. of a golden-colored essential oil having the penetrating odor of ambergris. Its sp. gr. is 1.011 at 15° C. Labdanum is a stimulant expectorant, formerly given in *catarrh* and *dysentery* and sometimes used in plasters.

Lac. *Lacca. Resina* (*Gummi*) *Lacca. Laque, Gomme lacque*, Fr. *Lack, Gummilack*, G.—A resinous substance obtained from several trees growing in the East Indies, India and Burma, particularly from *Croton laccifera* L. (Fam. *Euphorbiaceæ*); several species of *Ficus*, especially *F. religiosa* L. and *F. indica* L. (Fam. *Moraceæ*), *Schleichera trijuga* Willd. (Fam. *Sapindaceæ*), *Butea frondosa* Roxb., *Acacia arabica* Willd. and *Cajanus indica* Spreng., of the Fam. *Leguminosæ*, and *Zizyphus jujuba* Lam. (Fam. *Rhamnaceæ*). Stillman states that *Acacia Greggii* A. Gray (Fam. *Leguminosæ*) and *Covillea tridentata* (DC.) Vail. (*Larrea mexicana* Moric.) (Fam. *Zygophyllaceæ*), plants growing in Arizona, Colorado, and the Western territories, furnish both *shellac* and *lac dye*. (*A. J. P.*, 1880, 409.) *Lac* is found in the form of a crust, surrounding the twigs or extreme branches, and is generally supposed to be an exudation from the bark, owing to the puncture of an insect belonging to the genus *Coccus*, and denominated *C.* (*Tachardia*) *Lacca* Kerr (Fam. *Coccidæ*). Several varieties are known in commerce. The most common are *stick-lac, seed-lac* and *button lac.*

Many theories have been advanced to account for the formation of this substance, some claiming the resin to be secreted by the insects, others by the plant as a result of an irritation caused by the insects. According to C. S. Misra (*Pharm. Era*, 1919, lii, 95), lac is a secretion produced by a scale insect which sucks the juice of plants. The sap thus taken into the body being greatly transformed and given out uniformly through pores all over the body in the form of resin, which after a few days incases the insect completely. The lac-bearing branches are cut off and placed on trees having a sufficient number of succulent branches. When the young insects have swarmed out the old lac-bearing branches are removed and the resinous incrustation (stick-lac) is scraped off with a knife, ground in a mill, soaked in water and washed. The pure animal resin (seed-lac) thus obtained is mixed with colophony and orpiment, cooked over a slow fire and drawn out into thin sheets, in which form it is commercially known as shellac.

Most of the host plants of the lac insect belong to the *Leguminosæ.* All of these are said by Hassen to contain tannins, gums and substances like hydroxyacids. Tannin is asserted to be essential for the production of gums and so of lac. The lac insect lives upon sweet bacterial gums produced by tissue destroying bacteria.

Stick-lac is the resin as taken from the tree, still encrusting the small twigs around which it originally concreted. It is of a deep reddish-brown color, of a shining fracture, translucent at the edges, inodorous, and of an astringent, slightly bitterish taste. Its external surface is perforated with numerous minute pores, as if made by a needle, and when broken it exhibits many oblong cells, containing the dead insects which contain coloring matter. When chewed it colors the saliva red, and when burnt, diffuses a strong, agreeable odor. It is in great measure soluble in alcohol. It contains as its chief constituents resin, wax and coloring matter.

Seed-lac consists of minute irregular fragments, broken from the twigs and partially exhausted by water. It is of a light or dark brown color, inclining to red or yellow, feebly shining, almost tasteless and capable of imparting to water less color than the stick-lac, sometimes scarcely coloring it at all. It is occasionally mixed with small fragments of the twigs.

Button-lac consists of flat cakes of the resin.

Shellac is a product of *lac.* It is prepared by melting the *stick-lac* or *seed-lac*, previously deprived of its soluble coloring matter, with a small amount of orpiment and resin, straining it, and pouring it upon a flat smooth surface to harden, or pulling it out by hand into large thin orange-colored sheets, which are broken up after cooling.

According to John, lac consists of resin, coloring matter, a peculiar principle insoluble in alcohol, ether, or water, called *laccin*, a little wax, and various saline matters in small proportion. The resin, according to Unverdorben, consists of several distinct resinous principles differing in their solubility in alcohol and ether. The laccin is nearly or quite wanting in shellac, which also contains scarcely any of the coloring principle.

Stick-lac varies in its constituents according to Hassen (*A. J. P.*, 1922, p. 131), depending upon the tree from which it is obtained. When the lac insect is propagated on *Schleichera trijuga*, the product known as *Koosam-lac* is formed. This is claimed to be the richest source of shellac, containing 70 to 80 per cent. of resin. Most of the Koosam-lac comes from the central provinces of Western Bengal. Hatchett found in stick-lac 68 per cent. of resin, and 10 of coloring matter; in seed-lac 88.5 per cent. of resin, and 2.5 of coloring matter; in shellac 90.9 per cent. of resin, and 0.5 of coloring matter. The other constituents, according to this chemist, are wax and gluten, besides foreign matters. R. E. Schmidt (*Ber. d. Chem. Ges.*, 1887, 1285–1303) has prepared the lac dye in a pure crystallized state. He gives it the formula $C_{16}H_{12}O_8$ and calls it *laccaic acid.* It was obtained crystallized from ethereal solution. Caustic alkalies dissolve it, giving a magenta color. Baryta water forms a violet lake. Laccaic acid shows some analogy to carminic acid, but the colors they give on wool and silk are different. Laccaic acid is decomposed on heating with concentrated hydrochloric acid to 180° C., as well as on fusing with caustic potash.

Japanese lac from *Rhus vernicifera* was examined by A. B. Stevens. (See *Proc. A. Ph. A.*, 1905, 311.)

Lac in its crude state is slightly astringent, and was formerly used in medicine, but at present it is not employed. Shellac is wholly inert, unless contaminated with an arsenic compound, which is sometimes used to give it color. It is sometimes used in alcoholic solution as a glaze for confectionery. The use of such insoluble resinous glaze for a food product is prohibited in some states partly on account of its indigestibility *per se* and partly because in its preparation for varnish or pigment purposes arsenical compounds are used to heighten the color and many instances are on record where confectionery which had been coated with such glaze contained appreciable amounts of arsenic. A bleached form of arsenic-free lac has recently appeared in commerce, which would seem to be free from many of the objections previously urged against lac in coating confectionery. Stick-lac and seed-lac are used on account of the coloring principle which they contain. Shellac, as well as the other varieties, deprived of their coloring matter, is applied to numerous purposes in the arts. It is the chief constituent of *sealing wax.* The best red sealing wax is made by melting together, with a very gentle heat, 48 parts of shellac, 19 of Venice turpentine, and 1 of balsam of Peru, and mixing with the melted mass 32 parts of finely powdered cinnabar. But common rosin is often substituted in part for the lac, and a mixture of red lead and chalk for the cinnabar. For methods of detecting adulteration with rosin see *J. Soc. Chem. Ind.*, 24, 1905; also *Chem. Ztg.*, 1910, 991. The best black sealing wax consists of 60 parts of lac, 10 of turpentine, and 30 of levigated bone black; the best yellow sealing wax, of 60 parts of lac, 12 of turpentine, and 24 of lead chromate. (Berzelius.) Lac is also used as a varnish, and forms an excellent cement for broken porcelain and earthenware. It may be dissolved in alcohol, oil of turpentine, benzin, or naphtha. Lac has been highly recommended as an adhesive material for the dressing of *wounds, ulcers*, etc. It is prepared for use by dissolving, with the aid of a gentle heat, in alcohol contained in a bottle, sufficient lac to give it a gelatinous consistence, and then closing the bottle. It is used by spreading it on the bandages. For details of the preparation of shellac, see *U. S. D.*, 19th ed., p. 1543.

Lactagol.—Under this name has been introduced an extract from cotton seed. It occurs as a yellowish-white powder, which emulsifies when rubbed up with water.

Lactagol has been used for the purpose of increasing both the quantity and quality of milk in nursing women. According to Barlerin (*R. T.*, 1906, p. 393), it causes a marked increase in the percentage of fat and also of casein. Abramof (*Cb. G. T.*, 1906, p. 548) noted an increase in the quantity of milk with no change in its composition. Contrary to these experiences, Bruhn (*Ther. Neu.*, June, 1908, p. 161) was unable to notice any decided effect upon the lacteal glands.

Lactanin. *Bismuth Dilacto-monotannate.*—This is a yellow, odorless, tasteless powder, insoluble in water, which has been used in *doses* of three to five grains (0.2–0.32 Gm.) in *tubercular* and other *chronic diarrheas* of young children.

Lactic Acid Therapy.—It is a well known fact that most of the pathogenic bacteria do not grow well in acid medium. The late Professor Metchnikoff conceived the theory that many systemic disorders were due to the absorption of poisons formed by intestinal putrefaction and believed that the freedom of certain Balkan peoples from this group of diseases was due to their habit of drinking fermented milks which produced an acidity in the lower bowel. He attempted, therefore, to implant into the colon a lactic acid forming bacteria. For this purpose he chose the *Bacillus Bulgaricus*, the starter used by the Bulgarians to produce their fermented milk, *yoghurt* (see *Kephir*). This micro-organism is not a normal inhabitant of the intestinal canal and clinical experience has shown that it is very difficult, if not impossible, to produce a growth of it in the intestines. Various other acid forming bacteria have therefore been employed. Among these are the *B. Paralacticus, B. Bifidus* and *B. Acidophilus.* At present the last named is enjoying the greatest favor.

These bacteria are furnished commercially in three forms. (1) In the form of inoculated milk. This should contain, according to the standards of the *N. N. R.* 1924, not less than 50 million viable organisms per cc. It is, theoretically, the most rational form of administration because these bacteria grow best in a milk culture and require lactose in order to produce lactic acid. Bacillus acidophilus milk if properly made (that is, sterilized before implantation) may be stored for a week in a cool place without notable loss of efficacy. The ordinary dose of this milk is from one to three pints per day. (2) In the form of broth cultures. The latter are of two types: those intended for the home manufacture of inoculated milk and those that are intended to be taken as dispensed. These cultures should be marked with an expiration date beyond which they are not to be used and should be stored in a cold place. Most of them are given in doses of from one to three teaspoonfuls. It is advisable that milk sugar be administered simultaneously. (3) In the form of tablets. Although this would manifestly be the most convenient method for administering these bacteria, there is considerable doubt as to how long the lactic acid bacteria retain their viability in the dry state. Certain it is that many of the tablets of this nature contain practically no living organisms. Still another form is the agar jelly chocolate-coated block, each one of which contains as many viable organisms as a pint of acidophilous milk. The disadvantage of these is their instability and their tendency to mould.

On account of their antagonism to tissue-destroying bacteria, lactic-acid bacteria have been suggested and used as application to diseased surfaces and membranes of the body.

Cultures of lactic acid bacteria should be kept cold and used when fresh. Many inert products of this class have been placed on the market, but by shortening the date of expiration and improving the medium in which they are suspended, the manufacturers have largely succeeded in eliminating this defect. Cultures may be tested for activity and relative purity by inoculating sterilized milk and incubating at 37° C. for 24 to 72 hours to determine whether acid is produced without putrefactive odors or taste; strict aseptic precautions should be used throughout.

Lactucarium. *U. S. IX. Lettuce. Lactucarium Anglicum, Lactucarium Germanicum; Strong-scented Lettuce, Green Endive; Laitue virense,* Fr.; *Giftlattichsaft,* G.; *Lactucario,* Sp.—The plants of the genus *Lactuca* of *Compositæ* yield when wounded a milky-juice, to which, indeed, they owe their generic name. Narcotic properties have been attributed to the juice from several species including even the *Lactuca sativa* L., or *garden lettuce,* but only the *L. virosa* L. (strong-scented lettuce) is employed in medicine. This plant, whose dried juice was formerly official, is a biennial, with a stem from two to four feet high, erect, prickly near the base, above smooth and divided into branches. The lower leaves are large, oblong-ovate, undivided, toothed, commonly prickly on the under side of the midrib, sessile, and horizontal; the upper are smaller, clasping, and often lobed; the bracts are cordate and pointed. The flowers are numerous, of a sulphur-yellow color, and disposed in a panicle. The plant is a native of Europe.

It is lactescent, and has a strong disagreeable odor like that of opium, and a bitterish, acrid taste. Under the name of *thridace* the French Codex at one time recognized the expressed juice of the whole plant.

Lactucarium is cultivated in Scotland, Germany, Austria and France. It was officially described as follows: "Usually in quarter sections of hemispherical masses, or in irregular, angular pieces; externally dull reddish- or grayish-brown; fracture tough, waxy; internally light brown or yellowish, somewhat porous; odor distinctive, opium-like; taste bitter. Lactucarium is partly soluble in alcohol and ether and, when triturated with water, it yields a turbid mixture. Treat Lactucarium with boiling water and filter; the filtrate is clear while hot; on cooling it becomes turbid but clears upon the addition of ammonia water or alcohol; it is not colored blue by iodine T.S. (*starch*). An alcoholic solution of Lactucarium gives not more than a faint green color upon the addition of a drop of ferric chloride T.S. (*tannin*). The powder is grayish-brown to dark brown, consisting almost entirely of irregular fragments without any cellular structure: when mounted in hydrated chloral T.S., the fragments become clear, showing granular fragments, and from this deposit, numerous rod-shaped crystals and broad monoclinic prisms as well as aggregates of these, all of which polarize light. In the preparation of powdered Lactucarium, dry the crude drug at a temperature not exceeding 70° C. Lactucarium contains not more than 15 per cent. of moisture, and yields not more than 10 per cent. of ash." *U. S. IX.*

The drug of commerce usually has a growth of mold on the surface. If it has penetrated the drug to any extent it reduces its quality. Occasionally specimens are met with that are moldy throughout, and these should be rejected. In color, taste, and odor, lactucarium bears considerable resemblance to opium; and has been used to adulterate that drug; it is sometimes called *lettuce opium.* It yields nearly half its weight to water, with which it forms a deep-brown infusion. It is partly soluble in ether and alcohol.

From its resemblance in some of its properties and to opium, it was conjectured to contain morphine, or some analogous principle, but this conjecture is false. There is no doubt as to the complexity of the composition of lactucarium, but so feeble are its properties that it has largely gone out of active use, and its chemistry is of little practical importance.

About one-half of lactucarium is made up of a colorless, odorless and tasteless, crystallizable substance—*lactucerin* (*lactucon*). This substance fuses at 210° C., is soluble in ether and hot alcohol, but is not a fat. According to Hesse it is a mixture of the mono-acetyl and di-acetyl esters of *alpha-* and *beta-lactucerol,* $C_{18}H_{30}O$. Various bitter principles have also been described, namely *lactucin, lactucic acid* and *lactucopicrin;* there is, however, considerable uncertainty as to whether these substances are really proximate principles, and there is no evidence that any of them possess therapeutic activities.

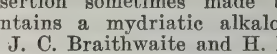
The assertion sometimes made that *Lactuca virosa* contains a mydriatic alkaloid has been denied by J. C. Braithwaite and H. E. Stevenson, *P. J.*, 1903, 148. Farr and Wright (*P. J.*, 1904, p. 16) claim, however, to have definitely established the presence of a mydriatic alkaloid, giving alkaloidal reactions with Mayer's and Thresh's reagents, and producing a powerful mydriatic effect upon the eye.

For an examination of *Russian lactucarium,* by L. Schiperovitch, see *Ph. Z. R.*, or *D. C.*, 1886.

Uses.—The ancients believed that lettuce had soporific properties, a superstition which has survived up to modern times probably because of the similarity to opium in appearance and odor. It has been employed in this country to some extent to allay *cough* and quiet *nervous irritation,* but what benefit is derived is probably purely psychical. One of the widely used proprietary preparations of lactucarium of former years owed its activity to morphine, which was later declared upon the label until its use died out.

Dose, ten to twenty grains (0.65–1.3 Gm.), but much larger quantities may be given without obvious effects.

Lactophenin. *Lactyl-p-phenetidin.*



$$C_6H_4\begin{cases}OC_2H_5\\NH.CO.CH.(OH).CH_3.\end{cases}$$

—A white crystalline powder, without odor, having a feeble bitter taste, soluble one part in five hundred of cold water, one in eight and a half parts of alcohol, and having a melting point of from 117.5° to 118° C. It is produced by the action of lactic acid on phenetidin in the presence of dehydrating substances, the lactic acid radical replacing the acetic acid radical of acetphenetidin.

We have very little definite knowledge in regard to the physiological action of lactophenin, but it is improbable that it differs materially in its effects from acetphenetidin. Some assert, however, that it has a somnifacient effect and it is also affirmed to be valuable in *rheumatism*, having specific curative properties inferior to but resembling those of the salicylates.

The statements which have been made that its use is free from danger are, however, not correct. It sometimes produces an exanthematous eruption, which may be macular or diffuse. Wenzel (*Cb. I. M.*, xvii, 1896) reports a case in which after the patient had been taking, for two weeks, fourteen grains of lactophenin a day, there was suddenly developed violent jaundice, with dark brown urine, without fever or slowing of the pulse, with colorless stools. Similar cases had been previously recorded by Franz Rield (*Zeitsch. f. Heilk.*, xvi, 1895). Kronig (*B. K. W.*, 1895) has reported a case of poisoning, with methemoglobin and cyanosis, followed by death. Lactophenin is eliminated, at least in part, by the urine as a paramidophenol.

Lactophenin may be given in *doses* of from five to twenty grains (0.32–1.3 Gm.), repeated in special cases up to a drachm and a half (5.8 Gm.) in a day.

Lakes.—These colors are compounds of vegetable or animal coloring principles with alumina or other metallic oxides, and are usually obtained by adding alum or stannic chloride to the solution of the coloring matter in water, and precipitating by means of an alkali. The alumina or stannic oxide unites with the phenolic bodies in coloring matter at the moment of separation, and forms an insoluble compound, usually of a very bright color. *Lakes* are obtained in this way, from cochineal, madder, Brazil wood, seed-lac, French berries, etc. (See also *Carminum*, Part I.)

Lamium. *Lamium album* Hart. (*L. maculatum* L.) *White Dead Nettle.* (Fam. *Labiatæ.*)—A hairy perennial herb introduced from Europe and found on roadsides and waste places in the United States. Hemostyptic properties were long since attributed by Lusitanus and by Florain to the flowers of this plant, and, according to the more recent researches by Kalabin (*Cb. G. T.*, xx, No. 12), their decoction produces a rise of the arterial pressure due to contraction of the peripheral vessels. The extract was found to cause firm, lasting contraction of the uterus, and the saturated tincture, in *doses* of twenty-five to forty minims (1.6–2.5 cc.) every two or three hours, to be useful in *hemorrhagic metritis* and *metrorrhagia.* Its effects in puerperal hemorrhage were not pronounced.

Lantana. *Lantana brasiliensis* Link. *Yerba Sagrada.* (Fam. *Verbenaceæ.*)—This Brazilian plant contains, according to Negrete, an alkaloid, *lantanine,* which is actively antiperiodic in *doses* of from fifteen to thirty grains (1.0–2.0 Gm.) in the twenty-four hours, given directly after the paroxysm. It is also claimed to be an intestinal antiseptic. (*T. G.*, 1885.) *Lantana camara* L., a small shrub, known in the West Indies as *sage tree* or *wild sage*, contains an alkaloid, *lantanine,* said to resemble quinine in its action.

Lanthanum Nitrate.—*Lanthani Nitras,* $La_2(NO_3)_6.12H_2O$, occurs in large rose-colored prisms which are soluble in water and alcohol. This salt is employed as an antiseptic, preventing the growth of bacteria when used in solutions of the strength of 1 in 2000. (See *Cb. B.*, 1897, xxi.)

Lanthanum Oxide. La_2O_3.—The oxide of lanthanum is an almost white, amorphous compound easily soluble in diluted mineral acids and insoluble in water. It is used as a source of production for other lanthanum salts and technically instead of calcium oxide in oxyhydrogen lights, being, it is said, superior to calcium oxide in many respects.

Lanthanum Oxalate is found in the mixture known officially as *Cerii oxalas* (see Part 1).

Larch Bark. *Laricis Cortex. Br.* 1885. *Ecorce de Mélèze,* Fr. *Lärchenrinde,* G.—The bark of *Larix decidua* Mill. (*Larix europæa* DC.) (Fam. *Pinaceæ*).

The European Larch is a deciduous tree attaining a height of 100 ft. with pyramidal to irregular crown, dark, grayish-brown bark, smooth, yellowish branchlets, soft, compressed, narrow, bright green leaves and purplish pistillate flowers. Its cones are up to 1¼ ins. long and possess nearly orbicular scales. The bark found by Aldridge to contain gum, starch, resin, and tannic acid of the kind which precipitates the salts of iron olive-green. John Stenhouse has obtained from it a peculiar volatile acid, *larixinic acid,* $C_{10}H_{10}O_5$ (*larixine*). For method of separation, see 16th edition, *U. S. D.* Larixinic acid occurs in beautiful white, lustrous crystals, often more than an inch long, of a peculiar somewhat empyreumatic odor, and a slightly bitter and astringent taste, inflammable, volatilizing at 93° C. and melting at 153° C., soluble in 87.88 parts of water at 13.3° C., very soluble in boiling water, soluble in cold but much more so in hot alcohol, and sparingly soluble in ether. It readily crystallizes from its solutions. A very singular and characteristic property is that of forming, when added, in strong solution, in excess, to baryta water, a bulky, transparent, gelatinous precipitate occupying the whole measure of the liquids if concentrated. The inner *larch bark* possesses astringent and gently stimulant properties, and is supposed to have a special tendency to the mucous membranes. It has been found particularly efficacious in *purpura* and other *hemorrhagic affections,* especially *hemoptysis,* and has been given in *bronchitis* with copious expectoration, and in diseases of the urinary passages. It has been used also, mixed with soap and glycerin, as a local remedy in *psoriasis, chronic eczema,* and other cutaneous affections. Of the extract from three to five grains (0.20–0.32 Gm.), of the tincture from thirty minims to a fluidrachm (1.8–3.75 cc.) or more may be given every three or four hours.

Lard Oil. *Oleum Adipis. U. S. VIII. Huile de Graisse,* Fr. *Schmalzöl, Specköl,* G.—"A fixed oil expressed from lard at a low temperature." *U. S. VIII.*

Lard oil is made in large quantities in this country by exposing lard to low temperatures and then subjecting it to very powerful pressure. In this way the stearin of the lard is separated from the olein, the latter oozing out from the presses in the form of a yellowish-white oil, while the stearin is found in the market in hard cakes, and is largely used in making soap. (See *Adeps.*)

Lard oil is "a colorless or pale yellow, oily liquid, having a peculiar odor and a bland taste. Specific gravity: 0.905 to 0.915 at 25° C. At a temperature a little below 10° C., it usually commences to deposit a white, granular fat, and at or near 0° C., it forms a solid white mass. Lard oil is almost insoluble in cold alcohol and only slightly soluble in boiling alcohol; easily soluble in ether, chloroform, benzene, and carbon disulphide. If 5 cc. of the Oil be thoroughly shaken in a test-tube with 5 cc. of an alcoholic solution of silver nitrate (made by dissolving 0.1 Gm. of silver nitrate in 10 cc. of alcohol, and adding 2 drops of nitric acid), and the mixture heated for about five minutes on a water-bath, the Oil should remain nearly or quite colorless, not acquiring a reddish or brown color (absence of more than about 5 per cent. of *cotton seed oil*). The Oil should be completely saponifiable with alcoholic potassium hydroxide T.S. and the resulting soap should be completely soluble in water, without separation of an oily layer (absence of *mineral oils*). If 2 cc. of Lard Oil be mixed in a test-tube with 2 cc. of equal volumes of amyl alcohol and carbon disulphide containing 1 per cent. of sulphur in solution, and the test-tube be immersed to one-third or one-half its depth in boiling salt water, no reddish color should develop in from ten to fifteen minutes (absence of *cotton seed oil* or of *certain other fats*)." *U. S. VIII.* Lard oil should show a saponification value of 195 to 197 and an iodine value between 56 and 74. It is not pure olein, but contains varying proportions of stearin, and is sometimes adulterated with paraffin oil. It was introduced into the U. S. P., 1880, for the purpose of rendering the ointment of mercuric nitrate softer and smoother in consistence, but it was not retained in the process of the U. S. P. IX, mainly owing to the difficulty of obtaining it of sufficient purity in commerce.

Lathyrus. *Lathyrus sativus* L. (Fam. *Leguminosæ.*) *Vetchling. Jarosse, Kasari* (Ind.).—The *White* or *Chickling Vetch*, the seed of which is used in Europe as a food both by man and animals, under the name of "*mutters*," produces, when taken too freely, a condition known as *lathyrismus.* Horses which have been fed on the plant for a considerable period drop while performing the lightest work, in consequence of paralysis of the hind extremities, and in many cases death has followed from bilateral paralysis of the recurrent laryngeal nerves and consequent asphyxia. This laryngeal affection does not occur in the human subject, and death very rarely takes place. In man the muscles of the lower extremities below the knee are apt to be especially affected, the abductors more than the adductors. The muscles of the face, neck, and upper extremities are very rarely, if ever, attacked. The reflexes and the general sensibility are usually not influenced; but Giorgieri has seen the tendon reflexes increased. According to Cantani, the galvanic contractility of the paralyzed muscle is altered, and the transverse markings of the muscles are nearly obliterated by fat globules. In fatal cases the spinal cord has been found normal. Astier obtained from the seeds a poisonous, alkaline, volatile liquid. According to him, this, being volatile, is not present in preparations such as pressed cakes made at a high temperature, which are consequently not poisonous. If, however, such cakes have been prepared at low temperature, they exhibit toxic properties, owing to the retention of the toxic principle. This is in conformity with the experience of the peasants in some parts of Europe, who mix the ground white-vetch seeds with wheat flour, and boil the mixture for food. E. M. Holmes states that these seeds should not be used in foods in any proportions, as they are poisonous. (*P. J.*, 1913, 795.) Stockman (*Ed. M. J.*, 1917, xix, 285) found in the seeds an alkaloid which paralyzed both the central nervous system and the peripheral motor nerves. Dilling (*J. P. Ex. T.*, 1919, xiv, 359) separated two alkaloids both of which appear to paralyze the central nervous system, including brain and spinal cord, and lower the excitability of muscle substance, one being also depressant to the peripheral motor nerves. Betaine and choline have both been reported present.

The *common vetch*, or *tare* (*Vicia sativa* L.), closely related to the above, is a troublesome weed in grain fields. The *V. ervilia*, or *black vetch* has long been known to be toxic; Wilcez and Tschumi (*Schweiz. Ap. Ztg.*, 1919) have reported on its pharmacognosy.

Laurotetanine.—This alkaloid, found in various of the *Lauraceæ* especially *Litsea* species, is said to be a powerful poison, acting like strychnine on the spinal cord. It gives with Froehde's reagent an indigo-blue color, which on the addition of water changes to yellow; with Erdmann's reagent, a transitory bright blue color, becoming brown, and with more nitric acid, it gives immediately a bright red-brown, and with pure nitric acid a dirty brown. It is soluble in excess of alkali. (*P. J.*, vol. xxi, 1891.)

Laurus. *Laurus nobilis* L. *Sweet Bay. Laurier commun,* Fr. *Lorbeer,* G.—The *sweet bay* is an evergreen tree of the Fam. *Lauraceæ*, inhabiting the countries bordering on the Mediterranean. It produces yellow flowers in early spring and later succulent, purple berries. The leaves are alternate, on short petioles, ovate-lanceolate or oblong, entire, pellucid-punctate, of a firm texture, smooth, shining, deep green upon their upper surface, paler beneath. They have a fragrant odor, especially when bruised, and a bitter, aromatic, somewhat astringent taste. They yield by distillation a greenish-yellow volatile oil which contains pinene, phellandrene, cineol, l-linalool, geraniol, eugenol and methyl eugenol; also acetic, isovaleric, and isobutyric acids and esters. The sp. gr. is 0.915–0.930; Opt. Rab. −15° to −22°; ref. ind. 1.4670 to 1.4775; acid number 1 to 3 and ester number 20 to 50. The volatile oil, of which the fruit yields 0.23 per cent., has a sp. gr. 0.88, and is solid at 0° C. (*Schim. Rep.*, April, 1897.) Water distilled from the leaves has their peculiar odor. The berries (*Fructus Lauri*) when dried are black and wrinkled, and contain two oval fatty seeds within a thin, friable envelope; or they may be considered as drupes, with a kernel divisible into two lobes. They have the same aromatic odor and taste as the leaves, but are more pungent. They contain besides a volatile oil, a fixed oil (*Oleum Lauri Expressum*), which, as obtained by expression from the fresh fruit, is of a greenish color, and aromatic odor from retained volatile oil. One of its chief constituents is the glyceryl ester of *lauric acid*, the so-called *laurostearine*, $C_3H_5(C_{12}H_{23}O_2)_3$, which fuses at 45° C. The free acid may be obtained from this by saponification. It cannot be distilled without decomposition. Another constituent of the crude fat is *laurin*, $C_{22}H_{30}O_3$, which can be extracted by alcohol. It forms neutral, easily fusible prisms without odor or taste. Lard, impregnated with the odorous principle of the berries, and colored green by chlorophyll or sometimes by indigo and turmeric, is said to be often substituted for the genuine expressed oil. This may be detected by boiling alcohol, which dissolves the true oil. The leaves, berries, and oil are excitant and narcotic, but are rarely used internally as medicines, and in this country are scarcely employed in any manner. E. M. Holmes, however, states that the berries have been used in Europe to promote miscarriages. (*P. J.*, 1910, 52.) Their chief use is to communicate a pleasant odor to external remedies. The leaves are also used for culinary purposes in communicating their aromatic flavor to soups, stews, etc. They come into commerce frequently as the packing around stick licorice extract from Mediterranean countries.

Lavender Flowers. *Lavandula. U. S.* 1880. *Lavandula vera* DC. (*L. officinalis* Chaix, *L. spica* L.) *Flores lavandulæ*, P. G. *Lavande, Fleurs de Lavande*, Fr. *Lavandelblüthen*, G. *Lavendola*, It. *Espliego Alhucema*, Sp.—Lavender is a small, labiate shrub with sessile, opposite, entire, linear, revolute leaves and terminal spikes of small, fragrant, lavender-colored, bi-labiate flowers. The plant is a native of Mediterranean regions, and covers vast tracts of dry and barren land in Spain, Italy, and the south of France. In England and America it is very largely cultivated. A number of cultural varieties have been produced. The cultivation of lavender has become an important industry and attempts are being made to cultivate the finer qualities of lavender in the United States. For details of lavender culture, see *U. S. D.*, 19th edition, p. 1546.

Lavender flowers have a strong fragrant odor, and an aromatic, warm, bitterish taste. They retain their fragrance long after drying. Alcohol extracts their virtues, and a volatile oil upon which their odor depends rises with that liquid in distillation. Hager obtained from a pound of the fresh flowers from half a drachm to two drachms of the oil. The flowers are frequently sold for packing away with clothing as a moth preventive. Most of the lavender flowers of commerce are obtained from France and England. Lavender is an aromatic stimulant and tonic, but is seldom given in its crude state. The products obtained by its distillation are much used in perfumery, and the volatile oil is official. (See *Oleum Lavandulæ*, Part I.)

Lawsonia. *Lawsonia inermis* L. (Fam. *Lythraceæ.*) *Henna Plant. Mehndi. Egyptian Privet.* —This is a shrub probably indigenous to North Africa and South Asia which is widely cultivated in tropical and sub-tropical countries, especially in Egypt, Persia, India, South Europe, West Indies, Florida and California. It is characterized by spinescent branches, opposite, ovate-lanceolate, entire, pale green leaves with acute apices and attenuated bases, small, 4-merous flowers arranged in panicles of cymes and globose, capsular fruits. The flowers vary from white (var. *alba* Hassk.) to cinnabar-red (var. *miniata* Hassk.) to rose-colored (pure species). Its leaves produce the well-known dye-stuff denominated *henna*, much used throughout the Mohammedan countries of the East. It is probably the substance referred to as *gopher* in the Old Testament. It is largely cultivated in Egypt. The flowers have a strong, pungent odor, and a distilled water prepared from them is used as a cosmetic. The fruit is thought to have emmenagogue properties. The powdered leaves, under the name of *henna* or *alhenna* are used to stain golden yellow the feet and hair of women of the harem. Abd-el-Aziz of Cairo, Egypt, found in it a brown substance, of a resinoid fracture, having the chemical properties which characterize the tannins and therefore named by him *hennotannic acid.* Tommasi (*D. C.*, 1921, lxv, 142) has isolated an oxynaphthoquinone which he claims is the dyeing principle. Henna has been employed both internally and locally, in *jaundice, leprosy*, and affections of the skin.

Most of the so-called henna hair preparations of the market owe their effect to other constituents than henna and a number do not even contain henna as an ingredient.

Lead Arsenate.—This is a white, heavy powder practically insoluble in water. It varies somewhat in composition but is approximately $PbHAsO_4$.

Lead arsenate is not used in medicine but is widely employed as an insecticide application to plants. Cases of chronic poisoning and serious disturbances to health have been ascribed to accidental poisoning from this agent from its use on plants.

Lead Carbonate. *Plumbi Carbonas, N. F. IV. Basic Lead Carbonate; Lead Oxycarbonate; Plumbi Carbonas; White Lead; Plumbum Carbonicum; Carbonas Plumbicus; Carbonate de Plomb, Céruse, Blanc de Plomb, Blanc de Ceruse*, Fr.; *Cerussa*, P. G.; *Bleiweiss*, G.; *Cerussa*, It.; *Albayalde o cerusa*, Sp.—The National Formulary IV recognized, under the title Plumbi Carbonas, "a mixture of lead carbonate and hydroxide [approximately, $(PbCo_3)_2Pb(OH)_2 = 775.32$]." *N. F. IV.*

Normal lead carbonate, $PbCO_3$, occurs in nature as *cerussite.* It may also be prepared by precipitating a solution of lead acetate with ammonium carbonate. It is little used either in the arts or medicine. The salt here referred to, basic lead carbonate, commonly called white lead, is prepared by several methods. By one method it is obtained by passing a stream of carbon dioxide through a solution of lead subacetate. The dioxide combines with the lead hydroxide of the basic salt, and precipitates it as lead carbonate, while a neutral acetate remains in solution. This, by being boiled with a fresh portion of oxide, is again brought to the state of basic salt, when it is treated with carbon dioxide as before. In this way the same portion of acetate repeatedly serves the purpose of being converted into subacetate and of being decomposed by carbon dioxide. The carbonate obtained is washed and dried with a gentle heat. This process, which produces white lead of the first quality, was invented by Thénard, about the year 1802, and is that which is usually pursued in France and Sweden, and known as the "Clichy process."

Another, called the "Dutch process" from its origin in Holland, consists in exposing lead to the vapor of acetic acid, and is the one usually pursued in England and the United States—but in England with some modifications. In this country the lead is cast into thin sheets which are rolled up so as to form cylinders five or six inches in diameter, and seven or eight high, each of which is placed in an earthen pot containing about half a pint of dilute acetic acid, and having within a few inches from the bottom three equidistant projecting knobs in the earthenware, on which the cylinder of lead is supported in order to keep it from contact with the acid. The pots thus prepared are placed side by side, in horizontal layers. The first layer is covered with boards, on which a stratum of tan-bark or of refuse straw from the stables is strewed, and fresh layers of pots, boards, and tan or straw are successively placed until the building is filled. The layers of pots are allowed to remain undisturbed for about six weeks, at the end of which time they are unpacked, and the cylinder of sheet lead in each pot, though still retaining its shape, is found almost entirely converted into a flaky, white, friable substance, which is the white lead. This is separated from the lead yet remaining in the metallic state, ground in mills in the presence of water and finally dried in long shallow reservoirs, heated by steam. Pelouze has succeeded in explaining these processes on one general principle. In Thénard's process it is admitted that the same portion of lead acetate unites with oxide, and gives it up again to carbon dioxide to form the carbonate. In the Dutch process the heat generated by the fermentation of the tan or straw volatilizes the acetic acid, which, with the assistance of the oxygen of the air, forms with the lead a small portion of subacetate. This, by reacting with the carbon dioxide resulting from the decomposition of the tan or straw, or derived from the atmosphere, forms lead carbonate, and is brought to the state of neutral acetate. The neutral acetate returns again to the state of subacetate and, by alternately combining with and yielding up the oxide, causes the whole of the lead to be finally converted into carbonate.

The temperature of the stacks of pots in the Dutch process is about 45° C. If it falls below 35° C., a part of the lead escapes corrosion, and if it rises above 50° C. the product is yellow. The "German" or chamber process differs from the Dutch process only in that the vessels containing the lead are placed in chambers having a perforated floor, through the openings of which the fumes of acetic acid rise acting upon the lead, while carbon dioxide from the burning of coke is passed in and through the chamber. This process is cheaper than the Dutch method, and is said to give an equally satisfactory product. In Carter's process, used in this country extensively, granulated metallic lead is moistened with acetic acid and submitted to the action of carbon dioxide gas in revolving barrels. A number of other methods have been suggested and used to a greater or less extent, but the Dutch process is the one most frequently employed.

The N. F. IV description was as follows: "A heavy, white, opaque powder, or as a pulverulent mass, without odor or taste; permanent in the air. Insoluble in water or alcohol, but dissolved by acetic acid or diluted nitric acid, with effervescence. When strongly heated it turns yellow without charring, and when heated in contact with charcoal it is reduced to metallic lead. Dissolve 2 Gm. of Lead Carbonate in a mixture of 2.5 cc. of nitric acid and 40 cc. of distilled water; not more than 0.01 Gm. of residue remains. Separate portions of this solution yield a black precipitate with hydrogen sulphide T.S.; a yellow precipitate with potassium iodide T.S.; and a white precipitate with diluted sulphuric acid. On completely precipitating 10 cc. of this solution with hydrogen sulphide, the filtrate, on evaporation, leaves not more than 0.01 Gm. of residue. Ignite 1 Gm. of Lead Carbonate in a porcelain crucible; it leaves a residue of lead oxide weighing not less than 0.83 Gm." *N. F. IV.*

It is sometimes adulterated with barium, calcium, and lead sulphates, particularly the first. A mixture of equal parts of white lead and barium sulphate is known as *Venetian white*, while *Hamburg white* is a mixture of 1 part of white lead and 2 parts of barium sulphate, and *Dutch white* of 1 part to 3 of barium sulphate. Louyet has examined samples of French white lead containing considerably more than half their weight of barium sulphate. Barium sulphate, if present, is left undissolved by nitric acid. Chalk or whiting is another adulteration. This may be detected by adding to the nitric solution of the white lead an excess of potassium hydroxide which will redissolve the lead monoxide first thrown down but leave a white precipitate of calcium hydroxide.

Uses.—White lead is largely used in the arts, especially in the preparation of paints. In medicine it has been employed externally as an astringent and protective application to *ulcers, excoriated surfaces, burns*, etc. Its free continued external use has produced lead poisoning and it has been, therefore, largely abandoned for less dangerous agents. Painters, and others whose work brings them in contact with this substance, are frequently victims of chronic lead poisoning (see *Plumbum*, Part I).

Lead Chloride. *Lead Chloride, Horn Lead.*—Lead chloride may be obtained by adding hydrochloric acid to a solution of lead acetate, until completely precipitated, collecting the precipitate on a filter and washing with distilled water. It occurs as a white crystalline powder, soluble in about 140 parts of water, permanent in the air, and with a sweetish, astringent taste. When heated it fuses and cools to a horny, translucent mass (*plumbum corneum*). It is completely soluble in strong hydrochloric acid from which it is precipitated by the addition of water.

The pigments known as *Turner's yellow, Paris* or *Cassel yellow* are mixtures of lead chloride and oxide. They are prepared by heating together the oxide, or carbonate, of lead with the chloride.

Lead chloride was formerly used as an astringent, caustic application to ulcerative epitheliomata, but it has almost completely gone out of use.

Lead Nitrate. *Plumbi Nitras. U. S. VIII. Nitrate of Lead. Nitras (Azotas) Plumbicus. Azotate de Plomb, Nitrate de Plomb*, Fr. Cod. *Salpetersaures Bleioxyd, Bleisalpeter*, G. *Nitrato di piombo*, It. *Nitrato plumbico, Nitrato de Plomo*, Sp. $Pb(NO_3)_2 = 331.12$.—Lead nitrate occurs in "colorless, transparent, octahedral crystals, when obtained by the spontaneous evaporation of cold solutions, or white, nearly opaque crystals, when formed by the cooling of hot solutions; without odor, and having a sweetish, astringent, afterwards metallic, taste; permanent in the air. Soluble in 1.85 parts of water at 25° C., and in 0.75 part of boiling water; almost insoluble in alcohol. When strongly heated, the salt decrepitates, emits nitrous vapors, and finally leaves a residue of lead oxide." *U. S. VIII.* It is largely used in dyeing and calico printing, for the preparation of mordants, and of chrome yellow.

Lead nitrate possesses the astringent and antiseptic properties of the soluble lead salts, but has largely passed out of vogue. It is occasionally applied to excoriated surfaces, and a solution made in the proportion of ten grains to an ounce of water, and colored probably with alkanet, has been used on the continent of Europe as a secret remedy in *sore nipples, chapped hands, cracked lips*, etc. *Ledoyen's disinfecting fluid* is a solution of *lead nitrate* in the proportion of a drachm to an ounce. Moerlonge and Vanzette ascribe remarkable efficiency to lead nitrate in *onychia maligna*, and their statements have been confirmed by other practitioners. It is applied by sprinkling the powder on the surface, and, according to J. Scott, of Belfast, Ireland, a complete cure may be relied on in from fourteen to thirty days.

Dose, one-fourth to one-half grain (0.016–0.032 Gm.).

Lead Oleate. *Diachylon.*—By precipitating a solution of sodium oleate with lead acetate is formed an insoluble lead oleate. It occurs in commerce either in the form of an ointment-like mass or as an unctuous granular powder. It is comparatively little used in this country although it represents the active ingredient in the official ointment of diachylon. (See *Emplastrum Plumbi.*)

Lead Phenolsulphonate. *Lead Sulphocarbolate.* $Pb(C_6H_4OHSO_3)_2 + 5H_2O$.—White, lustrous needles, soluble in water and alcohol and possessing astringent and antiseptic properties. It is used externally in *skin diseases* and *ulcers* instead of, and is stated to be better than, zinc sulphocarbolate.

Lead Saccharate. *Plumbi Saccharas. Saccharate of Lead.—Lead saccharate* is made by saturating a solution of saccharic acid in water with freshly precipitated lead carbonate gradually added. As the acid becomes saturated, the lead saccharate falls in the form of a white powder, being insoluble in cold water, and but very sparingly soluble in that liquid boiling hot. From this E. Hoskins prepared his *lead nitro-saccharate*, by dissolving the saccharate in diluted nitric acid, containing only one part of the acid in twenty parts of the mixture, filtering the solution, and gradually evaporating. The nitro-saccharate is deposited in yellow crystals in the form of regular six-sided plates or prisms. By dissolving one grain of this salt, with five drops of pure saccharic acid, in a fluidounce of distilled water, a solution was obtained which, though slightly acid to test paper, was perfectly bland. This solution was suggested to dissolve urinary *calculi* but is no longer employed in medicine.

Lead Tannate. *Plumbi Tannas.*—This is obtained by precipitating a solution of tannin with one of lead acetate, added drop by drop. It has been used locally in *chronic inflammations* of the *joints, ulcerations, bed sores*, and *sore nipples*, in 20 to 40 per cent. ointments. The preparation here described is a bitannate. Other lead tannates exist.

Lead Thiosulphate. *Lead Hyposulphite.* PbS_2O_3.—When freshly prepared this compound occurs as a white, amorphous powder turning black on exposure to air for some time, due to the formation of lead sulphide. It is soluble in solutions of the alkali thiosulphates and is used in this form in the external treatment of *rhus poisoning*. It is incompatible with acids or acid salts.

Lecin.—This is an elixir of iron albuminate. It is a permanent and non-gelatinizing preparation and asserted to be an extremely assimilable form of iron, containing 20 per cent. albumen and 0.6 per cent. iron.

Lecithin. *Ovolecithin. Phospholutein*, $C_{42}H_{84}NPO_9$, or $C_{44}H_{90}NPO_9$.—*Lecithin* consists of the esters of oleic, stearic, palmitic, or other fatty acid, with glycerophosphoric acid combined with choline; occurring in combination with proteids in many animal and vegetable tissues, especially nerve tissue and the yolks of eggs. The class of lecithins is now known to be widely distributed in both animal and vegetable tissues, although most familiar in its occurrence in the nerve tissues and embryonic cells. It is a yellowish-brown, waxy solid, of a peculiar odor, soluble in an equal volume of cold absolute alcohol and readily soluble in chloroform, ether, and benzine and fixed oils. It is insoluble in water, but swells, and eventually decomposes. It is hygroscopic on exposure in the air and decomposes according to the extent of moisture absorbed. Lecithin is incompatible with alkalies and should be kept in glass-stoppered bottles away from the light.

Lecithin contains 3.8 per cent. of phosphorus. The animal lecithin is *choline di-stearylglycerophosphate*, while the vegetable lecithin seems to be *betaine di-oleylglycerophosphate;* that is, the widely distributed vegetable base, *betaine* (*oxyneurine*), replaces the choline of egg lecithin and the oleic acid radical appears instead of that of stearic acid.

Vegi-lecithin has been studied chemically by C. Gordon Richardson. Besides the replacement of the choline by betaine and the difference in the fatty acids, it differs from *ovi-lecithin* (*vitellin*) in not being precipitated by acetone and being quite insoluble in alcohol, but soluble in all proportions in cold ether. Otherwise, it is readily soluble in all the solvents of ovi-lecithin. It seems to resemble somewhat the *cephaline* of Thudichum, which was obtained from the brain tissue and which is now known as lecithin, and is asserted to be better borne than ovi-lecithin.

Choline is a substance with well marked physiological properties, and is closely allied chemically to the alkaloid *neurine*, a poison of considerable power, which was discovered by Strecker (1849) and has been shown by Brieger (*Ueber Ptomaine*, Berlin, 1895) to occur in decomposing meat. These two substances are very similar in their effects upon the system. They are related physiologically to pilocarpine and muscarine in that they stimulate the peripheral ends of the autonomic nerves. Through this action on the nerve endings they cause an increase in various secretions, especially those of the salivary gland, slowing of the pulse, contractions of the pupil, and an increase in the peristaltic movements of the intestinal and probably other unstriped muscles. Besides these actions, they exercise a depressant influence upon the respiratory center, and in large doses also paralyze the peripheral motor nerves. Choline also lowers the blood pressure by dilating the blood-vessels. When injected into various organs choline produces, according to Hoffman (*W. K. W.*, 1905), destructive changes, similar to those caused by the X-ray. Exner and Sywek (*D. Z. Chir.*, 1906) confirmed these observations, and have had some encouraging results from injection of a 2 per cent. solution of choline in cases of inoperable *cancer*. Reid Hunt (*A. J. Phys.*, 1918, xlv, 231) has investigated the derivative, *acetylcholin* which he finds to be a vasodilator of such extraordinary potency that .000,000,003 milligm. will cause a distinct lowering of blood pressure in the cat.

When taken by the mouth lecithin is partially broken up by the fat-splitting ferments of the pancreas into its constituent parts, but appears also to be in part absorbed unchanged. The absorption of lecithin unchanged seems to be dependent upon the presence of bile in the intestines. The literature upon the effects of lecithin upon the body is enormous in volume and somewhat contradictory in character. In an elaborate review of the evidence published by the Ohio Agricultural Experiment Station (*Bull. No. 5*, March, 1914), Forbes and Keith reached the conclusions that although there is no convincing evidence that lecithin possesses unusual nutritive value in normal animals, in cases of impaired nutrition, especially where there is a condition of depleted phosporus reserve, lecithin encourages phosphorus retention and that while there is some contradiction in the testimony it is probable that lecithin accelerates the passage of food from the stomach and improves digestion in the intestines. Lecithin has been shown by H. C. Wood, Jr. (*U. P. M. B.*, May, 1902) to be non-toxic.

Danilewski found that, in young animals, it caused an increase in the number of red corpuscles, and a gain in weight. Billon (*International Congress of Medicine*, 1904) has confirmed these findings, and also observed a marked increase in the number of white corpuscles. Serono, as a result of studies on human beings, reached the conclusion that the output of nitrogen was increased. Lawrow and Woronzow (*A. I. P. T.*, 1912, xxi, 389), from experiments on the lower animals, reached the conclusion that lecithin had the power of restoring activity to a heart poisoned by various depressants such as chloral, etc. Hanschmidt (*Bio. Chem. Zeit.*, 1913, li, 171) found that the previous injection of lecithin increased the resistance of rabbits to strychnine, chloral and curare but lowered their resistance to ricin.

Lecithin was introduced into medicine with the idea that being a natural compound of phosphorus, it would exercise the tonic effect of this element upon the system without the disadvantages of its toxic action, and there is considerable clinical evidence of its utility in *tuberculosis, neurasthenia, chlorosis, scrofula* and *rickets*. Lancereaux and Paulesco recommend it also in *diabetes*, but Erben (*S. M.*, 1909) observed no benefit from its use in this disease. Although a portion of the lecithin is decomposed in the intestinal tract by the fat-splitting ferments, Slowtzoff asserts that a part of it is absorbed unchanged. Whether or not pure lecithin has any advantage over the yolks of eggs may be questioned. The *dose* of lecithin is from one to three grains (0.065–0.2 Gm.) in pills or emulsion.

There are a large number of proprietary preparations of lecithin on the market. Concerning the liquid forms, attention may be again called to the fact that lecithin is insoluble in water or alcohol, so that any transparent liquid preparation of lecithin must be suspected as containing little of the drug. The following are some of the more popular preparations:

Glyceritum Lecithini. Glycerol of Lecithin.—A 1.6 per cent. of lecithin in pure glycerin. *Dose*, one fluidrachm (4 cc.).

Lecibrin.—A preparation of lecithin from the brain, containing 33⅓ per cent. of lecithin with nucleo-proteins. It is marketed only in the form of gelatin-coated pills, each containing three grains (0.2 Gm.) of *lecibrin.*

Lecipon.—This is stated to contain 10.5 per cent. of lecithin in soluble form.

Lecithan.—A trade name for lecithin.

Lecithcerebrin.—Lecithin prepared from the brain substance.

Lecithmedullan.—A lecithin prepared from bone marrow.

Lecithol.—An emulsion of brain lecithin representing 1.5 per cent. of lecithin. *Dose*, one to two fluidrachms (4–8 cc.).

Neurolecithin.—A trade name for lecithin prepared from the brain and spinal cord of animals. *Dose*, one grain (0.065 Gm.).

Letalbin. (*Lecithin Albuminate.*)—This forms a yellowish, dry, stable powder of characteristic egg yolk taste. It contains 20 per cent. pure lecithin and is adapted as an addition to tablets, pastilles and infant foods.

Ledum. *Ledum palustre* L. (Fam. *Ericaceæ.*) *Crystal Tea. Marsh Tea. Rosmarinus Sylvestris. Marsh Cistus. Wild Rosemary. Lédon, Romarin sauvage*, Fr. *Porsch. Sumpfporsch, Wilder Rosmarin*, G.—A small evergreen shrub indigenous to Arctic regions and found as far south as Newfoundland in North America. It has linear to linear-oblong leaves which are revolute along the margin, dark green above and rusty-tomentose beneath. A variety of this species, *L. palustre dilatatum* Wahlenb., occurs as far south as Maine and is distinguished by its broader leaves which are sometimes glabrous and glaucous on the lower surface. The leaves have a balsamic odor, and an aromatic, camphoraceous, bitter taste, and contain, among other ingredients, volatile oil and tannin. For the properties of the volatile oil, see *J. P. C.*, 4e sér., xx, 244; also *Proc. A. Ph. A.*, xxv, 154. It contains *ledum camphor*, a stearopten, together with valeric and other volatile acids, and *ericinol*, $C_{10}H_{16}O$. The tannin has been named *leditannic acid*, $C_{15}H_{20}O_8$. On boiling with dilute mineral acids it is decomposed, and *ledixanthin*, $C_{30}H_{34}O_{13}$, separates as a yellowish or reddish powder. (Thal, *Ph. Z. R.*, 1883, 268.) Thal also extracted *ericolin*, $C_{34}H_{56}O_{21}$. This is a glucoside, which on heating with diluted sulphuric acid decomposes into sugar and *ericinol*, $C_{10}H_{16}O$, a colorless, peculiar-smelling oil, which turns brown in the air, owing to oxidation. The leaves are thought to be narcotic and diaphoretic, and have been employed in *dysentery* and in various cutaneous affections, particularly *leprosy* and *scabies*. In complaints of the skin they are used both internally and externally, in the form of decoction. In Germany they are sometimes substituted for hops in the preparation of beer.

Ledum grœnlandicum Oeder (*L. latifolium* Ait.) or *Labrador tea*, a larger plant than the preceding, is a native of North America, growing in damp places in Canada and the northern part of the United States. The leaves have an agreeable odor and taste, and were esteemed pectoral and tonic. They are said to have been used as a substitute for tea during the war for independence.

Leek. *Porrum. Porreau*, Fr. *Lauch*, G.—The bulb of *Allium Porrum* L. (Fam. *Liliaceæ.*) The *leek*, which is the national emblem of the Welsh, is a biennial bulbous plant with broad, often keeled leaves and white flowers, growing wild in Switzerland, and cultivated in the gardens of Europe and this country for culinary purposes. All parts of it have an offensive, pungent odor and an acrid taste, dependent on an essential oil, of which allyl sulphide, $(C_3H_5)_2S$, is the main ingredient. The bulb, which is the medicinal portion, consists of concentric layers, like the onion, which it resembles in medicinal properties, though somewhat milder. It is generally stimulant, with a direction to the kidneys. *Dose*, of expressed juice, a fluidrachm (3.75 cc.).

Leonotis. *Leonotis Leonurus* R. Br. (Fam. *Labiatæ.*) *Lion's Ear. Wild Daggar.*—This is a coarse perennial herb of shrubby habit indigenous to South Africa which is said to possess purgative and emmenagogue properties. (See *P. J.*, May, 1885.) The leaves of this plant which are hairy, lanceolate to oblong-lanceolate and serrate, are smoked by the Hottentots like tobacco. It is asserted that in overdose it has a narcotic effect. It is used by the South African aborigines as a cathartic, and in the treatment of *snake bite.* A decoction is also employed externally for various skin eruptions. (*P. J.*, 1907, lxxix.)

Leonurus. *Leonurus Cardiaca* L. (Fam. *Labiatæ.*) *Motherwort. Agripaume, Cardiaire,* Fr. *Herzespann, Wolfstrapp,* G.—An aromatic perennial herb indigenous to Europe but naturalized in North America. An infusion or decoction is sometimes used in *amenorrhea.*

Lepargyræa. *Shepherdia argentea* Nutt. (*Lepargyræa argentea* Greene.) (Fam. *Elæagnaceæ.*) *Buffalo Berry. Bull Berry. Grains de Bœuf,* Fr.—The acidulous fruit of this shrub produced in great profusion in the region of the upper Missouri, is largely used as an article of food. According to Henry Trimble, it contains a little more acid than currants. (*A. J. P.*, Dec., 1888.)

Levisticum. *Levisticum officinale* Koch. (Fam. *Umbelliferæ.*) *Lovage. Radix Levistici,* P. G. *Livèche. Ache de Montagne,* Fr. *Liebstöckel,* G.—This is a tall, perennial, aromatic herb native to South Europe and cultivated extensively in Germany for its rhizome system and fruits. It has bipinnate, cauline leaves with leaflets coarsely toothed at apex and greenish-yellow flowers.

The rhizome is vertical, from 5 to 10 cm. long and 2 to 4 cm. thick with a multiple crown often in longitudinal slices, annulate above and divided below into several subcylindrical flexible branches up to 10 mm. thick; externally yellowish-brown, reddish-brown or dark brown, longitudinally wrinkled; fracture short; texture spongy; inner surface showing a thick bark with numerous radially-arranged oil and resin reservoirs and a yellow porous and radiate wood surrounding a central whitish pith; wood-wedges separated by whitish medullary-rays which also contain oil and resin reservoirs; odor characteristically aromatic; taste aromatic, sweet, pungent and bitter.

The fruits are cremocarps which are ovate-oblong, somewhat flattened, about 4–5 mm. long and yellowish brown. In the drug, these are usually separated into mericarps, each of which shows five primary ribs, the lateral ones being the longest, as well as six vittæ. Both odor and taste are aromatic. Lovage is a stimulant aromatic, and has been employed as a carminative, diaphoretic, and emmenagogue. The best form for administration is that of infusion. The coloring principle has been isolated by M. J. Nicklés, who gives it the name of *ligulin;* it forms red solutions turning blue in the presence of alkalies.

Lewisia. *Lewisia rediviva* Pursh. *Spatlum. Chita. Bitter Root.*—The roots of this fleshy-leaved low perennial of the Fam. *Portulacaceæ,* abundant in the Northwestern United States, were very widely used by the Indians as an article of food. For analysis and description, see *A. J. P.*, 1889.

Liantral. *Lianthral.*—This substance is an extract of coal tar, obtained by treating with benzene, filtering from insoluble residue, and subsequently evaporating the benzene at a temperature not exceeding 80° C. It is a brownish-black viscous fluid which is insoluble in water, freely soluble in benzene, but dissolving only sparingly in fats, ethereal oils, alcohol, ether, acetone, petroleum benzin, and mixtures of these substances. Liantral has been commended by various clinicians as a substitute for coal and wood tars in the treatment of *eczema* and allied skin diseases. It is said to resemble wood tar in its action, but to be more energetic It has been used in ten per cent. solution with olive oil, applied with a brush, or in the form of a dusting powder made by triturating to dryness with the aid of starch, or talc.

Liatris. *L. spicata* (L.) Willd. (*Lacinaria spicata* Hill.) *Spike Gay-feather. Blazing Star. Button Snakeroot.*—An indigenous perennial composite plant growing in meadows and moist grounds from Massachusetts to Southern Ontario and Minnesota, southward. It has a tuberous root, and an erect annual stem, which terminates in a spike of beautiful, purple flower heads, appearing in August. The leaves are all linear. The root is said by Schoepf to have a terebinthinate odor, and a warm bitterish, terebinthinate taste; to be possessed of diuretic properties; and to be useful as a local application in *gonorrhea* and *sore throat.*

The leaves of the allied *Trilisa odoratissima* (Walt.) Cass. (*Liatris odoratissimus* Willd.), or *Vanilla leaf,* are very largely employed in the Southern United States to flavor tobacco, and to preserve clothing, etc., from moths. As a preservative it is worthless. The agreeable odor is due to coumarin, which may be frequently noticed in crystals upon the surface of the smooth spatulate leaves. (*A. J. P.*, Sept., 1881; xlvii, 116; *N. R.*, 1882, 66.) The roots of *L. scariosa* Willd. (*Lacinaria scariosa* Hill) and *L. squarrosa* Willd. (*Lacinaria squarrosa* Hill) (*rattlesnake's master*) have been employed to cure the bite of the rattlesnake. According to Wm. P. C. Barton, all the tuberous-rooted species of *Liatris* are active diuretics.

Libanol.—This is an ethereal oil obtained from the wood of *Cedrus atlantica* Manetti. (Fam. *Pinaceæ.*) It is a yellow liquid of pleasant odor and taste, soluble in alcohol and ether and insoluble in water. In diseases of the respiratory organs it is used as an antiseptic expectorant and also as an inhalation. It is claimed to be a valuable substitute for sandal wood oil in the treatment of *gonorrhea.* It has also been used externally in the form of an ointment in the treatment of *rheumatism. Dose,* fifteen to forty-five minims (0.9–2.8 cc.) several times a day.

Lignol.—This is an oily or tarry substance which is said to be obtained by the dry distillation of a bituminous fossilized wood. Lignol is asserted to be in bactericidal power equal to the 5 per cent. solution of phenol, and is recommended in *eczema, acne, pruritus,* and other chronic skin diseases, and in *doses* of fifteen minims (0.9 cc.) in pulmonary *tuberculosis.* Also, in chronic *irritation of the genito-urinary tract.*

Ligroine. *Ligroïn.*—This name has been applied to a petroleum product which is chiefly used as a solvent. It boils between 100° C. and 120° C. and has a specific gravity varying between 0.707 and 0.722.

Ligusticum. *Lovage.* (Fam. *Umbelliferæ.*)—A genus differing from *Levisticum* (also called Lovage) in having ternately compound leaves and mericarps with 6 to 10 vittæ on the commissural side and 2 to 6 vittæ between each two primary ribs on the dorsal side. The root of *Ligusticum sinense,* under the name of *kao-pên,* is largely used by the Chinese. In the Northwestern United States the large aromatic roots of *Ligusticum filicinum* S. Wats., *Osha Colorado cough-root*, are used to a considerable extent as stimulating expectorants. (See *A. J. P.*, 1890 and 1891.)

Ligustrum. *L. vulgare* L. (Fam. *Oleaceæ.*) *Troène*, Fr. *Rainweide, Hartriegel*, G. *Privet* or *Prim.*—A shrub having numerous varieties which is indigenous to the Levant and widely naturalized and cultivated as a hedge plant. It attains the height of 15 feet and bears opposite, deciduous to semi-evergreen, oblong-ovate, glabrous leaves and dense pyramidal panicles of small white flowers. The leaves, which have an astringent, bitter taste, and the flowers, which are small, snow-white, and of an agreeable odor, have been used in the form of decoction in *sore throat* and *aphthous* and *scorbutic ulceration of the mouth.* The berries are black, have a sweetish bitter taste, and are said to possess purgative properties, and to color the urine brown. They are sometimes used for dyeing. Death in a child between two and three years old is recorded by James Cheese (*P. J.*, 2d ser., viii, 607), as due to the eating of privet berries. The bark was analyzed by M. G. Polex, who found a peculiar substance, which he denominated *ligustrin*, insoluble in ether and absolute alcohol, but soluble in water and diluted alcohol. Strong sulphuric acid gives with *ligustrin* a deep indigo-blue color. Kromayer (*A. Pharm.* (2), cxviii, 19) proved that Polex's ligustrin was only impure *syringin*, $C_{19}H_{28}O_{10} + H_2O$. The large white crystals become anhydrous at 115° C., and fuse at 212° C. Mannite, sugar, muco-saccharine matter, starch, chlorophyll, bitter extractive, bitter resin, tannin, albumen, salts and a crystalline bitter principle, fusing at a little over 100° C., which Kromayer named *ligustron.* Pfau (*A. Pharm.*, 1925, ccxliii, 50) has made a further investigation of the coloring matter of privet berries, which have lately come to be used in Germany in the coloring of wine, and isolated a coloring principle which he obtained in red crystalline needles, and which he named *ligulin.*

Lilium. *Lilium candidum* L. (Fam. *Liliaceæ.*) *Annunciation Lily. Madonna Lily.*—This well-known plant is a native of Southern Europe from Corsica to the Caucasus Mountains and North Persia, but has been long cultivated in gardens. It is considered by many to be the lily mentioned in the Scripture. The plant possesses pure waxy white flowers of delicate fragrance and a subglobular imbricated bulb of white color tinged with pale yellow. The latter is without odor, but has a peculiar, disagreeable, somewhat bitter, and mucilaginous taste. It contains much mucilage, and a small proportion of an acrid principle. In the recent state it is said to have been employed with advantage in *dropsy.* Vomiting, purging, drowsiness, etc., are said to have been produced in a little girl by the pollen of the *tiger lily, L. tigrinum* Andr. (Jeffries Wyman, *Am. J. M. S.*, 1863.)

Limonene.—This terpene, $C_{10}H_{16}$, which is found in many volatile oils, has an odor resembling that of oil of lemon. It has been suggested by Kobert as a substitute for oil of turpentine. Zickgraf (*M. M. W.*, 1910, lvii) has used it with good effects in fetid *bronchitis, bronchiectasis, gangrene of the lung*, and *pulmonary tuberculosis.* He asserts that it is not only much more pleasant to the patient than is oil of turpentine, but is more efficient and less irritant to the kidneys. It may be administered either by inhalation or internally. The *dose* is ten to twenty drops (0.6–1.3 cc.) three times a day.

Linaria. *Linaria vulgaris* Hill. (*Antirrhinum Linaria* L.) (Fam. *Scrophulariaceæ.*) *Common Toadflax, Butter and Eggs. Ramsted. Linaire commune*, Fr. *Leinkraut, Flachskraut, Löwenmaul*, G.—This is a perennial herb whose spreading underground stem gives rise to many slender aerial shoots bearing numerous linear leaves and which terminate in racemes of yellow flowers, each of which shows a spurred, personate corolla with an orange-colored, bearded palate. It is a very common weed in waste places of America, Europe, and Asia. It should be collected when in flower, dried quickly, and kept excluded from the air. When fresh it has a peculiar, heavy, disagreeable odor, which is in a great measure dissipated by drying. The taste is herbaceous, weakly saline, bitter, and slightly acrid. Its constituents are stated to be two glucosides, *linarin* and *pectolinarin* (*P. J.*, lxxix, p. 316), with *linarosnin, linaracrin, antirrhinic*, tannic and citric acid. This plant is said to be diuretic and cathartic, and has been used in *dropsy, jaundice*, and *cutaneous eruptions.* It is most conveniently employed in infusion. The fresh plant is sometimes applied, in the shape of poultice or fomentation, to *hemorrhoids*, and an ointment of the flowers has been employed for the same purpose, and also locally in diseases of the skin. The flowers are used in Germany as a yellow dye.

Linden.—Boussingault calls attention (*J. P. C.*, 4e sér., xv) to a saccharine exudation which occurs upon the leaves of the European *Linden* (*Tilia europœa* L.), which he has found to have the same composition as Tamarisk manna.

Lint. *Linteum Carptum. Charpie*, Fr., G.—The term *lint* is applicable to a substance prepared from linen. It is in fact linen made soft and somewhat fleecy by various mechanical processes, so as to render it suitable for the dressing of wounds. It was formerly made from old linen thoroughly cleansed by washing with soap and water, or by boiling with a weak lye of soda or pearlash. Sometimes, when colored, it was bleached before being washed. Thus prepared, it was operated on by a simple machine, in which the rag, wrapped round a cylinder, was submitted to the interrupted action of a knife made to descend upon it at intervals of one-eighth of an inch, so as to cut the thread in one direction. On being removed from the machine, the cut ends of the thread became untwisted and loose, giving a flossy character to the fabric. To render it smooth, it was passed through rollers, and its ragged edges were trimmed.

In the progress of improvement, machines were invented and patented for manufacturing lint on the large scale. This so-called *patent lint* has almost completely displaced the older kind. It is generally prepared out of cloth manufactured for the purpose, and therefore has whatever advantage may be derived from uniformity of shape and consistence.

Cotton is in several respects inferior to linen for the preparation of lint, and, unless its presence in any manufactured article sold by this name be made known, it should be looked upon as a fraudulent substitution. Its fiber is less soft and therefore more likely to irritate. It has much less absorbing power, and it conveys heat less rapidly. The following are methods by which it may be distinguished (Elsner): (1) A linen thread when held erect, and set on fire, appears, after the flame is extinguished, in a smooth continuous form, while cotton thread similarly treated has a tufted aspect. (2) Under a microscope which magnifies 300 diameters, the linen fiber appears to be a straight nearly solid cylinder, with a slender central canal; the cotton, flattened as a piece of tape, with a wide canal, and often twisted like a corkscrew. (3) The potassium test, proposed by Böttger, consists in exposing the doubtful substance to the action of a boiling concentrated solution of potassium hydroxide. If made of linen, it will in two minutes assume a deep yellow color; if of cotton, it will either remain colorless, or will become very faintly yellow, and if the texture be composed of both, it will exhibit a streaked or mottled aspect. The examination must be quickly made, as the yellow color produced by the potassium becomes faint with time. (4) Sulphuric acid dissolves the linen fiber, while it leaves that of cotton little changed.

Tow, and hemp in the state of *oakum*, have been employed for dressing wounds; but they are only applicable as exterior dressings to absorb the pus, when the discharge of this is very copious. L. A. Sayre prefers picked oakum to lint as more absorbent. (*B. M. S. J.*, lxvii, 84.) *Charpie*, so much used by French surgeons, generally consists of bundles of straight threads, each four or five inches long, made by unravelling old and rather coarse linen.

Linum catharticum L. *Purging Flax.*—Purging flax is an European annual of the Fam. *Linaceæ*, six to eight inches high. The whole plant is very bitter and somewhat acrid, and imparts its virtues to water, which acquires a yellow color. It appears to owe its activity to a peculiar drastic principle, which has received the name of *linin*, and which is afforded most largely by the plant after the flower has fallen. Schroeder (*N. R. Pharm.*, xi, 11) obtained it in lustrous, white, silky crystals, which are neutral in reaction and have a strong persistent bitter taste in alcoholic solution. Purging flax has enjoyed some reputation in Europe as a gentle cathartic, useful in *muscular rheumatism*, *catarrhal affections*, and *dropsy* with disease of the liver. *Dose*, of the extract, from four to eight grains (0.26–0.5 Gm.); of the powder, one drachm (3.9 Gm.).

Lipoiodine. *Di-iodo-brassidinic acid ethyl ester. Ethyl diiodobrassidate—N. N. R.* 1924.—This occurs as white needles, melting at 37° C., readily soluble in alcohol, ether, chloroform and fatty oils, but insoluble in water. Its solution undergoes slow decomposition with the liberation of iodine. It is said to represent 41 per cent. of iodine. Loeb and Velden (*Th. M.*, 1911) assert that this preparation is absorbed unchanged from the intestinal tract, but that after absorption it undergoes slow decomposition, and thereby exercises a continuous iodine effect. Its action is similar to that of calcium iodobehenate (see Part I) and is used as a substitute for the alkaline iodides. It is marketed in the form of tablets, each containing 5 grains (0.3 Gm.), of from five to twenty-five grains (0.32–1.7 Gm.).

Lippia.—A genus of the *Verbenaceæ* comprising about 125 species of herbs and shrubs the majority of which are indigenous to tropical America. Their leaves are mostly opposite or 3-whorled; their flowers small with a 2-lipped, white, rose or purplish corolla, a 2–4 cleft persistent calyx, 4 didynamous stamens and a 2-celled ovary with a single ovule in each cell; their fruits mature as 2 separate nutlets. A number of the species of this genus contain aromatic oils, and several have been used in popular medicine. The *L. citriodora*, H. B. K., yields *verbena oil*, and is commonly known as *Lemon verbena.* From the *L. mexicana*, Podwissotzki (*Proc. A. Ph. A.*, 1886) separated an essential oil somewhat resembling that of fennel, as well as a camphor-like substance which he named *lippiol.* According to Maisch (*A. J. P.*, xlvii, p. 330), however, the plant used by Podwissotzki was probably the *Cedronella mexicana* Benth. Power and Tutin (*A. Pharm.*, 1907, ccxlv, p. 337) found in the *L. scaberrima* (Sonder), a native of South Africa, where it is popularly known as *Beukess boss*, an essential oil somewhat resembling lavender in its odor, a peculiar crystalline substance, which they named *lippianol*, having the qualities of a monohydric alcohol, and a number of other substances not peculiar to the plant.

Liriodendron. *Liriodendron Tulipifera* L. *Tulip Tree. American Tulip-poplar.* (Fam. *Magnoliaceæ.*) *White Tulip.*—The tulip-poplar is a beautiful, stately tree which is abundant in rich soil in the forests from Southern Ontario to Wisconsin and extending into the Southern States, the timber being commonly known as Poplar or White Wood. It is native to Pennsylvania, its fossil vestiges having been found in the Miocene formations within that state. It possesses simple leaves which are truncate and notched at the apex and greenish-yellow cup-shaped flowers marked with orange within at the base. Its formerly official bark was taken for use indiscriminately from the root, trunk, and branches, though that of the root is thought to be the most active. Deprived of the periderm, it is yellowish-white, the bark of the root being somewhat darker than that of the stem or branches. It is very light and brittle, of a feeble, rather disagreeable odor, strongest in the fresh bark, and of a bitter, pungent, and aromatic taste. J. U. Lloyd believes that the active principle is the alkaloid *tulipiferine*, discovered by him in 1886, and this, according to Bartholow, appears to possess toxic properties. (*Ph. Rund.*, 1886, 169.) The virtues of the bark are extracted by water and alcohol, but are injured by long boiling.

Emmett (*A. J. P.*, iii, p. 5) isolated a crystalline compound which he called *liriodendrin.* This was insoluble in water but dissolved by alcohol or ether and did not unite with either acids or alkalies. It had a slightly aromatic odor and a bitter, pungent taste.

Liriodendron is a stimulant tonic, with diaphoretic properties, and has been used in chronic *rheumatism* and *dyspepsia.* Dose, of bark in powder, from half a drachm to two drachms (2.0–7.7 Gm.); of saturated tincture, a fluidrachm (3.75 cc.).

Lithio-mercuric Iodide. $3LiI + HgI_2$.—Under the name of *mercuricide*, a compound iodide of the above formula has been brought out as a germicide. It is soluble without decomposition in water, alcohol and ether, and crystallizes in lemon-yellow crystals which are deliquescent. It is alleged that it is as actively germicidal as corrosive sublimate, but is not corrosive, less poisonous and not precipitable by blood serum, albumins or alkalies.

Mercury and Lithium Iodide, or *Hydrargyrum-Lithium Iodatum* of Merck, is a red and granular crystalline powder of the formula $HgI_2.2LiI$.

It is soluble in alcohol or ether, but wholly incompatible with water, forming a cloudy mixture which soon precipitates mercuric iodide. It has been used in Germany as an antisyphilitic, antilithic alterative, and especially in *gravel* complicated with *syphilis.*

Lithium Acetylsalicylate. *Hydropyrin. Lithiopyrin. Tyllithin.*—This is a hygroscopic soluble substance which, in the presence of moisture, decomposes into lithium salicylate and free acetic acid. It has been introduced as a substitute for acetyl salicylate acid in the treatment of *rheumatism* and *neuralgias.* It is, however, doubtful whether it has any advantage. The *dose* is from eight to fifteen grains (0.5–1 Gm.).

Lithium Agaricinate.—A white powder of a slight saline taste easily soluble in water. It is used as an anhydrotic in the treatment of phthisical *night sweats. Dose,* one and one-half to three grains (0.096–0.21 Gm.).

Lithium Bitartrate. $LiC_4H_5O_6 + H_2O$.—White crystals soluble in water; the resulting solution shows an acid reaction. It is used in the treatment of *gouty conditions* and *suppurative gingivitis.*

Lithium Iodide may be prepared by treating a warm solution of ferrous iodide with lithium carbonate and heating gently to promote complete decomposition. The liquid must be slightly alkaline. It forms a white hygroscopic salt very soluble in water and alcohol. It becomes yellow on exposure to the air due to liberation of iodine. It is used for the same purposes and in the same doses as potassium iodide.

Lithium Quinate. *Urosine.*—This is a mixture of lithium citrate and quinic acid containing 80 per cent. of the latter and 20 per cent. of the former. It is used in *uric acid diathesis* and as an antirheumatic.

Lithospermum. *Lithospermum officinale* L. (Fam. *Boraginaceæ.*) *Common Gromwell. Puccoon. Milium Solis.*—A European perennial, also found along roadsides and pastures of Canada and the Northern United States, the seeds of which are ovate, of a grayish-white or pearl color, shining, rather larger than millet seeds, and of a stony hardness, from which the generic name of the plant originated. They were formerly used as a stimulant diuretic, but are nearly inert.

Lithræa. *Lithræa venenosa* Miers. (Fam. *Anacardiaceæ*).—The leaves of this Chilian plant are said to act upon the skin in a manner similar to *Rhus toxicodendron,* and to contain a resin and an ethereal oil. The tincture of the fresh leaves has been used as a counter-irritant.

Litmus. *Lacmus. Turnsole. Tournesol. Lacca Cœrulea. Lacca Musica. Laquebleu,* Fr. *Lackmus,* G.—Litmus is yielded by some species of lichens from which cudbear is obtained (see *Persio,* Part I). It is prepared chiefly if not exclusively in Holland. The process consists in macerating the coarsely powdered lichens, in wooden vessels under shelter, for several weeks, with occasional agitation, in a mixture of urine, lime and potash or soda. A fermentation ensues, and the mass, becoming first red and ultimately blue, is, after the last change, removed, mixed with calcareous or silicious matter to give it consistence, and with indigo to deepen the color, and then introduced into small molds, where it hardens. It is said that ammonia may be substituted for urine in the manufacture of litmus, but that the reactions necessary for the production of the coloring matter of the litmus are due to the action of the enzyme which is found in the lichens. Litmus occurs in rectangular cakes, from a quarter of an inch to an inch in length, light, friable, finely granular, of an indigo-blue or deep violet color. It has the combined odor of indigo and violets, tinges the saliva a deep blue, and is somewhat pungent and saline to the taste. From most vegetable blues it differs in not being rendered green by alkalies. It is reddened by acids, and restored to its original blue color by alkalies. For a method of purifying commercial litmus by Foerster, see *Nat. Drug.,* 1904, 460.

Its chief use in pharmacy is as an indicator. For this purpose it is employed either in infusion or in the form of litmus paper. The infusion, formerly called *tincture of litmus,* may be made in the proportion of one part of litmus to twenty of distilled water, and two parts of alcohol may be added to preserve it. *Litmus paper* is prepared by first forming a strong clear infusion with one part of litmus to four of water, and dipping slips of white unsized paper into it, or applying it by a brush to one surface only of the paper. The paper should then be carefully dried, and kept in well-stoppered vessels, from which the light is excluded. It should have a uniform blue or slightly purple color, neither very light nor very dark. As a test for alkalies the paper may be stained with an infusion of litmus previously reddened by an acid, care being taken to avoid all excess. By gas light it is said that the change of color cannot be determined by the eye exactly, as the blue of litmus becomes mauve; but this may be obviated by watching the process through a green glass, by which the faintest trace of blue becomes discernible. (*P. J.,* 2d ser., vi, 479.) For the official method of preparing litmus paper, see *Tests, Test Solutions,* etc., Part III.

For chemical constituents of lichens, see *A. J. P.,* 1898, 455.

Loco Plants. *Crazy Weeds.*—These are plants of the Fam. *Leguminosæ* growing in the plains regions of far Western States, the eating of which by horses and cattle is believed to produce loss of flesh, disordered vision, delirium, convulsive movements, or stupor and death. The chief loco plants are *Astragallus Lamberti* Pursh. (*Oxytropis Lambertii* Greene), commonly known as *rattle weed* or *white loco,* extending from Alberta and Assiniboia in Canada south into Mexico and from Minnesota and Kansas to the Rocky Mountains, and *Astragalus mollissimus* Torr., the *purple loco, woolly loco* or *Texas loco* which ranges from South Dakota south to Mexico and through Western Nebraska, Kansas, Oklahoma, Texas, New Mexico, Eastern Arizona, Colorado and Southwestern Wyoming. There are quite a number of other plants causing heavy losses to stock men of the West.

Isaac Ott found a plant, which he believed to be *A. mollissimus,* to act as a violent spinal poison and mydriatic (*N. R.,* Aug., 1882), and, according to Carl Ruedi, the decoction produces in the rabbit great hilarity, excitement, and even ferocity, and contains an alkaloid, *locoine,* and an acid. (*Tr. Col. State Med. Soc.,* 1895.) On the other hand, O'Brien, of the State Agricultural College of Colorado, was not able to obtain any active chemical substance from six U. S. species of the genus, including the two previously mentioned, while in a very careful study of a plant which was neither in flower nor in seed, but whose identification as *A. mollissimus* was clear, H. C. Wood found that it was not poisonous to rabbits or dogs, a result which has been confirmed by Ingersoll (*Proc. A. Ph. A.*, 1890) and O'Brien (*Bulletin 25, Agricultural Experiment Station of Colorado*) and others. It would appear that *A. mollissimus* is not a poisonous plant. Other species of the genus, especially *A. Hornii* A. Gray, *A. Bigelovii* A. Gray, and *A. caryocarpus* Ker., Gawl, have had poisonous properties attributed to them, and in the fruit of the last-mentioned species G. B. Frankforter believes he has demonstrated the presence of an alkaloid. In 1908 Crawford brought forward the interesting theory that the poisonous effects of the *loco weed* were due to barium, but Alsberg and Black (*Bull. 246, U. S. Bureau of Plant Industry*, 1912) have shown that many other plants in the same localities contain equal quantities of barium, but do not produce the characteristic symptoms, and that the barium is in such an insoluble form as to render improbable that it would be absorbed in the intestinal tract. There can be no doubt that domestic animals are destroyed in the West in very large numbers from an affection which is known as "loco," and hundreds of thousands of dollars have been spent in bounties by the State of Colorado for the extirpation of the supposed poisonous astragalus. It is probable that many of the deaths attributed to loco have been from other causes. Thus, Ingersoll of the Colorado State Agricultural College, found in a large number of locoed sheep masses of *Tœnia expansa*, which he believed to be the cause of death. It is a probable explanation that the phenomena of loco disease are due to the fermentation of an astragalus or other plant in the intestines of the animals, and the production of one or more poisons which are absorbed and produce narcotic symptoms. If this be correct the loco disease is parallel in its etiology and nature to the lathyrismus of Europe. See *Lathyrus sativus;* also *N. Y. M. J.*, 1889, xlix. Similar effects are produced in horses by the pods of the mesquite (*Prosopis juliflora* DC.), when eaten too freely.

According to Haeckel (*Die naturlichen Pflanzen Familien*), the Russian grass *Stipa capillata* L. frequently kills sheep, not, however, by a direct poisonous action, but by its glumes working through the skin into the vital organs; and *Stipa Vaseyi*, which is said in some parts of New Mexico and Texas to be known by the name of "*sleepy grass*," is believed by some ranchers to be the cause of loco disease. Lescohier (*M. R.*, 1911, xx, p. 273) finds that the sleepy grass is an active respiratory poison, and also has some depressant action upon the heart muscle. He suggests that the apparent narcosis produced by the injection of it into the lower animals, is due to partial asphyxiation. This explanation, however, seems improbable in light of the symptoms which are reported in animals which have eaten the grass. Gillespie (*B. M. J.*, 1908, ii, p. 1059) reports that the drug is not only a narcotic, but also a diuretic and sudorific.

Lodal. (6: 7-dimethoxy-2-methyl-3: 4-dihydroisoquinolinium chloride.)—Under this name has been introduced a derivative of papaverine. It has been studied by Laidlaw (*Biochem. J.*, 1910, v, 243) who finds that it resembles hydrastinine in its physiological action, causing a rise in the blood pressure through a direct stimulating influence on the muscles of the heart and arteries. This stimulant influence on involuntary muscle is also shown most markedly in its effect upon the uterus in which it causes tonic contractions. It has been brought forward as a remedy for *menorrhagia* and *dysmenorrhea.* It is marketed in the form of tablets each containing one grain (0.065 Gm.).

Lolium. *Lolium temulentum* L. *Darnel. Bearded Darnel. Ivraie*, Fr. *Lolch, Taumelkorn*, G. —This grass, thought to be the "*tares*" of the Scripture, has spread over the world wherever wheat is cultivated, but is rarely found in the United States. It owes its importance to its growing especially with wheat, so that its ground seeds are eaten in the flour. From ancient times its seeds have been believed to produce an intoxication similar to that of alcohol; hence its specific Latin name and the French name, *Ivraie.* In the sweetish seeds, P. Antze (*A. J. P.*, 1891, 568) believed that he found a solid alkaloid, *temulentine*, and a volatile one, *loliine;* but Hofmeister (*A. J. P.*, 1892, 611) determined that the volatile alkaloid was an impure ammonia, while the temulentine was a mixture which contained a nitrogenous acid and an uncrystallizable alkaloid, *temuline*, of which the hydrochloride has the formula $C_7H_{12}ON_2.2HCl$.

It is alleged that *lolium* seeds produce vertigo, dizziness, headache, somnolence, and general intoxication in man, as well as in dogs, sheep and horses, while they are innocuous to hogs, cows, and poultry. Rivière and Maizière (*J. P. C.*, 1863, 280) have recorded death as occurring from the use of bread containing large amounts of darnel. P. Antze found that both *loliine* and *temulentine* are poisonous, causing violent gastro-intestinal irritation, dyspnea, and general depression. (*Cb. G. T.*, 1891.) M. P. Guerin believes the poisonous properties of darnel are due to the presence of a fungus. (*Morots Journ. de Bot.*, 1898.)

Lonchocarpus. *Lonchocarpus violaceus* (Jacq.) H. B. K. *Stinkwood.* (Fam. *Leguminosœ.*)—The wood of this papilionaceous tree is said to be used by the natives of Surinam as a fish poison. (*Ph. Cb.*, xxxix, 282.)

Lonicera. *Lonicera Caprifolium* L. *Honeysuckle.* "*American*" or *Italian Woodbine.* (Fam. *Caprifoliaceœ.*)—The flowers of this climbing honeysuckle are sometimes used in perfumery, and a syrup of the fruit has been commended in *asthma.* The fruit of all the species of *Lonicera* is said to be emetic and cathartic (Mérat and De Lens), and that of *L. xylosteum* L. to have caused serious poisoning. (*J. P. C.*, 4e sér., xviii, 65.)

Loretin. *Meta-iodo-ortho-oxyquinoline-ana-sulphonic Acid.* $C_9H_4IN.OH.SO_3H$.—This organic iodine compound, discovered by Claus of Freiburg, contains 36.2 per cent. of iodine and is a bright yellow, odorless, crystalline powder, insoluble in ether and oils, soluble in 500 to 1000 parts of cold water, and in 167 to 200 parts of boiling water; it forms neutral soluble salts with sodium, potassium, ammonium, and magnesium, yielding deep orange-yellow solutions. It is very stable for an iodine compound, not being affected by exposure to direct sunlight. It was found by Ammelburg to be much more powerful as a germicide than iodoform, with seven different pathogenetic germs essayed. Given hypodermically to guinea-pigs (5 cc. of a 5 per cent. solution for long periods), it produced no poisoning, and no iodine could be detected in the urine. (*Deutsche Zeitsch. für Thier. Med. und Vergleich. Path.*, 1894.)

It has been especially commended as a substitute for iodoform by Schinsinger and by Snow. (*B. M. J.*, 1891, ii.) It may be used as a dusting powder alone or mixed with calcined magnesia or starch; as collodion, from 2 to 10 per cent.; as ointment, 5 to 10 per cent.; and in solution, 1 to 2 per cent. of the soluble sodium salt. The soluble calcium salt, *calcium loretin*, has been especially recommended for the manufacture of antiseptic gauze. Snow states that the pure powder may be used without danger of poisoning or of local irritation.

A substance closely allied to loretin is known as *tryen* or *yatren*. Anselmino (*Ap. Ztg.*, 1914) believes that it is chemically identical with loretin, although there has been some difference of opinion on this point. According to Herzberg (*B. K. W.*, 1922, i, 1830) it is ortho-oxy-iodo-sulphonbenzol-pyridin. Tryen appears to be an active germicide and has been used by Blun (*D. M. W.*, 1913) and others in the treatment of *gonorrheal infections*, and by Bischoff (*D. M. W.*, 1913) as an insufflation in *diphtheria*. Pfeiler (*B. K. W.*, 1921, lviii, 1413) has obtained remarkable results from the intravenous injection of yatren in *actinomycosis* of cattle and suggest its use in human beings both in this condition and in the allied condition known as *Madura foot.* Muhlens and Menk (*M. M. W.*, 1921, lxviii, 802) report very favorable results from the use of yatren in amebic *dysentery*. They used rectal injections of 200 cc. (6 fluidounces) of a 5 per cent. solution or 1 Gm. (16 grains) by mouth three times a day. Zieler (*M. M. W.*, 1922, lxix, 664) has reported two cases with symptoms of acute yellow atrophy of the liver from intravenous use of yatren after several doses of 0.2 to 0.5 Gm. at intervals of one or two days.

An isomer of loretin has also been advanced under the name of *lorenit*, and is used for the same purposes as loretin. It is *para-iodo-ana-oxyquinoline orthosulfonic acid.*

Under the trade name of *griserin* the *sodium loretinate* has been introduced for the purpose of combating various systemic infections, as *tuberculosis, typhoid fever*, etc. It has, however, been violently condemned by a number of authors as not beneficial, but even actually harmful.

Bismuth loretinate is used as a surgical dusting powder, also internally in *tuberculosis enteritis* in doses of eight grains (0.5 Gm.) several times a day.

Lotus. *Lotus arabicus* L.—According to W. R. Dunstan and T. A. Henry, the leaves of this leguminous plant contain a yellow crystalline glucoside, *lotusin*, $C_{22}H_{19}NO_{10}$, and an enzyme, *lotase*, by which lotusin is converted into prussic acid and a yellow substance, *lotoflavin*. (*Proc. Roy. Soc.*, lxvii, 224.)

Luargol.—This is said to be an arsenobenzol reinforced with silver and antimony. Dalimier and Levy-Frankel (*P. J.*, 1916, xcvi) report successful results from it in the treatment of *syphilis;* they state that it causes an extraordinary rapid disappearance of the visible lesions of the infection such as gummata and skin eruptions although they have not investigated the final results. They claim it has the advantage over arsphenamin in that its solutions are relatively stable remaining unaltered for several hours. They also have found it useful in cases of *psoriasis*. They injected 0.1 Gm. (one and one-half grains) and upwards at a dose.

Disodo-Luargol is a new form of luargol freely soluble in water, giving a brown solution. The beginning dose is 0.05 Gm. gradually increased to 0.3 Gm. (one to five grains). (*Ph. Era*, 1918, li, 51.)

Luatol.—In 1921 Sazerac and Levaditi (*A. In. Past.*, 1922, xxxvi, 1) showed that certain bismuth compounds possessed a spirocheticidal power. They reached the conclusion that the most useful of these from a practical standpoint was *sodium and potassium tartro-bismuthate.* Under the name of *Luatol* has been introduced a 10 per cent. aqueous solution of this salt. This preparation is sold in the United States under the trade name of *bismosol*. *Trepol* is an oily suspension of the same substance.

While at the present writing there is not sufficient data to make an accurate judgment of the value of the bismuth compounds in *syphilis*, there is considerable evidence of their curative effect. Although, as far as we know, no serious poisonings in human beings had been reported, it should be remembered that the doses employed are certainly capable of toxic effects, the most important being stomatitis, the early symptoms of which are a foul breath, blue line on the gums and salivation. Lucke and Klauder (*J. P. Ex. T.*, 1923, xxi, 313) have shown that bismuth has a predilection for the kidneys and may give rise to serious nephritis. The *dose* of sodium and potassium tartro-bismuthate is about one and one-half grains (0.1 Gm.) injected intramuscularly every other day for one or two months.

Another form of bismuth which has been brought forward as an antisyphilitic is the *bismuth salicylate.* This is marketed in ampules, each containing two grains of the salt suspended in olive oil. The contents of one ampule may be injected intramuscularly twice a week (Ballenger and Elder, *T. G.*, March 15, 1925).

Luffa. *Luffa cylindrica* (L.) Röm. *Vegetable Sponge. Wash-rag Sponge. Gourd Towel.*—A cucurbitaceous plant, indigenous to Arabia and Egypt, furnishing a gourd fruit, which presents upon the removal of the epidermis a durable skeleton of interwoven woody fibers, which are used in place of sponge. For description of this plant see Weber. (*A. J. P.*, 1884, 6.) The fruit of *L. echinata* Roxb., of India, is a violent irritant poison, from which C. J. H. Warden has separated a principle allied to, if not identical with, *colocynthitin.* (*P. J.*, June, 1890.)

Lupinus. *Lupinus albus* L. *White Lupine. Lupin*, Fr. *Feigbohne, Wolfsbohne*, G.—A plant belonging to the *Leguminosæ*, and a native of Europe and Western Asia, which is sometimes cultivated in our gardens. Other species are also met with —*L. hirsutus* L., *L. luteus* L., *L. polyphyllus* Lindl., *L. densiflorus* Benth. The last two are indigenous to the Pacific slope and the West. The bitter principle *lupinin*, $C_{29}H_{32}O_{16}$, is a glucoside, and its solution in alkalies is of a dark brownish-yellow color. On boiling with dilute acids it is decomposed into *lupigenin*, $C_{17}H_{12}O_6$, and a fermentable, dextro-rotatory glucose. The bruised seeds of white lupin, after soaking in water, are sometimes used as an external application to *ulcers*, etc., and internally are said to be anthelmintic, diuretic, and emmenagogue. An instance has been recorded where a decoction used as an injection in the rectum caused symptoms which suggested a poisonous character for the drug. Schmidt (*A. Pharm.*, 1897, ccxxxv) has found an alkaloid, *lupanine*, $C_{15}H_{24}ON_2$, in *L. angustifolium*. *Hydroxylupanine*, $C_{15}H_{24}O_2N_2$, is also stated to be present. It is a pale, yellow, syrupy fluid of an intensely bitter taste and showing a green fluorescence. Two alkaloids, *lupinine*, $C_{10}H_{19}ON$, and *lupinidine*, $C_8H_{15}O_2N$, have been isolated from the seeds of *Lupinus luteus* and *L. niger*, the former a crystalline powder and the latter a syrupy liquid. According to Willstätter and Marx (*B. Chem. G.*, 1904, xxxvii) lupinidine is identical with sparteine. For study of the constitution of lupinine see Willstätter and Fourneau (*B. Chem. G.*, 1902, xxxv, 1914). Steiger (*J. Soc. Chem. Ind.*, 1886, 385) has also studied a carbohydrate analogous to dextrin, which Baeyer and Eichborn discovered in *Lupinus luteus*. He finds that it is not changed by yeast, that nitric acid converts it into mucic acid, and that diluted sulphuric or hydrochloric acid converts it into galactose.

According to Schwartz (*W. K. R.*, 1906) the seeds of the *Lupinus arabicus* contain *calcium-anhydro-oxydiamine phosphate*, to which he has given the name of *magolan* and which is a useful remedy in *diabetes mellitus*. It occurs in crystals which yield a green precipitate with copper acetate. The *dose* of magolan is three grains (0.2 Gm.) several times daily.

Lycetol. *Dimethylpiperazine Tartrate.* $NH(CH_2CHCH_3)_2NH + H_2C_4H_4O_6$.—This is the tartrate of a substitution product from piperazine, in which an atom of hydrogen in each of two CH_2 groups is replaced by the methyl group CH_3. *Lycetol* is a white powder melting at 250° C., readily soluble in water, having a taste which is described as pleasant and acidulous. Alkalies react on it, liberating from it the insoluble free base, and while anhydrous it is stated to be slightly hygroscopic. It is asserted that it is an active diuretic, exerting a powerful solvent influence upon uric acid, and causing no disturbance of digestion even when given continually in large doses. According to Hamonic, it acts very favorably in purulent *cystitis*, lessening suppuration and the tendency to decomposition of the urine. It has been used with asserted excellent results in *chronic* and *acute gout*, and in various other forms of *uric acid diathesis*, as well as for solution of *calculi*. *Dose*, of lycetol, from fifteen to thirty grains (1.0–2.0 Gm.) daily, administered in from one to two pints of water.

Lycium. *Matrimony Vine.* (Fam. *Solanaceæ.*) —Different species of *Lycium* have been used in various parts of the world for supposed medicinal virtues. *L. vulgare* Dun. (*L. halimifolium* Mill.), indigenous in the south of Europe and in Asia, is a thorny shrub, with long flexible branches, and is cultivated for hedges and arbors. Husemann and Marmé found in the leaves and stem an alkaloid, *lycine*, $C_5H_{11}O_2N$. (*A. J. P.*, 1864, 226.) Husemann believes that lycine does not exist in the plant, but is formed during the process of extraction, and also that it is identical with *betaine*, $C_5H_{11}NO_2$, the alkaloid obtained from beet juice by Scheibler, and with the oxyneurine of Liebreich (*A. J. P.*, xlvii, 209.) E. Schmidt found in *Lycium vulgare* traces of mydriatic alkaloids, resembling those of belladonna. (*Ap. Ztg.*, 1890, 511.) White, however, (*B. Sc. Pharm.*, 1921, xxviii, 503) failed to find any evidence of a mydriatic alkaloid. The young shoots of one of the species of *Lycium* are eaten in Spain as asparagus, and its leaves as salad, and the aborigines of Colombia used another species against *erysipelas*. The leaves of *L. vulgare*, as well as the fruit, are said to be used by the physicians of Japan.

Lycopodium Saururus Lam. *Piligan.*—In this Brazilian lycopod Adrian has found an actively poisonous alkaloid, *piliganine*. (*C. R. A. S.*, June, 1886; see also *B. G. T.*, cxi, 174.) Piligan is stated to contain also a resin which is mildly purgative. It has been used as an emeto-cathartic.

Other species of *Lycopodium*, as *L. selago* Dill. and *L. polytrichoides* of the Sandwich Islands, have been used as cathartics.

Lycopus. *U. S.* 1870. *Lycopus virginicus* L. *Lycope de Virginie*, Fr. *Virginischer Wolfsfuss*, G.—The *bugle-weed* is a labiate which grows throughout the greater part of the Eastern United States. The whole herb is used. Jos. L. Weil found 0.41 per cent. of fat melting at 50° C., 0.68 per cent. of a granular wax melting at 70° C., 0.43 per cent. of a crystallizable resin soluble in ether, a crystallizable glucoside, and a small quantity of gallic acid and tannin. (*A. J. P.*, 1890, 72.) It has a peculiar odor and a nauseous slightly bitter taste, which it imparts to boiling water.

Lycopus europœus L., a native of Europe, growing in waste places from Massachusetts to Virginia, is said to be frequently collected and sold for *L. virginicus*. The former may be distinguished by its acutely quadrangular stem, its narrow lanceolate leaves, of which the lower are somewhat pinnatifid, its more crowded flowers, and the acute segments of its calyx, armed with short spines. It has been employed in Europe as a substitute for quinine.

According to A. W. Ives, the bugle-weed is a mild narcotic and an astringent, useful in pulmonic and other *hemorrhages*. *Dose* of decoction (one ounce to one pint of boiling water), from one to four fluidounces (30–120 cc.).

Lycoris. *Lycoris radiata* Herb. (Fam. *Amaryllidaceæ.*)—According to Morishima (*A. E. P. P.*, 1897, xl, 121), this bulbous plant contains two alkaloids, *lycorine*, $C_{16}H_{17}O_4N$, which occurs in large colorless polyhedric crystals, and is physiologically active, resembling emetine in its action, and *sekisanine*, $C_{34}H_{36}O_9N_2$, which occurs in colorless, anhydrous columns and is quite inactive physiologically. More recent investigations indicate that lycorine is identical with narcissine (see *Narcissus*).

Lygosine. *Sodium Lygosinate.*—This is the sodium Salt of Diorthocumarketone. $CO(CH{:}CH.C_6H_4.ONa)_2 + 7H_2O$. It occurs as shining, metallic, green crystals, forming a red solution in water. According to Aujezki, it is feebly bactericidal, also capable of lowering the temperature in fevered rabbits. It has been used by Stray (*D. M. Zeit.*, 1909, No. 7) successfully in the treatment of *gonorrhea*, especially in women. For this purpose it is employed in solutions containing from one to five per cent.

Quinine lygosinate is a vivid orange-yellow color, representing approximately 70 per cent. of quinine. It is odorless and almost insoluble in water, but soluble in alcohol. Filep asserts that quinine lygosinate is actively bactericidal, and it has been employed clinically by Fürth (*Pharmakologische und Therapeutische Rundschau*, 1905, No. 12, p. 89) as a dusting powder in *old ulcers*, and for other surgical purposes. It is also claimed for the substance that it possesses styptic properties.

Lysidin. *Ethylen-ethenyl-diamine Hydrochloride. Methyl-glyoxalidin.* $C_4H_8N_2HCl$.—The article sold as *lysidin* is a 50 per cent. solution of the base *methyl glyoxalidin* which is chemically related to piperazine. The true base forms small colorless, extremely hygroscopic crystals, very soluble in water with an alkaline reaction, and giving the usual alkaloidal reactions. It is incompatible with acids and the salts of many metals and of the alkaloids. It is employed in the *uric acid diathesis,* thirty to one hundred and fifty grains (2–10 Gm.) being administered daily. The bitartrate forms the most stable salt. (*P. J.*, 1912, 371.)

Lythrum. *L. Salicaria* L. *Purple Loosestrife. Purple Willow-herb. Salicaire,* Fr. *Rother Weiderich,* G.—This is an elegant perennial herb of the Fam. *Lythraceæ,* a native of Europe, but naturalized from Quebec to Delaware. The dried herb is inodorous, and has an herbaceous, somewhat astringent taste. It is said to contain a glucoside, *salicarin,* which according to Caille (*P. J.*, 1920, civ) is the active principle. It has been used as a demulcent astringent in *diarrhea* and chronic *dysentery.* The *dose* of the powdered herb is about a drachm two or three times a day. A decoction of the root, prepared by boiling an ounce in a pint of water, may be given in the *dose* of two fluidounces (60 cc.).

Mace. *Macis. N. F. IV.*—"The arillode of the seed of *Myristica fragrans* Houttuyn (Fam. *Myristicaceæ*)." *N. F. IV.*

Mace was official in the U. S. Pharmacopœia 1890, and later in the National Formulary IV, but is now not recognized by either standard. It was described as follows: "In narrow bands, 25 mm. or more in length, somewhat branched and lobed above, united into broader bands; yellowish to brownish-orange, and oily. Odor fragrant; taste warm and aromatic.

"The powder is orange-buff to orange-brown. Mounted in water and examined microscopically, the powder exhibits elongated epidermal cells; parenchyma containing very small amylodextrin granules, which are colored red-brown by iodine T.S.; large oil cells the contents of which are not greatly changed in color on the addition of alkali.

"Powdered false Mace or Bombay Mace is yellow-brown to deep-brown in color and deficient in odor and taste. When mounted in water and examined microscopically it exhibits flattened, thick-walled epidermal cells and oil cells much more numerous than in true Mace and containing an orange-red resinous substance which is dissolved by alkalies forming a blood-red liquid.

"Moisten Mace with hydrochloric acid; no greenish color is produced (difference from and absence of the *arillode of Myristica malabarica* Lamarck or *Bombay Mace*). Add potassium chromate T.S. to an alcoholic extract of Mace (1 in 10); the precipitate formed is yellow and does not change to red on standing, nor does the solution develop a red coloration (difference from and absence of *Bombay Mace*). Saturate a piece of filter paper with an alcoholic tincture of Mace (1 in 10), and add one drop of potassium hydroxide T.S.; no blood-red coloration is produced (difference from and absence of *Bombay Mace*).

"Mace yields not less than 8 per cent. of volatile ether extract, and not less than 20 per cent. nor more than 30 per cent. of non-volatile ether extract. Mace yields not more than 3 per cent. of ash which is almost completely soluble in hydrochloric acid." *N. F. IV.*

Mace is inferior when it is brittle, less than usually divided, whitish or pale yellow, or with little taste and odor. The presence of starch granules or other microscopic particles different from those spoken of in powdered mace is proof of adulteration. Mace contains from 7 to 9 per cent. of a volatile oil, the greater portion of which consists of pinene, along with which is some *myristicin,* $C_{12}H_{14}O_3$. Wallach separated two odorous fixed oils; one yellow, soluble in ether, insoluble in boiling alcohol; the other red, soluble in alcohol and ether in every proportion.

Mackay Bean. (*Garbee Bean.*)—This is the seed of *Entada scandens* Benth. (Fam. *Leguminosæ*), a tropical woody climber; which has the reputation in Queensland of being strongly poisonous, and in which John Moss found saponin. (*P. J.*, vol. xviii, 242.) According to Raybaud (*C. R. S. B.*, 1921, lxxxv, p. 933), the *Entada Sudanica,* a small shrub found in French Equatorial Africa, yields an amber-colored gum of which 92 per cent. is soluble in cold water, the remainder acting like tragacanth.

Maculanin. *Potassium Amylate.*—Ogata Osaka (*D. M. W.*, 1907) prepares a caustic in the following manner: Well washed rice grains are scattered on the bottom of a glass dish, the latter being filled with a ten per cent. solution of potassium hydroxide and allowed to stand for six or eight hours, after which time the water is poured off, and the transparent mass rubbed up in a mortar. This is applied like a paste to the diseased tissue which has been previously cleansed.

Magnesium Benzoate. *Magnesii Benzoas.* $Mg(C_7H_5O_2)_2$.—A white, crystalline powder, permanent in the air, soluble in 20 parts of water or alcohol. Used for *gout, urinary calculi,* and *tuberculosis,* in *doses* of from three to fifteen grains (0.2–1.0 Gm.).

Magnesium Borate. $Mg(BO_2)_2.2Mg(OH)_2 + 7H_2O$.—This magnesium salt was primarily introduced under the trade name *antifungin.* It forms colorless micro-crystals possessing decided antiseptic value. It is used almost exclusively as a preservative, although it has been given as an internal antiseptic in *doses* of five to fifteen grains (0.32–1.0 Gm.).

Magnesium Bromide. *Magnesii Bromidum.* $MgBr_2 + 6H_2O$.—Made by neutralizing hydrobromic acid with magnesium oxide, evaporating and crystallizing. In the form of colorless, very deliquescent crystals, used as a nervine, in *doses* of from five to thirty grains (0.32–2.0 Gm.).

Magnesium Copaivate.—A yellowish powder, slowly soluble in alcohol and asserted to be an antiseptic, diuretic and laxative. It is used in *gonorrhea, leucorrhea* and *dysentery.*

Magnesium Glycerophosphate.—A white amorphous powder soluble in water, its solutions being neutral or faintly alkaline. It is used for the same purposes as the other glycerophosphates; *dose,* five to ten grains (0.3 to 0.6 Gm.).

Magnesium Hypophosphite.—White crystals, efflorescent, soluble in about 5 parts of water. It is used like the other hypophosphites. *Dose,* five to ten grains (0.3 to 0.6 Gm.).

Magnesium Iodide. $MgI_2 + 8H_2O$.—A deliquescent, crystalline powder melting at 45° C., and rapidly decomposing in aqueous solution. It is used as an alterative and sialagogue in the treatment of *scrofula, syphilitic* and *chronic rheumatism. Dose,* three to eight grains (0.2–0.5 Gm.).

Magnesium Lactate. *Magnesii Lactas.* $Mg(C_3H_5O_3)_2 + 3H_2O$.—In white, granular crystals, soluble in about 30 parts of cold water and 6 parts of boiling water, insoluble in alcohol. Used as a mild laxative in *doses* of from fifteen to forty-five grains (1–3 Gm.). A combination of magnesium lactate and magnesium phosphate known as *magnesium phospholactate,* is recommended as a tonic laxative. *Dose,* three to fifteen grains (0.2–1.0 Gm.).

Magnesium Perborate.—The exact composition of this salt is somewhat doubtful. The formula $MgBO_3 + 7H_2O$ has been suggested, but the commercial preparations rarely yield the amount of oxygen (11.9 per cent.) which would be indicated by such a compound. Magnesium Perborate is sparingly soluble in water with partial decomposition, the resulting solutions are faintly alkaline and contain hydrogen peroxide. It is used chiefly in the preparation of dentrifrices.

Magnesium Salicylate. *Magnesii Salicylas.* $Mg(C_6H_4(OH)CO_2)_2.4H_2O$.—This salt has been used as an intestinal antiseptic by Boas (*B. K. W.,* 1910, p. 89) in *intestinal fermentation,* and by Huchard in *typhoid fever.* The *dose* is from fifteen to thirty grains (1–2 Gm.) three times a day.

Magnesium Silicate. *Hydrated Magnesium Silicate. Meerschaum. Sepiolite. Ecume de Mer,* Fr. $3MgSiO_3 + 5H_2O$.—Meerschaum is one of several hydrated silicates of magnesium, asbestos, talc and serpentine being others of analogous formula. The most important deposits of meerschaum are in Anatolia, Asia Minor. It is used for the manufacture of tobacco pipes. It has been used as a substitute for bismuth subnitrate in *diarrhea* and has the advantage of not darkening the feces. It should be reduced to a very fine powder, and given in *doses* of from one to four drachms (3.9–15.5 Gm.) a day.

Magnesium Sulphite. *Magnesii Sulphis. U. S.* 1880. $MgSO_3.6H_2O$.—This salt may be prepared by double decomposition between magnesium sulphate and neutral sodium sulphite. Owing to the almost universal presence of sulphate in the sodium sulphite, J. P. Remington proposed to prepare it by suspending eight parts of pure magnesia in sixteen parts of water, and then adding gradually, with stirring, official aqueous sulphurous acid in excess. The crystals which form are washed with very cold water, drained, and dried. (*A. J. P.,* xl, 97.) "A white, crystalline powder, gradually becoming oxidized on exposure to air, odorless, having a slightly bitter, somewhat sulphurous taste, and a neutral or slightly alkaline reaction. Soluble in twenty parts of water at 15° C., and in nineteen parts of boiling water; insoluble in alcohol. When heated to 200° C., the salt loses its water of crystallization (50.9 per cent.), and is converted into magnesium oxide and anhydrous magnesium sulphate. The aqueous solution of the salt, mixed with ammonium chloride, yields, with excess of test-solution of sodium phosphate and water of ammonia, a white, crystalline precipitate soluble in acids. When treated with four times its weight of diluted hydrochloric acid, the salt dissolves completely and emits the odor of burning sulphur, without becoming cloudy (difference from hyposulphite). A one per cent. aqueous solution, strongly acidulated with hydrochloric acid, should not afford more than a slight cloudiness with test solution of chloride of barium (limit of sulphate)." *U. S.* 1880. Magnesium sulphite shares the general medicinal properties of the sulphites, but is better fitted for internal administration on account of its less solubility and less disagreeable taste, etc. (See *Sodii sulphis.*) The *dose* is from fifteen grains to half a drachm (1–2 Gm.).

Magnolia. *U. S.* 1880. *Magnolia Bark.*—Three species of *Magnolia* were formerly official as follows: *Magnolia glauca* L., *Small* or *Laurel Magnolia, M. acuminata* L. or *Cucumber-tree,* and *M. tripetala* L., commonly known as *Umbrella-tree* (Fam. *Magnoliaceæ*). In the fruit of the latter Wallace Procter found a neutral crystalline principle, *magnolin.* When pure, this is without odor and has at first little taste, in consequence of its insolubility in the liquids of the mouth, but after a time produces an irritant effect on the fauces. It is nearly insoluble in cold, but slightly soluble in hot water, very soluble in alcohol or ether. Procter considered it analogous to the liriodendrin obtained by Emmet, but quite distinct. It has been also found in other species. (See *A. J. P.,* 1872, 145; also Lloyd's paper in *Ph. Rund.,* 1866, 224.) W. F. Rawlins (*A. J. P.,* 1889, 7) obtained from the leaves of *M. glauca* a small quantity of a volatile oil of bright green color, with an odor resembling fennel or anise, but more pleasant. From the ethereal solution of this oil small crystals deposited. Indications were also obtained of a bitter glucosidal principle.

The bark and fruit of all the species of *Magnolia* are possessed of similar properties; but the bark only was official, and that of the root was thought to be most efficient. "The bark from young wood is quilled or curved, thin, externally orange-brown and glossy, or light gray, with scattered warts and somewhat fissured, internally whitish or pale brownish and smooth; fracture short, in the inner layer somewhat fibrous; inodorous; taste somewhat astringent, pungent, and bitter. The bark of old wood, deprived of the cork, is whitish or brownish, fibrous, and less pungent." *U. S.* 1880. The aromatic property, which resides in a volatile principle, is diminished by desiccation, and entirely lost when the bark is long kept. The bitterness, however, remains. The bark is destitute of astringency.

Magnolia is a gently stimulant aromatic tonic and diaphoretic. It has been used in *malaria* and in *rheumatism.* The *dose* of the recently dried bark in powder is from half a drachm to a drachm (2.0–3.9 Gm.), frequently repeated.

Malachite Green. *Tetra-methyl-diapara-amido-triphenyl-carbinol.*—(The term malachite green is usually applied to this coal tar dye although the native green copper carbonate has also been known as "malachite.") The closely allied *brilliant green,* or *diamond green* G., while by some considered identical, appears to be the sulphate of a compound similar to that above with the exception that the methyl groups are replaced by a tetra-ethyl. Malachite green of commerce occurs as either the zinc double chloride or double oxalate compound. The former is in brass yellow prismatic crystals while the latter is in green metallic-glistening plates. It is also called *benzaldehyde green.*

Malachite green is an active germicide but differs very greatly in its effects on various micro-organisms. Boer finds that one part in 40,000 destroys the anthrax bacillus in two hours and one in 8000 the diphtheria bacillus but that it requires one in 300 to destroy the typhoid bacillus. Fildes and Rajchman (*C. D.,* 1915, p. 156) find that one in 2000, is germicidal against the *Staphylococcus aureus.*

A number of surgeons have used it successfully as a wound antiseptic. According to Webb (*B. M. J.*, June, 1917, 870), it has the advantage of not interfering with granulation or phagocytosis. He uses a one to 1000 solution as a wound lavage and states that although it stains dead or nonvascular tissue (as the skin), it does not stain living vascular tissue. According to Löffler (*D. M. W.*, 1906, p. 269), it possesses such a marked influence over the *Bacillus coli communis* that it can be used as a means of separating this organism from the typhoid bacillus. Wendelstadt (*D. M. W.*, 1906, p. 863) has found it of service in the treatment of experimental trypanosomiasis, but we know of no clinical application of this result.

Malakin. *Phenosal. Salicyl-paraphenetidin.* $C_6H_4\left\{\begin{matrix}OC_2H_5\\ N:CH.C_6H_4(OH)\end{matrix}\right. + H_2O$.—This occurs in small, bright yellow, fine needles, melting at 92° C., insoluble in water, sparingly soluble in cold, but quite so in hot, alcohol, insoluble in carbonates of the alkalies, but soluble with a yellow color in sodium hydroxide solution. Weak mineral acids decompose it, forming salicylaldehyde and paraphenetidin.

Malakin contains about 57 per cent. of salicylic acid and 43 per cent. of phenetidin. In 1893 Jacquet called attention to it as an anti-rheumatic remedy, stating that it is decomposed in the stomach, yielding salicylaldehyde to the blood, and offering, therefore, a method of giving salicylic acid. On the other hand, while a number of clinicians have reported favorably of its effect in *acute rheumatism*, Ottolenghi (*Ther. Woch.*, ii, 1895) has found that the decomposition and after-absorption of it is exceedingly slow and uncertain. The contention of Bauer, that it is distinctly inferior to the older salicylates, is in all probability correct. Ottolenghi suggests that malakin must act on intestinal parasites, and may therefore prove useful as an anthelmintic. *Dose*, eight to fifteen grains (0.5–1.0 Gm.).

Malambo or Matias Bark.—A bark received from South America by Alex. Ure, under the name of *matias bark*, was found to have the characters of the *malambo bark*, which is held in high esteem in Colombia, where it is produced. According to H. Karsten, it is derived from a species of *Croton*, which he names *Croton Malambo* Karst. (Fam. *Euphorbiaceæ*). This is a small tree or shrub, growing on the coast of Venezuela and Colombia. The bark occurs in transversely curved pieces with a white outer and reddish-brown inner surface and a short fracture. It has a slightly aromatic odor and a bitter, pungent taste, and yields these properties to water and alcohol. Its active ingredients appear to be a volatile oil and a bitter extractive matter. Although formerly recommended as a febrifuge and antiperiodic it is probably nothing more than an aromatic tonic.

Malambo bark has been substituted for Winter's bark.

Malouetia. *Malouetia nitida* Spruce. *Guachamaca.* (Fam. *Apocynaceæ.*)—This plant, of Venezuela, contains an alkaloid, *guachamacine*, which Kobert believes to be identical with *curarine.* (*A. J. P.*, 1885, 560.)

Mandragora. *Mandragora autumnalis* Bertol. *Mandrake. Mandragora.* (Fam. *Solanaceæ.*)—A perennial, European plant, with spindle-shaped root, which is often forked beneath, and is therefore compared, in shape, to the human figure. In former times this root was supposed to possess magical virtues, especially when collected at certain times, and was used as an amulet to promote fecundity, etc., and the superstition is still cherished in some parts of Europe. The plant is a poisonous narcotic, somewhat similar in its properties to belladonna, to which it is botanically allied. See a paper by Ekert for the history of this drug. (*S. W. P.*, 1913, 425.) Crouzel isolated an alkaloid, *mandragorine*, which he found similar in properties to atropine. (*P. J.*, 1885, 1067.) Thoms and Wentzel (*B. Chem. G.*, 1901, xxxiv, p. 1023) state that this mandragorine is a mixture of hyoscyamine and scopolamine. Hesse (*J. P. C.*, 1901, lxiv, p. 274) finds in the plant, however, besides these two alkaloids a third substance to which the name mandragorine may be applied, $C_{15}H_{19}O_2N$.

Mandragora was much used by the ancients as a narcotic, and as an anesthetic agent before surgical operations. (*J. P. C.*, xv, 290.) *Morion* or *death-wine*, said to have been administered previous to the torture, was made from it.

Manganese. *Manganum.* Mn.—Atomic weight, 54.93. This element is a brittle grayish white metal, very hard, being capable of cutting glass and scratching tempered steel. It is susceptible of taking a high polish and has a specific gravity of 7.9. With oxygen it forms five or possibly seven compounds as follows—monoxide, MnO, of a light green color; sesquioxide, Mn_2O_3 (*braunite*), of a dark brown color; magnetic oxide, Mn_3O_4, which occurs in *hausmanite* as brownish black crystals; the dioxide MnO_2 described below; the highest oxide is acid forming yielding permanganic acid, $HMnO_4$ (see *Potassium permanganas.*) Manganese occurs in the mineral kingdom in the form of a silicate (*rhodonite*), as a carbonate (*rhodochrosite*) and as a dioxide (*pyrolusite*). The most abundant mines are in Russia, but it is also mined in various other countries. In the arts it is widely used in alloy with copper and zinc either as manganese bronze or German silver and for hardening steel.

Manganese is an occasional constituent of organic matter. It has been detected in minute quantity in various parts of the human body but is probably not a normal constituent of any human tissue. According to E. Davy, potassium hydroxide, dissolved in an equal weight of water, forms a delicate test for manganese, not obscured by the presence of other metals.

The citrate, glycerophosphate, and hypophosphite are recognized by the N. F. Several of its salts have been proposed as medicines, to be used as tonic and anti-anemic remedies.

Manganese Butyrate.—A solution of this salt has been brought forward as a remedy for *furunculosis* and other staphylococcic infections. The 1 per cent. solution is recommended to be injected intramuscularly in doses of fifteen minims (1 cc.); not more than two doses are to be given.

Manganese Carbonate. *Mangani Carbonas. Manganous Carbonate.* $MnCO_3$.—This salt may be obtained by double decomposition between molecular proportions of manganous sulphate and sodium carbonate, using the same precautions to prevent oxidation that are employed in making the preparations of ferrous carbonate. It is given in the form of pills of four or five grains (0.26–0.32 Gm.) each.

Manganese Chloride. *Mangani Chloridum.* $MnCl_2 + 4H_2O$.—Manganese chloride occurs as rose-colored deliquescent crystals. It has been used locally as a stimulant to *syphilitic* and other *indolent ulcers.* For process of preparing it, see *U. S. D.*, 19th ed., p. 1559.

Manganese Dioxide. *Mangani dioxidum. Mangani oxidum nigrum. Binoxide of Manganese. Manganese Peroxide, Manganum Hyperoxydatum; Oxydum Manganicum; Peroxide of Manganese; Deutoxide of Manganese, Black Oxide of Manganese, Pyrolusite; Braunstein,* G.

The U. S. P. 1890 recognized under the name of *Mangani dioxidum* the "native crude manganese dioxide." In the 8th revision this was substituted by a dioxide prepared by precipitation of manganese sulphate by a mixture of equal volumes of ammonia water and a solution of hydrogen peroxide. In the 10th revision the salt was entirely dropped. The *precipitated* Manganese dioxide (*Mangani Dioxidum Praecipitatum* U. S. IX) consisted "chiefly of manganese dioxide [MnO_2=86.93] with small amounts of other oxides of manganese, corresponding to not less than 80 per cent. of MnO_2." *U. S. IX.*

The formula for its preparation was as follows: "Manganese Sulphate, *fifty grammes;* Ammonia Water, *two hundred and fifty cc.;* Solution of Hydrogen Dioxide, *two hundred and fifty cc.;* Distilled Water, *a sufficient quantity.* Dissolve the manganese sulphate in *one thousand cc.* of distilled water. Dilute the ammonia water with an equal volume of distilled water, and mix it with the solution of hydrogen dioxide, which has also been diluted with an equal volume of distilled water. Pour the mixed solutions, slowly, with constant stirring, into the solution of manganese sulphate. Allow the mixture to stand for one hour, stirring frequently. Then decant the supernatant clear liquid from the precipitate, and wash the latter repeatedly by affusion and decantation with hot distilled water, using *one thousand cc.* each time. Collect the precipitate on a plain filter, and continue the washings with hot distilled water until the washings no longer have an alkaline reaction upon red litmus paper, and produce no turbidity when mixed with barium chloride test solution. Allow the precipitate to drain, then dry it at 150° C." *U. S. VIII.*

Manganese dioxide, as it occurs in nature, is very diversified in its appearance. Its sp. gr. varies from 4.7 to 4.9. It is found sometimes in brilliant needle-shaped crystals, often in compact masses having a metallic luster, but far more frequently in the form of a dull earthy-looking substance of a black or brown color. It is purest when crystallized. As it occurs in commerce, it is usually in the form of a black powder, insoluble in water, and containing more or less oxidized iron, calcium carbonate, barium sulphate, and earthy matter. Iron, which is rarely absent, is detected by the production of a green or blue tint on the addition of potassium ferrocyanide to its hydrochloric acid solution. When exposed to a red heat it yields a portion of its oxygen, and is reduced to manganoso-manganic oxide. Hence its use in obtaining that gas. Good samples, after being dried, lose, when heated to a whiteness, 12 per cent. of oxygen. It is distinguished from antimony sulphide which it physically resembles by its infusibility, and by causing the evolution of chlorine on being heated with hydrochloric acid. When of a brown color, it is not of good quality.

The U. S. Pharmacopœia described the precipitated manganese dioxide as "a heavy, very fine, black powder, without odor or taste; permanent in the air. It is insoluble in water or alcohol. When heated with hydrochloric acid, it is converted into manganous chloride and chlorine is evolved. At a red heat Precipitated Manganese Dioxide gives off oxygen and is converted into reddish-brown manganous-manganic oxide (Mn_3O_4). Add 2 drops of hydrochloric acid to about 0.1 Gm. of Precipitated Manganese Dioxide contained in a test tube, boil the mixture for one minute with 0.5 Gm. of lead peroxide and 5 mils of nitric acid and then add 5 mils of distilled water; the liquid assumes a reddish-violet color. Add 20 mils of distilled water to 1 Gm. of Manganese Dioxide and 2 Gm. of oxalic acid, follow this by 3 mils of sulphuric acid, and digest the mixture for several hours on a water bath; not more than 0.2 per cent. of residue remains (*insoluble substances*).

"Dissolve about 0.2 Gm. of Precipitated Manganese Dioxide, accurately weighed, in a mixture of 50 mils of tenth-normal oxalic acid V.S. and 3 mils of sulphuric acid, heat to 80° C. on a water bath, and titrate the residual oxalic acid with tenth-normal potassium permanganate V.S. It shows not less than 80 per cent. of MnO_2.

"Each mil of tenth-normal oxalic acid V.S. used corresponds to 0.0043465 Gm. of MnO_2. Each gramme of Precipitated Manganese Dioxide corresponds to not less than 184 mils of tenth-normal oxalic acid V.S." *U. S. IX.*

This salt appears to possess some stimulant action upon the uterine mucosa and is still used in the treatment of *amenorrhea.* Its ancient employment in *syphilis, scurvy,* and various *skin diseases,* does not appear to be founded on any rational basis.

The native oxide is used in the arts for obtaining chlorine in the manufacture of bleaching powder, for giving a black glazing to pottery, and for freeing glass from the color which it derives from iron. In the laboratory it is employed to obtain oxygen and chlorine, and to form the salts of manganese. It is also used for liberating chlorine from hydrochloric acid and from sodium chloride, and iodine from sodium iodide contained in kelp.

Dose, three to ten grains (0.2–0.65 Gm.).

Manganese Iodide. *Mangani Iodidum. Manganous Iodide.* MnI_2.—This very deliquescent salt may be prepared by adding manganese carbonate to aqueous hydriodic acid, filtering the solution, and granulating, carefully regulating the heat. This iodide may be administered in syrup or pill. For formula for these, see *U. S. D.*, 19th ed., p. 1559. According to Hannon, manganous iodide is particularly useful in the *anemia* attendant on *scrofula, phthisis,* and *cancer,* and in *syphilis.* It is also affirmed that when given with cinchona it removes the enlargement of the spleen of malarial fevers. *Dose,* two to four grains (0.12–0.25 Gm.).

Manganese Lactate.—This occurs as a pinkish powder or granules soluble in about ten parts of water. It has been used as a hematinic in *doses* of from one to five grains (0.06 to 0.3 Gm.).

Manganese Peptonate. *Peptonized Manganese.*—This is a brown powder representing about 3 per cent. of manganese. It is soluble in water. It has been used in the treatment of anemias in *doses* of ten to thirty grains (0.6–2.0 Gm.) (see also *Liquor Ferri Peptonatum et Mangani*).

Manganese Phosphate.—*Manganese Ortho-*

phosphate. Under the name of Manganese Phosphate is furnished either the dibasic or tribasic salt, although the latter seems to be the one most frequently intended. It is a pink powder insoluble in water but soluble in diluted mineral acids. It is employed usually in conjunction with iron in the treatment of *anemia,* in *doses* of one to five grains (0.06 to 0.3 Gm.).

Manganese Sulphate. (*U. S. P. VIII*). *Mangani Sulphas. Manganesii Sulphas. U. S.* 1870. *Manganum Sulphuricum. Schwefelsaures Manganoxydul,* G.—"It contains not more than 38 per cent. of water, and not less than 62 per cent. nor more than 68 per cent. of $MnSO_4$ (151.00)." *N. F. IV.*

This salt is no longer official in either the U. S. P. or N. F. It may be prepared by heating the native black oxide with concentrated sulphuric acid. For details of several methods of manufacture, see *U. S. D.*, 19th ed., p. 762. From its aqueous solution it crystallizes in rhombic prisms, which contain variable proportions of water of crystallization according to the temperature of the solution and other circumstances. "Manganese Sulphate occurs as pale rose-colored, translucent, tetrahedral prisms; slightly efflorescent when exposed to moist air. Odorless; taste slightly bitter and astringent. One gramme of the salt dissolves in about 1 cc. of water at 25° C., and in about 0.6 cc. of boiling water; insoluble in alcohol. An aqueous solution of the salt (1 in 20) is neutral or slightly acid to litmus." *N. F. IV.* For further tests see *U. S. D.*, 20th ed., p. 1483.

At one time manganese sulphate was said to be an active cholagogue and purgative, but it has failed to come into use as such. According to Thomas Thomson, of Glasgow, it resembles sodium sulphate both in taste and in effect, operating as a purgative in the dose of from one to two drachms (3.9–7.5 Gm.). A trial was made of it in *anemia,* as an adjuvant of the chalybeates, but the results have not been satisfactory and it is at present rarely given. *Dose,* as a tonic, from five to twenty grains (0.32–1.3 Gm.).

Mangosteen.—The pericarp of the fruit of *Garcinia Mangostana* L. (Fam. *Guttiferæ*), a handsome fruit tree widely cultivated in tropical countries. It is sometimes substituted for bael fruit (see *Belæ Fructus,* Part I). It is an active astringent, and has been used as such locally in various *catarrhs,* and also in *diarrhea* and in *leucorrhea.* Ambrose has used the toasted and pulverized rind of mangosteen in the treatment of tropical *dysentery* with asserted benefit. He gives *doses* of one drachm (4 Gm.) every two hours. The activity of the drug appears to reside in the neutral principle *mangostin. Dose,* of fluidextract, from half to one fluidrachm (1.8–3.75 cc.).

Manzanillo. *Manchineel. Hippomane Mancinella* L.—According to A. Betancourt, the milky juice of this euphorbiaceous tree, found near the coasts of Central America, West Indies and adjoining South America and Southern Florida, is a violent irritant, acting as a vesicant when applied to the skin, and when taken internally in doses of twenty drops causing a fatal gastroenteritis. In *doses* of two drops it acts as a powerful and very certain cathartic; it is also diuretic. In Cuba it has much repute in *tetanus.* (*L. M. R.*, Feb., 1889.)

Maranta. *Arrowroot. Arrowroot Starch.* (Fam. *Marantaceæ.*)—Under this name the U. S. Pharmacopœia, 1870, recognized the fecula or starch obtained from the rhizome of *M. arundinacea,* L.

The arrowroot plant is a native of the West Indies, where it is largely cultivated for the sake of its fleshy, irregularly cylindrical rhizomes whose cells are gorged with starch granules. It is cultivated also in the East Indies, Ceylon, Sierra Leone, and south of Africa, and formerly in our Southern States, especially Georgia and Florida. The plant is easily propagated by cuttings of the root. An analysis by Macdonald (*J. Soc. Chem. Ind.*, 1887, 336) gives the following as the composition of the St. Vincent root: Starch, 27.07 per cent.; fiber, 2.82; fat, 0.26; albumen, 1.56; sugar, gum, etc., 4.10; ash, 1.23; water, 62.96; total, 100.00. An analysis of the arrowroot starch from the same locality by Macdonald gave: Starch, 83.70 per cent.; fiber, 0.04; fat, 0.07; sugar, gum, etc., 0.18; ash and sand, 0.14; water, 15.87; total, 100.00. The fecula is prepared in the following manner. The rhizomes are dug up when a year old, washed, and then beaten into a pulp, which is thrown into water, and agitated so as to separate the amylaceous from the fibrous portion. The tissues are removed by the hand, and the starch remains suspended in the water, to which it gives a milky color. The milky fluid is strained through coarse linen, and allowed to stand that the starch may subside, which is then washed with a fresh portion of water, and afterwards dried in the sun.

The *Bermuda arrowroot* was formerly the most highly esteemed, but the production of it in the island has almost ceased. It occurs in somewhat hard and irregular whitish masses which when rubbed between the fingers are reduced to a smooth powder.

St. Vincent arrowroot is the variety now in the ascendency on the market. It differs from the Bermuda arrowroot in being slightly darker in color and in having many of its masses of grains larger than the preceding variety. For a list of other sources of arrowroot of commerce during different periods, see *U. S. D.*, 19th ed., p. 1561.

A spurious form, called *Florida arrowroot,* is derived from the stem of the *Zamia integrifolia* Willd. Langworthy and Denel (*J. Bi. Chem.*, 1922, lii, 251) have shown this is less easily digested.

Arrowroot starch is in the form of a light, white powder, or of small pulverulent masses, without odor or taste. It is firm to the touch when pressed between the fingers, and produces a faint creaking sound when rubbed. It is liable to become musty, and should then be rejected. The odor and taste are the best criteria of its quality. It should be perfectly free from odor and unpleasant flavor.

The microscope offers the best means of distinguishing the different varieties of fecula sold as arrowroot, or used for its adulteration. The grains of *Maranta arrowroot* are ovoid to ellipsoidal or oblong, from 10 to 70 microns in length with very fine, often indistinct, lamellæ, and a hilum varying from a circular to a linear or crescent-shaped cleft, situated in the center or toward the broad end of the grain. St. Vincent arrowroot exhibits grains with the larger number of transverse or crescent-shaped clefts.

Arrowroot affords a light, very mild, and easily digested article of diet, well adapted for the sick and convalescent, and peculiarly suited, from its demulcent properties, to bowel complaints. It is prepared by dissolving it in hot water or hot milk, with either of which it forms a pearly, gelatinous solution, and, if in sufficient quantity, a jelly-like mass on cooling. A tablespoonful will communicate sufficient consistence to a pint of water. It should first be formed into a perfectly smooth paste with a little cold water or milk, and the boiling water then gradually added with brisk agitation. The preparation may be then suitably flavored and sweetened.

Maretin. *Metatolyl-hydrazine-carbaminate.* $C_6H_4.CH_3.NH.NH.CONH_2$.—This may be regarded as a methyl-acetanilid in which the acetyl group is replaced by the carbamic group $NH.CONH_2$. It occurs as white, tasteless crystals practically insoluble in water or ether but readily dissolved by chloroform or acetone. It is claimed for the compound that the urea nucleus is so firmly combined that aniline is not liberated in the body; nevertheless, its effects are very similar to those of the other aniline derivatives. It has been used as an antipyretic and analgesic and is especially recommended in *acute articular rheumatism.* Heubner (*Th. M.*, 1911, xxv, p. 364, and 1913, p. 507) asserts that when used over long periods of time it causes destruction of the blood cells and may lead to a dangerous degree of anemia. The *dose* is from one and one-half to four grains (0.96–0.26 Gm.).

Marrubium. *Hoarhound. Horehound. White Hoarhound. Marvel. Herba Marrubii. Marrube Blanc,* Fr. Cod. *Andornkraut, Weisser Andorn,* G. *Marrubio,* It., Sp.—The U. S. P. formerly recognized "The dried leaves and flowering tops of *Marrubium vulgare* Linné (Fam. *Labiatæ*)." *U. S. VIII.*

Horehound has a perennial, fibrous root, and numerous erect, woolly annual stems, from twelve to eighteen inches high. The leaves are about 2.5 cm. long, roundish-ovate, crenate, wrinkled, downy above, hoary on the under surface, and supported in pairs on strong foot-stalks. The flowers are white, and in crowded axillary woolly whorls. Each consists of a sparsely hairy, tubular calyx with 10 hooked, bristle-like teeth, a bilabiate corolla, 4 parallel stamens and a bi-carpellary pistil with a 4-celled ovary.

Horehound has been adulterated with the leaves and flowering tops of *Ballota hirsuta* Benth., *Ballota nigra* L., *Marrubium peregrinum* L. and *Marrubium candidissimum* L. From all of these it may be readily distinguished by its characteristic calyx. *Ballota hirsuta* has been the most common recent adulterant. For detailed structural differences between *Marrubium* and *Ballota hirsuta* see article by H. W. Youngken in *A. J. P.*, 1919, pp. 147–156.

Horehound contains a volatile oil, resin, tannin, and a bitter principle called *marrubiin.* This marrubiin is slightly soluble in cold water, crystallizes from alcohol in prismatic and from ether in tabular crystals, is not precipitated by tannin, and has a very bitter and somewhat acrid taste. The fusing point of the crystals is 160° C., according to Kromayer. Matusow (*A. J. P.*, 1897, 201). He gives to it the formula $C_{30}H_{43}O_6$, and states the melting point of the purified substance to be from 154° to 155° C. According to him, it is not a glucoside.

Hoarhound is tonic, and in large doses laxative. It was formerly considered a valuable deobstruent, and was recommended in *chronic hepatitis,* and various other affections but it exerts no influence over any of them, and has passed mainly from the hands of physicians into domestic use, where it is used in the form of a confection for *sore throat.* It is employed occasionally in *bronchitis* with copious expectoration. The infusion, made in the proportion of an ounce of the herb to a pint of boiling water, may be given in wineglassful doses.

Dose, thirty grains to a drachm (2.0–3.9 Gm.).

Massoi Bark. *Lawang.*—In Eastern commerce, certain aromatic barks have occurred under the name of massoi barks. Of these, three are believed by F. Hekmeyer to be the products respectively of *Cinnamomum xanthoneurum* Blume, *Cinnamomum Burmanni* Blume (*C. Kianis* Nees), and *Massoja aromatica* Becc. (*Sassafras gœsianum* Teijsm. and Binn.), all of the Fam. *Lauraceæ.* For a description of these barks, by E. M. Holmes, see *P. J.*, 1888, 465. The *massoi bark* which comes from New Guinea, and from which Messrs. Schimmel have distilled an oil resembling that of nutmeg and cloves, probably has a different origin from the true massoi bark which has a cocoanut-like odor. (*Y. B. P.*, 1912, 473.)

Medeola. *Medeola virginiana* L. (*Gyromia virginiana* L.) *Indian Cucumber.*—An indigenous perennial herb of the Fam. *Liliaceæ,* growing in many parts of the United States. The tuber, which in shape and flavor bears a strong resemblance to a small cucumber, is said to have been eaten by the Indians, and was used by Barton to be useful as a diuretic in *dropsies.*

Melaleuca.—Under the names of *gomenol* and *Niaouli oil* there has been put upon the market a volatile oil obtained from the leaves of *Melaleuca viridiflora* Brong. and Gris., a tree growing in upper India, the islands of the Indian Ocean and Australia. Its sp. gr. is 0.922, and its rotatory power plus 0.42°. Its odor and taste are said to resemble those of camphor and peppermint. The chief constituent of the oil (66 per cent.) is cineol, and in addition to this is a crystallized terpineol, $C_{10}H_{18}O$, and the valeric ester of the same. These together make up 30 per cent. additional. It has been recommended in the *chronic catarrhs* of the pulmonary mucous membrane, and especially in *whooping cough* (see Carrière, *B. A. M.*, 1922, lxxxviii, 30). It may be given by the mouth or exhibited in the form of intramuscular injections being diluted with from four to ten parts of a sterilized fixed oil to one part of volatile oil. The hypodermic *dose* of a 10 per cent. solution is two and one-half fluidrachms to one-half fluidounce (9.3–15.0 cc.). The injections should be practised every other day. Gomenol has been used by Brimont (*Press. Med.*, 1910, p. 800) as a vermifuge in *ankylostomiasis,* in *doses* of five minims (0.3 cc.).

Melastoma. *Melastoma Ackermanni.*—This Colombian plant of the Fam. *Melastomaceæ* is used in South America as an antineuralgic. Its abundant essential oil resembles methyl salicylate, if indeed it be not identical with it. (See *N. R.*, Aug. and Sept., 1883.)

Meligrin.—This is a condensation product of dimethyloxyquinine and methylphenyl acetamid. It occurs as a white crystalline powder with a slightly burning, though not bitter taste. It is very soluble in water and is employed in the treatment of *migraine* and *neuralgia.*

Melissa. *U. S.* 1890. *Melissa. Common Balm.*—Under this name were formerly recognized by the U. S. P. the leaves and tops of *Melissa officinalis* L. (Fam. *Labiatæ*), the ordinary *balm* of Southern Europe, which has become naturalized in this country. Balm contains some tannic acid, and a yellowish, highly flavored essential oil which, however, is present in such small quantities that the plant has practically no remedial value. The allied *Satureja Calamintha* (L.) Scheele, var. *sylvatica* Brig., is said to contain sufficient aromatic volatile oil to be of possible commercial interest.

Under the name of *oil of lemon balm* or *oil of balm* the essential *oil of melissa* has been used as a diaphoretic in doses of from one to three minims (0.06 to 0.2 cc.). This oil is a yellow liquid with a specific gravity of 0.9 to 0.925. Its most important constituent is citral.

Melubrin. *N. N. R.* 1924. *Sodium Salt of phenyldimethylpyrazolon-amidomethansulfonic acid.* $C_{11}H_{11}N_2ONHCH_2SO_3Na$.—This occurs as a white crystalline powder, readily soluble in water, with difficulty in alcohol, and is almost tasteless. It has been brought forward as an antipyretic, antirheumatic and analgesic. According to Loening (*M. M. W.*, 1912), its effect in *acute rheumatic fever* is that of a specific. In its medical properties it seems to resemble antipyrine. The *dose* is fifteen to thirty grains (1–2 Gm.).

Under the name of *Novalgin*, a related, but not identical, compound has also been brought forward as an antirheumatic.

Menispermum. *U. S.* 1890. *Yellow Parilla. Canadian Moonseed. Texas Sarsaparilla.*—"The rhizome and roots of *Menispermum canadense* Linné (fam. *Menispermaceæ*)." *U. S.*, 1890.

M. canadense L.—This is a woody, climbing plant, which grows from Western Quebec and New England southward. It is specifically characterized by its peltate, three to seven-lobed leaves, its small clusters of greenish-yellow flowers, and its somewhat kidney-shaped, glaucous fruit, which is ripened in September. Menispermum was officially described as follows: "Rhizome 5 to 6 dm. long, 5 mm. thick, brown or yellowish-brown, somewhat knotty, finely wrinkled longitudinally and beset with numerous thin, rather brittle roots; fracture tough, woody; internally yellowish, the bark rather thick, the wood-rays broad, porous, and longest on the lower side; pith distinct. Nearly inodorous; taste bitter." *U. S.* 1890. Maisch found a white alkaloid, which he called *menispine* and a small quantity of berberine. H. L. Barber (*A. J. P.*, 1884, p. 401) obtained the white amorphous alkaloid for which Maisch proposed the name *menispine*. But H. M. Gordin states that berberine is not present in menispermum. (*Proc. A. Ph. A.*, 1909.) Menispermum has been used as a substitute for sarsaparilla but is probably inert. A *fluidextract* made with a menstruum of 2 parts of alcohol and one part of water was recognized by the U. S. P. 1890; *dose*, one-half to one fluidrachm (1.8–3.75 cc.).

Menosal. *Menthyl-salicylic-methyl ester, Methyl menthylsalicylate.* $C_{18}H_{26}O_3$.—This occurs as an oily, transparent liquid almost free from odor and taste. It is soluble in alcohol, ether, chloroform, and fatty oils, and has a specific gravity of about 1.037; it boils at 189° C. at 17 mm. Menosal is said to pass through the stomach unchanged, the salicyl radical being liberated in the intestines, thereby avoiding any gastric irritation. It is given as an antirheumatic in doses of 3 minims and it may also be employed externally in admixture with a suitable vehicle.

Mensalin. *Diphenyldioxycarbonate of Dimethylpyrazolonhexahydrocymolvalerate.*—This forms a white, hygroscopic powder and is recommended as a nervine and in the treatment of *painful menstruation.*

Mentha Aquatica L.—Under the name of *poco oil*, the volatile oil of this plant, which is a native of China, is used in the Island of Java as a popular remedy for *headache*, and also in *cholera.*

Mentha Pulegium L.—*European Pennyroyal. Pouliot commun*, Fr. *Polei*, G. *Pulegium vulgare* Mill. (Fam. *Labiatæ*).—This European labiate yields an oil which is known in England as the *oil of pennyroyal*, and must not be confounded with the American oil of the same name and which is yielded by *Hedeoma pulegioides* Pers. The oil, which is also known as the *oil of poley*, has been examined by Beckmann and Pleissner (*Ann. Ch. Ph.*, ccii, 1), who discovered as the most important constituent *pulegone*, $C_{10}H_{16}O$, an unsaturated ketone, which makes up 80 per cent. of the oil. The oil contains besides pulegone small quantities of l-limonene, dipentene, menthol and menthone. Its constants are sp. gr. 0.930 to 0.955; opt. rot. +15° to +25°; ref. ind. 1.4810 to 1.4865. The boiling point of pulegone is 221° C. Pulegone forms crystalline compounds with hydroxylamine and with hydrogen bromide. When reduced by sodium in ethereal solution pulegone is changed into menthol. Pulegone is most abundant in the Spanish oil, and less abundant in American and Algerian oils. (See also Wallach, *Ann. Ch. Ph.*, cclxxii, 122, and Semmler, *B. Chem. G.*, xxv, 3515.) Schimmel states that the oil is sometimes adulterated with eucalyptus oil. (*Schim. Rep.*, 1908, 67.) It is stated (*B. M. J.*, March, 1890) that the oil is largely used for the purpose of producing abortion, and is popularly believed to be safer and more certain than the other volatile oils. Taylor denies, however, that the oil is an abortifacient and it appears to be demonstrated that it is capable of causing fatty degeneration. (See *S. Jb.*, cclxvii, p. 230.)

Menthospirin. *Menthol Acetylsalicylate.*—It is a yellowish thick fluid, insoluble in water but soluble in alcohol, ether, and the fixed oils. It is used internally by Loewenheim (*Med. Klin.*, 1913) in the treatment of *colds* and various *catarrhs*, both acute and subacute, of the upper respiratory tract. It has also been employed locally in *laryngeal tuberculosis*. The *dose* is from eight to twelve grains (0.5–0.78 Gm.) several times a day, usually in capsules or pearls.

Menthyl Camphorate.—The camphoric ester of menthol, which forms a white powder which is insoluble in water and chloroform but soluble in alcohol and the fatty oils. Hot water decomposes it with the liberation of menthol. It is used in *tuberculosis.*

Menyanthes. *Buckbean. Marsh Trefoil. Bogbean. Water Shamrock. Folia trifolii Fibrini.*—The dried leaves of *Menyanthes trifoliata* Linné (Fam. *Gentianaceæ*). This perennial herb is a native both of Europe and Asia. It has become naturalized in North America, from Greenland to Alaska and south to Pennsylvania, Minnesota, and California. The leaves were formerly recognized by the N. F. They are collected in late spring and carefully dried.

It was described by the N. F. IV as "glabrous; petioles from 10 to 15 cm. in length, stout but soft and weak, the base more or less sheathed with broad, thin, and membranaceous, somewhat translucent stipules; blade ash-green, trifoliate; leaflets sessile or very short-petioled from 5 to 8 cm. in length and usually about two-thirds as broad, obovate, blunt, entire or occasionally coarsely and unequally crenate. Odor slight but characteristic; taste decidedly bitter. Menyanthes yields not more than 10 per cent. of ash." *N. F.* Its virtues depend on a bitter glucoside denominated *menyanthin,* which has a bitter taste, is soluble in alcohol and water, but not in pure ether, and is chemically neutral. Kromayer (1865) assigned to it the formula $C_{30}H_{46}O_{14}$, and stated that it breaks up on heating with diluted sulphuric acid into a fermentable sugar and *menyanthol,* a colorless difficultly volatilizable oil, with an odor like that of bitter almond. K. Leuderich (*A. Pharm.,* 1892, 38 and 48) has studied menyanthin, and gives it the formula $C_{33}H_{50}O_{14}$, and states that its decomposition products are a phenol-like body, menyanthol, $C_7H_{11}O_2$, a resinous product, and a left-rotatory sugar.

Vridevel (*P. J.,* 1910, lxxxv, p. 465) has separated a second glucoside from menyanthes, to which he gives the name of *meliatin.* It is a crystalline body, with a melting point of 217° C.

With the ordinary properties of the bitter tonics, menyanthes unites a cathartic power; in large doses it may cause vomiting. The *dose* of the powdered leaves or roots as a tonic is from twenty to thirty grains (1.3–2.0 Gm.); of an infusion, prepared with half an ounce to a pint of boiling water, from one to two fluidounces (30–60 cc.); and of the extract, ten or fifteen grains (0.65–1.0 Gm.), to be repeated three or four times a day. A drachm of the powder, or four fluidounces of the strong decoction, generally purges, and often occasions vomiting.

Merbaphen. *Novasurol.*—The double salt of sodium oxymercuric-chlorphenoxylacetate with diethylbarbituric acid. This organic compound is stated to contain 33.9 per cent. of mercury in a non-ionizable combination. It is marketed only in the form of a solution containing 10 per cent. of the drug.

This preparation was originally introduced for the treatment of *syphilis* by intramuscular injection. It has been claimed for it that it is much less toxic or locally irritant than the soluble mercurials and is better absorbed than the insoluble salts. More recently it has been observed that it possesses the diuretic powers of the mercurials and a number of clinicians have reported favorable results in *dropsies,* especially when due to cardiac insufficiency (see Neuhof, *T. G.,* January 15, 1924). The reports of Burwinkel (*M. M. W.,* 1922, lxix, 202) and others show, however, that while an active diuretic it is capable of causing serious mercurial poisoning in improperly selected cases.

It is recommended that the beginning dose be 0.75 cc. (12 minims) of the 10 per cent. solution which may be gradually increased if the patient shows no intolerance, up to 2 cc. (30 minims) once or twice weekly.

Mercuramine. *Mercury Ethylenediamin Citrate.*—This is a solution of 10 parts of mercury citrate and 4 parts of ethylenediamine in 86 parts of distilled water. Its 0.3 per cent. dilution is asserted to be equal in bacterial value to a 1 in 1000 solution of mercuric chloride.

Mercurialis. *Mercurialis annua* L. *Mercury Herb. French Mercury.*—An herbaceous European plant (Fam. *Euphorbiaceæ*) which has been employed from the most ancient times as a purgative, diuretic, and emmenagogue. When boiled, it loses its acridity, and in this condition has been used as an emollient. Another species, *M. perennis* L., or *dog's mercury,* also a native of Europe, is poisonous. Its leaves yield an unstable blue dye. Reichardt has discovered in *M. annua* a volatile alkaloid, which he named *mercurialine.* According to E. Schmidt (*P. J.,* vol. x, 29), *mercurialine* is identical with *methylamine,* CH_3NH_2, and is associated in the mercurialis with trimethylamine. It is a liquid of an oily appearance, narcotic odor, and alkaline reaction; boils at 140° C.; forms salts with the acids; absorbs carbon dioxide; has a strong affinity for water; on exposure to the air it is changed into a resin of a buttery consistence, and is said to be poisonous to man; but Hugo Schulz (*A. E. P. P.,* April, 1886, 88) found that neither the fluidextract nor the herb given as food was capable of killing either the pig or the rabbit, and that four and a half grains (0.29 Gm.) of the mercurialine hypodermically injected had no effect. Hoffmann (*P. J.,* 1919, cii, 426) has ascribed poisoning in horses to eating hay containing mercurialis. The urine is increased in quantity and colored reddish.

Mercuric Acetate. $(CH_3COO)_2Hg$.—Colorless, laminar crystals, soluble in 4 parts of water, also in alcohol and ether. Used internally as an antisyphilitic in *doses* of one-sixth to one grain (0.010–0.065 Gm.).

Mercurialized Serum. *N. N. R.* 1924.—In syphilitic diseases of the nervous system, especially of the spinal cord, mercury frequently fails to arrest the progress of the disease. This has been attributed to the inability of the mercury to penetrate into the central nervous system. With the idea of introducing mercury directly into the cerebro-spinal tract by intraspinal injection, a mercurialized serum has been prepared by treating normal horse serum with mercuric chloride and redissolving the precipitate in an excess of serum. (For method of preparation see Byrnes, *J. A. M. A.,* 1914, lxiii, p. 2182). It is upon the market only in the form of dosage packets which are made of various strengths, the stronger intended for intramuscular injection and the more dilute for intraspinal.

Mercuric Aminosuccinamate. *Mercury Asparaginate. Hydrargyri Aminosuccinamas. Asparagin Mercury.* $Hg(C_4H_7N_2O_3)_2$.—Made by dissolving mercuric oxide in a warm solution of amido-succinamic acid, or asparagin, and setting aside to crystallize. Colorless, needle-like crystals, insoluble in water, soluble in dilute acids. It is used hypodermically in the treatment of *syphilis* and is asserted to produce less irritation at the site of injection than other salts of mercury. The *dose* is one-twelfth to one-sixth of a grain (0.005–0.010 Gm.).

Mercuric Anilinate. *Hydrargyri Anilicum.* $Hg(C_4H_4.NH_2)_2$.—It is prepared by the action of a solution of bichloride of mercury on aniline and forms a white, micro-crystalline, odorless and tasteless powder containing 52.1 per cent. mercury. It is insoluble in water. Fedtscheutig has used this salt with success both hypodermically and by mouth in the treatment of *syphilis.* Hypodermically it may be given in a white oil suspension and by mouth, in a pill. It has also been used as an inunction with oleic acid and resorbin.

Dose, one-fourth of a grain (0.015 Gm.).

Mercuric Arsenate. $Hg_2H_2(AsO_4)_2$.—A yellow powder soluble in acids and insoluble in water. It is used in the treatment of *syphilis.* The *arsenite of mercury* (*mercurous arsenite*), Hg_3AsO_3, a brownish powder, soluble in acids and insoluble in water, is used in *syphilis.*

Mercuric Benzoate. *N. N. R.* 1924.—*Hydrargyri Benzoas,* $Hg(C_6H_5COO)_2 + H_2O$, is obtained by double decomposition between an alkaline benzoate and a mercuric salt; it is a white crystalline, odorless, and tasteless powder, which is sparingly soluble in water, but easily in alcohol as well as in aqueous solutions of sodium chloride, the latter effect being due to its property of forming easily soluble double salts with the haloids. E. Seger states that this solution quickly decomposes into mercuric chloride and sodium benzoate and is an incompatible mixture. (*Repertoire de Pharmacie,* 1919, ciii, 13.) R. W. Terry states that the mercuric benzoate of commerce is not a definite substance and confirms Seger's statement as to the reaction with sodium chloride (*Midland Druggist,* 1919, liii, 222). This salt is incompatible with acids, iron compounds and acid salts. It has been strongly recommended by Stukowenkow as a substitute for mercuric chloride, for intramuscular injections in *syphilis* and as a local remedy in *gonorrhea.* For urethral injections the solution may be 1 to 1000 or 2000, with an equal quantity of sodium chloride. The *dose* for intramuscular injection is from one-eighth to one-fourth of a grain (0.008–0.015 Gm.) every second day.

Mercuric Bromide ($HgBr_2$) *Mercury Dibromide.*—This is in the form of colorless crystals, or silvery lustrous scales, sparingly soluble in water, freely soluble in alcohol. Exposed to heat it melts and sublimes. This salt has been used in the treatment of *syphilis. Dose,* one-fifteenth to one-eighth of a grain (0.004–0.008 Gm.).

Mercuric Cyanide. *N. N. R.* 1924. *Hydrargyri Cyanidum. U. S.* 1890. $Hg.(CN)_2 = 252.62$. *Hydrargyri Cyanuretum. U. S.* 1850. The process for the preparation of this substance, given in the U. S. P., 1850, is based upon the following: Hydrocyanic acid is generated by the action of sulphuric acid on potassium ferro-cyanide, and, being received in a vessel containing water and a portion of mercuric oxide, reacts with the oxide, according to the reaction

$$(HCN)_2 + HgO = Hg(CN)_2 + H_2O$$

generating, by double decomposition, water, and mercuric cyanide which is held in solution. Sufficient mercuric oxide is not used at first to saturate the whole of the hydrocyanic acid generated, because should there happen to be any excess of the oxide there would be produced on evaporation, instead of the substance wanted, a peculiar salt composed of cyanide and mercuric oxide, which would crystallize in small acicular crystals. Hence a portion of the water still containing uncombined hydrocyanic acid is set aside, to be added to the liquid in which the acid had been completely saturated by the addition of mercuric oxide, and thus at least neutralize any mercuric oxide that might be present in it in excess. A surplus of hydrocyanic acid would not be detrimental, except for the loss of material incurred, as it is evaporated in the subsequent concentration. Mercuric cyanide should be kept in well-stoppered, dark amber-colored bottles.

It occurs as colorless or white, prismatic crystals, odorless, and having a bitter, metallic taste (the salt is exceedingly poisonous), becoming dark-colored on exposure to light. Soluble, at 15° C., in 12.8 parts of water, and in 15 parts of alcohol in 3 parts of boiling water, in 6 parts of boiling alcohol; very sparingly soluble in ether. It is often contaminated with the oxycyanide. The presence of the latter may be shown by the production of a white precipitate by ammonia.

Mercuric cyanide has been brought forward as a substitute for corrosive sublimate especially for germicidal purposes. The experiments of various investigators show that the antibacterial properties are much inferior to those of the bichloride. According to Hüne (*Desinfektion,* 1912, v), it requires a 1 in 1000 solution of mercuric cyanide to kill the staphylococci in thirty minutes, which corrosive sublimate will do in 1 in 10,000 solution, and Harrington (*B. M. and S. J.,* January 14, 1904) found that a 1 in 500 solution was not certainly fatal to the pus-forming organisms in thirty minutes.

Prochorow has used it hypodermically without causing local irritation, and with great asserted benefit, in *chronic syphilis.* Hill (*J. A. M. A.,* 1923, lxxx, 1365), however, was unable to observe any curative effect in experimental syphilis in rabbits. Chaleix (*Journ. de Méd. de Paris,* March, 1900) reports death from the use of a vaginal injection containing fourteen grains of mercuric cyanide. *Dose,* internally, from one-sixteenth to one-eighth of a grain (0.004–0.008 Gm.).

Mercuric Lactate. *Hydrargyri Lacticum.* $(C_3H_5O_3)_2Hg$.—It forms a white crystalline powder, soluble in water. This preparation has been used hypodermically in *dose* of one-sixth grain (0.010 Gm.) a day. Bouveyron (*S. M.,* 1905, p. 30) recommends that in cases of *syphilitic* lesions in the mouth, tablets of *mercury lactate* be allowed to dissolve slowly on the tongue.

Mercuric Oxycyanide. *N. N. R.* 1924. *Hydrargyri Oxycyanidum. Hydrargyri Oxycyanatum.* $HgO.Hg(CN)_2$.—This basic cyanide of mercury occurs as a white crystalline powder, soluble in 17 parts of water and turning litmus paper blue. The commercial preparations are frequently contaminated with the neutral cyanide of mercury. It has been brought forward as a substitute for mercuric chloride, both as a disinfectant and in the treatment of *syphilis.* The advantage is claimed for it as a germicide that it does not have an injurious effect upon steel instruments. Although Lehmann claimed that its germicidal power was equal to that of the bichloride, more recent experiments throw grave doubt upon this conclusion. Kruger, for example (*Desinfektion,* 1910, p. 456), reached the conclusion that its germicidal power was inferior to that of phenol. It is used in *syphilis* for hypodermic injection in the same doses as corrosive sublimate. Colombino (*G. Osp.,* 1917, xxxviii, 499) has irrigated the urethra with a 1 to 1000 solution for the abortion of *gonorrhea.*

Mercuric Pyroborate.—*Hydrargyri Pyroboras,* HgB_4O_7, is an amorphous, brown, insoluble powder, which has been commended by V. Tokayer (*Ph. Post,* 1892) as a local application in the treatment of specific and other ulcerations.

Mercuric Salicylarsinate.—*Hydrargyri Salicylarsinas. Enesol.*—By the interaction of molecular quantities of basic mercuric salicylate on methylarsenous acid, a white amorphous substance is formed which is difficultly soluble in water. The solution gives no reaction with hydrogen sulphide or with potassium iodide and may be sterilized without decomposition. The composition of the salt is mercury, 38.46 per cent., and arsenic, 14.4 per cent., with salicylic acid. Enesol is intended for subcutaneous injection in the treatment of *syphilis.* It is marketed in the form of a 3 per cent. solution.

The *dose* of the salt is from one-fourth to one grain (0.015–0.06 Gm.).

Mercuric Sozoiodolate. *Hydrargyrum Sozojodolicum.* $HgC_6H_2I_2OSO_3$.—This compound is a lemon-yellow powder, scarcely soluble in water, but more so in solution of sodium chloride. This preparation, which is said to contain 31 per cent. of mercury and 38 per cent. of iodine, has been especially recommended by Witthauer (*M. M. W.*, Aug., 1892) in the treatment of *syphilitic ulcerations, enlarged glands*, and *skin diseases*, in the form of a 1 per cent. ointment. The 1 per cent. solution is also used by Genzmer, as an injection into diseased joints, etc.

Mercuric Subsulphate, Yellow. *Hydrargyri Subsulphas Flavus. U. S.* 1890. *Mercuric Oxysulphate. Yellow Mercuric Subsulphate. Basic Mercuric Sulphate. Turpeth Mineral.* $Hg(HgO)_2SO_4$=729.87. *Hydrargyri Sulphas Flava. U. S.* 1870. *Hydrargyri Subsulphas.*

When normal mercuric sulphate is thrown into boiling or even warm water it is instantly decomposed, and an insoluble salt is precipitated, which is yellow mercuric subsulphate. Its composition is $Hg(HgO)_2SO_4$.

Yellow mercuric sulphate is a heavy, lemon-yellow powder, odorless and almost tasteless; permanent in the air. Soluble in about 2000 parts of water at 15° C., and in 600 parts of boiling water; insoluble in alcohol; readily soluble in nitric or hydrochloric acid. When heated, the salt turns red, becoming yellow again on cooling. At a red heat it is volatilized, evolving vapors of mercury and of sulphur dioxide, and leaving no residue. It was originally called *turpeth mineral*, from its resemblance in color to the root of *Ipomœa Turpethum*.

Yellow mercuric subsulphate is capable of acting as a mercurial and producing ptyalism. It is, however, in full dose violently emetic, and has been chiefly used in true *croup*. It is a dangerous remedy, especially with young children, several cases having been reported in which, failing to cause vomiting, it has produced death preceded by symptoms similar to those of corrosive sublimate poisoning. (See *M. News*, xliii, 1883; also, *London Med. Gaz.*, 1847.) Emetic *dose* for a child two years old, two or three grains (0.13–0.2 Gm.); for adult, three to five grains (0.2–0.32 Gm.), repeated in fifteen minutes if it does not operate. Alterative *dose*, one-fourth to half a grain (0.016–0.032 Gm.).

Mercuric Succinimide. *Hydrargyri Succinimidum. Hydrargol. N. N. R.* 1924. *Mercury Imidosuccinate.* $Hg[(CH_2.CO)_2N.]_2$.—This drug may be formed by heating together succinic acid, carbonic anhydride, and ammonia, which combine with mercuric oxide to form a compound which occurs as a white crystalline powder soluble in about 20 parts of water. This solution remains quite unchanged when kept. According to Vollert the solution of one and three-tenths grammes of this salt in one hundred of water is free from irritant properties, and when used hypodermically produces no disagreeable local or even secondary symptoms. (*Th. M.*, 1888.)

It was used by B. L. Wright with asserted extraordinary results in the treatment of *pulmonary tuberculosis*. Hartz (*J. A. M. A.*, 1911, lv, p. 915) and others were unable to see any beneficial effect from the drug in phthisical patients, except in those who were syphilitic. The *dose* employed was one-fifth of a grain (0.012 Gm.) injected intramuscularly every other day.

Mercuric Sulphate. *Hydrargyri Sulphas. Normal Mercuric Sulphate. Mercury Bisulphate. Sulfate Mercurique*, Fr. *Mercurisulfat*, G. $HgSO_4$ = 296.67.—Made by heating together 18 parts of mercury, 10 parts of concentrated sulphuric acid, 3 parts of water and 4 parts of 25 per cent. nitric acid, in a flask, on a sand bath, until reddish vapors cease to be given off, then drying with the aid of heat, in an open dish, constantly stirring. It is a heavy white crystalline powder, used in making turpeth mineral, and mercuric and mercurous chlorides. It has no use in medicine.

Mercuric Sulphide. *U. S.* 1880. *Hydrargyri Sulphidum Rubrum. Red Sulphide of Mercury. Cinnabar.* HgS=232.67.—This preparation, which was formerly official both in the United States and British Pharmacopœias, has been dropped from each. For process of making mercuric sulphide see *U. S. D.*, 19th ed., p. 1566.

Cinnabar is seldom prepared on a small scale, being made in large quantities for the purposes of the arts. Until within a few years it was nearly all manufactured in Europe, but it is now made to an enormous extent in this country. In Holland, where it is largely manufactured, the sulphur is melted in a cast iron vessel, and the mercury is added in a divided state, by causing it to pass through chamois leather. As soon as the combination has taken place, the iron vessel is surmounted by another, into which the cinnabar is sublimed. In the United States, Martin's method, consisting of the agitation together of quicksilver, sulphur, and an alkaline sulphide, appears to have the preference. Another process for its manufacture in the wet way very largely employed is Brunner's. (Wagner's *Chem. Tech.*, 13th ed., 1889, 552.)

Properties.—"Brilliant, dark red, crystalline masses, or a fine, bright scarlet powder, permanent in the air, odorless and tasteless, insoluble in water, alcohol, nitric or hydrochloric acid, or in dilute solutions of alkalies. It is dissolved by nitrohydrochloric acid with separation of sulphur. When heated, the salt becomes brown and then black, but, on cooling, it reassumes its red color. At a higher temperature it takes fire, burns with a bluish flame, emitting the odor of burning sulphur, and is finally volatilized without residue." *U. S.*, 1880. (For tests for purity, see *U. S. D.*, 19th ed., p. 1567.) In closed vessels at a red heat it sublimes without decomposition, and condenses in a mass, composed of a multitude of small needles. When duly levigated, it furnishes a brilliant red powder, which is the paint called *vermilion*. The same compound occurs native, being the sole ore—cinnabar—from which mercury is extracted. The preparation, if purchased in powder, should be carefully examined, as, in that state, it is sometimes adulterated with red lead, dragon's blood, or chalk. If red lead be present, acetic acid digested with it will yield a yellow precipitate (lead iodide) with potassium iodide. Dragon's blood may be detected by alcohol, which will take up the coloring matter of that substance, if present, and, if chalk be mixed with it effervescence will be caused on the addition of an acid.

Cinnabar is employed in medicine by fumigation, in *syphilitic affections*, when it is desired to obtain an immediate mercurial impression. Half a drachm may be thrown on a red-hot iron, in a close apartment, and fumes inhaled as they arise. These consist of sulphurous acid gas and mercurial vapor, the former of which must prove highly irritating to the patient's lungs. A better substance for mercurial fumigation is black mercurous oxide. It is also employed in the form of an ointment by Lassar (*Med. Klin.*, 1905, No. 3, 54), using red mercuric sulphide 1 Gm., sublimed sulphur 24 Gm., petrolatum 100 Gm., and oil of bergamot 30 drops. It is recommended in the treatment of *herpes tonsurans*.

Mercuric Sulphocyanate. *Hydrargyri Sulphocyanas.* $Hg(CNS)_2$.—This substance, formerly called *sulphocyanide of mercury*, is produced by mixing diluted solutions of mercurous nitrate and potassium sulphocyanate. The white precipitate which falls, after drying, swells up suddenly when ignited, giving off nitrogen, carbon disulphide, and poisonous vapor of mercury, leaving a voluminous gray residue, *mellon*, C_9H_{13}. The salt is used in the preparation of the toy, *Pharaoh's serpents*.

Mercuric Thymolnitrate. *Hydrargyri Thymolnitras.*—This salt, $(C_{10}H_{13}O)Hg.HgNO_3$, and *mercuric thymolsulphate* $[(C_{10}H_{13}O)Hg.Hg]_2SO_4$, have been used with asserted benefit in *syphilis*, in hypodermic *doses* of from one-twelfth to one-sixth of a grain (0.005–0.010 Gm.). (See *Merck's Jahresbericht*, 1891, 1892; also *W. K. W.*, March, 1892.) Besides these preparations *mercuric naphtholate*, a lemon-yellow powder, containing 30.8 per cent. of mercury, has been put upon the market; also under the name of *hydrargyrol*, *mercury paraphenylthionate* $(C_6H_4.OH.SO_3)_2Hg$, has been suggested as an antiseptic, but in proportion to its cost is probably of no practical value.

Mercuric Tribromphenol Acetate. *Hydrargyri Tribromphenol Acetas.*—A yellowish powder insoluble in water, containing 30 per cent. of mercury. It is employed as an antiseptic and antisyphilitic, best administered hypodermically in a white oil suspension containing about 25 per cent. of the salt. *Dose*, two grains (0.13 Gm.).

Mercuric and Zinc Cyanide. *Hydrargyri et Zinci Cyanidum.*—It is stated by Dunstan to be a true chemical compound, with the formula $Zn_4Hg(CN)_{10}$, but other authorities contradict this statement. It is a white powder, entirely insoluble in water. This substance has been very highly recommended by Lister as an antiseptic dressing, and is believed by him to be practically free from irritating or poisonous properties.

Mercurochrome. *Mercurochrome*-220 *Soluble. Mercuranine. N. N. R.* 1924.—The di-sodium salt of 2:7-dibromo-4-hydroxymercurifluorescein, containing from 23 to 24 per cent. of mercury.

This germicide was introduced by Young, White and Swartz (*J. A. M. A.*, 1919, lxxiii, 1483). The idea that led to its synthesis was that the combination of a stain with a potent germicide would carry the latter deeply into the tissues and thus reach bacteria which might have penetrated into the deeper layers of the mucous membrane. The compound that they called mercurochrome-220 is a combination of dibromfluorescein with mercury. Occurs as iridescent, green scales, slightly hygroscopic, readily soluble in water forming bright red solutions. Acids cause a precipitate. The original dye is an acid but is usually used in the form of the sodium salt. It is not precipitated by proteins nor by the normal acidity of the urine. In the strengths ordinarily used it is almost non-irritant.

Mercurochrome is a powerful germicide much less irritating than the chloride. Swartz and Davis (*J. A. M. A.*, 1921, lxxvi, p. 844) find that solutions as low as 1 in 4000 kill gonococci in five minutes, although it was less efficient against the *Bacillus coli*. Originally introduced as a urinary antiseptic, it has been extensively used in the treatment of *urethritis* and *cystitis* usually in strengths of about one per cent. It has also been employed as a general surgical disinfectant. Clapp and Martin (*J. A. M. A.*, 1920, lxxiv, 1224) have used it with favorable results in the treatment of *ophthalmia neonatorum*. They wash out the eyes with a 2 per cent. solution; this causes some burning sensation which, however, is only temporary. Gray and Meyer (*J. Inf. D.*, 1921, xxviii, 321) used it for the disinfection of the throat of *diphtheria* carriers with 98 per cent. of cures. It has also been used as a mouth wash in *gingivitis* and *pyorrhea alveolaris*.

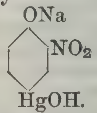
Swartz and Davis find that the solutions of mercurochrome, although undergoing no apparent change, become greatly weakened in their germicidal action on standing.

In 1924 Young and Hill (*J. A. M. A.*, lxxxii, 669) found by animal experimentation that the blood could be rendered bacterio-static by the intravenous injection of mercurochrome and reported a number of cases including general *septicemia, pyelitis, local abscesses*, etc., in which the intravenous injection was followed by prompt alleviation. The doses employed were from 3 to 5 milligrammes per kilo of body weight (approximately one-fiftieth to one-thirtieth of a grain per pound) usually in the form of a one per cent. solution.

Brill and Myers (*J. A. M. A.*, 1925, lxxxiv, p. 879) found, however, that 1 to 10,000 of mercurochrome in human blood did not prevent the growth of either streptococci or staphylococci, and when intravenously injected in cases of bacteremia had no apparent effect on the bacterial count of the blood nor the progress of the disease. Gatch, Trusler and Owen (*J. A. M. A.*, 1925, lxxxv, 894) find that it may exert a bacterio-static, though not a germicidal, effect in the blood and may in some cases be beneficial but that in large doses it is liable to do more harm than good.

One objection to the use of mercurochrome as a general surgical disinfectant is its vigorous staining qualities. It is said that the stains produced on the skin may be removed by the use of a 2 per cent. solution of potassium permanganate followed by 5 per cent. oxalic acid or by the use of solutions of the hypochlorites such as Dakin's Solution.

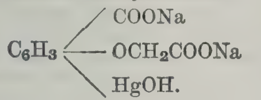
Mercurophen. *Sodium oxymercury-orthonitro phenolate.* Probably



This is an odorless, brick-red powder, sparingly soluble in water and freely soluble in hot water and yielding deep amber-colored solutions. It represents about 53 per cent. of mercury.

Mercurophen has been brought forward by Schamberg, Kolmer and Raiziss (*J. Inf. Dis.*, 1919, xxiv, p. 547) as a powerful disinfectant. They find that in strengths of from 1 in 400,000 to 1 in 2,000,000 it inhibits the growth of various bacteria; that its germicidal power is higher than that of mercuric chloride, especially in the presence of albumins. Moreover, it is much less irritant than the bichloride; a 1 to 1000 solution instilled in the rabbit's eye caused no visible effect and a 1 per cent. solution only slight congestion. They state that its toxicity is less than half that of corrosive sublimate and that it does not tarnish steel nor precipitate protein in germicidal strengths. Shivers (*J. of Urology*, 1922, viii, 35) has used it in *gonorrhea* in strengths of from 1 in 4000 to 1 in 10,000.

Mercurosal. *N. N. R.* 1924.—It is claimed to be di-sodium-mercuri-salicyl-acetate



$$\mathrm{C_6H_3}\begin{cases}\mathrm{COONa} \\ \mathrm{OCH_2COONa} \\ \mathrm{HgOH.}\end{cases}$$

This occurs as a pale yellow, almost white, amorphous powder, freely soluble in water and representing about 44 per cent. of metallic mercury. The solutions, if protected from light, remain unchanged for a limited time.

Mercurosal is intended for intramuscular or intravenous injection in the treatment of *syphilis.* The claims made for it are that it is free from corrosive property, that it does not precipitate blood serum and that it is only one-seventh as toxic as the mercuric chloride although it contains four-sevenths as much mercury. Smith (*Illinois Med. Jour.*, May, 1920), Marchand (*New Orleans Med. and Surg. Jour.*, May, 1921) and others have reported favorably on its clinical effects. It is marketed in sealed ampules of two sizes, containing 0.05 and 0.1 Gm. respectively (three-fourth and one and one-half grain).

Mercurous Acetate. *Hydrargyri Acetas. Mercury Acetate.* $Hg_2(C_2H_3O_2)_2$.—White, scaly crystals, soluble in about 330 parts of water, insoluble in alcohol and ether. It should be kept dry and away from light as it is decomposed, by boiling water and exposure, into mercury and mercuric acetate. Used internally in *doses* of from one-fifth to one grain (0.012–0.065 Gm.) for *syphilis.*

Mercurous Bromide.—*Hydrargyri Bromidum,* Hg_2Br_2, is formed by adding potassium bromide to mercurous nitrate. It falls as a white, curdy precipitate.

Mercurous Iodobenzolparasulphonate. *Anogon.*—It is a yellow, crystalline powder insoluble in all the ordinary solvents, representing 48.5 per cent. of mercury and 30.7 per cent. of iodine. It is used in suspension in olive oil, and as an intramuscular injection in the treatment of *syphilis.* The *dose* is fifteen minims (0.9 cc.) of a 10 per cent. suspension.

Mercurous Sulphide. *Hydrargyri Sulphidum Nigrum. Black Sulphide of Mercury. Ethiops Mineral.* Hg_2S.—This now disused remedy was prepared as follows: "Take of Mercury, Sulphur, each, *a pound.* Rub them together till all the globules disappear." *U. S.*, 1850 For properties, see *U. S. D.*, 14th ed., 1259.

Mercurous Tannate. *Hydrargyri Tannas.* $Hg_2.3(C_{14}H_9O_9).OH$. *Hydrargotin.*—*Mercurous tannate,* which was first brought forward by Lustgarten (*N. Y. M. J.*, March, 1892), has received some favor at the hands of syphilographers, and is official in the Austrian Pharmacopœia (1906), under the name of *Hydrargyrum tannicum oxydulatum.* It is declared that it has the especial advantage of being unabsorbed in the stomach, but decomposed by the alkaline juices of the duodenum, in such a way as to yield very minute globules of metallic mercury. It may be prepared either by precipitating concentrated solution of tannic acid and mercurous nitrate or by rubbing together tannic acid and mercurous nitrate. According to Lustgarten, the first process yields the better preparation. It is asserted that it does not irritate the alimentary canal. In *syphilis,* three grains (0.2 Gm.) may be given to the adult daily, increasing to five grains (0.32 Gm.) or more.

Mercury Atoxylate. *Mercury Paraminophenylarsenate. Atoxyl Mercury. Aspirochyl. Asiphyl.* $C_{12}H_{14}O_6N_2As_2Hg$.—This occurs as a white powder insoluble in water, and represents 31.8 per cent. of mercury. It has been introduced as an antisyphilitic with the idea that it would combine the effects of its two constituents. Manteufel (*Med. Klin.*, 1908, p. 1651) found it to be actively destructive to *spirilli, spirochete* and *trypanosomes,* and obtained favorable clinical results in *syphilis.* Bergrath (*D. M. W.*, 1910), however, reached the conclusion that it had no advantage over other forms of mercury. It is administered by intramuscular injection in the form of a 10 per cent. emulsion in olive oil. Of this emulsion from eight to fifteen minims (0.5–1.0 cc.) may be injected once or twice a week. It is also used in the form of an ointment (1 in 20).

Mercury Resorcinol Acetate. *Resorcinol Mercury Acetate.*—A yellow, crystalline powder containing 69 per cent. mercury. It is soluble in strongly alkaline solutions and in hydrochloric acid, but insoluble in alcohol and water. It is used as an antisyphilitic hypodermically in liquid paraffin and melted lanolin solution. Three minims (0.2 cc.) of a solution of eighty-five grains (5.6 Gm.) of the salt in the same amount of paraffin oil and thirty grains (2.0 Gm.) of anhydrous lanolin is injected twice weekly, the mixture being warmed to 25° C. before being used.

Mergal. *N. N. R.* 1924.—Under this name there has been introduced into medicine a mixture which is asserted to contain one part of *mercuric cholate,* $Hg(C_{24}H_{39}O_5)_2$, with two parts of albumin tannate. It occurs as a yellowish-white powder, practically insoluble in water, but dissolving in alkaline solutions. Mergal has been highly lauded by a number of authors as a satisfactory means of exhibiting mercury in the treatment of *syphilis.* According to Barges (*Fort. Med.*, 1907, No. 27) mercury appears in the urine within four hours after its exhibition by the mouth, and elimination —which is partially through the kidneys and partially through the intestinal glands—goes on with great regularity, so that the prolonged use of the remedy is less liable to lead to undesirable results than with the ordinary form of mercury. It contains approximately 4.4 per cent. of mercury and is dispensed in capsules, which contain 0.05 Gm. each (three-quarters of a grain) of mercuric cholate and one and a half grains (0.096 Gm.) of albumin tannate. Of these from five to ten may be given daily.

Meroxyl. *N. N. R.* 1925.—A mixture containing approximately 50 per cent. of the sodium salt of 2,4-dihydroxy-3,5-dihydroxy-mercuribenzophenone-2-sulphonic acid, with foreign matter consisting of ammonium-2,4-dihydroxy-benzophenone-2-sulphonate, sodium acetate and water. It represents about 27 per cent. of mercury.

It has been brought forward as a local germicide by Young, White, Hill and Davis (*Surgery, Gynecology and Obstetrics,* 1923, xxxvi, 508. It is used for wet dressings of wounds, and also for irrigation of wounds and infected bladders.

Meroxyl occurs as a pinkish powder easily soluble in hot water up to 10 per cent. Solutions of 2.5 per cent., or stronger, gel or form a deposit on cooling. The color of the solution varies with concentration; a 0.5 per cent. solution has a brownish pink color with greenish fluorescence, the color becoming browner in more concentrated solutions.

It is used in strengths of from 0.1 to 0.5 per cent.

Mesembryanthemum. *Mesembryanthemum crystallinum* L. *Ice Plant. Diamond Fig.*—A biennial plant of the Fam. *Aizoaceæ,* a native of the south of Europe, now distributed to the Canary Islands, Southern Africa, Australia and California. The stem and under surface of the leaves are covered with crystalline drops, which give the plant the appearance of being coated with ice. H. Mangon obtained as much as 43 per cent. of salts of potassium and sodium from the dried leaves. (*A. J. P.*, 1883, 370.) The herb is without odor, and has a saline, somewhat nauseous taste. It is considered demulcent, diuretic, and has been used in *inflammations* of the *pulmonic* and *genito-urinary* mucous membrane.

Holmes (*P. J.*, 1918, ci, 317) grew some seeds which were found in a Moroccan soap substitute called *ghassoul,* and found them to yield the *M. crystallinum* L. and the *M. nodiflorum* L. The cleansing power is due to the presence of saponin.

In the *Mesembryanthemum expansum,* Hartwich and Zwicky (*Ap. Ztg.*, 1914, xxix, p. 925) found an alkaloid *mesembrine,* $C_{16}H_{19}O_4N$, with a cocaine-like action.

Mesenna. *Musenna. Bisenna. Musena. Moucéna,* Fr. *Musennarinde,* G.—Under these different names has been brought into notice, as a powerful *tænifuge,* the bark of an Abyssinian tree, *Albizzia anthelmintica* Brongn. (Fam. *Leguminosæ*). The bark is in flat pieces from five to ten inches long, smooth, slightly fissured, of a rusty gray color exteriorly, and pale yellow and fibrous within. It consists of four layers, one of which contains very large cells, with thick coats and is supposed to be the active part. E. Caventou and Legendre found in the bark no alkaloid, but a peculiar, acid, acrid, resinous substance. The *musennin* of Theil is probably the same, although not as yet in a pure state. The Abyssinians employ the powdered bark, in the *dose* of about two ounces, suspended in water or other liquid, or mixed with flour in the form of bread, or made into a confection with honey, butter, etc. It is taken in the morning, three or four hours before breakfast, and no other precautions are used. It produces no pain nor any disturbance of the functions, not even purging actively. Fragments of the worm are voided the same evening, and the greater portion of it the next day.

Mesotan. *Salmester. Salicylic Acid Methyloxymethylester. Ericin. N. N. R.* 1924. $C_6H_4OHCOO(CH_2OCH_3)$.—This preparation is a yellow, clear fluid with a peculiar odor, miscible in all proportions with ordinary oils, sp. gr., 1.2, boiling point, 162° C. It has been brought forward as a local application in all forms of *rheumatism.* In from half an hour to an hour after its local application the presence of salicylic acid can be demonstrated in the urine. When applied pure to the skin and confined by waxed paper or other appropriate dressing it produces redness and sometimes pronounced burning pains, so that it should be diluted with olive oil, castor oil, petrolatum or liquid petrolatum. Even when diluted, mesotan may produce eczematous, urticarial, or other eruption upon the skin, requiring its removal or further dilution. From one and a half to two and a half fluidrachms (5.5–9.3 cc.) of an oily solution, containing 20 to 50 per cent. of mesotan, may be applied daily to the affected part.

Mesothorium.—This is the name which has been applied to the first product of the disintegration of thorium. It appears to give off, like radium, three types of rays and an emanation. It has been used by Voigts (*M. M. W.*, 1913, lx, 1186) in *uterine hemorrhages.* It is probable that mesothorium has therapeutic properties very similar to those of radium. See also Emsmann (*B. K. W.*, 1911, p. 2108), and *P. J.*, 1913, 608. Mesothorium is obtained from the monazite sand in Brazil.

Mespilus Germanica L. *Medlar.* (Fam. *Rosaceæ.*)—The fruit of this tree has been recommended by Mercier (*A. G. M.*, 1907) in the treatment of *chronic enteritis* and *colitis.* It may be either eaten fresh or preserved. The method he employed was to put the patient on a diet consisting of two quarts of milk and eight ounces of medlar daily, no other food being allowed.

Metaferrin.—This is an iron albumen combination representing 10 per cent. of iron. It is a brownish, odorless powder, insoluble in water and dilute acids, but soluble in alkalies. It is supposed to pass through the stomach unchanged, and be absorbed from the intestinal tract, and hence not to affect gastric digestion. It is used in *anemia.* The *dose* is four grains (0.26 Gm.) three times a day generally in tablet form. There is also a "liquid form of metaferrin," *metaferrose,* the *dose* of which is one tablespoonful.

Metaphen. Bisacetoxymercuri-4-nitro-2-cresol. $(CH_3COOHg)_2:(C_6H.CH_3.OH.NO_2)$. *N. N. R.* 1924.—This is a yellow, odorless, tasteless powder almost insoluble in water, but soluble in the presence of sodium hydroxide; it contains from 58 to 60 per cent. of mercury. According to Raiziss and Severac (*J. Lab. Clin. M.*, 1923, ix) it is a more powerful germicide than corrosive sublimate and is only half as toxic. Moreover it does not precipitate protein and is practically non-irritant to mucous membranes.

It is stated to be without deleterious influence on metallic instruments. It has been brought forward as a surgical disinfectant and as a local application in cases of gonorrheal *urethritis.* For disinfection of the skin instruments, etc., solutions of 1 in 1000, made with the aid of sodium hydroxide, may be employed, while for urethral irrigation solutions of from 1 in 5000 to 1 in 10,000 are recommended.

Methacetin. *Para-acetanisidine. Para-oxymethylacetanilide.* $C_6H_4(OCH_3).NHC_2H_3O$.—This differs from acetanilide in having an atom of the nucleus replaced by the oxymethyl group (OCH_3) or from acetphenetidin by having oxymethyl instead of oxyethyl as a replacing group. It forms lustrous crystals free from color, odorless, melting at 127° C., and distilling at higher temperatures unchanged. It is scarcely soluble in cold water, readily soluble in hot water, soluble in alcohol, acetone, chloroform, glycerin, and fatty oils. When triturated with chloral, bromal or phenol it liquefies and with resorcin it forms a mass. Its color and identity reactions are similar to those of phenacetin from which substance it may be distinguished, however, by the fact that when it is heated with a quantity of water insufficient for solution it melts to an oily liquid, while phenacetin does not. According to F. Manhnert, when given in toxic dose to rabbits, it causes convulsions and death through its action on the central nervous system, and is germicidal in 1 per cent.

solution. Methacetin appears to be a powerful antipyretic, producing in fever a very marked fall of temperature, with a slow afterrise; this effect being accompanied by a violent sweating, which especially in *phthisis* and allied diseases, greatly interferes with the practical use of the drug. It has also been much used in *acute rheumatism,* but is not as effective as the salicylates. As an analgesic, in *ataxic* and *neuralgic pains,* it appears to be distinctly inferior to phenacetin and antipyrine. No eruption from it has been noticed. During its administration the urine responds to Trommer's test, but does not contain sugar, nor is there hemoglobinuria. *Dose,* for adults, eight grains (0.5 Gm.).

Methanol. *Methyl Alcohol. Methylic Alcohol. Carbinol. Spiritus Pyroxylicus Rectificatus. Br.* 1864. *Pyroligneous Spirit. Pyroxylic Spirit. Wood Spirit. Wood Alcohol. Wood Naphtha. Alcool méthylique, Alcool formique, Alcool de Bois, Esprit de Bois, Esprit pyroligneux,* Fr. *Holzgeist,* G. CH_3OH.—Methyl alcohol was discovered in 1812 by Taylor. When wood is subjected to destructive distillation, there is formed, besides acetic acid, tar, and other products (see *Creosotum,* Part I), about 1 per cent. of an inflammable volatile liquid, which, when separated and purified, constitutes methyl alcohol. The crude liquor, derived from the wood, separates on standing into two liquids; the heavier containing the tarry matters, and the lighter consisting of water, acetic acid, methanol, etc. The lighter liquid is saturated with lime, and subjected to distillation, whereby the impure methyl alcohol first comes over, mixed, however, with various compounds, among which are aldehyde and pyroacetic spirit (acetone). This, after having been redistilled and deprived of water by repeated rectifications from lime, forms the methyl alcohol of commerce. The commercial spirit may be purified by adding to it as much calcium chloride as it can dissolve, and allowing the mixture to stand for a few days. The methanol unites with the calcium chloride, and the compound formed is subjected to distillation to separate certain contaminating substances, which distil over. Finally, the methanol is separated from the calcium chloride by the addition of water and a new distillation, and from water by rectification from dry lime. Methyl alcohol, like the other monatomic alcohols, can also be formed synthetically in a variety of ways—from marsh gas, from formic acid, and from formaldehyde. Pure anhydrous methanol is a mobile, colorless liquid, possessing a hot, pungent taste, and a peculiar odor. It mixes in all proportions with water, alcohol, and ether. It burns like alcohol, but with a less luminous flame. Its sp. gr. as a liquid is 0.8021 at 15.5° C. Its vapor is irritating to the eyes. It boils at 65° C. As a solvent it resembles alcohol, most substances soluble in that menstruum being likewise soluble in it.

It is desirable to be able to distinguish the presence of methanol in ethyl alcohol, and in preparations which may have been made from the methylated instead of the pure spirit. For this purpose the official test is the best which has been proposed. See test for methyl alcohol under *Alcohol* (Part I); see also *Ph. Centralh.,* 1913, No. 29.

Columbian spirit is simply a brand of wood alcohol of a high quality, free from empyreumatic odor and with only a slight trace of acetone as impurity. *Colonial spirit* is also a purified methyl alcohol.

Methylated spirit, much used in England, contains nine parts of ethyl alcohol to one part of methanol.

Crude methyl alcohol is very largely used in the arts as a solvent, especially in the manufacture of varnish and other resinous solutions. It is also considerably employed as a source of heat, but the ordinary varieties of the spirit during burning give off an offensive odor.

Methanol is capable of producing an intoxication similar to that caused by ethyl alcohol, but distinct in the slowness of the onset and the extraordinary duration of the symptoms, which may last from three to four days after the comparatively moderate dose of the drug. The symptoms which have been observed in methyl alcohol poisoning are marked fall of the body temperature, convulsions, sometimes of a tetanic character, at others of a choreic type, vomiting, dilatation of the pupil, frequently nystagmus. The reflexes at first are increased, but after a period of a day or two loss of sensation and also of reflex power may occur. Quite characteristic of the poisoning is the loss of vision which begins generally within twenty-four hours and may progress to complete blindness. *Per se* methyl alcohol is less toxic than ethyl alcohol and the severity of the symptoms which it causes indicates that the effects must be due to some decomposition product, and the present evidence is strong that this educt is formic acid. Krol (*A. E. P. P.,* 1913, lxxii) has called attention to the similarity of the symptoms of wood alcohol poisoning with those of acidosis. Harron and Benedict (*J. A. M. A.,* 1920, lxxii, p. 25) reports a case of methanol poison in which chemical examination of the blood showed a great diminution in the alkali reserve and the presence of considerable amount of both lactic and formic acid in the urine, as well as acetone bodies; the administration of large quantities of alkali caused, in this case, immediate relief from the acute symptoms, although the patient was left with permanent impairment of vision. Both Reid Hunt and Schmiedeberg have demonstrated that methanol is oxidized in the body to formic acid. Autenrieth (*M. M. W.,* Aug. 1, 1919) has recovered from the urine a quantity of formic acid equivalent to more than 5 per cent. of the ingested spirit.

The amblyopia is due to an inflammation of the optic nerve with eventually, in severe cases, complete optic atrophy. In 90 per cent. of cases there is permanent impairment of vision. It is probable that this predilection for the optic nerve is part of the general tendency towards the nerve trunks for Jelliffe (*M. News,* 1905, lxxvi, p. 387) reports a case of multiple neuritis. For review of the literature on this subject, see Holloway, *N. Y. M. J.,* 1911, xciii, p. 1030.

Many of the cases of poisoning have been due to the innocent use of liquor, or even essence of ginger, which have contained more or less wood alcohol. The use of this substance for the purpose of denaturing grain alcohol, although at present officially permitted by the U. S. Internal Revenue Service, is a dangerous practice. It should be noted that it is not necessary for this poison to be swallowed in order to produce its characteristic effects. A number of cases of permanent blindness have followed the inhalation of its fumes by workmen using varnish containing it or from various dyes in which it is a solvent. Several cases have also been reported in which the external application of methyl alcohol, either as a liniment or accidentally, has led to serious poisoning, and it is therefore highly probable that enough of it may be absorbed through the skin to exercise its injurious effects. (See case reported by Woods, *J. A. M. A.*, 1913, lx, p. 1762.)

In the treatment of wood alcohol poisoning the first step is to thoroughly empty the stomach, which is best accomplished by means of the stomach tube, and the intestines, with a saline purge. The probability that the toxic symptoms are due to acidosis strongly suggests the use of alkalies to combat subsequent symptoms and Isaacs (*J. A. M. A.*, April 10, 1920) has reported favorable results from the use of 45 grains (3 Gm.) of sodium bicarbonate every two hours, or in sufficient quantity to keep the urine alkaline. If the patient be comatose or the cyanosis very marked he recommends the administration of the alkali intravenously. Venesection is sometimes advisable. Haskell, Hillman and Gardner (*A. I. M.*, January, 1921), although they found an acidosis, were not greatly encouraged by the results of the alkaline treatment in experimental poisoning.

Methyl alcohol is a so dangerous remedy that its use for any medical or pharmaceutic purpose is unjustifiable and under no circumstance should it be employed by pharmacists as a menstruum or as a solvent for medicinal preparations of any kind.

Methyl Atropine.—Two salts are on the market, namely the bromide (*methyl-atropine-bromide* of *Mydriasine*), $C_{16}H_{20}O_3N(CH_3)_2Br$, and the nitrate (*methyl-atropine-nitrate* or *Eumydrin*), $C_{16}H_{20}O_3N(CH_3)_2NO_3$.

Atropine Methylbromide occurs as white crystals with a melting point between 222° to 223° C., freely soluble in either water or alcohol. *Atropine methyl nitrate* is a white, crystalline, odorless powder, soluble in both water and alcohol. Its solutions are permanent but have the incompatibilities of alkaloids in general.

Methyl-atropine closely resembles ordinary atropine in its effects on the system, but requires somewhat larger quantities to produce the same effect. As a mydriatic it is employed in strengths of from 1 to 4 per cent. The dilatation of the pupil comes on more promptly than after atropine and is of less duration. Hudovernig (*B. K. W.*, 1906) asserts that it has a marked analgesic action and is a useful remedy in various types of *headaches* and *neuralgia.* It has been found useful for many of the purposes in which atropine is employed especially for the control of *night sweats* and in the treatment of *gastric ulcer.* A spray containing 0.3 per cent. of methyl atropine bromide with 1 per cent. of anasthesin has been recommended as an inhalation for the relief of *asthma.* The dose of either salt is from one-sixtieth to one-twentieth grain (0.001–0.003 Gm.).

Methyl Chloride. *N. N. R.* 1924.—*Monochlormethane,* CH_3Cl, is obtained by the action of hydrochloric acid gas upon methyl alcohol, best in the presence of a little zinc chloride. It is a colorless gas, condensing to a liquid at –23° C., and is very soluble in alcohol, which dissolves thirty-five volumes of it, but is insoluble in water. On account of its extreme volatility, methyl chloride, when applied in the form of a spray, produces extreme cold and freezing of the part. It has been used in this way as a local anesthetic. At very low temperatures it forms with water a hydrate. According to Richet and Marcille (*S. M.*, 1902), methyl chloride acts upon the animal as an efficient anesthetic, which has practically no influence upon the circulation. Its usefulness seems to be limited by its failure to produce complete muscular relaxation. We know of no clinical reports upon its activity.

Methyl Iodide. *Iodomethane.* CH_3I. *Iodure de Methyl,* Fr. *Jodmethyl,* G.—This is a heavy, sweet-smelling liquid, boiling at 43° C., and has a sp. gr. of 2.23 at 15° C. In the cold it unites with water to form a crystalline hydrate, $CH_3I + H_2O$. It turns brown, gradually, on exposure to light. It is made by the action of dry hydrochloric acid gas upon a mixture of potassium iodide and anhydrous methyl alcohol.

R. Kirk (*L. L.*, Oct., 1885) commends *methyl iodide* as a vesicant, applied on lint under a watch glass, a drop or two of soda solution being added to neutralize the free iodine that may be present. It produces at once a tingling, burning, biting sensation, like pricking with a number of needle points. The maximum pain is reached in a few minutes, when the substance is to be removed. The blister produced is said to be as full of serum as that caused by cantharides.

Methyl Ether. $(CH_3)_2O$. *Methylic Ether. Methyl Oxide. Hydrate of Methylene. Ether méthylique, Oxyde de Méthyl,* Fr. *Methyläther, Holzäther Formäther,* G.—This substance was employed as an anesthetic by B. W. Richardson in 1867. He prepared it by mixing one part pure methyl alcohol with two of strong sulphuric acid, heating, collecting and washing repeatedly with potassium hydroxide solution the methyl ether which passes over. It is a gas even at low temperature. A saturated solution of the gas in ethyl oxide was at one time suggested as a surgical anesthetic under the name of *methyl-ethylic ether.*

Methylal. *Methylene Dimethyl Ester. Formal.* $CH_2(OCH_3)_2$.—This is made by distilling methyl alcohol with sulphuric acid in the presence of manganese dioxide, or by abstracting one molecule of water from a mixture of one molecule of formaldehyde and two of methyl alcohol. It is a limpid colorless liquid, of sp. gr. 0.855 at 17° C. and boils at 42° C. It is soluble in water, alcohol, ether, and fatty and ethereal oils. It was originally proposed as an anesthetic and hypnotic by B. W. Richardson in 1868. Richardson, Motrokhin, and Personali are in general accord as to its physiological action. It produces in man a sleep closely resembling the normal sleep; or, if the dose has been large enough, a profound coma in which reflex actions are suspended. Recovery is rapid on account of its rapid elimination. The arterial pressure is reduced, as is also, according to Motrokhin, the irritability of the cerebral cortex. Both Personali and Motrokhin found that it arrests the tetanic spasms produced by small doses of strychnine, although in Motrokhin's experiments, when large doses of strychnine were given, methylal seemed to accelerate rather than put off death. It has been employed as an hypnotic, and is said to be free from danger and unpleasant effects; but in most cases patients become so rapidly accustomed to it that its influence soon disappears, unless enormous doses are used. The *dose* is from one-half to one fluidrachm (1.9–3.75 cc.), given in emulsion.

Methylene Dichloride. *Methylene Chloride. Dichloro-methane. Bichloride of Methylene.* CH_2Cl_2.—It may be prepared by exposing to sunshine, in a glass globe, pure chlorine and gaseous methyl chloride. Methylene dichloride is a colorless liquid, of an odor resembling that of chloroform, of the sp. gr. 1.344, and the boiling point 40° C. The vapor is inflammable, burning with a brilliant flame, and yielding, as the result of combustion, carbon dioxide and hydrochloric acid. Methylene dichloride mixes readily with absolute ether, and, as the boiling points of the two approach nearly, they volatilize evenly and equably. It is neutral to test paper; an acid reaction in any specimen would be an evidence of the presence of hydrochloric acid, and should preclude its use. To prevent the generation of the acid, the liquid should be kept carefully secluded from the sunlight, and the addition of a small quantity of absolute alcohol is recommended.

Methylene dichloride was suggested by Richardson as a general anesthetic, the advantages of being quick and powerful. It enjoyed considerable popularity at one time but some years ago H. C. Wood examined a sample of methylene dichloride supplied by one of the most reputable English firms and found that it contained practically none of this compound and was largely chloroform. Gutzart, as the result of the examination of several German specimens, states that they are mixtures of alcohol, methylene dichloride and chloroform in varying proportions. Merck states that the product used by Richardson, which they call *methyl dichloride,* is really a mixture of one volume of methyl alcohol with three of chloroform.

As yet methylene dichloride cannot be regarded as a safe anesthetic. Even the mixture of methylene dichloride and absolute ether, which Richardson introduced under the name of *methylene ether* (*M. T. G.*, ii, 1872; i, 1873), has caused death. (*P. M. T.*, iii, 718; *M. T. G.*, July, 1873.) The methylene dichloride may be given internally in the *dose* of from ten to thirty minims (0.6–1.8 cc.), which may be dissolved in dilute spirit.

Metol. *Monomethylpara-amido-metacresol-sulphate.* $(C_6H_3[OH]CH_3[NH]CH_3)_2H_2SO_4$.—A white powder, soluble in water and extensively used as a developing agent in photography and in X-ray processes.

Micrampelis. *Micrampelis fabacea* (Naud.) Greene. (*Megarrhiza californica* Torr., *Echinocystis fabacea* Naud.) *Man Root. Big Root. Gerba marra.* (Fam. *Cucurbitaceæ.*)—J. P. Heaney has obtained a substance from this root of resinous character which he calls *megarrhizitin,* and another which he believes to be a glucoside and calls *megarrhizin.* It is said to be actively cathartic. (*A. J. P.*, 1876, 451.) A second glucoside was obtained by W. M. Young (*A. J. P.*, 1883, 195), to which the name of *megarrhin* was given. It resembles saponin, and possesses the property of dilating the pupil. Young also found two resins, one soluble in alcohol and the other soluble in ether.

Microcidin. *Betanaphthol Sodium.*—Under this name the varying compounds of *sodium naphtholate* with other naphtholates and phenates have been put upon the market, and used as surgical antiseptics in solution varying from three to five per cent. As a nasal or aural douche a 0.1 per cent. to 0.5 per cent. solution is recommended.

Micromeria. *Micromeria Chamissonis* (Benth.) Greene. *Yerba Buena.*—This sweet-scented labiate, which is popularly known as *yerba buena,* is a trailing perennial, indigenous to the Pacific Coast. Power and Salway have obtained besides 0.16 per cent. of a volatile oil with a mint-like odor, two new alcohols, which they named *micromol,* and *micromeritol,* and a phenol, *xanthomicrol.* (*J. Am. C. S.*, 1908, 251.) The fluidextract prepared from this plant has been used popularly as an emmenagogue. *Dose,* one-half to two fluidrachms (1.8–7.5 cc.).

Midrol. *Iodomethylate of Phenylpyrazolon.*—*Midrol* forms white, bitter and water soluble crystals. It is used as a mydriatic, in 5 to 10 per cent. strength. One drop of a 10 per cent. solution introduced into the conjunctiva causes at first contraction, then dilation, of the pupil which lasts about two hours.

Migrol. *Pyrocatechin-monoaceto-dimethylamidophenyldimethyl-pyrazolon.*—It forms colorless crystals of an intensely bitter taste, of slight acid reaction and soluble in water and alcohol. It is used in 0.5 gramme (8 grain) doses in *neuralgia* and *rheumatism.*

Miré.—This is a shrub found growing in Central Bolivia whose rhizome and roots, stems and leaves are used by the aborigines of that country as a muscular paralyzant and remedy for cutaneous parasites. H. W. Youngken investigated the gross and microscopic structure of the plant from material collected in 1921 by members of the Mulford Biological Exploration Party in Central Bolivia. He determined it to be a species of *Brunfelsia* belonging to the Fam. *Solanaceæ,* the structure of the stems and leaves of which bears a striking similarity to *Brunfelsia hydrangæformis* (Phol.) Benth. (See *Jour. A. Ph. A.*, 1925, p. 195.)

According to H. H. Rusby (*J. A. Ph. A.*, 1924, xiii. p. 101) the natives of the region in which this plant is found boil the drug to extract its active principle and claim the perspiration which follows the internal use of this drug is capable of killing cutaneous parasites, further that it paralyzes the voluntary muscles precisely like alcoholic intoxication.

T. S. Githens (*J. A. Ph. A.*, xiii, 102) states that miré causes paralysis of voluntary motion by its action on the spinal cord and that it stimulates the salivary and sweat mechanism as well as the peripheral motor apparatus.

Momordica. *Momordica Balsamina* L. *Balsam Apple. Balsamina.* (Fam. *Cucurbitaceæ.*)—An annual climbing East Indian plant, cultivated in our gardens for the sake of the ornamental fruit. The latter is ovate, attenuated towards each extremity, angular, warty, not unlike a cucumber in appearance, of a lively red or orange-yellow color, easily falling when touched, and spontaneously separating into several pieces. A liniment formed by infusing the fruit, deprived of its seeds, in olive or almond oil, is applied to *chapped hands, burns, piles, prolapsus ani,* etc.; and the mashed fruit is sometimes used as a poultice. According to Descourtilz, two or three drachms taken internally will kill a dog. An extract prepared from it is said to be useful in *dropsy. Dose,* six to fifteen grains (0.4–1.0 Gm.).

Monarda. *Monarda punctata* L. *Horsemint. Menthe de Cheval,* Fr. *Pferdeminze, G.*—This is an indigenous perennial or biennal labiate, growing in light gravelly or sandy soils from New York to Texas and west to Wisconsin. The whole herb is employed. It has an aromatic odor, and a warm, pungent, bitterish taste, and abounds in a volatile oil, which may be separated by distillation with water. Herman J. M. Schroeter (*A. J.*

P., 1888, 120) found the oil to consist of a hydrocarbon, $C_{10}H_{16}$ (56 per cent.), thymol, $C_{10}H_{14}O$ (25 per cent.), and higher oxygenated compounds, $C_{10}H_{18}O$. Kremers (*Ph. Rev.*, 1896, 223) examined the oil from authentic specimens and found it to yield from 56 to 61 per cent. of a phenol (thymol). Horsemint is stimulant and carminative, but is seldom used in regular practice. In the state of infusion it is occasionally employed as a domestic remedy for flatulent *colic* and sick stomach, and for other purposes to which the aromatic herbs are applied. *Monarda fistulosa* L., *wild bergamot*, an active diuretic (see *Proc. A. Ph. A.*, 1895, 256; 1896, 238), contains, according to J. W. Brandel and E. Kremers, *hydrothymoquinone, thymoquinone,* besides cymene, carvacrol and limonene. (*Ph. Rev.*, 19.) The oil of *Monarda citriodora* Cerv., or *prairie bergamot*, according to Brandel (*P. J.*, 1894, liii, 547), contains 65 per cent. of a phenol and 1.2 per cent. citral. See also *Midland Druggist*, 1910, 526, and a paper by Nellie Wakeman in the *Proc. A. Ph. A.*, 1910, 979. For the composition of monarda oils see *Ph. Archiv.*, 1899, 73.

Mon-Arsone.—This is di-sodium ethyl arsonate, hence related to sodium cacodylate and more nearly to arrhenal. It has been suggested as a substitute for arsphenamine in the treatment of *syphilis.* Nichols (*J. A. M. A.*, 1921, lxxvi, 1335) has found that while in rabbits it has some spirocheticide effect the dose required is large enough to kill the animal, *i.e., in* sub-lethal doses it has no value.

Monesia.—A South American vegetable extract, which is derived from the bark of *Pradosia latescens* Radlkofer. (Fam. *Sapotaceæ*), a tree of moderate size, growing in the forests near Rio Janeiro and elsewhere in Brazil. The bark, which has also entered commerce, is in pieces, some of which are three or six mm. thick, is very compact and heavy, of a deep brown or chocolate color, contrasting strongly with the grayish color of the epidermis when this remains, and of smooth fracture. The extract is of a dark brown almost black color, very brittle, the fracture neither very dull nor very shining, and of a taste at first sweet, then astringent, and ultimately acrid, the acridity being very persistent. It is entirely soluble in water. The bark contains glycyrrhizin and, according to Peckolt (*A. J. P.*, 1884, 626), a saponin, *monesin;* an acrid, amorphous body, *lucumin;* a peculiar tannin, *monesiatannic acid;* tartaric and citric acids, wax, etc. *Monesin*, $C_{32}H_{54}O_{18}$, was in transparent, yellowish scales, which were easily pulverized, forming a white powder. It was uncrystallizable, readily soluble in alcohol and water, to the latter of which it gave the property of frothing, and insoluble in ether. It was without odor, but had a slightly bitterish taste, followed by a decided and permanent acrimony in the posterior mouth and fauces. Monesia owes its activity probably to this principle and to tannic acid.

Monesia is stomachic and feebly astringent, and has been used with asserted advantage in *diarrhea, hemoptysis, menorrhagia, scrofula, scurvy,* also as a local remedy in *leucorrhea, ulcerations of the mouth and fauces* and *ulcers.* It is applied to ulcers either by being sprinkled in powder upon the surface or in the form of ointment made with one part of the extract and seven parts of simple ointment. The *dose* of the extract is from two to ten grains (0.13–0.65 Gm.), repeated every one to three hours. Monesin has been given internally in the *dose* of about half a grain (0.032 Gm.), and has also been applied to ulcers. It is said to be a powerful oxytocic, but is seldom used.

Mongumo Bark.—For analysis of this Madagascar bark, which is said by E. M. Holmes to resemble the bark of *Ochrosia borbonica* J. F. Gmel. (Fam. *Apocynaceæ*), see *P. J.*, ix, 816. It was examined by Dragendorff, who found *mongumic acid*, resin, waxy substance, a glucoside soluble in water and alcohol, metarabic acid, fatty matter, calcium oxalate and a substance insoluble in alcohol and soluble in water.

Monsonia.—According to John Maberly (*L. L.*, Feb., 1897; July, 1898), certain South African plants belonging to the family of *Geraniaceæ*, having large fleshy roots, are valuable remedies in the treatment of both acute and chronic *dysentery;* such are especially *Monsonia ovata* Cav. and *M. Burkeana* Planch., also certain *Pelargoniums.* Under the name of *t'Namie*, the natives of Namaqualand are said to use the root of *Pelargonium antidysentericum* Kostel. Maberly believes that the *Pelargoniums* are especially valuable in ulceration of the stomach and upper portions of the intestinal tract, and the *Monsonias* when the disease is low down in the intestines. The *dose* of monsonia is given as half an ounce (15.5 Gm.). It is believed that the plants are not poisonous.

Morinda.—From the wood of the *Morinda tinctoria* Roxb. (Fam. *Rubiaceæ*), or *Indian Mulberry,* Anderson (*P. J.* 1886) claimed to have obtained a glucoside *morindin,* which yielded on hydrolysis trihydroxy-methyl-anthraquinone. Oesterle (*A. Pharm.*, 1907, ccxlv), however, was unable to find this glucoside, but did obtain a monomethyl-ether of tri-oxymethyl-anthraquinone, $C_{16}H_{12}O_5$. *M. umbellata* L., *M. citrifolia* L., and the *M. longiflora* G. Don., all yield anthraquinone derivatives. (See Barrowcliff and Tutin, *Trans. British Chem. Soc.*, 1907.) The flowers of *M. citrifolia* contain a red, and the roots a yellow, coloring principle. These plants are used by the African aborigines as remedial agents, but there is no reliable evidence of their therapeutic value.

Morphine Hydrobromide, or *Morphine Bromide* ($C_{17}H_{19}O_3NHBr + 2H_2O$), is made by double decomposition between morphine sulphate and barium bromide (*A. J. P.*, xliv, 447.)

Morphine Meconate. *Morphine Meconas.* ($(C_{17}H_{19}O_3N)_2C_7H_4O_75H_2O$.—This is obtained by the interaction of morphine alkaloid and meconic acid. It occurs in minute, colorless crystals or a yellowish-white powder slightly soluble in water but more so in alcohol. It contains 66.3 per cent. anhydrous morphine and is used after the manner of other morphine salts.

Morphine Methyl Bromide. *Morphosan.* $C_{17}H_{19}O_3NBrCH_3$.—This occurs in needle-like crystals soluble in 20 parts of water. It is asserted that it is free from any of the unpleasant secondary effects of morphine and it has been suggested as a substitute for the latter in the treatment of the morphine habit. The *dose* is one twelfth to one-half of a grain (0.005–0.032 Gm.).

Morphine Stearate. $C_{17}H_{19}O_3N.C_{17}H_{35}.COOH$.—This is made by the combination of morphine hydrochloride with sodium stearate. It forms a white scaly product with a melting point of 85° C. A sweet almond oil solution (1 to 100) of this substance is known as *morphinol* and is used as an anodyne application.

Moxa. *Moxa,* Fr. *Brenncylinder,* G.—These are small combustible masses used to produce an eschar by being burned in contact with the skin. In Japan and China they are made from the leaves or the downy hairs on the leaves and stems of one or more species of *Artemisia. A. chinensis* L. and *A. indica* Willd. (*A. vulgaris* L.) were indicated by the Dublin College; but Lindley states that it is the *A. moxa* of De Candolle which is employed. A similar *moxa* has been made in France, by a similar process, from the leaves of *A. vulgaris.* Moxa were prepared by the Pawnee Indians of North America from the stems of an unidentified species of *Aster.* According to Percy, the dried stem of the ordinary sunflower may be used for moxa. Artificial moxas may be made by impregnating cotton with saltpeter.

Cauterization by fire has been used from time immemorial among savages, half-civilized, and intelligent communities, and is said to have been reintroduced into Europe by the early Portuguese navigators from the Far East. Though at one time much employed for the purposes of revulsion, this form of cauterization has fallen into complete desuetude. The details of its application are described in the 18th edition, *U. S. D.*

Muawin Bark.—This is the bark of a Mozambique tree, which in Eastern Africa is used as an ordeal poison. In appearance and structure it closely resembles the erythrophlœum bark obtained from numerous species of *Erythrophlœum* (Fam. *Leguminosæ*). An alkaloid, *muawine,* was discovered in it by E. Merck, 1891. The hydrobromide, a yellowish powder soluble in water and alcohol. The characteristic test is said to be that with vanadinsulphuric acid, which gives with muawine first a pale green, passing into a pale blue. (H. Jacobsohn, *In. Dis.,* Dorpat, 1892; see also *Merck's Jahresbericht,* 1891.) According to Jacobsohn, the hydrobromide when injected subcutaneously does not cause any irritation, but produces in frogs symptoms similar to those caused by digitalin, and in warm-blooded animals slowing of the pulse, increase of the heart action, elevation of blood pressure, and contraction of the arterioles. The action of muawine is, therefore, like that of digitalin, but is distinguished by being very temporary.

Mucuna. *Mucuna pruriens* De Cand. *Cowhage. Cowage. Setæ Siliquæ Hirsutæ. Pois velus, Pois à gratter,* Fr. *Kratzbohnen, Kuhkrätze,* G.—This is a leguminous climbing plant which grows in the West Indies and tropical countries of both hemispheres. The fruit is a coriaceous pod, shaped like the Italic letter *f*, about four inches long, and covered with brown bristly hairs, which easily separate, and when handled stick in the fingers, producing an intense itching sensation.

The spicula are said to be very destructive to the *round worm,* acting mechanically by penetrating their bodies. Neither the tincture nor the decoction is effective. Cowhage is efficient, but so disagreeable that it has passed out of vogue. The usual mode of preparing it is to dip the pods into syrup or molasses, and scrape off the hairs with the liquid, which is in a proper state for administration when it has attained the consistence of thick honey. The *dose* of this preparation is a tablespoonful (15 cc.) for an adult, a teaspoonful (3.75 cc.) for a child three or four years old, to be given every morning for three days, and then followed by a brisk cathartic.

Muira-Puama.—The dried root of *Liriosma ovata* Miers [*Dulacia ovata* (Miers) Lyons] (Fam. *Oleaceæ*), a Brazilian tree. (For a description of this drug see Youngken, *J. A. Ph. A.,* 1921, x, 690.) According to Th. Peckolt, it contains an alkaloid, *muira-puamine,* and is used by the Brazilian aborigines as an aphrodisiac, also in the treatment of *dysentery.* In *impotence,* ten to twenty minims (0.6–1.3 cc.) of the fluidextract may be taken three or four times a day. (See *M. R.,* 1902.)

Mulberry.—There are in the United States six species of which the three best known are the following: the indigenous *Morus rubra* L., with dark purple fruit; *M. alba* L., introduced from Europe, and at one time extensively cultivated as a source of food for the silk worm, having a white fruit; and *M. nigra* L., a tree of middle size, supposed to have been brought originally from Persia into Italy and widely cultivated. The fruit of the last species has a sweet, mucilaginous, acidulous taste, and abounds in a deep red juice having the sp. gr. 1.060. (*Mori Succus,* Br., 1885.) For analysis of mulberries see *U. S. D.,* 19th ed., p. 1573. In amount of grape sugar the mulberry is surpassed only by the cherry, 10.79, and the grape, from 10.6 to 19.0. Mulberries are refreshing and laxative, and serve to prepare a grateful drink well adapted to febrile cases.

Murexide. *Acid Ammonium Purpurate.* $C_8H_4(NH_4)N_5O_6 + H_2O$.—A fine purple dye-stuff, made by the reaction of nitric acid on uric acid. As resulting from the action of nitric acid on urine, it was supposed by Prout to consist of purpuric acid and ammonia (which belief has been confirmed by further investigation), and hence was named *ammonium purpurate.* It was later made from guano. This was first treated with hydrochloric acid to remove foreign substances, and then with soda to dissolve the uric acid, which is separated by neutralizing the soda with hydrochloric acid. The uric acid is dissolved in nitric acid, the solution is heated, and after it cools ammonia or its carbonate is added, which develops the purple color. Murexide is obtained in crystals, which have a square form, and are a rich green color by reflected, but of a purple-red by transmitted, light. It is slightly soluble in cold water, more so in boiling water and insoluble in alcohol and ether. With potassium hydroxide it forms a rich purple solution. It has been replaced as a dye by aniline colors.

Muscari. *Muscari comosum* (L.) Mill. *Grape Hyacinth* (Fam. *Liliaceæ.*)—In the bulbs of this plant, which grows in Europe and Asia, Curci (*Rép. de Pharm.,* March, 1889) has found *comosic acid,* which he believes to act physiologically like saponin.

Musculus. *Musculus venenosus.*—That certain mussels, or that mussels in a certain condition, are actively poisonous is well ascertained. F. Crumpe (*Dublin Q. J.,* Oct., 1873) has reported collapse with complete paralysis of the voluntary muscles as produced by the mussel. M. Breiger (*D. M. W.,* 1885) has isolated out of mussels the base *mytilotoxine* ($C_6H_{15}O_2N$), which he has demonstrated to possess physiological properties closely resembling those of curare. These poisonous principles are all probably ptomaines, and disappear when the mussel is boiled with sodium carbonate; so that boiling the mussel in an alkaline solution (three and a half grammes per liter of water) renders it harmless.

Musenna Abyssinica.—A substance known as *tœniol* which is claimed to be derived from the rind of the *Musenna abyssinica*, has been recommended as a vermifuge especially for the treatment of *anchylostoma*. According to Liermberger (*B. K. W.*, 1905, p. 390), it is an efficient and nontoxic anthelmintic. The only unpleasant symptom produced was slight giddiness. It is marketed only in the form of capsules of which 10 to 15 may be taken at intervals of ten minutes. After the sixth or seventh capsule there should be allowed an interval of an hour.

Mushrooms and Toadstools. (*Edible and Poisonous Fungi.*)—Notwithstanding the fact that it has been shown that edible fungi, when compared with other articles of food, do not possess a high food value, the interest in the study of the fungi, as well as the consumption of edible forms, is constantly increasing. The study of the fungi is one of the most highly specialized, as there have been up to the present time no less than 64,000 species described. From a food standpoint the differentiation of the edible from the poisonous is one of the most difficult that the novice can undertake, as it is almost impossible to lay down any invariable rules.

The fungi are divided into a number of classes, each of which is again subdivided into sub-classes, orders, and families. The class *Basidiomycetes* includes the largest and most conspicuous of the fungi and all of the mushrooms and toadstools.

The *Basidiomycetes* are divided into two subclasses, the *Hymenomycetes*, or those which have their spore-bearing surface exposed, and the *Gasteromycetes*, or those with their spore-bearing surface inclosed.

It is commonly believed that mushrooms are edible and that toadstools are poisonous; in reality, however, no such distinction should be made. The word "mushroom" is best used in application to any or all of the higher fleshy fungi whether good, bad, or indifferent in respect to edible qualities.

The sporophores (fruiting bodies) of the *Hymenomycetes* are characterized in general in that they arise from a mass of colorless threads, known as "mycelium" or "spawn," produced in the ground, bark of trees, etc. Their first appearance above ground is marked by the production of small solid balls (called buttons), which gradually enlarge, and at length shoot up into a stem or stipe bearing at its summit the umbrella top or "pileus," which is at first closed around the stalk like a closed umbrella and then expands more or less widely, according to the species. The under side of the pileus is the part which bears the spores, which correspond to the seeds of higher plants. In some cases the under surface consists of a series of gills resembling knife blades, which radiate from the top of the stalk to the circumference, like the spokes of a wheel, as in *Agaricaceœ;* in others it consists of a mass of small pores or tubes packed closely together, side by side, as in *Polyporaceœ;* in others of teeth, as in *Hydnaceœ;* in others only slightly wrinkled or undulated, as *Thelephoraceœ*, etc. The *Basidiomycetes* include about 14,000 species which are included in nine orders and subdivided into twenty-five families. A few of the important are the following:

1.—*Agaricaceœ* (the mushrooms and toadstools proper) comprises about 4600 species, some of which are poisonous, as the *Amanitas* (Fly and Deadly Agarics) *Lactarius* (with a milky juice), whereas others are edible, as *Agaricus campestris* L., the common mushroom, *Cantharellus cibarius*, Fr., the *chanterelle*, etc.

2.—*Polyporaceœ* (pore-fungi) includes about 2000 species, many of which are parasites on trees and destructive to timber; some are edible, as *Boletus edulis* Bull., whereas others are poisonous, as *B. satana* Lenz.

3.—*Hydnaceœ* (teeth-bearing fungi): Most of the species are too small and woody to be eaten. *Hydnum repandum* forms "fairy rings" in woods.

4.—*Thelephoraceœ:* Most of the species are small, and the larger species are tough and leathery.

5.—*Clavariaceœ* (coral-shaped fungi) includes some large fungi; none are poisonous and some, as *Clavaria flava* Schaeff, are palatable.

Of these, the most important group are the *Agaricaceœ* both from the point of view of the toxicologist and the epicure.

It is not possible in this limited space to even mention the various poisonous and edible fungi that experience has demonstrated as such. The number of species which have been eaten or experimented with, however, is small compared to the number recognized by botanists. Many students of fungi have formulated rules for distinguishing edible from poisonous fungi. "The different popular tests for distinguishing edible from poisonous fungi, such as, for instance, the blackening of a silver coin or spoon when placed in a mass of poisonous fungi while they are being cooked, are all absolutely worthless." The only safe rule is to use no mushroom which the collector is not absolutely sure from previous experience is edible.

The *common mushroom* (*Agaricus campestris* L.) is practically the only species cultivated in this country, and is the only fresh species sold in the northern markets during the winter months. It is found wild in open grassy fields and pastures in great abundance in August and September. It is not common on the mountains, never found in woods, and never grows on trees or fallen trunks. The color of the stalk and pileus varies from a whitish shade to drab, but the color of the gills, a point which should never be overlooked, is at first pinkish and then a brownish-purple. The stalk is cylindrical and solid, and has, rather more than half way up, a membranous collar called the ring; but there is no membrane or scales found at the base of the stalk, which appears to come directly out of the ground. "In specimens which are not fully expanded there is a thin membrane or veil which extends from the stalk to the margin of the pileus. When the veil is ruptured, exposing the gills behind, a part remains attached to the stalk forming the ring already referred to. In older specimens the ring shrinks, but generally a mark remains showing where it has been attached."

Two of the most poisonous forms resembling the common mushroom, and which have been eaten in mistake for it, are the deadly agaric and fly agaric.

The *fly agaric* (*Amanita muscaria* (L.) Pers.), so called because decoctions have been used for killing flies, is in some localities much more abundant than the common mushroom. It is seldom found in the grassy pastures preferred by the common mushroom, but more generally in poor soil, especially in groves of coniferous trees. "It grows singly and not in groups and differs from the common mushroom in having gills which are always white, never pink or purple and in having a hollow stem, which is bulbous at the base and clothed with irregular fringy scales on all the lower part.

The pileus varies in color from a brilliant yellow to orange and a deep red, the yellow and orange being more frequent than the red. The surface is polished, and has scattered over it a larger or smaller number of prominent, angular warty scales which can be easily scraped off. The gills and stalks are white, and there is a large membranous collar which hangs down from the upper part of the stem."

The *deadly agaric* (*Amanita phalloides* (Pers.), Fr.), so named because it probably has been more frequently the cause of death than any other fungus, prefers a damper and less sandy soil than the fly agaric and is not pre-eminently an inhabitant of grassy pastures. It is common in woods and like the fly agaric grows singly. "The pileus is often a shining white, but may be of any shade from a dull yellow to olive, and when wet is more slimy than the common mushroom or the fly agaric. It has no distinct scales and only occasionally a few membranous patches on the pileus. The gills and stalks are white, and the latter has a large ring like the fly agaric and is hollow, or when young, is loosely filled with cottony threads, which soon disappear. The base of the stalk differs from that of the fly agaric in having more bulbous volva, the upper part bordered by a sac-like membrane."

The list of edible and poisonous fungi are relatively long, and while most belong to the *Hymenomycetes*, some are also yielded by the *Gasteromycetes*, as the puff-balls and carrion fungi. The *giant puff-ball, Lycoperdon bovista* (*L. giganteum* Batsch), found in the region of San Francisco Bay, is not rarely forty inches in diameter.

We may conveniently consider the poisonous mushrooms in four groups following the divisions of Kobert. (*Ueber Pilzvergiftung*, 1891.)

In the first group is the genus *Lactarius* which owe their toxic properties to the presence of an irritant resin. Some of this genus, as *L. deliciosus*, are stated to be edible, but most of them produce severe or even fatal gastric enteritis.

The second group contains species belonging to the genus *Helvella*, whose juice contains *helvellaic acid*, isolated by Boehm. It is asserted that these fungi, when thoroughly dried, are not poisonous, and that hot water also extracts from them the poisonous acid, so that boiling makes them edible. The chief physiological action of the acid seems to be to destroy the red blood corpuscles, and, probably by such action, to produce vomiting, hemoglobinuria, jaundice, irritation of the kidneys, etc.

The third and most important group are the *Amanitas*. They are the most common source of mushroom poisoning, not only because of their resemblance to many of the edible species, but also because of the virulence of their effects. The most important of this species is the *A. phalloides*, or *skunk mushroom*. According to Ford (*J. P. Ex. T.*, 1910, 1, p. 275), they contain two poisonous substances, one being hemolytic, and the other causing degenerative changes in the various internal organs, especially the liver, kidneys, spleen and muscles. The *amanita-hemolysin*, which is probably identical with the *phallin* of Kobert, appears to be glucosidal, and because it is destroyed by heat, probably plays little part in human poisoning. The nature of *amanita-toxin* is not yet determined, but poisons of a similar nature appear to be widespread throughout the whole of the genus.

In the fourth group are included those which contain *muscarine*. This alkaloid was first obtained from the *Amanita muscaria*, but is also found in the *A. pantherina*, the *Russula emetica*, in *Boletus luridus*, *B. Satanus*, and, according to Ford (*J. P. Ex. T.*, 1911, ii, p. 549), occasionally also in the *Clytoscybe dealbate*, which has by some been classed as an edible fungus. Decoctions of the *Amanita muscaria* are used to poison flies, whence the common name of the *fly agaric*. The inhabitants of the Caucasus also use this fungus as an intoxicant. The *A. pantherina* is used in Japan for like purposes.

Muscarine was first obtained in a state of purity by Schmiedeberg and Koppe. (*Das Muscarin*, Leipzig, 1869.) The alkaloid may be produced artificially by gently heating choline platino-chloride with strong nitric acid. Potassium chloride is used to decompose the muscarine platino-chloride and produce muscarine hydrochloride; treatment with moist silver oxide yields the muscarine as a hydrate ($C_5H_{15}O_3NH_2O$). Muscarine is closely related in its chemical composition and structure to betaine and choline. Muscarine resembles pilocarpine in its physiological action, and is antagonistic to atropine. It increases the secretions of the sweat, salivary and lachrymal glands, contracts the pupil, slows the pulse, and causes motor weakness. The reduction in the pulse rate is due to stimulation of the pneumogastric nerve, and after very large doses diastolic arrest of the heart occurs. If atropine be given so as to paralyze inhibition the cardiac movements reoccur. The vasomotor nerves are said to be paralyzed. There is a stimulation of the muscles of the intestines, bladder and spleen. The abdominal secretions are greatly increased.

The symptoms of mushroom poisoning will vary greatly according to the special fungus which has been ingested. In the case of the deadly agaric (*Amanita phalloides*) which is the most common source of toadstool poisoning, the symptoms usually do not appear for several hours after the fungus has been eaten. They consist of great prostration and collapse, cold sweats, stupor, sometimes preceded by delirium, convulsions, frequently cyanosis and not rarely icterus. There is usually, also distinct fever, and either hemoglobinuria or methemoglobinuria, and evidence of irritation of the kidney is shown by the presence of albumen, or partial suppression of the urine. When the poisoning is produced by fly agaric, to these symptoms will be added those of muscarine poisoning, namely, profuse salivation, contracted pupils and slowing of the pulse. In the poisoning by the lactarii the symptoms are those simply of violent inflammation of the alimentary tract, vomiting, purging and collapse. In poisoning by the *Helvellæ* the symptoms resemble those produced by the *Amanitas*.

After the poison has once entered the system but little can be done to save the patient. Our utmost efforts should be directed to preventing absorption. A promptly acting emetic, such as apomorphine, should be administered to produce vomiting. Secheyon (*P. J.*, 1910, liiiv, p. 492) highly recommends animal charcoal for the purpose of adsorbing the poison, and thus preventing its entrance into the system. At least a tablespoonful, stirred up in water, should be administered, and repeated libitum. It is also advisable to administer atropine hypodermically in one-sixtieth-grain doses (1 mgm.), as it is the physiological antagonistic to muscarine, and may prove a life-saving remedy in poisoning by fly agaric, and by its general stimulant effect will also exercise a feeble influence in combating the collapse even although due to other forms of poisoning. A rapidly acting cathartic should also be administered to cleanse the intestinal tract. Aside from these measures, the treatment is purely symptomatic—the use of opium if necessary to check the diarrhea and vomiting, and various stimulants to maintain the circulation and respiration.

Musk. *Moschus* U. S. IX, *Deer Musk. Musc,* Fr., *Bisam,* G., *Muschio,* It., *Almizcle,* Sp.—"The dried secretion from the preputial follicles of *Moschus moschiferus* Linné (Fam. *Moschidæ*). Preserve it carefully in glass-stoppered bottles." *U. S. IX.*

Musk is no longer recognized by either the U. S. or British Pharmacopœia.

The *musk-deer* is a small animal about 20 inches in height, differing from other deers in that there are no antlers in either sex. It is an extremely wary animal of a deep iron gray color, inhabiting the mountainous districts of Central Asia where it is hunted for its hide as well as for the peculiar secretion known as musk. This latter is contained in an oval, hairy, projecting sac, found only in the male, situated between the umbilicus and the prepuce, from two or three inches long, and from one to two broad, opening by a small hairy orifice at its anterior part, and marked posteriorly by a groove or furrow which corresponds with the opening of the prepuce. It is lined internally by a smooth membrane, thrown into a number of irregular folds, forming incomplete partitions. In the vigorous adult animal, the sac sometimes contains six drachms of musk; but in the old, seldom more than two drachms, and none in the young. As soon as the animal is killed, the sac is cut off, dried, and sent into the market.

The so-called *Tonquin musk* (which really comes from the province of Sze-Chuen in China) and the *Tibetan musk,* which are the preferred varieties, appear in commerce as flattish, circular or oval cakes called "pods," of about 5 to 7 centimeters in diameter and 2 or 3 cm. in thickness. They are convex and hairy on one side, flat and destitute of hair on the other. The hairs are brownish-yellow, grayish, or whitish, stiff and short, and arranged concentrically around the orifice of the sac. The pods of the *Yunan musk,* which is obtained in the Chinese province of that name, may easily be distinguished by their more nearly spherical outline. The *Assam* and *Nepaul musk* are in spherical pods which are much smaller than those of the Tonquin variety. A variety known as *Cabardine musk* is exported from China into Japan, but does not appear to enter this country.

Fresh musk is an unctuous, brownish, semi-liquid—but in the dried condition, as it appears in our markets, is in grains or lumps concreted together, soft and unctuous to the touch, and of a reddish-brown or ferruginous color resembling that of dried blood. Some hairs of the pod are generally mixed with it. It was officially described as "usually in small irregular granules, not more than 2 mm. in thickness, blackish with a few brown fragments and becoming somewhat grayish on aging; glistening and somewhat oily; odor peculiar, penetrating, powerful and peristent; taste somewhat bitter. Add a few granules of Musk to 2 mils of water in a watch crystal and stir with a glass rod; a light brown solution is obtained. The undissolved portion consists of irregular fragments containing a finely granular substance, numerous rod-like bacteria and occasionally the hyphæ of a fungus. Add a drop of iodine T.S. to a few granules of Musk on a slide and examine it under the microscope; the particles are not colored blue or bluish-black (*starch*). Add a few granules of Musk to 2 mils of alcohol contained in a watch crystal; the grains sink to the bottom, and upon stirring with a glass rod, a pale brown, slightly cloudy solution is obtained, leaving a somewhat oily stain upon the upper portion of the watch crystal as the alcohol evaporates; the undissolved portion or residue resembles that obtained with the aqueous mixture, except that the particles are less disintegrated. Add a few granules of Musk to 2 mils of chloroform in a watch crystal; the grains float on the surface and upon stirring with a glass rod, the solution remains nearly colorless, and as it evaporates there separates around the particles a small quantity of a whitish, oily or fatty substance. Not less than 50 per cent. of Musk is soluble in water, the solution having a strong, distinctly characteristic odor, and a slightly acid reaction. Not less than 10 per cent. of Musk is soluble in alcohol, the solution being of a light, yellowish-brown color and becoming slightly turbid upon the addition of water. Musk loses not more than 15 per cent. of moisture when dried to constant weight in a desiccator over sulphuric acid. Musk yields not more than 8 per cent. of ash." *U. S. IX.*

The odor is strong, penetrating and so diffusive that one part of musk communicates its odor to more than 3000 parts of inodorous powder. (Fée.) In some delicate individuals it produces headache and other disagreeable symptoms, and it has even caused convulsions. The color of the powder is reddish-brown. Musk is inflammable, burning with a white flame, and leaving a light spongy charcoal. It yields, upon analysis, a great number of proximate principles. Among these are fatty substances—such as stearin, olein and cholesterin—various proteins, various inorganic salts, and a small amount of a thick, colorless oily substance, apparently related to the ketones; this, which has been called *muskone,* possesses a powerful musk-like odor. Geiger and Reinman found a peculiar bitter resin, a peculiar substance in part combined with ammonia, and lactic acid both free and in combination. The action of potassium hydroxide upon musk is accompanied with the extrication of ammonia and an increase of its peculiar odor. By the influence of heat and moisture long continued, ammonia is developed, which acts upon the fatty matter, producing a substance resembling adipocere. When kept in glass bottles, in a situation neither moist nor very dry, it remains for a great length of time without material change. The odor of musk is very much diminished by mixing it with emulsion or syrup of bitter almond, or with cherry-laurel water. From the experiments of Wimmer, it appears that musk loses its odor when rubbed with golden sulphide of antimony, and reacquires it on the addition of a little solution of ammonia. Camphor rubbed up with musk is also said to destroy its odor.

The price of this medicine is so high, and its sources are so limited, as to offer strong temptations to adulteration, and little genuine unmixed musk is to be found in the market. A common practice in the East is to open the sac and to introduce all sorts of substances as dried blood, sand, resins, lead shot, etc. Some of these adulterations are obvious on even a casual observation but others are difficult of detection. The only safe rule is to purchase the musk in the sac, which should present no evidence of having been opened. The slit is sometimes carefully sewed up, sometimes glued together. The former condition may be discovered by close inspection, the latter by immersion in hot water. When the bag is made from any other portion of the skin, the difference may be detected, according to Neligan, by the microscope. The genuine hairs exhibit innumerable cells, which are wanting in the spurious. (*Chem. Gaz.*, Feb., 1846, p. 79.) Musk which burns with difficulty, has a feeble odor and a color either pale or entirely black, feels gritty to the finger, is very moist so as to lose much weight in drying, or contains obvious impurities, should be rejected. For an account of the effects of numerous reagents on musk, and other modes of identification, as well as of detecting adulterations, see Bernatzik (*A. J. P.*, 1861).

There are a number of other animals that secrete substances with strong odors, more or less resembling that of true musk. Among these is the beaver (see under *Castor*) and civet cat (see *Civet*). Under the name of *American musk* a product of the *musquash* or *muskrat* (*Fiber Zibethicus*) has been used as a substitute for true musk in perfumery, although the odor is not identical.

By the preceding generation of physicians, musk was one of the most highly esteemed remedies; of recent years, however—whether because of difficulty in obtaining it or the lack of real virtue is uncertain—it has very largely passed out of vogue. It was attributed with remarkable restorative powers in the nervous exhaustion of *low fevers*, such as *typhoid* or *adynamic pneumonia*. It was also highly esteemed for its antispasmodic action, especially in *hiccough* and in *laryngysmus stridulus*. According to some authorities, musk rapidly loses its power of influencing the nerve centers, and for this reason, and on account of its costliness, its employment should always be delayed until severe nervous exhaustion becomes alarming. It may be given in pill or emulsion. The U. S. IX recognized a 5 per cent. tincture made with a menstruum of diluted alcohol.

Dose, from five to fifteen grains (0.32–1.0 Gm.).

Musk, Artificial. *Moschus Factitius.*—An artificial musk introduced as a patented preparation, called "*Musk Baur*," from the name of the discoverer, A. Baur, is *trinitrometabutyltoluene*, $C(CH_3)_3.C_6H(NO_2)_3CH_3$. It is prepared by adding tertiary metabutyltoluene slowly in the cold to five times its weight of a mixture of concentrated nitric and sulphuric acids, and afterwards heating the mixture for from eight to nine hours on a water bath. There are several closely related compounds, all derived from butyltoluene, which are commercially known as "artificial musk." They melt at temperatures ranging from 89° C. to 96° C. They are insoluble in water but soluble in alcohol, ether, benzene, chloroform, and petroleum benzin.

Artificial musk has been esteemed to be antispasmodic and has been highly commended in *whooping cough* and *spasm of the glottis* of children. *Dose*, ten grains (0.65 Gm.); for a child two years old, from half a grain to a grain (0.032–0.065 Gm.), every two or three hours.

Mutisia. *Mutisia viciæfolia* Cav.—This composite, a native of Chile, is stated to be a valuable anti-spasmodic, useful in *hysteria* and *croup;* it is also a cardiac tonic.

Myrtus. *Myrtus communis* L. *Myrtle.* (Fam. *Myrtaceæ.*)—This is a handsome shrub with strongly scented leaves and flowers, indigenous to Mediterranean countries. From the leaves of this plant is distilled a volatile oil which, under the name of *myrtol*, is employed in medicine. This oil contains pinene, cineol and a characteristic alcohol, *myrtenol*. The mixture usually known as *myrtol* is collected between 160° and 180° C. Myrtol has been recommended as an antiseptic and a powerful stimulant to the pulmonic and genito-urinary mucous membranes, and useful in chronic *bronchitis*, *cystitis*, or *pyelitis*. Barker and Rowntree (*J. H. H. B.*, 1918, xxix, 215) have described cases of poisoning from myrtol with symptoms similar to those caused by oil of eucalyptus. *Dose*, from one to two minims (0.06–0.13 cc.), given in capsules, from four to eight times a day. A. de Vevey (*R. T.*, lxiii, 1896) has used the 10 per cent. solution in sterilized olive oil hypodermically in doses of eighty to one hundred and sixty minims (5–10 cc.) once or twice in twenty-four hours.

Nabalus. *Prenanthes alba* L. *Rattlesnake Root. White Lettuce. Cancer Weed. Gall of the Earth. Lion's Foot.* (Fam. *Compositæ.*)—In certain portions of Virginia and North Carolina, where this perennial herb grows, great value was attached to it in *rattlesnake bite*. The milky juice is taken freely internally, and its leaves steeped in water which is locally applied and frequently changed. The plant is also used in *dysentery*, and N. B. Williams has found tannin in the rhizome. (*A. J. P.*, 1887.)

Nance Bark.—This bark is believed to be obtained from the *Malpighia glabra* L. (*Barbados Cherry*) (Fam. *Malpighiaceæ.*), a glabrous shrub with opposite, ovate to elliptic leaves and umbels of red flowers, found growing from South Texas to northern South America and in the West Indies. It is much used in Mexico for tanning, and, according to F. Holberg, contains 26.2 per cent. of tannin. (*A. J. P.*, xvi, 239.)

Naphthalan. *Naftalan.*—This is a greenish-black soft mass, prepared by the fractional distillation of naphtha obtained from the Armenian highlands, having a slightly empyreumatic odor, a neutral reaction, and a specific gravity of 0.89. It melts at 70° C., is insoluble in water and glycerin, but mixes readily with fats and oils, and is soluble in ether and petroleum benzin. It has been recommended by Rosenbaum and others as very efficacious in the treatment of *pruritus* and *burns*, as well as in *chronic eczema*, *sycosis*, and other parasitic skin affections, and as having a range of usefulness closely parallel to that of the oil of cade. Applied as a paste, 50 per cent. naftalan, 25 per cent. each of zinc oxide and of starch, with or without 2 to 5 per cent. of menthol. (See *Praktitchesky Vratch*, vol. i, No. 31.)

Kupzis recommends a naftalan which is a combination of the higher boiling portions of Caucasus naphtha from the naphtha residues, having a sp. gr. 0.94–0.97, and deprived of odor by vacuum distillation, by dissolving from 6 to 8 per cent. of perfectly neutral stearine soap in it. (*Ph. Ztg.*, 1905, 499.)

Naphthalene. *Naphthalenum. U. S. VIII. Naphtalin. Naphthalin. Tar Camphor.* $C_{10}H_8 = 128.06$.—"A hydrocarbon obtained from coal-tar, and purified by crystallization. It should be kept in well-stoppered, amber-colored bottles." *U. S. VIII.*

This may be obtained by subjecting coal-tar to distillation, when it passes over in the middle oil and heavy oil; in the fractions of the latter it often constitutes the main constituent, causing it to become almost solid on cooling. It is frequently produced during the dry distillation of organic bodies. It is made very extensively and cheaply at present, the sublimed commercial product being nearly pure. It is a white, shining, crystalline substance, fusible at 80° C. and boiling at 218° C., but volatilizing with vapor of water. According to Kopp, its sp. gr. in the liquid state is 0.9774; according to Alluard, at 98.8° C., 0.9628.

It was officially described as in "colorless, shining, transparent laminæ, having a strong, characteristic odor resembling that of coal-tar, and a burning, aromatic taste; slowly volatilized on exposure to air; by exposure to light acquiring a brownish color. Insoluble in water, but when boiled with it, the water acquires a faint odor and taste; soluble in 13 parts of alcohol at 25° C. and very soluble in boiling alcohol; also very soluble in ether, chloroform, carbon disulphide, and fixed or volatile oils. Naphthalene volatilizes slowly at ordinary temperatures, but rapidly when heated. It also volatilizes with the vapors of water or alcohol. At 80° C. it melts, and at 218° C. it boils. Its vapor is inflammable, burning with a luminous but smoky flame. When ignited, it is consumed, leaving no residue. Naphthalene is neutral to litmus paper moistened with alcohol. On shaking a small portion of naphthalene with concentrated sulphuric acid, the acid should remain colorless, and should not acquire more than a pale reddish tint if the mixture be heated for five minutes on a water-bath (absence of *impurities derived from coal-tar*)." *U. S. VIII.*

Naphthalene is possessed of antiseptic properties, and is poisonous to most fungi and probably to most insects. Under the name of "*tar camphor*," it has largely supplanted true camphor as a means of preventing the deposition by moths of eggs in woollen clothing, and of preventing the destruction by insects in natural history museums. Castellani and Jackson (*Jour. of Tropical Medicine and Hygiene*, 1915, xviii, p. 253) rank naphthalene as the most practical insecticide powder for the protection of the body against vermin and hence against the diseases, such as *typhus fever*, carried by them; fleas exposed to its vapors were killed within 30 to 60 minutes and although it required a longer time to kill lice it seems to exercise a strong deterrent effect. Blaschko (*B. M. W.*, 1915, xli) highly recommends the use of a 5 per cent. naphthalene petrolatum as protective against typhus fever. It has been used for its antiseptic action in various *skin diseases* and to a less extent as a surgical dressing. In internal medicine it has been employed with asserted excellent results both as vermifuge and as an intestinal antiseptic in *enteritis*. For these latter purposes, however, it has been almost entirely superseded by its derivative, naphthol. *Dose*, one to five grains (0.06–0.3 Gm.) Eighty grains are said to have been given in a day without deleterious effects, but J. A. Otte (*Chinese Med. Missionary Journ.*, xi, 1897) violently poisoned himself by eight grains of naphthalene. The symptoms were excessive vomiting and purging and great abdominal pain, followed by nephritis. Moreover, employees in gutta-percha works, where it is largely used, are said to be occasionally thrown into a peculiar condition of delirious intoxication.

Narcissus. *Narcissus Pseudo-narcissus* L. *Daffodil. Trumpet Daffodil. Narcisse des prés, Porillon*, Fr. *Gelbe Narcisse*, G. (Fam. *Amaryllidaceæ.*)—Both the bulb and the flowers of this common and widely cultivated popular European garden plant have been used in medicine. The bulb is tunicated and averages one and one-half to two inches in diameter. The flowers are about two inches long, pale yellow, the corona crenate to somewhat crenate-fimbriate, the six stamens inserted near the base of the perianth and much shorter than the corona. The flowers have a feeble peculiar odor, and both have a bitter mucilaginous taste. They are an uncertain emetic. It is probable that the flowers of the wild European plant are more powerful than those of the cultivated. Gerrard found in 1877 in these bulbs a crystalline neutral principle and an alkaloid *narcissine* (*pseudonarcissine*). This base, which occurs in a number of the *Amaryllidaceæ*, has been shown by Asahina and Sugii (*A. Pharm.*, 1913, ccli, 357) to be identical with *lycorine*, $C_{16}H_{17}O_4N$, found by Morishima (*A. E. P. P.*, 1897, xl). It crystallizes in colorless prisms with a melting point of 270° C. According to Ruiger, the alkaloid obtained by Gerrard from the bulb of the flowering plant dries the mouth, checks perspiration, dilates the pupil, especially when applied locally, quickens the pulse, and acts on the heart of the frog antagonistically to muscarine and pilocarpine, while the alkaloid taken from the bulb after flowering causes salivation and perspiration, internally taken contracts the pupil, and topically applied dilates it slightly. (*J. P.*, i, 436.) In France, narcissus flowers have been used as an antispasmodic. The *dose* of the powder, to produce an emetic effect, varies, according to the statements of different physicians, from twenty grains to two drachms (1.3–7.7 Gm.); while the extract is said to cause vomiting in the *dose* of two or three grains (0.13–0.20 Gm.). The bulb is most powerful in the recent state.

Narcophine. $C_{22}H_{23}O_7N.C_{17}H_{19}O_3N.C_7H_4O_7 + 4H_2O$.—This is a double salt containing one molecule of morphine and one of narcotine united to meconic acid. Although it corresponds to only 38 per cent of morphine hydrochloride, according to Straub (*Biochem. Zeit.*, 1912, xlii, p. 316), it equals the latter salt in narcotic power. On the other hand Zehbe (*M. M. W.*, 1912) finds that it is somewhat weaker in equal dose than morphine, but the dose may be safely increased without the production of the common secondary effects of morphine. It is given in *doses* of from one-sixth to one-half grain (0.010–0.032 Gm.).

Narcyl. *Ethyl-narceine-hydrochloride.* $C_{25}H_{31}O_8N.HCl$.—It is sparingly soluble in cold water, readily soluble in alcohol; its solubility in water is greatly increased by the presence of organic acids. The various alkaloidal reagents precipitate it and the addition of chlorine water followed by ammonia will show a cherry-red color with a fresh solution of this compound. The precipitate formed by the addition of sodium hydroxide redissolves in an excess of the precipitant (distinction from narceine). According to Pouchet and Chevalier (*B. G. T.*, 1904, p. 779), its physiological action is very similar to that of codeine. It has been used as a cough sedative in *phthisis*, *bronchitis*, and *whooping cough*. *Dose*, half to one and a half grains (0.032–0.096 Gm.).

Nard.—Several aromatic rhizomes were known to the ancients under the name of *nardus*, distinguished, according to their origin or place of growth, by the names of *Nardus indica*, *Nardus celtica*, *Nardus montana*, etc. They are supposed to have been derived from different valerianaceous plants. Thus, the *Nardus indica* is referred to *Nardostachys Jatamansi* (Roxb.) DC. (*Valeriana Jatamansi* Roxb.), of Bengal, the *Nardus Celtica* to *V. celtica* L., inhabiting the Alps, Apennines, etc., and the *Nardus montana* to *V. tuberosa*, which grows in the mountains of the south of Europe. The *Indian nard*, sometimes called *Syrian nard*, is still occasionally to be found in commerce under the name of "*Nardus Root*." It is a dark gray, short rhizome from one to three inches long, beset with a tuft of soft, light brown, slender fibers, of an agreeable odor, and a bitter aromatic taste. It was formerly very highly esteemed as a medicine, but is now almost out of use. Its properties are analogous to those of valerian.

Naregamia. *Goanese Ipecacuanha.*—The root of *Naregamia alata* Wight and Arn. (Fam. *Meliaceæ*), of Western India, has been employed as an emetic, as an hepatic stimulant in *dysentery*, and in small doses as an expectorant in *bronchitis*. Drasche, of Vienna, confirms the value of the drug. (*Cb. G. T.*, 1890.) In it Hooker has found an alkaloid, *naregamine*, an oxidizable fixed oil, and a wax. (See *P. J.*, vol. xv, 1887.) The *dose* of a concentrated tincture (1 to 4) is from five to ten minims (0.3–0.6 cc.); as an emetic, from fifteen to thirty minims (0.9–1.8 cc.).

Nastin.—This substance which was originally prepared by Deycke and Reschad (*D. M. W.*, 1907, p. 89) from a culture of the bacilli of leprosy is stated by the discoverers to be a peculiar paraffin-like substance of fruity odor and composed of a glycerin ester and *nastinic acid* (a fatty acid of high molecular weight). It was at one time thought to be characteristic of these bacteria, but has been found in the bodies of other bacteria. It is claimed that the injection of this substance causes the death of the leprosy germs and hence arrests the disease. It is not claimed for it that it will cure the lesions which are already present, but simply that it prevents further progress of the disease. It is employed in the form of a 1 per cent. solution in warm sterile olive oil of which at first eight minims (0.5 cc.) and later 1 cc. is injected weekly. Kupffer (*Cb. G. T.*, 1909, p. 311) has also obtained favorable results from its employment.

Neopyrin. *Valinopyrin. Valeryl-amino-antipyrine.*—This is in the form of odorless crystals, of very bitter taste, and a melting point of 203° C. It is sparingly soluble in water, more so in alcohol, and freely so in chloroform.

Bachem (*Th. M.*, 1909, p. 588) has experimented upon the lower animals with valeryl-amido-antipyrine and also with its bromine derivative. The latter, however, he finds is too toxic to give promise of therapeutic usefulness, although it exercises a marked antipyretic action. He finds *neopyrine* is less poisonous than antipyrine and believes that it may prove a useful antipyretic. *Dose*, five to ten grains (0.32–0.65 Gm.).

Nerium. *Nerium Oleander* L. *Oleander*, *Rose Bay*. *Laurier Rose*, *Laurose*, Fr. *Oleander*, *Rosenlorbeer*, G. (Fam. *Apocynaceæ.*)—This widely cultivated ornamental evergreen shrub is a native of the Mediterranean region and Asia. It flowers in summer, the blooms being salver-shaped, variously colored and arranged in terminal cymes. Its leaves are lanceolate and are arranged in whorls of 2 or 3. It is affirmed to have been used from time immemorial in portions of Southern Europe for destroying rats, and a number of cases of poisoning by it have been reported. (For collection, see *T. G.*, July, 1888.) The symptoms have been vomiting, abdominal pain with frequent cries, dilatation of the pupil, vertigo, convulsive movements, insensibility, small, very slow pulse, and in fatal cases epileptiform convulsions with coma ending in death. The action on the heart has in some cases in which death has not ensued, been very pronounced, the pulse for five days remaining as low as forty per minute. The infusion made from four ounces of the root is affirmed to have taken life.

The active principle of oleander seems to be the glucoside *oleandrin*, discovered by Leukowsky, but more closely studied by Schmiedeberg (*A. E. P. P.*, 1883, xvi, 145), who proved its glucosidal character and found it to be a powerful cardiac poison of the digitalis type. A number of other supposedly active principles have been described but their existence cannot be considered as definitely established. Among these may be mentioned the *neriodorin* of Greenish (*A. J. P.*, 1881, 350), the *neriin* of Schmiedeberg and the *karabin* of Bose (*P. J.*, 1901, 553). Dubigadoux and Durieu affirm that they have obtained strophanthin from the oleander of Algeria. Leulier found in oleander bark a glucoside which seems to be identical with the lævo-strophanthin of Thoms. (*P. J.*, lxxxvii, p. 407.) Pieszczek obtained from oleander bark a principle which he named *rosaginin*, which was very poisonous, resembling strychnine in its action. (*A. Pharm.*, ccxxviii, 352.) (See also *M. R.*, 1911, and *J. P. C.*, 1912, 108.)

Pouloux (*B. G. T.*, May 15, 1888) and Freiherr (*Aerzt. Rund.*, 1899) have used oleander clinically in the treatment of *heart disease* as a substitute for digitalis with asserted success. Its diuretic action is said to be very marked, and not rarely it acts as a cathartic. Freiherr asserts that it is safer than digitalis in atheromatous diseases. Freiherr used it in infusion or tincture, representing as the daily dose from three-quarters to one and a half grains (0.048–0.096 Gm.) of the dried oleander bark, one and a half to three grains (0.096–0.2 Gm.) of the fresh bark, one and a quarter to three and a half grains (0.08–0.23 Gm.) of the dried fruit. Pouloux's dose of the extract was three-quarters of a grain (0.048 Gm.). Orfele has used the dried flowers—dose, three grains (0.2 Gm.) in substance, or from ten to twenty minims (0.5–1.0 cc.) of a 10 per cent. tincture—with success.

Nervocidine.—This is a yellow, amorphous, hygroscopic powder, readily soluble in water, which is affirmed to be an alkaloid, obtained from the East Indian plant, *Gasu Basu*, and to be a powerful local anesthetic, its 1 per cent. solution producing marked anesthesia of the cornea. It is stated to be so irritant that its 2 per cent.

solution will cause in dogs and rabbits an ulcerative keratitis along with an anesthesia which lasts for days. It is affirmed, further, to be a paralyzing poison, causing such symptoms as to almost invalidate its usefulness and render it unsafe. (*L. L.*, 1902, 1.)

Neuraltein. *Neraltein. Sodium p-ethoxyphenyl-amino-methane-sulphonate.* $C_2H_5O.C_6H_4NH.CH_2SO_3Na + H_2O$.—This is in the form of white crystals which are soluble in 10 parts of water, and very soluble in boiling water.

It is claimed that it has the advantage over other derivatives of paramido-phenol of being much less toxic. Astalfoni (*W. K. W.*, 1909, p. 119) has found that it causes an increase in the blood pressure with slowing of the pulse. The primary phase of hypertension lasts about an hour and is not followed by depression. Gottlieb (*Cb. I. M.*, 1909, xxx, p. 1049) has employed it in a number of febrile conditions. He finds that it exercises in many cases a distinct antipyretic effect but that its analgesic action is much inferior to that of other coal-tar antipyretics. Skutetzki (*M. M. W.*, 1909, p. 2314) on the other hand has obtained a marked relief of pain in *rheumatic fever* and believes that it is of value rather as an analgesic than an antipyretic. It may be given in *doses* of eight grains (0.5 Gm.) three to six times a day.

Neurodin. *Acetoxane. Acetyl-p-oxy-phenyl-urethane.* $C_6H_4(OCOCH_3)NH.COOC_2H_5$.—Forms colorless, odorless crystals, fusing at 87° C., soluble in 1400 parts of cold water. It is used as an anodyne in *neuralgia* in *doses* of from fifteeen to twenty grains (1–1.3 Gm.).

Neurolæna. *Neurolæna lobata* R. Br.—From the leaves of this composite plant, used in the Windward Islands as a substitute for quinine, and in *dysentery*, B. H. Paul and A. J. Cownley obtained an uncrystallizable alkaloid. (*P. J.*, ix.)

Neuronal. *Acetobromal. Diethylbromacetamid.* $Br(C_2H_5)_2CO.NH_2$.—A crystalline substance slightly soluble in cold water, but decomposed in hot water. It possesses a camphoraceous odor and a bitter cooling taste. Melting point 66° to 67° C. It has been used as a somnifacient by a number of clinicians with more or less satisfactory results. While apparently a useful drug in the treatment of the milder forms of *insomnias*, it does not seem to possess sufficient power in the severer cases. Heineicke (*Med. Clin.*, 1906, 572) observed that when used repeatedly, the remedy is liable to lose its power. The *dose* is from fifteen to thirty grains (1–2 Gm.).

Neutral Red. *Dimethyldiamidotoluphenazine Hydrochloride.—Toluylene red* has been employed by Schlaepfer (*M. M. W.*, 1908, No. 36) as a means of testing the motor function of the stomach. Nine cc. of a one-half per cent. solution of the dye is mixed with a meal and the passage of the gastric contents through the pylorus is indicated by the coloration of the urine. The remainder of the contents of the stomach are then siphoned out and the activity of the digestion may also be approximately ascertained by a degree of change in the color of from red to yellow which is caused by the gastric secretions.

New Sidonal. *Neusidonal.*—This preparation is asserted by its promotors to be the inner anhydride of quinic acid, but analysis has proved it to be irregular proportions of quinine, $C_7H_{10}O_4$, and quinic acid, $C_7H_{12}O_5.H_2O$, usually containing 75 per cent. of the former and 25 per cent. of the latter. It is administered in the treatment of *gout*, one hundred and fifty grains (9.8 Gm.) being given daily in divided *doses*.

Nickel. *Niccolum.*—T. P. A. Stewart (*A. E. P. P.*, Bd. xviii, 154) finds that in frogs soluble preparations of nickel produce palsy with convulsive movements which are due to an action upon the nerve centers, the muscles remaining intact, the heart also being affected, as it is believed, by an action upon its motor ganglia. In mammals the chief symptoms produced by nickel are paralysis, with motor disturbance bearing some resemblance to chorea, with convulsions and great irritation of the gastro-intestinal tract, and a marked fall of the blood pressure, due to paralysis of the vasomotor center. Large doses of *nickel* seem, however, to be necessary for a toxic influence, and the use of nickel in culinary instruments appears to be entirely safe. Riché (*B. A. M.*, 1888), as the result of experiments made upon dogs and guinea-pigs, reaches the conclusion that nickel is not more poisonous than iron. Thus, a dog absorbed over five drachms of it in sixty days, and increased in weight. The results obtained by Riché have been confirmed in Germany by von Hamel Roos and by Schulz. (*P. J.*, Dec., 1887.)

Nickel Bromide.—*Nickelous Bromide*, $NiBr_2$, is a greenish-yellow powder, of a sharp, almost burning taste, freely soluble in water, and making a grass-green solution. It was first brought forward by J. M. da Costa as a remedy for *epilepsy* and kindred disorders, and its value has been confirmed by R. Leaman. (*Med. Gaz.*, April 18, 1885.) It has been physiologically investigated by H. A. Hare, who finds (*T. G.*, vol. ii, 297) that it is a powerful paralyzant to the spinal cord, the motor and sensory nerve trunks, and also to the voluntary muscle. In sufficient dose it causes immediate diastolic cardiac arrest. In smaller doses it lessens the arterial pressure by depressing the heart and the vasomotor center.

Dose, five to ten grains (0.3–0.6 Gm.).

Nickel Carbonate. *Nickelous Carbonate. Niccoli Carbonas.* $NiCO_3 + Ni(OH)_2$.—Made by precipitating the solution of a nickel salt with potassium carbonate. It is from pale green to dark green, of variable composition. At one time it was employed in *anemia* in *doses* of two grains (0.13 Gm.).

Nickel Carbonyl. *Carbonic Oxide Nickel. Nickel-Kohlenoxyd*, G. $Ni(CO)_4$.—This substance is of interest because of the toxicity of its vapors. (See A. Mittasch, *A. E. P. P.*, xlix, 367; *L. L.*, 1903, i). Langlois (*C. R. S. B.*, 1891), also McKendrick and Snodgrass (*B. M. J.*, June, 1891), have shown that it acts by being broken up in the body and yielding carbon dioxide to the hemoglobin. For physical properties and methods of preparation, see authors quoted.

Nickel Chloride. *Niccoli Chloridum. Nickelous Chloride.* $NiCl_2 + 6H_2O$.—A green, very deliquescent salt. The anhydrous chloride is yellow and sublimes in yellow scales, without melting.

Nickel Sulphate. *Niccoli Sulphas*, $NiSO_4.7H_2O$.—It is in the form of emerald-green crystals efflorescent in the air, soluble in three parts of water, but insoluble in alcohol and ether. It has a sweet, astringent taste. Simpson found this salt to act as a gentle tonic, useful in *migraine* in *doses* of from half a grain to one grain (0.032–0.065 Gm.) three times a day. In large doses it is liable to produce nausea and vomiting, especially when the stomach is empty. (See *Braithwaite's Retrospect*, xxvii, 446.) Kolipinski (*J. A. M. A.*, 1911, lvii) states that *nickel sulphate* has a strong parasiticidal effect, that in solutions from one to two per cent. it is a useful application in *impetigo contagiosa, tinea,* and other parasitic skin diseases.

Nicotine Salicylate. *Nicotinæ Salicylas.* $C_6H_4(OH)COOH.C_{10}H_{14}N_2$. *Eudermol.*—This substance occurs in colorless crystals, soluble in water and alcohol, fusing at 118° C. Under the name of *eudermol* a substance composed chiefly of lanolin, containing 0.1 per cent. *nicotine salicylate,* has been put upon the market and highly commended for the treatment of *scabies* and other parasitic diseases of the skin, also of *itching eczema.* Ointments containing a larger per cent. are said to be dangerous. (*Th. M.*, 1898.) The application of the ointment should be followed after some hours by a soap bath. L. C. Fettich has used the 1 per cent. lanolin ointment of nicotine salicylate in cases of *mange* of dogs. When the mange is of the acaridic variety the treatment should be assisted by baths containing 2 to 4 per cent. of potassium sulphide.

Nierenbergia Hippomanica Miers. *Cup-flower. Chus-chu.*—This solanaceous plant is the not infrequent source of poisoning to cattle in Argentine where it is a native. Laveuir and Sanchez (*J. P. C.*, 1907, xxvi) have isolated a poisonous alkaloid to which they give the name *nierenbergine.* Apparently this alkaloid resembles saponin in some of its properties. They were not able to find the glucoside *hippomanin* which had previously been reported.

Nigella. *Nigella sativa* L. *Nutmeg-flower. Small Fennel-flower. Faux Cumin,* Fr. *Schwarzkümmel,* G. (Fam. *Ranunculaceæ.*)—A small, annual plant, growing wild in Syria and the south of Europe, and cultivated in various parts of the world. The seeds, *semen nigellæ,* are ovate, somewhat compressed, from 2.5 to 3.5 mm. in length, and less than 2 mm. in thickness, usually three-cornered, with two sides flat and one convex, black or brown externally, white and oleaginous within, of a strong, agreeable, aromatic odor, like that of nutmegs, and a spicy, pungent taste. (*P. J.*, 1882, 681.) Their chief constituents are a volatile and a fixed oil (1.5 per cent. of the former and 35 per cent. of the latter), and an amorphous glucoside, *melanthin,* which is decomposed by diluted hydrochloric acid into *melanthigenin* and sugar. This seems to be an acid saponin and Schulz (*Arb. Pharmacol. Inst. Zu Dorhat,* 1892, xiv, 112) has shown that it is extremely poisonous, the fatal dose for the cat intravenously being 1.5 milligrammes. The *nigellin* of Reinsch does not seem to have been a pure substance. Rochebrune has found a powerful paralyzing alkaloid, to which he gives the name of *nigelline.* (*Toxicol. Africaine,* vol. i.). In India the seeds are considered as stimulant, diaphoretic, and emmenagogue, and are believed to increase the secretion of milk. They are also used as a condiment, and as a corrigent or adjuvant of purgative and tonic medicines. In the seeds of the *Nigella Damascena* L., Schneider (*Ph. Centralh.*, 1890, xxxi, p. 173) found an alkaloid which he called *damascenine,* $C_{10}H_{15}O_3N$, whose construction was studied by Pommerehne and Keller. (*A. Pharm.*, 1904, ccxlii, p. 295.) They were unable to find any alkaloid in *N. sativa.* (See also Ewins, *Tr. Chem. Soc.*, 1912, ci, 544.)

Nigrosine. *Aniline Black. Coupier's Blue.*—A series of blue to black dyes prepared by oxidizing various proportions of nitrobenzene, aniline and toluidine. The process is purely empirical and admits of great variation in the resulting product. It is used as a black dye and in the manufacture of aniline inks.

Ninhydrin. *Triketol.*—This is phenyl-1:2-triketo-cyclopropane hydrate. It occurs in the form of colorless, water-soluble crystals. It is not employed therapeutically, being used solely as a reagent to demonstrate the presence of albumen, peptone, polypeptid, and amino acids, especially in the diagnosis of pregnancy after Aberhalden's method.

Nirvanin. *Glycocaine.*—The *hydrochloride of diethylglycocoll-p-amido-o-oxybenzoic-methylester.* It occurs in colorless prismatic crystals, with a melting point of 185° C., affording a violet reaction with ferric chloride, and soluble in water.

Nirvanin has been brought forward as a local anesthetic, with a claim that it is only about one-tenth as toxic as cocaine, and is as effective as a local anesthetic. It is also alleged to be actively antiseptic, the 1 per cent. solution effectively preventing the growth of bacteria. The 5 per cent. solution placed in the eye produces a temporary irritation followed by lasting anesthesia. It has been used to a considerable extent as a substitute for cocaine in infiltration anesthesia, the strength of the solution used varying from one-tenth to one-third of 1 per cent. Nirvanin has also been used to a considerable extent in dentistry; eight grains (0.5 Gm.) are stated to have been given to an adult, hypodermically without the production of toxic symptoms. (Elsberg, *Ther. Prog.*, April, 1900.)

Nirvanol. *Phenyl-ethyl-hydantoxin.* — This should not be confounded with nirvanin (see above). In its chemical composition this compound is analogous to that of barbital, glycolyl-urea, however, being substituted for malonyl-urea. It occurs as a colorless, odorless, crystalline powder insoluble in water, but is usually employed in medicine in the form of its soluble sodium salt. It is intended as a hypnotic. Although a number of cases of poisoning by this agent have been reported, Gelma and Schwartz (*Paris Méd.*, 1922, xii, 162) have found it a powerful and satisfactory somnifacient. The *dose* is from five to ten grains (0.3 to 0.7 Gm.).

Nitrated Alcohols.—The following substances of the possible series of nitrated alcohols have been studied by J. B. Bradbury (*B. M. J.*, 1895, ii):

Methyl Nitrate, (CH_3NO_3), *Glycol (Ethylene) Dinitrate* $C_2H_4(NO_3)_2$, *Glycerol Trinitrate (Nitroglycerin)* $C_3H_5(NO_3)_3$, *Erythrol Tetranitrate* $C_4H_6(NO_3)_4$, *Arabinol Pentanitrate* $C_5H_7(NO_3)_5$, *Mannitol Hexanitrate* $C_6H_8(NO_3)_6$.

Of the group the first three are liquid. The others are crystalline, colorless solids, stable in the dark at a moderately low temperature, turning yellow and exploding when heated above 150° C., or percussed. Of slight solubility in water, soluble in alcohol and ether, responding when heated to the meta-phenylene-diamine test.

Bradbury has shown that all these substances have similar physiological action, differing among themselves and from amyl nitrite simply in the rapidity and fugaciousness of influence. Glycol dinitrate in one-hundredth-grain (0.0006 Gm.) *doses* markedly influences arterial tension in the human being, but its effect is not maintained longer than sixteen minutes. Erythrol and mannitol nitrates were found to be slow in action but of remarkable permanence and influence, their effect on the lower animals lasting more than four or five hours. Methyl nitrate was feeble and fugacious in its influence.

Both erythrol and mannitol nitrates have been used by Bradbury and others in *angina, aneurism, Raynaud's disease, asthma, headache,* and various other affections for which nitroglycerin has been employed. Erythrol nitrate, as more soluble, appears to be preferable to mannitol nitrate. It is less easily exploded than nitroglycerin, but great care must be practised in any attempt at powdering, as a very serious explosion has occurred from rubbing it in a mortar with sugar of milk. It is usually administered in tablet form in *doses* of one-half to two grains (0.03–0.12 Gm.). The *dose* of the 1 per cent. alcoholic solution of mannitol nitrate is one and a half fluidrachms (5.5 cc.).

Nitrobenzene. *Nitrobenzole. Oil of Mirbane.* $C_6H_5NO_2$.—*Nitrobenzene* is formed by the action of strong fuming nitric acid upon benzene,

$$C_6H_6 + HNO_3 = C_6H_5 + H_2O.$$

The product, after having been washed with water, is an oily, yellowish, intensely sweet liquid, with an odor like that of oil of bitter almond. Its sp. gr. is 1.186, and boiling point 209° C. It has become of commercial importance, being produced as an intermediate product in the manufacture of aniline oil, and, under the name of *artificial oil of bitter almonds,* or *oil of mirbane,* being employed for scenting soaps and pomades. Its use in articles of food and for flavoring, as a substitute for bitter almond oil, is properly forbidden under pure food regulation. For method of detecting nitrobenzene in oil of bitter almond, see *Oleum Amygdalæ* (Part I). It is of commercial importance, as being used in the manufacture of aniline.

In manufactories where nitrobenzene is made, headaches, with sleepiness, are not infrequently produced by inhalation of the fumes; much more serious poisoning is liable to occur, and there have been a number of deaths produced by nitrobenzene. The symptoms may come on almost immediately, or they may be delayed for some hours. According to Filehne (*A. E. P. P.*, Bd. ix), the slowness of action is chiefly dependent on the fact that nitrobenzene, when mixed with the contents of the stomach and intestines, is absorbed with very great slowness; for if the drug be injected directly into the blood of the rabbit, it produces death in convulsions in less than a minute. The first symptoms of poisoning are headache, with muscular weakness, and a peculiar bluish color of the face, and disturbance of consciousness. In the fully developed poisoning the whole surface of the body is a deep bluish color, and the mucous membranes a bluish-gray; the pupils are dilated; the muscular relaxation is complete, except that sometimes the jaw is rigidly set; consciousness is lost; respiration rapid, but shallow and irregular; pulse rapid and thready, or entirely absent. The urine contains urobilin, indican, and acetone. Recovery may occur, as in a case reported by Stevenson (*Guy's H. R.*, vol. xxi, 1876), after many hours of unconsciousness, the bluishness of the skin and the headache remaining for several hours longer. After death, the blood is of a deep chocolate brown.

There have been a number of cases of nitrobenzene poisoning recorded from its use for various purposes in the arts. Apparently it can be absorbed through the skin in sufficient quantity to cause poisoning as in the series of cases reported by Stifel (*J. A. M. A.*, 1919, lxxii, 395) from the use of shoe dye containing nitrobenzene. Poisoning has also been caused by inhalation of the vapors.

The symptoms of nitrobenzene poisoning are due in part to the action of the poison on the nerve centers and in part to its destructive effect upon the blood. After death the blood is found of a deep, chocolate-brown color similar to that of methemoglobin but there is some doubt as to whether the compound formed is methemoglobin or some other chemical compound as some authorities report a different spectrum from that of methemoglobin. Loeb and Fitz (*Am. J. M. S.*, 1921, clxi, 539) in two cases of human poisoning found a very striking reduction in the oxygen-carrying power of the blood. Not only is there change in the chemical composition of the hemoglobin but also actual destruction of the red blood cells. According to Caspar, death from prussic acid and nitrobenzene may be distinguished by the fact that when the body is left open for some hours, the odor of prussic acid leaves, while that of nitrobenzene persists. The minimum fatal dose is not known; according to Taylor, fifteen drops (0.75 cc.), taken by the mouth, have proved fatal, and in Stevenson's case, twenty-three minims (1.42 cc.), taken in seven doses, in forty-eight hours produced unconsciousness and respiratory arrest, so that death would probably have occurred if treatment had not been instant.

In the treatment of nitrobenzene poisoning the first thing is to prevent further absorption by washing out the stomach, or removing the patient into fresh air, or removing the poison from the skin, according to the source of its entrance. Remembering the reduced hemoglobin, the use of oxygen inhalations naturally suggests itself. Both Werner (*B. K. W.*, 1884, xxi) and Loeb and Fitz have reported remarkable results from venesection followed with transfusion of blood. Circulatory and respiratory stimulants such as strychnine and atropine should be used as required.

Dinitrobenzene, Dinitrobenzol. 1–3 $C_6H_4(NO_2)_2$.—On boiling benzene with fuming nitric acid, there is formed chiefly *metadinitrobenzene,* fusing at 90° C., with small amounts of the ortho and para compounds. By crystallizing out of alcohol, the meta compound can be obtained pure. Dinitrobenzene has attracted considerable attention on account of the number of cases of poisoning by it occurring among the workmen in aniline works. The symptoms are said to be jaundice, enlargement with tenderness of the liver, diarrhea with colorless stools, and dark brown urine in which dinitrobenzene can be located by the phenylenediamine test. The toxicology has been especially studied by Strassmann and Strecker (*Friedreich's Blätt. f. Gerich. Med. u. Sanitätspolizei,* Heft iv, 1896), who add to the symptoms already given, headache, a peculiar bluish discoloration of the face and general surface, a tendency to fainting, with excessive sweating, vomiting, fall of temperature, great muscular weakness, and finally collapse. It is noted also that in animals experimentally poisoned there has been destruction of the red blood corpuscles with consequent hemoglobinuria and wide-spread fatty degeneration.

According to White and Hay (*L. L.*, 1901, ii) chemically pure dinitrobenzene is less poisonous than the commercial substance which contains the mononitrobenzene because the latter acts as a solvent for the dinitrobenzene and increases its absorption through the skin. The fact that the dinitrobenzene is absorbed through the skin of the workmen is so generally recognized that in most commercial laboratories the workmen are required to wear specially close fitting clothing over the body and head, and to practise absolute cleanliness.

Nitro-Propiol.—*Ortho - nitro - phenyl - propiolic acid,* when heated with grape sugar in the presence of soda, forms indigo, according to the following equation:

$$2C_6H_4(NO_2).C \equiv C—COOH + 4H = C_{16}H_{10}N_2O_2 + 2CO_2 + 2H_2O$$

The formation of indigo is rendered evident by a blue coloration of the fluid. The compound therefore serves as a qualitative test for the glucose in urine. Von Gerhardt recommends the following method for carrying out the test: Place 10 to 15 drops of the urine under examination in a test tube, add one hundred and sixty minims (10 cc.) distilled water and a *nitro-propiol tablet,* and carefully heat the mixture for two to four minutes. In the presence of sugar the fluid first becomes green and subsequently intensely blue. This reaction is sufficiently sensitive to indicate with certainty 0.3 per cent. of sugar and possesses the advantage that it only takes place if grape sugar is actually present in the urine.

Nizin. *Zinc Sulphanilate.* $Zn[C_6H_4(NH_2)SO_3]_2 + 4H_2O$.—It is intended as an astringent and antiseptic injection in the treatment of chronic gonorrheal *urethritis.* It is recommended to be employed in about one-half per cent. aqueous solution.

Njimo Wood.—The wood of *Sarcocephalus esculentus* Afzel. (Fam. *Rubiaceæ*), known as *Njimo,* was introduced into Germany from the Cameroons with the statement that it had digestive properties similar to those of pepsin. Schulz (*Ph. Ztg.,* June 12, 1886), however, was unable to perceive any digestive action. The bark of this same plant called "Dundaki," according to Heckel and Schlagdenhauffen (*Compt. Rend.,* 1885, 69) contains an alkaloid, *dundakine.*

Nosophen. *Tetraiodophenolphthalein. Iodophen.* $C_{20}H_{10}I_4O_4$.—*Nosophen* is obtained by the action of iodine on solutions of phenolphthalein. It is an impalpable, yellowish-gray, odorless, tasteless powder, containing 61.7 per cent. of iodine in combination. It may be heated up to 220° C. without decomposition. It is insoluble in water and acids, soluble with difficulty in alcohol, glacial acetic acid, ether, and chloroform, but readily soluble in alkalies, with the last of which it forms salts from which it is easily freed at low temperature by carbon dioxide. In the presence of heat it liberates carbon dioxide from its alkaline salts. By virtue of its two hydroxyl groups, nosophen is an acid, readily soluble in alkalies with replacement of the hydrogen atoms of both hydroxyl groups by a metal. Three of the salts of nosophen have been put upon the market—the sodium salt (antinosine), the bismuth salt (eudoxine), and the mercury salt (apallagin).

Antinosine has the following formula:

$$(C_6H_2I_2ONa)_2C.O.C_6H_4O.$$

It is a dark blue, amorphous powder which is readily soluble in water and alcohol.

Eudoxine, $(C_6H_2I_2OBi_2)_3C.OC_6H_4O$, is a reddish-yellow, tasteless, odorless powder, insoluble in water, which is decomposed by alkalies into bismuth oxide and a soluble salt of tetra-iodophenol-phthalein. It contains 52.9 per cent. of iodine and 14.5 per cent. of bismuth.

Apallagin. Mercury Tetra-iodo-phenol-phthalein.—A gray powder which is recommended as a powerful antiseptic.

Medicinal Properties and Uses.—Nosophen and its derivatives are asserted to possess disinfectant and local alterative powers. Nosophen, itself, is used especially as a surgical dusting powder, the advantages over iodoform being claimed for it not only being due to its lack of odor but also that it is non-toxic. It has been especially recommended as a dusting powder in nasal and laryngeal conditions. It has also been used internally as an intestinal antiseptic in *doses* of 5 to 8 grains (0.32 to 0.5 Gm.).

For intestinal use, however, eudoxin is usually preferred because it combines the action of bismuth with that of nosophen. This compound is believed to be decomposed by the alkaline juices of the intestines, liberating its constituent parts, and is used in *diarrhea* and various gastric and intestinal inflammations. *Dose,* five to eight grains (0.3–0.5 Gm.).

Antinosine, being soluble, may be applied where a non-toxic, antiseptic wash is desired as in *gonorrhea, cystitis, otitis media* and the like. It is used in strengths ranging from ½ to 2 per cent.

Novaspirin. *Salicitrin. Methylene-citric-acid-ester of Salicylic Acid. N. N. R.* 1924.—This is a white, crystalline powder representing 62 per cent. of salicylic acid. It is almost insoluble in water, but dissolves readily in alkaline solutions or alcohol. Its melting point is 150° to 152° C. This substance is used for those various conditions in which aspirin has been found of service, such as acute and chronic *rheumatism, neuralgia,* etc. It is stated that it is better borne by the stomach than aspirin and less likely to produce excessive sweating and the other undesirable sequelæ sometimes seen after the older remedy. Lehmann (*D. M. W.,* 1907, No. 10) has found, however, that it is less powerful in its effects than aspirin, especially in acute *rheumatic fever.* Gresic (*K. T. W.,* 1908, No. 4) has found it also of service in the treatment of *asthma,* both to prevent and to relieve the paroxysms. It is incompatible with iron compounds and with acids or strongly acid salts. The *dose* of novaspirin is from ten to thirty grains (0.65–2 Gm.) three or four times a day or oftener if needed.

Noviform. *Tetrabrom-pyrocatechin-bismuth.*—This is a yellow, insoluble powder. It is used as a surgical dressing in much the same way that iodoform has been employed.

Nuclein. *Nucleinum. Nucleol.* $C_{29}H_{49}N_9P_3O_{22}$.—The term *nuclein* is applied to a group of substances containing proteins which possess a *nucleinic acid* group in their structure, $C_{40}H_{54}N_{14}O_{27}P_4$. These proteins are derived from tissues rich in cell nuclein. The nuclein, however, probably does not exist as such in the cell but is produced by decomposition of the nucleo-proteids. It may be separated by digesting the cells with artificial gastric juice by which means the investing protoplasm is dissolved leaving the nuclein unaffected. The term *pseudonucleins* or *paranucleins* is applied to a group of bodies somewhat resembling the real nucleins, which are produced by the peptic digestion of proteins containing phosphorus but not nucleinic acid. *Nucleinic,* or *nucleic acid,* may be obtained from nuclein by the action of alkalies or by tryptic digestion. It occurs as an amorphous, white powder, strongly acid in reaction, sparingly soluble in water, but readily soluble in alkalies, and insoluble in alcohol or ether.

When nuclein-containing foods are taken, the nuclein is partly separated but not destroyed by the gastric digestive juices. In the intestines, however, the nuclein is broken up and nucleic acid liberated. Some of this may be further destroyed in the intestines but the larger part is absorbed. The nuclein absorbed is partially eliminated as purin bodies—allantoin, uric acid, etc.—and probably in part broken up into urea. As an almost constant accompaniment of the introduction of nucleic acid into the system, whether from the ingestion of food rich in nuclein or from the parenteral absorption of nucleinic acid or its salts, there is a great increase in the number of white blood corpuscles. Renner (*Mitt. Grenz. M. C.*, 1905, xv, p. 89) has reported as high an increase in the number of leucocytes as 452 per cent., and several authors have noted more than double the number of normal. This leucocytosis is usually preceded by a hypoleucocytosis of six or eight hours' duration. Fox and Lynch (*A. J. M. S.*, 1917, cliii, 235, 571) were unable to maintain the leucocyte count high by repeated injections.

Nucleinic acid has a distinct bactericidal effect; according to Kossel 0.5 per cent. of nucleinic acid kills streptococci *in vitro* in two hours and staphylococci after six hours. As has been shown by Vaughan and confirmed by Parlavecchio (*A. K. C.*, 1909, xc) and others, nucleinic acid also possesses bacteriolytic properties and even precipitates bacterial toxalbumins and in the body increases the formation of agglutinins and alexins. Chantemesse (*B. A. M.*, 1907, lvii) and others have noted an increase in the opsonic index.

These effects of nuclein should tend to increase the bodily resistance to bacterial infections and the drug has consequently been largely used in the treatment of *septicemia, furunculosis, tuberculosis, diphtheria*, and other diseases of bacterial origin. While the clinical reports have not been uniformly flattering they have been sufficiently encouraging to justify the further trial of this remedy in infectious conditions. In addition to this it has been used to a lesser extent for its influence upon metabolism in *anemia, neurasthenia*, and similar diseases. Donath (*M. M. W.*, 1912) asserts that it is a useful drug in parasyphilitic diseases, such as *general paresis*. He injects from eight to fifteen grains (0.5–1.0 Gm.) of *sodium nucleinate*, in the form of a 10 per cent. solution, gradually increasing the *dose* to sixty to seventy-five grains (3.9–5.0 Gm.), or until there is a febrile reaction.

Nuclein is frequently used in the crude form as found in various foods, such as yeast (see *Cerevisia*). There are, however, a considerable number of proprietary preparations more or less purified. Some of these are as follows:

Nuclein from yeast, a grayish-white, amorphous powder, sparingly soluble in water, but soluble in alkaline solutions. *Dose*, eight grains (0.5 Gm.) four to six times a day.

Protonuclein.—This is stated by the manufacturers to be prepared from the lymphoid structures and glandular organs of the body. *Dose*, three to ten grains (0.2–0.65 Gm.).

Nucleol.—This is stated to be pure nuclein. It occurs as a white powder, readily soluble in water.

Neucleic Acid (*Nucleinic Acid*).—There are several varieties of nucleic acids, all related but differing somewhat in their exact chemical composition. They are insoluble in either water, alcohol or ether but form salts with the alkalies which are water-soluble. When pure they do not give the biuret reaction characteristic of the albumins.

Nucleinic acid from yeast is a white or grayish-white powder obtained from yeast nuclein; it is practically insoluble in water, but is readily soluble in alkalies. *Rhomnol* is a trade name for *nucleinic acid.*

The ordinary *dose* of nucleic acid is from one-half to two grains (0.03–0.06 Gm.).

Animal Nucleinic Acid.—A yellowish powder prepared from the thymus gland and other similar animal glands containing nuclein; it has almost the same solubility as nucleinic acid from yeast.

Sodium Nucleinate.—A yellowish-white powder prepared from nucleinic acid from yeast. It is readily soluble in water and contains approximately 4.5 per cent. of sodium.

Sodium Tritico-nucleinate. Sodium Nucleate from Wheat.—Another form of sodium nucleinate is prepared by treating the aqueous extract of the wheat germ with sodium chloride and hydrochloric acid; the precipitate formed is digested with pepsin, neutralized with sodium hydroxide and precipitated with alcohol. This is marketed in the form of an aqueous solution—*Liquor Sodii Tritico-nucleinate*—containing about 10 per cent. of the salt.

Quinine Nucleinate.—A yellowish-white powder, slightly soluble in water, rather more soluble in alcohol (50 per cent.) and in dilute glycerin. It contains 40 per cent. of quinine.

Copper Nucleinate, Cuprol.—Cuprol occurs as a greenish powder, soluble in water, containing about 6 per cent. of metal. It is used as an astringent application in all those cases in which the older copper salts have been employed. In *conjunctivitis* a 5 to 10 per cent. solution has been recommended.

Ferric Nucleinate. Ferrinol.—Ferrinol is a brown powder, freely soluble in water, containing about 6 per cent. of iron.

Mercury Nucleinate. Mercury Nucleide.—Two forms of this compound are known to medicine, the one a direct combination of mercury with nucleinic acid known as *mercurol*, and the other known as *levurargyre*, made by acting upon yeast with mercuric chloride.

Mercurol is a colorless or brownish-white powder, containing 10 per cent. of mercury, soluble in water with a weak alkaline reaction, and has been used both internally and locally as a substitute for corrosive sublimate, over which it has the advantage of not coagulating albumin. In *syphilis* from half to one grain (0.032–0.065 Gm.) of *mercurol* may be given hypodermically. Two grains (0.13 Gm.) are said to have produced salivation. Another preparation similar to mercurol is called *Rhomnogyre.*

Levurargyre.—*Nuclein mercurate* is a grayish-white powder, soluble in water, and unaffected in solution by hydrogen sulphide. It is given in the treatment of *syphilis*, usually hypodermically, in *doses* of one-sixth to one-half grain (0.010–0.032 Gm.).

Mercedan is a proprietary preparation asserted to be a mercury-sodium paranucleinate.

Argentic Nucleinate. Nargol. Silver Nucleinate.—This is a light, brownish-white powder, readily soluble in water, contains 10 per cent. of silver. It has been recommended as a local application in those conditions for which silver

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nitrate has been used. It may be used in solution up to 25 per cent. on most mucous membranes. The solution should be recently made, as it undergoes change after a few weeks.

Nymphæa.—The terms *water lily*, or *pond lily*, are popularly applied to two genera of the Fam. *Nymphæaceæ*, of which several species have been used more or less in medicine. These are aquatic perennial herbs with thick horizontal rootstocks and usually floating leaves and solitary showy flowers. The petals are numerous; in the Nymphæa small and stamen-like, in the Castalia large and white but gradually passing into stamens.

Castalia odorata (Dryand.) Woodv. and Wood (*Nymphæa odorata* Ait.) is popularly called *Sweet-scented Water Lily*, *Water Nymph* or *Water Cabbage*. It has large flowers which are deliciously fragrant; the numerous white petals, sometimes tinted with rose, afford an attractive contrast with the bright yellow of the stamens. The orbicular or reniform floating leaves are from four to twelve inches in diameter, green and shining above, purplish beneath. The plant grows in ponds and sluggish streams throughout the eastern United States. The root contains, according to Bigelow, large amounts of tannic and gallic acid. It was formerly used as an astringent in application in *sore-throat* and *leucorrhea*, also internally in *diarrhea*. The *dose* employed in the latter condition was about thirty grains (2 Gm.).

Castalia alba Presl. (*Nymphæa alba* L.); the European white water lily, was formerly official in the French Codex under the name of *Nenuphar blanc*. The root (*Rhizoma Nymphææ*) contains, according to Grüning (*A. Pharm.*, 1882), an alkaloid closely related to nupharine (see below) and several astringent principles including *nymphæatannic acid*. It was used not only as an astringent but was at one time supposed to possess anaphrodisiac properties. The flowers of this species were also recognized by the Codex. They are astringent and apparently also sedative, and were used locally in gonorrhea and leucorrhea.

In the seeds of the *Nymphæa lutea* L. (*Nuphar luteum* Sibth. and Smith), European *Yellow Pond Lily* or *Spatterdock*, Grüning (*A. J. P.*, 1883, 96) found an amorphous, bitter alkaloid, *nupharine*. The presence of this alkaloid has been confirmed by Goris and Crété (*J. Chem. S.*, 1910) who demonstrated its occurrence in the fresh rhizome. They assign to it the formula $C_{18}H_{24}O_2N_2$. The rhizome also yields a large amount of a tannin, *nuphar-tannic acid*, $C_{56}H_{56}O_{37}$. This, like the previous species, was attributed with power of allaying sexual irritability and used in spermatorrhea, as well as for its astringent effects in diarrhea.

Nyssa. *Nyssa aquatica* Marsh. *Tupelo. Sour Gum. Swamp Tupelo.* (Fam. *Cornaceæ.*)—A large tree growing in deep swamps in the Southern United States. The root, known as *Tupelo root*, has been recommended for surgical tents. (*A. J. P.*, 1883.)

Ochres.—These are native mixtures of argillaceous or calcareous earth with iron and manganese oxides, employed in painting. They are prepared for use by elutriation. The color of the *ochres* varies with the state of oxidation of the iron, and with the proportion which the iron bears to the other ingredients, and is sometimes artificially modified by the agency of heat. Several varieties are known in commerce under different names, according to their color or place of origin. Such are *brown ochre*, *yellow ochre*, *red ochre*, *Roman ochre*, which is of a brownish-yellow color, changing by heat to a purple-red, *Oxford ochre*, of a brownish-yellow color less deep than the Roman, and *French ochre*, which is yellow. The *Indian red*, from the Persian Gulf, and *Spanish brown* and *Venetian red* may also be ranked in this class of pigments. Sometimes ochres come in powder, and sometimes in hard masses known as *stone ochres*.

Ocimum. *Ocimum Basilicum* L. *Basil. Sweet Basil. Grand Basilic*, Fr. *Basilienkraut*, G. (Fam. *Labiatæ.*)—An annual, aromatic plant, a native of India and Persia, and cultivated in Europe and in this country in gardens. It yields by distillation from 0.02 to 0.04 per cent. of a yellowish, volatile oil. The French and German oil have a penetrating odor resembling estragon, the Réunion has a camphor-like odor, a higher specific gravity and is dextrogyrate. Basil has the ordinary properties of the aromatic plants, and is used as a condiment. The seeds are said by Ainslie to be used in India in *gonorrhea*.

Œnanthe. *Œ. crocata* L. *Water Hemlock. Water Dropwort. Dead Tongue.*—A perennial, umbelliferous, aquatic, European plant, exceedingly poisonous both to man and inferior animals. The root, which has a sweetish not unpleasant taste, is sometimes eaten by mistake for other roots, often with fatal results. The symptoms produced are those of irritation of the stomach, besides failure of circulation, and great cerebral disturbance, indicated by giddiness, convulsions, and coma. (See *P. J.*, 1874, 202.) Externally applied, the root produces redness and irritation of the skin, with an eruption. It is said to be sometimes used empirically as a local remedy in *piles*. Other species of *Œnanthe* are poisonous, and the whole genus should be suspected. We have two or three indigenous species. In cases of poisoning, the stomach should be at once evacuated, and symptoms met as they arise. A peculiar resinoid principle, denominated *œnanthin*, has been found by Gerding in *Œnanthe fistulosa* L., the common water hemlock of Europe, of which half a grain (0.032 Gm.), given to an adult, produced long-continued irritation of the fauces, and a grain (0.065 Gm.), occasional vomiting. (See *A. J. P.*, xxi, 68.) Poehl (*A. E. P. P.*, 1895, xxxiv, p. 258) claimed to have isolated a toxic principle, to which he gave the name of *œnanthotoxin*, and assigned a formula $C_{17}H_{22}O_5$. Tutin, however (*P. J.*, Aug. 26, 1911), asserts that this body is not a pure principle but a mixture of neutral resins of unknown nature. He confirms the conclusions that the resin is an active poison. He also examined the tuberous roots of *O. crocata* and found *triacontane*, $C_{30}H_{62}$, and *hentriacontane*, $C_{31}H_{64}$. In the *P. J.*, vol. xvi, 357, is a paper by Henry William Jones upon the recognition of *Œ. crocata* in cases of suspected cattle poisoning; he found that the starch granules possessed characters which enabled him to distinguish the tubers from all others.

Œnanthe aquatica Lam. (*Œnanthe Phellandrium* Lam., *Phellandrium aquaticum* L.) *Fine-leaved Water Hemlock. Water Fennel. Fructus Phellandrii. Wasserfenchel*, G. *Phellandrie aquatique, Fenouil d'Eau*, Fr.—A biennial or perennial, umbelliferous, European water plant, the fresh leaves of which are said to be injurious to cattle, producing a kind of paralysis when eaten. By drying, they lose their deleterious properties. The cremocarp fruits are from 4 to 5 mm. in length (about 2 mm. broad), ovate-oblong, narrow above, somewhat compressed, marked with ten delicate ribs, and crowned with the remains of the calyx, and with the erect or reverted styles. Their color is yellowish-brown; their odor peculiar, strong, and disagreeable; their taste acrid and aromatic. Among their constituents is a volatile oil, upon which their aromatic flavor depends. C. Fronefield found a volatile alkaloid, analogous to, if not identical with, coniine. (*A. J. P.*, May, 1860, 211.) The ethereal oil of water fennel which is present to the extent of 1 to 2½ per cent. is a yellow liquid of strong, pleasant characteristic odor and burning taste. It has a sp. gr. of 0.85–0.89 and is dextrorotatory. It contains about 80 per cent. of phellandrene, $C_{10}H_{16}$. In overdoses the seeds produce vertigo, intoxication, and other narcotic effects. They have been used in chronic pectoral affections, such as *bronchitis, pulmonary consumption*, and *asthma;* also in *dyspepsia, intermittent fever*, obstinate *ulcers*, etc. The *dose* of the seeds, to commence with, is five or six grains (0.32–0.4 Gm.), so repeated as to amount to a drachm (3.9 Gm.) in twenty-four hours. They should be given in powder. *Dose*, of the alcoholic extract, three grains (0.2 Gm.). (*P. J.*, xii, 591.)

Œnothera. *Œnothera biennis* L. (*Onagra biennis* (L.) Scop.). *Evening Primrose. Night Willow-herb. Tree Primrose. Sun-drop. Onagre*, Fr. *Nachtkerze*, G. (Fam. *Onagraceæ*).—This is a native, annual, or biennial herb from one to several feet in height with more or less pubescent stem and lanceolate sessile leaves. The bright yellow flowers are composed of four petals and are one to two inches broad, usually opening about dusk of the evening.

The stem contains considerable tannin as well as mucilage.

Many years ago R. E. Griffith highly recommended a strong decoction of the plant in *tetter* and other skin diseases; an ointment made by boiling the herbage in lard or tallow was also used for the same purpose. Internally the drug was used as a gastro-intestinal demulcent and astringent; it was also attributed with antispasmodic properties and recommended in *whooping cough* and spasmodic *asthma. Dose*, of fluidextract, from a half to one fluidrachm (1.8–3.75 cc.). The ointment may be made by incorporating four ounces of the fluidextract in a pound of vaseline or lard.

Oil of Akee.—This is a yellow, non-drying, butter-like fat obtained from *Blighia sapida* Kon. (Fam. *Sapindaceæ*), a tree with paripinnate leaves and axillary racemes of white flowers, native to Guinea, but cultivated in Jamaica and South Florida. (*P. J.*, lxv, p. 691.)

Oil of Aleurites Triloba.—The *Aleurites triloba* Forst., or *Candle-Nut*, is a small tree belonging to the *Euphorbiaceæ.* It is widely diffused throughout the tropics. The fruit is a nut nearly as large as a walnut, consisting of a thick shell enclosing a kernel containing much protein and rich in oil, of which it is said to yield nearly one-half its weight by expression. The nuts strung together on the fibers of the palm leaf were formerly used in many Pacific islands as a substitute for candles. The oil has been long known in the various countries inhabited by the plant, being called in Jamaica *Spanish walnut oil*, in India *Belgaum walnut oil*, in Ceylon *kekune oil*, and in the Hawaiian Islands *kukui* oil. It is very fluid, of an amber color, without odor, of a nutty, pleasant taste, congealing at 0° C., insoluble in alcohol, readily saponifiable, "and very strongly drying." It is said to be a mild cathartic, acting like castor oil, but more promptly and without griping effects. (*J. P. C.*, 3e sér., xxiv, 228.) The *dose* is from one-half to one fluidounce (15–30 cc.), the smaller quantity generally answering. The cake left after the expression of the oil, given to a dog in the *dose* of about half an ounce (15 Gm.), produced no vomiting, but acted strongly as a purgative.

The oil of the *Tung Tree, Aleurites cordata* R. Br., is used to a large extent in the arts in China, under the name of *Chinese wood oil* or *tung oil.* (This must not be confounded with the Indian "oil of wood," see *Oil of Gurjun.*) It is prepared in China by a crude process of expression from the seeds which contain about 53 per cent. of oil. It occurs in two forms, *white oil*, a moderately thick, yellowish, transparent liquid, and the *black oil*, which is thick, black, and opaque; the latter is considered an inferior grade. Wood oil is used in China and Japan either as a direct application to wood or mixed with various substances, as lacquer varnish, or paint. Its most remarkable characteristic is its extraordinary drying property, which is said to exceed that of any known oil. When applied to wood it forms a resinous layer which is affirmed to be impermeable by water and ordinary solvents. Wood oil is largely imported into this country, where it is used in the making of varnishes and linoleum.

According to R. H. Davies, its sp. gr. at 15.5° C. is 0.94015; it remains liquid at –13.3° C. (*P. J.*, 1885, 636.) E. M. Holmes believes that the dark colored oil is made by boiling the kernels previous to expression, the cold drawn oil being colorless, inodorous, and nearly tasteless. The latter, according to Cloëz (*C. R. A. S.*, 1875, vol. lxxxi, 469), has the sp. gr. 0.9362, congeals at –18° C. to a transparent mass, solidifies rapidly when exposed to light in a closed vessel, and is the most drying oil known. (*C. D.*, May, 1902.) (See also *Proc. A. Ph. A.*, 1897, 677; and *Chem. News*, 1912, 14.) The official requirements of the Hong Kong Government, according to Browne (*Chem. News*, 1916, civ, 123), are: Spec. grav. (at 15° C.) not less than 0.9400; refractive index not less than 1.5204 at 15° C. He also gives the iodine value as 167 and saponification value as 191. It has been used in *ulcerations* and *skin diseases.* The seeds of the tung tree are used in China for killing rats, and are also affirmed to have emetic properties.

Oil of Anda.—A fixed oil procured by expression from the seeds of *Joannesia princeps* Vell. (*Anda gomesii* Juss.) (Fam. *Euphorbiaceæ.*) The bark of *J. princeps*, growing in the maritime provinces of Brazil, yields on being wounded a milky juice, which is said to be poisonous, and to be used for stupefying fish. The fruit, which is about as large as an apple, ash-colored, with two larger and two smaller ridges, encloses a two-celled nut, containing two seeds, about the size of a chestnut. Like the seeds of other euphorbiaceous plants, these are actively purgative, one seed, according to Martius, being the *dose* for a man. By expression these seeds yield a pale yellow, transparent oil, with little odor or taste, which is said to be used in Brazil for burning and painting. It has a sp. gr. 0.927, and in properties belongs to the class of semi-drying oils. (*P. J.*, 1905, 910.)

Mello Olliveria has found in it an alkaloid, *johannesine,* which Couty affirms to be inert. (*N. R.*, 1881, 260.) Norris, who tried the oil at the Pennsylvania Hospital, found it to operate on the bowels moderately in the *dose* of fifty drops (2.5 cc.), and copiously when more largely given. Maneol de Castro and other Brazilian physicians assert that in *doses* of from one-half to one fluidrachm (2–4 cc.) it acts in a manner very similar to castor oil, over which it has the great advantage of not being nauseous to the taste.

Oil of Anise Bark.—There has appeared in the European markets a bark, closely resembling Massoi bark, and is supposed to be derived from a species of *Illicium,* probably *I. parviflorum* Michaux, growing in Madagascar, which yields fully three and a half per cent. of a light, yellow oil, the odor of which slightly resembles safrol. It has a spicy taste, but is only slightly sweet. Its specific gravity is 0.969 at 15° C. Optical rotation –0° 46′ in a 100-mm. tube. Refractive index at 16° 1.52510. It contains a small quantity of ordinary anethol, but consists principally of the isomeric fluid anethol, the *methylchavicol* of Eykman, $CH_3O.C_6H_4.CH_2.CH:CH_2$.

Oil of Ben. *Behen Oil.*—This is a fixed oil extracted from the seeds of *Moringa arabica* Pers., and from *M. pterygosperma* Gaertn. (*M. Oleifera* Lam.) (Fam. *Moringaceæ*). It should not be confounded with oil of benne from *Sesamum indicum* L. (Fam. *Pedaliaceæ*).

These trees inhabit different parts of India, Arabia, Syria, etc., and have been introduced into the West Indies. The pungent taste of the root, which is sometimes eaten, has given the name of *horseradish tree* to *M. pterygosperma.* According to Henry Schachan (*Nouv. Rem.*, 1890), the tincture of the root is very actively diuretic and useful in cardiac *dropsy.* The oil of the seeds has long been known, though used in the arts rather than in medicine. It is prepared in Europe from the seeds brought from Egypt; and it would appear, from the statements of Macfadyen, that the idea generally prevailing that it is also extracted in the West Indies is incorrect. The oil has a sp. gr. of from 0.912 to 0.917; it solidifies at about 0° C.; indeed at 7° C. it begins to deposit the solid fats. It is inodorous, clear, and nearly colorless, and keeps long without becoming rancid. It resembles olive oil, and is used for similar purposes. Mérat and De Lens say that it is purgative; but most of the fixed oils are so in sufficient doses. According to Völcker, the oil contains palmitin, olein, and a peculiar fatty matter yielding an acid by saponification, which he names *benic* (or *behenic*) *acid* (*J. P. C.*, xvi, 77); this is one of the normal fatty acid series, possessing the formula $C_{22}H_{44}O_2$.

Oil of Callitris.—The genus *Callitris* (Fam. *Pinaceæ*) includes about 15 species of trees and shrubs which are native to Australia, New Caledonia and Africa. The wood of these plants is of great value as building timber because of the fact that it is not attacked by white ants. According to Baker and Smith ("Research on the Pine Trees of Australia," 1910) this protection is due to the presence of a phenol-like body, to which they give the name *callitrol.* The constitution of this substance which they have obtained from the wood of *C. glauca* R. Br., they have not as yet determined. Several of the Australian species yield a resin with the same properties as those of sandarac, but at present they have not been employed commercially as sources of this resin. The term *cypress pine* is applied in Australia to a number of these trees.

Oil of Cavete.—This is obtained from the seeds of the *Omphalea diandra* L. (*O. megacarpa* Hemsl.), Fam. *Euphorbiaceæ,* a Brazilian tree. It acts as a brisk cathartic in about three hours after taking, without pain or much continuance. (*P. J.*, 1918, ci, 95.) Cash (*J. P.*, 1911, xxxvi, p. 488) obtained from the *Omphalea triandra* L. seed, 56 per cent. of a pale yellow oil, with a specific gravity of 0.924, which, in doses of 0.5 Gm. exercised a cathartic and diuretic action. From the *O. diandra* L., he obtained an oil, somewhat darker in color than the preceding, which had a specific gravity of 0.922 and a saponification value of 190.3 and an iodine value of 119.7. This oil was also a cathartic and diuretic, although somewhat larger doses were required than in the oil from the *O. triandra* L. From the allied plant, *Garcia nutans* Rohr., he also obtained a cathartic oil.

Oil of Chione.—The bark of this West Indian tree, *Chione glabra* DC. (Fam. *Rubiaceæ*) yields on distillation 1.5 per cent. of a light yellow volatile oil, consisting chiefly of *o-oxyacetophenone,* C_6H_4-$OH.CO.CH_3$. A compound obtained synthetically from *o-nitrocinnamic acid* proved to be identical with that isolated from the oil. (See *J. Chem. S.*, vol. lxxv, 1899.)

Oil of Citronella.—There are a group of closely allied grasses which yield sweet-scented volatile oils. Of these volatile oils, which are sometimes spoken of collectively as *Indian Grass Oils,* there are at least five commercial varieties, namely, *Oils of Citronella, Lemon Grass, Palmarosa, Ginger Grass,* and of *Vetiver.* The botany of the sweet-scented grasses from which perfumery oils are obtained, has been somewhat confused. Stapf (see *Schim. Rep.*, April, 1907, p. 20) divides them into three groups, the *Cymbopogon, Andropogon* and *Vetiveria.*

Andropogon nardus L. (*Cymbopogon Nardus* Rendle) (Fam. *Gramineæ*) yields *citronella oil.* It grows in Ceylon, the Malaccan Peninsula, India and to some extent in tropical East Africa. There are two principal varieties, the one, *Lana Batu,* grows widely in Ceylon and yields an oil relatively poor in geraniol and is the principal source of the oil of commerce. The second variety, known as *Maha pangiri,* is generally cultivated in the Straits Settlements and in Java. This latter oil has a lower specific gravity, a lighter color and is claimed to be superior in quality.

Oil of citronella is produced in Ceylon, the Straits Settlements, close to Malabar, the Malay Peninsula and Java, the last named being the most highly esteemed. Oil of citronella is of a yellowish-green color, having a characteristic odor and pungent taste. Its sp. gr. is, according to Gildemeister and Hoffmann, 0.886–0.900. It mixes with alcohol in all proportions, and the test for purity given by Schimmel and Co. is based upon its behavior towards alcohol of 80 per cent: "One volume of the oil must form an absolutely clear solution with two, or at least two and a half, volumes of 80 per cent. alcohol at a temperature not below 20° C. A cloudy mixture indicates the presence of turpentine, certain fixed oils, and other essential oils which are sometimes used to adulterate it." The most important ingredients in this oil are *geraniol* and *citronellal* which together may make up as much as 93 per cent. of the oil. It is not used in medicine, but is largely used in the arts, for perfuming cheap soaps, especially so-called honey soap. An ointment containing 25 per cent. of the oil of citronella affords an excellent protection against the bites of mosquitoes and other insects.

Oil of lemon grass is official in the British Pharmacopœia (1914). (See *Oleum Graminis Citrati*, Part I.)

The *Palmarosa oil* is produced chiefly in India. It was formerly attributed to the *Cymbopogon Schoenanthus* Spreng. but Stapf (*Kew Bulletin*, No. 8, 1906) maintains that it is from a new species, *C. Martini* Stapf.

The *ginger grass oil* closely resembles palmarosa oil but contains a much smaller percentage of geraniol. It appears to be obtained from a variety of the *C. Martini* (Pearson, *P. J.*, 1916, xcvii, 251).

From the roots of the *vetiver* or *cus-cus grass, Vetiveria zizanoides* Stapf. (*A. muraticus* Retz), which grows in the island of Rèunion and in the Philippine Islands, is distilled a volatile oil. The odoriferous principle of this oil is at present unsettled. It has been attributed by Genivesse and Landlois to a peculiar alcohol which they named *vetivenol*, but this has been denied by Bacon. (*Philippine Journal of Science*, 1909, iv, p. 118.)

Various other allied grasses, such as the *Cymbopogon polyneuros* Stapf., or *Delft Grass*, and the *C. Coloratus* Stapf., etc., yield sweet-scented oils which have, however, not become commercially important.

Oil of Coconut. *Coconut Oil. Cocoanut Butter. Oleum Cocos*, P. G. *Oleum Cocois. Beurre de Coco*, Fr. *Kokosnussöl*, G.—This must not be confounded with the fixed oil of the chocolate nut, which is often called *cocoa butter.* (See *Oleum Theobromatis*, p. 797.) The substance here considered is the fixed oil of the coconut, which is the seed of the cocoanut palm, *Cocos nucifera* L., universally known as the *coconut tree*, or *cocoanut tree.* The oil is obtained either by expression or decoction, often by insolation—*i.e.*, exposing the rasped nuts to the heat of the tropical sun. It is of a fine white color, of the consistence of lard at ordinary temperatures, becoming solid, like suet, between 4.4° C. and 10° C., and liquid at about 26.7° C., of a bland taste, and a peculiar, not disagreeable odor. It is readily dissolved by alcohol. It contains large quantities of the glycerides of myristic and lauric acids, with smaller quantities of the glycerides of palmitic and oleic acids. It has also been found to contain several volatile acids, as caproic, caprylic, and capric acids. (Lewkowitsch, *Chemical Analyses of Oils, Fats, and Waxes*, 2d edition, 1898, 538.)

The oil has been used for various purposes in medicine and pharmacy. It has been employed as a substitute for cod liver oil—especially in the form of a proprietary preparation, *coco-olein*—a most unfortunate substitution as it contains neither the vitamines nor the peculiar fatty acids to which cod-liver oil owes its unique value. In Germany it has been used in pharmacy, to a considerable extent, as a substitute for lard, to which, according to Pettenkofer, it is preferable on account of its lesser tendency to rancidity, its more ready absorption when rubbed on the surface of the body, and its lesser liability to produce chemical changes in the substances with which it is associated. Besides, it takes up one-third more water, which is a useful quality when it is desirable to apply saline solutions externally. To prepare it for use, nothing more is ordinarily necessary than to melt it at a moderate heat, and strain it through linen. If colored, it may be digested with powdered animal charcoal, and subsequently filtered through paper. (*A. J. P.*, xxix, 331.) When chilled and pressed, a solid residue, which is *coco-stearin*, is obtained. This is extensively used as a substitute and adulterant of the genuine cocoa butter in the confectionery trade. Coconut oil is employed in the manufacture of soap, particularly of the transparent varieties, and the so-called "*marine soaps*" and *filled soaps;* it is also largely used for giving firmness and lathering qualities to the ordinary soap; this property also permits of the addition of a large quantity of water to the soap. Unfortunately, coconut oil soap is very apt to contain free caprylic acid; and the persistent rancid odor, resembling that of infants' vomit, left upon the skin after washing with its soap is an effectual bar to its very extended use. Besides the oil itself, the dried pulp of the coconut is sent to European and American markets in large amounts under the name of *copra.*

According to Parisi, the endocarp or meat of the coconut is a powerful tenicide. The patient should drink the milk and then eat the flesh of the nut. The coconut is said to be largely used in India as a vermifuge and the matter appears to have practical importance.

Powdered coconut shells were at one time largely used in America as an adulterant for spices. Their débris is readily recognized under the microscope by the peculiar elongated stone cells which have brownish-yellow walls and dark-brown contents.

Oil of Colza.—An oil expressed from the seed of *Brassica campestris* L. var. *oleifera* DC., or *field cabbage*, a cruciferous plant which is largely cultivated in France and Germany for the sake of this oil. *Colza oil* is used in Europe as a burning oil, as a lubricating oil, and, after purification by heating with starch, as a table oil. The raw oil has a sp. gr. of 0.915, and the refined oil 0.9136. Chilled to –4° C. stearin separates out, and at –6° C., it becomes a yellowish buttery mass. The oil contains the glycerides of stearic, *erucic* (or *brassic*) *acid*, $C_{22}H_{42}O_2$, and an acid isomeric with, but differing in some respects from, ordinary oleic acid. A similar oil is derived from *rape-seed* (*Brassica napus*). For analysis of commercial samples, see *C. D.*, 1894, 140.

Oil of Cypress. *Oleum Cupressi. N. N. R.* 1924.—An oil derived from the leaves and young branches of the Cypress tree, *Cupressus sempervirens* L. (Fam. *Pinaceæ*), an evergreen tree indigenous to S. Europe and W. Asia. It has a specific gravity of 0.88 to 0.89 at 15° C. and an optical rotation of + 4° to + 18°. It contains furfural, d-pinene, d-camphene, cymene, d-sylvestrene, d-terpineol, and esters of the same, l-cadinene and cypress camphor.

It has been strongly recommended by Bravo in *whooping cough;* it is used by sprinkling the oil upon the clothes, bed, etc., of the patient.

Winterseel (*In. Dis.*, Bonne, 1908) has studied *cypress oil* physiologically and finds that its action is similar to the other essential oils, but is of relatively low toxicity. When the reflexes are excited by spinal stimulants it acts as a depressant to the spinal cord. He confirms the favorable results of its inhalation in cases of *whooping cough.*

Oil of Dœgling. *Oleum Chœnoceti. Dœgling Oil. Dœgling Thran. Huile de Rorqual Rostré,* Fr.—The oil derived from the Norwegian whale, *Balœna rostrata,* is said by Gustave Guldberg to possess a lower specific gravity than any other animal oil (0.876 at 15° C.), and also remarkable penetrative properties. It is affirmed that if mixed in equal quantities with chloroform it carries the latter agent through the skin, and enables it to act as a local anesthetic in *pruritus, neuralgia,* etc. Mixed with wax, it is highly recommended as a basis for ointments by the same authority.

Oil of Egg Yolk.—A fatty oil obtained by expression from the yolks of fresh eggs. It has been used in lotions and as a popular remedy on the continent in the treatment of *corneal opacities.*

Thorpe's Dictionary gives the following composition and properties of egg oil: specific gravity, 0.9144; solidification point, 8°–10° C.; melting point, 22°–25° C.; acid value 1.2; saponification value 184.4–190.2; iodine value 68.5–81.6; insoluble fatty acids and unsaponifiable matter 95.16 per cent.

Benedikt states that the refractive index of egg oil is 1.4655 and that it gives the elaidin reaction. It is also stated that the oil obtained by expression differs from that extracted by solvents in that the latter contains cholesterol and lecithin.

Oil of Eulachon.—The fish known by the North Pacific Indians under the name of *Eulachon* or *Oulachon* and by the English as *Hoolakins* or *Candle fish,* the *Thaleichthys pacificus* of scientists, yields a great abundance of an oil which has been proposed as a substitute for cod liver oil. According to the editor of *N. R.* (1881, 356), this oil first begins to congeal and become opaque at −7° C., although authorities state that at ordinary temperatures it grows solid and lard-like. Specific gravity at 15.5° C., 0.907; mixed with one-half its volume of nitric acid, specific gravity 1.37, it develops a beautiful pink color which fades slowly to amber, and after standing fifteen hours it is considerably thickened and its color is changed to a deep amber of a reddish cast. It contains about 20 per cent. of palmitic and stearic acids, and 60 per cent. of oleic acid and 13 per cent. of an unsaponifiable substance, which resembles the similar constituent of sperm oil. (*T. G.*, Sept. 15, 1884.)

Oil of Euphorbia.—A fixed oil, obtained from the seeds of *Euphorbia Lathyris* L. (Fam. *Euphorbiaceœ*), or *Caper Spurge,* an annual plant naturalized in eastern U. S. A., though indigenous to Europe. It is often found near gardens and in cultivated fields, and is generally called *mole plant,* under the impression that moles avoid the ground where it grows. It is the *caper plant* of England. Like the other species of *Euphorbiaceœ,* it contains a milky juice which is extremely acrid, and the whole plant possesses the properties of a drastic purge; but the oil of the seeds is the only part used in medicine. This may be extracted by expression, or by the agency of alcohol or ether. In the first case, the bruised seeds are pressed in a canvas or linen bag, and the oil which escapes is purified by decanting it from the whitish flocculent matter which it deposits upon standing, and by subsequent filtration. By the other process, the bruised seeds are digested in alcohol, or macerated in ether, and the oil is obtained by filtering and evaporating the solution. According to Soubeiran, however, the oils obtained by these different processes are not identical. That procured by expression is probably the purest.

Oil of euphorbia is colorless, inodorous, and, when recent, nearly insipid; but it speedily becomes rancid, and acquires a dangerous acridity. Soubeiran has ascertained that it has a complex composition, containing, besides the pure oil, four distinct proximate principles. (*J. P. C.*, xxi, 259.) From 40 to 44 parts are obtained by expression from 100 of the seed. It is a powerful purge, but in *doses* of from five to ten drops is stated by continental physicians to act kindly upon the bowels. In this country, however, it has been found very uncertain in its effects, and very liable to cause vomiting. (*A. J. P.*, iv, 124.)

Oil of Gurjun. *Wood Oil. Gurjun Balsam.*—This oil must not be confounded with the *Chinese* wood oil, which is used as a varnish. (See *Oil of Aleurites*, p. 1515.) It is obtained from *Dipterocarpus turbinatus* Gaertn. f., and several other species of *Dipterocarpus* growing in East India (Fam. *Dipterocarpaceœ*), large trees which form forests in Pegu and other parts of Farther India. A large notch is cut in the trunk of the tree, between two and three feet from the ground, and a fire made so as to char the wound. The juice then begins to flow, and is received in suitable vessels. Every three or four weeks the charred surface is cut off and burned anew. A single tree sometimes yields forty gallons in a season. *D. tuberculatus* Roxb. yields a liquid known in Burma as *In oil,* which is sometimes sold as gurjun balsam. (*Proc. A. Ph., A.* 1913, 223.) It is at first turbid, but may be clarified either by filtration or deposition.

After filtration, it is a clear, dark brown liquid, of the sp. gr. 0.964 (Hanbury), and, in consistence, odor, and taste, bears a close resemblance to copaiba for which it was at one time substituted and in which it is still occasionally used as an adulterant.

Gurjun oil is soluble in two parts of alcohol, with the exception of a very small proportion of darkish flocculent matter, which subsides on standing. According to Lowe, it contains 65 per cent. of volatile oil, 34 of resin, and 1 of acetic acid and water. A characteristic property noticed by Lowe, by which it may be distinguished from copaiba, is that, when heated in a closed vial to 266° F., it becomes slightly turbid and coagulates, so that the vial may be inverted without changing the position of its contents, and this consistence is retained when the liquid cools. By a gentle heat with agitation the fluidity returns; but the liquid again coagulates if heated to 266° F. According to D. Brandis, this property of coagulation is characteristic of the wood oil from *D. alatus* Roxb. (*P. J.*, xxv), a wood oil which is further to be distinguished by the greenish opalescence of its surface.

Guibourt states that wood oil does not solidify, like copaiba, with one-sixteenth of magnesia, and the two separate on standing. (*J. P. C.*, xxx, 192.) According to De Vrij, with an equal volume of the wood oil, benzene forms a turbid mixture, from which, after a long time, a resinous matter is deposited in flocculi; with copaiba it forms a transparent solution.

The volatile oil from gurjun balsam is a yellow, somewhat thick liquid, of sp. gr. 0.915 to 0.930, and has at times a high optical rotation—viz., −35° to −130°. The oil boils in larger part at 255° to 256° C. and consists of a sesquiterpene, $C_{15}H_{24}$. With hydrochloric acid it yields a deep blue color. The resin left after distilling off the volatile oil is essentially *gurjunic acid,* $C_{22}H_{34}O_4$. This when purified dissolves readily in ether and strong alcohol, and slowly in benzene. It melts at 220° C. and congeals again at 180° C. Flückiger has also described a neutral resin from gurjun balsam, which is insoluble in caustic potash, fuses at 126° C., and is of the composition $C_{28}H_{46}O_2$. Flückiger (*A. Pharm.*, 1876, 420) noticed that wood oil may be recognized by the violet color it assumes if dissolved in twenty parts of carbon disulphide and mixed with a drop of a cold mixture of equal parts of concentrated sulphuric and nitric acids.

According to O'Shaughnessy, the oil of dipterocarpus is little inferior to copaiba in the diseases for which that medicine is employed. It has been used in *gonorrhea* given in the *dose* of a teaspoonful two or three times a day. It probably has a remedial influence similar to the different turpentines. The juice may be given in emulsion, in *doses* of from fifteeen to forty minims (0.9–2.5 cc.); the volatile oil from ten to twenty minims (0.6–1.3 cc.).

Oil of Jasmine.—This oil is obtained from the flowers of the *Spanish jasmine* (*Jasminum grandiflorum* L.). Alternate layers of the fresh flowers, and of cotton saturated with the oil of ben or other fixed oil, are exposed in a covered vessel to the warmth of the sun, the flowers being renewed until the oil becomes impregnated, when it is separated from the cotton by pressure. This method is necessary, as the flowers do not yield their aroma by distillation. According to Gildemeister and Hoffmann, jasmine oil contains 65 per cent. of benzyl acetate, and in addition linalyl acetate, benzyl alcohol, and linalool. The oil is used only as a perfume. W. H. Hall records (*M. S. Rep.*, Jan., 1861) the case of a child poisoned by the fruit of a jasmine, probably the common white species. The symptoms were coma, widely dilated pupil, and snoring respiration, with a cold pale surface, and slow and feeble pulse, followed by violent convulsions, with rigidity of the muscles about the head and throat.

Oil of Kuromoji.—Under this name there have entered commerce two fragrant Japanese oils—one, *Kouro motsi*, said to be obtained from the *Lindera sericea* Bl., and one, *Kuro matsi*, yielded by *Lindera umbellata* Thunb. (Fam. *Lauraceæ*). (See *Schim. Rep.*, 1904.)

Oil of Linaloe.—This volatile oil which is produced in Mexico, according to Seyffert (*Schim. Rep.*, Oct., 1907), is obtained from the wood of two species of *Bursera*, one of which is known in the Spanish as *Linaloe*, and the other as *Copal limon.* The latter tree is probably the *B. aloexylon* Engl. Better grades of this oil have a pleasant odor resembling a mixture of lemon and jasmine, while the poorer grades have a caraway-like odor. It is important in perfumery as the source of *linalyl acetate,* and is used as a substitute for oil of bergamot.

Oil of Maize. *Corn Oil.*—Our American maize or Indian corn yields a bright golden-yellow oil, of peculiar pleasant odor and taste. It is moderately thick, and has a sp. gr. at 15° C. of 0.916 to 0.924. It consists of olein and palmitin, and solidifies at –10° C. The oil is contained in the germs of the seed alone. Reckoned on the whole weight of the seeds the oil constitutes about 5 per cent., reckoned on the weight of the germ itself, after separation from the starchy body of the seed, the oil amounts to nearly 50 per cent. It is now being extensively produced in connection with the working of starch and glucose factories. It is used as a lubricant and for soap making, and as a substitute for cotton seed oil.

Oil of Neat's-foot. *Oleum Bubulum. Oleum Pedum Tauri. Axungia Pedum Tauri. Huile* (*Graisse*) *des Pieds du gros Bétail*, Fr. *Klauenöl, Ochsen Klauenfett*, G.—This formerly official oil is obtained by boiling for a long time the feet of the ox, previously deprived of hoofs. The fat and oil which rise to the surface are removed and introduced into a fresh portion of water, heated nearly to the boiling point. The impurities having subsided, the oil is drawn off, and, if required to be very pure, is again introduced into water, which is kept for twenty-four hours sufficiently warm to enable the fat which is mixed with the oil to separate from it. The liquid being then allowed to cool, the fat solidifies and the oil is removed and strained, or filtered through layers of small fragments of charcoal free from powder. The oil is clear and yellowish in color, of sp. gr. 0.916 at 15° C., and, when properly prepared, inodorous and of a bland taste. It thickens or congeals with great difficulty, and is, therefore, very useful for greasing machinery. It is also used for softening leather and in grinding metals. It was formerly given as a substitute for cod liver oil in scrofulous diseases but is no longer used in medicine.

Oil of Palm. *Palm Oil. Huile* (*Beurre*) *de Palme*, Fr. *Palmöl, Palmbutter*, G.—This highly valuable fixed oil is the product of *Elœis guineensis* Jacq., a palm growing on the western coast of Africa, and cultivated in the West Indies and South America. It is among the handsomest trees of its graceful family which flourish in the tropical regions of Africa. The oil is obtained by expression from the fruit. It is brought to this country chiefly from Liberia and other places on the African coast, although prepared also in the West Indies, Cayenne, and Brazil. It is not improbable that various species of *Palmaceæ* contribute to the supply of this article of commerce. At present the chief ports for its shipment are Cape Palmas and Lagos, prima and secunda Lagos being the choicest varieties.

Palm oil has the consistence of butter, a rich, orange-yellow color, a sweetish taste, and an agreeable odor, compared by some to that of violets, by others to that of the Florentine orris. By age and exposure it becomes rancid and of a pale yellow or nearly white color. It melts with the heat of the hand, and when perfectly fluid passes readily through blotting paper. Highly rectified alcohol dissolves it at common temperatures, and in ether it is soluble in all proportions. Its constituents are *tripalmitin* and *triolein*, $C_3H_5(C_{16}H_{31}O_2)_3$ and $C_3H_5(C_{18}H_{33}O_2)_3$. Palm oil undergoes more rapid spontaneous hydrolysis than any other fixed oil, as much as 75 per cent. of the oleic acid present being liberated within a few months. This makes the oil more easily saponifiable and may account for the preference given it by soapmakers in the days of empiric soap manufacture. Palm oil is said to be frequently imitated by a mixture of lard and suet, colored with turmeric, and scented with Florentine orris. It is much employed in the manufacture of toilet soap, which retains its pleasant odor. It is sometimes used to impart a yellow color to mixtures of fats or manufactured products, such as oleomargarine. In the latter case it is considered as an artificial coloring matter which necessitates the payment of ten cents per lb. additional tax. It is detected in the presence of other fats by a color reaction developed when sulphuric acid is added to a mixture of the suspected oil and an equal volume of acetic anhydride. This is known as Crampton-Simons test for palm oil, but it has been attacked by A. G. Gill (*J. I. E. C.*, 1917, p. 136) as being fallacious due not to a specific substance present in palm oil only, but to the presence of *carotin*, which is present in butter and some other constituents likely to be normally present in oleomargarine, to which this test is usually applied for the purpose of detecting the palm oil as an added coloring matter. Subsequently the method was improved and now consists of two separate tests, both of which must be positive. As now recommended it is carried out as follows:—Preparation of Sample: The sample should be kept in a cool dark place until tested, as exposure to light and air or the presence of water, alcohol, ether or similar reagents, interferes with the tests. Immediately before testing, the sample is filtered as quickly as possible at a temperature not exceeding 70° C. First Test: Dissolve 100 cc. of the fat in 300 cc. of petroleum ether and shake out with 50 cc. of a 0.5 per cent. potassium hydroxide solution. Draw off the aqueous layer, make distinctly acid with hydrochloric acid and shake out with 10 cc. of pure carbon tetrachloride. Separate the carbon tetrachloride solution, transfer a portion to a porcelain crucible, add 2 cc. of a mixture of one part colorless, crystallized phenol and two parts of carbon tetrachloride, then 5 drops of hydrobromic acid (sp. gr. 1.19) and mix by gentle agitation. The almost immediate development of a bluish-green color is indicative of palm oil. Second Test (usually preferred): Shake out 10 cc. of the melted and filtered fat with an equal volume of colorless, chemically pure, acetic anhydride, add 1 drop of sulphuric acid (sp. gr. 1.53) and shake the mixture for a few seconds longer. If palm oil is present the lower layer, on settling, will be found to be colored blue with a tint of green. The color in this as well as in the preceding test is transient.

Oil of Patchouli.—The genuine oil is obtained from *Pogostemon Patchouli* Pellet (*P. Heyneanus* Benth.) (Fam. *Labiatæ*), a plant cultivated in the Straits Settlements and in Penang. The plant has also been cultivated in the West Indies and in Paraguay. A small amount of oil is also obtained from *Microtæna cymosa* Prain, a plant cultivated in the mountainous districts of Assam. The patchouli herb is sometimes dried and sent into commerce. It is not infrequently adulterated with a number of other plants, the latter being present to the extent of 80 per cent. The oil as found in commerce is of two kinds. The best is that distilled in the East in the neighborhood of the patchouli plantations, from selected fresh leaves; the other kind is distilled in Europe from imported leaves; the latter often arrive in a more or less damaged condition, and are frequently adulterated. *Oil of patchouli* is a thick, brownish-yellow oil with a green tint and was shown by Gladstone to contain cœrulein, the blue compound found in oils of absinthium, matricaria, etc. The oil has the sp. gr. 0.970–0.990 at 15° C., and is lævorotatory. Rodie states that the odor improves by age and hence perfumers prefer the older oils. It deposits a solid, *patchouli alcohol*, $C_{15}H_{26}O$, which crystallizes in hexagonal prisms, melts at 56° C., and boils at 206° C., while cadinene, $C_{15}H_{24}$, remains; oil of cedar and oil of cubeb are frequently used to adulterate the oil. They may be detected by fractional distillation. Oil of patchouli is used in perfumery mainly for its valuable property of conferring upon other odors lasting qualities; its characteristic and persistent odor when uncombined is usually not popular among Caucasians.

Oil of Perilla.—This valuable oil is produced from seed of the *Perilla ocymoides* L., an Asiatic mint commonly grown in Japan and Korea. The oil is used in Japan in the manufacture of paints, paper umbrellas, and for similar purposes for which boiled linseed oil is used in the United States. It is claimed that it is superior to the latter for use in paints. It is also used as a food stuff.

Oil of Turtle. *Turtle Oil.*—In South America an oil is prepared from the eggs of turtles, and in the Seychelle Islands and in Jamaica from the fat of the turtle itself. These oils are said to be of equal value with cod liver oil for strumous persons and others in whom the nutritive processes are defective. (See *P. J.*, vol. xv, 573.) C. E. Sage examined *Turtle oil* as sold in London drug auctions and found the sp. gr. 0.919 at 25° C. The oil was yellow and semi-solid, having an odor of beef-drippings. (*C. D.*, 1906, 691.)

Oil of Ylang Ylang. *Cananga Oil. Oleum Anonæ. Oleum Unonæ.*—This is a volatile oil obtained from the flowers of *Cananga odorata* Hook. f. and Thoms (Fam. *Anonaceæ*), a large tree inhabiting most parts of Southern Asia; the oil from the Philippine Islands is especially esteemed. According to Schimmel & Co. (*Schim. Rep.*, April, 1897), it contains pinene, linalool, geraniol, esters of acetic and benzoic acids, cadinene, and para-cresol-methyl ester. It is used only as a perfume. The so-called *Macassar hair oil* is said to be a solution of it in coconut oil. (See *A. J. P.*, 1881, 123; also *A. J. P.*, 1893, 529.)

Ointment of Casein. *Unguentum Caseini Unna. Caseinsalbe*, G.—Prof. Francis Hemm quotes Dr. Unna's formula for casein ointment as follows: Take milk from which the cream or fat has been entirely removed and curdle it by the addition of rennet at a temperature of 30° to 40° C. Collect the coagulum and wash freely with cold water until the washings are no longer acid. Dry carefully and reduce to powder. Dissolve 34.5 parts of caustic potassium hydroxide and 8.5 parts of caustic sodium hydroxide in 5000 parts of water and dissolve 1400 parts of casein in this solution. Now add 700 parts of glycerin and 50 parts of phenol, and when dissolved incorporate 2100 parts of white petrolatum and 50 parts of zinc oxide and finally enough water to make 10,000 parts. (*M. B. D.*, 1906, 192.) It has the consistence of thick cream, is incompatible with acids and acid salts, but mercury, tar, balsam of Peru, zinc oxide, resorcinol, pyrogallol, and ichthyol may be incorporated with it. Certain forms of casein creams are known as rolling creams because when rubbed over the surface of the skin they take the dirt out of the pores by rolling up into small particles which can be brushed off. They are extensively used as cosmetics.

Ointment of Cucumber. *Cucumber Ointment.*—Emollient ointments prepared from the common cucumber (fruit of *Cucumis sativus* L., Fam. *Cucurbitaceæ*), were formerly considerably employed in irritated states of the skin. They have been largely superseded by non-fatty cosmetics. Several formulas for cucumber ointments are given in the *U. S. D.*, 20th ed., p. 1524.

The most frequently used preparation of cucumber at the present time is the cosmetic preparation known as *cucumber jelly,* which is used as a soothing application in roughness of the skin, etc. It consists of a jelly of tragacanth, quince seed, or some similar mucilaginous drug flavored with cucumber juice which imparts to the preparation a characteristic odor.

Olibanum. *Thus. Oliban, Encens,* Fr. *Weihrauch,* G.—*Olibanum,* the *frankincense* of the ancients, was erroneously ascribed by Linnæus to *Juniperus phœnicea* L. (*J. lycia* L.), but really is derived from several species of *Boswellia,* viz., *B. Carterii* Birdw. (furnishes what is known as *Luban Bedowi* or *Luban Sheheri*), and *B. Frereana* Birdw. (furnishes *Luban Meyeti* or *Luban Matti*). These are small trees of the Family *Burderaceæ,* growing in Somaliland and Arabia. They contain schizogenous gum-oleo-resin reservoirs in this bark. The natives incise the bark and collect the gum resin as soon as this exudation has dried. The drug is carried to Aden and thence to Bombay from which it enters commerce. It appears that the resin of *B. papyrifera* Hochst. is not gathered at all. The product of *B. serrata* Roxb. (known as *Salaigugul*) is not sent into general commerce, but is employed medicinally only in India.

The Arabian or African frankincense is in the form of yellowish tears, and irregular, reddish lumps or agglutinated masses. The tears are generally small, oblong, ovoid, clavate or pyriform, brittle, with a dull and waxy fracture, softening in the mouth, and bearing some resemblance to mastic, from which, however, they differ in their want of transparency. The odor is aromatic, balsamic; the taste slightly bitter. When triturated with water, the drug forms a milky emulsion. The reddish masses soften in the hand, have a stronger taste and odor than the tears, and are often mixed with fragments of bark and small crystals of calcium carbonate which are visible under the microscope.

The Indian frankincense, or olibanum, consists chiefly of yellowish, somewhat translucent, roundish tears, larger than those of the African, and generally covered with a whitish powder produced by friction. It has a balsamic resinous odor, and an acrid, bitterish, somewhat aromatic taste. When chewed it softens in the mouth, adheres to the teeth, and partially dissolves in the saliva, which it renders milky. It burns with a brilliant flame and a fragrant odor. Triturated with water, it forms a milky, imperfect solution. Alcohol dissolves nearly three-fourths of it, and the tincture is transparent.

Tschirch (*Harze und Harzbehälter,* 1900, p. 253) found in olibanum: resins 65 per cent.; volatile oil 6 per cent.; water soluble gum, 20 per cent.; bassorin, 6–8 per cent.; plant residue, 2–4 per cent. The resins were composed of *boswellic acid,* $C_{32}H_{52}O_4$, a resin acid of which well crystallized salts were obtained, and *olibanoresin,* $C_{14}H_{22}O$, a neutral resin. In the essential oil Wallach identified 1-pinene and dipentene, while the chemists of Schimmel & Co. found in addition phellandrene.

Olibanum is stimulant like the other gum-resins, but is now very seldom used internally. Delioux has obtained advantage from the inhalation of its fumes, when heated, in chronic *bronchitis* and *laryngitis.* (*B. G. T.*, Fév. 28, 1861.) It is chiefly employed for fumigation and in unofficial plasters. *Dose,* fifteen grains (1.0 Gm.), which may be increased to a drachm (3.9 Gm.) or more.

Canadian olibanum is reported by Karl Dieterich to be an American substitute for olibanum, which formerly came into the drug market from Hamburg. Its melting point is 77–78° C. Thus occupies a place about midway between Canadian olibanum or gum thus. It is a valuable American pine resin, which, however, containing no gum and therefore is not a gum resin. (*Ph. Centralh.*, 1912, 652–654.)

Omorol.—A compound of albumin and silver. It is a yellow powder, said to represent 10 per cent. of silver. It is insoluble in water, but soluble in physiological saline solution, and in the various body fluids. This silver compound is used as an antiseptic in the treatment of *catarrhs* of various mucous membranes, such as *pharyngitis, conjunctivitis,* etc., and also for its antiseptic influence on infected *wounds* and old *ulcers.* It is claimed that it is non-irritating and because of its relative insolubility the powerfully antiseptic effect is much more persistent than the ordinary preparations of silver. Viett (*Med. Klin.*, 1906, p. 436) has found it useful in the treatment of *diphtheria;* he dusts a finely powdered preparation on the infected area for one or two hours after previous cleansing of the throat with a gargle.

Onion. *Cepa.*—The bulb of *Allium Cepa* L. (Fam. *Liliaceæ.*) Fourcroy and Vauquelin obtained from the ordinary onion a white, acrid, volatile oil containing sulphur; also albumen, much uncrystallizable sugar and mucilage, phosphoric acid, both free and combined with lime, acetic acid, calcium citrate, and lignin. The expressed juice is susceptible of the vinous fermentation. The oil is essentially the same in chemical composition as the oil of *Allium sativum* L., and consists largely of allyl sulphide, $(C_3H_5)_2S$. (See *A. Pharm.*, 1892, 434.) Perkin and Hummel found *quercetin* in the outer skin of onion bulbs, and the skins have been used in dyeing.

The onion is sometimes used in domestic medicine as an expectorant in subacute *bronchitis,* and the onion poultice is sometimes employed as a mild irritant.

Ononis. *Radix Oncnidis. Rest Harrow. Ononis spinosa* L. (Fam. *Leguminosæ*).—This common European plant has the root more or less flattened, twisted and slightly branched; from 10 to 60 cm. in length and 1 to 2 cm. in thickness; externally it is grayish-brown, deeply wrinkled; the odor resembles that of licorice, the taste being sweetish, mucilaginous, afterward bitter. Kobert (*Pharm. Weekblad.*, 1918, lv, 49) has found in the ononis two saponins closely related to glycyrrhizin, one of which was previously described by Reinsch under the name of *ononin. Onocerin,* a di-secondary alcohol, $C_{26}H_{42}(OH)_2$, was isolated by Thoms, who proposed to change its name to *onocol.* (*A. Pharm.*, 1897, 28.) Cow (*A. E. P. P.*, 1912, lxix, p. 393) has found that in the dog, the aqueous extract of *ononis* exercises a diuretic effect approaching in power that of juniper, which conclusion has been clinically confirmed by Breitenstein. It also contains tannin.

Ophioxylon. *Radix mustelæ. Rauwolfia serpentina* Benth. (*Ophioxylon serpentinum* L.) (Fam. *Apocynaceæ.*)—In the root of this plant, which is used in East India as a purge and anthelmintic, Wefers-Bettink found a yellow crystalline principle, *ophioxylin*, melting at 72° C., and possessing the formula $C_{16}H_{12}O_6$; also a volatile oil. (*A. J. P.*, 1890.) It is widely used in India as an antidote against bites of serpents, stings of insects, etc.

Opopanax.—A concrete juice or oleo-gum-resin of *Opopanax chironium* Kch. (*Pastinaca Opopanax* L.) (Fam. *Umbelliferæ*), a plant closely allied to the common *parsnip*. It is a native of the Levant, and grows wild in the south of France, Italy and Greece. When the base of the stem is wounded, a juice exudes, which, when dried in the sun, constitutes the *opopanax* of commerce. Some authors state that it is obtained from the root. A warm climate appears necessary for the perfection of the juice, as that which has been collected from the plant in France, though similar to opopanax, is of inferior quality. The drug is brought from Turkey.

It is sometimes in tears, but usually in irregular lumps or fragments, of a reddish-yellow color, speckled with white on the outside, paler within, and when broken, exhibiting white pieces intermingled with the mass. Its odor is strong, peculiar, and unpleasant, its taste bitter and acrid. Its sp. gr. is 1.622. It is inflammable, burning with a bright flame. It is a gum-resin, with an admixture of other ingredients in small proportion. Tschirch found opopanax to consist of resin, 19 per cent.; ethereal oil, 6.5 per cent.; gum and plant tissues, 70 per cent.; water and loss, 4.5 per cent. (*A. Pharm.*, 1895, 209.) Schimmel states that the oil consists of an alcohol with a sesquiterpene as the chief constituent. (*Schim. Rep.*, 1904, 67.) Water by trituration dissolves about one-half of the gum-resin, forming an opaque milky emulsion, which deposits resinous matter on standing, and becomes yellowish. Both alcohol and water distilled from it retain its flavor; but only a very minute proportion of oil can be obtained in a separate state. Opopanax was formerly employed, as an antispasmodic and deobstruent, in *hypochondriasis, hysteria, asthma*, and chronic visceral affections, and as an emmenagogue; but it is now scarcely ever used. *Dose*, ten to thirty grains (0.65–2.0 Gm.).

Optochin. *Numoquin. Ethylhydrocupreine.*—$C_{21}H_{28}O_2N_2$. Under the name of *Cuprea Bark* the bark of the *Remijia pedunculata* Triana and the *R. purdieana* Triana, trees closely allied to the cinchonas, were at one time used in medicine. They contain a number of the cinchona alkaloids including quinine, quinidine, cinchonine and a related alkaloid, *cupreine*. Quinine is a methyl cinchonine while cupreine is hydroxy-cinchonine. The base is a white or faint yellowish amorphous powder with a bitter taste, practically insoluble in water but easily soluble in alcohol or ether. It forms a crystalline hydrochloride which dissolves in twice its weight of water or in 5 parts of alcohol.

Ethylhydrocupreine was shown by Morgenroth (*B. K. W.*, 1910 and 1911) to have specific germicidal powers against the pneumococcus and has been used both in true *pneumonia* and various local pneumococcus infections. While its general antibacterial effects are comparatively feeble Schiemann and Ischaivara (*Z. Hyg.*, 1914, lxxvii, 49) found that in the strengths of one part in 400,000 it kills the pneumococcus even in the presence of blood serum. These results, however, have been contradicted by Bedell (*J. A. M. A.*, 1920, lxxv, 928) who found that although in more concentrated solutions it was pneumococcicidal, in 1/400,000 it actually stimulated the growth of the pneumococcus. Although Waetzhold (*Ther. Geg.*, 1915, lvi, 262) and others reported favorably on its clinical value in *pneumonia* more recent studies have thrown great doubt on its clinical usefulness for this purpose. Moore and Chesney (*A. I. M.*, 1918, xxi, 659) have used it in 75 cases of pneumonia and were unable to perceive any noteworthy therapeutic benefit. In 12 per cent. of the cases there was temporary amblyopia. Objection has been made to the conclusions of Moore and Chesney, however, on the ground that they used the hydrochloride instead of the base itself. It is asserted that when the base is given by the mouth a markedly pneumococcicidal effect is accomplished without serious danger to the patient. The present evidence indicates strongly that the toxicity of optochin for human beings is so high that it is unsafe to give doses large enough to influence pulmonary infections without serious danger to the patient. On the other hand, there is considerable evidence that in local infections, as *pneumococcus conjunctivitis*, the installation of a one or two per cent. solution of the soluble optochin hydrochloride is of real value. Kolmer (*J. Ex. M.*, 1921, xxxiii, 693) has recommended the intraspinal injection of ethylhydrocupreine hydrochloride in pneumococcic *meningitis*.

Because of its toxicity it is not safe to give more than 1.5 Gm. (23 grains) in 24 hours to the ordinary adult. This may be conveniently divided into 8 doses of 0.15 Gm. (2 grains) every three hours. Smith and Fantus (*J. P. Ex. T.*, 1916, viii, p. 53) report a study of its physiological action with a review of the literature. They find that it is decidedly more toxic to infusoria than corresponding solutions of quinine. It is also somewhat more poisonous to animals, its toxicity for white mice as compared to quinine being as 7 to 5. As an antipyretic it is less efficient than quinine. When given to frogs in large doses it causes first exaggerated reflexes followed by paralysis of the peripheral nerves. They state that quinine produces the same symptoms. In mammals it causes motor weakness with exaggeration of reflexes and death from respiratory failure. In large quantities it depresses the heart but has less effect on the circulation than quinine. In solutions of more than 1 per cent. optochin is irritant to the conjunctiva, and later anesthetic. Recently it has been found by Liefmann (*Th. M.*, 1915, xxix, p. 260) to cure *malaria* which had resisted quinine. Two compounds closely related to optochin have been introduced as surgical antiseptics. These are the *isoamyl-hydrocupreine* known by the trade name of *eukupin*, and the *isoctyl-hydrocupreine* called *vuzin*. They are used in the form of their di-hydrochlorides. Bruhn (*Th. M.*, Dec., 1919) has found that the Gram positive bacteria—which include streptococci, staphylococci, pneumococci, diphtheria bacilli, etc.—are killed by these compounds in as dilute solution as one part in 10,000 but that even a 1 to 1000 solution is unable to restrain the multiplication of other bacteria.

Eukupin also possesses local anesthetic properties. The combination of this with its antiseptic influence makes it a valuable local application in *cancerous ulcers, carbuncles* and other painful infections. It is claimed to be especially efficacious for the sterilization of *diphtheria* carriers and meningococcus carriers. It has been used to a slight extent internally as a substitute for quinine in *malaria* and *influenza*. For internal use the base itself is recommended in *doses* of three to four grains (0.2–0.25 Gm.) every 3 or 4 hours. For local application the soluble dihydrochloride may be employed in strengths of 0.5 to 1 per cent. solution.

Opuntia. *Opuntia vulgaris* Mill. (Fam. *Cactaceæ.*) *Prickly Pear. Barberry Fig. Indian Fig. Figue de Barbarie*, Fr. *Indische Feige*, G.—A common cactus composed of flattened, prickly or spinose jointed stems, and occurring in sandy soil from Nantucket to South Carolina. For analyses of fruit of this cactus, see *A. J. P.*, 1884, 3, and 1896, 170.

Orange Red. *Orange Mineral. Sandix.*—Red lead oxide, prepared by calcining lead carbonate. It is of a lighter color than *minium*, and is used as a pigment.

Orcin. *Dihydroxytoluene. Dihydroxymethylbenzene. Orcinol.* $C_6H_3(CH_3)(OH)_2.[1:3:5]$.—The U. S. IX recognized this among the reagents and described it as in "monoclinic prisms, white with a reddish tint, which fuse at about 58° to 60° C. Orcin has an intensely sweet and astringent taste; very soluble in hot water, less soluble in cold water, readily soluble in alcohol or ether. The anhydrous substance fuses between 106° and 108° C. Anhydrous crystals are deposited from an ether solution. When exposed to light or air the crystals assume a reddish-brown color. The addition of a few drops of ferric chloride T.S. to an aqueous solution of orcin (1 in 20) produces a deep blue color. Warm 10 mils of an aqueous solution of orcin (1 in 10) with 10 mils of sodium hydroxide T.S. and add a few drops of chloroform; the solution assumes a purple-red color, then bright red, and, after diluting with distilled water, shows an intense, greenish-yellow fluorescence. Aqueous solutions of orcin (1 in 20) tested separately do not yield precipitates upon the addition of test solutions of either mercuric chloride, cupric sulphate, tannic acid or lead acetate; with basic lead acetate T.S., a white precipitate is obtained (characteristic of *resorcinol derivatives*)." *U. S. IX.*

It also gave an assay process requiring not less than 85 per cent. of anhydrous orcin.

Orcin is said to resemble resorcinol in its local action and to be useful in the same class of skin diseases. A coloring matter obtained from *orcin* by the action of ammonia is known as *orcein*, $C_{28}H_{24}N_2O_7$. It is used in microscopic staining. According to J. Andeer (*Med. Chron.*, Dec., 1885), orcin is distinctly antiseptic, and in poisonous doses produces death by a direct action upon the heart muscle.

Oreodaphne. *Umbellularia californica* (Hook. et Arnott) Nutt. (Fam. *Lauraceæ.*)—The *California Bay Laurel* is an evergreen tree of considerable size, rather abundant throughout the State. Its wood is much prized on account of the beauty of its grain and its immunity from the attacks of insects. The leaves yield about 4 per cent. of a neutral, straw-colored, limpid, volatile oil, which has a warm camphoraceous taste and a pungent aromatic odor, resembling somewhat that of a mixture of oils of nutmeg and cardamom. It is soluble in 1000 parts of water, and in alcohol and ether in all proportions. It is said, when inhaled, to cause dizziness and headache. John P. Heamy, (*A. J. P.*, 1875, 105) finds it to consist of a pure hydrocarbon, sp. gr. 0.894, boiling at 175° C., and an oxygenated, pungent portion which boils at 210° C. This he calls *oreodaphnol. Oreodaphene* was obtained by distilling oreodaphnol with glacial phosphoric acid. For the reactions, see Heamy's paper.

Orexin. *Phenzoline. Cedrarine. Tannexin. Phenyldihydroquinazoline Hydrochloride.* $C_{14}H_{12}N_2.(C_{14}H_{10}O_9)$.—A complex derivative of quinoline. It forms colorless, odorless, lustrous crystals with bitter, pungent taste, freely soluble in hot water. *Orexin* was first brought forward by F. Penzolt as a stomachic. It appears to be practically free from toxic properties, two grains of it per pound not being sufficient to kill a rabbit. It appears to be a very active remedy in those cases of failure of appetite in which simple bitters are indicated, and to be contra-indicated by hyperacidity of the stomach, gastric catarrh and gastric ulcer.

The *tannate* is affirmed to be more efficient than the hydrochloride, which salt it has practically replaced in the market. The tannate is a yellowish powder, tasteless, odorless, insoluble in water, freely soluble in acid solutions. It is very highly praised in all forms of *atonic dyspepsia, loss of appetite* in convalescence, and similar conditions. It is affirmed also to be very useful in the treatment of *vomiting*, following the use of narcotics, such as opium, chloroform, etc. It is chemically incompatible with iron salts. It is best administered in the form of powder, five to ten grains (0.3–0.7 Gm.) given in capsules, one to two hours before meals.

Organotherapeutic Extracts. *Endocrines.*—The use of the extracts of various organs as medicinal agents is one of the oldest known therapeutic measures. Thus, Pliny mentions the use of the brains of animals in the treatment of *jaundice*, and it is probable that this drug was used also by the ancient Egyptians. The modern use of organic extracts may be dated from the investigations of Brown-Sequard. (*A. de P.*, 1889, p. 51.) Since this time extracts of nearly every portion of the body have been tested therapeutically. From many of these extracts there is no reason to expect any beneficial influence in diseased conditions. On the other hand, it is impossible to deny that many of the glandular organs of the body deliver their secretions directly into the blood stream, and that these secretions are essential for the maintenance of health and it is *a priori* not unreasonable to expect that the artificial administration of these secretions will have a beneficial influence in certain diseased conditions. It is among the last group of drugs that *opotherapy* finds a justification for its existence. Two of these organs of internal secretion have achieved so fixed a place in medicine as to have received official recognition, namely, the suprarenal capsule and the thyroid gland. Although the pancreas probably also delivers an internal secretion, the pancreatin of the Pharmacopœia represents an external and not an internal secretion of the pancreatic gland. There are some which have firmly established their claims, although not yet included in the U. S. P., but the great mass of them are still in the experimental stage. The fact that attention is paid to the following preparations does not imply the opinion that they are proper endocrine organs, but merely that they are of sufficient commercial or scientific interest to deserve mention.

Cerebrin. Cerebrum Siccum.—The dried *brain* substance has been used by Babes and others (*K. T. W.*, 1900) in the treatment of *neurasthenia*, *insanity* and *epilepsy*. The treatment, however, has no scientific foundation. Wassermann (*B. K. W.*, 1898, p. 4) has shown that an emulsion of the brain is capable of neutralizing the tetanus toxin. It has subsequently been shown also that this holds true for strychnine and morphine and is probably due to its cholesterin content (see under *Cholesterin*). On this evidence an emulsion of the dried brain substance has been used in the treatment of *tetanus* and *rabies*. (Kowalski, *K. T. W.*, 1900, No. 5.) The *dose* of the dried brain substance is 30 to 60 grains (2–4 Gm.).

Ciliary Body. Corpus Ciliaræ.—The extract of the ciliary body, as well as the *vitreous body* has been used in sympathetic *ophthalmia* by Dor and by Wecker. (*Annals d'Oculistique*, August, 1902.) *Oculin* is a name applied to a glycerin extract of the ciliary body and vitreous humor.

Kidneys. Renes Siccum.—There is considerable evidence that the kidneys supply an internal secretion, but that failure of this internal secretion is the cause of uremia, as claimed by some, has certainly not been established. Although a number of authors have claimed beneficial results from the administration of the kidney substance in *nephritis* and *uremia*, it is probable that the treatment is useless. The *dose* recommended is from four to fifteen grains (0.26–1.0 Gm.) several times daily. *Nephritin* is a proprietary extract of this class.

Hypophysis. N. N. R. 1924.—As described in Part I the hypophysis cerebri or *pituitary body* consists of a posterior lobe which is made up of tissue which seems to be related to the nervous system, and it is therefore improbable that it has any secreting function. The *anterior lobe*, however, is composed of glandular tissue and is generally regarded as one of the organs with an internal secretion. The hormone which is furnished by this gland to the blood is especially important in the young as it apparently controls the growth of the bony and sexual systems. A deficiency of pituitary secretion in the young leads to dwarfism, failure of development of the sex organs, deposition of fat and often mental sluggishness. An excessive activity of the gland leads to gigantism (or in adults acromegaly), sexual precocity, and overgrowth of hair.

As a drug the extract of the anterior lobe of the pituitary gland has been employed for the correction of those failures of growth which seem to be attributable to pituitary deficiency.

Tethelin is a lipoid isolated by T. B. Robertson in 1916 and by him believed to be the growth controlling principle of the anterior lobe (see *A. J. P.*, 1919, xci, p. 349).

The dose of the desiccated anterior lobe of the pituitary is from one to five grains (0.06–0.3 Gm.).

Insulin.—It has long been known that destruction of the islands of Langerhans in the *pancreas* caused an increase in the blood sugar and the appearance of glucose in the urine. It is generally acknowledged that most, if not all, cases of diabetes mellitus are due to pancreatic disease. Various extracts of pancreas have been therefore tested in the treatment of diabetes but without any brilliant success. In 1922, Banting and Best (*J. Lab. Clin. M.*, 1922, vii, 251) evolved the hypothesis that the islands of Langerhans secreted a hormone which was essential for the metabolism of sugar and that the reason of the failure of previous pancreatic extracts was that the digestive enzymes present in these extracts destroyed the glycolytic hormone; and that if they could find a means of bringing about degeneration of the enzyme-secreting portions of the pancreas without affecting the islands of Langerhans it would be possible to prepare an active glycolytic extract. This they accomplished by ligation of the pancreatic ducts which led to atrophy of the pancreatic cells. From such glands they prepared an extract which, in normal animals, greatly increases the combustion of sugar and leads, therefore, to a reduction in the amount of glucose in the blood. In sufficient dose the blood sugar may be reduced below the necessary minimum and fatal effects follow.

Animal experimentation and numerous clinical trials have established beyond cavil the power of insulin to increase the metabolism of sugar in most cases of *diabetes mellitus*. This increased carbohydrate combustion has led, in the great majority of patients, to the reduction of the glykemia to normal limits, to the consequent disappearance of sugar from the urine and the subsidence of all clinical manifestations of the diabetes. Many of these patients are able, under the insulin treatment, to utilize a diet containing a normal percentage of carbohydrates without the occurrence of glycosuria. On the other hand, it must be remembered that the use of this extract simply provides the system with an absent hormone; it has no effect in restoring health to the diseased cells of the pancreas. In other words, it is not properly to be regarded as a curative agent as it does not tend towards a restitution of normal function. Just as in the case of cretinism it is necessary to continue the use of thyroid indefinitely, so in these cases of diabetes the complete withdrawal of the insulin is followed by a return of the carbohydrate intolerance. It has been found clinically, however, that after a few weeks' treatment with insulin the dose employed may be very greatly reduced; in other words, there is a partial recovery of normal pancreatic power just as has been observed frequently from the ordinary dietetic treatment. Banting, Campbell and Fletcher (*B. M. J.*, January 6, 1923, p. 8) and others, have shown that even in diabetic coma it may bring about, not merely a reduction in the excessive glucose in the blood, but also a restoration of the normal alkalinity of the body and consequent recovery in apparently morbid cases of acidosis. Strouse and Schultz have found it of great value in the treatment of various *infections*, either local or systemic, occurring in diabetic patients. Thalhimer (*J. A. M. A.*, 1924, lxxxii, 692) has found it of service in nondiabetic *acidosis* and the *vomiting* of pregnancy.

While insulin must be regarded as a very important addition to our remedial agents it must not be forgotten that improperly used, it is equally potent for injurious or even fatal effects. Too large doses may lead to dangerous and probably fatal reduction in the percentage of blood sugar. Fortunately, this reduction is signalized by very marked symptoms before it reaches fatal proportions and can be promptly relieved by the administration of available carbohydrate such as glucose. The symptoms of dangerous reduction of the blood sugar are weakness and a sense of fatigue, with extreme hunger and nervous restlessness; the most characteristic but somewhat later symptom is profuse sweating usually accompanied with tremors and followed by unconsciousness.

A remedy so potent for both good and evil as insulin is clinically useless unless the dose can be standardized. In the absence of definite knowledge of its chemical composition the present standardization of insulin is a physiological one based upon the amount required to effect glycolysis in the rabbit and the dose is expressed in units. One unit is one-third of the amount required to reduce the blood sugar to less than 0.045 per cent. in a rabbit of two kilogrammes weight that has been previously starved for 24 hours. This unit is known as the H unit. In 1923 a new unit, designated by the letter U and representing a 40 per cent. increase of strength, was introduced. For details of the method of testing insulin see *A. J. Phys.*, lxii, p. 162 and Voegtlin & Dunn, *U. S. Pub. Health Rep.*, August 3, 1923. The ordinary beginning *dose* is from 10 to 30 units daily, which must be given hypodermically or intramuscularly. In severe cases, with proper control by quantitative determinations of the blood sugar, much larger doses may be employed for short periods of time. In any case it is important that its use be regulated by frequent examinations of the urine or, better yet, estimations of the blood sugar.

(For references to the literature on this subject see Allen, *J. Metabolic Research*, 1922, ii, p. 125, and Joslin, *J. A. M. A.*, 1923, lxxx, p. 1581, and an editorial in *J. A. M. A.*, June 2, 1923, p. 1618.)

The chemical nature of the glycolytic hormones, as well as the mode of its action in the body, are entirely unknown. It is interesting to note, however, that a number of investigators have prepared extracts from a variety of sources, including yeast, raw potato juice, etc. (See Thalhimer and Perry, *J. A. M. A.*, 1923, lxxx, p. 1614), which have an effect upon carbohydrate metabolism apparently similar to those of insulin.

Liver. Hepar Siccum.—Gilbert and Karno (*S. M.*, 1897, p. 184) believe that there is some substance in the liver which leads to a retention of the glycogen out of the blood in the liver, and that the administration of this substance is of benefit in the treatment of *diabetes*. Gyr asserts that the extract of the liver is also useful in *hepatic cirrhosis* (*R. M. S. R.*, June 20, 1908), and in *hemeralopia* by Roncagliolo (*Med. Klin.*, 1905, p. 909). The *dose* of the dried liver is one-half to one ounce (15–31 Gm.) per day.

Mammary Gland. Mammæ Siccatæ.—On the theory that there is some relation between the uterus and the mammary gland, the latter has been used by Shober (*Phila. M. J.*, Nov., 1899) and others, in the treatment of *menorrhagia, fibromata, dysmenorrhea*, etc. The *dose* of the dried gland is five to ten grains (0.32–0.65 Gm.) three times a day.

Ovaries. N. N. R. 1924.—That the ovaries deliver an internal secretion which while not essential to life, certainly modifies in some way metabolism, is almost universally accepted. One of the strongest proofs of this is seen in the symptoms which occur at the menopause or after double oöphorectomy. The *corpus luteum*, according to Ott and Scott (*Proc. of the Soc. of Exper. Biol. and Med.*, 1910, viii, p. 49), has a marked stimulating effect upon the mammary gland, but the ovarian substance when deprived of this was without such action. There is strong clinical evidence that the administration of the ovarian substance will at least temporarily relieve the symptoms seen at the menopause, whether the latter is natural or artificial. Richter (*D. M. W.*, 1899) has found that there is a marked increase in the fatty metabolism under the feeding of the ovarian substance. These investigations have been confirmed by Thumim. (*Ther. Geg.*, 1900, p. 451.)

The ovarian substance has also been used in the treatment of *neurasthenia* by Vidal (*Press. Med.*, 1900, p. 173) as well as in a host of other diseases in which there was much less likelihood of benefit following its administration. (For review of the literature, see Offergeld, *D. M. W.*, 1911, p. 1172.)

The *corpus luteum* has been used for various disturbances of *pregnancy* on the ground that these were due to the natural intermission in this function. Hirst (*J. A. M. A.*, 1921, lxxvi, 772) who has had excellent results with the extract of corpus luteum for the relief of the *vomiting* of pregnancy maintains that the cause of frequent failure after its oral administration is the destructive influence of the digestive secretions. He prefers to give it intravenously using 2 cc. (30 minims) of a solution which represents 0.4 Gm. (6 grains) of the dried gland twice daily for 4 doses. Taylor, however, objects to the intravenous injection and prefers to give the drug intramuscularly. He gives an extended review of the literature (*Pa. M. J.*, 1923, xxvi, 252). The corpus luteum has also been used in the treatment of menopausal disturbances and various menstrual disorders. Proprietary preparations of the ovarian substance are *glandnovin, ovadin, ovarial, ovarigen, oophorin, ovaron, lutein, ovariin* and *overaden*.

Dose, of desiccated ovarian substance, one to three grains (0.06–0.2 Gm.). The dried corpora lutea is given in *doses* of one to five grains (0.065–0.32 Gm.) two or three times a day.

Parotid Gland. Parotis Siccum. Glandula Parotidis.—Believing that there is some connection between the parotid and the sexual organs, Bell (*Ther. Woch.*, 1896, p. 659) has employed the parotid gland in the treatment of *dysmenorrhea, ovarian neuralgias*, and other disorders of the pelvic organs. The dried substance is usually administered in tablet form in *doses* of from one to three grains (0.065–0.2 Gm.) three times a day.

Parathyroids. N. N. R. 1924. *Glandula Parathyroidea.*—These are four small bodies growing near the lateral lobes of the thyroid gland. Because of their anatomical proximity it was at one time believed that their function in the body was similar to that of the thyroid body, but it is now known that these two organs are in no way physiologically connected. The parathyroid bodies, however, play some important rôle in the bodily metabolism. Although the view formerly held that their removal was certainly fatal has been shown to be incorrect, yet their extirpation gives rise to very violent symptoms which destroy life unless actively combated. The most prominent of these symptoms are violent tetanic convulsions and a marked reduction in the blood calcium. Some believe that the convulsions are due to the absorption of toxins from the intestines, while others believe that they are due to the withdrawal of lime salts from the nerve system. (See Vines, *B. M. J.*, 1922, i, 791.) Ott and Scott (*Amer. Med.*, 1910) have found that the parathyroid extract has a powerful diuretic influence. The dried parathyroid gland has been used in the treatment of *tetany.* (Loewenthal, *Med. Klin.*, 1907, p. 1012.) It has also been used by Meyer (*Ther. Geg.*, 1913, 354) and Berkley (*N. Y. M. J.*, Nov. 23, 1907) in treatment of *paralysis agitans.* The *dose* is one-tenth of a grain (0.006 Gm.) two or three times a day.

Spleen. Lien Siccus.—It can hardly be considered definitely established that the spleen furnishes any internal secretion. According to Danilewsky and Salensky (*A. G. P.*, 1895, p. 264), however, the subcutaneous injection of the splenic extract produces an increase in the percentage of hemoglobin, and in the number of red blood cells. It is also asserted that there is an increase in the number of the white corpuscles. It is possible that these effects are not due to any substance peculiar to the spleen, but to the nucleinic acid which it contains. Accordingly, the splenic extract has been used in the treatment of *anemias,* with more or less beneficial results. Leake and Bacon (*J. P. Ex. T.*, 1924, xxiii, 353) have shown that feeding splenic extract causes a marked increase in the number of red blood cells, but the effect is especially noteworthy if it is combined with simultaneous administration of bone marrow. Carpenter (*D. M. Ztg.*, 1907, p. 571) asserts that it has a specific action in *malaria.* H. C. Wood (*A. J. M. S.*, 1897, p. 511) has found it useful in *Graves's disease.* It has also been recommended in various forms of *insanity.* One of the difficulties in the use of this drug is to obtain a preparation which is active and yet will be borne by the stomach. The dried powder is given in *doses* of four to fifteen grains (0.26–1 Gm.) three times a day. It is doubtful, however, how far it entirely represents the drug. Under the name of *eurythrol,* an aqueous extract has been marketed. The *dose* of this is one to two teaspoonfuls, given generally in soup. *Lienaden* and *opo-lieninum* are proprietary preparations of spleen.

Suprarenals. Suprarenalum Siccum, U. S. IX, *Glandulæ suprarenales,* U. S. VIII. *Adrenals.*—The suprarenal glands are small organs found in all mammals, situated in the neighborhood of the kidney. They consist of an outer layer, or *cortex,* composed of tissue similar to that of the glandular organs and an inner layer—the medulla, which in its development and histology seems to be related to nerve tissue. The extirpation of these organs in the lower animals is almost invariably fatal within one or two days. Although the evidence is strong that this death is due to the destruction of the cortex rather than of the medulla (see Houssay and Lewis, *C. R. S. B.*, 1921, lxxxv, p. 1210) we know very little as to the precise function of this portion of the suprarenal bodies. The medullary part contains a nitrogenous body that has a very pronounced effect on the various functions of the system (see *Epinephrina*). There is considerable evidence that stimulation of the peripheral of the splanchnic nerve causes a discharge of epinephrine into the general circulation and many physiologists regard this substance as a true internal secretion.

The U. S. IX defined the dried suprarenals as: "The suprarenal glands of animals which are used for food by man, cleaned, dried, freed from fat, and powdered, and containing not less than 0.4 per cent. nor more than 0.6 per cent. of epinephrine, the active principle of the suprarenal gland. One part of Dried Suprarenals represents approximately 6 parts of fresh glands, free from fat. If assayed biologically one gramme of Dried Suprarenals contains the equivalent of ten milligrammes of lævo-methylamino-ethanol-catechol." *U. S. IX.* When freed of their fat and dried they may be pulverized. This powder is a "light yellowish-brown, amorphous powder, having a slight, characteristic odor; partially soluble in water. Dried Suprarenals contain not more than 7 per. cent. of moisture, and the yield of ash does not exceed 7 per cent.

"*Assay.*—Add 0.005 Gm. of finely powdered manganese dioxide and 10 mils of distilled water to 0.01 Gm. of Dried Suprarenals; thoroughly shake the mixture several times during one hour and filter. Compare the color of the filtrate in a test tube or in any convenient manner, with the color of cobaltous chloride T.S. and diluted gold chloride T.S. (see Reagents, Part III) combined as follows: Mix 1.85 mils of cobaltous chloride T.S. with 0.95 mil of diluted gold chloride T.S. and 7.2 mils of distilled water; the color corresponds to 0.2 per cent. of epinephrine in the filtrate obtained above; 2.95 mils of cobaltous chloride T.S. with 1.25 mils of diluted gold chloride T.S. and 5.8 mils of distilled water corresponds in color to 0.4 per cent. of epinephrine; 4.05 mils of cobaltous chloride T.S. with 1.35 mils of diluted gold chloride T.S. and 4.6 mils of distilled water corresponds in color to 0.6 per cent. of epinephrine; 5.15 mils of cobaltous chloride T.S. with 1.55 mils of diluted gold chloride T.S. and 3.3 mils of distilled water corresponds in color to 0.8 per cent. of epinephrine. The percentages of epinephrine indicated by the above color standards are based upon the maceration of 0.01 Gm. of the Dried Suprarenals in 10 mils of distilled water, as directed above, and filtering. In samples containing more than 0.8 per cent. of epinephrine, 0.005 Gm. of the Dried Suprarenals may be taken, in which case the percentage stated above, as indicated by the color standards, should be doubled. The standard color solutions keep unchanged, if sealed in glass tubes." *U. S. IX.*

It will be noted that the chemical and biological assays differed, the latter requiring the presence of 1 per cent. of active principle, the former only 0.5 per cent. How this discrepancy was to be reconciled surpasses conjecture.

Seidel and Fenger (*U. S. Hygienic Lab. Bull.* No. 100, 1914) have found that the percentage of epinephrine in the suprarenal gland of the beef runs distinctly higher than those of either sheep or swine, varying in the beef glands from 0.4 to 1 per cent., in hogs and sheep from 0.1 to 0.4.

Uses.—An aqueous solution of the dried suprarenals will produce all the effects described under *epinephrine* (see Part I), but because of its greater convenience the alkaloid is universally preferred. There are one or two conditions, however, in which the whole drug is to be preferred. Foremost among these is that syndrome known as *Addison's disease.* According to S. Solis-Cohen, the administration of the suprarenal gland by the mouth every two or three hours is sufficient to prevent the occurrence of the *asthmatic paroxysm.*

Dose, three to ten grains (0.2–0.65 Gm.).

Testicles. Testes Sicci. Orchic Substance.—The basis of the famous elixir of Brown-Sequard, *Liquor spermaticus,* was the fluid contained in the testicles. The persistent use of the various imitations and modifications of the *Brown-Sequard Elixir* would argue that it must possess some therapeutic virtue. It is claimed by those who use it that it has a powerful tonic effect, not merely improving the strength, but also exercising a beneficial influence upon the metabolism, so as to lead to a permanent augmentation of power. It has been recommended for *neurasthenia, diabetes, locomotor ataxia, arteriosclerosis,* and a large number of other chronic complaints.

The dried testicular substance is given in *doses* of from five to thirty grains (0.3–2 Gm.), but it is generally recommended as a liquid preparation, and that it should be given hypodermically. Among the preparations which contain testicular fluid as their important ingredient are the *succus e testibus paratus, orchidin, Hawley lymph, testaden, testidin* and *teston.*

A salt solution of the hydrochloride of the amine *spermin* ($C_5H_{14}N_2$), a normal constituent of the spermatic fluid is used as a nerve tonic and stimulant in a variety of infectious diseases, as *typhus, syphilis,* etc. *Dose,* subcutaneously, sixteen minims (1 cc.) of a two per cent. solution; by mouth, ten to thirty drops (0.6–1.8 cc.) of a four per cent. solution.

Thymus Gland. Glandula Thymi Sicca.—This body, which is the ordinary *sweet-bread,* is found only in young animals, disappearing as adult life comes on. Physiologists are not agreed to its exact importance or function. It appears to have some connection with the growth of bone and also of the formation of the white corpuscles of the blood. It has been used in medicine chiefly for two purposes, namely, in the treatment of *exophthalmic goiter,* and for the purpose of stimulating body growth in *rickets* and *ununited fracture.* It should be remarked that thymus contains a larger percentage of nuclein than any common food stuffs, and for this reason its use is generally forbidden to gouty patients. The *dose* of the fresh gland is from one drachm to half an ounce (2–15 Gm); of the dried gland from two to five grains (0.12–0.3 Gm.).

Bone Marrow. Medulla Ossium.—Leake (*J. P. Ex. T.,* 1923, xxii, 401) in experiments in human beings found that desiccated bone marrow caused an increase of about 15 per cent. in the number of red blood cells; when spleen substance was administered at the same time the increase was even greater. It has been used by Gullan (*Lancet,* 1907, p. 520), and others in the treatment of *pernicious anemia.* Gullan administered it by spreading the fresh red bone marrow on bread, which is taken at meal times. It is very prone to produce nausea. The *dose* of the fresh marrow is one to three ounces (31–93 Gm.); of the dried marrow two to five drachms (7.7–20 Gm.). *Opo-osslin* and *ossagen* are proprietary preparations made from bone-marrow.

Oridine.—*N. N. R.* 1925. This is the calcium salts of the iodized fatty acids of cotton seed oil analogous therefore to calcium iodobehenate. It occurs as a light brown powder almost odorless and tasteless, practically insoluble in water and only sparingly soluble in the ordinary organic solvents. It represents from 23 to 25 per cent. of iodine. It is used as a substitute for the alkaline iodides and presumably has the same advantages as the official calioben.

Origanum. *Wild Marjoram. Marjolaine sauvage,* Fr. *Wilder Majoran* (*Meiran*), G.—Two species of *Origanum* (Fam. *Labiatæ*) have been used in medicine. *O. marjorana* L. (*Majorana hortensis* Moensch) or *sweet marjoram,* and *O. vulgare* L., or common marjoram. The former, which is widely used as a seasoning herb, grows wild in Portugal and Andalusia, and is cultivated as a garden herb in other parts of Europe and in the United States. *Sweet marjoram* has a pleasant odor, and a warm, aromatic, bitterish taste, which it imparts to water and alcohol. By distillation with water it yields a volatile oil. It is tonic and gently excitant, but is used more as a condiment than as a medicine. In domestic practice its infusion is employed to hasten the tardy eruption in *measles* and other exanthematous diseases.

Sweet marjoram is a perennial herb indigenous to the Mediterranean region and Asia. In this country it grows along the roadsides, and in dry, stony fields and woods, from Pennsylvania to Virginia, and is in flower from June to October; but is not very abundant, and is seldom collected for use in the wild state.

The parts used consist of the dried leaves but parts of the flowering tops are usually admixed with these. Most of the drug is imported from France, Spain and Germany.

Sweet marjoram imported during recent years from Europe was found to be adulterated by mixing with it broken fragments of leaflets of the poisonous *Coriaria myrtifolia.* (See LaWall, *Proc. Penna. Pharm. Assoc.,* 1917, xl, 241.)

Two kinds of *oil of origanum* are now known commercially: the Trieste oil, of dark color and high specific gravity, and the Smyrna oil, of lighter color, lower specific gravity, and milder taste. The former contains from 60 to 85 per cent. of carvacrol, $C_{10}H_{14}O$, a trace of another phenol, and cymene, $C_{10}H_{14}$. The latter contains from 25 to 60 per cent. of carvacrol and, in addition, linalool and cymene. The specific gravity of the Trieste oil ranges from 0.94 to 0.98, while that of the Smyrna oil is from 0.915 to 0.945. (Gildemeister and Hoffmann, *Aetherische Oele,* pp. 813, 814; see also *Schim. Rep.,* 1913, 76.)

The *French oil of marjoram* is said to be distilled from *Clinopodium Nepeta* (L.) Kze. (*Calamintha Nepeta* Link. and Hoffm.). It is colorless, but gradually turns yellow on exposure. It is neutral in reaction, sp. gr. 0.904 at 16° C., and optical rotation $[a]_D = + 18° \ 39'$ in chloroform solution. On fractionating, three constituents were isolated, *lævo-pinene, calaminthone,* and *pulegone. Calaminthone* is a new ketone, $C_{10}H_{16}O$. (See *P. J.,* March, 1903.)

Origanum floribundum, of Algeria, yields largely of a volatile oil containing 25 per cent. of thymol. (*P. J.,* Feb., 1903.)

Oroxylon. *Oroxylon indicum* Vent. (Fam. *Bignoniaceæ.*)—This bark yielded by a tree indigenous to Southern Asia is said to be not only a tonic and astringent, useful in *diarrhea,* but also a powerful sudorific. A yellow crystalline substance, *oroxylin,* has been separated from the bark by Naylor and Chapman (*P. J.,* Sept., 1890), and from the seeds by Hooper (*P. J.,* vol. lxi). The seeds have been used in veterinary medicine.

Orpiment. *King's Yellow.* As_2S_3.—A native *arsenic trisulphide.* It is in masses of a brilliant lemon-yellow color, composed of flexible laminæ, and slightly translucent. It exists in various parts of the world, but is obtained for use from Persia and China. (Guibourt.) It is sometimes mixed with realgar, which gives it a reddish or orange hue. A similar sulphide may be made artificially by passing hydrogen sulphide through a solution of arsenic trioxide in hydrochloric acid or by fusing together equal parts of arsenic trioxide and sulphur. (Turner.) In Germany, according to Guibourt, it is prepared by subliming a mixture of these two substances. In this case, however, it retains a large portion of the acid undecomposed, and is therefore highly poisonous. Guibourt found a specimen which he examined to contain 94 per cent. of arsenic trioxide and only 6 per cent. of the trisulphide.

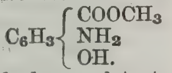
Orpiment is an ingredient of certain depilatories. *Atkinson's depilatory* is said to consist of one part of orpiment and six parts of quicklime, with some flour and a yellow coloring matter. (*Ann. Ch. Ph.*, xxxiii, 348.) But this arsenical sulphide is chiefly used in fireworks and as a pigment.

Orsudan. *Sodium 3-methyl-4-acetylaminophenylarsenate.*—This is soluble in three times its weight of water, and contains 25.4 per cent. of arsenic.

Orsudan has been brought forward as a means of obtaining the anti-syphilitic action of the organic compounds of arsenic. Although favorable results have been reported, the experience of Lane (*B. M. J.*, 1910, ii, p. 599), who reports a case of permanent total blindness following its use, would make one hesitate greatly before employing it. The *dose* ordinarily administered is ten grains (0.65 Gm.) deeply injected into the muscles on alternate days until ten doses have been given.

Orthoform. *Orthocaine.* *N. N. R.* 1924.

Methyl amino-paraoxybenzoate.



$$C_6H_3\begin{cases}COOCH_3\\NH_2\\OH.\end{cases}$$

This compound forms a white, odorless and tasteless powder, almost insoluble in water, easily soluble in alcohol, melting at 141°–143° C. It is sometimes called *orthoform-new* to distinguish it from a closely similar compound which was formerly used.

Orthoform was introduced into practical medicine by Einhorn and Heinz (*M. M. W.*, 1897). Its hydrochloride is soluble in water, but is so acid in its reaction as to interfere with its use.

The physiological action of orthoform is only so far made out as to show that, probably on account of its insolubility, it has very little influence upon the system whether given by the stomach or hypodermically, Heinz having found that ninety grains produce no distinct symptoms in the lower animals, and seven hundred grains have been applied to a facial ulcer in a week without injurious effect (*L. L.*, 1897); also, according to Neumayer (*M. M. W.*, xliv, 1897), sixty grains taken by a man in the course of a day produced no symptoms whatever, not even evidences of gastro-intestinal irritation.

The chief value of orthoform is as a local anesthetic. Because of its insolubility its field of usefulness is practically the same as that of benzocaine (see Part I). The studies of Sollmann (*J. P. Ex. T.*, 1919, xiii, 429) have shown that at least as far as the effects on mucous membranes are concerned, orthoform is decidedly the weaker. According to Neumayer, its local analgesic action is not accompanied by abolition of the sense of touch.

Orthoform has been widely employed to relieve the *pain* in various ulcerated conditions such as *tuberculosis, laryngitis, cancerous sores*, etc. In *keratitis* with ulceration, Boisseau commends an ointment made with one drachm each of lard and lanolin and twenty-four grains of orthoform. In many cases orthoform may also be added with advantage, on account of its anesthetic properties, to ointments containing medicinal substances. Böttcher (*B. K. W.*, 1919, lvi, 1084) recommends a 10 per cent. ointment in *pruritus vulvæ.*

Gustav Spiess found that insufflations into the posterior part of the pharynx may greatly alleviate the paroxysms of *whooping cough.*

Internally, orthoform in *doses* of eight grains (0.5 Gm.) has been used with asserted good results in *cancerous* and other *ulcerations of the stomach* and has been found useful in the treatment of *gastralgia.*

Externally, orthoform may be used either as a dusting powder, ointment or solution.

According to Yonge (*B. M. J.*, i, 1898), for many purposes the saturated solution of orthoform in collodion is most effective. In diseases of the larynx the parts may be sprayed with a solution of five grains of orthoform and fifty minims each of alcohol and water, which soon coats the diseased surface.

Orthoform has been believed to be actively antiseptic, but Lichtwitz and Sabrazes (*B. M.*, xi, 1897) found that bouillon saturated with it was still capable of serving as a culture medium. The antiseptic influence of orthoform is probably due to its decomposition by ulcerated surfaces.

Occasionally orthoform produces marked irritation and even violent inflammation at the seat of its application, and several cases have been reported in which it has produced sloughing, which has been compared to that caused by pure phenol. According to the majority of clinical reports, orthoform is of little value except as a local remedy, though relief has been claimed from it in the treatment of *syphilitic headaches.*

Doses of five to ten grains (0.32–0.65 Gm.) may be given three to four times a day.

Orthosiphon. *Orthosiphon stamineus* Benth. *Java Tea.* (Fam. *Labiatæ.*)—This drug occurs in commerce in the form of small, oval, finely toothed, green leaves, rolled up like tea. Van Itallie has discovered in it a volatile oil and a crystalline glucoside, *orthosiphonin*, and potassium salts. (*Ph. Ztg.*, Sept., 1886; see also *Répertoire de Pharm.*, 1887, 191.) It is said to be a powerful diuretic, and is highly recommended in *gravel*, and *ascites.* It has also been used in *diabetes.* The *dose* is from fifteen to thirty grains (1.0–2.0 Gm.) a day.

Ortizon. *Perhydrit, Peraquin.*—Under these names has been introduced a combination of hydrogen dioxide and urea containing about 35 per cent. of hydrogen dioxide. This occurs as a white crystalline powder without odor, permanent in dry air and soluble in 2.5 parts of water, the hydrogen dioxide being split off by solution. It is intended as a convenient method of carrying hydrogen dioxide for the preparation of solutions. Bactericidal properties of the solutions prepared from this compound have been used by Ungermann. (*Hyg. R.*, 1913, p. 1137.)

Osha Root.—This is the root of *Ligusticum filicinum* Wats. (Fam. *Umbelliferæ*), a perennial herb indigenous in Utah and neighboring States and known as *Colorado cough root.* It was formerly used as an expectorant. H. Haupt found in it an acid, *oshaic acid*, closely resembling angelic acid. (*A. J. P.*, 1867, 1868, 1873.)

Osmic Acid. *Osmium Tetroxide. Osmic Anhydride.* OsO_4.—A volatile, odorous, crystalline compound, produced by the action of nitrohydrochloric acid on osmium or either of its lower oxides.

Its vapor is very pungent and poisonous, attacking the eyes and respiratory organs. Claus recommends as an antidote to its action cautious inhalation of hydrogen sulphide. Osmic acid melts to a colorless liquid at 90° C., softening at a temperature of 35° C. It is slowly soluble in water; soluble in alcohol and ether; but these solutions are unstable, depositing black *osmic hydroxide*, $Os(OH)_4$. *Potassium osmate*, $K_2OsO_4 + 2H_2O$, is made by adding potassium hydroxide to an alcoholic solution of osmium tetroxide, and separating the crystals by careful evaporation. In the form of deep, garnet-red crystals, readily soluble in water, but decomposing when in solution or moist air; permanent in dry air. It is incompatible with organic substances, phosphorus, ferrous sulphate and iodides.

Osmic acid is used largely as a histological stain. We have no definite knowledge as to its influence upon the animal system when given in small doses. It has, however, been used internally especially in the form of potassium osmate in *rheumatic affections*, such as *sciatica*, and in *epilepsy*. The *dose* is one-sixtieth of a grain (0.0011 Gm.) at short intervals up to a daily dose of one-quarter of a grain (0.016 Gm.). In 1887 Stekoulis (*L. L.*, Aug. 13, 1887) suggested the injection along the course of the nerve trunks for the relief of *sciatica*. The method has been extended to include other painful diseases of the peripheral nerves, such as *tic doloureux*. According to Hammerschlag (*A. K. C.*, 1906, lxxix), while it generally gives temporary relief it rarely causes permanent cure. From five to fifteen minims (0.32 to 1 cc.) of a 1 to 2 per cent. solution are injected immediately into the nerve trunk. Auerbach (*Journ. of Laryngology and Rhinology*, June, 1891) recommends osmic acid for the destruction of morbid growths.

Ovogal. *N. N. R.* 1924.—This is a product obtained by the combination of bile acids with egg albumen. Alkalies dissolve *ovogal* with decomposition into its primal constituents. Ovogal is a yellowish-green powder, insoluble in water and acid solutions, but in the presence of alkalies it dissolves with decomposition. It therefore should not be prescribed in combination with alkalies.

It has long been well known that the salts of the bile are the most potent stimulants to hepatic secretion that we possess and this combination of cholic acid with albumin has been shown by Worner (*Med. Klin.*, 1906, p. 547) to increase the secretion of bile. The favorable results obtained by him in *intestinal dyspepsia, atonic constipation, acute* and *chronic catarrh of the biliary passages* has been confirmed by a number of authors. From ten to fifteen grains (0.65–1.0 Gm.) may be given four or five times a day. Rahn (*M. M. W.*, 1907, No. 10) proved the harmlessness of the drug by taking himself one and one-half teaspoonfuls without any evil results. It may be administered either as a dry powder or enclosed in capsules.

Oxalic Acid. *U. S.* Reagent (see Part III). *Acidum Oxalicum. Acide oxalique ou carboneux*, Fr. *Oxalsaure, Kleesaure*, G. $H_2C_2O_4.2H_2O = 126.05$.

This acid is found both in animals and vegetables. It is generated occasionally in disease, and it may be deposited in the bladder as calcium oxalate, forming the *mulberry calculus*. In vegetables, it occurs in a free state in the bristles of the chick pea (*Cicer arietinum* L., Fam. *Leguminosæ*), as an acid potassium oxalate in *Rumex Acetosa* L. (Fam. *Polygonaceæ*), or common sorrel, in *Oxalis Acetosella* L. (Fam. *Oxalidaceæ*), or wood sorrel, in *Chenopodium Quinoa* Willd. (Fam. *Chenopodiaceæ*), *Amaranthus caudatus* L. (Fam. *Amaranthaceæ*), *Mesembryanthemum crystallinum* L. (Fam. *Aizoidaceæ*), and in many other plants. It is said to be formed in the leaves. (*J. Chem. S.*, 1886.) Combined with calcium in microscopic crystalline forms, it is abundant in almost every portion of the vegetable kingdom.

Saccharomyces Hausenii has the property of producing a fermentation which forms oxalic acid out of sugar.

Many substances yield oxalic acid by the action of nitric acid, such as molasses, rice, potato starch, gum, wool, hair, silk, and many vegetable acids. This reaction was formerly the chief commercial source. For details of this process, see 15th edition *U. S. D.*, p. 90. The yield of oxalic acid from a given quantity of material has been much misunderstood. If properly treated with nitric acid, 100 lbs. of good sugar will yield from 125 to 130 lbs. of oxalic acid, and the same weight of molasses from 105 to 110 lbs.

The oxalic acid of commerce is now obtained by heating sawdust or wood shavings with a mixture of sodium hydroxide and potassium hydroxide. Sodium hydroxide alone will not generate the acid, and potassium hydroxide is too costly to be used by itself for the purpose; but Dale ascertained that, by mixing the two in the proportion of two molecules of sodium hydroxide to one of potassium hydroxide, the same or an even better result was obtained than from the latter alone. The mixture of caustic alkalies and sawdust is made into a thick paste and then heated for several hours to a temperature which is gradually brought to 240° C. The gray mass is then washed with sodium carbonate, whereby the potassium is removed as carbonate, the less soluble sodium oxalate remaining. This is converted into calcium oxalate by milk of lime, and the calcium salt then decomposed with sulphuric acid and the resulting crude oxalic acid purified by recrystallization.

Oxalic acid occurs in colorless crystals, efflorescent in dry air, possessing considerable volatility, and a strong, sour taste. It is soluble in 4.5 parts of dehydrated alcohol, in 2.5 parts of alcohol, and almost insoluble in ether, chloroform, benzene, and petroleum benzin. The crystals should dissolve in ten parts of water at 25° C.; soluble in 3 parts of boiling water.

It fuses in its water of crystallization at 98° C., although continued exposure to a heat of from 60° C. to 70° C. will render it perfectly anhydrous. Solutions of oxalic acid at 100° C. lose acid by sublimation, and at 157° C. the anhydrous acid itself sublimes rapidly. If the heat rise to 160° C., partial decomposition, with consequent loss of acid, occurs. (See also *Oxalic Acid* under Reagents, Part III.)

It is a dibasic acid and combines with salifiable bases, forming oxalates. The most important of these are the three *potassium oxalates*, severally called *oxalate*, $K_2C_2O_4 + H_2O$, *binoxalate*, $KHC_2O_4 + H_2O$, and *quadroxalate*, $KHC_2O_4.H_2C_2O_4 + 2H_2O$, and *calcium oxalate*. Potassium binoxalate and quadroxalate, both popularly called *salt of sorrel* (*sal acetosella*), are also sometimes called by the dangerous misnomer *essential salt of lemons* (or *sal limonis*), are employed for removing iron mold from linen, and act by their excess of acid, which forms a soluble salt with the ferric oxide constituting the stain. Salt of sorrel is also used extensively in the bleaching of straw goods and other vegetable fibers. Oxalic acid is used for removing ink stains and iron mold, for cleaning the leather of boot tops, and for discharging colors in calico printing. Prussian blue dissolves in aqueous oxalic acid to clear blue liquid which is often employed as a *blue ink.*

Oxalic acid is a powerful and rapidly acting poison. From the general resemblance of its crystals to epsom salts fatal mistakes have occurred. It may, however, at once be distinguished by its sour taste. It acts on the economy in two principal ways, according as its solution is concentrated or dilute. When concentrated it causes great pain, followed by violent retching with bloody vomit, then sudden dulness, languor, and great debility, and finally death without a struggle. When dissolved in 20 times its weight of water oxalic acid possesses no corrosive and scarcely any irritating properties but is still capable of causing death by its depressant action upon the central nervous system and the heart. In such cases the symptoms have been great muscular weakness with twitchings of the muscles and more rarely convulsions; the respirations become slow, pulse weak and there maybe either pallor or cyanosis of the face. In fatal cases coma precedes the termination.

After death from oxalic acid the mucous membranes of the alimentary canal are either soft and pultaceous or entirely destroyed. The stomach usually contains a dark fluid, resembling coffee grounds, consisting chiefly of altered blood. In a few cases no morbid appearances have been discovered.

In 1879 Kobert and Kürsner announced that in animals oxalic acid may produce glycosuria; this has since been confirmed, and Sarganeck has noted the symptom in human poisoning, so that it is probably a constant phenomenon.

In the treatment of poisoning by oxalic acid, the remedial measures must be employed with great promptitude. Vomiting may be encouraged and the stomach tube used, but unless the antidote be at hand death will rarely be averted. The proper antidote is chalk or magnesia, mixed with water, and as soon as either can be procured, it must be administered in large and repeated doses. In many cases whitewash or some other preparation of lime can be obtained sooner than chalk, and should be at once administered; tooth powder can usually be obtained quickly, and generally (not always) consists chiefly of calcium carbonate. These substances act by forming with the poison an insoluble, inert calcium or magnesium oxalate. The soluble salts of oxalic acid, as ammonium oxalate and potassium oxalate, are equally poisonous, and the antidotes for them are lime water or solutions of magnesium salts.

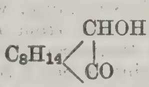
Oxalic acid has been strongly recommended by Poulet and by Marsh (*T. G.*, 1891) in *amenorrhea.* Marsh has also found it serviceable in *cystitis.* It is a very active germicide, and its solution is used in conjunction with potassium permanganate for the disinfection of the surgeon's hands. *Dose,* half a grain (0.032 Gm.) from three to five times a day.

Oxalis. *O. Acetosella* L. (Fam. *Oxalidaceæ.*) *Wood Sorrel. Acetosella. Allêluia, Surelle, Pain de Coucou,* Fr. *Sauerklee, Hasenklee,* G.—Wood sorrel is a small, creeping plant having radical leaves and scapes from 5 to 15 cm. high. It is a native of Europe and naturalized in the Northern United States. Other indigenous species of *oxalis* possess similar properties to *O. Acetosella.* The whole herbaceous portion may be used.

Wood sorrel is without odor, and has an agreeable sour taste. It owes its acidity to *acid potassium oxalate* or *potassium binoxalate* (HKC_2O_4).

The fresh plant, eaten raw, is useful in *scurvy.*

Oxalis crassicaulis Zucc., a Peruvian species, yields edible tubers and, by expression from its leaves, a very sour and astringent juice, which is employed, in the form of syrup, in *hemorrhages, chronic catarrh,* and *gonorrhea,* with asserted advantage.

Oxycamphor.  $C_8H_{14}\left\langle\begin{array}{l}CHOH\\ \;|\\ CO\end{array}\right.$. This oxidation product of camphor is a white crystalline powder, melting at from 203° to 205° C. and volatile in a current of steam. Soluble to a slight degree in cold water; more soluble in hot water. It is decomposed by prolonged exposure to the air.

It is stated that oxycamphor acts as a stimulant to the cardiac muscle and also to the centric and peripheral vasomotor nervous system, and as a calmative to the respiratory centers. It has been used with asserted good results for the relief of both cardiac and pulmonic *dyspnea. Dose,* from eight to fifteen grains (0.5–1.0 Gm.). A fifty per cent. solution of *oxycamphor* in alcohol is sold under the trade name of *oxaphor.*

Oxychinaseptol. *Diaphtherin.* $C_6H_4(SO_2)\text{-}\begin{cases}O—NH.C_9H_6(OH)\\ O—NH.C_9H_6(OH)\end{cases}$. This substance is made by uniting two molecules of oxyquinoline, $C_9H_6N\text{-}(OH)$, with one molecule of phenol-sulphonic acid, $C_6H_5(HSO_3)OH$. It occurs in yellowish hexagonal crystals, melting at 85° C., very soluble in water and diluted alcohol. Its solution is decomposed by alkalies. According to the researches of Emmerich (*M. M. W.*, 1892), it is much more powerful as an antiseptic than phenol; two-tenths of one per cent. solution is sufficient to kill the comma or diphtheria bacilli in ten minutes, and three-tenths of one per cent. solution destroys the pus organisms in thirty minutes. It is also asserted that it is practically innocuous to higher animals, the subcutaneous injection of five cubic centimeters of a 5 per cent. solution producing no serious effects upon guinea-pigs. It has been used in practical surgery, especially by Kronacher, who has employed from ½ to 1 per cent. solution with great satisfaction for the general purposes of the antiseptic treatment of wounds. Such solution produces no irritation except in some cases a momentary burning. Rohrer (*Corresp. f. Schweiz. Aerz.*, Nov., 1892) commends the remedy as a local application in disease of the nasal mucous membrane. The solution does not stain the hands, but forms on steel instruments a black deposit which is readily washed off.

Oxydendrum. *Oxydendrum arboreum* (L.), DC. *Sour Wood. Elk Tree. Sorrel Tree.* (Fam. *Ericaceæ.*)—The leaves of this indigenous tree possess an acrid taste, whence the common names of the tree, and are said by eclectic physicians to be a powerful diuretic, useful in *dropsy.* A semi-solid extract may be made, one part representing five of the drug; *dose,* from five to fifteen grains (0.32–1.0 Gm.). Of the fluidextract the *dose* is from a half to two fluidrachms (1.8–7.5 cc.).

Oxysparteine. $C_{15}H_{24}N_2O$.—This is an alkaloidal oxidation product of sparteine, originally described by F. Ahrens (*B. Chem. G.*, 1891, xxiv).

It occurs in white, somewhat hygroscopic needles, melting at about 84° C., soluble in water, alcohol, ether, and chloroform. It has been found by Hurthle (*A. E. P. P.*, 1892) to be a cardiac stimulant, decreasing the pulse rate, but markedly increasing the arterial pressure and heart work. The hydrochloride, which occurs in large needles (often consolidated together) and is very soluble in water, has been used hypodermically by von Oefele in cases of *heart failure.* The *dose* is half a grain (0.032 Gm.), rapidly increased to one and a half grains (0.096 Gm.). The system is said soon to become accustomed to it.

Ozokerite.—This substance, which is found in Galicia, in Austria, and from near the Caspian Sea, as well as in Southern Utah, is in its crude state, a solid, varying in color from a dirty green to nearly black. When purified by treatment with sulphuric acid and alkali and subsequent filtration, while melted, through bone black or other filtering medium, it is a hard, white, spermaceti-like substance, and is extensively used in England as well as in Austria in the manufacture of candles. (See *Ceresin.*) It is a mixture of natural paraffins. It is said to resemble tar in its therapeutic properties, and, mixed with glycerin or linseed oil, has been employed in *skin diseases* as a substitute for that remedy. (See *Am. Drug.*, 1892, 40.)

Ozone (O_3) is recognized as an active modification of the element oxygen. It is considered to differ from the common form in being more condensed and at the same time more active. It has a peculiar odor, somewhat resembling that of diluted chlorine. *Ozone* changes gradually at the ordinary temperature into common oxygen, and at 237° C. the change is instantaneous. It is one of the most powerful oxidizing agents known, attacking and at once destroying organic substances, such as caoutchouc, paper, cork, etc. It also decolorizes most organic pigments. It is slightly soluble in water, imparting to water its peculiar odor, as well as its oxidizing power. According to Carius, 1000 volumes of water dissolve 4.5 volumes of ozone, and it is much more soluble in certain ethereal oils. The power of these latter as carriers of oxygen and deodorants is thus explained. At one time ozone was thought to be peroxide of hydrogen, but Marignac and De la Rive demonstrated its true nature. Hautefeuille and Chappius (*C. R. A. S.*, xciv, 1249) succeeded in producing "liquid ozone" by applying a pressure of 125 atmospheres to richly ozonized oxygen at −100° C. It is stated to be of a dark indigo color.

Ozone has not been obtained free from oxygen; indeed, it is probable that 1 per cent. of ozone is the highest concentration reached in its production. It is prepared by the decomposition of water by the battery, by the passage of the silent electric discharge through air or oxygen, by the slow oxidation of phosphorus in moist air and in other cases of slow combustion, and, lastly by the action of sulphuric acid upon barium dioxide and potassium permanganate.

The presence of ozone in the air or in gases is indicated by its action on paper moistened with potassium iodide and starch solution. This is turned blue, and if reddened litmus paper is moistened with potassium iodide, this is also blued. Another test is found in the use of paper moistened with an alcoholic solution of guaiacum, which is changed to light blue. Ozone may be readily determined in extreme dilution by the decolorizing effect which it has on fluorescein solution.

Its presence in the air is now fully established, although in thickly inhabited districts it is almost always absent, as it is reduced to ordinary oxygen by the organic emanations constantly sent out into the air. In the air of the country, and especially in sea air, the presence of ozone can often be recognized by its peculiar odor. The probable cause of the formation of ozone in the air has been pointed out by Gorup-Besanez, as he has shown that ozone is invariably formed when water evaporates, and it is to this source, rather than to the electrical discharges, that the production of ozone must be traced. Ozonizing machines, in which the gas is generated by the passage of an electrical spark, are used in some industrial establishments and cold storage plants for the purpose of deodorizing and purifying the air.

Contrary to the common superstition ozone has no disinfectant virtues. There is no evidence that it has any more therapeutic use than ordinary oxygen.

Pæonia. *Pæonia officinalis* L. *Peony. Pentecost Rose. Pivoine*, Fr. *Gichtrose, Pfingstrose*, G. (Fam. *Ranunculaceæ.*)—The subterranean portion of this garden peony consists of a thick rhizome which sends off in all directions spindle-shaped roots, which gradually taper into thread-like fibers, by which they hang together. It has a strong, peculiar, disagreeable odor, and a nauseous taste, which is at first sweetish, and afterwards bitter and somewhat acrid. The odor is lost, or much diminished, by drying. Peony "root" was in very great repute among the ancients as a charm and as a medicine in *epilepsy.* In modern times it has been used as an antispasmodic. Its expressed juice is milky and of a disagreeable odor and taste. According to Rochebrune (*Toxicolog. Africaine*, i), it contains an active alkaloid, *pæonine* which has been used as a styptic. The *seeds* are roundish-oval, about as large as a pea, externally smooth, shining, and nearly black, internally whitish, inodorous when dry, and of a mild oleaginous taste. By some authors they are said to be emetic and purgative, by others antispasmodic. The *dose* of the fresh root or seeds is from two drachms to an ounce (7.7–31.0 Gm.), boiled in a pint of water down to half a pint, which should be taken daily. It is said to be less active when dried.

W. Will obtained from an aqueous distillate of the root of the Japanese *Pæonia Moutan* Simson, an aromatic ketone in colorless crystals. (*B. Chem. G.*, xix, 1777.) According to Nagae, this substance has the formula $C_9H_{10}O_3$. (*Ibid.*, xxiv.) It has been prepared by Schimmel & Co., under the name of *peonol.* It has a pleasant aromatic odor, and crystallizes in large needles. No essential oil was found in the root. (*Schim. Rep.*, Oct., 1890.) Dragendorff has found in the seed of *P. peregrina* Mill., a fixed oil, an alkaloid, and *pæonic acid.* (*Jahresb.*, 1879.)

Palicourea. *Palicourea rigida* H. B. K. (Fam. *Rubiaceæ.*)—The leaves of this tree are used in Brazil as a diuretic and diaphoretic. In 1866 Peckholdt found in them an alkaloid and three organic acids. One of these acids consisting of a yellow, oily liquid with an overpowering odor, was found to be distinctly poisonous, one drop injected into a pigeon being enough to cause death. This was called *myotonic acid.* A crystalline *palicouric acid*, an amorphous tannin, and another amorphous non-toxic bitter principle were also isolated. Santesson has confirmed the presence of an alkaloid. (*A. Pharm.*, 1897, ccxxxv.)

Palladious Chloride. *Palladous Chloride. Palladii Chloridum.* $PdCl_2$.—This is a blackish-brown mass, soluble in water, which has been recommended as a reagent for determining the malic acid in wine. It has been used to some extent in medicine as a local germicide, and has been recommended in the treatment of *phthisis* in *doses* of one-fourth to one-third of a grain (0.016–0.021 Gm.) three or four times a day.

Under the name of *leptynol* an emulsion of *palladium hydroxide*, $PdOH_2$, has been employed as an injection for the treatment of *obesity* by Kauffmann. (*M. M. W.*, 1913, p. 1260.) Two cc. of this preparation, containing 50 mgm., are injected once a week into the abdominal fat.

Panase. *N. N. R.* 1924.—This is a combination of the digestive enzymes of the pancreas, derived from the pancreatic glands of the pig. It is a light, yellowish-white powder, having a slight animal odor and a somewhat mucilaginous taste. It is not entirely soluble in water or in glycerin, due to a small amount of proteid present. This can, however, be filtered out without impairing the digestive quality of the solution. *Panase* is incompatible with strong alcohol, acids, alkalies and other substances which destroy the activity of ferments. It is used for the same purposes as pancreatin. *Dose*, two grains (0.13 Gm.).

Panbotano Bark.—The root of the Mexican leguminous tree, *Calliandra Houstoni* Benth., has been highly recommended by Valude as an antiperiodic, although Villejean was not able to find in it either an alkaloid or a glucoside. (*Journ. de Sci. Méd. de Lille*, 1890.) Pouchet (*Nouv. Rem.*, 1896), however, states that he has found in panbotano, besides a saponin, an alkaloid which produces death by systolic arrest of the heart. Both Dinau (*Thèse de Paris*, 1896) and Crespin confirm its antiperiodic value. (*B. G. T.*, Aug., 1895.) A tincture representing two ounces of the root is taken in four *doses* during twenty-four hours.

Pancreon (*pankreon*) is a preparation obtained by the action of tannic acid on pancreatin containing 8 per cent. of the former in combination. It is a grayish, odorless powder soluble in water and acidulated liquids and is affirmed to have strongly trypsilytic, amylolytic, and emulsifying properties. It is further claimed to be superior to pancreatin in not losing its activity in the stomach. *Dose*, eight to fifteen grains (0.5–1.0 Gm.).

Pangium. *Pangium edule* Reinw. (Fam. *Bixaceæ.*)—This East Indian tree, which is said to possess anthelmintic and narcotic properties, and to be capable of causing death, according to Blume, contains an alkaloid resembling *menispermine.*

Pantopon. *N. N. R.* 1924. **Omnopon.**—Sahli introduced, in 1908, this combination of the alkaloids of opium as being more actively narcotic in proportion to its poisonous properties than morphine and having the advantage over crude opium that it was fitted for hypodermic administration. Both Straub (*Biochem. Zeit.*, 1912, xli, p. 419) and Macht (*J. P. Ex. T.*, 1915, vii, p. 339) have shown that narcotine is stimulating to the respiratory center and therefore antagonistic to morphine and codeine. There are, therefore, scientific grounds for this combination and the conclusions of Sahli have received considerable clinical confirmation. The *dose* of *pantopon* should be about double that of morphine. From one-sixth to one-third of a grain (0.010–0.021 Gm.) may be given by mouth.

A similar combination of opium alkaloids is sold under the name of *toponal* (*D. C.*, 1915, p. 580).

Pao-Pereira Bark. *Pereiro Bark.*—Under this name a bark is employed in Brazil as a febrifuge. It is supposed to be the product of *Geissospermum læve* (Vell.) Baill. (Fam. *Apocynaceæ*). O. Hesse (*B. Chem. G.*, 1893, xxvi, 1045) has found an alkaloid, *geissospermine*, $C_{19}H_{24}O_2N_2 + H_2O$, in it, but he seems to have been preceded in this discovery by Santos (*A. J. P.*, 1878, 184.) Peretti has discovered in the root a second alkaloid, *pereirine*, $C_{19}H_{24}N_2O$, which, according to Guimaraes (*B. M. J.*, vol. i, 1887), in sufficient doses causes paralysis with elevation of temperature, ending in death. It has been given to man as an antiperiodic in *doses* of thirty grains (2.0 Gm.) a day. (See also *A. J. P.*, 1886, 278.) Later a third alkaloid, *vellosine*, $C_{23}H_{28}O_4N_2$, was found by Freund and Favet (*Ann. Ch. Ph.*, 1894, cclxxxii, 247). This forms colorless crystals, melting at 189° C., insoluble in water, easily soluble in alcohol and ether. In concentrated nitric acid it dissolves with a purplish-red color, which is very stable.

Papaya. *Melon Tree. Papaw.*—The *Carica Papaya* L. (Fam. *Caricaceæ*) is an unbranched tree growing to the height of 20 feet, with large palmately 7-lobed leaves and fruits which frequently attain the size of a human head. It is commonly cultivated in tropical countries for the sake of its fruit. The ovoid fruit sometimes attains a length of 30 cm. and weight 4 or 5 kilogramme. This tree should not be confused with the indigenous *Asimina Triloba* which is, unfortunately, commonly known as the American papaw; there is neither botanical nor medicinal relationship between these trees (see *Asimina*). According to Peckholdt (*P. J.*, Nov., 1879), the milky juice is contained in all parts of the tree, but in such small quantity, save in the unripe fruit, that it is always procured from the latter. One fruit will yield about 33 Gm., which is obtained by scratching through the skin in various places; the process does not interfere with the ripening of the fruit, but it is said that the seeds will not germinate. The milk-juice is collected in porcelain-lined receptacles and allowed to evaporate to a granular condition whence it is marketed as crude papaïn. The juice has an acid reaction, an astringent bitterish taste, and a sp. gr. of 1.023. Upon standing for a few minutes it separates into two parts, an aqueous liquid and a white, somewhat coagulated pulpy mass. In the aqueous portion is an albuminous substance, possessed of enzymic properties, to which the names of *papaïn* and *papayotin* have been given. According to the researches of S. H. C. Martin, papaw juice contains besides papaïn, a milk-curdling ferment, globulin, albumin, and two phytalbumoses. No peptones occur in the juice, but leucine and tyrosine are present. (*J. Chem. S.*, 1886, 642; see also *P. J.*, 1885, 129.) In a representative preparation the ferment action seems to be most marked when all the proteids are associated together in the natural form. In its action upon albumin the enzyme of the papaw produces substances which have a close relation to those produced by tryptic and peptic digestion. In the action of the papaw ferments on milk there is first curdling in which the casein is separated into a soft flocculent precipitate, and afterwards a digestion of the proteids, during which process they are converted into soluble and diffusible products. The amount of starch-converting ferment is not large, but sufficient in the fresh latex to promptly act upon starch paste, thinning it, and converting a portion at least into soluble starch and dextrin. The report of the presence of rennet ferment and pectase requires further investigation.

According to Wurtz, fibrin is dissolved whether the solvent solution be alkaline or acid. Brunton and Wyatt and also Martin affirm, however, that one-half per cent. of hydrochloric acid will prevent digestion, but Albrecht reasserts that hydrochloric acid hastens the action of the ferment, and states that the official preparation in use in Paris hospitals is an acid one. In order entirely to convert fibrin into pure peptone so that nitric acid will produce no precipitate, the proportion of the ferment should be as great as 3 per cent., and digestion must continue for forty-eight hours at 50° C.

The seeds of the papaw tree contain a glucoside, *caricin*, which resembles sinigrin. These seeds also contain the ferment, myrosin, and by the reaction of the two a volatile pungent body is produced, suggestive of oil of mustard in odor. An alkaloid, *carpaine*, $C_{14}H_{25}O_2N$, has been obtained from the leaves by Greshoff; it has been more closely studied by Barger (*B. P. G.*, 1914, xxiv). Physiologically, this alkaloid is said to affect the heart like digitalis. (*A. J. P.*, 1901, 336 and 383.)

Under the name of *papayotin*, *papaïn*, or *papoid*, the dried juice of the *Carica Papaya* is put upon the market. As it occurs in commerce, papaïn is a grayish, fine powder, which in appearance, odor, and taste strongly suggests pepsin. It is frequently adulterated with starch, which is not naturally present in the fruit. Its digestive power is far below the claims formerly made for it. It is asserted for it that, when the stomach is acid, it is much superior to pancreatin, because its action is not markedly affected by contact with the acid. In experiments made by H. C. Wood with a papoid from one of the most renowned manufacturers no digestion occurred, and it is probable that much of the article of commerce is inert. It has been used as an internal medicine in *dyspepsia* and *gastric catarrh*, and as a local application for the destruction of false membranes, *warts*, *tubercles*, walls of old sinuses, and even of *epithelioma*. (See Branch, *B. M. J.*, 1907.) Jacobi affirms (*T. G.*, vol. ii) that diphtheritic membranes are dissolved in a few hours by the hourly application of a mixture of one part of papaïn with two parts each of water and of glycerin. It is stated that from time immemorial the fresh leaves of the papaya plant have been used by the Indians to wrap meat in to make it tender, and as a dressing to *foul wounds*. According to Brunton, the *dose* is from five to ten grains (0.32–0.65 Gm.). Injected into the venous circulation it acts as a powerful poison, of which a single grain is sufficient to kill a rabbit.

Paradimethylaminobenzaldehyde (Dimethyl-p-amino-benzaldehyde), $(CH_3)_2N.C_6H_4.CHO$.—"Colorless scales fusing at 73° C.; soluble in hot water. The addition of an alcoholic solution of benzidine (1 in 100) to a slightly acidified solution of paradimethylaminobenzaldehyde produces a brick-red precipitate after standing." *U. S. IX.*

It is used in testing urine for bile pigments (see *Diagnostic Reagents.*)

Paralaudin.—This is stated to be a *diacetyldihydromorphine* and is used as a substitute for diacetyl-morphine and in the same dose.

Parameria. *Parameria vulneraria* Radlkofer. (Fam. *Apocynaceæ.*)—This tree yields the *Balsamo de Taguloway* of the Malays. (See *A. Pharm.*, Nov., 1885.)

Paramidoacetophenone. $C_6H_4.NH_2.CO.CH_3$.—This substance occurs in crystals soluble in boiling water, alcohol, and ether, and melting at 106° C. It has been used in the practical application of Ehrlich's *diazo test.* (See *Diagnostic Tests.*)

Paramorfan. *Dihydromorphine hydrochloride*, $C_{17}H_{21}O_2N.HCl$.—It is a white, crystalline powder, soluble in water and slightly in alcohol. It is used for the same purposes as morphine. It is given in *doses* of from one-sixth to one-third of a grain (0.01–0.02 Gm.).

Parsley. *Ache, Persil*, Fr.; *Petersilie*, G.; *Prezzemolo*, It. *Petroselinum sativum* Hoffman (*Apium petroselinum* L.).—The *common parsley*, which is used extensively as a culinary herb, is a hardy biennial bearing pinnately-compound leaves which in the cultivated varieties are greatly divided. During its early stages the leaves are arranged in rosettes and the plant is six inches or less above the ground; the flowering and fruiting plant, however, is from 2 to 3 feet in height. It is a native of Sardinia and was introduced into England in 1548, and is naturalized in salt marshes on the coast of California. It has been cultivated as a sweet herb since earliest times and was used by the ancient Greeks and Romans as a part of their festive garlands on account of retaining its color so long.

Both the root and the fruit of parsley have been used in medicine. The fruit, often incorrectly called *parsley seeds*, consists of two dried mericarps which in the fresh state are joined along the center commissure. The U. S. P. IX described them as follows: "Mericarps usually separated, ovoid-crescent shaped, from 2 to 3 mm. in length and about 1 mm. in diameter; externally grayish-brown, becoming grayish or brownish on aging, having 5 yellowish, filiform, prominent ribs, alternating with the coarsely roughened furrows; in transverse section nearly hemispherical, the commissural surface with 2 vittæ or oil-tubes, the dorsal surface usually with a single vitta, occasionally 2 vittæ in the groves between the primary ribs; endosperm large, oily, enclosing a small embryo; odor and taste characteristic and aromatic, especially when bruised. Under the microscope, sections of Parsley Fruit show an epidermal layer with thick cuticularized walls having numerous small centrifugal projections; several layers small thin-walled parenchyma cells, being usually considerably collapsed and occasionally containing a rosette aggregate of calcium oxalate; a single, large, brown, elliptical vitta or oil-tube between each of the primary ribs and surrounded by a layer of comparatively large yellowish-brown, tangentially elongated cells; a singe fibrovascular bundle more or less surrounded by a few or occasionally numerous sclerenchymatous fibers; inner epidermis of narrow, thin-walled elongated cells closely cohering with the brownish tabular cells of the seed-coat; commissural surface usually with 2 large vittæ, a very few stone cells and showing a slight separation of pericarp and seed-coat; endosperm of polygonal, thick-walled parenchyma cells containing fixed oil and numerous, small aleurone grains, usually containing a small rosette aggregate of calcium oxalate. The vittæ usually contain yellowish oil globules or a resin-like mass adhering to the walls, and occasionally are divided by a radial wall. The powder is grayish-brown; mostly of large, irregular fragments; cells of endosperm with aleurone grains, each usually containing a rosette aggregate of calcium oxalate, from 0.003 to 0.007 mm. in diameter; fragments with light yellow vittæ and the yellowish-brown cells of the pericarp; fragments with narrow tracheæ and more or less lignified sclerenchymatous fibers." *U. S. IX.*

Parsley root (*Petroselini Radix, N. F. IV*) was described as "The entire fusiform root, measuring up to 20 cm. in length and up to 2.5 cm. in thickness at the crown, or broken or cut into pieces; usually cut lengthwise into two or four sections; externally light yellowish, wrinkled longitudinally, somewhat annulate, root scars distinct and corky; fracture tough when damp, brittle when dry; internally, cortex whitish and characterized by numerous, reddish-brown oleoresin cells, cambium zone distinct and brownish; wood about the same thickness as the cortex, slightly radiate and light yellow. Odor aromatic; taste sweetish and pungent. The powdered drug, when examined under the microscope, shows numerous truncate or somewhat angular starch grains up to 0.03 mm. in diameter, reticulate tracheæ up to 0.06 mm. in width and thin-walled, lignified fibers with simple pores. Parsley Root yields not more than 6 per cent. of ash." *N. F. IV.*

All parts of the plant contain a volatile oil, to which it owes its odor and mainly its taste, as well as its use in seasoning. This oil consists of a hydrocarbon, $C_{10}H_{16}$, probably pinene, and apiol. Braconnot (*B. Chem. G.*, 1876, 1121) obtained from the herb a peculiar substance, resembling pectic acid in appearance, which he named *apiin*. This has been stated to be a glucoside but Joret and Homolle believe it is identical with pectin. It is soluble in hot water and on cooling forms a gelatinous mass. When purified it forms silky needles of the formula $C_{27}H_{32}O_{16}$. *Apiol*, or *parsley camphor* occurs as a white crystalline solid with a faint odor of parsley, insoluble in water but soluble in alcohol, ether and fixed oils. It is the di-methoxymethylene ether of allyl-tetraoxybenzene, $C_{12}H_{14}O_4$.

Ciamician and Silber (*Ph. Post*, 1888, 391) have investigated apiol, and state that the pure substance occurs in white crystals having the composition $C_{12}H_{14}O_4$, melting at 30° C., and boiling at 294° C. *Isapiol, apiolic acid, apiolaldehyde,* and *apion* are decomposition products. They state that isapiol has physiological properties resembling those of pure apiol.

The term "apiol" or "liquid apiol" is often applied to the *oleoresin* (*Oleoresina petroselini* U. S. IX) also often known as *oil of parsley seed.* The method of preparation of this was as follows:

"Parsley Fruit, in No. 60 powder, *five hundred grammes;* Ether, *a sufficient quantity.* Place the parsley fruit in a cylindrical glass percolator provided with a stop-cock and arranged with a cover and a receptacle suitable for volatile liquids. Pack the powder firmly and percolate slowly with ether, added in successive portions until the drug is exhausted. Recover the greater portion of the ether by distillation on a water bath, and, having transferred the residue to a dish, remove the remaining ether by spontaneous evaporation in a warm place, stirring frequently. Allow the Oleoresin to stand without agitation for four or five days, decant the clear liquid portion from any solid residue, and preserve it in well-stoppered bottles." *U. S. IX.*

Parsley root was used chiefly as a diuretic in dropsies and various inflammatory conditions of the urinary organs. Cow (*A. E. P. P.*, 1912, lxx, p. 393) has shown, however, that it has very feeble physiological action.

The oleoresin of parsley contains a number of bodies of considerable physiological power. The most important of these are crystalline apiol, white apiolin, and myristicin. According to the experiments of Lutz (*Bull. Sci. Pharm.*, 1910, xvii, p. 1) the actions of these substances are similar in kind. They produce marked slowing of the pulse with fall of the blood pressure, tremors, and weakness of the extremities, followed by paralysis with epileptiform convulsions and gasping respirations. After death there was found marked congestion in the lungs and in the pelvic organs. Rimini and Dilitala (*Archiv. di. Farmacologia e. Terap.*, 1908, xiv) have shown that apiol produces in the cat fatty degeneration of the liver of the same type as is caused by myristicin (see under *Oleum Myristicæ*). They also noted that it had a direct weakening action on the voluntary muscles.

Apiol has been attributed with the possession of antiperiodic properties, but is chiefly employed in *dysmenorrhea* and other uterine disorders. There is, however, no satisfactory evidence that we know of, either experimental or clinical, that it possesses any real therapeutic value.

Glatard (*Journ. de Med. et Chir. Prat.*, 1910, p. 674) report a case of apiol poisoning in a pregnant woman who took six grammes in a period of forty-eight hours. There was vertigo, nausea and vomiting, urticaria, liver swollen and painful, mild icterus, urine scanty and high colored, but free from albumen; pregnancy was not interrupted. Sardou (*A. G. M.*, 1906) recommends apiolin as an antispasmodic in *intestinal colic.*

The *dose* of parsley-root is about 30 grains (2 Gm.); a fluidextract was formerly official. The oleoresin may be given in doses of five to fifteen minims (0.3–1 cc.).

Parietaria. *Parietaria officinalis* L. *Wall Pellitory. Pariétaire, Perce-muraille,* Fr. *Glaskraut,* G. (Fam. *Urticaceæ.*)—A perennial European herb, growing on old walls and heaps of rubbish. It is diuretic and refrigerant, and was formerly used in urinary complaints and *dropsy*, in the form of decoction or of the expressed juice.

Paris Green. *Schweinfurt Green. Aceto-Arsenite of Copper.* $Cu(C_2H_3O_2)_2.3Cu(AsO_2)_2$.—This substance, which was originally made for a pigment, is now used to an enormous extent for dusting on potato vines to destroy the so-called *potato bug*, or *Colorado beetle, Doryphora decemlineata.* It is made by mixing five parts of verdigris with sufficient water to form a thin paste, and adding to this a boiling solution of four parts of arsenic trioxide in fifty parts of water, keeping the mixture at the boiling temperature, and adding a little acetic acid to cause it to retain a brilliant color. Numerous cases of poisoning have occurred through carelessness in its use as an insecticide. The treatment would be the same as that for poisoning by arsenic.

Parkia. *Parkia biglandulosa* W. and A. (*P. africana* R. Br.) *African Locust. Nitta* or *Nutta Tree. Doura. Houllé. Neretou.*—This is an African leguminous tree, from the dried seeds of which a farinaceous food is prepared by the natives. According to DeRochebrune (*Toxicolog. Africaine,* 1898), it contains a peculiar crystalline alkaloid, *parkine*, which resembles, in its physiological activity, physostigmine.

Parthenium. *Chrysanthemum Parthenium* (L.) Bernh. *Feverfew. Matricaire*, Fr. *Mutterkraut*, G. (Fam. *Compositæ.*)—A tall, strongly scented, perennial, branching herb, with bipinnately divided leaves, the segments being oblong or elliptic-oblong and cut, and small flower-heads arranged in a corymb. It is a native of Europe, but cultivated in our gardens and naturalized in some places. The whole aerial part is used. The plant has an odor and taste analogous to those of chamomile, which it resembles also in the appearance of its flowers and in its medicinal virtues. It yields a greenish volatile oil which boils between 165° and 220° C., and separates on standing, *pyrethrum camphor*, $C_{10}H_{16}O$.

The flower-heads of this and of a closely resembling species, *Matricaria parthenoides* Desf., (*Chrysanthemum parthenoides* Voss), are said to be used in France, to a considerable extent, indiscriminately with those of the true chamomile plant, *Anthemis nobilis*, which they closely resemble, especially when double. They may, however, be distinguished, in this state, by their peculiar odor, their small receptacle, which is, moreover, rounded and flattened above, instead of being conical and somewhat pointed as in the *Anthemis*, and by the tubular five-toothed central florets, which in the chamomile are small, few, and scarcely visible, but in the two former species are large, very numerous, and very long.

Parthenium Hysterophorus L.—José Torar has found *parthenine* and four other alkaloids besides *parthenic* acid, in this cuban plant which is used by the natives as a febrifuge and antiperiodic. Of the alkaloids, *parthenine* is crystallizable and is apparently the active principle. It has been extracted and studied again by H. V. Arny (*A. J. P.*, 1890, 121), who believes it to be a bitter glucoside and not an alkaloid. In doses of three grains (0.2 Gm.) it is said to quicken the heart, and in doses of fifteen grains (1.0 Gm.) to slow cardiac action, while fifty grains (3.2 Gm.) not only lessen the arterial pressure and respiratory frequency but reduce the bodily temperature. In *doses* of from seven to ten grains (0.45–0.65 Gm.) it is affirmed to be useful in *neuralgia.* (See *Journ. de Méd. de Paris*, March, 1887; *A. J. P.*, 1897, 169.)

Parthenium integrifolium L., *American Feverfew. Prairie Dock. Wild Quinine* (Fam. *Compositæ*) is an herbaceous perennial, growing abundantly in the prairies of the Southwestern States, which has been used as a tonic and antiperiodic; two ounces (62 Gm.) of the flowering tops may be given in infusion.

Paulowilhelmia. *Paulowilhelmia speciosa* Hochst.—This acanthaceous plant is used by the Aquapine tribe on the Gold Coast, as a fish poison, under the name of *adubiri.* (*P. J.*, xx, 1890.)

Peach Leaves. *Prunus Persica* (L.) Sieb. et Zucc. (Fam. *Rosaceæ.*) *Pechier*, Fr. *Pfirsich*, G. —The peach tree is a native of China, but flourishes everywhere in the warm temperate zone. Peaches are among the most grateful and wholesome of our summer fruits. They abound in saccharine matter, which renders their juices susceptible of the vinous fermentation, and a distilled liquor prepared from them has been much used, in some parts of the country, under the name of *peach brandy.* The kernels of the fruit resemble, physically and chemically, bitter almonds, for which they are frequently substituted in commerce. The flowers, leaves, and bark also have the peculiar odor and taste of bitter almonds, and yield hydrocyanic acid. The leaves afford a volatile oil by distillation. The distilled water prepared from them was found in one instance to contain 1.407 parts of hydrocyanic acid in 1000, and in another only 0.437 parts in the same quantity. From some experiments it is inferred that the proportion of acid is greatest where there is least fruit. (*A. J. P.*, xxiv, 72.)

Peach kernel oil made by expression has found its way into Western Europe from the Levant, and is used in Italy and Southern France largely as an adulterant of almond oil. It is described as of a light yellow color, having the taste and odor of almond oil. It thickens at –9° C. or –10° C., and solidifies at –18° C. The sp. gr. at 15° C. is 0.915. It gives with strong nitric acid a dark brown color, with sulphuric acid a dark brown becoming lighter, with solution of zinc chloride a purplish-brown; forming with the elaidin test in two hours a mass of butter-like color and consistence. Peach kernel oil has a saponification value of 189–192 and an iodine figure of 93.5. (See *Oleum Amygdalæ Expressum*, Part I.)

The leaves of the peach are said to be laxative, and have also been used with asserted advantage in *whooping cough, irritability of the bladder*, etc. The dried leaves may be employed (an ounce to a pint of hot water) in infusion. The flowers of the peach are affirmed to be laxative and vermicidal, in half-fluid-ounce (15 cc.) doses when fresh, given in the form of syrup. Cases of fatal poisoning in children from their use are on record. The peach kernels are distinctly active, and when rubbed up with cold water form an emulsion which may be used in place of cherry-laurel water or other preparations of hydrocyanic acid.

Peganum. *Peganum Harmala* L. *Wild Rue.* (Fam. *Rutaceæ.*)—A tall herbaceous plant growing in the Mediterranean region of Europe and Africa and extending into Thibet. In the seeds of this plant Goebel (1837) found the alkaloid *harmaline*, and Fritzsche (1847) a second alkaloid, *harmine.*

Harmine, $C_{13}H_{12}ON_2$, crystallizes in rhombic prisms which melt at 257°–259° C. (See Fischer, *B. Chem. G.*, 1912, xlv and 1914, xlvii, 99; also Perkin and Robinson, *Tr. Chem. Soc.*, 1919, cxv, 967.)

Harmaline or *harmine dihydride*, $C_{13}H_{14}ON_2$, is in the form of trimetric, octahedral crystals. It is soluble in alcohol and ether and slowly so in water. It melts at about 238° C. with decomposition. Flury (*A. E. P. P.*, 1911, lxiv, p. 105) finds that harmaline in moderate doses produced symptoms in the dog similar to those produced by cannabis and in toxic quantities it caused salivation. Its anthelmintic effect he attributes to a paralytic action upon the muscular tissues of the worm. The seeds of *peganum* were used by the ancient Greeks in the treatment of eye diseases. In modern times it has been used as an emmenagogue, anthelmintic and sedative.

Pegnin. *Milk-sugar Rennet.*—Under this name is marketed the milk curdling enzyme of calf's rennet diluted with milk-sugar and a little sodium chloride. It is a fine, white powder, having a sweet saline taste, readily soluble in water, forming a solution that rapidly coagulates the casein of milk. It is used mainly in the extemporaneous preparation of infant food and in stomachic disturbances, such as *hyperacidity* and *flatulence.*

Pelargonium. *Pelargonium odoratissimum* Willd. *Rose Geranium. Nutmeg Geranium.* (Fam. *Geraniaceæ.*)—The *Pelargoniums*, commonly referred to as *geraniums*, are indigenous to South Africa and largely cultivated as decorative plants. Some of the species are cultivated for the distillation of the volatile oil, in France, Spain, Algiers, and the Island of Réunion. According to Guibourt, several species of *Pelargonium* yield a volatile oil by distillation, closely analogous in odor to that of the rose: such are the species above named, *P. capitatum* Ait., and *P. roseum* Willd., which is probably a variety of *P. radula* Ait. The oil is obtained from the leaves. The oil which occurs in commerce, purporting to be the oil of *P. odoratissimum*, is fluid at ordinary temperatures, of a pale brownish-yellow color, and the characteristic odor of the plant, merely recalling that of the rose. This oil is now much used in perfumery. Piesse states that, as this oil is used to adulterate that of roses, so is it in its turn adulterated with the cheaper oils of species of *Andropogon*, especially the oil known as *oil of palmarosa* (see *Oil of Citronella*). Jallard states that the true oil of rose geranium, from *P. roseum*, is freely soluble in 70 per cent. alcohol. The oils likely to be used to adulterate it are insoluble in this liquid. If, therefore, six drops of the suspected oil be mixed with 5 cc. of 70 per cent. alcohol, there should be no separation. F. W. Semmler (*B. Chem. G.*, xxiii, 1098) has shown that the chief ingredient in the various geranium oils is an alcohol, *geraniol*, $C_{10}H_{18}O$, which boils at from 231° to 232° C., and has a sp. gr. 0.884 at 15° C. When oxidized by chromium trioxide mixtures, it is changed into *citral*, $C_{10}H_{16}O$, an aldehyde found in many of the essential oils, and this when oxidized by silver oxide yields *geranic acid*, $C_{10}H_{16}O_2$. The geraniol is both free and combined as tiglic acid ester. The oil also contains citronellol. (*Schim. Rep.*, April, 1897.) Geranium oil is sometimes adulterated with dimethyl sulphide, $(CH_3)_2S$. (*Schim. Rep.*, 1909, 55; see also *Am. Perf.*, Jan., 1913.)

Pengawar Djambi. *Paku Kidang. Golden Moss.*—This is composed of silky, long, yellow or brownish hairs, very soft, which are obtained in Java, Sumatra, from the base of the fronds of various ferns, especially *Cibotium Barometz* Link, *C. glaucum* Hook. et Arnold, *Alsophila lurida* Bl., etc. (Fam. *Cyatheaceæ*). (See also *S. W. P.*, 1910, No. 43, 361.) It has the power of causing rapid coagulation of blood, and, when properly used, of mechanically arresting hemorrhages from capillaries. It has been much used in the physiological laboratories of Europe and this country, and was employed in human medicine during the Middle Ages under the name of *Agnus Scythicus.* The medieval drug was composed of pieces of the rhizome with the attached scales and petioles so cut as to resemble animals. (See *L. M. R.*, Dec., 1887.)

Peralga. *Veramon.*—This is a compound of amidopyrine and barbital. It occurs as a yellow powder, sparingly soluble in cold water but readily soluble in hot water and various organic solvents. Its melting point is 95° to 97° C.

Peralga is intended for the relief of various pains such as *headache, dysmenorrhea, neuritis,* etc. It is asserted that it will even relieve traumatic *pains.* The *dose* is from five to nine grains (0.2 to 0.6 Gm.).

Penthaclethra. *Penthaclethra macrophylla* Benth. (Fam. *Leguminosæ.*) *Owalá Grains.*—The mussel-shaped seeds of this plant, which grows in the Congo States, are said to contain an alkaloid, *paucine*, crystallizing in yellow foliaceous crystals, melting at 126° C., insoluble in ether and chloroform, having the formula $C_{27}H_{38}O_5N_5$. (*P. J.*, lix); it is stated to be physiologically inactive. These seeds had formerly been employed as a Physostigma adulterant.

Peptones.—The general name of a class of albuminoids resulting from the hydrolysis of the nitrogenous elements of food (such as albumin, fibrin, casein, etc.), by the action of the digestive juices. This conversion is caused by the gastric ferment pepsin, and also by trypsin present in the pancreatic juice.

The physiologists of the preceding generation considered peptones to be the final product of digestion of proteins. It is now believed, however, that the peptones are further broken down into so-called *amino-acids.* The peptones cannot be regarded as final products of digestion and it has been definitely established that they cannot be utilized by the body tissues. Indeed, if introduced into the circulation, they have a distinctly toxic action.

Peptones are soluble in water, are not precipitated by potassium ferrocyanide in the presence of acetic acid, and are not coagulated by heat.

The commercial peptones, such as *Witte's peptone*, are the results of incomplete digestion, being mixtures of various *proteoses* and peptones. They vary considerably in their physical appearance and may occur either as powders or pastes. More usually they are in the form of a dark brown paste with a characteristic odor suggesting that of roast meat, soluble in water.

The peptones have the nutritious properties of the proteins from which they are derived. They are frequently employed in diseased conditions with the idea that being already partially digested they make less demand on the digestive organs. They have been also used for the purpose of exciting the protein reaction in the treatment of certain infections. (See *Protein Therapy*). They are also used for technical purposes especially in bacteriology. The U. S. P. IX recognized, among the reagents, *beef-peptone* describing it as: "The dried product of the pancreatic digestion of meat. A yellow powder of a slightly bitter but not disagreeable taste and an odor resembling that of meat extract. Soluble in all proportions in water, yielding a yellowish-brown liquid of faintly acid reaction. Slightly soluble in diluted alcohol, insoluble in alcohol or ether. An aqueous solution of peptone (1 in 20), upon the addition of tannic acid T.S. or mercuric chloride T.S., yields a precipitate. On the addition of 0.5 mil of potassium hydroxide T.S. to an aqueous solution of peptone (1 in 20), followed by a solution of copper sulphate (1 in 50), added drop by drop with agitation, an intense, red-violet color is produced (biuret reaction). Pour an aqueous solution of peptone (1 in 20) into an excess of alcohol, allow the resulting precipitate to settle and decant the clear supernatant liquid; the residue left on evaporating this liquid is completely soluble in alcohol and no coagulation occurs. One Gm. of peptone dissolves in 20 parts of water with but slight turbidity. When an aqueous solution of peptone (1 in 200) is heated to boiling, no precipitation occurs; the addition of nitric acid does not cause turbidity (*coagulable albumin*).

Saturate an aqueous solution of peptone (0.5 Gm. in 20 mils) with powdered zinc sulphate; not more than a slight flocculent precipitate appears (*proteoses*). Dry 1 Gm. of peptone at 100° C., it loses not more than 7 per cent. in weight; ignite this dried product; not more than 0.005 Gm. of ash remains. Peptone contains not less than 12.5 per cent. of nitrogen when determined by the Kjeldahl method, corresponding to about 78 per cent. of pure peptone." *U. S. IX.*

The term peptone has been greatly abused in commercial usage, being applied to a variety of preparations containing partially digested foodstuffs, both carbohydrate and protein, some also containing considerable amounts of alcohol. Vinous solutions containing from 5 to 10 per cent. of partially digested proteins are largely employed under various trade names as accessory foods. Their nutritive value is generally less than that of milk, and even this is due in large part to the alcohol they contain.

Perezia Root.—This root is obtained from several Mexican plants, *Perezia Wrightii* A. Gray, *P. Nana* A. Gray, and *P. Dugesii* A. Gray. (Fam. *Compositæ.*) It contains *pipitzahoic acid*, $C_{15}H_{20}O_3$, a substance which crystallizes in beautiful golden yellow needles. R. Anschütz and J. W. Leather obtained this acid also from the dried roots of *P. adnata* A. Gray. (*Trixis Pipitzahoac* Schaffner). It melts at from 103° to 104° C., sublimes readily, and is easily soluble in alcohol, ether, chloroform, benzene, and glacial acetic acid. It is a quinone, and bears great resemblance, when recrystallized from diluted alcohol, to *oxythymoquinone*, which, recrystallized from the same liquid, is scarcely distinguishable from it. (*A. J. P.*, 1884, 185, and *Ph. Rund.*, 1883, 245; *A. Pharm.*, 1887, 183.)

Under the name of *perezol* the 0.5 per cent. alcoholic solution of *pipitzahoic acid* has been recommended by Duyk as an alkalimetrical indicator. By acids it is at once decolorized; with alkalies it becomes reddish. Boric, and perhaps other acids, and acetates, borates, bicarbonates, and carbonates act with respect to the solution like alkalies. For a paper on pipitzahoic acid by Altamirans, see *Analen del Instituto Mex.*, Nat. 7, p. 21, or *P. J.*, 1905, 553.

Periploca. *Periploca græca* L. *Silk-Vine.* (Fam. *Asclepiadaceæ.*)—From the bark of this deciduous shrub, growing in the neighborhood of the Black Sea, has been separated by Lehmann (*A. Pharm.*, 1897, p. 157) a colorless glucoside, *periplocin*, $C_{30}H_{48}O_{12}$, soluble in 125 parts of water, freely soluble in alcohol. According to the experiments of Burschinski (*St. P. M. W.*, 1897), it is an active cardiac poison belonging to the digitalis group. It has been used as a cardiac tonic by Cholewa (*Th. M.*, 1904, p. 292), Silberberg (*In. Dis.*, Odessa, 1909), and others, in the treatment of *heart disease.* Silberberg asserts that it is better suited for intravenous injection than strophanthin. The *dose* is from one one-hundred-and-twentieth to one-sixtieth of a grain (0.0005–0.0011 Gm.).

Peronine. *Benzyl-morphine Hydrochloride.* $C_{17}H_{18}NO_2.O.C_6H_5CH_2HCl$.—This is the hydrochloride of morphine benzyl-ester, produced by replacing the hydrogen of the hydroxyl group in morphine, which is analogous to the hydroxyl group of phenols, with the alcohol radical ($C_6H_5CH_2$). *Peronine* occurs as a bitter, odorless, white powder, consisting of prismatic crystals. At 65.5° C. it dissolves in water in the proportion of 7.5 to 1000, but dissolves readily in 10 parts of boiling water, the aqueous solutions having a bitter taste and being neutral to litmus. It is soluble in 218 parts of 95 per cent. alcohol. Although precipitated from its solutions by the general alkaloidal reagents, peronine differs both in its solubilities, and also in its behavior towards special reagents, from morphine and codeine.

Peronine was first therapeutically investigated by Schröder (*Th. M.*, 1897), and the conclusion reached that in its medicinal activities it is intermediate between morphine and codeine. The physiological action of the drug has been partially studied by Mayor (*Revue Méd. de la Suisse Romande*, 1898), who finds that it produces in guinea-pigs and rabbits exaggerated reflexes, ending, if the dose have been large enough, in convulsions and death by asphyxia. The lethal dose for rabbits, according to Mayor, is 2.5 Gm. per kilo, or little less than one-third that of codeine. On the other hand, Pierart affirms, as the result of his experiments, that peronine is more poisonous than morphine. Clinically, peronine has been used to some extent as a substitute for morphine, having analgesic and hypnotic powers inferior to those of that alkaloid, but being of distinct value in the treatment of *phthisis, chronic bronchitis,* and other pulmonary diseases. The *dose* is from one-third of a grain to one grain (0.021–0.065 Gm.).

According to Bufalini, confirmed by Gevaert, the 1 to 2 per cent. solution of peronine placed in the conjunctival sac produces a complete anesthesia which lasts for many hours. The drug, however, has not been used for this purpose on account of its causing pain, edematous swelling, and even serous chemosis of the conjunctiva.

Peroxides.—There have been introduced into medicine a series of superoxygenated compounds with various inorganic bases. The theoretical basis for the introduction of these compounds into medicine is that in the presence of water they part with an atom of their oxygen, which unites with the elements of the water to form hydrogen peroxide, as in the following reaction:

$$MgO_2 + H_2O = MgO + H_2O_2$$

and that the hydrogen peroxide which is formed under these circumstances will exercise the well-known disinfectant properties of that substance. It is to be remembered, however, that hydrogen dioxide is very unstable in the presence of an alkali, and since, in the above reaction, an alkaline salt is left behind, there will be a rapid decomposition of the hydrogen dioxide, with the liberation of free oxygen. The more highly alkaline the oxide which is left after the splitting off of one atom of oxygen, the more rapidly will the resulting hydrogen dioxide be broken up. Of this group of salts, the sodium perborate has received official approbation, and the following are of sufficient importance to deserve mention.

Magnesium Peroxide. Magnesii Peroxidum. N. N. R. 1924.—*Magnesium dioxide* is an odorless, white powder, practically insoluble in all the ordinary solvents. It should contain not less than 15 per cent. of MgO_2 equivalent to 4.3 per cent. of available oxygen. It has been used as an antiseptic with asserted good results in the treatment of gastric and intestinal disorders, but it does not seem probable that whatever benefit may have followed this treatment can be laid to the disinfectant properties of the drug. It will, in these cases, evidently act as an antacid and laxative as does the ordinary magnesium oxide. It has also been used internally as a substitute for the ordinary oxide in the treatment of *rheumatism, gout* and *hyperacidity of the stomach,* and also, with less reason, in the treatment of *diabetes.*

Although the germicidal power of magnesium peroxide has not been as yet satisfactorily determined, the experiments of Park indicate that it is a germicide of considerable power. Croner states that the addition of 0.7 Gm. of magnesium peroxide per liter drinking water exercised a bactericidal effect, but did not produce complete sterility of the water. It has been used locally as a dusting powder in infectious conditions of the throat, such as acute *tonsillitis,* but chiefly as an ingredient of dentrifrices. Magnesium peroxide is also known under various brand names, such as *Magnesium Perhydrol, Magnesium Superoxyl, Biogen, Novozone,* and *Magnodat.* The *dose* for internal administration is from five to twenty grains (0.32–1.2 Gm.).

Sodium Peroxide. N. N. R. 1924.—This occurs as a white or yellowish powder which dissolves in water with the development of heat and the evolution of oxygen. It should contain at least 90 per cent. of Na_2O_2, equivalent to 18.4 per cent. of available oxygen. It is largely used as a bleaching agent in the arts and is also used by dentists for bleaching teeth. Unna recommends a sodium peroxide soap made of 3 parts of liquid petrolatum, 7 of dried soap, and from 2½ to 7 per cent. of sodium peroxide. It is said to impart to a pale and excessively cornified facial skin pitted with comedones, a healthy, rosy color and a softened surface. It has also been used in *rosacea pustulosa.* A proprietary preparation of fused sodium peroxide, containing also some catalytic agent is sold under the name of *oxone.*

Calcium Peroxide. N. N. R. 1924.—*Calcium Peroxidatum* or *gorit,* CaO_2, occurs as a cream colored, odorless and tasteless powder, which is practically insoluble in water. The standard of the N. N. R. requires 60 per cent. of CaO_2 corresponding to 13.3 per cent. available oxygen. It is chiefly used as an addition to dentifrices, but often in such small quantities as to be absolutely incapable of any antiseptic action in the mouth. It has also been used as an antacid and disinfectant in gastric and intestinal disorders in *doses* of five to fifteen grains (0.32–1.0 Gm.).

Strontium Peroxide. N. N. R. 1924.—This is a white, odorless and tasteless powder containing at least 84 per cent. of SrO_2, equivalent to 11.2 per cent. of available oxygen. It is almost insoluble in water. It is employed in medicine as a dusting powder and in the form of an ointment.

Zinc Peroxide. N. N. R. 1924.—This occurs as a white or yellowish insoluble powder, representing at least 45 per cent. of ZnO_2, equivalent to 7.4 per cent. of available oxygen. It is used in medicine as an antiseptic in various ulcerated conditions, such as *burns,* old *leg ulcers,* and the like. It has been recommended as a local application in various *skin diseases.* It may be used either mixed with talc as a dusting powder, or in the form of an ointment in strengths of 5 to 25 per cent. *Ektogan, Zinc Perhydrol,* and *Zinconal* are proprietary forms of zinc peroxide.

Persulphates.—Persulphates are obtained by the electrolysis of solutions of sulphates. Sulphuric acid is decomposed into H_2 and SO_4, and the SO_4 ion unites with a molecule of the normal sulphate, as:

$$Na_2SO_4 + SO_4 = Na_2S_2O_8.$$

They have been brought forward for use in medicine and dentistry on account of their germicidal properties and as a source of nascent oxygen. According to Friedländer (*Th. M.,* Feb., 1899), the half per cent. aqueous solution checks the growth of pathogenic bacteria, and the 5 per cent. solution kills them. They are said to be actively poisonous, 0.5 gramme per kilo rapidly causing death in the rabbit, and to be violently irritant to mucous membranes; one and one-half to five per cent. solutions have been used to some extent in the dressing of *wounds.*

The important persulphates are *ammonium persulphate,* $(NH_4)_2S_2O_8$, which occurs in colorless crystals, making a turbid solution with water; *potassium persulphate,* $K_2S_2O_8$, which occurs in colorless crystals, very slightly soluble in water; and *sodium persulphate,* $Na_2S_2O_8$, a colorless crystalline powder, sparingly soluble in water.

Sodium persulphate has been recommended internally as an aperitive stimulant to digestion, in *hypochondria, chlorosis,* and *neurasthenia.* Lumière (*Lyon Chirurgical,* October, 1915) has found sodium persulphate useful in the treatment of *tetanus.* From experiments in the test tube as well as in the lower animals he concludes that its effect is due to the destruction of the toxin. It has been used in various intestinal conditions as a stimulant and antiseptic. Cannaday (*Press. Med.,* 1905, p. 286) reports favorably upon its action in *typhoid fever.* The *dose* in a day is three grains (0.2 Gm.).

Persodine is the one and three-tenths aqueous solution which has been supplied commercially in France.

Ammonium persulphate has been strongly recommended by Strzyzowski (*Schweizer Wochen. f. Chemie u. Pharmacie,* 1898, No. 48) as a urinary reagent; if its ten per cent. solution is poured down the inside of a test tube containing urine the presence of albumin will be revealed by a whitish-gray zone at the juncture of the two liquids. The development of a green tint indicates the presence of biliary pigments. The salt is readily soluble in water, and its solutions keep unchanged for weeks unless they be heated or in contact with easily oxidizable bodies. (*Th. M.,* 1899, 99.)

Pertonal. *Acetyl-amido-ethoxybenzene.*—This compound is said to resemble acetphenetidin in its action but to be less depressant (*A. J. P.,* 1919, xci, 365). *Dose,* ten to twenty grains (0.6–1.2 Gm.).

Perugen.—A synthetic imitation of Peru balsam obtained through solution of aromatic gum resins and balsams in aromatic esters. It behaves similarly to the true balsam in its action towards solvents, etc., but can be distinguished by the difference in its lower saponification number and iodine number, that of *perugen* being 206 and 33.7, respectively.

Petroleum. *Rock Oil. Oleum Petræ. Huile minéral,* Fr. *Bergöl,* G.—*Petroleum* is a native mixture of hydrocarbons with very small amounts of oxidation or alteration products admixed. The hydrocarbons may be gaseous, liquid, or solid, and in crude oil, fresh from the wells, all three classes are present. The hydrocarbons belong to several of the homologous series known to organic chemistry. The researches of Pelouze and Cahours, of

Warren, and more especially of Schorlemmer, have established the presence of the paraffin series, C_nH_{2n+2}, beginning at methane and continuing through the liquid members, which constitute the bulk of the oil, to the solid hydrocarbons known commercially as "paraffine"; of the olein series, C_nH_{2n}; of the benzene series, C_nH_{2n-6}. After the oil has been heated, as in distillation, pyrogenic products form, so that in the residues of petroleum, distillation, naphthalene, anthracene, and other higher hydrocarbons have been detected. In Caucasian petroleum, Beilstein and Kurbatow (*A. J. P.*, 1880, 612) have also found another homologous series of hydrocarbons, *hexahydrobenzene*, C_6H_{12}, and its homologues known as the *naphtenes*. These same hydrocarbons under the name of *polymethylenes* have been shown by Richardson to make up California petroleums and to be present in other asphalt base oils.

Pennsylvania petroleum consists in great part of paraffins, and the individual hydrocarbon making the bulk of illuminating oil is *heptane*, C_7H_{16}. The oxidation products accompanying petroleum constitute usually only a small fraction of 1 per cent., and have not been very fully studied. It is known, however, that these alteration products are largely acid in character. Prolonged atmospheric exposure may, however, cause a petroleum to thicken, at least superficially. In this way the semi-solid deposits of California are explained, as well as Rangoon tar and Trinidad pitch or bitumen. When the bitumen is in the solid state it is called *asphaltum*. This is black and sometimes dry, friable, and is insoluble in water or alcohol. Not infrequently asphaltum exists in nature mixed with more or less of the liquid substance, and this semi-solid mixture is distinguished by the name of *maltha* or *mineral tar*.

Petroleum has been known from the earliest historical period. Within the limits of the United States it has long been known to exist in a few localities. On the borders of Seneca Lake in the State of New York small quantities of it were collected, and to some extent used in medicine under the name of *Seneca oil* in colonial days. In Western Pennsylvania, on Duck Creek in Ohio, near Scottsville in Kentucky, and on the Kanawha in Virginia, it attracted local attention, and a certain locality in Western Canada had acquired some notoriety by its burning spring. But little attention was paid to it until the year 1859, when, the preparation of oil for burning, distilled from bituminous shales, having proved very profitable, and a strong resemblance having been shown to exist between this and petroleum, enterprise was directed towards some of the known resources of the latter liquid, and, being greatly stimulated by success, soon led to further and astonishing discoveries. At first the most productive locality of petroleum was in Western Pennsylvania; but it is now obtained in many States. After the Pennsylvania field, in order of development, is that of Ohio; but most of the oil produced in this State is from a different geological horizon—viz., the Trenton limestone—and contains a persistent sulphur impurity. This renders the Ohio oil (popularly known also as *Lima oil*, from the town of Lima, Ohio) more difficult and expensive to refine. It is hence very largely used in the crude state as *fuel oil*, and as such has been of the greatest industrial value, being shipped by pipe line or tank cars to great distances. Within recent years large quantities of petroleum have been found in California, Texas, Louisiana, Kentucky, and Kansas, but in the main it is of a grade much inferior to that known as Pennsylvania oil, being largely used as fuel oil. Petroleum is found in commercial quantities in many parts of the earth. The more important oil-fields are in various sections of the United States, Mexico, Russia, Mesopotamia, India, etc.

In the early days of the petroleum discovery the oil was gathered as it floated on the surface of the water in springs or small streams. In 1859 the first oil well, the Drake well, was sunk near Titusville, Pa., and the oil-bearing strata were reached at a depth of seventy-one feet, with the result of some eight barrels per day. In 1861 and 1862 the first large flowing wells were struck in drilling for oil. The explanation of these flowing wells is simply that in new territory the gaseous hydrocarbons have accumulated with the liquid oil in such amount that they exert an enormous pressure, causing a flow of oil of several thousand barrels per day. Often, however, the pent up gas escapes with enormous force without any accompanying oil. These *gas wells*, as they are termed, are well known througout the oil regions, and they have been utilized on a large scale as sources of gaseous fuel for manufacturing and domestic purposes. Sadtler has analyzed numerous samples of this *natural gas*, and finds it to consist chiefly of methane and its homologues, with traces of the olefines and of carbon monoxide. In one case free hydrogen was present. (*Proc. Amer. Philos. Soc.*, xvi, 585, 1877.) After a well has flowed oil for a time, it will continue to yield on pumping. Indeed many smaller wells never have flowed, and have to be pumped from the start. In some districts "torpedoing" with nitroglycerin has been largely resorted to after a well has begun to decline in power, in order to increase the flow. The explosion effects this by shattering the sandstone and pebble conglomerate which holds the oil, so that new channels are opened.

Oil wells are of various depths. The first or Drake well, as stated, was only seventy-one feet deep, while in Washington County and other localities in the southwestern part of Pennsylvania the oil was obtained from a depth of 2000 feet.

There are two theories as to the origin of petroleum. According to one, it is simply a product of distillation from the bituminous shales which underlie almost the whole of this oil producing country. The gas and the liquid oil are equally products of this distillation. According to the other, it represents the decomposition of marine plants and animal life which accumulated in these sand rock formations. These decomposition products may have also been in part subjected to distillation. Studies by Engler (*B. Chem. G.*, 1888, 1816) on the distillation under pressure (ten atmospheres) of fish oils and of olein and other fats show that large amounts of light oils, composed of pentane, hexane, heptane, octane, and nonane, can be obtained, thus making the second theory very probable. S. P. Sadtler has shown that linseed oil, distilled under pressure, may be made to yield hydrocarbons of the paraffin series, and has obtained products of all gravities from light benzin to solid scale paraffin. Thus, Engler's theory must be broadened sufficiently to allow of the vegetable seed oils being taken as original sources of petroleum production as well as animal oils.

Crude petroleum is occasionally of a clear color when taken from the earth, but is generally of a greenish color, appearing claret-red by transmitted light. The green color may, however, become so dark as to be almost black. In gravity it varies from 0.865 to 0.777, or from 32.5° to 52° Baumé.

The method of purifying petroleum is analogous to that already described for purifying coal tar. The crude oil is put into large retorts of wrought iron and exposed to a heat rising gradually to between 315.5° C. and 426.6° C., by which all the volatile ingredients are distilled, leaving from five to ten per cent. of solid residue, constituting a sort of coke. The liquids thus obtained are comparatively colorless, though still retaining the strong odor of the crude oil. The several fractions are collected separately and show very varying gravity and volatility, and are applied to different uses. An average result of a normal distillation may be stated as follows: Gasoline 1½ per cent., refined naphtha 10 per cent., benzin 4 per cent., refined petroleum or kerosene (sometimes called coal oil), 55 per cent., lubricating oil 17½ per cent., paraffin 2 per cent., loss, gas, and coke 10 per cent. As the greater demand for illuminating oil makes it desirable to get the maximum quantity of this fraction, the distillation is generally so conducted that by the process of "cracking" the yield of burning oil is increased at the expense of the lubricating oil and heavy naphtha. Many distilleries obtain, therefore, from 75 to 80 per cent. of illuminating oil from the crude material. A crude distillate, however, would not be adapted for the purposes of an illuminating oil, so the distillate must be treated with acid. It is placed in the treating tank or "agitator" and 1 or 2 per cent. of strong sulphuric acid is added, when, by the aid of an air blast introduced below, the whole is violently agitated. The acid combines with the impurities of the oil and forms a tarry substance, called "*sludge acid*," which settles to the bottom and, after the whole has subsided, is removed. The oil is then washed with water and again agitated, the process being repeated once or twice. It is then treated with caustic soda solution and again washed. The oil is now clear and almost colorless. It is then placed in large settling tanks to allow the water to separate. If it does not have the desired fire test, it is "steam stilled" and the lighter vapors taken out until the desired test is obtained. In most States of the Union the legal fire test for illuminating oil is 43.3° C.; that is, it must not evolve inflammable vapors below the temperature of 43.3° C. Many special brands of illuminating oil have a much higher fire test, as high even as 148.8° C.

Lubricating oils, on the other hand, are valued according to their "cold test"; that is, they must not congeal except at very low temperatures. A lubricating oil, therefore, consists of the heavy liquid hydrocarbons of the paraffin and olefin series, but is free from the solid paraffin.

Medicinal Properties and Uses.—Petroleum has been deemed a stimulating antispasmodic, expectorant, and diaphoretic. In large quantities it may prove poisonous, as shown by a case recorded in the *J. P. C.* (March, 1869, 227), in which, after swallowing by mistake a quantity of rectified petroleum, a workman was seized almost immediately with violent inflammation of the throat, with colicky pain, and a desire to vomit, followed in an instant by a fearful tetanic seizure, and a general rigidity, attended by the most frightful cries. After a relaxation of ten minutes the symptoms returned with still greater violence; and life was probably saved only through the prompt action of the powerful emeto-cathartic medicines administered.

Bjerrum (*Ugeskrift for laeger*, Copenhagen, June 27, 1918) reports death in a child of fifteen months from drinking a quantity of petroleum, estimated at 4 or 5 Gm. There was violent vomiting soon after the petroleum was ingested, but the child died within a few hours with symptoms of heart failure.

The more volatile fractions of petrolatum are also highly poisonous to insect life and various distillates under trade names are sold as insecticides.

Petroleum is used as a folk remedy in the treatment of acute *bronchitis*, but probably with no beneficial action in this condition save by virtue of its nauseating effect. The inhalation of asphalt vapors have been recommended by Floer (*Ther. Geg.*, 1909, p. 405) in the treatment of *pulmonary tuberculosis*. It is stated that the influence of these fumes is not merely upon the bronchial mucous membranes, but that there is a marked improvement in the appetite and in the digestive power. In Germany it has been used successfully as a remedy against the *tape worm*. Schwartz's formula in such cases is a mixture of one part of petroleum with one and a half parts of tincture of asafetida, of which forty drops were given three times a day. Externally, petroleum is employed in *chilblains*, *chronic rheumatism*, affections of the joints, *paralysis*, and diseases of the skin, and is said to be very effectual in *psora* and *prurigo*. (See also *Petrolatum* and *Petrolatum Liquidum*.) It is an ingredient in the one time popular remedy called *British Oil*. It is affirmed that many cases of *asthma* are much benefited by inhaling petroleum vapors.

The lighter fractions of petroleum are capable of absorption and are highly toxic substances. There have been a number of cases of serious and even fatal poisoning reported both from the swallowing and inhalation of various products of this nature. The symptoms have been dizziness, cyanosis, rapid small pulse, respiration slow and labored. If the dose is large enough the patient becomes stuporous and occasionally delirious. When taken by the mouth to these symptoms are added gastro-intestinal irritation. H. C. Wood, Jr. (*Phila. Medical Journal*, 1899), has shown that the mixture known as benzin is a direct depressant to the heart and vasomotor system. Various of these substances are used by depraved humanity as intoxicants.

Extraordinary claims have been made for various commercial emulsions containing some form of petroleum, but there is no certain substantiation of these claims. The *dose* of petroleum is from thirty to sixty minims (2–4 cc.).

A water and alcohol soluble combination of petroleum oil has been originated by Max Doenhardt (*Ph. Ztg.*, 1913, p. 266), who discovered that when petroleum is mixed with terpineol and the solution treated with triolein and potassium hydroxide solution, the mixture develops heat spontaneously, a product resulting in a short time which forms a perfectly clear solution with alcohol, which in turn may be diluted with water to produce a permanently clear solution. The proportions of the ingredients depend upon the amount of petroleum, an excess of alkali always being necessary. The author has patented a product called "*Terpipetrol*" made by the above process.

Peucedanum. *Chucklusa. Hog Fennel. Sulphurwort.*—This is the root of *Peucedanum officinale* (Fam. *Umbelliferæ*), originally an European plant but now growing in North America. The active constituent of the root is *peucedanin*, $C_{16}H_{16}O_4$, stated to be diuretic and emmenagogue.

Peucedanum palustre Mnch. *Marsh Parsley. Marsh Smallage. Persil de Marais*, Fr. *Radix Olsnitii. Sumpfsilge, Elsenich*, G.—The root of this European umbellifer is, when dried, of a brown color externally, having a strong aromatic odor, and an acrid, pungent, aromatic taste. Peschier found it to contain a volatile oil, a fixed oil, and a peculiar acid which he calls *selinic*. It was formerly used for *epilepsy* in Russia. *Dose*, from twenty to thirty grains (1.3–2.0 Gm.).

Peucedanum sativum Benth. and Hook. which had been claimed to contain a volatile alkaloid by Wittstein has been reinvestigated by VanCook (*Pharm. Weekblad*, 1919, lvi, 1391) who claims to have found fatty material, starch, sugars, and small amounts of a non-volatile alkaloid which is present in all parts of the plant. There is also an ether soluble crystalline substance which is neither alkaloidal nor glucosidal.

Phaselin.—This substance is represented as the active constituent of the bean of *Dilkas Mexicano*, a South American plant. It is used similarly to papain as a digestive in *doses* of eight to fifteen grains (0.5–1.0 Gm.).

Phaseolus. *Phaseolus vulgaris* L. *Common Kidney* or *String Bean*. (Fam. *Leguminosæ*.)—Of this species there are some 70 cultivated varieties. Soltsien found an alkaloid, *phaseoline*, in the legumes of the common bean. He, during a toxicological analysis, traced the source of the alkaloid which might, under other circumstances, have been mistaken for a ptomaine, to the beans found in the stomach under examination. The new substance is not crystallizable in the free state, but it crystallizes as a hydrochloride. (*A. Pharm.*, 1884.)

According to Dunlop (*P. J.*, 1917, xcviii, 257) the *Phaseolus lunatus* L. (*Civet Bean*), from a variety of which we derive the well-known *lima bean*, produces also a variety having a dark purple bean (*Java Bean, Burma Bean*), which is highly toxic. The toxicity of this bean depends upon the presence of *phaseolunatin*, $C_{10}H_{17}O_6N$, a cyanogenetic glucoside which forms prussic acid in the stomach.

Phenacaine.—There is formed by the condensation of molecular amounts of phenacetin and paraphenetidin, a base known as *Holocaine*. This is *p-Diethoxyethenyl diphenylamidine. Phenetidylacetphenetidin*,

$$C_6H_4\begin{cases}OC_2H_5\\NH.C.(CH_3)=N.C_6H_4(OC_2H_5).\end{cases}$$

The free base crystallizes well, is insoluble in water, and melts at 121° C. It is insoluble in fixed oil, a point which should be borne in mind, inasmuch as it is a frequent method of using holocain to prescribe it in a castor oil solution. The hydrochloride is, however, soluble in oils and should be dispensed when the other is called for. It should not be dispensed in alkaline solutions, being rapidly decomposed.

Phenacaine (*Holocaine*) *Hydrochloride*, *N. N. R.* 1924, forms colorless, lustrous, odorless crystals, melting at 189° C. It is soluble in 50 parts of water and readily in alcohol. It readily dissolves in boiling water, leaving on cooling a saturated solution containing about 2½ per cent. of the hydrochloride. This solution is slightly bitter, neutral in reaction, and keeps many months without change. In boiling, a porcelain vessel should always be used, as the solution at 100° C. is affected by the alkalinity of the glass.

Phenacaine is used chiefly as a local anesthetic for the eye. Although Eggleston and Hatcher (*J. A. M. A.*, Oct. 25, 1919, p. 1256) have shown that it is one of the most poisonous of the cocaine group of local anesthetics this fact is of small moment in ophthalmological practice because of the minute quantities of the drug required. The advantages claimed for it in ocular practice (see *J. A. M. A.*, 1921, lxxvii, 1730) are that its action is quicker than that of cocaine, that it does not dilate the pupils nor dry the cornea and that it is distinctly antiseptic. It is usually applied in 1 per cent. solution. According to the experiments of Heinz and Schlosser (*Klin. Monat. f. Augen.*, xxxv, 1897), the ½ of 1 per cent. solution affects bacteria, while the 1 per cent. solution is a powerful germicide, rapidly killing the lower organisms, including infusoria. Even in small doses it causes in frogs and in mammals violent convulsions which appear to be of cerebral origin, since after division of the spinal cord in the mouse the convulsions were confined to the anterior portion of the body. Holocaine is an active muscle poison, the 1 per cent. solution rapidly killing voluntary and cardiac muscles in the frog, and it exerts also a curare-like influence upon the motor nerves. According to Winselmann, its 1 per cent. solution exceeds in anesthetic power the 3 per cent. solution of cocaine.

Phenegol. $C_6H_5(O.NO_2.SO_3K):Hg:(KSO_3.NO_2.O)C_6H_5$.—Nitrated derivatives of paraphenolsulfonic acid unite readily with mercury, forming compounds known as *egols*. According to the phenol selected these products are called *phenegol*, *cresegol* or *thymegol*. Phenegol is a red-brown, soluble, tasteless powder, containing one-third mercury. It is asserted to be free from irritating action, and to be germicidal in 0.4 per cent. solution.

Phenoco. *N. N. R.* 1924.—This compound is said to be a mixture of coal tar creosote and higher phenol homologues suspended in a soap solution. It contains 8 per cent. phenol homologues. With water it forms a milky white emulsion of a high antiseptic value. The phenol coefficient test showed a germicidal value over 15 times that of phenol. (*U. S. Hygiene Bull.*, vol. viii, No. 1, 1911.) It is used in dilutions of 0.1 to 0.5 per cent.

Phenocoll. *Amido-aceto-para-phenetidin. Glycocoll-para-phenetidin. Phenamine.*

$$C_6H_4\begin{cases}OC_2H_5\\NH.COCH_2NH_2H_2O.\end{cases}$$

—This is formed by the action of glycocoll (amidoacetic acid) upon phenetidin. It is a white, finely crystalline powder, soluble at 17° C. in sixteen parts of water; also soluble in warm alcohol. The hydrochloride of phenocoll has almost entirely displaced the base as a therapeutic agent. Ammonia, alkalies, and alkaline carbonates throw down the pure base phenocoll from the solution of the hydrochloride, in the form of white needles with one molecule of water of crystallization.

Phenocoll closely resembles the other phenetidin compounds in its physiological action. Hertel and Herzog (*D. M. W.*, 1891) find that its antipyretic action is prompt, and that the sweating which is a common accompaniment may be readily controlled with small doses of atropine. Antiperiodic powers have also been attributed to it, but without any convincing evidence. The *dose* of the hydrochloride is from eight to fifteen grains (0.5–1.0 Gm.).

Phenocoll Salicylate, Salocoll,

$$C_6H_4\left\{\begin{array}{l}OC_2H_5\\NH.COCH_2.NH_2.C_6H_4(OH)COOH,\end{array}\right.$$

has been put upon the market as an antirheumatic. It may be used in the *doses* of ten to twenty grains (0.65–1.3 Gm.).

Phenoltetrachlorphthalein. *N. N. R.* 1924.—This dyestuff is made by the condensation of phenol with tetrachlorphthalic acid. It differs in its composition from the official phenolphthalein in having four chlorine atoms in the place of four of the hydrogen atoms.

It occurs as an odorless pink powder practically insoluble in water but soluble in alcohol or acetone. In alkaline solution it dissolves forming purple—or, when very dilute, bluish—solutions. This enables it to be easily distinguished from phenolphthalein which forms red solutions.

Phenoltetrachlorphthalein was suggested some years ago as a hypodermic purgative (see Abel and Rowntree, *J. P. Ex. T.*, 1909, i, p. 231) but did not achieve popularity for this purpose. As it was found to be excreted from the blood almost exclusively by the liver, it has been used to a very considerable extent as a test of the functional activity of the liver. The test is performed by injecting the disodium salt, intramuscularly or intravenously—the recommended *doses* have ranged from one to six grains (0.06–0.4 Gm.)—and afterwards estimating the amount of the dye either in the feces (Rowntree, *J. A. M. A.*, 1914, lxiii, 1533), in the duodenal contents (Aaron, Beck and Schneider, *J. A. M. A.*, 1921, lxxvii, 1631) or in the blood (Rosenthal, *J. P. Ex. T.*, 1922, xix, 385).

Phenoval. *Fenoval, Bromvaletin,* alpha-bromisovaleryl-phenetidin.—This occurs as tasteless, odorless crystals insoluble in water. It has been recommended as an hypnotic and anti-neuralgic, in *doses* of from eight to thirty grains (0.5 to 2 Gm.).

Phenoxycaffeine. $C_8H_9(OC_6H_5)N_4O_2$.—This product forms a white, crystalline powder, fusing at 142° C. It is used as an analgesic in neuralgias in *doses* of four to five grains (0.26–0.32 Gm.).

Phenoxy-proprandiol. *Glycerine-monophenylether. Antodyne.* $C_6H_5OCH_2CHOH.CH_2OH$.—This occurs as white crystals, freely soluble in both water and alcohol, and melting at 69° to 70° C. It is used as an analgesic in *neuralgia, gonorrhea, arthritis* and other painful conditions. It appears to differ from other coal-tar anodynes in that it is not antipyretic. The *dose* is from five to ten grains (0.3–0.6 Gm.).

Phenyform is a condensation product of phenol and formaldehyde, and occurs as a grayish, odorless powder, insoluble in water, but dissolving in alkaline solutions, or alcohol. It is asserted by Schuftan (*Th. M.*, 1906, 249) that phenyform is completely non-toxic. Brenning (*All. W. M. Z.*, 1906, 182) has used it as a dusting powder in various suppurating processes and states that it not only checks the formation of pus, but also acts as a deodorizer and favors the formation of healthy granulations. It has also been employed in *urethritis*, a finely powdered preparation being blown into the urethra, under which circumstances it is asserted that it adheres firmly to the mucous membranes.

Phenylchinoline. *Phenylquinoline.* $C_9H_6(C_6H_5)N$.—According to Tappeiner (*D. A. K. M.*, lvi, 1896), the action of this substance on the lower organisms is almost identical with that of quinine and about equal to it in strength.

Phenylenediamine. $C_6H_4(NH_2)_2[1{:}4]$.—*Paraphenylenediamine* and *meta-phenylenediamine* have been physiologically studied by Dubois and Vignon (*C. R. A. S.*, cvii, 533), who find that in *doses* of 0.01 Gm. per kilogramme it causes in the dog vomiting, diarrhea, and fatal coma, with peculiar symptoms.

Under the name of *ursol* and various other trade names paraphenylene-diamine has been used for dyeing the hair and coloring furs. This has given rise to a large number of cases of violent dermatitis, accompanied by itching and burning, in some cases much edema of the skin so that the eye-lids may be almost completely closed; the inflammation is not limited to the areas with which the irritant comes into direct contact. According to Olson (*J. A. M. A.*, March 18, 1916) the irritation is due to an intermediary product of oxidation of the dye, *quinone dichlor-diamin.* According to Blaschko (*D. M. W.*, 1913, xxxix, 2406) sufficient of the dye may be absorbed through the skin to give rise to constitutional symptoms such as vomiting, vertigo, ringing in the ears, etc. Gibbs (*J. P. Ex. T.*, 1922, xx, 221) has shown that when administered internally it causes a remarkable edema of the head and neck; doses of 1 Gm. per kilo proving fatal, in the cat, from pulmonary edema. He suggests that these effects may be due to a disturbance of the colloidal balance of the blood. Thompson (*N. Y. M. R.*, 1920, xcvii, 401) reports a case of constitutional poisoning with vertigo, diplopia and violent dermatitis from the use of a hair dye of this type. (For literature on this subject see Knowles, *Penna. M. J.*, Sept., 1916; also see Nostrum and Quackery, *A. M. A.*, vol. i.) Colman and Loewy (*D. M. W.*, 1911), however, have found that by combining it with reducing substances, the toxic properties of paraphenylenediamine were reduced. They recommend as a hair dye a solution of *paratoluylenediamine* with neutral sulphites, which is put upon the market under the name of *primal.*

Phenylhydrazine. $C_6H_5NH.NH_2$.—This is prepared from diazobenzene hydrochloride (resulting from the action of sodium nitrite upon aniline hydrochloride) by reduction with stannous chloride or sodium sulphite. The various compound derivatives of this substance have been tested by Heinz (*B. K. W.*, 1890) and others, and found to be too toxic for use in practical medicine. Phenylhydrazine is a colorless, slightly yellowish, highly refractive liquid, while the hydrochloride is a white crystalline powder, melting at about 200° C. *Phenylhydrazine hydrochloride* has been employed as a test for sugar in the urine. (*Fischer's Test.*) (See *Diagnostic Reagents.*)

Phenylhydrazine is an active irritant and toxic agent, producing in warm-blooded animals violent disturbances of breathing, with gastro-enteritis. It is remarkable for the changes which it produces in the blood, causing that fluid to become of a distinct green color when seen in thin sheets. The coloring matter appears not to be due to a derivative of phenylhydrazine, but to have at least spectroscopic relations to acid hematoporphyrin and to chlorophyll. (See *Z. B.*, N. F., xxiv, 1901.)

Phenylhydroxylamine. $C_6H_5.NH.OH$.—This substance has no known application to the treatment of disease, but requires notice on account of the occasional poisoning by it of those who are engaged in the manufacture of certain chemicals. For cases, see Hirsch and Edel (*B. K. W.*, xxxii, 1895), L. Lewin (*A. E. P. P.*, Bd. xxxv). The symptoms, which have developed with great suddenness, have consisted of coma, cyanosis, pulselessness, abolition of corneal and pupillary reflexes, chocolate-colored blood, methemoglobinuria, grayish-blue lips, and intense blue-red surface of limbs. The treatment of these cases should consist in active artificial respiration, together with hypodermic injections of strychnine and of digitalis.

Phenylurethane. *Euphorin. Ethyl Phenylcarbamate. Carbamilic Ether.* $C_9O_2H_{11}N$, or $CO\left\{\begin{matrix}OC_2H_5\\NH(C_6H_5)\end{matrix}\right.$.—This is a white, crystalline substance, having an aromatic odor and clovelike taste, and is made by the action of ethyl chloroformate (or ethylic ether) on aniline. It is almost insoluble in cold water, very soluble in boiling water, alcohol, and ether, and melts at 51° C. It has been physiologically investigated by Giacoasa, who finds that its 2 per cent. solution is antiseptic and that its toxicity is low but in large doses it depresses the central nervous system. It has been used by Sansonia (*Th. M.*, 1892, p. 452) as an antiseptic in obstinate *ulcers*, and in chronic *ophthalmia*, and by others in the treatment of *rheumatism*, but it has failed to establish its value in these conditions. Stroll (*M. M. W.*, 1907, p. 2262) has asserted that it is an extraordinarily powerful local anesthetic, and of great service in painful *ulcers* of the foot.

The similarity of names has led to euphorin being confused with europhen. *Dose*, eight to fifteen grains (0.5–1.0 Gm.).

Phlorizin. *Phloridzin. Phlorrhizin. N. N. R.* 1924. $C_{21}H_{24}O_{10} + 2H_2O$.—This is a bitter principle, discovered by De Koninck, of Germany, in the bark of the apple, pear, cherry, and plum trees. It is most abundant in the bark of the root, and derived its name from this circumstance (from two Greek words, φλοιός, bark, and ῥίζα, a root). It is light, white, crystallizable in silky needles, of a sweet, afterwards bitter taste, soluble in about 1000 parts of cold and freely soluble in boiling water, very soluble in alcohol and methyl alcohol, scarcely soluble in ether, cold or hot, dissolved without change by solutions of the alkalies. It loses its water of crystallization at 100° C., and fuses at a somewhat higher temperature. The ammoniacal solution becomes red on exposure to the air on account of the formation of *phlorizein*, $C_{21}H_{30}N_2O_{13}$ Phlorizin is a glucoside. When heated with diluted hydrochloric or sulphuric acid, it is converted into sugar and a peculiar substance called *phloretin*, $C_{15}H_{14}O_5$. To obtain phlorizin, the fresh bark of the root of the apple tree should be selected, as the dried bark is said to contain it in much smaller proportion. It is obtained by extracting the bark with boiling water and allowing the glucoside to crystallize out by cooling; the crude substance later being purified with animal charcoal. Rochleder states that the leaves contain a principle, *isophlorizin*, isomeric with phlorizin.

When given to the lower animals in very large doses (from seven to ten grains to the pound), phlorizin produces polyuria and glycosuria. (See Coolen, *Archiv. de Pharmacod.*, vol. ii, 1896; also Kossa, *Z. B.*, xl, 1900.) These effects are due to an irritant action on the kidney. Leclerq (*Paris Médical*, 1919, ix, 248) has used phlorizin, in *doses* of 5 to 10 milligrammes (one-twelfth to one-sixth grain), as a diuretic. Formerly it was considerably employed as a test of renal efficiency but has been latterly supplanted by various dyes. (For further information see *U. S. D.*, 20th edition, p. 1547.)

Phloroglucin. *Phloroglucinol.*—This is a trihydroxybenzene and therefore isomeric with pyrogallol. "It occurs as a white to cream colored crystalline powder readily soluble in water, alcohol or ether. When rapidly heated it melts between 217° and 219° C., when slowly heated between 200 and 209° C. Introduce a few crystals of phloroglucinol in a test tube with about 1 cc. each of sulphuric acid and acetic anhydride and heat in boiling water for from 5 to 10 minutes; no blue color develops (diresorcinol)." *U. S. IX.* Phloroglucin is used as a test for hydrochloric acid in the gastric contents (see under *Diagnostic Reagents*).

Phosphorescent Powder or Paint.—Made by mixing calcined oyster shells, 100 parts; caustic lime, 100 parts; calcined sodium chloride, 25 parts; then incorporate about 55 parts of sulphur and from 8 to 18 parts of calcium, barium, strontium or magnesium sulphide. It may be used as a paint by mixing it with varnish. If the substance has been exposed to sunlight, it becomes luminous in the dark. Radio-active substances are now used for this purpose as they do not require exposure to sunlight to render them luminous and are said to retain this property indefinitely. *Canton's phosphorus* consists of 2 parts of oyster shells and 1 part of sulphur.

Photoxylin.—This is a nitro-cellulose, which is said to be entirely soluble in a mixture of equal parts of concentrated ether and alcohol. According to Beringer, a 3 per cent. solution leaves on evaporation a very tough collodion-like film. *Photoxylin* is made from wood pulp, by methods of nitration similar to those given under pyroxylin, which is its chemical counterpart.

Physalis. *Physalis Alkekengi* L. *Alkekengi. Strawberry Tomato. Common Winter Cherry. Coqueret*, Fr. *Judenkirsche, Schlutte*, G.—A perennial herb belonging to the *Solanaceæ*, growing wild in Europe and Asia, cultivated in our gardens and said to be escaping locally. The fruit is a round red berry, about as large as a cherry, enclosed in the inflated calyx, and containing numerous flat kidney-shaped seeds. All parts of the plant are bitter, especially the leaves and the capsules enveloping the fruit. The berries are very juicy, and have an acidulous, bitter taste. By drying they shrink, and become a brownish-red color. Dessaignes and Chautard found a yellowish, bitter principle, *physalin*, very slightly soluble in cold water and freely soluble in alcohol and chloroform, especially with the aid of heat. Its composition is $C_{14}H_{16}O_5$. (*J. P. C.*, 3e sér., xxi, 24.) The berries are said to be aperient and diuretic, and have been recommended in *suppression of urine, gravel*, and *gout*. An extract of alkekengi berries to which lithium salt has been added is sold under the name of *lithal*. From six to twelve berries, or half an ounce of the expressed juice, may be taken for a *dose;* and much larger quantities are not injurious. They are consumed to a considerable extent in some parts of Europe as food and are coming into use to a certain degree for this purpose in America.

The berries of *Physalis viscosa* L., of this country, are said by Clayton to be diuretic.

Physostigmine Borate. *Eserine Borate.*—This eserine salt is advanced by Merck as possessing the advantage over the sulphate or salicylate of forming permanent aqueous solutions that do not become irritant. Its uses are the same as those of other eserine salts. (See Part I.)

Physostigmine Sulphite. *Eserine Sulphite.* $(C_{15}H_{21}O_2N_3)_2H_2SO_3$.—This salt of physostigmine has been brought forward as being more permanent than either the sulphate or salicylate. Its uses are precisely the same as those of the official salt. (See Part I.)

Phytelephas.—*Phytelephas macrocarpa* Ruiz. and Pav., or *negrito-palm*, of Colombia, Venezuela and Ecuador, yields the *Tagud nut*, from which is derived the hard white substance, *vegetable ivory* or *corajo*. The nuts contain a fixed oil. The ground nuts have been used as an adulterant in ground coffee and cattle powders. They may be detected in these by their endosperm cells which have extremely thick walls of reserve cellulose.

Phytin. *Calcium-magnesium Salt of Anhydro-oxymethylene-diphosphoric Acid.* $(C_2H_6O_9P_2)_2$-MgCa.—It is a white powder, slowly soluble in water, with a somewhat acid taste. Phytin, which was discovered in 1900 by Posternak (*C. R. S. B.*, lv, p. 1190), who has obtained it from the seeds of the hemp, sun-flower, sesame, peas, beans, and other plants. So universal is its distribution that he believes it an ingredient in all seeds, bulbs, and roots, and that it represents 70 to 90 per cent. of the entire phosphorus content of the plant seeds. It contains 22.8 per cent. of phosphorus. It is a heavy white powder, which when rubbed up with water forms a milky emulsion which is almost without taste.

Phytin was introduced into medicine on the supposition that being an organic form of phosphorus it would be more readily assimilated by the system, but the experiments of Mendel and Underhill (*A. J. Phys.*, 1906, xvii, 75), who find that it is eliminated as an inorganic phosphate, throw grave doubt on this supposition.

The preparation has been employed in *rickets, anemia, tuberculosis, neurasthenia* and other conditions in which phosphorus is useful. It is doubtful, however, whether this preparation possesses any very valuable therapeutic properties. The beginning *dose* is fifteen grains (1 Gm.) a day, given in divided doses.

Phytolacca Acinosa Roxb. (Fam. *Phytolaccaceæ.*)—This Asiatic plant has long been used in Japan as a diuretic, and is said to be violently poisonous. C. Nagai has separated from it an amorphous resin, *phytolaccotoxin*, which appears to be a spinal convulsant, and at the same time stimulant to the circulation, probably through the vasomotor centers. (*Sei-i-kwai Med. Journ.*, April, 1891.)

Pichurim Beans. *Semen Pichurim. Sassafras Nuts. Fèves Pichurim, Noix de Sassafras*, Fr. *Pichurimbohnen, Sassafrasnüsse*, G.—The seeds of *Nectandra Puchury-major* Nees, and of the *N. Puchury - minor* Nees (*Ocotea Puchury - minor* Mart.) (Fam. *Lauraceæ*), yielding respectively "*Fabæ Pichurim majores,*" or larger pichurim seeds, and "*Fabæ Pichurim minores,*" smaller pichurim seeds. The two species are closely allied and both have been known to botanists as *Ocotea Pichurim* H. B. K. (*Laurus Pichurim* Willd.). The trees grow in Brazil, Guiana, Venezuela, and other parts of South America, and are sometimes spoken of as *Brazilian* or *South American Sassafras.* The seeds of commerce usually consist of the separated cotyledons. They are plano-convex, from 3 to 5 cm. in length and nearly 2 cm. in width. Externally they are smooth and blackish-brown, being internally light brown. They have an aromatic odor combining that of nutmegs and sassafras, and a spicy pungent taste.

Pichurim beans contain a fatty matter of the consistency of butter, consisting largely of *laurostearin*, and a concrete volatile oil, *pichurim camphor* which appears to be identical with *laurel camphor.* A liquid product brought from South America and known as the *native oil of laurel* or *sassafras*, is obtained by incising the trunk of the *Nectandra puchury.* This is believed to be the same as that with which the copaiba from Maracaibo is adulterated. It may be distinguished from copaiba by its ready solubility in alcohol of 0.838 and by the fact that its volatile oil is acted on by potassium.

In South America pichurim seeds are said to be used as a substitute for nutmeg, and have even been called by that name. They are rare in this country. The oil obtained from the tree is said to impart its odor to the perspiration and urine, and to be useful in *rheumatism, gout*, etc.

Picoline. *Alphamethylpyridine. Alphapicoline.* $C_5H_4.N(CH_3)$.—This is obtained by the dry distillation of bones or coal. It is a colorless liquid having a specific gravity of 0.952, and is miscible with both water and alcohol. It has been used as a nerve sedative and to lessen heart action when diseased.

Picrasma. *Picrasma quassioides* (Ham.) Benn. (Fam. *Simarubaceæ.*)—The wood of this upright shrub or small tree, which grows in the subtropical Himalayas, and resembles closely the *Ailanthus* in its appearance, has an intensely bitter taste, and has been proposed as a substitute for quassia. W. Dymok and C. J. H. Warden have found in it a crystalline principle which they believe to be quassin, and to exist in the probable proportion of from 0.02 to 0.03 per cent. The same investigators believe that the drug has in it a peculiar alkaloid. (*P. J.*, xx, 1889.) A principle analogous to quassin was isolated by Shimoyamo from the bark of *P. eilantoides.* (*Ap. Ztg.*, 1892, 439.)

Picrotoxin.—This is a feebly acid principle found in the *Cocculus Indicus* (see Part I). It was formerly official in both the U. S. P. 1890 and the British Pharmacopœia, 1898. It occurs as: "Colorless, flexible, shining, prismatic crystals, or a micro-crystalline powder, odorless, and having a very bitter taste; permanent in the air. Soluble, at 15° C., in 240 parts of water, and in 9 parts of alcohol; in 25 parts of boiling water, and in 3 parts of boiling alcohol; also soluble in solutions of the alkalies, and in acids. Very slightly soluble in ether or chloroform. Picrotoxin is neutral to litmus paper. When heated to 200° C., picrotoxin melts, forming a yellow liquid, and upon ignition it is consumed, leaving no residue. Concentrated sulphuric acid dissolves Picrotoxin with a golden-yellow color, very gradually changing to reddish-brown, and showing a brown fluorescence. On mixing about 0.2 Gm. of powdered sodium nitrate with 3 or 4 drops of sulphuric acid, in a small, flat-bottomed capsule, sprinkling a minute quantity of Picrotoxin over it, and then adding, from a pipette, concentrated solution (1 in 4) of sodium hydrate, drop by drop, until it is in excess, the particles of Picrotoxin will acquire a brick-red to deep red color which fades after some hours. On diluting 2 cc. of alkaline cupric tartrate volumetric solution with 10 cc. of water, and adding a small portion of Picrotoxin, red cuprous oxide will be separated within half an hour at ordinary temperatures, and much more rapidly upon the application of heat. The aqueous solution of Picrotoxin should remain unaffected by mercuric or platinic chloride test-solution, tannic acid test-solution, mercuric potassium iodide test-solution, or other reagents for alkaloids (absence of *alkaloids*)." *U. S.*, 1890. It may be separated from acidulated aqueous solution, but not from alkaline, by shaking out with chloroform.

By the action of hydrochloric acid it is deposed into two dilactones called *picrotin*, $C_{15}H_{18}O_7$, and *picrotoxinin*, $C_{15}H_{16}O_6$. Picrotoxinin shows a brick-red color, when tested with the Langley reaction, while picrotin is indifferent in this case. See a paper by Meyer and Bruger, *Ap. Ztg.*, 1890, 67. In Europe, picrotoxin was at one time added to malt liquors in order to give them bitterness, and intoxicating properties,—but the practice is forbidden by law, in England, under heavy penalties and is rarely, if ever, practised now. For method of detection see *U. S. D.*, 20th edition, p. 1550. To procure picrotoxin, the aqueous extract of the seeds is triturated with pure magnesia, and then treated with hot alcohol, which dissolves the picrotoxin, and yields it upon evaporation. In this state, however, it is impure. To obtain it colorless it must be again dissolved in alcohol, and treated with animal charcoal. After filtration and due evaporation, it is deposited in the crystalline form.

Picrotoxin is a violent poison to all classes of vertebrates, producing, when in sufficient dose, violent convulsive attacks with periodic arrest of respiration, slowing of the heart beat, and finally death. In mammals the pupils are usually contracted although later dilated, there is salivation, frequently vomiting, and stupor deepening into coma. The precise mechanism of the convulsive attacks is not known but there appears to be an intense stimulation of the whole central nervous system, including the cerebrum, medulla and spinal cord. In frogs the convulsions persist after removal of the cerebrum but are abolished by destruction of the medulla; in mammals they are modified by removal of the cerebrum and disappear when the pons is destroyed. Koppen (*A. E. P. P.*, 1892, xxix) has shown that in mammals picrotoxin antagonizes the somnifacient effects of chloral hydrate and according to Kossa (*Ungar. Arch. f. Med.*, 1892, i) it increases the toxicity of morphine. The exciting effect upon the medullary centers is shown by the rise in blood pressure due to an action upon the vasomotor center, by the slowing of the pulse from stimulation of the cardio-inhibitory center, by the rapid respirations, and by the emesis. There is salivation, contraction of the pupil, and sweating, also due to an action upon the nerve centers. According to Hayashi (*A. E. P. P.*, 1903, l, p. 247) the drug has a marked antipyretic effect even in doses too small to cause convulsions. Tatum (*J. P. Ex. T.*, 1922, xx, 385) finds that small doses increase the amount of sugar in the blood. In man picrotoxin acts as it does in the lower animals and a number of cases of serious and even fatal poisoning have been produced by it or the plants in which it is found.

Picrotoxin has been used in various nervous diseases such as *epilepsy, hystero-epilepsy* and *chorea.* It has also been used in the treatment of *night sweats;* such effect as it may have in this condition is due to its stimulant action upon the circulation and respiration. Paterson (*S. M.*, 1907) recommends it for the prevention of post-anesthetic *vomiting. Dose,* from one-hundredth to one-thirtieth of a grain (0.0006 to 0.002 Gm.).

Pidan.—This name is applied to a Chinese egg food which is a product of bacterial change brought about by long keeping. The changes that are produced are similar to those occurring in the ripening of cheese.

Pinckneya. *Pinckneya pubens* Michx. *Georgia Bark. Bitter Bark. Fever Tree.* (Fam. *Rubiaceæ.*)—A large shrub or small tree, native to South Carolina, Georgia, and Florida, in marshy banks of streams within the pine barrens. It bears ovate or oblong, opposite leaves and large showy cymes of white, tubular flowers, dotted with red. The bark is bitter and has been used with alleged advantage in *intermittent fever.* E. H. Naudain (*A. J. P.*, April, 1885) found in it a glucoside, *pinckneyin*, but no alkaloid.

Pineapple. *Ananas sativa* Schult. f. (Fam. *Bromeliaceæ.*)—This is an herb indigenous to tropical America and cultivated in Florida and other subtropical districts for its delicate fruit. The fruit consists of a dense spike of connate fleshy berries and bracts, forming together an ovoid or subglobular compound fruit, which is seedless through cultivation, and crowned by a tuft of rigid leaves. Some years ago V. Marcano discovered that the juice of the ordinary *pineapple* has the power of digesting proteid vegetable and animal substances. R. H. Chittenden (*Trans. Connecticut Academy*, vol. viii, 1891) found that the fresh pineapple juice is a constant and powerful digestant of albuminous matters; that the ferment is decidedly active in the presence of either acids or alkaline carbonates, but is most energetic in neutral solution; that it is most active between 50° and 60° C.; still digests at 30° C., but is destroyed at a temperature of 70° C.; the ferment, to which the name *bromelin* has been given, is more nearly related to trypsin than to pepsin, forming during its action not only proteoses and peptone, but also leucine and tyrosine.

E. V. Flack found in fresh pineapples grown in Cape Colony: Crude fat 1.11 per cent., proteins 0.49 per cent., crude fiber 0.33 per cent., nitrogen-free extract 13.51 per cent., ash 0.70 per cent., silica 0.069 per cent., lime 0.047 per cent., potash 0.358 per cent., phosphoric oxide 0.024 per cent., and moisture 83.86 per cent. (*Chem. News*, 1912, 99.)

Pimpinella. *N. F. IV. Pimpernel Root. Pimpinella Saxifraga* L. *Small Burnet Saxifrage. Saxifraga. Radix Pimpinellæ,* P. G. *Grand Boucage,* Fr. *Pimpinell, Bibernell,* G.—"The dried rhizome and roots of *Pimpinella Saxifraga* Linné, or *Pimpinella magna* Linné (Fam. *Umbelliferæ*)." *N. F. IV.*

Pimpinella Saxifraga L. is a smooth-stemmed perennial herb attaining a height of 1 to 2 ft. It bears pinnate leaves, the leaflets of which are ovate to sub-orbicular, serrate below and narrow-lobed above. Its flowers are white and arranged in compound umbels. *P. magna* L. resembles the former species but has all of its leaflets ovate-serrate, somewhat cut, the terminal one being 3-lobed. Both of these herbs are indigenous to Europe. They are also naturalized, growing along roadsides and in waste places in the northern United States and Canada. The root has a strong, aromatic, yet unpleasant odor, and a sweetish, pungent, biting, aromatic, bitterish taste. Pimpinella was described by the N. F. as "cylindrical or slightly tapering, from 10 to 20 cm. in length and from 1 to 1.5 cm. in diameter at the crown, frequently branching, sometimes split longitudinally or broken into pieces; the upper or rhizome portion annulate, with undeveloped stem buds and a few attached stem remains which should not be over 5 cm. in length; roots longitudinally wrinkled, slightly annulate, cortex thin, easily detached; fracture short when dry, tough and flexuous when damp; externally light yellowish-brown; internally porous; cortex broad and whitish with numerous groups of projecting radial bast fibers and reddish-brown oleoresin cells; wood yellowish, usually with a few indistinct fibers, medullary rays interrupted, cambium zone distinct. Odor aromatic; taste sweetish, pungent and acrid.

"The powdered drug, when examined under the microscope, shows numerous simple or two- to four-compound starch grains, the individual grains being from 0.004 to 0.01 mm. in diameter; secretion canals from 0.05 to 0.06 mm. in diameter; tracheæ reticulate or scalariform, from 0.035 to 0.07 mm. in breadth; fibers, thin-walled numerous, thick-walled with simple pores few (*P. magna*).

"Pimpinella yields not more than 5 per cent. of ash." *N. F. IV.*

The commercial supplies of this drug are imported from Germany.

Its active constituents are volatile oil and an acrid resin. The yellow volatile oil has an odor recalling parsley, and a biting taste. Buchheim obtained from the alcoholic extract a crystalline principle, which he called *pimpinellin*, $C_{13}H_{10}O_5$. It is insoluble in water and petroleum ether, but soluble in alcohol. It is considered diaphoretic, diuretic, and stomachic, and has been used in *chronic catarrh, asthma, dropsy, amenorrhea*, etc. The *dose* in substance is about half a drachm (2.0 Gm.), and in infusion two drachms (7.7 Gm.). The root is used also as a local stimulant in toothache, etc.

Pinguicula Vulgaris L. and **Pinguicula Alpina** L. (Fam. *Lentibuliariaceæ.*) *Butterwort.*—These carnivorous plants of the northern United States and Canada are used as a folk medicine in the treatment of wounds and as a purgative. It has been asserted that *P. vulgaris* contains a proteolytic ferment; this has been used in combination with the extract of thyme in the treatment of whooping-cough under the name of "*diatussin.*" The *dose* of diatussin for a child of five years is one to three drops twice a day.

Pini-Pini. *Arra Diabo.*—This is the bark of *Jatropha urens* L. (Fam. *Euphorbiaceæ*). This stinging, spiny Brazilian plant has been long used by the natives of Southern America as a blistering agent. Very little is known of its constituents.

Piper Novæ-Hollandiæ Miq. (Fam. *Piperaceæ.*)—The berries of this Australian pepper contain a volatile oil, and are said to be useful in *gonorrhea* and allied diseases.

From the leaves of *Piper ovatum* Vahl, a plant found growing in Trinidad, Dunstan and Carr (*Chem. News*, 1895, 278) extracted a crystalline principle, *piperovatine*, $C_{16}H_{21}NO_2$. It is insoluble in water, but soluble in alcohol. It is said to act as a depressant of both motor and sensory nerves, and as a stimulant to the spinal cord.

Piperazine. *Arthriticine. Diethylene-diamine. Piperazidine.* $N_2\left\{\begin{matrix}H_2 + 6H_2O\\(C_2H_4)_2\end{matrix}\right.$.—This is formed by the action of ammonia upon ethylene bromide or chloride. A mixture of bases from this reaction is fractionated, and from the fraction boiling between 130° and 180° C., the dietnylenediamine separates on cooling. It forms glassy lustrous tables, melting at from 104° to 107° C., and boils at 145° C. Piperazine is very soluble in water and slightly less so in alcohol. Exposure to air is said to cause its eventual decomposition, due to the fact that it absorbs carbon dioxide from the air. It is strongly alkaline and combines with acids to form salts, and is incompatible with alkaloids; almost all oxidizing agents decompose it. Iron salts or compounds precipitate it from solution and when triturated dry with acetanilid, phenacetin or antipyrine it forms a liquid compound. In experiments made by Bock upon rabbits, no evidence of stimulating properties could be obtained. The blood pressure was never increased, but if the dose were large enough was temporarily depressed. In a cold aqueous solution it is said to dissolve twelve times as much uric acid as will lithium carbonate, and one part of uric acid and piperazine dissolves in fifty parts of water, while lithium urate requires three hundred and sixty-eight times its own weight to dissolve it.

Piperazine was introduced into medicine because its power of dissolving uric acid in the test tube led to the hope that it would exercise a similar solvent action in the system, and prove a valuable remedy, not only in the treatment of uric acid *gravel* and *calculi*, but also in *gout*. While piperazine enjoyed for a time a wide popularity in the treatment of *gout*, the present evidence is that it is of little if any value. Hanzlik (*J. Lab. Clin. M.*, Feb., 1917, 308) has found that in quantities corresponding to the therapeutic dose it does not increase the solvent action of the urine upon uric acid. Umpfenbach's statement that it is a powerful diuretic is denied by Hanzlik. During the taking of piperazine the urine usually is reddish-brown, and the drug can be readily obtained from the urine. Piperazine may be given hypodermically in a 2 per cent. solution, which is said to produce some pain but no abscesses; or, better, fifteen grains (1.0 Gm.) of it may be administered during the day in a quart of plain or carbonated water. It is so hygroscopic that it cannot well be given in pill or powder.

Under the name of *ichthyolidin* the ichthyolate of piperazine has been proposed as a more effective method of administering this drug.

Piperazine Quinate. *Sidonal.*—This is introduced with the idea of combining the powers of quinic acid, which hastens uric acid elimination, with the solvent properties of piperazine. It is a white crystalline powder with a faintly acid reaction, readily soluble in water. It is used in *gout* and in *neurasthenia* in *doses* of from ten to twenty grains (0.65–1.3 Gm.), but is of very doubtful service.

Piperonal. *Heliotropin.*—This interesting substance, although used almost exclusively in perfumery, has been recommended by Fraggani (*Ph. Centralh.*, xxviii, 253) as an antiseptic and antipyretic and by Moore (*J. A. M. A.*, 1918, lxxi) as a protective against lice. It may be obtained by the oxidation of piperic acid. This piperonal is the aldehyde of *piperonylic acid*, $C_6H_3(COOH)\genfrac{}{}{0pt}{}{O}{O}>CH_2$, which, as the formula indicates, is the methylene ester of protocatechuic acid, $C_6H_3CO\text{-}OH(OH)_2$. See also *Schim. Rep.*, 1903, 133.

Pipi Root.—The root of the *Petiveria alliacea* L. (Fam. *Phytolaccaceæ*). The root of this shrub, which grows in Mexico, attracted some notice in the latter part of the 19th century as a stimulating expectorant and diaphoretic. For further description see *U. S. D.*, 20th ed., p. 1554.

Piscidia. *Piscidia Erythrina* L. *Jamaica Dogwood. Fish-Poison Tree. Écorce du Bois de chién. Écorce de Piscidie. Mulungu. Murungu.*—This is a leguminous tree growing throughout the West Indies and the neighboring countries, being found in Florida, Texas, Mexico, and the northern portion of South America, and yielding to commerce a very valuable wood. It is characterized by having imparipinnate leaves with 7–11 oblong or elliptical leaflets, purplish-white flowers and legumes with 6–8 black seeds. From time immemorial the bark has been used for catching fish. The leaves, twigs, and root bark are collected, macerated with the residue from the distillation of rum or with lime water, then transferred into baskets, and the latter dragged up and down the water until the fish are stupefied.

The bark is in pieces of 5–10 cm. in length and about 8 cm. in width, having a thickness of 1.5 cm. The outer surface varies from a yellowish to a dark brown and is frequently studded with flattened protuberances of a lighter color than the surrounding cork. The central part of the bark is much lighter colored, and, when wet or freshly broken, is of a peculiar blue-green color. The bark has a strong odor resembling opium. It is acrimonious, and produces a burning sensation in the mouth and pharynx.

E. Hart obtained a neutral principle, $C_{29}H_{24}O_8$, to which he gave the name *piscidin.* (*A. J. P.*, 1883, 369.) Berberich (*A. J. P.*, Sept., 1898) showed that the principle was glucosidal and found their melting point to be 192° C. Paul C. Freer and A. M. Clover (*A. Pharm.*, Feb., 1901) found this principle to consist of two distinct chemical compounds. The first of these forms colorless, highly refracting rectangular prisms, melting at 201° C.; composition $C_{23}H_{20}O_7$. The second separates from alcohol in fine yellow needles, melting at 216° C.; composition $C_{22}H_{18}O_6$. The authors found also in the aqueous extract of the bark *piscidic acid* soluble in water; insoluble in chloroform, benzene or ligroin. It forms acicular crystals, which melt at 182° to 185° C.; composition $H_2.C_{11}H_{10}O_7$.

Ott (*T. G.*, March, 1883) has shown that the Jamaica dog wood has narcotic properties and that it causes dilatation of the pupil, increases secretion of sweat and rise of blood pressure. Pittenger and Ewe (*A. J. P.*, 1919, p. 580) find that it affects dogs very similarly to cannabis but requires approximately 17 times the dose of the latter drug.

The exact practical value of the drug has not been determined, nor are the results produced in man, by doses approaching toxic, known. Hamilton took a drachm, when suffering with severe toothache, on going to bed. He first felt a violent sensation of heat internally, which gradually extended to the surface, and was followed by profuse perspiration, with profound sleep for twelve hours. On awaking, he was quite free from pain, and without the unpleasant sensations which follow a dose of opium. Various practitioners have reported good results from its use as an anodyne in *neuralgia, nervous insomnia, whooping cough*, etc., but in other hands it has failed to do good. H. C. Wood found it in one case of neuralgia to produce great nausea and gastric distress without evincing the slightest narcotic effect. (For formula for fluidextract by Lemberger, see *U. S. D.*, 19th ed., 1616.) The *dose* of the fluidextract is a fluidrachm (3.75 cc.), to be carefully increased.

Pithecolobium. *Pithecolobium Saman* Benth. (Fam. *Leguminosæ.*)—A shade-tree, growing from Mexico to Brazil, and planted for shade in Japanese coffee plantations, which yields a poisonous alkaloid, *pithecolobine-saponin*, whose physiological action is analogous to that of sapotoxin.

Plantain. *Plantago major* L. *Rib Grass. Ribwort. Ripple Grass. Plantain*, Fr. *Wegerich*, G. (Fam. *Plantaginaceæ*).—The leaves are saline, bitterish, and acrid to the taste; the root is saline and sweetish. The common plantain weed was formerly considered refrigerant, diuretic, deobstruent, and somewhat astringent. The ancients esteemed it highly, but it is at present never used, except externally in domestic practice as a stimulant application to sores. The leaves are applied whole or bruised in the form of a poultice. *Plantago media* L., or *hoary plantain*, and *P. lanceolata* L., or *rib grass*, which are also naturalized in America, possess properties similar to those of *P. major*, and may be used for the same purposes.

For results of examination of the leaves of *P. major*, see Rosenbaum (*A. J. P.*, 1886, 418.) J. F. Strawinski found in the rhizome a substance which he believes to be either phlobaphene or protocatechuic acid. (*A. J. P.*, 1898, 189.)

Bourdier (*A. Pharm.*, ccxlvi) has found in a number of species of *plantago*, including the *P. major*, a glucoside *aucubin*, which was isolated from the *Aucuba japonica.*

Plasmon.—The freshly precipitated casein of skimmed milk, after mixing with a slight amount of sodium bicarbonate, is kneaded and dried at a temperature of 70° C., in an atmosphere of carbonic acid gas. It contains a large amount of proteids and is asserted to be a highly nutritious and palatable food for convalescents and invalids.

Platinum. Pt. 195.2. *Platine, Orblanc*, Fr. *Platin*, G.—A silvery white metal of the group also including gold and iridium. Sp. gr. 21.5, melting point 1750° C. It is unaffected by alkalies and also by acids excepting nitro-hydrochloric. Halogens readily combine with it. The richest deposits of platinum are found in Russia although small amounts are mined in the United States of Colombia, in New South Wales, Australia, in the Ronda Mountains of Spain and in parts of Germany. *Platinum* and its salts are of much importance for various chemical manipulations. On account of its resistant properties platinum is used for dishes, crucibles and other apparatus used in analytical and manufacturing chemistry. Because of the high cost of platinum, substitutes which can be used in its place for laboratory apparatus, are constantly being sought. Among these are alloys of gold and platinum. Crucibles of this type are not suitable for electrolytic work nor for temperatures above 1000° C., but may be used for estimating $CaCO_3$,$BaSO_4$,Fe_2O_3, or ZnO. Such an alloy containing 89 parts of gold and 11 of platinum is known as *platino*. *Stellite* is an alloy of cobalt and iridium; *platinite* of chromium and steel. Alloys of palladium and gold have been proposed under the names of *palau* and *rhotanium*. *Illium* is an alloy of secret composition intended for the same purpose.

The *platinum sponge* is an active catalyzing agent, and is used for various oxidation processes. *Colloidal platinum*, formed by the action of an electric arc between platinum wires under water forms in water a deep black liquid, which has a strong catalytic effect, resembling in many respects the action of organic ferments. Under the name of *platinum chloride* there is used to a wide extent as a precipitant for alkaloids, and for various other chemical purposes, *chloroplatinic acid*, $H_2PtCl_6.6H_2O$. This is made by dissolving the metal in nitro-hydrochloric acid, and evaporating with hydrochloric acid until all the nitric acid is removed. *Platinum tetrachloride*, $PtCl_4.5H_2O$, may be obtained by mixing an aqueous solution of chloroplatinic acid with a solution of silver nitrate; a precipitate containing the silver, combined with some platinum and chlorine, separates, and the yellowish-red solution yields on evaporation fine, large, red crystals of platinum chloride. Under the name of *bichloride of platinum*, the double *chloride of platinum and sodium* was formerly used in medicine to a small extent in the treatment of *syphilis*, but has been abandoned. When injected into the circulation in *doses* of fifteen to thirty grains, the soluble salts of platinum cause in the lower animals a primary stage of motor excitement, followed by paralysis of the central nervous system and later of the muscles themselves. The *dose* of platinum and sodium chloride is from one-half to two grains (0.032–0.13 Gm.) two or three times a day, generally in pill form.

Plevacol.—This is a mixture of tri-cresol, formalin and *amido-benzoyl-eugenol*, which is employed in dentistry for the purpose of filling roots and capping amputated pulp. It forms yellowish-white, or colorless crystals, melting at 155° to 156° C., soluble in acetone, benzol, alcohol, and in glacial acetic acid on warming.

Plumbago Europea L. *Leadwort. Dentellaria.* (Fam. *Plumbaginaceæ.*)—A perennial, herbaceous plant, growing in the south of Europe. It has an acrid taste, and, when chewed, excites a flow of saliva. This is particularly the case with the root, which has been long used to relieve toothache; hence its French name *dentelaire*. A decoction of the root in olive oil has been highly recommended for *itch*. A crystallizable, acrid principle, called *plumbagin*, has been extracted from the root by Dulong. (*J. P. C.*, (2), xiv, 441.) *Plumbago zeylanica* is said to be a very powerful diaphoretic.

Plumiera. *Pagoda Tree.*—The bark of *Plumiera sucuuba* Spruce (Fam. *Apocynaceæ*), a plant growing in South America which the natives of Brazil have long used in the treatment of fevers. It is asserted also to be an anthelmintic and emmenagogue. Plumier, the French botanist, first brought this plant to the attention of the medical profession. The important constituents of the plant are *plumierin* (*agoniadin*), $C_{21}H_{26}O_{12} + H_2O$, and *plumieric acid*, $C_{20}H_{24}O_{12}$. The *P. acutifolia*, said to contain an alkaloid, $C_{57}H_{72}N_{33}$, has been used in the treatment of *gonorrhea*.

Poison Gas.—Duringthe World War a number of poisonous gases were employed by various methods. The methods employed may be divided into two groups, those in which large cylinders of the gas were opened in a favorable wind and allowed to drift towards the enemy and those in which various containers, either artillery shells or hand grenades, were exploded in the neighborhood of the enemy. Norris (*J. A. M. A.*, 1918, lxxi, p. 1822) divided the gases into five groups as follows: 1. Lacrimators. These include the bromo-acetone, $CH_2BrCOCH_3$, xylene, bromide and benzyl bromide, $C_6H_5CH_2Br$. Their action is to cause intense irritation in the eye with lachrymation and temporary functional blindness. 2. Sternutators. These, of which *diphenylchlorarsin*, $(C_6H_5)_2AsCl$, is the most important example, irritated the mucous membrane of the upper respiratory tract causing sneezing, and coughing often with headache and vomiting. Their action is very rapid and they were employed chiefly as a preliminary to bombardment with more fatal gases in order to prevent the putting on of protective gas masks. 3. Lung irritants, including chlorine, *phosgen* (*carbonylchloride*, $COCl_2$) *diphosgen* (trimethylchloraforminate), and oxychlorcarbon. These gases cause intense irritation of the respiratory tract resulting in pulmonary edema. 4. Vesicants, of which the best known are the so-called *mustard gas* (*dichlorethylsulphide*) $(CH_2ClCH_2)S$ and *dichlormethylether* $(CH_2Cl)_2O$. These caused, when in contact with the skin, blistering, followed by ulceration and if inhaled intense irritation of the larynx, trachea and bronchii. In the latter cases death was due to broncho-pneumonia. 5. Blood-poisons. Carbon monoxide, which caused asphyctic death by combining with hemoglobin, and arsin which caused hemolysis.

The most deadly of these cases were lung irritant groups. The earliest used was chlorine gas which was afterwards replaced by phosgen (also known as *palite*), which in turn was later replaced by the *diphosgen* or *superpalite*. The latter is so intense an irritant that, in sufficient concentration, when inhaled may kill by laryngeal spasm. In the more common groups of cases from the inhalation of less concentrated vapors, death was due to asphyxiation caused by pulmonary edema. Vapors as dilute as one part in one million are toxic if breathed over a considerable period of time. Cow (*L. L.*, May 29, 1915) recommends the use of atropine combined with inhalations of oxygen in the treatment of chlorine-gas poisoning. Diphosgen in contact with water forms hydrochloric acid. The fatal cases from this gas usually died within 24 hours. The treatment consists of absolute rest, body warmth, venesection, cardiac stimulation and inhalation of oxygen. All opiates and anodynes are contraindicated. Expectorants and depressants are also to be avoided.

Mustard gas, also known as *yperite*, has a faint odor similar to that of French mustard and is not immediately irritant so that soldiers often remained in contact with the gas for several hours before becoming conscious of its presence. The symptoms usually appeared in from 1 to 3 hours. The early symptoms were smarting and redness of the eyes which was followed by photophobia and lachrymation. Later there is widespread purulent irritation, in all the upper respiratory tracts. These cases generally also showed destructive irritation of the skin as clothing saturated with the gas is irritant enough to destroy the epidermis.

According to Marshall (*J. A. M. A.*, 1919, lxxiii, 684) the so-called mustard gas is really not a gas but an oily liquid which vaporizes slowly in the air. Animals exposed to an atmosphere containing one part per million die after 8 hours' exposure. There may be an absorption of the gas through the lungs in which case systemic poisoning may be caused. This, however, is not common in conditions of actual warfare. The symptoms following the systemic ingestion of this gas are salivation, hyper-excitability and convulsion, vomiting and diarrhea and slow irregular heart. He says that negroes are much more resistant to the gas, at least as far as the skin lesions are concerned, than white men.

For studies of the pathology of mustard gas poisoning see Marshall, Lynch and Smith (*J. P. Ex. T.*, 1918, xii, 265).

The treatment of mustard gas poisoning should consist of thorough cleansing of the entire body with soap and water, douching of the eyes, nose and mouth with a 1 per cent. solution of sodium bicarbonate, followed by installation of a bland oil containing ½ per cent. of dichloramin-T, which acts not only as an antiseptic but as a chemical antidote by virtue of its chlorine content. Skin burns should be treated with alkaline dusting powders.

Pollantin (Fall). *Dunbar's Serum.*—A hay fever serum prepared by introducing the pollen of golden rod and other plants into the blood of animals. After a certain period of time, blood is drawn and from this the serum is prepared. While the claims made for this product by its manufacturers are no doubt exaggerated, yet clinical evidence has proven it to be of value in some cases. It is used by installation in the eye and nostrils, and not intended for hypodermic use. This serum may also be obtained in powder form, which is merely the evaporated serum powdered and diluted with milk sugar.

Polygala. *Polygala polygama* Walt. (*P. rubella* Muhl.) (Fam. *Polygalaceæ.*) *Bitter Milkwort. American Bitter Polygala. Polygale, Laitier*, Fr. *Kreutzblume, Milchwurz*, G.—*Bitter polygala* is a perennial herb, up to 1 foot in height which grows from Nova Scotia to Florida and Texas. It bears numerous cleistogamous flowers. It was formerly official. It has a strong and permanent bitter taste, which it yields to water and alcohol. In small doses bitter polygala is tonic, in larger, laxative and diaphoretic. It appears to be closely analogous in medicinal virtues to *Polygala amara* L., of Europe, which is used for a similar purpose. From the seeds of the *P. butyracea* Heck. and Schlag., an African plant, the natives prepare an edible fat. (See *P. J.*, 1889, xx.)

A senega which was first used in Japan, and which has been referred by some writers to *P. japonica*, by others to *P. tenuifolia*, has been examined by Reuter, who finds in it 0.8 per cent. of resin, traces of methyl salicylate, and 8.8 per cent. of an oil which has somewhat the odor of patchouli.

Polygonatum. *Polygonatum officinale* (L.) All. (*Convallaria Polygonatum* L., *Polygonatum uniflorum* Gilib.) *Sealwort. Solomon's Seal. Sceau de Salomon, Genouillet*, Fr. *Weisswurzel, Salomons Siegel*, G. (Fam. *Liliaceæ.*)—A perennial, herbaceous European plant, whose root is inodorous. It is said to be emetic. In former times it was used externally in *bruises*, especially those about the eyes, in *tumors, wounds*, and *cutaneous eruptions* and was highly esteemed as a cosmetic. At present it is not employed. The berries and flowers are said to be acrid and poisonous. *Polygonatum multiflorum* L. (All.) (*C. multiflora* L.), which grows in Europe and Asia, is analogous to the preceding in properties.

Polymnia. *Polymnia uvedalia* L. *Leafcup. Bear's Foot.* (Fam. *Compositæ.*)—A tall, rough-hairy, shrubby plant, growing in rich soil from New York to Missouri and southward. Great virtues as a remedy in *malarial splenic enlargements* have been attributed to this plant.

Polypodium. *Polypody. Fern Root.*—Various species of this genus of ferns are asserted to have medicinal properties. *Polypodium vulgare* L., very common both in Europe and America, was believed by the ancients to be an active cholagogue purgative, and has been used in modern times as an expectorant in chronic *catarrh* and *asthma. Dose*, from one to eight drachms (3.9–31 Gm.), usually given with a cathartic. The rhizome, as it usually occurs in commerce, is from 2 to 12 cm. in length and 3 to 8 mm. in thickness, somewhat contorted, covered with brown, easily separable scales, which should be removed before being used. Its color is reddish-brown, with a tinge of yellow, its odor disagreeably oleaginous, its taste peculiar, sweetish, somewhat bitter, and nauseous. *P. adiantiforme*, of Porto Rico, is believed by the natives to be a powerful antisyphilitic. It must be used freely for several months in the advanced stages of the disease. *P. friederichsthalianum*, of Central America, has had similar properties attributed to it.

Polytrichum. *Polytrichum juniperinum* Hedw. (Fam. *Polytrichaceæ.*) *Herba Adianti Aurei. Rock-brake Herb. Female Fern Herb. Perce Mousse. Frauenhaar. Jung Fernhaar. Widertot. Wolfgerste. Hair Cap Moss. Robin's Rye. Golden Maidenhair.*—This indigenous moss was esteemed by some physicians of the past generation to be actively diuretic and therefore useful in *dropsy*.

Pongamia. *Pongamia pinnata* W. F. Wight. (Fam. *Leguminosæ.*)—*Pongamia* or *kurung oil* is expressed from the seeds of an East Indian tree. It is deep yellow to reddish-brown, fluid at 15.6° C., but below that it is solid with sp. gr. of 0.9352 (*P. J.*, 72, p. 492). It is especially commended in *pityriasis versicolor* and other parasitic skin diseases. (*P. J.*, Feb., 1883.)

Poppy Capsules. *N. F. IV. Papaveris Fructus. Papaveris Capsulæ.* Br. 1898. *Papaver*, U. S., 1870; *Capsules de Parot blanc ou Pavot officinal*, Fr. Cod.; *Fructus Papaveris immaturi*, P. G.; *Unreife Mohnköpfe, Kapseln des Weissen Mohns, Mohnkapseln, mohnköpfe*, G.; *Papavero*, It.; *Cabezas de amapola*, Sp.—"The dried, fully grown, unripe fruit of *Papaver somniferum* Linné (Fam. *Papaveraceæ*). Separate and reject the seeds before using the fruit in pharmaceutical preparations." *N. F.*

Poppy capsules were formerly official in the Br. (1898) and in the N. F. (IV.) but have been dismissed from both. In England the poppy has been largely cultivated for its capsules, which are gathered as they ripen, and taken to market enclosed in bags. The N. F. directs them to be collected before they are quite ripe, as they then contain more of the active milky juice. When ready for collecting they are a yellowish-green color. They are employed chiefly in preparing Syrup of Poppy Capsules.

Dried *poppy capsules* vary in size from the dimensions of a small egg to those of the fist. They differ also in shape according to the variety of the poppy from which they are procured. On the Continent two sub-varieties of the white poppy are recognized, the *long*, and the *round* or *depressed*. Of these, according to Aubegier, the long are richest in morphine, and his conclusions are confirmed by Meurein, who also found the largest capsules most efficient. Those commonly found in commerce are spheroidal, flattened below, and surmounted by a crown-like expansion —the persistent stigma—which is marked by numerous diverging rays that rise somewhat above the upper surface and appear to be prolongations of partial septa, or partitions, proceeding along the interior circumference of the capsule from the top to the bottom. In the recent state, the seeds, which are very numerous, adhere to these septa, but in the dried capsule they are loose in its cavity, and the N. F. directed that they should be separated before the capsule is used. They were described in the N. F. as "globular or ovoid, usually from 3 to 3.5 cm. in diameter, but varying in size, more or less sunken or depressed on the sides, contracted at the base into a sort of neck immediately above a tumid ring at the point of attachment with the stalk; crowned at the summit with the seven- to fifteen-rayed stigma disk; outer wall of pericarp smooth, hard, grayish-yellow to brownish-yellow, often marked with black spots; interior surface rugose, finely striated transversely, and bearing thin, brittle, membranous placentæ which extend from the sutures toward the center, and bear on their faces and edges numerous, minute, conspicuously reticulated, reniform white seeds. Odorless; taste slightly bitter.

"The powdered drug is grayish-yellow, and, when examined under the microscope, exhibits fragments of the epicarp composed of thick-walled polygonal cells, the cells of the outer layer non-porous, up to 0.05 mm. in diameter and with occasional stomata, the latter up to 0.035 mm. in length; the cells of the inner layer of the epicarp often with numerous simple pores; portions of the soft, spongy sarcocarp consisting of isodiametric or irregular parenchyma and branching milk ducts, the latter up to 0.06 mm. in width, of variable length and with thin, non-porous walls; fragments of the inner wall of the pericarp and the outer wall of the placental tissue composed of polygonal or somewhat elongated cells with porous walls, up to 0.06 mm. in width and up to 0.3 mm. in length, the walls of the latter cells often slightly lignified; spiral and annular tracheæ up to 0.035 mm. in width and reticulate tracheæ up to 0.06 mm. in width; sclerenchyma cells few with simple or oblique pores; starch grains few, small, somewhat rounded; fragments of the reticulately pitted seed-coat very few or absent. Poppy Capsules yield not more than 10 per cent. of ash." *N. F. IV.*

Poppy capsules contain the same active ingredients as opium but in smaller proportion. They were used chiefly in the form of a syrup as a mild narcotic. The *dose* is from ten to twenty grains (0.65–1.3 Gm.).

Portulaca. *Portulaca oleracea* L. *Garden* or *Common Purslane.* (Fam. *Portulacaceæ.*)—This is a fleshy, prostrate annual indigenous to Europe but naturalized in the United States and found frequently both on cultivated and waste grounds. It has been considered a cooling diuretic, and recommended in *scurvy* and urinary affections. The seeds have been considered anthelmintic, but are inert.

Potassio-Mercuric Iodide. *N. N. R.* 1924. *Potassii et Hydrargyri Iodidum. Mercuric Potassium Iodide. Mercury and Potassium Iodide. Potassium Iodohydrargyrate. Mayer's Reagent.* K_2HgI_4.—Mercuric iodide unites with the iodides to form a series of double salts known as *Iodohydrargyrates.* The potassium salt in the anhydrous state represents approximately 25.5 per cent. of mercury but it also crystallizes with either 1, 2 or 3 molecules of water. The anhydrous form occurs in commerce in yellow crystalline pieces, deliquescent in moist air. When mixed with its weight of water it forms a clear solution results, but on dilution mercuric iodide is slowly precipitated, unless an excess of potassium iodide be added; when dissolved in water containing sufficient potassium iodide it forms the compound $HgI_2 2KI$. Under the name of *Mercuric potassium iodide test solution* this liquid is official in the U. S. P. (See Part III.) Clayton suggests the practical method of simply evaporating *Nessler's solution* and collecting the crystals. (*Chem. News,* 1894, 102.)

This is an active preparation, which may be given in the same dose and for the same purposes as corrosive sublimate. It is formed when its components are prescribed together extemporaneously. It is not decomposed by the compound syrup of sarsaparilla, which is frequently used as a vehicle for it. Potassio-mercuric iodide was suggested by F. L. Winckler as a qualitative test of the organic alkaloids. F. F. Mayer subsequently employed, for volumetric analysis, a solution made with 13.546 grammes of corrosive sublimate, 49.8 grammes of potassium iodide, and a liter of distilled water. (See *Mercuric Potassium Iodide Test Solution, U. S. D.,* Part III.)

Potassio-mercuric iodide is a powerful germicide, rivaling mercuric chloride in its potency, and frequently used as a succedaneum for that salt. It has the advantage of not being precipitated by albumin. Its solutions are proven to undergo decomposition unless an excess of potassium iodide be present. Tablets containing the proper quantities of the potassium iodohydrargyrate and potassium iodide for making antiseptic solutions are now marketed by various manufacturing chemists.

Potassium Bisulphate. *Potassii Bisulphas. Acid Potassium Sulphate.* $KHSO_4 = 136.18$.—This is a by-product in various chemical operations, being left as residue when potassium salts are decomposed by sulphuric acid in excess. It is a white salt, the crystals having the form of right rhombic prisms so flattened as to be tabular. The salt has a bitter and extremely acid taste. It is soluble in twice its weight of cold and in less than its weight of boiling water. Alcohol does not dissolve it, but when added to an aqueous solution, precipitates the neutral sulphate. Exposed to the air, it effloresces slightly on the surface, and when moderately heated readily melts, and runs like oil. At a red heat it loses water and the excess of acid, and is reduced to a neutral sulphate. Owing to its excess of acid, it acts as an acid on the carbonates, causing them to effervesce. It is incompatible with alkalies, alkaline earths, and their carbonates, with many of the metals, and with most oxides. This salt was formerly called *sal enixum*. It is aperient. It answers, according to Barker, for preparing a cheap aperient effervescing draught. Equal weights—a drachm, for instance—of the bisulphate and of sodium carbonate may be dissolved separately, each in two fluidounces of water, then mixed, and taken in the state of effervescence. *Dose,* one or two drachms (3.9–7.7 Gm.).

Potassium Bromate. $KBrO_3 = 167.02$. *Potassii Bromas. Bromate de potase,* Fr. *Kaliumbromat, Bromsaures Kali,* G.—This salt is formed in the process employed for making the bromide and may be separated by crystallization. Colorless, cubical or tabular crystals, soluble in 15 parts of cold and 2 parts of hot water. Like potassium chlorate it oxidizes matter like sugar and sulphur and must be mixed with great caution with readily oxidizable substances. It is an ingredient in *Koppeschaar's solution,* which is employed in titrating phenol. (See *Tenth-normal Bromine Volumetric Solution,* Part III.)

Potassium Chloro-Platinite. *Potassium Platinochloride.* K_2PtCl_6.—Eight grains (0.5 Gm.) of this salt, which is used as a toning agent in photography, caused death in an infant of two months, preceded by violent gastro-enteritis and collapse. (*B. M. J.*, i, 1896.)

Potassium Cobalti-Nitrite. $CO_2(NO_2)_{12}K_6 + 2H_2O = 934.32$.—When potassium nitrite is added to a cobalt salt solution acidified with acetic acid, nitrogen is set free, and in course of time the double cobaltic and potassium nitrite separates as a yellowish crystalline powder, almost totally insoluble in acid solution. Wolcott Gibbs having suggested that this nitrite might be less fugacious than other nitrites, on account of its stability and relative insolubility, J. W. Roosevelt tried it in doses of from one-quarter to one-half grain (0.016–0.032 Gm.), every two hours, in kidney cases with high arterial tension and dyspnea, in *asthma,* and also in *cardiac valvular diseases.* He stated that the effects of the drug are similar to those of the nitrites, beginning in fifteen minutes and lasting from two to four hours.

Potassium Cyanide. *Potassii Cyanidum. U. S. VIII. Cyanide of Potassium. Potassii Cyanuretum. U. S.* 1850. *Cyanuret of Potassium. Kalium Cyanatum, Kaliumcyanid, Cyankalium,* G. *Cianuro potasico,* Sp. $KCN = 65.11$.—This salt is no longer official. It occurs in "white, opaque, amorphous pieces, or a white, granular powder, odorless when perfectly dry; deliquescent in the air and exhaling the odor of hydrocyanic acid. *Great caution should be used in tasting and handling this salt.* Soluble in about 2 parts of water at 25° C. Boiling water dissolves its own weight of the salt, but rapidly decomposes it. In alcohol it is but sparingly soluble. At a low red heat the salt fuses." *U. S. VIII.*

For processes of manufacture and tests of purity see *U. S. D.*, 19th edition, p. 996.

Besides the very extensive use of potassium cyanide and sodium cyanide in preparing electroplating solutions for gilding and silvering by electro-deposition, and in photography, large quantities are now consumed in the extraction of gold and silver from the fine residues or "tailings" where amalgamation fails to take up the precious metals. From such solutions of gold in potassium cyanide the metal is thrown out by the action of metallic zinc. Potassium cyanide has the power of dissolving silver oxide and may be used for the removal of silver nitrate stains from clothing. According to Guthrie a solution of three grains (0.2 Gm.) to the ounce (30 cc.), dropped in the eye every other day, will remove olive colored stains from the conjunctiva caused by silver nitrate. Owing to the large use of potassium cyanide for the recovery of gold, numerous accidental cases of poisoning occur in the reduction works. Potassium cyanide acts precisely like hydrocyanic acid as a poison. (See *Acidum Hydrocyanicum Dilutum.*) Five grains of it have repeatedly taken life. It is of no value as a medicine but was formerly employed occasionally as a substitute for hydrocyanic acid in *doses* of from one-eighth to one-quarter of a grain (0.008-0.015 Gm.).

Potassium Ferricyanide. *Ferricyanide of Potassium. Red Potassium Prussiate.* $K_3Fe(CN)_6$.—This is formed by passing a current of chlorine through a solution of potassium ferrocyanide, until the liquid ceases to form a precipitate with a solution of ferric chloride, a proof that the whole of the ferrocyanide has been converted into the ferricyanide. The solution, by due evaporation, yields the compound in question. It may also be prepared, in the dry way, by agitating finely powdered ferrocyanide with chlorine as long as it is absorbed. The reaction is explained by the following equation:

$$2K_4Fe(CN)_6 + Cl_2 = 2K_3Fe(CN)_6 + 2KCl$$

The radical ferricyanogen is supposed to be formed by the coalescence of two molecules of ferrocyanogen, and is sometimes represented by the symbol FCy. This salt, discovered by Gumelin, is in beautiful, deep, hyacinth red, anhydrous crystals, which are soluble in four parts of water. Its solution forms a delicate test for ferrous salts, with which it produces a blue precipitate; but with ferric salts it only produces a green or brown color. It is used in dyeing and calico printing. (See *Test Solutions,* Part III.)

Potassium Ferrocyanide. $K_4Fe(CN)_6 + 3H_2O = 422.35$. *Potassii Ferrocyanidum. U. S. VIII. Potassæ Prussias Flava. Ferrocyanide of Potassium. Yellow Prussiate of Potash. Ferroprussiate of Potash. Prussiate of Potash. Protocyanure jaune de Fer et de Potassium,* Fr. *Kalium Ferrocyanatum, Kalium Borussicum, Cyaneisenkalium, Ferrocyankalium, Gelbes Blutaugensalz,* G.—Potassium ferrocyanide was formerly prepared on the large scale by heating animal matters, such as dried blood, hoofs, chips of horn, woollen rags, old leather, the refuse of tallow chandlers called *greaves,* and other substances rich in nitrogen, with the pearlash of commerce and scrap iron.

In recent years almost all potassium ferrocyanide is prepared from the spent ferric oxide which is obtained in abundance during the purification of coal gas.

Potassium ferrocyanide is in "large, soft, transparent, yellow, four-sided, monoclinic, tabular crystals or prisms; odorless, and having a mild, saline taste. Slightly efflorescent on exposure to the air. Soluble in about 4 parts of water at 25° C., and in 2 parts of boiling water; insoluble in alcohol. When heated to 60° C., the salt begins to turn white from loss of water of crystallization, and when heated at 100° C., it is rendered anhydrous." *U. S. VIII.*

For further description and tests of purity see U. S. D., 20th ed., p. 1560.

Pure potassium ferrocyanide is almost non-toxic. Callies, as quoted by Pereira, found the commercial salt slightly poisonous, but the pure salt unproductive of harm innocuous.

This salt is manufactured on a large scale, chiefly for the use of dyers and calico printers. In chemical manufacturing it is employed to prepare diluted hydrocyanic acid, Prussian blue, and potassium and silver cyanides. Its only medicinal value is as an antidote in *copper sulphate poisoning*. *Dose,* five to ten grains (0.32–0.65 Gm.).

Potassium Glycerophosphate. *Potassii Glycerophosphas.* $K_2C_3H_5(OH)_2PO_4$.—The salt is very hygroscopic and has an alkaline reaction. This salt appears in commerce to-day as a colorless to yellowish liquid, miscible with water in all proportions, and containing from 50 to 75 per cent. of the salt. It is used for the same purposes as sodium glycerophosphate in *doses* of from three to six minims (0.2–0.4 cc.).

Potassium Iodate. *Potassii Iodas. Iodate de Potasse,* Fr. *Kaliumjodat, Jodsaures Kali,* G. KIO_3.—A white crystalline powder, very soluble in water. Demarquay and Custin assert that potassium iodate is superior to potassium chlorate as a local remedy in ulcerative and gangrenous *stomatitis, ptyalism, diphtheria,* and other diseases of the pharyngeal and buccal mucous membrane. *Dose,* from four to eight grains (0.26–0.5 Gm.).

Potassium Nitrite. *Potassii Nitris.—Nitrite of potassium* ($KNO_2 = 85.11$) is most readily obtained by fusing saltpeter with lead, which withdraws one atom of oxygen from the former, and forming thereby litharge. It is a white, fusible, and uncrystallizable mass, usually cast into sticks like the hydroxide. It is very deliquescent, and absorbs carbon dioxide from the air. It shares the activities of the nitrites, producing in animals their physiological effects, and being capable of replacing them in the treatment of disease. Its influence is comparatively slow and permanent. Five grains (0.32 Gm.) have produced mild poisoning. *Dose,* one to three grains (0.065–0.2 Gm.).

Potassium Percarbonate, $K_2C_2O_6 + H_2O$, is a colorless powder which slowly decomposes under the action of water, as follows:

$$K_2C_2O_6 + H_2O = 2KHCO_3 + O$$

In the presence of sulphuric acid, potassium percarbonate decomposes and forms hydrogen peroxide.

$$K_2C_2O_6 + 2H_2SO_4 = 2KHSO_4 + 2CO_2 + H_2O_2$$

This substance has not as yet been used in practical medicine, but is believed to be the material known as *antihypo,* much used in photography, and which has been recommended by Müller for the purposes of decolorizing and counterstaining tubercular bacilli. He washes the preparations for this purpose in 50 to 70 per cent. alcohol and places them for fifteen minutes in a 5 to 10 per cent. solution of potassium percarbonate, and after differentiating rinses in water and counterstains with methylene blue.

Potassium Perchlorate. *Potassii Perchloras. Hyperchlorate of Potassium.* $KClO_4 = 138.56$.—This salt is prepared by fusing potassium chlorate until it begins to assume a pasty condition. The cooled mass consists of potassium perchlorate and chloride. The absence of undecomposed chlorate may be known by a sample failing to communicate a yellow color to hydrochloric acid. The mass must be dissolved in the smallest possible quantity of boiling water, when perchlorate crystallizes out. It is sparingly soluble in water, and insoluble in alcohol. It is used in analytical chemistry as an oxidizing reagent and is formed in the estimation of potassium salts by the use of perchloric acid. Its effects are wholly different from those of potassium chlorate.

Potassium Persulphate. $K_2S_2O_8$. *Potassii Persulphas. Kaliumpersulfat,* G. *Anthion.*—Obtained by electrolyzing a solution of potassium bisulphate. It forms colorless crystals, soluble in about 50 parts of water. Used in photography, owing to its oxidizing of sodium thiosulphate to sulphate.

Potassium Phenolsulphonate. *Potassium Sulphocarbolate.* $C_6H_4(OH)SO_3K + H_2O$.—This forms white crystals soluble in water and alcohol, and melting at 400° C. Therapeutically it is very little used, but it has some use as an antiphylloxerin in checking the ravages of the grape vine parasite.

Potassium Phosphate. *Potassii Phosphas. Dibasic Potassium Phosphate,* $K_2HPO_4 = 174.25$.—The *potassium phosphate* which has come into use as a medicine is the *dipotassic orthophosphate,* having a composition precisely analogous to that of the medicinal sodium phosphate. It may be formed precisely as sodium phosphate is prepared; or by nearly saturating, by means of potassium carbonate, common or orthophosphoric acid, H_3PO_4. The medicinal potassium phosphate is a white, amorphous, deliquescent salt, crystallizing with difficulty. It has been given as an alterative in *scrofula* and *phthisis* with supposed advantage. The *dose* is from ten to thirty grains (0.65–2.0 Gm.), three times a day, dissolved in a teaspoonful of water.

Potassium Picrate. *Potassium Trinitrophenate. Potassii Picras. Kaliumpikrat, Pikrinsaures Kalium,* G. $C_6H_2(NO_2)_3OK$.—This salt may be made by neutralizing a hot solution of 20 parts of picric acid with 7 parts of potassium carbonate and crystallizing in a cool place. Small, yellow crystals, or a yellow powder of a bitter taste, soluble in 230 parts of cold water and 15 parts of hot water; nearly insoluble in alcohol. It must be handled with care, as it explodes by a blow or when heated.

Potassium Silicate. *Potassii Silicas.—Silicate of potassium,* also known as *soluble glass,* is prepared in the same way as the sodium salt. It varies commercially but is usually of the formula, $K_2Si_6O_7$. It may be used as a substitute for plaster of Paris in the preparation of rigid surgical dressings. The solution is applied of a syrupy consistence, by means of a brush, to the bandages, upon which it rapidly hardens, requiring only five or six hours for this result. The facility of removing the bandages by means of hot water is the advantage which *potassium silicate* possesses over most other dressings.

Potassium Sozoiodolate. *Potassium Diodoparaphenolsulphonate.* $C_6H_2I_2.OH.SO_3K$.—A colorless, inodorous, crystalline powder, soluble in 50 parts of water. It is used as a 10 per cent. dusting powder or ointment in the treatment of *herpes* and *eczema*, etc., and as a 25 per cent. ointment in *laryngitis, adenitis*, etc.

Potassium Sulphite. *U. S. VI. Potassii Sulphis. Kali Sulfurosum, Sulfis Kalicus. Schwefligsaures Kali*, G. $K_2SO_3.2H_2O = 194.30$.—Potassium sulphite is in "white, opaque, obliquely-rhombic, octahedral crystals, or a crystalline powder, somewhat deliquescent, odorless, having a bitter, saline, and sulphurous taste, and a neutral or feebly alkaline reaction. Soluble in 4 parts of water at 15° C. and in 5 parts of boiling water; only sparingly soluble in alcohol. When gently heated, the salt loses its water of crystallization (18.5 per cent.); at a red heat it is decomposed and leaves a residue of an alkaline reaction. The aqueous solution of the salt yields a white, crystalline precipitate on the addition of a saturated solution of bitartrate of sodium. Addition of diluted hydrochloric acid to the aqueous solution gives rise to the odor of burning sulphur, and the solution does not become cloudy (difference from *hyposulphite*)." *U. S. VI.* It decrepitates when heated. In the air it effloresces, absorbing oxygen, and being partially converted into the sulphate.

The medicinal uses of this salt are essentially those of the other sulphites. It acts as a slight laxative and diuretic. It escapes from the system with the urine, and may be found for some hours unchanged; at the end of twenty-four hours potassium sulphate is found in the urine instead of the sulphite, proving that the salt undergoes oxidation in the body. It is used for the same purposes as sodium sulphite, over which, however, it has no advantages. *Dose*, from fifteen grains to a drachm (1.0–3.9 Gm.).

Potassium Sulphocyanate. *Potassii Sulphocyanas. Potassium Thiocyanate. Potassium Rhodanide. Potassium Thiocyanide.* $KSCN = 97.18$. *Sulfocyanure de Potassium*, Fr. *Kalium Sulfocyanat, Rhodankalium*, G.—Potassium sulphocyanate, formerly called *potassium sulphocyanide*, is in long, striated, anhydrous prisms, deliquescent in a moist atmosphere, very soluble in alcohol, and having a cooling, somewhat biting taste. It was at one time suggested as a substitute for hydrocyanic acid but as far as we know is no longer used as a medicine. For method of making it see *U. S. D.*, 20th ed., p. 1563.

Potentilla.—*Cinquefoil. Potentilla reptans* L., the *creeping cinquefoil* of Europe, is naturalized from Massachusetts to Ohio, and *Potenilla canadensis* L., one of the common cinquefoils of America (Fam. *Rosaceæ*), have each been used as astringents in *diarrhea, chronic catarrhs, night sweats*, etc. According to J. C. Peacock (*A. J. P.*, 433, 1900), dried *P. norvegica* L. contains four, and *P. canadensis* thirteen, per cent. of tannic acid. (See *P. J.*, 1911, 350.)

Powder of Algaroth. *Pulvis Algarothi. Oxychloride of Antimony. Nitro-muriatic Oxide of Antimony.*—A powder rarely used now. For a description of its uses, properties, etc., see 14th edition, *U. S. D.*

Primula. *Primrose, Cowslip.*—The leaves of various species of primrose, especially the *Primula obconica*, produce in certain persons when handled an active dermatitis somewhat resembling that produced by the poison ivy. The toxic principle is contained in the glandular hairs. Its precise nature is unknown although Simpson (*J. A. M. A.*, 1917, lxix, 95) has presented evidence suggesting that it is of resinous character.

Primula obconica Hance (Fam. *Primulaceæ*) is a popular, perennial, winter-blooming house plant which has been introduced into the U. S. A. and Europe from China and now is commonly cultivated by florists. It is characterized by possessing a dense rosette of long-petioled, ovate-oblong or round-oblong leaves with irregularly scalloped-toothed margins and many long-stalked umbels of lilac or light purple flowers. Its leaves possess numerous glandular hairs, the heads of which contain an irritating principle.

From the roots of *Primula grandiflora*, Bongault and Alland have separated a crystalline polyatomic alcohol, *primulite*, which is said to be identical with the hepatomic alcohol, *volemite*. (*C. R. A. S.*, cxxxv, 796.) Two glucosides, *primeverin* and *primulaverin*, and an enzyme, *primverase*, were isolated by Goris and Mascnè. (*Chem. Cb.*, 1910, No. 3.) and later in the *P. officinalis* (*J. P. C.*, 1920, xxi, 284).

Prinos. *Black Alder. Winterberry. Feverbush. Prinos*, Fr., G.—The U. S. P. formerly recognized under this name the bark of *Ilex verticillata* (L.) A. Gray (*Prinos verticillatus* L.) (Fam. *Ilicaceæ*). This shrub, of which there are 3 well recognized varieties, grows in the United States from Canada to Florida and west to Missouri and Wisconsin, frequenting low, wet places. The berries, which have a bitter, sweetish, somewhat acrid taste, are sometimes used medicinally for the same purposes as the bark. The dried bark occurs in "thin, slender fragments, about 1 Mm. thick, fragile, outer surface brownish ash-colored, with whitish patches and blackish dots and lines, the corky layer easily separating from the green tissue; inner surface pale greenish or yellowish; fracture short, tangentially striate; nearly inodorous, bitter, slightly astringent." *U. S.*, 1880.

Black alder has been considered tonic and astringent, and has been used in *diarrhea* and as a substitue for Peruvian bark, but has no antiperiodic properties. In cases of flabby or ill-conditioned *ulcers* it is popularly used both locally and internally in decoction (two ounces in three pints of water boiled to a quart); *dose*, from two to three fluidounces (60–90 cc.).

Prioria. *Prioria Copaifera* Griseb. (Fam. *Leguminosæ.*)—The *oil tree* is a native of the West Indies. The seeds are edible and in Panama are sold under the names of *Cativa* or *Amanza muger*. The tree yields an exudate which is known as the *gum of the oil tree*. This is a thick, adhesive liquid, resembling copaiba, usually turbid on account of a greenish substance, which, however, finally subsides, leaving a clear, brownish-yellow liquid. For chemical study, see *A. J. P.*, Jan., 1898.

Propaesin. *Propylis Amino-benzoas. Propylamine Benzoate. Paramido-benzoic Acid Propyl Ester.*—It occurs as a white, crystalline powder, very sparingly soluble in water, but freely soluble in both alcohol and ether. Perl (*Med. Klin.*, 1909, v, p. 1892) has found it useful to relieve the pain of *sore throat*, and, internally, to quiet *vomiting* and the pain of *gastric ulcer*. The internal *dose* is approximately one to four grains (0.065–0.25 Gm.), although Cluger asserts (*Th. M.*, 1909, p. 77) that fifteen grains (1 Gm.) may be given without harmful symptoms.

Proponal. *Propal. Propytal. Dipropyl Barbituric Acid.* $(C_3H_7)_2C(CONH)_2CO$.—It occurs as colorless crystals which melt at 145° C., sparingly soluble in cold, but more so in boiling water and easily soluble in dilute alkalies. This hypnotic appears to be closely allied in its range of therapeutic usefulness, as it is in its chemical structure, to barbital. According to Bumke (*Med. Klin.*, 1906) it is one-half again as powerful a somnifacient as barbital, but Ziehen (*D. M. W.*, 1908, p. 583) found that although it was more rapid in its action it was not so certain. It appears also to be less liable to be followed by unpleasant consequences, especially by post-nocturnal drowsiness. The *dose* is from two to eight grains (0.13–0.5 Gm.).

Propyl Alcohol (normal propyl alcohol, $C_2H_5.CH_2OH$) is formed in the fermentation of certain sugar and wine residues, as from the marc of grapes, and is separated from the fusel oil of this fermentation. It is a colorless, pleasant-smelling liquid, boiling at 96° C. See also *Isopropyl Alcohol.*

Propylamine. *Mono-propylamine.* $CH_3.CH_2.CH_2.NH_2$.—For many years this compound was considered to be identical with trimethylamine, but at the present time it is known to be an entirely different product, although isomeric, and to possess distinctive properties. The boiling point of *propylamine* is 49° C., trimethylamine 93° C. Pure propylamine is a clear, highly refractive fluid, pure trimethylamine is a gas. It is generally prepared by heating propyl nitrate with a 10 per cent. alcoholic ammonia solution and is a clear alkaline fluid with a powerful ammoniacal, fishy odor, and soluble in both water and alcohol. In 1854 it was brought forward by Awenarius, of St. Petersburg, as an antirheumatic, but it is rarely used to-day for this purpose. It has also been used as a sedative in *chorea* and *hysteria. Dose,* two to five grains (0.13 to 0.32 Gm.) several times daily. As much as fifteen to forty-five grains (1–3 Gm.) has been administered in the course of a day.

Propylamine Hydrochloride. $CH_3.CH_2.CH_2.NH_2.HCl$.—Deliquescent colorless crystals, easily soluble in water. Uses and properties same as preceding. The *sulphate of propylamine,* $(CH_3CH_2CH_2NH_2)_2H_2SO_4$, well formed crystals, has also been used.

Propylene. *Propene.* C_3H_6.—This occurs in common illuminating gas and is also a by-product in the refining of petroleum. It may be prepared synthetically by heating glycerin with zinc dust. It is a gas which liquefies at −48° C.

Propylene has been suggested as a surgical anesthetic. Brown (*J. P. Ex. T.*, 1924, xxiii, 485) finds that concentrations of 37 per cent. will produce anesthesia and that in 65 per cent. it causes toxic symptoms with fall of blood-pressure. Riggs (*Proc. Soc. Exper. Biol.*, 1925, xxii, 269) finds that the anesthetic potency is considerably higher than that of ethylene and that the recovery is rapid after withdrawal. As far as we know it has not been tested on human beings.

Protea. *Protea mellifera* Thunb. (Fam. *Proteaceæ.*) *Sugar Bush.*—A large bush with linear-oblanceolate leaves, white flowers and showy involucre, indigenous to South Africa. From the leaves Merring Beck, in 1886, obtained *proteacin.* Merck and Hesse subsequently named the principle *leucodrin.* Hesse found the leaves to yield from 2 to 5 per cent. of *hydroquinone* associated with *proteacic acid.* (*P. J.*, 1896, 426.)

Protein Therapy. *Foreign protein therapy. Non-specific protein therapy.*—In 1913 Ichikawa, in studying the treatment of typhoid fever by vaccines, noted that the injection of killed typhoid bacilli was beneficial in cases of infection by the para-typhoid bacillus as well as by the typhoid bacillus. As the antibodies and antitoxins are known to be narrowly limited in their antidotal effects to single specimens or even strains of bacteria, it was surmised that the injections of killed bacteria must have some other effect upon the system than increasing the formation of specific antibodies. Subsequent studies have shown that the parenteral introduction of foreign protein increases the bodily resistance to a large number of pathogenic micro-organisms. Various foreign proteins, including killed bodies of bacteria, milk and proteose, have been employed in a considerable number of infectious diseases, in some cases with marked benefit.

The reaction to intravenous injection of a foreign protein seems to be the same no matter what the type of protein which is used. Unless the dose of the protein be large enough to call forth a fairly vigorous reaction it is not likely that there will be any beneficial effect upon the course of the infection. The typical course of the reaction is about as follows: About half an hour after the injection the patient is seized with a chill of varying severity accompanied with increase in the pulse rate, with more or less headache which may be quite severe—and often nausea and cyanosis. Within 15 to 30 minutes the chill is followed by a fever, the body temperature reaching a point sometimes as high as 105° F.; this fever lasts from a few hours to one or two days. At the time of the chill there is usually a slight reduction in the number of white blood corpuscles but soon after there occurs a great increase in the number of these cells, the leucocytosis reaching its maximum in from 4 to 12 hours after the injection. At the height of the leucocytosis there is ordinarily from 20,000 to 30,000 white cells per cubic millimeter in the blood but as high as 100,000 has been reported. This leucocytosis continues generally for 24 to 48 hours. At the time of the chill there is usually a slight increase in the blood pressure but immediately after there occurs a marked fall.

Most of the early studies of this method of treatment were made with *typhoid vaccine.* Miller (*J. A. M. A.*, 1917, lxix, 765) has reported on 175 cases of various forms of *arthritis* which were treated with this method. In the great majority of cases there was either complete cure or marked benefit in the joint conditions. Complicating endocarditis was not favorably influenced. He gave doses of from 40,000,000 to 115,000,000 killed typhoid bacilli at a dose.

Among the proteins which have been used may be mentioned especially the following: Miller (*J. A. M. A.*, 1917, lxix, 765) uses killed typhoid bacilli in doses of from 40,000,000 to 150,000,000. Gow (*B. M. J.*, Feb. 28, 1920) has employed killed bacillus coli in doses up to 50,000,000. Several authors have used the so-called *Witte's peptone* in doses of 0.5 to 1 Gm. (8 to 16 grains) usually in about a ten per cent. solution. These are generally given intravenously. Schulman (*N. Y. M. R.*, July, 1920) and others have used intramuscular (not intravenous) injections of sterilized milk in doses of 5 cc. (75 minims) and upwards. Barker and Nelson (*J. A. M. A.*, 1924, lxxii, 190) believe the reaction following milk injections is due to the bacteria in it as they failed to obtain the effect from milk of low bacterial count. Various proprietary albumoids, intended for this use, are on the market. Among these may be mentioned *Vaccineurin, Sanarthrit, Caseosan* and *Albusol.*

The following are some of the diseases in which this method of treatment has been employed. In *typhoid fever,* Kraus and Mazza, using typhoid vaccine, reported abrupt termination in about 20 per cent. of their cases and marked favorable influence in about 40 per cent. more. That these results were not due to the vaccine effect of the bacilli is shown by the fact that Ludke (*M. M. W.*, 1915, lxxii, 321) obtained equally favorable results with deutero-albumose. Miller reports 93 cases of acute arthritis, some apparently *rheumatic fever,* in 80 of whom there was marked relief of the joint symptoms. He did not observe, however, any favorable influence upon complicating endocarditis. In sub-acute and chronic *arthritis* he noted results favorable enough to justify further study of the subject. Schulman has used the method of treatment in *gonorrheal arthritis* with apparent good effect and Trossarello (*Rif. Med.*, April 3, 1920) has used it in various forms of gonococcus infections, as in *salpingitis,* with encouraging results but in urethritis, prostatitis and arthritis no apparent benefit. Cowie and Beaven (*J. A. M. A.*, 1919, lxxii, 1117) have employed the treatment in *influenzal pneumonia* but with no striking effect on the general mortality. Miller (*J. A. M. A.*, Jan. 29, 1921) has observed apparent benefit in some of his cases of *pneumonia.* Cowie (*N. Y. State J. Med.*, 1921, xxi, 395) has had favorable results in *furunculosis* and other suppurative diseases, especially in the treatment of inflammatory eye conditions as, *iritis, panophthalmitis,* etc. It has also been used in puerperal and other *septicemias, tuberculosis,* etc., but the present evidences of its value are insufficient to draw conclusions.

Prunella. *Prunella vulgaris* L. *Self-heal. Heal-all. Carpenter Weed. Brunella vulgaris. Paquerette,* Fr. *Braunelle, Braunheil,* G.—A small perennial labiate herb with 3-flowered axillary clusters of purplish to pinkish flowers arranged in a close spike. While native to Europe, it is common both in Europe and the United States. It was formerly used in *hemorrhages* and *diarrhea,* and as a gargle in *sore throat.*

Prussian Blue. *Ferri Ferrocyanidum. U. S.* 1870. *Ferri Ferrocyanuretum. U. S.* 1850. *Ferrocyanide of Iron. Ferric Ferrocyanide. Ferrocyanuret of Iron.* $Fe_4Fe_3(CN_6)_3$.—A blue amorphous powder, insoluble in water, soluble in acids and alkalies; produced by the interaction of solutions of a ferric salt and potassium ferrocyanide. It was discovered by Diesbach in 1710.

Prussian blue at one time was manufactured on a large scale by the action of fused alkali and iron salts on nitrogenous organic matter, as dried blood, but it is now prepared by electrolytic combination.

For further information concerning Prussian blue see *U. S. D.*, 20th ed., p. 1565. It is no longer used in medicine. In by-gone days it was employed as a tonic in *doses* of from three to five grains (0.20 to 0.32 Gm.), repeated several times a day, and gradually increased until some effect is produced.

Psidium. *Psidium Guajava* L., *P. pomiferum* L., *P. pyriferum* L., and other species of *Psidium.* (Fam. *Myrtaceæ.*) *Guava.*—These are shrubs or trees indigenous to tropical and subtropical America. Hartwich has examined the root, bark, and leaves of these plants from India. (See *Ph. Rev.*, 1896, 257.) The fruits, which somewhat resemble apples, are largely used as a food in the form of jelly.

Psoralea. *Scurfy Pea.*—This genus (Fam. *Leguminosæ*) is represented by about 115 species of strongly scented herbs, shrubs and undershrubs which are glandular-punctate, and possess pinnate or trifoliate leaves, racemes or spikes of blue, purple or white papilionaceous flowers with an unequally 5-toothed calyx and short, ovoid, 1-seeded pods. The tubers of *P. esculenta* Pursh. were employed by the Indians of the Northwestern United States, and by the settlers, as articles of food, being the *prairie turnip* or *prairie potato,* the *tipsinah* and *taahgu* of the Indians. C. Richardson found in it nearly 70 per cent. of starch, and 5 per cent. of a new, rapidly crystallizing sugar, which has not been further investigated. *P. glandulosa* L., *culen, yolochiahitl,* of the Mexican Pharmacopœia, yields a leaf which is used as a tonic or anthelmintic, and an emetic root. *P. bituminosa* L., of Arabia, and *P. physodes* Dougl., of California, are popularly considered tonic and emmenagogue, the former being presented under the name of *Herba Trifolii Bituminosi. P. pedunculata* (Mill.) Vail. (*P. melilotoides* Michx.) (*Congo root, Bob's root, Samson's snakeroot*), of Virginia, has been recommended as an aromatic bitter tonic, especially useful in *chronic diarrhea.* The part employed is the root, from which MacNair obtained about 2 per cent. of a volatile oil, having the specific gravity 0.93, a pungent and bitter taste, and a neutral reaction; also a bitter principle, but not tannin. For further description, see *A. J. P.*, July, 1889; also 14th and 16th editions of *U. S. D. P. corylifolia* L., of India, yields an oleoresin which is used in the treatment of *leucoderma* and other skin diseases. (*P. J.*, Sept., 1881.) Mann and Griffiths obtained from the seeds of *P. corylifolia* 13.7 per cent. of a thick brownish oil and 37.2 per cent. of an alcoholic extract which yielded by purification 9.2 per cent. of a resinoid. (*P. J.*, 1912, 260.)

Psyllium. *Semen Psyllii; Semences de Psyllium,* Fr.—This name has been applied to the seeds of several species of European *Plantago.* The best are those of *Plantago Psyllium* L., or *fleawort,* which grows in the south of Europe and in Northern Africa. They are ovoid, about 3 mm. in length, and 1 to 1.5 mm. in width, convex on one side, concave on the other, dark reddish-brown in color, shining, inodorous, and nearly tasteless, but mucilaginous when chewed. They are demulcent and emollient, and may be used internally and externally in the same manner as flaxseed, which they closely resemble in medicinal properties. They are used as a mild laxative in *chronic constipation* in *doses* of one or two teaspoonfuls 3 times a day. *Spogel seed,* used in India as a demulcent in intestinal irritation, is derived from *P. Isphagula* Roxb., probably a variety of *P. ovata* Forsk. (See *Journ. Méd. de Paris,* Sept., 1887.)

Ptelea. *Ptelea trifoliata* L. *Wafer Ash. Wing Seed. Shrubby Trefoil. Hop Tree. Orme à trois feuilles,* Fr. *Hopfenbaum, Kleebaum,* G. (Fam. *Rutaceæ.*)—This is a shrub or small tree with 3-foliate leaves growing in rocky places from Lake Ontario to Minnesota and southward.

The root bark has a peculiar somewhat aromatic odor, and a bitter, persistently pungent, and slightly acrid, yet not disagreeable taste. Within recent years the bark has been found admixed with Euonymus as well as substituted for it. It may be readily distinguished from the latter by its absence of caoutchouc fibers and by its characteristic broad transverse lenticels and waxy, pale yellow fractured surface. For structural details of *Ptelea* bark see article by H. W. Youngken in *A. J. P.*, 1918, 160. Steer obtained from it an oleoresin of an acrid and bitter taste and the alkaloid berberbine. An alkaloid, *arginine*, $C_6H_{14}O_2N_4$, is stated also to be present in the root. (*A. J. P.*, 1867, 337.) It was formerly employed among the physicians of the Western States in the treatment of *dyspepsia*, and generally in diseases requiring a mild, non-irritating, bitter tonic.

Ptomaines.—Under this name are included alkaloid-like bases obtained from animal tissue after decomposition has commenced, hence sometimes called *cadaveric alkaloids.* Bence Jones and Dupré (*Ph. Centralh.*, xvi, No. 10) first published a notice of the finding of an alkaloid-like base from a decomposing human liver. Its sulphate solution fluoresced, and in other ways resembled quinine, yielding precipitates also with the usual alkaloidal reagents, potassio-mercuric iodide, phosphomolybdic acid, and gold and platinic chlorides. It appears, however, that Marquardt had isolated such bases even previous to this. The chief investigators of this class of alkaloids have been Selmi, who first systematically studied them and gave them the name *ptomaines*, and Brieger, who in the latter part of the 19th century published a series of elaborate studies and has classified their reactions.

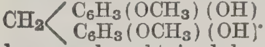
Brieger's researches established the fact that ptomaines are found during the earlier stages of decay, and that they are in general of a non-benzenoid character, but that as putrefaction continues they gradually disappear and give place to well-known benzenoid compounds, phenol, cresol, indol, etc. The bases are of two classes. At first are obtained oxygenated bases, like *choline*, $C_5H_{15}O_2N$, *muscarine*, $C_5H_{15}O_3N$, *neurine*, $C_5H_{13}ON$, *gadinine*, $C_7H_{18}O_2N$, and *tetanine*, $C_{13}H_{20}O_4N_2$. These seem later to disappear, and amines seem to be almost the only products. Among those mentioned, the simplest are *dimethylamine*, $(CH_3)_2NH$, *trimethylamine*, $(CH_3)_3N$, and *triethylamine*, $(C_2H_5)N_3$. A number of the others seem to be diamines, like *putrescine*, $C_4H_{12}N_2$, *cadaverine*, $C_5H_{14}N_2$, *saprine*, $C_5H_{16}N_2$, *neuridine*, $C_5H_{14}N_2$—all four discovered by Brieger in the cadaver—*collidine*, $C_8H_{11}N$, *hydrocollidine*, $C_{11}H_{13}N$, *parvoline*, $C_9H_{13}N$, and *tyrotoxicon* (*diazobenzene*), $C_6H_5N_2$, discovered by Vaughan in poisonous cheese and in ice cream which had been allowed to become stale.

Barger and Walpole (*J. P.*, 1909, xxxvi) separated from putrescent horse meat *parahydroxyphenylethylamine* which is formed by the decomposition of tyrosine (see *Tyramine*). This base also occurs in ergot. Dale and Dixon (*J. P.*, xxxix) have shown that this base as well as *isoamylamine*, which also occurs in putrescent meat, acts upon the system like adrenalin, causing marked rise in the blood pressure.

Brouardel and Bontury (*C. R. A. S.*, xcii, 1056) state that ptomaines can be distinguished from the vegetable alkaloids by their reaction with potassium ferricyanide. This salt when treated with a solution of a pure vegetable alkaloid is unaffected by it; while, under the same conditions, it is instantly reduced to the state of ferrocyanide by a ptomaine, and thus becomes capable of forming Prussian blue with a ferric salt. Up to the present but two exceptions to this rule have been found—morphine, which readily reduces potassium ferricyanide, and veratrine, which gives traces of such reduction. It is possible, however, that in this last case the reducing action is due to certain impurities which the investigators were unable to remove completely from the veratrine employed by them.

Ptomaines are not used as medicines, but are of great interest to the toxicologist, not only from a chemical standpoint, but also from the fact that many are violently poisonous. The well-known action of putrescent flesh, the curious poisonings sometimes produced by certain crustaceans and mollusks which feed upon carrion, are in all probability caused by them. Salkowski and Brieger found in living mussels a ptomaine that they named *mytilotoxine.* (See *Musculus.*) In regard to treatment of poisoning by putrid animal matters, our present knowledge only justifies the immediate evacuation of the stomach and bowels and the meeting of the various indications as they arise. For fuller information as to the formation of ptomaines, their detection, separation, and clinical features, see *Ptomaines and Other Animal Alkaloids*, by A. C. Farquharson, M.D., Bristol, Eng., 1892.

Pulmoform. *Methylene-diguaiacol.*



$$CH_2\left\langle\begin{matrix}C_6H_3(OCH_3)(OH)\\ C_6H_3(OCH_3)(OH)\end{matrix}\right.$$

This is a yellow tasteless powder obtained by the action of formaldehyde upon guaiacol. It is used as a substitute for creosote, especially in the treatment of *chronic bronchitis* and *tuberculosis.* The *dose* is eight grains (0.5 Gm.).

Pulmonaria. *Pulmonaria officinalis* L. *Lungwort. Pulmonaire*, Fr. *Lungenkraut*, G. (Fam. *Boraginaceæ.*)—An herbaceous perennial, European plant having tufts of ovate-oblong, coarsely hairy, spotted leaves and cymes of red flowers fading to violet. It is commonly cultivated. The leaves have been employed in *catarrh, hemoptysis,* and *consumption*, but their virtues are doubtful.

Purgatol. *Purgatin. Anthrapurpurine-diacetate. Diacetyl Ester of Anthrapurpurine*, or *Trioxyanthraquinone.* $C_{14}H_5(OH)(OC_2H_3O)_2.O_2$.—This substance occurs as an orange-colored crystalline powder, melting at 175° to 178° C., insoluble in water and in dilute acids, but slowly soluble in weak alkali and splitting up with development of a deep violet-red coloration.

Purgatol is said to be a laxative similar to emodin, to which it is chemically allied. It is absorbed to some extent, causing the urine to become red. It has been recommended in *chronic constipation* in *doses* of eight grains (0.5 Gm.), increased if necessary, and is said to act in from three to twelve hours without pain.

Pycnanthemum. *P. flexuosum* (Walt.) Bsp. (*P. linifolium* Pursh., *Koellia flexuosa* (Walt.) MacM.) *Mountain Mint. Basil. Dysentery Weed.*—This American mint was popularly used in bowel complaints; its hot infusion is diaphoretic. (See *A. J. P.*, 1894, 65, 169; *Ph. Rund.*, 1896, 32.)

The volatile oil from *P. lanceolatum* Pursh. contains carvacrol, pulegone, geraniol, dipentene, and terpenes, and a second ketone, probably thujone. The carvacrol content runs from 14.5 to 58 per cent., usually 25 per cent. or more. (*Chem. Abstracts*, 1918, xii, 1410.)

Pyocyanase.—This is the name which is given to a solution of bacterial proteids, obtained by the process of autolysis, from the *Bacillus pyocyaneus.* The method of preparation is as follows: The bacilli are grown in bouillon until they cause to multiply; this cessation of growth is believed to be due to the production of a ferment which eventually leads to a solution of the bodies of the bacteria. The bouillon is then filtered through porcelain filters to free it from any bacteria which may be present. This solution contains a substance which has the power of dissolving not only the *Bacillus pyocyaneus,* but many other forms of bacteria, including those which cause diphtheria, typhoid fever, streptococci, etc. The tubercle bacillus, however, does not appear to be affected by it. Muhsam (*D. M. W.,* 1908, xxxiv, 231) added one drop of *pyocyanase* to eighty minims (5 cc.) of a bouillon culture of diphtheria and found that in twenty-four hours these germs were all destroyed. He also injected into guinea-pigs 2 cc. of diphtheria culture to which was added at the time of inoculation from one to five drops of pyocyanase and found that in every instance the latter protected the animals against the acquirement of the disease.

Pyocyanase has been used as a local antibacterial agent in a number of conditions. It has been found serviceable when applied directly to the membranes in cases of *diphtheria,* and is stated to be capable of sterilizing the throat. It has also been employed with asserted good results in various other suppurative and infectious conditions of the mouth, nose and throat. Pringsheim (*Med. Klin.,* 1909, p. 1678) dissents from the chorus of praise and states that it is not superior in its practical effects to other disinfectants in common use. Bernbach (*M. M. W.,* 1908, lv, 120) finds that when injected subcutaneously it is followed by local redness, swelling and pain, and chill followed by a fever reaching as high at times as 40° C., which ends in five hours with a critical sweat.

Pyocyanase is applied either by means of a swab or an atomizer, from fifty to eighty minims (3.0–5.0 cc.) being used.

Mavinaveitia has separated the blue coloring matter formed by these bacteria to which he gives the name *pyocyanin.* (*D. C.,* 1917, lxi, 132.)

Pyoktanin Mercury.—A combination of mercury, with methyl violet. It forms a violet powder almost insoluble in water and alcohol. It is used as an antiseptic in *gonorrhea* in 1–2000 solutions and in *burns,* diluted with equal amounts of starch.

Pyoktanin Yellow. *Imino-tetramethyl-diamido diphenyl-methane Hydrochloride. Apyonin. Medicinal Auramine,* $C_{17}H_{21}N_3HCl$.—This is a yellow powder insoluble in water and alcohol, used as an antiseptic in *skin diseases* and in ophthalmic practice. It is used as a dusting powder, 1 or 2 per cent., or 2 to 10 per cent. ointments.

Pyramidon Camphorate.—There are two combinations of camphoric acid with pyramidon on the market. The neutral pyramidon camphorate, $(C_{13}H_{17}N_3O)_2C_{10}H_{16}O_4$, is a white, crystalline powder, fusing between 80° and 90° C., soluble in 15 parts water and 2 parts alcohol. The acid camphorate (*pyramidon bicamphorate*), $C_{13}H_{17}N_3O.C_{10}H_{16}O_4$, has a faintly acid reaction, fuses between 84° and 94° C., and is soluble in twenty parts of water or four of alcohol. The purpose of these combinations is to overcome the tendency of pyramidon to produce excessive sweating, indeed it is asserted that the bicamphorate is useful to control the *night sweats* of *phthisis.* The two salts are used for much the same purposes as pyramidon. *Dose,* of either, is eight to fifteen grains (0.5–1.0 Gm.).

Pyramidon Salicylate. *Amidopyrine Salicylate.* $C_{13}H_{17}N_3O.C_7H_6O_3$.—This substance has been proposed as a substitute for the older salicylates, and may be used in their stead in subacute and chronic cases. The *dose* is eight to twelve grains (0.5–0.75 Gm.).

Pyranum. *Pyrenol. Thymol-sodium Benzoyloxybenzoate.*—This is a white, hygroscopic, crystalline powder with an aromatic odor and a sweetish taste. It dissolves readily in water, one part to five, and in alcohol, one part to ten. This substance, which apparently undergoes change in the system (salicylic acid and thymol having been detected in the urine after its administration), was brought forward by Schlesinger (*Th. M.,* Feb., 1903) as an antipyretic and antineuralgic. He used it in various forms of fevers and asserts that it is superior to salicylic acid in acute *rheumatism,* and has very remarkable analgesic properties. Burchand (*Ther. Geg.,* 1905) recommends pyranum in *hysteria* and *neurasthenia. Dose,* fifteen grains (1 Gm.) repeated up to forty-five grains (3 Gm.) in a day, if required.

Pyridine. C_5H_5N.—*Pyridine* is the first of a series of homologous bases which are found in coal tar naphtha, in shale oil, in peat tar, in tobacco smoke, and more especially in the product known as *Dippel's oil,* obtained by the distillation of bones and other animal matter. Pure pyridine is a colorless liquid, with a powerful and persistent odor, of sp. gr. 0.9746, and boils at 116° to 118° C. It is miscible with water in all proportions, but is precipitated from its solution by excess of sodium hydroxide. It is also miscible with alcohol, ether, chloroform, benzene, and fatty oils. It is used as a solvent in the rubber and paint industries. It has been used as an antiseptic and germicide, and is employed as one of the constituents for "denaturing" alcohol for manufacturing uses. In toxic dose pyridine is a violent poison, producing cyanosis, methemoglobinemia, great muscular weakness from paralysis both of the motor centers and nerves, and finally death from failure of respiration. De Renzi asserts that in small doses it stimulates the heart, increases the blood pressure, and is a useful remedy in *angina pectoris.* It was first introduced into practical medicine, as a remedy for *asthma,* by Germain Sée, whose statement has since been confirmed by various clinicians. Sée employed it by exposing about a drachm upon a plate in a small room, in which the patient remained from twenty to thirty minutes, the process being repeated several times a day; or from five to ten minims in two ounces of water may be taken by an atomizer; or five minims may be inhaled directly. De Renzi has given it internally in the daily *dose* of six minims (0.3 cc.) gradually increased to twenty-five (1.6 cc.). Under the name of *pyrilin* is marketed a solution of *pyridin ethylphosphinate,* recommended in diseases of the air passages.

Pyridine Tricarboxylic Acid. $C_5H_2(COOH)_3N$.—This derivative of pyridine may be prepared by the oxidation of methyl-pyridine (*picoline*), or is obtained from certain natural alkaloids, such as quinine, quinidine, and cinchonidine, by boiling with an alkaline solution of potassium permanganate. It forms prisms melting at 244° C. This substance is said to be an active antiseptic and antipyretic, and was recommended by Rademaker (*Medical Herald*, 1887) in *malaria, asthma* and *typhoid fever*, in *doses* of from one to ten grains (0.06–0.6 Gm.).

Pyrochinin is a quinine-pyramidon double salt of camphoric acid, containing 43 per cent. quinine, 30 per cent. pyramidon and 26 per cent. camphoric acid. It has been proposed as an antipyretic and analgesic.

Pyrosal. $C_9H_8O_5C_{11}H_{12}N_2O$.—*Antipyrine acetylsalicylate* forms colorless needles or plates of an acid but not bitter taste which are difficultly soluble in water. *Pyrosal* is said to contain about 50 per cent. of antipyrine, 36 per cent. of salicylic acid, and 14 per cent. of acetic acid. It is asserted to be broken up in the intestinal canal into its constituents, and to exert their influence in the human system, and has been used in *polyarthritis*, severe *influenza, febrile cystitis, migraine*, and *sciatica*, in *doses* of from eight to fifteen grains (0.5–1.0 Gm.), from two to six times daily.

Quamacai.—The wood of *Paullinia thalictrifolia* Juss. (Fam. *Sapindaceæ*), a twining shrub indigenous to Brazil, has been used in *beri-beri* and *rheumatic affections*. It is also used externally in diaphoretic baths.

Quebracho Bark. *Aspidosperma, U. S. IX.*—The name quebracho is derived from the two Spanish words, *quebrar* and *hacha*, signifying "The axe breaks." There are several trees whose wood is hard and to which the term "quebracho" is popularly applied, among others the *Thouinia striata* (Fam. *Sapindaceæ*). The name *quebracho colorado* is applied to the *Schinopsis Lorentzii* (Griseb.) Engl. (Fam. *Anacardiaceæ*) which grows in Argentine. The wood of this plant yields as extract which is largely used in tanning of leather. Perkin and Gunnel (*A. J. P.*, 1896) found in it also a yellow coloring matter apparently identical with fisetin (see *Fustic*). Under the name of "quebracho flojo," the wood and bark of *Iodina rhombifolia* Hook. et Arn. (Fam. *Santalaceæ*) are substituted and sold for quebracho colorado in Southern Brazil, Argentina and Uruguay.

Quebracho blanco is the popular name for the *Aspidosperma quebracho-blanco*, which was formerly official. This is a large evergreen tree which sometimes reaches the height of one hundred feet, and is remarkable for its erect stem and its wide-spreading crown reaching out over the cacti and lower bushes among which it grows. The tree is indigenous to the western provinces of Argentine and is also found growing in Chili, Bolivia and Southern Brazil. The bark has been used for a long time in South America as a febrifuge but was not introduced into Europe until about 1878. The commercial supply of the drug used in the United States comes from the Argentine Republic.

Quebracho bark is remarkable for the extreme thickness of the corky layer which often constitutes more than half of its entire substance, and is separated from the lower layer by a more or less sharply defined outline. The corky layer is usually externally dirty gray, or where it has been rubbed appears yellowish-red. "In irregular chips or in longitudinal pieces attaining a length of 14 cm. and a thickness of 35 mm.; outer corky layer from 3 to 25 mm. in thickness, brownish-gray or reddish-brown and deeply furrowed, frequently somewhat reticulate with longitudinal and shallow transverse fissures, the crevices being occasionally lined with the mycelia of a grayish mould; outer surface of bark, from which the cork has been separated, light brown or reddish-brown and usually more or less roughened; inner surface occasionally with adhering wood, otherwise light yellowish-brown to light reddish-brown, longitudinally finely striate and finely porous; fracture short-fibrous with projecting bast-fibers; nearly inodorous, taste bitter and slightly aromatic. Under the microscope, transverse sections of Aspidosperma show a number of successive layers of cork separated by large groups of stone cells, isolated bast-fibers and parenchyma; inner bark with starch-bearing medullary rays 1 to 5 cells in width, separating narrow wedges composed of large prominent groups of stone cells in which are occasionally included one or more thick-walled bast-fibers; bast-fibers usually single, very thick-walled, strongly lignified and surrounded with crystal fibers and starch-bearing parenchyma. The powder is reddish-brown; bast-fibers single, very long and surrounded by crystal fibers, the crystals being in prisms frequently terminated by pyramids and from 0.008 to 0.03 mm. in length; stone cells in large thick groups composed of numerous more or less tabular cells; cork cells more or less polygonal in outline with thick, slightly lignified walls; starch grains single or 2- to 4-compound, the individual grains spherical, ovoid or more or less plano-convex, from 0.003 to 0.025 mm. in diameter." *U. S. IX.*

In 1878, Fraude (*B. Chem. G.*, 1878, p. 2189; 1879, p. 1560) discovered in the quebracho blanco an alkaloid, *aspidospermine*, $C_{22}H_{30}O_2N_2$, but Hesse has found five other alkaloids, *aspidospermatine*, $C_{22}H_{28}O_2N_2$, and isomeric with it *aspidosamine*, $C_{22}H_{28}O_2N_2$, *quebrachine*, $C_{21}H_{26}O_2N_2$, and isomeric with this *hypoquebrachine*, $C_{21}H_{26}N_2O_2$, and *quebrachamine*, *quebrachol*, $C_{20}H_{34}O + H_2O$, *quebrachit*, $C_6H_{11}(OCH_3)O_5$. (*Ber. d. Chem. Ges.*, xiii, 2308.) A. J. Ewins (*Tr. Chem. Soc.*, 1914, p. 2738) investigated aspidosperma, but could not confirm the list of alkaloids found by Hesse, with the exception of aspidospermine and quebrachine. He believes that the other alkaloids reported are decomposition products of aspidospermine and quebrachine. According to Fourneau and Page (*Bull. Sci. Pharm.*, 1914, xxi, 7), quebrachine is identical with yohimbine.

Aspidospermine is a brownish-yellow amorphous powder or needle-shaped crystals, fusing at 205° to 206° C., is soluble in about 6000 parts of water at 15° C., the solution having a decidedly bitter taste, soluble in about 48 parts of absolute alcohol, in 106 parts of ether, insoluble in glycerin; it dissolves readily in fats and fixed oils, cod liver oil dissolving a larger proportion than it does of quinine. Its sulphate and hydrochloride are very soluble in water. The citrate is crystallizable, and very soluble. The yield of aspidospermine is small, 0.33 per cent. of the bark. *Aspidospermatine* is crystalline, and fuses at 162° C.; *aspidosamine* is amorphous, and fuses at 100° C.; *quebrachine* in colorless crystals fuses at 214° to 216° C.; *hypoquebrachine* is a yellowish mass resembling albumin, and fuses at 80° C.; *quebrachamine* forms colorless silky needles, only slightly soluble in alcohol, ether, chloroform, and benzin, and fuses at 142° C. Vanderkleed reports two samples of quebracho assaying 0.95 and 1.22 per cent. of alkaloids respectively. (*J. A. Ph. A.*, 1915, p. 983.) Newcomb reports the ash content of aspidosperma to range from 5.9 to 6.8 per cent. (*A. J. P.*, 1915, p. 115.) Two new sugars have also been extracted by Tanret, *quebrachite* and lævogyrate inosite. Tannin and starch have also been found in the bark. According to H. C. Wood, Jr., the most important principle is quebrachine. (*U. P. M. B.*, 1910, xxiii.)

When a preparation of aspidosperma is injected into the circulation it causes an enormous increase in the rate and depth of the respiration with some fall in the blood pressure. Pentzold, who first described the effects of this drug on the respiration, believed that the breathing was dyspneic in type and that the drug acted by preventing the red corpuscles from giving up their oxygen. He based his belief on the fact that after death from the poison the blood had the same color in both arteries and veins, but Wood and Hoyt (*U. P. M. B.*, Sept., 1903) showed that the blood retained its normal oxidizing powers after aspidospermine and believed that the arterial hue in the veins was due to the violence of the respiration. The fall of blood pressure is due primarily to weakness of the heart, although larger doses also cause dilatation of the blood vessels—according to Cow (*J. P. Ex. T.*, 1914, v, p. 341), by a depressant action on the medullary centers. The increase in the respiration which is the most marked effect of aspidosperma appears to be due to a direct action upon the respiratory center as H. C. Wood, Jr. (*U. P. M. B.*, 1910, xxiii), has shown that it does not affect the circulation in the lungs, and Cow that it does not affect the bronchioles.

All of the alkaloids of aspidosperma as far as they have been studied are possessed of similar physiological properties, although to different degree. Both Wood and Cow agree that quebrachine is the most active alkaloid in the drug.

Aspidosperma is used in medicine for the relief of various types of dyspnea, especially in *emphysema* and *asthma*. In the latter condition it is not generally useful to interrupt the paroxysm, but in many cases if used continuously will greatly reduce the frequency and severity of attacks.

Under the name of *amorphous aspidospermine* there has entered in commerce a mixture of the various alkaloids of this drug. *Dose* of this preparation is from a quarter to one grain (0.016–0.065 Gm.); that of the crystalline aspidospermine is from one-fortieth to one-twentieth of a grain (0.0016–0.003 Gm.).

The fluidextract (*Fluidextractum Aspidospermatis*) was formerly official. *Dose*, fifteen minims (1 cc.).

Quina Morada.—This drug, growing in Bolivia and the Argentine Republic, and there credited with the therapeutic values of cinchona is produced by *Pogonopus Tubulosus* (Rich.) K. Sch. (Fam. *Rubiaceæ*). It has been studied by Arata and Canzoneri, who find in it a blue fluorescent substance, *moradin*, and an alkaloid, *moradeine*. (*P. J.*, April, 1890.)

Quinanaphthol. *Quinaphthol. Quinine-beta-naphthol-monosulphonate.* $C_{20}H_{24}O_2N_2.(OHC_{10}H_6.SO_3H)_2$.—This is a yellow crystalline powder, soluble in alcohol and water. It fuses at 185° to 186° C., and contains 42 per cent. quinine. It is used in *typhoid fever, intestinal tuberculosis, dysentery* and *acute rheumatism* in *doses* of five to fifteen grains (0.3–1 Gm.).

Quinate of Urea. *Urol. Urea Quinate.* $C_7H_{12}O_6.2CO(NH_2)_2$.—A combination of two molecules of urea and one of quinic acid. It forms prismatic crystals melting at 106° to 107° C. It is recommended by Van Noorden in *doses* of thirty to forty-five grains (2–3 Gm.) dissolved in a tumblerful of hot water, on rising, and going to bed, as a solvent for uric acid.

Quinic Acid. *Acidum Quinicum. Kinic Acid. Hexahydro-tetraoxybenzoic Acid.* $C_6H.H_6.(OH)_4.COOH$.—Forms colorless, rhombic prisms, easily soluble in water, difficultly soluble in strong alcohol, which fuse at 162° C. Found naturally in cinchona bark, in the coffee bean, and other sources. Led by the belief that the decrease in the elimination of uric acid, which is said to be produced by strawberries, is due to *quinic acid*, Weiss, of Basel, experimentally determined that quinic acid checks the formation of uric acid in the body, and was led to propose it and its salts as remedies in the treatment of *gout*. This theory of the action of quinic acid is certainly not established and of doubtful correctness, but has given rise to practical trials of quinates by various clinicians in gout with asserted good results. Quinic acid is converted in the system, first into benzoic, and second into hippuric acid. Various combinations of quinic acid have appeared in commerce, often under proprietary names among which are urosin, urol, chinotropin, sidonal and new sidonal; these are described elsewhere in this work.

Quinine Acetyl Salicylate. *Quinine Aspirin. Xaxaquin.*—Acetyl salicylate of quinine, $CH_3.CO.O.C_6H_4.COOH.C_{20}H_{24}O_2N_2$, is a white, crystalline powder, sparingly soluble in water, more readily in alcohol and in chloroform; melting point 157° C. It has been used by Rivolta in *pleurisy*. Boshuwers has used it (*Ther. Neu.*, March, 1908) as a symptomatic remedy in *influenza* and *tonsillitis*. The *dose* is three to ten grains (0.2–0.65 Gm.).

Quinine Æsculinate (Neutral). *Escoquinine.*—It is stated to be prepared by chemically combining quinine with esculin, the glucoside obtained from the common horsechestnut, *Æsculus Hippocastanum* L. It is a yellowish, amorphous, water insoluble powder, bitter tasting and containing 50 per cent. quinine. It is claimed to have been used with signal success in the treatment of *catarrh* and lung complications. *Dose*, one and one-half to three grains (0.096–0.2 Gm.).

Quinine Antimonate.—A white powder insoluble in water. It is used in the treatment of *rheumatism, gout, herpes*, etc. *Dose*, one and one-half to seven grains (0.096–0.45 Gm.).

Quinine Arrhenalate. *Quinine Methyl-arsenate. Quinine Monomethyl-arsenate.* $(C_{20}H_{24}O_2N_2)_2AsO.(OH)_2CH_3$.—This salt forms colorless, bitter crystals, fusing at 139° to 141° C., which are insoluble in cold and slightly soluble in warm water.

Quinine Arsenate. *Quininæ Arsenas.* $2(C_{20}H_{24}O_2N_2).H_3AsO_4 + 8H_2O$.—Made by precipitating a solution of 10 parts of quinine hydrochloride in 200 parts of water with a solution of 3.9 parts of sodium arsenate dissolved in 100 parts of water. The precipitate is washed and purified by recrystallization. It forms white, prismatic crystals, slightly soluble in cold water, very soluble in hot water. The salt contains 69.39 per cent. of quinine and 12.30 per cent. of arsenic acid. *Dose*, one-fifteenth to one-eighth of a grain (0.004–0.008 Gm.).

Quinine Eosolate. *Quininæ Eosolas.* $C_9H_7S_3O_{12}(C_{20}H_{24}O_2N_2)_2$.—This is the commercial name of the neutral quinine salt of *trisulpho-acetyl-creosote*. Very active anti-periodic properties have been claimed for it. *Dose*, three to eight grains (0.2–0.5 Gm.) three times a day.

Quinine Glycero-phosphate. *Quininæ Glycerophosphas. Kineurine, Neo-quinine.*—This salt was formerly recognized by the N. F., but was dropped at the last revision. It represents about 72 per cent. of quinine. It was officially described as follows: "Quinine Glycerophosphate occurs as fine, white crystalline needles or as a powder; odorless and having a very bitter taste. One gramme dissolves in about 850 cc. of water, or 75 cc. of alcohol at 25° C.; very soluble in boiling alcohol; very slightly soluble in chloroform or ether; soluble in 20 parts of a mixture of one volume of alcohol and two volumes of chloroform. Quinine Glycerophosphate slowly loses part of its water of crystallization at room temperature and when heated to 100° C. becomes anhydrous. Incinerate 0.2 Gm. of the salt; no weighable residue remains. The salt yields a clear solution with diluted sulphuric acid. An aqueous solution is not fluorescent, but becomes so upon the addition of a few drops of diluted sulphuric acid. Add 1 cc. of bromine T.S. to 10 cc. of a saturated aqueous solution of the salt, and then follow with 1 cc. of ammonia water; the liquid acquires an emerald-green color. When the salt is heated with potassium bisulphate the odor of acrolein is given off. An aqueous solution of 0.1 Gm. of the salt in 10 cc. of distilled water, made with the aid of acetic acid, does not produce a precipitate on the addition of ammonia oxalate T.S. (*calcium*). Dissolve 0.1 Gm. of the salt in 10 cc. of diluted hydrochloric acid; the solution does not become more than faintly turbid upon the addition of a few drops of barium chloride T.S. (*sulphate*). Dissolve 0.1 Gm. of the salt in 10 cc. of diluted nitric acid; the solution is not rendered more than faintly turbid on the addition of silver nitrate T.S. (*chloride*). Add a slight excess of ammonia water to a saturated aqueous solution of the salt, and filter; the clear filtrate does not show more than a slight turbidity with magnesia mixture T.S. (*phosphate*). Mix about 2.5 Gm. of the salt in a separatory funnel with 15 cc. of distilled water, add 5 cc. of ammonia water, shake with three successive portions of 25, 15 and 10 cc. of chloroform, respectively, and evaporate the chloroform solutions to dryness on a water bath. Dissolve 1.5 Gm. of this dry residue in 25 cc. of alcohol, add 50 cc. of hot distilled water, neutralize the liquid with normal sulphuric acid V.S., using methyl red T.S. as indicator and evaporate the liquid to dryness on a water bath. Powder the residue, mix it with 20 cc. of distilled water and maintain the temperature of the mixture at 65° C., for thirty minutes, agitating frequently. Now cool the mixture to 15° C., macerate it at this temperature for two hours with occasional shaking, then filter it through a dry filter, of from 8 to 10 cm. in diameter, into a dry test tube. Transfer 5 cc. of this filtrate to a test tube and mix it gently (without shaking) with 7 cc. of ammonia water, which must contain not less than 10 per cent. nor more than 10.2 per cent. of NH_3, must have a temperature of 15° C., and be added at once. A clear liquid is produced (*other cinchona alkaloids*). If the temperature during the maceration has been 16° C., add 7.5 cc. of ammonia; if 17° C., add 8 cc." *N. F. IV.* This substance has been recommended as an antiperiodic in *doses* of five to ten grains (0.32–0.65 Gm.). The tonic *dose* is set down as one and one-half to three grains (0.096-0.2 Gm.).

Quinine Salicylate. *Quininæ Salicylas,* U. S. IX; $C_{20}H_{24}O_2N_2.C_7H_6O_3+H_2O$. *Salicylate de Quinine Basique,* Fr. *Chininsalicylat. Salicylsaures Chinin,* G. *Salicilato quinico,* Sp.—Quinine salicylate may be made by adding a solution containing 3.9 parts of sodium salicylate dissolved in 30 parts of water, to a hot solution made by dissolving 10 parts of quinine sulphate in 75 parts of boiling water. The precipitate is collected, washed and dried and recrystallized from its solution in alcohol.

It was officially described as in "colorless, odorless needles, having a bitter taste, permanent in the air. It often assumes a pinkish color on keeping. One Gm. of Quinine Salicylate dissolves in 14 mils of alcohol, 13 mils of glycerin, 25 mils of chloroform, and in 160 mils of ether at 25° C.; slightly soluble in water. Its saturated aqueous solution is alkaline to litmus and when this solution is treated with a drop of ferric chloride T.S., a violet color develops. Add 1 or 2 drops of bromine T.S. to 10 mils of an aqueous solution of Quinine Salicylate and then introduce an excess of ammonia water; an emerald-green color is produced due to the formation of thalleioquin. Quinine Salicylate loses not more than 5 per cent. of its weight when dried to constant weight at 100° C. Incinerate about 2 Gm. of Quinine Salicylate; not more than 0.05 per cent. of ash remains. Shake about 0.4 Gm. of the salt with 20 mils of distilled water and 1 mil of nitric acid; separate portions of 10 mils each of the filtered solution are not rendered more than slightly turbid by the addition of a few drops of barium chloride T.S. (*sulphate*), nor more than slightly opalescent by a few drops of silver nitrate T.S. (*chloride*). Mix 2.21 Gm. of Quinine Salicylate in a separator with 10 mils of distilled water, add 5 mils of ammonia water, and shake the liquid with three successive portions of 25, 20 and 10 mils, respectively, of ether. Evaporate the combined ether solutions to dryness on a water bath, dissolve the residue in 20 mils of alcohol, dilute it with 50 mils of hot distilled water, and neutralize the liquid with normal sulphuric acid V.S., using methyl red T.S. as indicator. Evaporate it to dryness on a water bath, powder the residue, mix it with 20 mils of distilled water in a test tube, and complete the test for other cinchona alkaloids as directed under *Quininæ sulphas.*" *U. S. IX.*

Under the name of *Quinisal* has been introduced a compound of quinine with salicylo-salicylic acid (see *Diplosal*). This is a fluffy crystalline powder practically insoluble in water but decomposes in the presence of either acids or alkalies into its constituents. It represents a still larger proportion of salicylic acid than the normal salicylate which is rather to be regarded as a disadvantage.

Quinine salicylate represents approximately 27 per cent. of salicylic acid, and 69 per cent. of anhydrous quinine. It is believed by many practitioners to be a valuable remedy in the advanced stages of an *acute rheumatism,* in *subacute rheu-*

matism, and in mild *gouty* conditions, but the proportion of salicylic acid seems too small to exercise any pronounced effect on the system.

Dose, from five to ten grains (0.32–0.65 Gm.).

Quinine Salts.—A number of salts of quinine whose effects do not differ materially from those official and whose advantage is very doubtful, have been put on the market; they are used for the same purposes and in practically the same dosage as the official salts. In addition to those described elsewhere in this work the following seem to merit a brief word of mention of their physical properties:

Quinine Acetate, $C_{20}H_{24}O_2N_2.C_2H_4O_2$.—White crystals of a somewhat acetous odor, sparingly soluble in cold water, soluble in alcohol; 84.38 per cent. quinine. It is said also to possess diuretic properties.

Quinine Benzoate. $C_{20}H_{24}O_2N_2.C_7H_6O_2$.—White crystalline powder, soluble in about 350 parts of water; 72.65 per cent. quinine. Incompatible with either alkalies or acids.

Quinine Bitartrate, $C_{20}H_{24}O_2N_2.C_4H_6O_6$.—White crystals, slightly soluble in water or alcohol; 81 per cent. of quinine.

Quinine Citrate.—Varies somewhat in its composition; generally occurs as white crystals, sparingly soluble in water; represents from 72 to 87 per cent of quinine.

Quinine Carbonate. Acid Carbonate of Quinine. $C_{20}H_{24}O_2N_2.H_2CO_3 + H_2O$.—Fine, needle-like crystals soluble in water or alcohol; 73.66 per cent. of quinine. The neutral carbonate is described under *Aristochin.*

Quinine Ferrocyanide. Quinine Hydroferrocyanide. $(C_{20}H_{24}O_2N_2)_4H_4Fe(CN)_6 + 7H_2O$.—Yellow powder very slightly soluble, represents 79.13 per cent. of quinine. It is used in *night-sweats.*

Quinine Formate. Quinoform. $C_{20}H_{24}O_2N_2CH_4O_2$.—White crystals, neutral in reaction, soluble in water or alcohol; 87.6 per cent. of quinine. Especially suited for hypodermic use.

Quinine Hydrochlorsulphate. Quinine Chlorhydrosulphate. $(C_{20}H_{24}O_2N_2)_2H_2SO_4(HCl)_2 + 3H_2O$.—Colorless or faintly yellowish crystals, soluble in 1 part of water; 74.23 per cent. of quinine. Its solutions are acid.

Quinine Hydrofluoride. Quinine Fluoride. $C_{20}H_{24}O_2N_2.HF$.—White powder or crystals, insoluble in water, soluble in alcohol; 94.17 per cent. quinine. Used also in *rickets.*

Quinine Iodide. Quinine hydriodide. Quinine hydriodate. $C_{20}H_{24}O_2N_2HI$.—Pale yellow crystals, slightly soluble in water, freely in alcohol; 71.71 per cent. of quinine.

Quinine Iodohydriodide. Iodized Quinine Hydriodide. Quinine Periodide. $C_{20}H_{24}O_2N_2HI + I_2$.—A reddish-brown amorphous powder, insoluble in either water or alcohol: 45.9 per cent. of quinine. Used chiefly for iodide effect in *syphilis* and *rheumatism.*

Quinine Diiodide. Acid Quinine. Hydriodide. $C_{20}H_{24}O_2N_2.2HI + 5H_2O$.—Yellowish crystals or scales, soluble in 20 parts of water; 48.4 per cent. quinine.

Quinine Lactate.—Soluble in 6 parts of water, very soluble in alcohol: 78.26 per cent. of quinine. Also used locally in *gonorrhea.*

Quinine Phosphate. $C_{20}H_{24}O_2N_2.H_3PO_4 + 8H_2O$.—colorless crystals, soluble in water or alcohol; it represents from 70 to 77 per cent. of quinine according to varying amount of water of crystallization.

Quinine Tartrate. $(C_{20}H_{24}O_2N_2)_2C_4H_6O_6 + 2H_2O$.—Colorless crystals, slightly soluble in water, soluble in alcohol; 77.7 per cent. quinine.

Quinine Urate was thought by Pérayre, of Bordeaux, to be peculiarly efficacious in obstinate intermittents. It is prepared by boiling 10 parts of crude quinine in water, adding gradually 20 parts of crystallized uric acid, and, after sufficient ebullition, filtering and evaporating. A yellow salt is obtained, sometimes amorphous, more frequently crystalline, soluble in hot and less so in cold water, and, according to the author, capable of curing intermittent fever in smaller doses than the sulphate, with less cerebral disturbance, less bitterness, and easier tolerance by the stomach. (*J. P. C.*, 3e sér., xxxvii, 139.)

Quinine Valerate. *Quininæ Valeras. Quinine Valerianate.*—This salt was official in the N. F. IV, as an ingredient in the elixir of quinine and strychnine valerate. As the amount of valeric acid represented was so small as to be incapable of modifying the effect of the alkaloids, this elixir has very properly been omitted. The salt which represents approximately 73 per cent. of quinine was described as follows: "Quinine Valerate occurs as white, lustrous crystals, having an odor of valeric acid and an intensely bitter taste. It is sparingly soluble in cold water, soluble in hot water, becoming less soluble with age on account of loss of valeric acid; readily soluble in alcohol. Its aqueous solution is neutral or slightly alkaline to litmus. Add a few drops of bromine water to 10 cc. of an aqueous solution of the salt (1 in 1000), then add an excess of ammonia water; an emerald-green color is produced. An aqueous solution of the salt, acidulated with sulphuric acid, exhibits a blue fluorescence and has the odor of valeric acid. Incinerate 1 Gm. of Quinine Valerate; not more than 0.1 per cent. of ash remains. About 0.1 Gm. of the salt dissolves in 5 cc. of sulphuric acid without producing more than a light yellow color (*readily carbonizable impurities*). Ten cc. portions of the cold, saturated aqueous solution of the salt do not give more than a slight turbidity with barium chloride T.S. when acidulated with hydrochloric acid (*sulphate*); nor with silver nitrate T.S. when acidulated with nitric acid (*chloride*). To test this salt for excessive amounts of *other cinchona alkaloids* proceed as directed under *Quininæ Glycerophosphas.*" *N. F. IV.*

Quiniodol.—This is made by treating powdered red cinchona bark with an ethereal solution of iodine. Two strengths are made containing respectively 5 and 10 per cent. of iodine. It is employed as a surgical dusting powder for infected *wounds.*

Quinoa.—The *Chenopodium Quinoa* Willd. (Fam. *Chenopodiaceæ*), is largely cultivated in Southern Peru and Southern Chili, often above the elevation at which barley and rye will ripen, for the sake of its seeds. These are about the size of white mustard seeds, but flatter, and afford a flour resembling somewhat oatmeal. The starch grains are very small, and constitute about 40 per cent. of the seed, which also contain 5 per cent. of sugar, 7.5 of casein, and 11 of albumen and other protein compounds. One variety, the *red quinoa,* contains a bitter principle in the seed husks, and is used to some extent as an emetic and antiperiodic. (*A. J. P.*, 1872, 559.)

Quinoline. *Chinoline. Leucoline. Chinolin,* G. $(C_9H_7N.)$—This is a tertiary base, resembling an alkaloid, found in coal tar. It may be prepared by the destructive distillation of quinine or cinchonine with potassium hydroxide, and also synthetically by König's and Skraup's processes by the action of sulphuric acid and glycerin upon nitrobenzene and aniline, or a mixture of these two latter substances. *Chinoline* is a colorless, strongly refractive, oily liquid, having a specific gravity of 1.094, boiling at 238° C., without decomposition, the oily stain left on bibulous paper disappearing readily on exposure. Its odor is aromatic, resembling that of oil of bitter almond. It is sparingly soluble in cold water, more so in hot water, soluble in alcohol, and mixes in all proportions with ether, carbon disulphide, methyl alcohol, etc. It easily dissolves camphor and resin. It gradually turns reddish-brown in color on exposure to the air. It forms readily crystallizable salts with acids, the tartrate now being a commercial article; these salts are decomposed by contact with fixed alkalies and the peculiar odor of quinoline developed. A number of compounds and derivatives are known among which are the following: *Quinoline tartrate,* $(C_9H_7N)_3.(C_4H_6O_6)_4$, is in the form of a whitish, micaceous, crystalline powder, melting at 125° C. It dissolves in 80 parts of cold water, in about 150 parts of alcohol, and in 300 parts of ether, having a peculiar pungent odor and a rather sharp, though not unpleasant taste. *Quinoline hydrochloride,* $C_9H_7N.HCl$, melts at 94° C. and sublimes unchanged. It dissolves in water, alcohol, and chloroform. *Quinoline salicylate,* $C_9H_7N.C_7H_6O_3$, is a white crystalline powder, soluble in water and glycerin, very soluble in alcohol, ether, vaseline, and fatty oils. (See also *Crurin.*)

While quinoline was originally brought forward as a substitute for quinine, experience has shown that it possesses only feeble antiperiodic properties. It is, however, an active antipyretic and is also a powerful germicide. It is a depressant to the central nervous system and in 1 per cent. solution will prevent the coagulation of the blood. It is used chiefly as an antiseptic, especially in the treatment of *gonorrhea* for which purpose an 0.7 per cent. solution may be employed. Quinoline has been highly commended as a preservative for anatomical specimens. For physiological study of quinoline derivatives see *Trans. College of Physicians of Edinburgh* (*Laboratory*). 1893; also Laidlaw (*Biochem. J.*, 1910, v, 243).

Quinotoxin. *Chinotoxin.*—This name was originally applied by Ostermayer to the *diquinolindimethyl sulphate,* a synthetic compound possessing toxic properties similar to those of curare. The term was afterwards applied to the decomposition product resulting from the action of acetyl-salicylic acid upon quinine. According, however, to Sollmann (*J. A. M. A.*, 1921, lxxvi, p. 999) this latter product is the same as quinicine and is of very low toxicity.

Quisqualis.—The seeds of the *Quisqualis indica* L. (Fam. *Combretaceæ*) (*Rangoon Creeper*) have been used as an anthelmintic and occasionally substituted for santonica. According to Davenport (*Schweitz. Apoth. Zeit.*, 1918, lvi, 522) they contain an active principle resembling santonin. The *dose* of the seeds is 7.5 Gm. (2 drachms).

Radium. Ra = 226.4.—*Radium* is an elemental substance, possessing remarkable chemical and physical properties, discovered in pitchblende, a complex uranium ore, by Professor and Madame Curie of the University of Paris, in 1900. It belongs below barium in the periodic system and on the same line with thorium and uranium, these three elements having the highest atomic weights of any known. The discovery that certain substances are radio-active was made by Henri Becquerel in 1896, who showed that *uranium* was capable of affecting a photographic plate in the same way as light. Shortly after this, it was shown that a number of other substances were radio-active. The characteristics of radio-active bodies are four: (1) They affect photographic plates; (2) they produce phosphorescence in certain substances; (3) they cause the surrounding air to become a conductor of electricity; (4) they produce heat. In 1899 Madame Curie, while investigating the radio-activity of certain minerals, came to the conclusion that the uranium ore, known as *pitchblende,* from Joachimsthal in Austria, must contain some substance more actively radiant than uranium itself. This led her to the separation of the element radium, which showed two million (2,000,000) times as much activity as uranium.

After tedious and difficult experimentation involving the recrystallization, precipitation, and concentration of a ton of the ore down to a few decigrammes of purified product, a barium-like element was discovered which was many thousand times as active as uranium in its radio-activity, and which was therefore named radium by its discoverers. England manufactures some radium, the Cornish pitchblende being richer in radium than that from Joachimsthal. *Autunite* from Portugal and China and also *torbenite* contain traces of radium. At present the main radium supply of the world is from *carnotite* which is found in large quantities in Colorado. In testing specimens of unknown ores for radio-activity, the photographic plate is used and an exposure is made of the unopened plate with a small metal object placed between the ore sample and the plate. After leaving the objects in this relative position for twelve hours or more the plate is developed in the regular way and is examined for evidence of a photographic outline or image of the metal object. The extraction of radium salts from radium containing ores includes three stages. First the ores are roasted; the roasted ores are then treated with sulphuric and nitric acids which takes out the uranium compounds and leaves the radio-active metals behind as sulphates; the residue is then treated alternately with alkalies and acids and is finally separated by fractional precipitation as sulphate.

One ton of uranium residues furnishes from 17 to 22 pounds of radio-active barium residue, which upon final concentration yields a few drachms of radium bromide of high radio-active power. Some ores like autunite contain but two or three milligrammes of radium to the ton of original ore. The yield of pure radium bromide from a ton of pitchblende is about 0.25 Gm. The yield from carnotite is somewhat larger.

Radium in the elemental form has recently been prepared and observed. It is a brilliant white metal fusing at about 700° C. It is bivalent and closely allied to barium.

Properties.—Radium gives off three groups of rays, which are known by the first letters of the Greek alphabet, *alpha, beta,* and *gamma rays.* The alpha and beta rays are universally acknowledged to be material substances, while the gamma rays are by some considered waves of ether, and by others as electrons. Besides these, in solution radium liberates a gaseous element which is known as *emanation.* This gas is formed in the radium while in the dry state, but is completely absorbed, and only given off from solutions of salts of the metal. The most widely accepted theory concerning the origin of these rays is that of Rutherford. According to this, radio-activity is a sign of atomic destruction, particles of matter being given off, and the element being changed into another form of element with a lower molecular weight. Thus uranium gives off alpha particles, and the residue is *ionium;* this gives off alpha particles, the residue being radium. The decomposition of radium forms emanation, which in turn gives off alpha particles, forming a series of active deposits known as Radium A., Radium B., C., D., E., F. (Polonium), and eventually Radium G., which is by some believed to be identical with lead.

This spontaneous transformation of radium goes on at a constant rate, independent of the physical state or chemical combination of the element. The rate is such that nearly 2000 years will elapse before half of any given quantity will be changed. The following table showing the disintegration of products and the length of time required for disintegration of half of each substance is taken from the *N. N. R.*, 1924:

RADIUM AND ITS DISINTEGRATION PRODUCTS

Substance	Chemical Nature	Atomic Weight	Half Value Periods
Radium	Metal	226	1,780 yrs.
Radium emanation	Inert gas	222	3.85 days
Radium A	Solid non-metal identical with polonium	218	3.0 min.
Radium B	Identical with lead	214	26.7 min.
Radium C1	Identical with bismuth	214	19.5 min.
Radium C2	Identical with thalium	210	1.4 min.
Radium C′	Identical with polonium	214	10.6 sec.
Radium D	Identical with lead	210	15.8 yrs.
Radium E	Identical with bismuth	210	4.85 days
Radium F	Polonium	210	136 days

The alpha rays, which constitute about nine-tenths of the radiation of radium are positively charged electrons with a mass about four times that of hydrogen, moving with a velocity approximately one-tenth that of the light wave. By some they are supposed to be identical with the element *helium*, or rather to represent helium in the process of formation. Their power of penetration is relatively small. They can pass only through three inches of air, and are stopped by a heavy sheet of note-paper.

The beta rays are negatively charged electrons, and are by many believed to be identical with the cathode stream formed in a Crooke's tube. Their velocity is about equal to that of light, and their penetration is quite considerable, it requiring a sheet of lead one centimeter in thickness to certainly stop them. The beta rays travel in the opposite direction to the alpha rays and are deviable by a magnetic field which the alpha and gamma rays are not.

The gamma rays form less than one per cent. of the total radiation. Of their nature comparatively little is known. Their penetration is extraordinary, exceeding that of the X-ray. Because of the fact that they are not deflected by a magnetic field it was formerly believed that they were non-material, but the theory has been brought forward that they are discrete particles, electrically neutral.

Emanation (or *radon*) is constantly being formed in radium. It is absorbed by the salts of the metal when in a dry state, but is liberated when the salt is dissolved. It is a gaseous element, called *niton* which may be liquefied at a temperature of −150° C., and has an atomic weight of 222. When freshly liberated it is radio-active but becomes exhausted within a relatively short time, one-half of its power being dissipated within four days. Any substance exposed to emanation becomes temporarily radioactive. This is due to a deposit of the solid matter into which emanation is transferred after giving off its alpha rays.

The approximate estimate of the radio-active power in given substances can be reached by the degree of its influence upon photographic plates or the degree of fluorescence imparted to a platinocyanide screen but accurate measurements are based upon their ionizing power, that is, upon the degree of electrical conductivity they impart to the air. For this purpose, an apparatus known as the electroscope is employed. A *Curie* is the amount of emanation in equilibrium with one gramme of radium. A micro-curie is one-millionth of this and is equivalent to the amount of emanation in one milligramme of radium and equals 2700 "Maché units."

Besides the therapeutic uses of radium described below it is being much used in activating luminous paints for watch, clocks, etc.

It has been estimated that the total amount of radium separated and in use in 1921 was less than 100 Gms.

Most of the radium which is used therapeutically is in a more or less impure state, and it becomes necessary to have some knowledge of the radio-active power of any known specimen before it is used for medical purposes. Because of its affinity for oxygen, it is very difficult to prepare radium in the elemental state and it is therefore usually marketed in the form of one of its salts. Of these the *carbonate* $RaCO_3$, the *chloride* $RaCL_2$, and the *sulphate* $RaSO_4$ are most frequently employed. The salts sold under these names do not pretend to be pure salts of radium but are mixtures with the corresponding salts of barium. They are usually sold on the basis of their radium content as measured electroscopically. Manufacturers of radium generally supply with each sample of the metal, a statement of its power.

Therapeutic Uses.—The medical value of radium depends in the first place upon the destructive action of the rays upon the certain pathological tissues, and secondly upon the alterations in functions which are produced by the internal administration of emanation. The widest use of radium has been as a destructive agent in various types of *neoplasms.* For this purpose it is applied in various forms of containers, the most popular being a sealed glass tube, which is enclosed within a thin aluminum capsule to protect it from breaking.

The earliest investigations of the action of radium rays upon living protoplasm appear to be those of Schwarz (*A. G. P.*, 1903), who showed that when hen's eggs were exposed to the metal there was a decomposition of the lecithin within them. London (*B. K. W.*, xlii) found that rabbits kept for two weeks in a cage on top of which was placed 25 mgm. of radium lost their hair, the ears necrosed and the sexual organs degenerated; he believes that the emanations have no effect on fibroid tissue. The alpha rays have considerable germicidal action, as apparently does also emanation, but neither of these have any great penetrative power, so that the anti-bacterial effect of radium is not likely to prove of practical utility.

When applied to the skin, radium produces no immediate effect, but lesions appear after considerable periods of incubation, which may be as long as two weeks. If the dose has been small there is merely redness, but after longer exposure an ulcer is formed which heals very slowly. Although there is left behind, when these ulcers heal, a white supple cicatrix, destruction to the hair follicles, sweat and sebaceous glands may have been the result of the action of the rays upon the skin. It is possible, however, to profoundly influence the deeply lying structures with much less danger of causing dermatological injuries than with the X-rays. This can be accomplished by screening off the relatively superficially acting alpha and beta rays which allows the deeply penetrating gamma rays alone to act.

Radium has been largely used for the destruction of *malignant growths* and ulcers such as *carcinomata, sarcomata, rodent ulcers, epitheliomata*, and the like, especially in *cancer of the uterus*. While there is no doubt that it exercises a beneficial action there is a considerable difference of opinion as to its precise value, some authorities going so far as to rank it superior to surgical operations while others maintain that it is to be classed as a palliative rather than a curative. (For discussion of its value in uterine cancer see *J. A. M. A.*, 1921, lxxvii, 604, et seq.)

It is also of great service in the treatment of *menorrhagia* and *metrorrhagia*. The mode of its action in these cases is not definitely known; it has been suggested that it is due to its effects upon the ovaries but Maury (*J. A. M. A.*, 1920, lxxiv, 1711) from experiments upon the lower animals concluded that its action was upon the mucous membrane of the uterus. Levin (*J. A. M. A.*, 1921, lxxvii, 930) has used it with asserted good results in *Hodgkin's disease* and in *lymphatic leukemia*.

The dosage of radium is generally expressed in terms of pure radium and time. For instance, if the quantity of the salts equivalent to one milligramme of pure radium is to be applied for one hour, the dosage set is "one milligramme, hour." If an impure preparation is employed, as is usually the case, its activity must be calculated to that of pure radium. For instance, if the salt represent five-hundred-thousand units, it would require four milligrammes to exercise the same effect as one milligramme of pure radium.

Emanation when introduced into the system appears to have an influence upon the circulation, but especially upon metabolism. According to Theis and Bagg (*J. Bi. Chem.*, 1920, xli, 525) radium emanations cause a marked increase in the elimination of nitrogen. According to Loewi (*B. K. W.*, 1912, xlix, p. 198), the inhalation of emanation produces a contraction of the vessels of the lungs, and dilation of the vessels of the brain, with some tendency to lower the general blood pressure. The effect upon metabolism is shown in an increased elimination of uric acid. Although His (*B. K. W.*, xlviii, p. 197) found after the exhibition of radium marked diminution in the amount of uric acid in the blood, Fine and Chace (*J. P. Ex. T.*, 1914, vi, 219) could find no such change. Armstrong (*Practitioner*, 1912, lxxxviii, p. 156) and a number of German writers have described beneficial results from the drinking of water containing emanation, and also from the inhalation of the gas itself in *gout*.

While it seems evident that radium emanation has some marked effect on metabolism the precise nature of this alteration remains as yet obscure. Clinically, radium has been used internally in the treatment of *gout, arthritis deformans* and other diseases of the joints; in muscular *rheumatism*, in *sciatica, neuralgia* and other painful conditions. Some believe that the beneficial effects obtained by drinking mineral waters is due to their radium content; but while it is a fact that many of the famed medicinal springs are radio-active it remains to be shown that this explains their beneficial action. Indeed, the whole use of radium as an internal remedy is still in the experimental stage. (For a list of some of the proprietary radium specialties see *A. Ph. A. Year-book of Pharmacy*, 1912, p. 302.)

Raisins. *Uva Passa. U. S.* 1870.—The dried ripe fruit of the *Vitis vinifera* L. (Fam. *Vitaceæ*), is no longer recognized by the Pharmacopœia. The grape vine itself is too well known to require description. The plant is a native of the southern shores of the Caspian Sea and Armenia, and has been cultivated in Europe and Northern Africa from the remotest antiquity, and is now spread over all the temperate civilized regions of the globe. Its leaves and tendrils are somewhat astringent, and were formerly used in *diarrhea, hemorrhages*, and other morbid discharges. The juice which flows from the stem was also thought to be possessed of medicinal virtues, and the idea still lingers among the vulgar in some countries. The unripe fruit has a harsh, sour taste, and yields by expression a very acid liquor, called *ver-juice*, which was much esteemed by the ancients as a refreshing drink when diluted with water. It contains malic and tartaric acids, and an acid called *racemic acid*, a compound isomeric with tartaric acid, but differing from it in being optically inactive. M. A. Petit has ascertained that grape leaves contain both glucose and sucrose, as well as tartaric acid. (*J. P. C.*, 1874.) The seeds afford from 15 to 18 per cent. of a bland fixed oil, which is occasionally extracted, and from 5 to 6 per cent. of tannic acid, which also exists in the skin of the fruit. The grape, when ripe, is among the most pleasant and grateful fruits, and is admirably adapted, by its refreshing properties, to febrile complaints. If largely taken, it proves diuretic and gently laxative. The ripe fruit differs from the unripe in containing more sugar and less acid, though never entirely destitute of the latter. The fruit is exceedingly influenced by soil and climate, and the varieties of the plant which have resulted from culture or situation are innumerable.

Several varieties of raisins are known in commerce. The best of the European fruit are the

Malaga raisins, imported from Spain. They are large and fleshy, of a purplish-brown color and sweet, agreeable taste. Those produced in Calabria are similar. The *Smyrna raisins* are also large, but of a yellowish-brown color, slightly musky odor, and less agreeable flavor. They are originally brought from the coast of Syria. The *Corinthian raisins*, or *currants* as they are commonly called in this country, are small, bluish-black, with a vinous odor and a sweet, slightly acid taste. Their name is derived from the city in the vicinity of which they were formerly cultivated. At present they are procured chiefly from Zante, Cephalonia, and the other Ionian Islands. In the older Pharmacopœias they are distinguished by the title of *uvæ passæ minores.* Within recent years the production of raisins in California has become an industry of the highest importance. These raisins are coming into large use in the United States and have largely replaced those obtained from Europe. The ripe grapes are cut from the vines, spread out on a clay floor, and dried by exposure to the heat of the sun. The drying process usually requires about ten days' time. Artificial heat is used to dry them in rainy weather; sometimes the grapes are partially dried on the vines; this is done by cutting the stalks of the ripe grapes half way through, and allowing the bunches to remain for a few weeks, a portion of the bark of the vine being removed also to facilitate the process. If it is desirable to remove the waxy bloom on the grapes, the bunches are steeped for a short time in weak alkaline solution, washed and then thoroughly dried.

Raisins usually contain more sugar than do fresh grapes. It is often so abundant that it effloresces on the surface or concretes in separate masses within the substance of the raisin. The average composition of raisins is, in parts per hundred: moisture 18.61, protein 3.09, fat 2.86, sugars 70.49, ash 2.70. The *sugar of grapes* (*dextrose*) differs from that of the cane, being less sweet, less soluble in cold water and much less so in alcohol. In these respects it does not differ from artificial dextrose, which is now made in enormous quantities and consumed in food products and candies; the artificial product is made by acting on starch with hydrochloric acid (see *Glucosum*).

The chief medicinal use of raisins is to flavor demulcent beverages. Taken in substance they are gently laxative, but are also difficult of digestion, and, when largely eaten, sometimes produce unpleasant effects, especially in children.

Radish. *Raphanus sativus* L.—The juice of this well known plant has been used by Grumme in the treatment of *cholelithiasis* as an aid in preventing the formation of biliary calculi. He employed the expressed juice of the crushed bulbs in *doses* of two to four fluidounces (60–120 cc.).

Saki reports the presence of an amylolytic enzyme in radish juice. (*J. P. C.*, 1906, 561.)

Sacher recommends the coloring matter from red radishes as a sensitive indicator in alkalimetry; the fresh peels are treated with alcohol and the solution is turned red with acids and green by alkalies.

Randia. *Randia dumetorum* Lam. (Fam. *Rubiaceæ.*)—The fruit of this spiny Asiatic shrub is used by the natives as a fish poison, and is said to act in man as an irritating emetic. According to the *Pharmacographia Indica*, each fruit contains about four grains (0.26 Gm.) of a saponin, besides valeric acid. The tincture has been used by James Sawyer (*L. L.*, 1891) as an antispasmodic.

Ranunculus. *Crowfoot. Renoncule*, Fr. *Hahnenfuss*, G.—Most of the plants belonging to the genus *Ranunculus* have similar acrid properties, and, from their close resemblance, are confounded under the common name of *buttercup. R. bulbosus* L. was formerly in the Secondary List of the U. S. Pharmacopœia; but *R. sceleratus* L. had attracted more attention in Europe, and *R. acris* L. and *R. flammula* L. were recognized by the Dublin College. In all these species the plant itself is a violent irritant, producing when chewed excessive inflammation in the mouth and throat, and, when swallowed toxic gastritis which may be fatal. Clarus discovered, in *R. sceleratus* L., besides an acrid volatile oil, a nearly inert resin, and *anemone camphor* (see under *Pulsatilla*). The volatile oil is soluble in ether, and is decomposed, on standing, into a white amorphous substance having acrid properties (*anemonic acid*), $C_{15}H_{14}O_7$. (*Brit. and For. Med.-Chir. Rev.*, 1859, 181.) Rochebrune states that he has separated from *R. aquatilis* L., *R. flammula* L., *R. sceleratus* L. and *R. bulbosus* L., crystalline alkaloids to which he has given the name of *ranunculine*, although their identity is doubtful. These alkaloids are violent irritants and active cardiac poisons. (*Toxicolog. Africaine*, i.) Before the introduction of cantharides the green butter-cup plants were much employed as vesicants.

Realgar. As_2S_2. *Red Orpiment.*—This is *arsenic disulphide.* It is found native in Saxony, Bohemia, Transylvania, and in various volcanic regions. *Realgar* is artificially made by melting arsenic trioxide with about half its weight of sulphur. Thus prepared, it is of a crystalline texture, of a beautiful ruby-red color, of a uniform conchoidal fracture, somewhat transparent in thin layers, and capable of being sublimed without change. Native realgar is said to be innocuous when taken internally, while that artificially prepared is poisonous, in consequence, according to Guibourt, of containing a little free arsenic trioxide. Realgar is used only as a pigment.

Red Chalk. *Reddle.*—A mineral substance of a deep red color, of a compact texture, dry to the touch, adhering to the tongue, about as hard as chalk, soiling the fingers when handled, and leaving a red mark when drawn over paper. It consists of clay and ferric oxide, and is intermediate between *bole* and *red ochre*, containing more ferric oxide than the former and less than the latter. It is used for drawing lines upon wood, etc., and is sometimes made into crayons by levigating and elutriating it, then forming it into a paste with mucilage of gum arabic, molding this into cylinders, and drying it. It has been used internally as an absorbent and astringent.

Resaldol. *Resoldol. Resorcin-benzoyl-carbonic acid-ethyl-ester.* $C_{20}H_{14}O_5(CH_3CO)_2$.—Resaldol is made by acetylating the product of the reaction between chlormethyl-salicylic aldehyde and resorcinol. It is an amorphous yellowish-brown powder of an astringent taste, insoluble in water and dilute acids, but soluble in alkalies. According to Impens (*D. M. W.*, 1913, p. 1827), it acts much like cotoin (see *Coto*), over which it has the advantages of being tasteless and nonirritant. It is used in *tuberculous* and other forms of *enteritis*. The *dose* is eight grains (0.5 Gm.) several times a day.

Reseda. *Reseda Luteola* L. *Weld. Dyer's Weed. Herbe Jaune, Gaude,* Fr. *Wau, Gelbkraut, Harnkraut,* G. (Fam. *Resedaceæ.*)—An annual European plant, naturalized on roadsides and ballast from Massachusetts to Pennsylvania. The plant grows to a height of 6 dm., possesses alternate lanceolate leaves and small greenish-yellow flowers. It is inodorous, and has a bitter taste, which is very persistent. Volhard showed that allyl thiocyanate, $C_3H_5.SCN$ (volatile oil of mustard), was present in the root, and Chevereul obtained from it by sublimation a peculiar yellow coloring matter, which he called *luteolin.* Hlasiwetz and Pfaundler (1895) assign to it the formula $C_{15}H_{10}O_62H_2O$ and find it to be tetrahydroxyflavone. This forms yellow crystals of silky luster, insoluble in water, soluble in alcohol. It dissolves in alkalies with deep yellow color. It is used especially in silk dyeing. A. G. Perkin (*J. Chem. S.*, 1896) investigated the salts of luteolin, and called attention to the similarity of its properties to those of fisetin (see *Fustic*). In medicine it has been employed as a diaphoretic and diuretic, but it is now used only for dyeing purposes.

Resineon.—This is a volatile oil obtained from black tar oil by distillation and stated to be free of phenol. It boils at 148° C. and is used externally as a dressing for wounds and injuries and as an antiseptic in *skin affections.* A 1 to 8 ointment is applied by inunction in *chronic eczema.*

Resorbin.—An ointment vehicle made by emulsifying almond oil and water by means of a little yellow wax, gelatin, and soap, to which is added some lanolin. It is asserted that it greatly facilitates the absorption of medicaments.

Resorcin Acetate. *Resorcinol Monoacetate, N. N. R.*, 1925.—This is a thick, yellow liquid, sparingly soluble in water but more soluble in alcohol and the organic solvents. It has a faint odor and a sharp taste. Its boiling point is 283° C.

Resorcin acetate is used in the treatment of skin diseases, such as *acne, chilblains, seborrhea,* etc. Its action is said to resemble that of resorcin but to be milder and more lasting.

Retinol. *Codoil. Rosinol. Rosin Oil.* $C_{32}H_{16}$.—A product obtained by the distillation of rosin. It forms a yellowish oil boiling at temperatures over 280° C. It is stated that *retinol* does not irritate the skin, is unaltered by light, is mildly antiseptic, does not become rancid, and is very inexpensive; qualities which, taken along with its extraordinary solvent power, bid fair to make it a valuable vehicle for ointments. Among the substances dissolved by it are: salol, 1–10; iodol, 1–50; naphthol, 1–50; thymol iodide, 1–50; camphor, 1–20; chrysophanic acid, 1–40; cocaine, 1–30; codeine, 1–40; and strychnine, 1–40. It is miscible in all proportions with oil of juniper, phenol, terpentine, alcohol, and ether. Resorcinol, if dissolved in glycerin, may be mixed with retinol, and so may iodoform if it be dissolved in a little ether. Iodol is dissolved, but soon precipitates as a resinous mass. Phosphorus is also dissolved, and the solution remains unchanged indefinitely. Retinol mixes readily with fats, oils, vaseline, lard, lanolin, glycerin, cacao butter, etc, and may be used in ointments. In cases where a liquid is not undesirable, retinol, owing to its antiseptic properties, can with great advantage replace these bodies. Upon the mucous membrane retinol seems to act as a mild stimulant antiseptic; it has been used with alleged excellent results locally in *otitis, vaginitis, rhinitis* and other mucous diseases. Injections of it in *gonorrhea* are said to be remarkably effective. As a means of administering phosphorus it is especially recommended.

Rhigolene.—This name was given by H. J. Bigelow of Boston, to a very light, inflammable liquid, obtained by distilling petroleum, and separating the liquids of the lowest boiling point by redistillation, until one is obtained which boils at about 18° C. It was used for producing local anesthesia by its rapid evaporation when sprayed upon the part, but has been displaced by ethyl chloride. The vapor is inflammable and care should be exercised in using it near a flame.

Rhizophora Mangle L.—This is a tree with coriaceous, elliptic to elliptic-ovate leaves and large yellow flowers belonging to the *Rhizophoraceæ* and forming thickets along the coast of Florida and in the tropics. The red bark of the *mangrove tree* has been used for many years by the natives of South America as a febrifuge. Duque and Moreno (*S. M.*, 1905, p. 479) have claimed that it is a specific in *leprosy.* They administer a beginning *dose* of one fluidrachm (3.75 cc.) of the fluidextract twice a day which is gradually increased until the patient is taking a fluidounce and a half (45 cc.) daily.

Rhododendron. *Rhododendron Chrysanthemum* Pall. *Yellow-flowered Rhododendron. Rosebay. Snowrose. Rosage,* Fr. *Alpenrose, Schneerose, Gichtrose,* G. (Fam. *Ericaceæ.*)—The leaves of this rhododendron have long been employed in Siberia as a remedy in *rheumatism,* and to a less extent in *gout* and *syphilis.* They yield their virtue to water and alcohol, and, according to von Archangelski, contain three proximate principles; *rhododendrol,* $C_{10}H_{12}O_2$; *rhododendrin,* $C_{16}H_{22}O_7$; and a glucoside resembling digitalin and very toxic. The *dose* of the dried leaves is said to be two drachms (7.7 Gm.), given in infusion. There have been several reports of sheep being poisoned through eating rhododendron leaves. De Zaayer found in *R. ponticum* the neutral principle, andromedotoxin. Hardikar (*J. P. Ex. T.*, 1922, xx, p. 17) confirms its presence in an unnamed species of rhododendron which he investigated, and made a careful study of its physiological action. (See *Andromeda.*)

G. F. Kuehnel found in leaves of the "great laurel," *Rhododendron maximum* L., a common shrub in the Alleghenies from New York to Georgia, arbutin, ericolin, and ursone. (*A. J. P.*, 1885.)

Rhus.—The genus *Rhus* contains various species which have the property of so violently irritating susceptible skins as to produce severe dermatitis. Of these poisonous species there are six which are indigenous to the United States.

R. vernix L. (*R. venenata* DC.)—*Swamp Sumac, Poison Sumach, Poison Elder* is our most poisonous species. It is a handsome shrub or small tree, usually ten or fifteen feet high. The bark of the trunk is dark gray, of the branches lighter. A prominent characteristic is the color of the extreme twigs and petioles, which is pale to deep red. The leaves are pinnate, with three to six pairs of opposite leaflets, and an odd terminal one. These are oblong or oval, entire or slightly sinuate, acuminate, smooth, and, except the one at the end, nearly sessile. The flowers are polygamous, very small, greenish, and in loose or slender axillary panicles. The berries are small, roundish, and greenish white. The tree grows in swamps and low grounds from Canada to Carolina, and flowers in June and July. It was confounded by the older botanists with *R. vernicifera* DC., of Japan, the Japanese lacquer tree, which has similar poisonous properties. Its activity is said to depend upon *urushic acid.*

Rhus Michauxii Sargent (*R. pumila* Michx.) is a rare Southern species, growing in upper Carolina and Georgia, and not more than a foot in height. It is characterized by its pubescent branches and petioles, by its pinnate leaves, with many pairs of oval, nearly acuminate, incised-dentate leaflets, downy beneath, and by its silky fruit. According to Pursh, it is the most poisonous of the genus.

Rhus diversiloba Torrey and Gray (*R. lobata* Hooker) is found on our Pacific border. It is there generally known as *Poison Oak,* and closely resembles *R. Toxicodendron* L.

Rhus Metopium L. (*Metopium Linnæa,* Engelm.), *Mountain Manchineel, Coral Sumac,* is a West Indian species, growing also in the "hummock" lands of Southern Florida. It is a small tree, the bark, when wounded, exuding a gum-resin to which medicinal properties are ascribed. This is known locally as *hog-gum,* but should not be confounded with the Asiatic *Hog-gum* or *Bassora.* The leaves are pinnate with fine leaflets. To the acid red fruit is due the name Coral Sumac. It is exceedingly poisonous.

Rhus Toxicodendron L. (*R. radicans* L.), *Poison Oak, Poison Ivy,* whose fresh leaves were formerly official in the U. S. Pharmacopœia under the name of *Rhus Toxicodendron,* U. S. 1890, is a woody vine climbing by numerous aerial rootlets to considerable heights and showing considerable variation. The leaves are 3-foliate, the leaflets being ovate or rhombic, 2.5 to 15 cm. long, entire or sparingly dentate or sinuate, acute or short-acuminate, the lateral sessile or short-stalked, are inequilateral, the terminal ones stalked. The flowers are green, 3 mm. broad, in loose axillary panicles, 2 to 8 cm. long; the fruit globose-oblong, whitish or cream colored, resembling that of *R. Vernix.*

The milky juice, of the poisonous species of *Rhus,* becomes black on exposure to the air, and leaves upon linen or other cloth a stain, which cannot afterwards be removed by washing with soap and water, or by alcohol either hot or cold, but deepens by age. It has been proposed as an indelible ink. Ether dissolves it; applied to the skin it frequently causes inflammation and vesication

The toxic principle of poison sumacs is generally believed to be *toxicodendrol,* an acid resin, but McNair concludes that it is a polyhydric phenol which he calls *lobinol* (*J. Am. C. S.,* 1921, xliii, 159). As toxicodendrol is non-volatile many have hesitated to accept it as the sole active principle because of the well-known fact that susceptible persons may be poisoned without actual contact with the plant, but Youngken and Slothower (*A. J. P.,* 1920, xcii, 695) have shown that the hairs on the leaves of the poison ivy contain the toxic principle. The latter may be carried by air currents or may be transported on clothes, or tools, or animals, which after brushing against the plant are able to transfer the poison to susceptible persons.

In the treatment of *ivy poisoning* a great variety of remedies have been lauded as specifics; among these may be mentioned fluidextract of grindelia, solution of lead subacetate, solution of formaldehyde, zinc sulphate, potassium permanganate, etc. Perhaps as successful treatment as any is to remove the poison from the skin with alcohol—it is not sufficient simply to bathe the part with alcohol as this serves only to spread the poison, it must be thoroughly washed. Afterwards apply a lotion of sodium thiosulphate of about 10 per cent. strength to which may be added one or two per cent. of phenol to allay itching. Thorough washing with soap—if due precaution against the transference of the poison to other parts of the body is observed—is probably also a valuable means of removing the poison; indeed it has been recommended that a thick lather of laundry soap be allowed to dry on the inflamed part as a curative. Schamberg (*J. A. M. A.,* 1919, lxxiii, 1213) succeeded in desensitizing persons against ivy poisoning by the use of ascending doses of a tincture of the drug by the mouth, and Strickler (*J. A. M. A.,* 1923, lxxx, 1588) has employed hypodermic injections of an extract as a curative. Warren (*A. J. P.,* 1913, p. 548) was unable to detect a poisonous principle in the pollen grains of *Rhus Vernix.* See also Tschirch and Stevens, *A. J. P.,* 1906, p. 63. Besides the poisonous principle of rhus there is present an iron greening tannin, chlorophyll, wax, fixed oil, resin, sugar, albumen, pectin, gum, starch, and oxalic acid.

The poisonous rhus when taken internally appears to be possessed of narcotic besides irritant properties, vomiting, drowsiness, stupor, dilated pupils, convulsive movements, delirium, and fever having been present in poisoning by them. The tincture of rhus has been used by homeopathic practitioners in the treatment of *subacute* and *chronic rheumatism,* and the practice has found imitation. Some years ago H. C. Wood made extended trials of the remedy, using a homeopathic tincture obtained from a homeopathic pharmacy, in various doses (homeopathic, small, and large), upon a large number of cases of various types of rheumatism, in the Philadelphia Hospital, but he was not able to perceive that the patients progressed more rapidly when taking it than when they were simply nursed.

Rhus canadensis Marsh. (*R. aromatica* Ait) (Fam. *Anacardiaceæ*).—This indigenous shrub, growing in dry soil from Maine and Southern Ontario to Florida and westward, has been highly recommended in the treatment of *nocturnal incontinence* of urine by a number of clinicians of repute (See *G. H. M. C.,* 1889; also *Annals of Gynæc.,* 1890.) The adult *dose* is twenty or thirty minims (1.3–1.8 cc.) of the fluidextract of the bark, three times a day, given in aromatized solutions.

Ricin is the name given by Kobert and Stillmark to the toxic constituent of castor beans (*Ricinus communis* L.). It belongs to the class of albuminoids and is of the character of an enzyme. It is a white powder which forms a turbid liquid in a 1 per cent. solution of sodium chloride. It has been proposed by Jacoby to detect the presence of pepsin in liquids by using *ricin.* (*M. R.,* 1907.) For a valuable paper by Finnemore and Deane read before the British Pharmaceutical Conference, 1905, see *M. R.*, 1906, 165. The toxic symptoms, which frequently do not come on for several hours after the ingestion of the poison, are due primarily to the intensely irritant action of the substance, and consist of diarrhea, with suppression of the urine, and frequently jaundice, probably from irritation of the mucous membrane of the biliary ducts. Müller (*A. E. P. P.*, 1899, xlii) states that the poison also has a direct action upon the medulla, leading to the fall of blood pressure and lessened respiratory activity.

The effects of ricin in many directions bear a striking resemblance to the effects of bacterial toxins. Thus, for example, it produces a leucocytosis and an agglutination of the red corpuscles. The most interesting, however, of these resemblances is the production of immunity and the formation of antitoxic substances.

Rimu Resin.—The resin of the *Dacrydium cupressinum* Solander, the New Zealand red pine or *rimu*, a large coniferous tree of New Zealand, is characterized by its rose color and its crystalline appearance. It is composed chiefly of a crystalline acid resin, *rimuic acid.* (*Chem. News*, lxxxviii, 20.)

Ristin.—This is the mono-benzol ester of ethylene glycol. It is marketed only in the form of a 25 per cent. alcoholic solution. The latter is asserted to possess antiseptic properties and is used in the treatment of *scabies* mixed with equal parts of glycerin.

Robinia. *Robinia Pseudo-Acacia* L. *Black Locust Tree. Yellow Locust. False Acacia. Robinier*, Fr. *Falsche Akasie*, G. (Fam. *Leguminosæ.*)—This well-known indigenous tree has a place in the materia medica of the eclectics. The root and inner bark are poisonous but the leaves are said to offer a wholesome food for foraging animals. This would seem confirmed by the experiment of Paven, who failed to find in them any poisonous principles. Kobert (*M. Bull.*, April, 1891) found in the bark an albumoid enzyme, which he named *robinalbin*, similar to, but not identical with, ricin. Power (*P. J.*, Aug. 17, 1901; *A. J. P.*, 1913, 339) summarizes the results of a more detailed investigation of this bark. He names the poisonous proteid *robin* and states that it belongs to the class of nucleoproteids. He finds evidences of one or more alkaloids; by hydrolysis he obtained *syringic acid*, $C_9H_{10}O_5$, and a red amorphous substance, *syringenin.* These products indicate the glucoside *syringin*, $C_{17}H_{24}O_9$. He also considers that *glucosyringic acid*, $C_{15}H_{20}O_{10}$, may pre-exist in the bark. In the bark of the locust tree grown in Japan Tasaki and Tanaka (*J. Soc. Chem. Ind.*, 1919, xxviii, 267) found a poisonous glucoside, *robitin.* The most striking toxic effects of this were fever and paralysis of the hind legs. Robin has emetic and purgative properties. Z. T. Emery (*N. Y. M. J.*, Jan. 22, 1887) reports the poisoning of thirty-two boys from chewing the inner bark of the tree. The symptoms in the mildest cases were vomiting and flushed face, dryness of the throat and mouth, and dilated pupils. In the severest cases, to these were added epigastric pain, extremely feeble, intermittent heart action, and stupor. The air dried seeds have been examined by van Berk (*Pharm. Weekblad.*, 1917, liv, 1278.) and found to contain, water 13 per cent., fat 8.5 per cent., albumin 38 per cent., soluble carbohydrates 18 per cent. Feeding experiments showed the seeds to be harmless to animals.

Robinia Nicou Aubl., now known as *Lonchocarpus Rufescens* Benth.—According to the researches of Geoffroy (*Annal. de l'Inst. botanico-geologique colon. de Marseille*, 1895), this leguminous plant, which is used in Guiana for the purpose of stupefying fish, contains an active principle, *nicoline* (C_3H_4O), which crystallizes in oblique, rhomboidal tables. It has been found by E. Boinet (*C. R. S. B.*, 1886, 10 s., iii) to produce in the lower animals a short primary stage of excitation, followed by one of stupor, great muscular relaxation, enfeeblement of sensibility, mydriasis, fall of temperature, cyanosis, and death through centric paralysis of the respiration, though there is also fall of arterial pressure. In the dog there was salivation and vomiting.

Rosa.—Of the genus *rosa* at least four species have been, and probably to some extent are still, used in medicine—namely, *Rosa canina* L., *Rosa centifolia* L., *Rosa damascena* Mill., and *Rosa gallica* L.

Rosa canina.—The *Dog Rose, Wild Brier*, or *Hip Tree*, of Europe, North Africa and West Asia is an upright shrub characterized by having branches with stout hooked prickles, imparipinnate leaves with 5–7 oval or elliptic, doubly serrate leaflets and light pink flowers with usually 5 obcordate fragrant petals. The fruit consists of a fleshy, hollow receptacle, bearing on its inner surface a number of hairy achenes. The ripe fruit, which is usually employed in the fresh condition, is ovoid, smooth, shiny and red in color. Rose hips possess a pleasant, sweet, acidulous taste. It was formerly official in the British Pharmacopœia under the name of *Rosæ Caninæ Fructus.* It contains about 30 per cent. of sugar, combined with citric and malic acids, also salts of these acids, and a trace of tannin. A confection is sometimes used as a pill excipient. Vanillin has also been found present in the petals.

Rosa centifolia, the *Cabbage Rose* or *Pale Rose*, has prickly stems and the leaves consist of two or three pairs of leaflets, with an odd one at the summit closely attached to the common footstalk, which is rough, but without spines. The leaflets are ovate, broad, serrate, pointed, and hairy on the under surface. The flowers are large, with many petals, generally of a pale red color, and supported upon peduncles beset with short bristly hairs. The varieties of *R. centifolia*, produced by its almost universal cultivation, are very numerous, but the plant is said to grow with single flowers in its native home, which is the eastern part of the Caucasus. It is very closely allied to *R. gallica*, Regel considering it a variety of *R. gallica.* The petals, which were recognized by the U. S. P., 1890, as *pale rose*, are roundish-obovate and retuse, or obcordate, pink, fragrant, sweetish, slightly bitter, and faintly astringent. They contain volatile oil, malic and tartaric acids, tannin, fat, resin, sugar, and a coloring matter which seems to be identical with that of the red rose. They should be collected when the flower is fully expanded but has not begun to fall. Their fragrance is impaired but not lost by drying. They may be preserved for a considerable time by compressing them with alternate layers of common salt in a well-closed vessel, or beating them with twice their weight of that substance. A rose water is often prepared from them by distillation.

Rosa damascena or *Damask Rose* is not known in the wild state. It was introduced into Europe from Asia Minor in the 16th century. It is the rose which is cultivated mainly on the southern side of the Balkan mountains, in Bulgaria, and yields the commercial *otto of rose.* (See *Oleum Rosæ.*) It is a tall shrub with usually double, red, pink, white, or striped flowers of moderate size, having several on a branch, though not clustered. Its volatile oil is the base of rose water.

Rosemary. *Rosmarinus. Folia Rosmarini, s. Roris Marini. Folia Anthos. Feuilles de Romarin,* Fr. Cod. *Rosmarin, Rosmarinblätter,* G. *Rosmarino,* It. *Romero,* Sp.—"The leaves of *Rosmarinus officinalis* (Fam. *Labiatæ*)." *U. S.,* 1880. *Rosemary* is a small evergreen shrub, with an erect stem, divided into many long, slender, ash-colored branches. The leaves are numerous, sessile, opposite, about 2.5 cm. long, rigid, linear, entire, obtuse at the summit, folded backward at the edges, of a firm consistence, smooth and green on the upper surface, whitish, woolly, and glandular beneath. The flowers occur in pale blue verticillasters. The plant is native to the countries which border on the Mediterranean, and is cultivated in the gardens of Europe and the United States. The leaves, which have already been described, have a strong balsamic odor, which is possessed, but in a less degree, by all parts of the plant. Their taste is bitter and camphoraceous. These properties are imparted partially to water, completely to alcohol, and depend on the volatile oil. (See *Oleum Rosmarini,* Part I.) The present commercial supplies of this drug are from France. The tops lose a portion of their sensible properties by drying, and become inodorous by age. Rosemary is gently stimulant, and has been considered emmenagogue. In the practice of this country it is scarcely used; but in Europe, especially on the continent, it enters into the composition of several syrups, tinctures, etc., to which it imparts its agreeable odor and excitant property. It is sometimes added to sternutatory powders, and is used externally in connection with other aromatics in the form of fomentation. In some countries it is employed as a condiment; and its flowers, which are much sought after by the bees, impart their peculiar flavor to the honey of the districts in which the plant abounds.

Rotten Stone. *Terra Cariosa.*—An earthy mineral, occurring in light, dull, friable masses, dry to the touch, of a very fine grain, and of an ash-brown color. It is obtained from Derbyshire, in England, and is used for polishing metals. For a particular account of it, see *A. J. P.,* 1860, 463.

Rourea. *Rourea oblongifolia* Hook. and Arn. (Fam. *Connaraceæ.*)—This Mexican creeper is affirmed to contain an alkaloid, and to act as a violent convulsant poison. (*El Estudio,* 1890.)

Rubia. *Madder. Garance,* Fr. *Krappwurzel, Färberröthe,* G. *Robbia,* It. *Rubia de tintoreros, Granza,* Sp.—Under this name the U. S. P. 1870 recognized the root of *Rubia tinctorum* L. (Fam. *Rubiaceæ.*) The root of *dyer's madder* is perennial, and consists of numerous long, succulent fibers, varying in thickness from the size of a quill to that of the little finger, and uniting at the top in a common head, from which also proceed side-roots that run near the surface of the ground, and send up many annual stems. The quadrangular stems are furnished with short prickles by which they adhere to neighboring plants, upon which they climb. The leaves are arranged in whorls at the joints of the stem. The flowers are small, yellow and terminal. The plant is a native of Southern Europe. The root, which is dug up the third summer, enters commerce either in the form of the whole root deprived of its cuticle, or in the form of a reddish-brown powder.

Madder contains as its most important constituent *alizarin,* $C_{14}H_6(OH)_2O_2$, and with it as coloring matter of secondary importance *purpurin,* $C_{14}H_5(OH)_3O_2$. Besides these two technically important constituents there have been recognized *pseudopurpurin,* an orange dye color, and a yellow one (*xanthopurpurin*). These coloring matters, however, are probably decomposition products from glucosides existing in the fresh plant. Thus, alizarin is known to result along with glucose from the treatment with dilute acids of *rubianic* or *ruberythric acid,* $C_{26}H_{28}O_{14}$. The most interesting of the coloring substances is the *alizarin,* and this is now termed *dihydroxyanthraquinone,* $C_6H_4(CO)_2.C_6H_2(OH)_2$. This occurs as orange-red crystals, almost insoluble in cold water, but readily soluble in alcohol, ether, the fixed oils, and alkaline solutions. The alcoholic and aqueous solutions are rose-colored; the ethereal, golden yellow; the alkaline, violet and blue when concentrated, but violet-red when sufficiently diluted. A beautiful rose-colored lake is produced by precipitating the solution of alizarin with alum. Alizarin was recognized by Graebe and Liebermann in 1868 as a derivative of anthracene, $C_{14}H_{10}$, and elaborated a method for preparing it commercially from anthracene. Upon this arose rapidly a great chemical industry, and the cultivation of madder, has, of course, decreased correspondingly.

Madder when taken into the stomach imparts a red color to the milk and urine, and to the bones of animals, without sensibly affecting any other tissue. Under the impression that it might effect some change in the osseous system, it has been prescribed in *rachitis,* but without favorable result. It was also formerly used in *amenorrhea. Dose,* about half a drachm (2.0 Gm.), repeated three or four times a day.

Rubidium.—Rb–85.45. A soft silvery white metal belonging to the alkali metal group with potassium and sodium, easily oxidized in air, only stable when kept immersed under a hydrocarbon. Sp. gr. 1.532, melts at 39° C.; and boils at 696° C. Decomposes water when brought into contact with it, dissolved by acids to form salts. Salts of *rubidium* may be obtained much more cheaply than in former years, on account of Erdmann's process for the recovery of these salts from the Stassfurt potash deposits. Several salts have been brought forward for use in practical medicine.

Rubidium Carbonate. $RbCO_3.H_2O$.—A white powder, deliquescent and strongly caustic. Decomposes upon exposure to the air with the formation of rubidium bicarbonate ($RbHCO_3$) which is crystalline, permanent in air and with a faint alkaline reaction.

It is used in preparing salts of rubidium.

Rubidium iodide, RbI, which occurs in white lustrous crystals, or a white powder, freely soluble in water, has been recommended by Harnack, Neisser, and others as a substitute for potassium iodide, than which it is asserted to be better borne by the stomach. The dose is that of potassium iodide. G. Jacontini affirms that rubidium iodide is a specific in *coryza.* It has also been used as a substitute for the other iodides in *syphilis. Dose,* one to five grains (0.06–0.3 Gm.).

Rubidium bromide, RbBr, may be used as a substitute for, and in the dose of, potassium bromide, than which it is said to be better borne, especially by feeble patients.

Rubidium and Ammonium Bromide ($RbBr + 3NH_4Br$).—A white or slightly yellowish, crystalline powder, readily soluble in water. Its taste is somewhat cooling at first, and pungently saline afterwards. This salt, one hundred parts of which contain thirty-six parts of rubidium bromide and sixty-four of ammonium bromide (NH_4Br) is used as a sedative, similar in action to potassium bromide. *Dose,* from one to two drachms (3.9–7.7 Gm.) in a day.

Rubidium Sulphate. Rb_2SO_4.—This occurs as large, rhombic crystals with a taste resembling potassium sulphate. It is soluble in water and is stated to be a very active cathartic.

Rue.—*Ruta.* U. S. 1870. *Garten-Raute,* G.; *Ruda,* Sp. The U. S. P. formerly recognized the leaves of the *Ruta graveolens* L. (Fam. *Rutaceæ*). It is a low, shrubby plant, with several shrubby branching stems, which, near the base, are woody and covered with a rough bark, but in their ultimate ramifications are smooth, green, and herbaceous. The leaves are fleshy, 2- to 3-pinnatifid, the ultimate lobes or divisions being obovate-cuneate. The flowers are yellow, and disposed in a terminal branched cyme. The plant is a native of the south of Europe, locally established in pastures in the United States and cultivated in our gardens. The leaves have a strong, disagreeable odor, especially when rubbed. Their taste is bitter, hot, and acrid. When recent, and in full vigor, they have so much acrimony as to inflame and even blister the skin, if much handled; but the acrimony is diminished by drying. Their virtues depend chiefly on a volatile oil, which is contained in glandular vesicles, apparent over the whole surface of the plant. They contain, also, a peculiar acid, *rutinic acid,* $C_{27}H_{32}O_{16}$. Rutinic acid is the coloring principle of rue, and has been found in various other plants; though, like quercitrin, yielding quercetin and sugar, it has been shown to be distinct.

Rue yields a very small proportion of a yellow or greenish volatile oil (*Oleum Rutæ, U. S.,* 1880), which becomes brown with age. According to Zeller, the yield from the fresh herb is 0.28 per cent., that from the seeds about 1 per cent. The oil has the strong unpleasant odor of the plant, and an acrid taste. Kane gives its sp. gr. at 0.837, its boiling point at 230° C. "A neutral reaction. Sp. gr. about 0.880. It is soluble in an equal weight of alcohol." *U. S.,* 1880. It consists mainly of an oxidized constituent, which Strecker proved to be *methyl-nonyl-ketone,* $CH_3.CO.C_9H_{19}$. This accounts for its yielding under treatment with oxidizing agents, pelargonic acid, $C_9H_{18}O_2$. The methyl-nonyl-ketone, when pure, is a colorless liquid, fluorescing blue, boiling at 225° C., and crystallizing at about 15° C. Schimmel & Co. (*Schim. Rep.,* 1892, 31) state that pure oil of rue consists of 90 per cent. of methyl-nonyl-ketone, and solidifies even at a moderate temperature to a solid, crystalline mass, and has the sp. gr. 0.837.

According to von Soden and Henle, *Algerian oil of rue* differs from the ordinary oil in that it is chiefly composed of methyl-heptyl-ketone, with but small quantities of methyl-nonyl-ketone. Its specific gravity at 15° C. is 0.842; and it does not solidify at –15° C. (*Ph. Ztg.,* 46.) Power and Lees (*Trans. Chem. Soc.,* 1902) find in Algerian oil 80 per cent. of the two ketones, 10 per cent. of the corresponding carbinols (alcohols), pinene, l-limonene, cineol, methyl salicylate, ethyl valerate, and some free fatty acids.

Rue is said to have been used by the ancients as a condiment. In modern times it has been employed in *hysteria, worms, colic,* and atonic *amenorrhea* and *menorrhagia.* Its medicinal activity depends upon its volatile oil, which is a powerful local irritant, causing, when applied to the skin persistently, burning, redness, and vesication, and when taken internally in large doses, violent gastric pains and vomiting, great prostration, confusion of mind, convulsive twitching, and in pregnant women, abortion. It has been considerably used in Europe for the production of criminal abortion, in a number of cases with fatal results. The experiments of Prochnow (*A. I. P. T.,* 1911, xxi, 314) demonstrate, however, that it has only a feeble influence on the uterus. In a case of fatal poisoning in a man, reported by G. F. Cooper, there were vomiting, violent tormina and tenesmus, with bloody stools, great abdominal distention, with tenderness and severe strangury. (*Med. Exam.,* N. S., ix, 720.) The *dose* of the oil is from two to five minims (0.12–0.3 cc.) every two or three hours. The rue itself is sometimes given in the *dose* of from ten to thirty grains (0.65–2.0 Gm.).

Ruthenium. Ru–101.7.—A grayish black brittle metal. Sp. gr. 8.6, melting point about 2000° C. Soluble in aqua regia. This is one of the platinum group of rare metals. Several of its salts have been proposed for use in medicine or as reagents.

Ruthenium Chloride. *Ruthenium Sesquichloride.* Ru_2Cl_6.—A deliquescent, crystalline mass of a brownish-red color and soluble in water and stated to possess a high antiseptic value.

Ruthenium Red. *Ruthenium Oxychloride Ammoniated.* $Ru_2(OH)_2Cl_4.7(NH_3) + 3H_2O$.—A brownish-red powder, soluble in water. It is used as a microscopic stain and reagent for pectin, plant mucin, and gum. In bacteria staining there must be added to the *ruthenium red* a small amount of acetic acid.

Rye. *Secale cereale* L. (Fam. *Gramineæ.*) *Roggen,* G. *Leigle,* Fr. *Centeno,* Sp.—*Rye* is a tall annual cereal allied to wheat and barley. Its native country is somewhat doubtful, but is said to be found wild throughout the Mediterranean countries, extending to Central Asia. Hackel believes the species to have been derived from *Secale montanum* Guss., a wild perennial indigenous to the mountains of South Europe and Central Asia. There are two prominent varieties known as "Winter" and "Spring" rye, the difference being due to cultivation mainly. Rye is now cultivated in all temperate latitudes. The average composition of rye as a cereal may be thus stated: fat, 1.43 per cent.; starch, 61.87 per cent.; sugar (as sucrose), 4.30 per cent.; albumen (insoluble in alcohol), 9.78 per cent.; nitrogenous matter (soluble in alcohol), 5.09 per cent.; cellulose, 3.23 per cent.; mineral matter, 1.85 per cent.; moisture, 12.45 per cent. (Sadtler, *Industrial Organic Chemistry,* 3d ed., p. 169.) *Rye flour* is used, in the dry state, as an external application to *erysipelatous inflammation* and other eruptive affections, the burning and unpleasant tingling of which it tends to allay, while it absorbs the irritating secretions. In the form of mush it is an excellent laxative article of diet, and, mixed with molasses, it may be given with great advantage in *hemorrhoids* and *prolapsus ani,* connected with *constipation.*

Sabadilla. *Cevadilla.*—The dried ripe seeds of *Schoenocaulon officinale* (Schlecht.) A. Gray [*Asagræa officinalis* (Cham. and Schlecht.) Lindl.], were recognized by the Br. Pharm. of 1885. At one time cevadilla was generally believed to be derived from *Veratrum Sabadilla* Schiede. The plant grows in the Andes of Mexico and in the mountains of Guatemala and Venezuela. It is also cultivated. The fruit is a capsule having three locules in each of which there are from three to four seeds. A resemblance, existing or supposed, between this fruit and that of barley is said to have given rise to the Spanish name cevadilla, which is a diminutive of barley. The seeds are elongated, pointed at each end, flat on one side and convex on the other, somewhat curved, 5 to 8 mm. long, wrinkled, slightly winged, black or dark brown on the outside, whitish within, hard, inodorous, and of an exceedingly acrid, burning, and bitter taste. The powdered drug is sternutatory.

Cevadilla contains about 0.3 per cent. of alkaloids for account of which see under *Veratrina.*

Cevadilla is an acrid, drastic emeto-cathartic, operating occasionally with great violence, and in overdoses capable of producing fatal effects. Known in Europe as early as 1752, and formerly used to some extent as a tænicide, in *doses* of from five to twenty grains (0.32–1.3 Gm.), it was official solely as the source of veratrine. It is the principal ingredient of the *pulvis capucinorum,* sometimes used in Europe for the destruction of vermin in the hair.

Sabbatia. *American Centaury. Centaurée Américaine,* Fr. *Sabbatie,* G.—The overground plant of *Sabatia* (*Sabbatia*) *angularis* (L.) Pursh. (Fam. *Gentianaceæ*), an herb found in rich soil throughout the Eastern and Central United States and Ontario. The stems are much branched, distinctly 4-angled, and from 3 to 9 dm. high. The leaves are ovate, 5-nerved, having a heart-shaped clasping base. The flowers are rose-pink and on drying become pinkish brown. The fruit is a 2-valved capsule, dark brown and covered with a resin. It is more or less used in popular medicine as a tonic and antiperiodic. It is a simple bitter of some activity, and may very well be substituted for the foreign remedies of its class. Rodney H. True found American centaury adulterated with *Rhexia mariana* L., also known as *deer grass* or *meadow beauty.* (*A. J. P.,* 1905, 213.) John F. Huneker found in *sabbatia* a small proportion of *erythrocentaurin,* $C_{27}H_{24}O_8$, previously discovered by Méhu in *Erythræa Centaurium* Pers., of Europe.

In the southeastern United States, the *Sabbatia Elliottii* Steud., or *Quinine flower,* and in the southwestern United States the *Sabbatia campestris* Nutt. have been employed like the *S. Angularis* in the north. According to Merck the *S. Elliottii* contains a glucoside, *sabbatin,* as its active principle. Of the *S. angularis* and the *S. campestris* the whole plant is used, the *dose* being a drachm (3.9 Gm.), given in the form of fluidextract or in decoction. Of the quinine flower, the root is employed; *dose,* of the fluidextract, one fluidrachm (3.75 cc.); in intermittent fever to be repeated at short intervals.

Sabina. *U. S. VIII. Savin. Sabinæ Cacumina. Summitates* (*Herba*) *Sabinæ. Savine Tops. Sabine,* Fr. Cod. *Sadebaumspitzen. Sevenkraut,* G.—"The tops of *Juniperus Sabina* Linné (Fam. *Coniferæ*)." *U. S. VIII.* An evergreen, spreading or prostrate, rarely erect, shrub, with several varieties, from three to ten feet high, with numerous pliant branches. The leaves, which completely invest the younger branches, are numerous, small, firm, smooth, pointed, dark green, glandular in the middle, opposite, and imbricated in four rows. The fruit is a blackish-purple galbalus of globular shape, and containing three seeds. Although savin is a native of the mountains of Europe and West Asia, it grows wild in the neighborhood of the northwestern lakes of the United States.

The ends of the branches, and the leaves by which they are invested, are collected for medicinal use in the spring. They were officially described as "short, thin, subquadrangular branchlets bearing leaves which are rather dark green, in four rows, opposite, scale-like, ovate-lanceolate, more or less acute, appressed, imbricated, having on the back a shallow groove containing an oblong or roundish gland; odor peculiar, terebinthinate; taste disagreeable, resinous and bitter." *U. S. VIII.* They have a strong, heavy, disagreeable odor, and a bitter, acrid taste. These properties, which are less striking in the dried than in the recent leaves, are owing to a volatile oil.

In America the tops of *Juniperus virginiana* L., or common *red cedar,* also commonly referred to as *savin,* are sometimes substituted in commerce for savin, which they resemble closely, but from which they can be distinguished by some of their leaves being obtuse or acutish and the fruits being smaller, purplish and containing fewer seeds. In Europe savin is said to be adulterated with the tops of *J. phœnicea* L., which contain volatile oil similar to that of *J. communis* L. Such substitution is to be detected by the fact that in *J. phœnicea* the imbricated leaves occur in spirals of five, and the berries are large, shiny, and vary in color from yellow to reddish-yellow. In the mesophyll there occur large stone cells which are either single or in groups.

The proportion of volatile oil obtained from savin varies from 1 to 2.5 per cent. The *oil of savine* (*Oleum Sabinæ, U. S. VIII*) is "a colorless or yellowish liquid, having a peculiar terebinthinate odor, and a pungent, bitter, and camphoraceous taste. Specific gravity: 0.903 to 0.923 at 25° C. The oil is dextrogyrate, the angle of rotation varying between $+40°$ and $+60°$ in a 100 mm. tube, at a temperature of 25° C. Soluble in about one-half volume or more of 90 per cent. alcohol." *U. S. VIII.* According to Schimmel & Co. (*Schim. Rep.,* April, 1897), it contains pinene, $C_{10}H_{16}$, cadinene, $C_{15}H_{24}$, and an alcohol, $C_{10}H_{16}O$, *sabinol,* which is present both in the free state and as acetic ester. With iodine it becomes heated, detonates, and gives off yellow and violet-red vapors. (Flaschoff.)

Savin is highly irritant, and is supposed to have a special direction to the uterus. It has been much used in *amenorrhea* and *atonic menorrhagia,* and occasionally as a remedy for *worms.* Chapman strongly recommended it in *chronic rheumatism,* and it is employed in Germany, both internally and externally, in *chronic gout.* In overdoses it may produce dangerous gastro-intestinal inflammation, and it should therefore be used with caution. The oil of savin is a powerful local irritant, producing, when persistently applied to the skin or the mucous membrane, violent inflammation. It has been much used for the purpose of producing criminal abortion, and in a number of such cases has caused death, the symptoms being violent abdominal pain, bloody vomiting and purging, diminution or suppression of urine, disordered respiration, unconsciousness, convulsions, and fatal collapse. Although Prochnow (*A. I. P. T.*, 1911, xxi, p. 316) has found that small doses of savin have a slight stimulating effect upon the uterus, it is manifest that any abortifacient results must be due to general disturbance of the health rather than to any local action. The fluidextract which was official in the U. S. P. VIII, is rarely used internally but the stated *dose* is from five to ten minims (0.3–0.6 cc.). The *dose* of the oil of savin is from one to three minims (0.06–0.2 cc.).

Safrol. *Safrolum. U. S. VIII. Synthetic Oil of Sassafras.* $C_{10}H_{10}O_2 = 162.08$.—"The methylene ether of allyl pyrocatechol [$C_6H_3.C_3H_5.OOCH_2$) 1 : 3 : 4], found in oil of sassafras, camphor oil, and other volatile oils, purified, if necessary, by repeated chilling and crystallization." *U. S. VIII.* Safrol is found in oil of sassafras often in the proportion of 80 per cent., but commercially it is obtained from the red oil of camphor, by fractional distillation, the portion boiling at about 230° C. contains the safrol, this is cooled and the crystals separated.

Safrol appears to be widely distributed in the vegetable kingdom, probably existing in the bark of the *Mespilodaphne Sassafras* Meissn. in the *Sassafras nuts* (see *Pichurim Beans*, Part II), both of Brazil, in the bark of *Atherosperma moschatum* Labill. and in many other plants. It was officially described as "a colorless or faintly yellow liquid with a sassafras-like odor. Specific gravity: 1.098 to 1.100 at 25° C. Boiling point: about 233° C. It is optically inactive. On cooling to −20° C. or below, it solidifies to a mass of crystals, which do not melt below 11° C. Soluble in about an equal volume of strong alcohol, and in about 30 parts of 70 per cent. alcohol. Miscible in all proportions with ether and chloroform." *U. S. VIII.* Physiologically and therapeutically, safrol is equivalent to oil of sassafras. *Dose,* three to eight minims (0.2–0.5 cc.).

Sagapenum.—This gum-resin, formerly highly esteemed, but at present very rarely met with even in Eastern commerce, is the concrete juice of a Persian plant, *Ferula Persica* Willd. (Fam. *Umbelliferæ*), related to those that yield galbanum. It is in irregular masses, composed of agglutinated fragments, slightly translucent, of a brownish-yellow, olive, or reddish-yellow color externally, paler internally, brittle, of a consistence somewhat resembling that of wax, and often mixed with impurities, especially with seeds more or less entire. It has an alliaceous odor less disagreeable than that of asafetida, and a hot, nauseous, bitterish taste. According to Tschirch (*Harze und Harzbehälter,* 229), it contains 23.3 per cent. of gum; 19.2 per cent. of essential oil, containing sulphur; and 57.5 per cent. of a resin which is free from sulphur and melts at 74° to 76° C. The ether soluble resin of *sagapenum* can be separated by saponification into *umbelliferone* and *sagaresitannol,* $C_{24}H_{27}O_4.OH$. This latter yields on oxidation *oxypicric acid.* The oil is pale yellow, very fluid, lighter than water, and of a disagreeable alliaceous odor. Sagapenum was formerly used in *doses* of from ten to thirty grains (0.65–2.0 Gm.) in *amenorrhea, hysteria,* etc.; also externally in plasters as a discutient.

Sage. *Salvia. U. S. VIII. Garden Sage. Meadow Sage. True Sage. Save. Sauge,* Fr. *Folia Salviæ,* P. G. *Salbei,* G.—"The dried leaves of *Salvia officinalis* Linné (Fam. *Labiatæ*)." *U. S. VIII. Sage* is a perennial low shrub or subshrub, up to two feet high, with a quadrangular, pubescent, branching, shrubby stem, furnished with opposite, petiolate, ovate-lanceolate, crenulate, wrinkled leaves, of a grayish-green color, sometimes tinged with red or purple. The flowers are blue, variegated with white and purple, and are disposed on long terminal spikes, in distant whorls, each composed of a few flowers, and provided with ovate, acute, deciduous bracts. The calyx is tubular and striated, with two lips, of which the upper has three acute teeth, the under two. The corolla is tubular, bilabiate, ringent, with the upper lip concave, and the lower divided into three rounded lobes, of which the middle is the largest. The filaments are supported upon short pedicels, to which they are affixed transversely at the middle. The fruits are black nutlets borne in open cups.

Sage grows spontaneously in Southern Europe, and is cultivated abundantly in our gardens. There are several varieties, differing in the size and color of their flowers, but all possessing the same medicinal properties. The flowering period is in June, at which time the plant should be cut, and dried in a shady place. The leaves were officially described as "long and stoutly petiolate, the blade elliptical or ovate-oblong, 3 to 7 Cm. long, obtuse or subacute at the summit, rounded or subcordate at the base, finely crenulate, thick, grayish-green, very pubescent, especially on the under surface, conspicuously reticulate-veined; odor aromatic; taste aromatic, bitter, and somewhat astringent." *U. S. VIII.*

Within recent years sage of commerce has been adulterated with or substituted by *Spanish sage* and *Greek sage.* Spanish sage consists of the leaves of *Salvia lavandulæfolia* Vahl., a perennial herb indigenous to Mexico. Its leaves differ from those of true sage in being usually smaller, whorled on the stems and having a less distinctly crenulate margin and a much smoother surface. *Greek Sage* is the leaves of *Salvia triloba* L., a perennial herb indigenous to countries bordering the Mediterranean. It may readily be distinguished from sage by having usually broader, thicker, shorter and more woolly leaves with a less pronounced crenulate margin and by its odor which is distinct from that of true sage.

Both the leaves and the flowering tops of sage have a strong, fragrant odor, and a warm, bitterish, aromatic, somewhat astringent taste. They abound in a volatile oil, which may be obtained separate by distillation with water. Muir (*J. Chem. S.*, xxxvii, p. 678) found it to contain a terpene boiling at 156° C., another boiling at 171° C., thujone, $C_{10}H_{16}O$, a liquid boiling at from 197° to 203° C., and ordinary camphor, $C_{10}H_{16}O$. In the fresh oil the first terpene predominates. On standing, the amount of thujone increases, and then the camphor. The oil from English leaves contains also a sesquiterpene, $C_{15}H_{24}$, of the boiling point 260° C. Wallach (*Ann. Ch. Ph.*, 1889) states that the first portions contain pinene and cineol, but the greater portion consists of thujone, $C_{10}H_{16}O$ (formerly called *salviol*). Ferrous sulphate strikes a black color with infusion of sage.

By the ancients sage was highly esteemed; it is at present little used, except as a condiment, but has been given in *dyspepsia*, also for *colliquative sweats.* According to Cadéac and Meunier (*Lyons Méd.*, May, 1891,) the volatile oil of sage is a violent epileptiform convulsant, resembling in its action the oil absinthe, but less powerful.

The *dose* of the powdered leaves is from twenty to sixty grains (1.3–3.9 Gm.). *Dose,* of the infusion (one oz. in one pint of boiling water), two fluidounces (60 cc.).

Although the *Salvia officinalis* was the only species of this genus which was recognized by the U. S. P. VIII, many other species share the feeble medicinal properties of sage. *S. pratensis* L., *S. Æthiopis* L., *S. glutinosa* L., and *S. Sclarea* L., or *clarry,* have been officially recognized in Europe, but are less agreeable than is *S. officinalis* and are not much used; the leaves of *S. Sclarea* are said to be introduced into wine in order to impart to it a muscatel taste. The infusion of the *Rocky Mountain sage,* probably *S. lanceolata* Willd., is affirmed by A. Comstock (*T. G.*, 1887, 660) to be valuable as a diaphoretic in *malarial* and *rheumatic fevers,* taken in the form of hot infusion, and when cold to be distinctly tonic and astringent. The *dose* of fluidextract is half a fluidrachm (1.8 cc.).

The seeds of various sages contain enough farinaceous and mucilaginous material to make them useful as food. In the Western United States the ordinary sages of the plains are highly esteemed for fattening cattle, which eat their ripened tops freely (these sages must be distinguished from the so-called "sage brushes" of the West, which belong to the genus *Artemisia*). *Chia* is the seeds of one or more species of *salvia* largely used in Mexico and Southern Arizona by the natives as food. It is affirmed that the variety known as *Chia pinoli* is yielded by *S. columbariæ* Benth. (see *Report U. S. Geogr. Surveys, 100th Merid.*, vol. vi, 48). *S. Chia* was described in the Farmacopea Mexicana as a new species, yielding *chia,* but Mariano Báscena affirms (*La Naturaleza,* 1881) that the common chia-yielding sage of Mexico is *S. polystachya* Ort., while *Chia azul* is yielded by *S. patens* Cav. Guibourt is probably in error in ascribing chia to *S. hispanica* L. The chia seeds are used as food and for the making of mucilaginous poultices. For description of these seeds see (*A. J. P.*, May, 1882, 227–229). The European species, *Salvia verticillata* L., *S. Verbenacea* L., *S. horminum* L. and *S. viridis* L., all indigenous to Central or Southern Europe, are also noted for the mucilaginous character of their seeds, and have on this account been employed to remove foreign substances from the eye. *S. Verbenacea* is sparingly naturalized in waste places in the Middle and Southern States.

Sago. *Sagou,* Fr. *Sago,* G., It. *Sagu,* Sp.—Under this name the U. S. P. formerly recognized the starch obtained from the *sago* palms Numerous trees, inhabiting the islands and coasts of the Indian Ocean, contain a farinaceous pith from which is extracted the starch in enormous quantities. In India and the East Indies it is obtained from several palms, viz: *Metroxylon Rumphii* Mart., *M. læve* Mart., *M. Sagu* Rottboell and allied species (Fam. *Palmæ*). It has also been obtained from *Cycas revoluta* L. and other cycads.

The fruit of the *Cycas circinalis,* according to J. van Donjen, contains a poisonous glucoside, *pakoëine.* (*P. J.*, May, 1903.)

According to H. von Rosenberg (*Proc. A. Ph. A.*, xxvii, 140), pith cells of these palms consist mostly of starch when the large leaves have fallen off and the flowers are just taking their place. At this time the tree is felled, and the trunk cut into billets six or seven feet long, which are split in order to facilitate the extraction of the pith. This is obtained in the state of a coarse powder, which is mixed with water in a trough having a sieve at the end. The water, loaded with farina, passes through the sieve, and is received in convenient vessels, where it is allowed to stand till the insoluble matter has subsided. An average palm about fifteen years old will yield from 300 to 400 kg. of sago starch. It is then strained off, and the farina which is left may be dried into a kind of meal or molded into whatever shape may be desired. For the consumption of the natives it is usually formed into cakes of various sizes, which are dried, and extensively sold in the islands. The commercial "Pearl" sago is prepared by forming the meal into a paste with water, and rubbing it into grains. It is produced in the greatest abundance in the Moluccas, but of the finest quality on the eastern coast of Sumatra. The Chinese of Malacca refine it so as to give the grains a fine pearly luster. Malcolm states that it is also refined in large quantities at Singapore.

Pearl sago is that which is now generally used. It is in small grains, about the size of a pin head, hard, whitish, of a light brown color, in some instances translucent, inodorous, and with little taste. *Common sago* is in larger and browner grains, of more unequal size, of a duller aspect, and frequently mixed with more or less of a dirty looking powder.

Sago meal is imported into England from the East Indies. It is in the form of a fine amylaceous powder, of a whitish color, with a yellowish or reddish tint, and of somewhat musty odor.

Sago starch grains occur both in the altered and unaltered condition in the commercial article. They are avoid, muller-shaped or irregularly 3- or 4-sided with rounded angles; simple or 2-, 3- or 4-compound, the larger grains 30 to 60 or rarely up to 80 microns in length; the hilum circular, excentric and often radiately fissured; lamellæ excentric and concentric; polarization crosses distinct.

Common sago is insoluble in cold water; but by long boiling unites with that liquid, becoming at first soft and transparent, and ultimately forming a gelatinous solution. Pearl sago is partially dissolved by cold water, probably owing to the heat used in its preparation. Chemically considered, it is a very pure natural starch, as the nitrogenous mater rarely amounts to more than one per cent. and the ash to one-half per cent., the remainder being starch and moisture.

Potato starch is sometimes prepared so as to resemble bleached pearl sago, for which it is sold, But, when examined under the microscope, it exhibits larger granules, which are also more regularly oval or ovate, smoother, less broken, and more distinctly marked with lamellæ than are those of sago, and the hilum often cracks with two slightly diverging slits. Imitation sago is now made in the United States from various kinds of starch.

Sago is used exclusively as an easily digestible, non-irritating food. It is given in the liquid state, and in its preparation care should be taken to boil it long in water, and stir it diligently, in order that the grains may be thoroughly dissolved. Should any portion remain undissolved, it should be separated by straining. A tablespoonful to the pint of water is usually sufficient.

Salacetol. *Salicyl-acetol. Salantol.* $C_6H_4(OH)CO.OCH_2CO.CH_3$.—A synthetic product, the ester of salicylic acid and acetylcarbinol, introduced as a substitute for salol, to avoid the elimination of phenol in the system. Crystallizes out of alcohol in white or pinkish needles, fusing at 71° C., slightly soluble in cold water and alcohol, readily soluble in ether, chloroform, and petroleum benzin. It may be used when salol is indicated, in *doses* of from fifteen to forty-five grains (1.0–3.0 Gm.).

Salamander Alkaloids.—*Salmander maculosa*, and probably other newts, produce a poisonous secretion from the skin, from which Hoppe-Seyler and Zalesky separated an active body, *salamandarine*. E. S. Faust (*A. E. P. P.*, xliii) has secured crystalline salts from this body which produce in the lower animals restlessness, excited reflex activity, and convulsions ending in total paralysis. A second alkaloid, *salamandaridine*, was also separated by Faust.

Salep. *Tubera Salep*, P. G.—This name is given to the dried tuberous roots of many species of the genus *Orchis*, and other allied genera of the *Orchidaceæ*. At present the salep of European commerce is prepared chiefly in the Levant, but to some extent in Germany and other parts of Europe. The tubers are collected from wild plants growing in Asia Minor, Southwest Asia, France and Germany. They are divested of their brown outer covering, washed, boiled and dried. The German salep is said to be more translucent than the Levant.

The commercial supplies of salep are shipped chiefly from Smyrna and Constantinople and to a limited extent from Germany.

Salep is in small, oval, irregular, ovoid or oblong tubers, rarely palmate (as tubers from *Orchis maculata* and *Orchis latifolia*) hard, horny, semi-transparent, of a yellowish color, a feeble odor, and a mild insipid mucilaginous taste. It is sometimes kept in the state of powder. In composition and relation to water it is closely analogous to tragacanth, consisting of bassorin with a smaller amount of a water soluble gum and minute quantities of saline matters. It also occasionally contains a little starch. It is highly nutritive, and may be employed for the same purposes as tapioca, sago, etc. Its medieval and Oriental reputation as an aphrodisiac is unfounded. On account of its hardness, salep, in its ordinary state, is of difficult pulverization; but the difficulty is removed by macerating it in cold water until it becomes soft, and then rapidly drying it. *Royal salep*, said to be much used as a food in Afghanistan, has been identified by J. E. T. Aitchison as the product of *Allium Macleanii* Baker. (Fam. *Liliaceæ*.) (*P. J.*, Sept., 1889.)

E. Reeb stated that salep possesses, like diastase, the property of coagulating milk, which he attributes to *erythrodextrin*, but finds that this body, in distinction from diastase, will retain its coagulating property even after heating it to 100° C. (*Journ. der Pharm. v. Elsass-Lothringen*, 1912, No. 8.)

Sal-ethyl. *N. N. R.* 1924. *Ethyl-Salicylate.* $C_6H_4(OH)COOC_2H_5$.—This proprietary ester is used after the manner of, and for the same purposes as, methyl salicylate. It is a colorless volatile fluid of pleasant odor and taste. Sp. gr. 1.184 and boiling at 231.5° C. The *dose* is five to fifteen minims (0.3–1 cc.).

Saligallol. *Pyrogallol Di-salicylate.*—A resinous solid, soluble in two parts of acetone and fifteen parts of chloroform. Its solution in acetone has been used as an external application in skin diseases.

Saligenin. *N. N. R.* 1924. *Ortho-oxybenzyl alcohol*, $C_6H_4.OH.CH_2OH$, is the decomposition product of the glucoside *salicin*. Under the name of *antiarthrin*, a substance has been introduced into commerce which is said to be a combination product between *saligenin* and tannin. It readily undergoes decomposition. It has been used in chronic *rheumatism* and *gout* in doses of eight to twenty grains (0.5–1.2 Gm.) four to six times a day.

It has been recommended as a local anesthetic by Wethall and Thomas (*Jour. of Urol.*, 1922, vii, p. 329). See also under *Salicinum*, Part I.

Salimenthol.—*Samol. Salicylic Ester of Menthol*, $C_6H_4(OH)COO.C_{10}H_{19}$, is an almost colorless fluid, insoluble in water, but miscible with alcohol, ether, chloroform and fatty oils in all proportions.

It is supposed to exercise the virtues of both of its constituents and is employed in various rheumatic and painful conditions by external application with the idea that it will act as a local anodyne by virtue of its menthol radical and being absorbed will exercise the analgesic effect of salicylic acid. It may be applied in the form of a 25 per cent. ointment. It has also been administered internally in *doses* of eight to fifteen drops (0.5–1.0 Gm.), generally enclosed in capsules.

Salipyrin. *N. N. R.* 1924. *Antipyrine Salicylate. Salazolon.* $C_{11}H_{12}N_2O.C_7H_6O_3$.—Prepared by the action of salicylic acid upon antipyrine, either at 100° C. or in solution. It occurs as a white, coarsely crystalline powder, odorless, with a somewhat sweetish taste. It is readily soluble in alcohol and in benzene, and crystallizes from the former in hexagonal tables with a melting point of 91.5° C. According to Guttmann and to Kollmann (*Internat. Klin. Rundsch.*, Sept., 1890; also *M. M. W.*, Nov., 1890), it is an active antipyretic and antirheumatic, which rarely produces toxic symptoms, although an eruption resembling that caused by antipyrine has been noted. Kollmann states that it sometimes causes vomiting, and the daily *dose* should not exceed forty-five grains (3.0 Gm.), and always be less than this in the beginning, as some individuals are intolerant of it. *Salipyrin* has been used to a considerable extent in all forms of *rheumatic diseases*, in *influenza*, in various *fevers*, in *migraine*, and in the whole class of diseases in which its component constituents have been found to be useful; also locally in *coryza*. Salipyrin has been very highly praised by Beuttner as a sedative antihemorrhagic remedy, in all forms of *metrorrhagia* not dependent upon severe organic disease, in threatened *abortion*, and in *dysmenorrhea*. The usual *dose* is from seven to fifteen grains (0.45–1.0 Gm.), in capsule or tablet, repeated every three or four hours, until not over 45 grains (3 Gm.) have been taken.

Salit. *Salicylic Ester of Borneol.* $C_{10}H_{17}O.CO.C_6H_4.OH$.—It occurs as an oily fluid, insoluble in water, but readily soluble in alcohol, ether, and oils. It is incompatible with alkalies and alkaline salts.

Salit is employed for the purposes of the endermic administration of salicylic acid in *neuralgia*, and acute and chronic *rheumatic disorders*. In a few instances its application has given rise to a slight irritation of the skin. It should generally be diluted with equal portions of olive oil, and one-half to one teaspoonful of the mixture applied with friction or by painting over the infected part and covering with an impermeable dressing.

Salix. *Willow-bark. Weidewinde,* G. *Ecorce de Saule,* Fr.—Most of the species of the large genus *Salix* are possessed of similar medicinal properties. (For elaborate study of various willow barks see *Wellcome Chemical Research Laboratory Report,* No. 39.) *S. fragilis* L. or *Crack Willow,* which has been introduced into this country from Europe, is said by Sir James Smith to be the most valuable species. *S. purpurea* L., the *Basket Willow,* a European species, is stated by Lindley to be the most bitter, and *S. pentandra* L., or *Laurel-leaf Willow,* is preferred by Nees von Esenbeck. Many native species are in all probability equally active with the foreign.

Salix alba L., the species formerly recognized by the U. S. Pharmacopœia (1880), is the common European or *white willow.* It has sparingly escaped from cultivation, growing from New Brunswick and Ontario southward to Pennsylvania. It is a large tree with a rough grayish bark, the twigs being brittle at the base, and in this respect somewhat resembling *S. fragilis.* The leaves are pubescent on both surfaces and finely serrulate. It hybridizes with other species of *Salix.* It flowers in April and May, and the bark is easily separable throughout the summer. That obtained from the branches rolls up when dried into the form of a quill, from 0.5 to 1 mm. thick, has a brown, more or less finely warty periderm, is flexible, fibrous, and of difficult pulverization. The inner surface is brownish-white, and smooth, separating in thin layers. Willow bark has a feebly aromatic odor and a peculiar bitter astringent taste. It yields its active properties to water, with which it forms a reddish-brown decoction. Pelletier and Caventou found among its ingredients, tannin, resin, a bitter yellow coloring matter, a green fatty matter, gum, wax, lignin, and an organic acid combined with magnesia. The proportion of tannin is so considerable that the bark has been used for tanning leather. The characteristic constituent of all species of willow, however, is *salicin.* (See *Salicinum.*) Robert W. Beck (*A. J. P.*, 1891, 581) has determined the relative percentages of salicin and tannin as follows:

	Salicin.	Tannin.
Leaves of *S. lucida* Muhl	0.30 per cent.	6.48 per cent.
Bark of *S. lucida* Muhl	1.09 " "	3.58 " "
Bark of *S. alba* L............	0.56 " "	4.26 " "
Bark of *S. nigra* Marsh......	0.73 " "	3.29 " "

Jowett and Potter made an examination of thirty-three samples of willow and poplar, and found in but one (*Salix discolor* Muhl.) the related glucoside *salinigrin,* which Jowett had previously discovered in an unknown sample of willow bark. This compound has the formula $C_{13}H_{16}O_7$, and on hydrolysis yields glucose and meta-hydroxybenzaldehyde. (*Wellcome Chem. Research Laboratory Report,* No. 28.)

The green aments or floral buds have been recommended by certain eclectic practitioners as a sexual depressant, useful in *spermatorrhea,* and other forms of *sexual excitement,* and in the nervous disturbances of the menstrual period. From twenty to thirty minims (1.3–1.8 cc.) of the fluidextract are to be given four times a day.

Salocoll. *Phenocoll Salicylate.* $C_6H_4(OC_2H_5)$-$NH.COCH_2.NH_2C_7H_6O_3$.—This substance forms fine white crystalline needles of sweet taste and soluble in hot water. It combines the properties of phenocoll and salicylic acid, being used in *rheumatic affections* in *doses* of nine to fifteen grains (0.6–1.0 Gm.) several times daily.

Salophen. *Phenetsal. N. N. R.* 1924.—*Acetylparaminophenol Salicylate,*
$C_6H_4\left\{\begin{matrix}OH\\COOC_6H_4.NH(C_2H_3O)\end{matrix}\right.$, is formed by the combination of salicylic acid with acetylparamidophenol, and contains 51 per cent. of salicylic acid. It forms small white crystalline scales melting at 187° C., and is almost insoluble in cold water; moderately soluble in alcohol and ether. In warm alkaline solution it undergoes decomposition into salicylic acid and acetylparamidophenol. According to Siebel (*Th. M.*, Jan., 1892), this reaction takes place in the intestines. It has been used by various clinicians in all forms of *rheumatic diseases* and is undoubtedly effective, though less certain in its action than are the simple salicylates. It is also used to some extent as an analgesic in the pains of nervous diseases and as an intestinal antiseptic. Locally it is sometimes applied to relieve *itching* in various *skin diseases.*

Dose, ten to fifteen grains (0.65–1.0 Gm.); not more than seventy-five grains should be given daily.

Saloquinine. *Salochinin.* $C_6H_4.OH.CO.O.C_{20}$-$H_{23}N_2O$.—This is the quinine ester of salicylic acid and occurs in colorless crystals, insoluble in water, freely soluble in alcohol and ether, fusing at 130° C. Acids or strongly acid salts decompose it, splitting it up into its constituents. It is tasteless and is said not to disturb the digestion or to cause tinnitus aurium, although it is very slowly absorbed. It is said to contain 70 per cent. of quinine, and has been used successfully as an antiperiodic, but is reputed to be of special value in the treatment of malarial and other *neuralgias,* also in fulgurant pains, and has also been highly commended in *typhoid* and other *fevers* as an antipyretic. If in a fever it be administered directly after the cold bath, it begins to powerfully impress the system about the time the effect of the immersion is going off. It may be given in the single *dose* of from fifteen to thirty grains (1–2 Gm.), repeated within twenty-four hours in bad cases of *rheumatic affections.*

Saloquinine Salicylate. *Rheumatin.* C_6H_4.-$OH.CO.O(C_{20}H_{23}ON_2).C_6H_4OH.COOH$.—A white, tasteless powder. Slightly soluble in water, readily in chloroform and ether. It is used in *neuralgia, rheumatism,* etc., in fifteen-grain (1 Gm.) *doses.*

Samandera Bark.—This is the inner bark of *Samandera indica* Gärtn., a tree belonging to the *Simarubaceæ,* growing in Ceylon and the East Indies. It is intensely bitter, and probably contains quassin. For further particulars, see ***P. J.***, 1872, 541.

Sandarac. *Sandaraca. Gum Juniper.*—A resinous substance obtained from the *Callitris quadrivalvis* Vent. (*Thuja articulata* Vahl.), an evergreen tree (Fam. *Pinaceæ*) growing in the mountains of northwestern Africa.

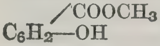
Sandarac is a resinous exudation which occurs as a natural secretion in schizo-lysigenous reservoirs in the bark. It exudes naturally, but an increase in yield is obtained by cutting through the bark. The exuding resin hardens and is collected. It is sent by the natives to Mogador, Casablanca and Nazagan, from which points it is shipped to London, Trieste, Marseilles and Hamburg. It occurs in small, irregular, roundish oblong grains or tears, of a pale yellow color, and with a dusty surface, more or less transparent, dry and brittle, breaking into powder under the teeth, of a faint, agreeable odor increased by warmth, and of a resinous, slightly acrid taste. It melts with heat, diffusing a strong balsamic odor, and easily inflames. It is almost entirely soluble in ordinary alcohol, and entirely so in that liquid when anhydrous, and in ether. Heated oil of turpentine also dissolves the greater part of it, but very slowly. According to Unverdorben, it consists of three resins, varying in their relations to alcohol, ether, and oil of turpentine. The *sandaracin* of Geise, which remains after sandarac has been exposed to the action of ordinary alcohol, is a mixture of two of these resins. Tschirch (*Harze und Harzbehälter*) has isolated and described an acid, *sandaracolic acid,* $C_{44}H_{64}O_4(OH)COOH$, making up 85 per cent. of the natural resin and *callitrolic acid,* $C_{64}H_{82}O_5(OH)COOH$, of which 10 per cent. is present. In Australia and Tasmania *Callitris verrucosa* R. Brown trees grow in vast numbers, and produce a sandarac which is almost colorless, having highly refractive power, and a pleasant aromatic odor, becoming dark by age, and sometimes assuming a superficial mealiness. This *Australian sandarac* softens easily, but does not melt in boiling water, is gritty to the touch, and can scarcely be distinguished from the African drug. (*P. J.*, Jan., 1890.) It is claimed by Greenish (*M. M.*, 1920, p. 471) to contain more volatile oil and more inactive pimaric acid than the African article. For an elaborate description of Australian sandarac, see also *A. J. P.*, 1896, 215.

Sandarac was formerly used internally, and as an ingredient of various ointments and plasters. At present it is used chiefly as a varnish and as incense; its powder, termed *pounce,* is rubbed upon paper to prevent ink from spreading after letters have been scratched out. It is sometimes adulterated with mastic, rosin and dammar. A false sandarac has been described by R. Haneke. It resembled the real article, being lemon-yellow in color, transparent, and the tears elongated and rounded at the tips. When chewed it broke into fine powder and stuck to the teeth, while it softened on the water bath and flowed together into a resinous mass. Examination showed it to consist largely of colophony. (*O. Z.*, liv.)

Sanicula. *Sanicula marilandica* L. *Sanicle,* Fr. *Sanikel,* G. (Fam. *Umbelliferæ*).—The root of this indigenous perennial herb is popularly known in some parts of the country by the name of *black snake-root.* It is fibrous and of an aromatic taste, and, according to C. I. Houck (*A. J. P.*, vol. xiv, 463), contains a volatile oil and a resin. It has been used in *intermittent fever,* and also in *chorea* by Zabriskie. *Dose* of powder to children eight years old, half a drachm (2.0 Gm.) three times a day.

Sanitas.—This name is given to a fluid prepared by forcing air through a mixture of Russian turpentine oil and water, heated at 60° C. for a period ranging from 4 to 12 days. Among the various oxidation products is a soluble camphor ($C_{10}H_{16}O_3$), remaining dissolved in the oil, also a peroxide. It is used as an application for *burns, sores,* and *skin diseases,* and as a general disinfectant for sick rooms.

Sanoform. *Di-iodo-methyl Salicylate.*



$$C_6H_2\begin{matrix}\diagup COOCH_3\\ —OH\\ \diagdown I_2\end{matrix}$$

.—This substance is obtained by the action of iodine on methyl salicylate. It is a crystalline, colorless, odorless, and tasteless powder, permanent in the light and air, and melting at 110° C., but may be heated up to 200° C. without decomposing. It is soluble in 200 parts of cold or 10 parts of hot alcohol, and readily in ether, chloroform, benzene, and carbon disulphide, but almost insoluble in water or glycerin. It contains 62.7 per cent. of iodine. It forms, with caustic alkalies, salts which are sparingly soluble in water.

Sanoform, first introduced as a substitute for iodoform by A. Arnheim, would appear to afford an efficient antiseptic dressing for wounds. As it remains unchanged at high temperatures, it is readily sterilized, while its odorlessness gives it a great advantage over iodoform. Its absorption is extremely slow, as it does not appear in the urine after having been administered hypodermically until twenty-four hours have elapsed, and does not entirely disappear until after fourteen days. It is seemingly, therefore, less poisonous than iodoform. It may be used as a dusting powder or in the manufacture of a 10 per cent. gauze which can be sterilized by heating; or a 1 per cent. solution in collodion, or a 10 per cent. ointment may be employed. It has been employed with satisfaction in ophthalmic surgery by Radziejewski and by Jacobsohn.

Santolina.—A composite plant, commonly called *Holy herb, Heiligenpflanzen, Cypress herb, Cypressenkraut* (*Santolina Chamæcyparissus* L.), is stated to have long been used popularly against the *round worm* in Scotland. Maben (*P. J.*, xvi, 301) found in it a volatile oil and a considerable percentage of resin, with a bitter principle, which he believed to be an alkaloid and the active principle of the drug. The decoction of the plant may be made by boiling half an ounce in a pint of water for half an hour, straining and making up to a pint. It is given in *doses* of five fluidounces (150 cc.) to adults and half that quantity to children, repeated for four mornings, and then followed by a brisk cathartic.

Santalol compounds.—There have been put upon the market a number of proprietary derivatives of oil of sandalwood. These are used like the oil itself as urinary antiseptics, especially in *urethritis.* The advantage claimed for these compounds over the oil is generally that they are less irritating to the stomach.

Santalol Carbonate. Santalyl Carbonate.—There are on the market two preparations claiming to be carbonic acid esters of santalol. These are known under the trade names of *Blenal* and *Carbosant.* They each occur as yellowish, oily liquid, almost tasteless and odorless, representing 94 per cent. of santalol. They may be given in *doses* of fifteen to twenty minims (1 to 1.3 cc.).

Santalol Camphorate. Camphosal. Camphoral. Santalyl Camphorate.—This is stated to be the neutral camphoric ester of santalol. It is a yellowish brown oil with a faintly aromatic odor and bitter taste. *Dose,* five to fifteen minims (0.3–1 cc.).

Santalol Salicylate. Santalyl Salicylate. Santyl. N. N. R. 1924.—A yellowish oil with a faint balsamic odor and taste and a specific gravity of 1.07. It yields on saponification approximately 40 per cent. of salicylic acid and 60 per cent. of santalol. Besides its use as a urinary antiseptic in *gonorrhea* and *cystitis,* Menier (*B. K. W.,* 1907) has found it of service as a local remedy in *ozena.* The *dose* is fifteen to twenty-five minims (1 to 1.5 cc.).

Thyresol.—This is said to be the methyl ether of santalol. It occurs as a colorless liquid with a slight sandalwood odor freely soluble in alcohol or ether. According to Knauth (*D. M. W.,* 1909) it does not liberate santalol in the body but appears in the urine as a glycuronic compound. He, however, finds it a useful remedy in *urethritis. Dose,* five to ten grains (0.3 to 0.6 Gm.).

Santalol Formaldehyde.—This combination of formic aldehyde with oil of sandalwood and some inorganic acid is a balsamic yellow fluid which, in the presence of water, is asserted to break up into its components.

Santalol Allophanate.—The allophanic ester (see *Allophanic Acid*) of santalyl is upon the market under the trade name of *allosan.* It occurs as colorless tasteless crystals insoluble in water and representing about 72 per cent. of santalol. The usual *dose* is fifteen grains (1 Gm.).

Sapindus.—Various tropical plants belonging to this genus of the *Sapindaceæ* contain saponin, and are largely used for cleaning purposes. The berries are commonly used, being called "*Soap berries.*" Thus, in India are employed the pulp of the fruit of *Sapindus Mukorossi* Gaertn., the capsules of *S. trifoliatus* L., and in South America the oil and seed vessels of *S. Saponaria* L. The fruits of *S. rarak* DC., according to O. May, contain saponin and a fixed oil. (*A. Pharm.,* 1906, 25.) Asahina and Shimidzu (*J. P. C.,* 1916, xiv, 188) extracted from the pericarp of *S. mukurosi* a pure saponin exhibiting an optical rotation of + 13.28° at 20° C. and hydrolyzing to form sapogenin and arabinose.

Sapium. *Sapium sebiferum* (L.) Roxb. *Chinese Tallow Tree. Vegetable Tallow. Tankawang Fat.*—This is a species of the family *Euphorbiaceæ,* cultivated in the Chinese provinces of Kiangse, Kiang-sou, and Chih-kiang for the sake of the solid fixed oil which covers the seeds. The "tallow" occurs in hard, brittle, opaque, white masses of about eighty pounds' weight. It consists chiefly of palmitin with a little stearin and is said to be nearly pure stearin. The oil is largely used for lighting purposes. The remnants of the nut are employed as fuel and as manure. (See *P. J.,* 1883, 401, and 1887, 901.)

Saponaria. *Saponaria officinalis* L. *Soapwort. Bouncing Bet. Fuller's Herb. Sheep Weed. Saponaire. Savonnière,* Fr. *Seifenwurzel,* G. (Fam. *Caryophyllaceæ.*)—A perennial herb, having oblong-lanceolate, 3-nerved leaves and panicled cymes of pink or nearly white flowers. Though indigenous to Europe, it is common along roadsides and waste places in the United States. The rhizome and roots are employed. The rhizomes are cylindrical, from 5 to 12 cm. long and 5 to 12 mm. thick, outer surface being reddish-brown. The fracture is short and even. They are inodorous, and of a taste at first bitterish and slightly sweetish, afterwards somewhat pungent, continuing long, and leaving a slight sense of numbness on the tongue. They impart to water the property of forming a lather when agitated, like a solution of soap, whence the name of the plant was derived. This property, as well as the medicinal virtues of the plant, resides in *saponin,* $C_{32}H_{54}O_{18}$. This principle constitutes, according to Bucholz, its discoverer, 34 per cent. of the dried root which contains also a considerable quantity of gum and a little bassorin, resin, and altered extractive, besides lignin and water.

Saponin.—The term saponin is applied to a number of glucosidal principles which have in common the property of foaming when shaken with water and of forming emulsions with fixed oils and resinous substances and of preventing the deposition of finely divided precipitates.

They are homologous substances having the general formula $C_nH_{2n-8}O_{10}$. They vary considerably in physiological action, the more powerful ones being called *sapotoxins.* They are colloids and not dialysable.

They usually have a biting acrid taste and are powerfully sternutatory.

The saponins can be separated by several methods, the earliest suggested being that of Gehlen who dissolved them out of the crude drug with boiling alcohol from which on cooling they spontaneously separate or may be precipitated by ether. Some of them, however, are soluble in cold alcohol and therefore not recoverable by this method. A second method is that of Tromsdorf who precipitated the saponin from either a decoction or a hot alcoholic extract, first with neutral lead acetate, which precipitates in an acid saponin, and the filtrate is then treated with basic lead acetate which precipitates the neutral saponins. A third method depends upon their precipitation with saturated solution of caustic baryta. By this method it is probable that there is some change in the chemical composition of the molecule. The fourth method, which is useful for some of them, is that suggested by Kobert of salting out with ammonium sulphate.

The saponins are mostly neutral in reaction although there is a small group which are acid. Both the acid and the neutral saponins, however, will form salt-like combinations with barium and other bases. On heating with diluted mineral acids they are decomposed, yielding some kind of sugar. When heated with caustic alkalies a fatty acid complex is separated. They are therefore classed as glucosides. (See Kobert, *Bio-Chemisches Hand lexikon,* 1912, vii.)

The saponins are widely distributed through the vegetable kingdom. Among the plants, considered elsewhere in this work, which yield saponin are quillaia, dioscorea, guaiacum, helonias, aesculus, senega, sarsaparilla, ginseng, cainca, saponaria, digitalis, etc.

Saponin has been found in many other plants, among them some species of *Silene, Dianthus,* and *Lychnis,* in *Vaccaria vulgaris* Host., and in *Agrostemma Githago* L., all belonging to the Fam. *Caryophyllaceæ.* Serious poisonings by the mixture of the seeds of *Agrostemma Githago* with wheat have been reported. (*D. M. W.,* 1903.) According to Augustine Henry, there are at least eleven species of trees whose products are used in China for washing purposes and probably contain saponin, which is also found to the extent of 10 per cent. in the seeds of the Chinese tea oil tree, and is left in such large proportion in the refuse after the extraction of the oil that the "tea seed cake" is used as a fish poison. (*Am. Drug.*, 1896.) In California the *Indian Soap Root*, *Chlorogallum pomeridianum* (Ker.) Kunth., is much used for washing clothes; it probably contains saponin.

Yucca filimentosa L., familiarly known as *Adam's needle* or *Spanish bayonet*, a liliaceous Mexican plant, has long been used by the Indians as a cleansing agent and contains a considerable amount of a special saponin. It has become a plant of some commercial importance in Kansas under the colloquial name of *soap weed.* (See *D. C.*, 1917, lxi, 42.)

The saponins have been employed in beverages to give a frothy or foaming effect. The detection of small amounts is very difficult. One method that has been suggested is to test the hemolytic effect of the separated froth.

Many of the saponins are highly poisonous and are therefore known as *sapotoxins.* The toxic effects appear to be due to their affinity for cholesterin and perhaps also lecithin. By virtue of this combination with these important lipoid bodies they are irritant to mucous membranes and when introduced into the circulation destroy the red blood cells and exercise potent effects upon the central nervous system. The variability in their toxic powers may be gauged by the fact that diocin, when mixed with blood, in as dilute solution as 1 in 400,000, will cause hemolysis while chamaelirin (from Helonias) requires a concentration of 1 in 700. Most of the toxic saponins are unable to pass through the intestinal mucous membranes and when taken by the mouth cause only local irritation of the alimentary canal; agrostemma is a noteworthy exception to this rule.

When introduced into the circulation in moderately toxic doses the most obvious symptoms produced by the sapotoxins, are usually on behalf of the nervous system; convulsions followed by motor weakness, and even complete paralysis. Accompanying these nervous symptoms there is often weakness of the heart and evidence of irritation of the serous membranes and eliminating organs. After larger quantities, there is, besides the nervous manifestations, marked failure of the circulation, and vomiting and purging—the ejecta often being bloody. Death is usually due to respiratory failure, but may occur after some days of general exhaustion. When locally applied sapotoxins destroy the contractility of the muscles and the conductivity of the nerves. For studies of the physiological effects of saponins see Ransom (*D. M. W.*, 1901, xxvii, p. 194), Brandl (*A. E. P. P.*, 1905, liv, p. 245 and 1908, lix, p. 299), Yagi (*A. E. P. P.*, 1911, lxiv, p. 141) and Kobert (*Biochem. Handlex*, 1914, vol. vii).

Sarcocolla. *Sarcocolle*, Fr. *Fleischleimgummi*, *Fischleimgummi*, G.—This peculiar gum was formerly thought to be an exudate of the *Penœa fulcata* L. (*Penaceæ*), a small shrub growing in Cape of Good Hope, but according to Tschirch (*Schweiz. Apoth. Zeit.*, 1920, lviii, 113) is a secretion of the stem of the *Astragalus sarcacolla* (*Leguminosæ*) a native of Persia. *Sarcocolla* occurs in the form of small, roundish, irregular grains, somewhat spongy, sometimes agglutinated in masses, at times admixed with fine hairs, friable, opaque or semi-transparent, of a yellowish or brownish-red color, inodorous unless heated, when they have an agreeable odor, and of a peculiar, bitter sweetish, and acrid taste. Sarcocolla, according to Pelletier, consists of 65.3 per cent. of a peculiar substance, considered by Thomson as holding an intermediate place between gum and sugar, and called *sarcocollin*, $C_{13}H_{23}O_6$, 4.6 of gum, 3.3 of a gelatinous matter having some analogy with bassorin, and 26.8 of lignin, etc. It is said to be purgative, but at the same time to produce serious inconvenience by its acrid properties. The Arabian physicians used it internally, and by the ancients it was employed as an external application to wounds and ulcers, under the idea that it possessed the property of agglutinating the flesh, whence its name.

Sarracenia. *Side-saddle Plant. Pitcher Plant. Huntsman's Cup. Water Cup. Sarracenie*, Fr., G. —This is a genus of carnivorous plants belonging to the *Sarraceniaceæ* which includes 7 species indigenous to swamps and savannas of the eastern half of North America. According to E. P. Porcher, the roots of *Sarracenia flava* L., and *S. variolaris* Michx., were at one time used in the southern United States in *dyspepsia.* Sheppard found them to contain lignin, coloring matter, resin, an acid salt of lime, and probably an alkaloid. Stan Martin asserts that he has found in the root—(1) an alkaloid which he proposes to name *sarracenine*, a resin, and a yellow coloring principle. (*Ann. Thér.*, 1866, 73.) E. Schmidt, however, found no alkaloid but discovered *sarracenic acid.* (*A. J. P.*, 1872, 213.) *Dose*, of tincture (two ounces in one pint), a fluidrachm (3.75 cc.); of fluidextract, from ten to twenty minims (0.6–1.3 cc.).

Sassy Bark. *Nkasa. Doom Bark. Casca Bark. Mancona Bark. Saucy Bark. Ecorce de Mançoine*, Fr. *Manconarinde*, G.—This bark is interesting chiefly from its employment by the natives of Western Africa as an ordeal in their trials for witchcraft or sorcery. (For details, see *P. J.*, lxv, 2.) It is obtained from *Erythrophleum guineense* Don, which is a large tree with spreading branches, doubly pinnate leaves, flowers in spike-like racemes, and leguminous fruit. The bark, which is collected from the trunk and branches, occurs in flat or transversely curved pieces, externally of a dull gray, grayish-black or reddish-brown (very old bark) color and marked by reddish-brown warts or circular whitish spots, the old bark being irregularly ridged; fracture hard and granular; inner surface dull black or reddish-brown; odor indistinct; taste astringent and slightly bitter. A comprehensive description of *sassy bark* is given in the *Commentar zur oesterreichischen Pharmacopœia*, 1890, by Vogl; and in the *Résumé de la Matière Médicale et Toxicologique Coloniale*, by Corre and Lejuanne, the plant, fruit, seeds, etc., are carefully illustrated. Gallois and Hardy obtained the poisonous principle *erythrophleine.* This alkaloid is a colorless, crystalline solid, soluble in water, acetic ether, alcohol, and amyl alcohol, insoluble in chloroform, benzin, and ether. In contact with sulphuric acid and black manganese oxide, a violet color (less intense than that produced with strychnine) is developed. Harnack and Zabrocki (*A. E. P. P.*, xv, 404) also prepared *erythrophleine*, $C_{28}H_{43}O_7N$, and by the action of hydrochloric acid upon it obtained an acid they call *erythrophleic acid*, and a volatile alkaloid they call *mançonine.* The bark yields its virtues to water. Power and Salway examined sassy bark in 1912 and confirmed the presence of erythrophleine as described by Harnack. (*A. J. P.*, 1912, 337.)

The physiological action of erythrophleine has been studied by various observers, especially by Harnack and Zabrocki, and Lauder Brunton, with results which are fairly concordant. Erythrophleine exercises a digitalis-like action on the circulation causing a slow, strong pulse, with a rise in the arterial pressure. These changes are certainly in great part due to the direct action upon the heart, but are also seemingly in part produced by a stimulating influence upon the muscle fibers or nerves in the walls of the arterioles. Purging was also noted as the result of an increased peristalsis, thought to be due to the local action of the poison. Vomiting is believed by Lauder Brunton to be the result of an influence upon the nerve centers, because it occurs when the alkaloid is given hypodermically. In fatal poisoning in the lower animals, convulsions are pronounced, and the respiration is also markedly affected. In 1888 Lewin asserted erythropleine to be a powerful local anesthetic, whose action is more pronounced than that of cocaine. His paper gave rise to an extraordinary controversy, the outcome of which appears to be that, although the alkaloid is possessed of moderate anesthetic powers, it is for various reasons practically not useful. (See *U. S. D.*, 17th edition, p. 1739.) A 50 per cent. solution in eugenol has been used under the name of *throphleol* to devitalize dental pulp.

Germain Sée asserts (*Méd. Mod.*, Dec., 1891) that, although sassy bark does not act well upon the heart, it gives great relief in *dyspnea*, the number of respirations being lessened and the inspirations being extraordinarily increased in depth. He gave of the alkaloid from one-fortieth to one-thirtieth of a grain (0.0016–0.002 Gm.); of the extract, from one-fourth to one-third of a grain (0.016–0.021 Gm.).

Satureja. *Satureia hortensis* L. *Summer Savory; S. Montana* L. *Winter Savory. Sarriette,* Fr. *Bohnenkraut,* G.—Annual labiate plants resembling thyme in odor and flavor, growing spontaneously in the south of Europe, cultivated in our gardens as culinary herbs, and sparingly naturalized from New Brunswick to Michigan and southward.

Saururus. *Saururus cernuus* L. *Lizard's Tail.* (Fam. *Saururaceæ.*)—D. L. Phares, of Newtonia, Miss., considered this indigenous swamp plant of the eastern and central United States useful in irritation of the kidneys, bladder, prostate, and urinary passages generally. The *dose* of the strong infusion was, with the plant either fresh or dried, from one to four fluidounces (30–120 cc.) every fifteen or thirty minutes, or three or four times a day. (*A. J. P.*, 1867, 468.)

Saxifraga. *Saxifrage. Rockfoil.* (Fam. *Saxifragaceæ.*)—Garreau and Machelast have isolated from *S. crassifolia* L. and other species of this genus a crystallizable bitter substance, *bergenin.* It is obtained by boiling the stems of the plants with absolute alcohol, after the tannin has been removed by ether. It crystallizes in alcohol, has a bitter taste, melts at 140° C., and is soluble in 167 parts of 90 per cent. alcohol and in 830 parts of water. Its formula is given as $C_6H_3O_3.H_2O$. Bergenin is asserted to be intermediate in its action between salicylic acid and quinine. (*A. Pharm.*, 1881, 293.) The rhizome of *Saxifraga ligulata* Bell, which is used in India in *dysentery*, has been found by David Hooper to contain about 16 per cent. of gallic and tannic acids, but no other active principles. (*P. J.*, Aug., 1888.)

Scarlet Red. *N. N. R.* 1924. *Amido-azotoluol-azo-β-naphthol. Biebreich scarlet. Rubrum Scarlatinum.* $CH_3C_6H_4.N{:}NC_6H_3(CH_3)N{:}N.C_{10}H_5.OH$.—A compound of betanaphthol and diazotized amido-azo-ortho-toluol.

It is a dark brownish-red powder, nearly insoluble in water, slightly soluble in benzene and acetone and easily soluble in chloroform, oils, fats and phenols. It is slightly soluble in cold alcohol, more soluble in hot alcohol, more readily soluble in petrolatum and paraffin. It softens at 175° C., melts between 181° and 188° and decomposes at 260° C. The saturated aqueous solution is of a clean scarlet red color which has a bluish tinge upon dilution or in thin layers. In 1906 Fisher (*M. M. W.*, 1906, liii, 2041) discovered that the dye stuff known as scarlet red had the power of greatly stimulating the growth of epithelial cells. This observation was confirmed by Helmholz (*J. H. H. B.*, 1907, xviii, 365), and in 1908 Von Schmieden (*Cb. C.*, 1908, xxxv, 153) applied it practically for the purpose of stimulating epithelial growths in various surgical conditions, as *chronic ulcers, unhealthy granulations,* and the like. Since then it has been employed by a number of surgeons to stimulate the formation of skin not only in these conditions, but in *bed sores,* in unhealed *ulcers,* following extensive injuries or *burns,* and to promote skin formation after operations. It is usually applied in the form of an ointment containing from 4 to 8 per cent. of the curative agent. When the ulcer is very large it is recommended that the salve should be applied around the edges rather than over the whole surface of the denuded area. It has also been employed by Wolfrum and Cards (*M. M. W.*, 1909, p. 242) in the treatment of *corneal ulcers* after the loss of cornea whether due to injury or ulceration and by Rabaudi (*S. M.*, 1909, p. 344) in *sore nipples* and *erosions of the uterus.*

When the wound is suppurating profusely, scarlet red is of little value. It should be reserved for clean, dry ulcers which show little tendency to heal. It may be applied either in the form of the eight per cent. ointment or as a powder diluted with boric acid. It is not an entirely harmless remedy, for Lyle (*N. Y. M. R.*, Nov. 16, 1912) has reported a case of serious poisoning, characterized by nausea and vomiting, epigastric pain with fever following the application of scarlet red over extensive ulcerated surfaces. Irritation of the kidney has also been attributed to its use.

The success which followed the use of scarlet red has led to the introduction of a number of related substances for similar use. Hayward (*M. M. W.*, 1909, p. 1836) from his experiments concluded that *ortho-amido-azotoluol,* a substance closely allied to scarlet red, was even more efficacious than scarlet red. Amido-azotoluol has the chemical formula $CH_3C_6H_4N.NC_6H_3(CH_3)(NH_2)$. Amido-azotoluol forms red crystals or a reddish-brown powder melting at 100° C. It is insoluble in water but readily soluble in alcohol, chloroform and ether. It is also soluble in fatty oils. Curbski (*Cb. Chir.*, 1910) has reported a case of poisoning from the use of an ointment of this in which the symptoms resemble those of aniline poisoning. According to Curschmann (*Th. M.*, 1911, p. 717) the acetylization of amido-azotoluol diminishes its toxicity and does not affect its therapeutic value. Preparations of this type are on the market under the names of *azodermin* and *epithermol.*

Diacetyl-amido-azotoluol has been marketed under two proprietary names—*pellidol* and *dimazon.* Similar therapeutic properties are claimed for sodium dimethylaminoazobenzene-*m*-sulphonate, which is sold under the name of *azophen. Azodolen* is a mixture of equal parts of pellidol with an iodol compound called *iodolen.*

Schinus. *Schinus Molle* L. *Peruvian Mastic-Tree. California Pepper-Tree.* (Fam. *Anacardiaceæ.*)—The *pepper tree* of Peru yields a drupe the size of a pea, having a flavor similar to a mixture of pepper and fennel. It has been introduced as a shade tree in Southern California. (*A. J. P.*, 1896, 215.) The leaves contain a volatile oil which is readily discharged, as after a rain when the air is filled with fragrance. Schimmel & Co. examined the volatile oil distilled from the berries; it had the sp. gr. 0.850, the odor of phellandrene, and was soluble in alcohol. (*Ph. Rev.*, 1897, 114.) It has been used in *gonorrhea* as a substitute for cubeb. The leaves, bark, and gum resin have also been employed medicinally. (See *A. J. P.*, 1890; *P. J.*, 1887.)

Scolopendrium. *Scolopendrium vulgare* Smith. *Scolopendrium Scolopodendrium* (L.) Karst. *Asplenium Scolopendrium* L. *Phyllitis Scolopendrium* (L.) Newman. *Hart's Tongue.* (Fam. *Polypodiaceæ*).—The fronds of this fern, which is indigenous in Europe and Asia, have a sweetish, mucilaginous, and slightly astringent taste, and, when rubbed, a disagreeable oily odor. They were used as a deobstruent in visceral affections, as an astringent in *hemorrhages* and fluxes, and as a demulcent in pectoral complaints.

Scopola. *Scopolia. Belladonna Scopola. Scopola Belladonna. Japanese Belladonna* (incorrectly).—"The dried rhizome of *Scopola carniolica* Jacquin (Fam. *Solanaceæ*), yielding, when assayed as directed below, not less than 0.5 per cent. of its alkaloids." *U. S. VIII.* The genus *Scopola* is the connecting link between *Atropa* and *Hyoscyamus*, resembling *Atropa* in leaf and flower and in the microscopical character of its rhizome, but differing in that its fruit is not a berry but is a pyxis, so resembling that of Hyoscyamus. For description of drug and its histological study, see Kraemer, *A. J. P.*, 1908, p. 459. The Japanese plant, *S. japonica* Maxim., is so closely allied to *S. carniolica* that its specific distinction is very doubtful; it has been separated upon the characters of the style being curved, the calyx-teeth unequal and the leaves less obovate and having much longer petioles than *S. carniolica;* but Holmes has shown that the curved style occurs in *S. carniolica. S. carniolica* is a common plant in Bavaria, Austro-Hungary, and Southwestern Russia, usually in the hilly districts, where it grows in damp, stony places. Its general appearance is that of the belladonna, but it is much shorter, rarely growing above a foot in height, has thinner leaves, and is especially distinguished by its fruit being a transversely dehiscent capsule (pyxis), and by the presence of a distinct rhizome.

The rhizome was officially described as "of horizontal growth, more or less curved and shortly and sharply flexuous, cylindraceous and somewhat flattened vertically, occurring mostly in pieces from 2.5 to 7.5 Cm. long and 0.8 to 1.6 Cm. broad, often split before drying; upper surface marked with closely set, large, cup-shaped stem scars, margins irregularly contracted; externally varying from yellowish-brown to dark brownish-gray, finely and irregularly wrinkled longitudinally, obscurely annulate and more or less nodular-roughened; fracture short and sharp, exhibiting a yellowish-white bark, its corky layer dark brown, or pale brown, wood indistinctly radiate, and central pith rather horny; nearly inodorous; taste sweetish, afterwards bitterish and strongly acrid." *U. S. VIII.*

The Japanese rhizome is from 5 to 15 cm. long, about 1 cm. in diameter, rarely branched, cylindrical or slightly compressed, knotty, bent, with circular disk-like scars, of a pale brown color, not whitish when abraded, with a slightly mousy, narcotic odor, and a taste nearly free from bitterness.

Histologically, Scopola can readily be distinguished from belladonna root by its characteristic reticulate tracheæ and absence of tracheæ with elliptical-shaped bordered pores.

Scopola yields approximately 0.6 per cent. of total alkaloids (see Williams, *Proc. A. Ph. A.*, 1899, 285) of which about 80 per cent, is hyoscyamine and the rest scopolamine and atroscine.

The U. S. VIII recognized a fluidextract (*Fluidextractum Scopolæ*) which was made with a menstruum of 75 per cent. alcohol.

The physiological action and therapeutic effects of scopola very closely resemble those of belladonna. H. C. Wood, Jr. (*T. G.*, April 15, 1901) showed, however, that the scopola was slightly more depressant to the spinal cord than belladonna (evidence of scopolamine action) and that the extracted total alkaloids of scopola were much more toxic than the extracted total alkaloids of belladonna. Scopola has been very little used in this country as an internal medicine but was at one time extensively employed for the manufacture of belladonna plaster. It is also a commercial source of scopolamine and hyoscyamine.

Extract of Scopola, U. S. VIII, was made by evaporating the fluidextract and assaying it so that it contains 2 per cent. of mydriatic alkaloids. *Dose*, one-eighth to one-fourth of a grain (0.008–0.016 Gm.).

Dose, of the drug, one to two grains (0.65–0.13 Gm.); of the fluidextract, one-half to three minims (0.03–0.2 cc.).

Scrophularia. *Scrophularia marilandica* L. (*S. nodosa* var. *marilandica* Gray). *Figwort. Scrofula Plant. Carpenter's Square. Square-stalk. Heal All. Scrofulaire*, Fr. *Kropfwurz. Kontenwurz*, G. (Fam. *Scrophulariaceæ.*)—This rather tall herb, having a knotted root, a square stem, opposite leaves and slender panicles of small, greenish-purple flowers, grows in rich open woods from New York to North Carolina and west to Kansas. Its leaves have, when fresh, a rank fetid odor, and a bitter, somewhat acrid taste; but these properties are diminished by drying. Water extracts their virtues, forming a reddish infusion, which is blackened by ferric sulphate. For histological study of root, see *P. J.*, 1896. Walz has obtained from it two proximate principles, which he names respectively *scrophularin* and *scrophularosmin.* Figwort leaves were formerly employed internally as an alterative and externally as a discutient and as a local application in *hemorrhoids.* Van de Moer (*P. J.*, 1896) affirms that the seeds are toxic, belonging to the digitalis group.

Sedoheptose.—This is a new sugar produced from *Sedum spectabile* B. by La Forge, and Hudson. It has the formula $C_7H_{14}O_7$ and is reducible but not fermentable.

Sedum. *Sedum acre* L. *Biting Stonecrop. Wall Paper. Small Houseleek. Mossy Stonecrop. Joubarbe âcre. Poivre des Murailles*, Fr. *Mauerpfeffer, Steinkraut*, G. (Fam. *Crassulaceæ.*)—This European plant has escaped to some extent from the gardens and grows wild in New England. It is spreading moss-like, possesses small, very thick leaves and yellow flowers. It causes vomiting and purging, and applied to the skin produces inflammation and vesication. The fresh herb and the expressed juice have been used as an antiscorbutic, emetic, cathartic, and diuretic, and have been applied locally to old *ulcers, warts,* and other excrescences. Other species are less acrid, and are even eaten as salad in some parts of Europe. Such are *Sedum rupestre* L., and *S. album* L. *S. Telephium* L. was formerly employed externally to cicatrize wounds, and internally as an astringent in *dysentery* and *hemoptysis,* and is still esteemed by the common people in France as a vulnerary. Ernst Mylius found in 100 parts of *Sedum acre* 2.2 parts of a soft, not acid resin, 12.80 parts of uncrystallizable sugar, and 12.40 parts of a soft acid resin, besides an alkaloid and inert substance. (*J. P. C.*, 4e sér., xvii, 81.)

Selenium. Se = 79.2.—A steel-gray non-metallic element with a high luster and showing a crystalline surface upon being broken. Also in dark red crystals or powder soluble in carbon disulphide and melting between 170° and 180° C. It burns in air with a bluish-red flame evolving selenium dioxide. Sp. gr. 4.27, m. pt. 217° C. It occurs in copper ores and is obtained as a by-product in the copper industry. It is used in the electrical sciences on account of its distinctive property of being a good conductor of electricity when exposed to light but a poor conductor in the dark. This widely distributed element, discovered by Berzelius in 1817, belongs to the sulphur group, and its compounds occur in nature associated with sulphur compounds. It is also extracted from the lead chamber deposits of the sulphuric acid works. The presence of *selenium* in sulphuric acid has been objected to on account of its coloring substances yellow, even minute quantities present in sulphuric acid giving a yellow tint to cellulose. (*P. J.*, 1912, 47.) The physiological actions of the compounds of this metal have not been widely studied, but Chabrié and Sépicque (*C. R. A. S.*, cx) have shown that *selenous acid* is an irritant poison. According to Merck, a solution of selenous acid (0.5 per 100) is a valuable reagent for detecting alkaloids. (*M. R.*, 1900.) Wassermann (*D. M. W.*, 1911) from experiments upon mice reached the conclusion that selenium had a destructive action on *cancerous growths* which has led to some clinical trials of various compounds of the element, especially the combination of *eosin-selenium* and the colloidal forms known as *seleniol* and *electro-selenium.* The treatment must be regarded as still in an experimental stage.

Selenium oxychloride has recently come into use as a solvent. It has selective solvent properties which are peculiarly uncommon and is capable of dissolving such resistant materials as rubber, enamels, hydrocarbons, phenol-formaldehyde condensation products, etc. (*Ph. Era.*, 1921, liv, 120.)

Semecarpus. *Semecarpus venosa* (Fam. *Anacardiaceæ*), the *Tschongott Tree.*—The highly poisonous nature of the bark of this tree, which is a native of the Caroline Islands, is, according to Thoms and Mannich (*Ph. Ztg.*, 1902), due to the presence of *cardol* (*anacardic acid*).

Sempervivum. *Sempervivum tectorum* L. *Common Houseleek. Hen-and-Chickens. Grande Joubarbe,* Fr. *Hauswurz, Hauslauch, Dachwurz,* G. (Fam. *Crassulaceæ.*)—A succulent, perennial, Eurasiatic plant with imbricated leaves and scorpioid cymes of rose-purple flowers arranged on a panicle. It is extensively cultivated. In Europe the bruised recent leaves of this plant are employed as a cooling application to burns and other external inflammations. The juice is said to cure *warts.*

Septovince. *Trichloracetyl-diphenol-diiodide.*—This compound was introduced under the name of *iodal,* but as this title properly belongs to the triiodaldehyde the name was changed to septovince. It is claimed by Sorapure to have specific curative properties in *acute articular rheumatism* (*P. J.*, 1916, xcvii, 463). The method of use is as follows: One part of septovince is shaken with 7 parts of water and allowed to stand for 6 hours at the end of which time there is a dark, tarry deposit and a clear, brown, supernatant liquid. The latter is injected intramuscularly in *doses* of one fluidrachm (5 cc.) daily and also applied locally.

Serums. *Normal Horse Serum. Normal Sheep Serum. Normal Goat Serum.*—These liquids are obtained from the blood of the respective animals by inserting a large sterile needle into a vein and allowing the blood to flow through rubber tubing connected with the needle into covered vessels of one or more liters capacity. The blood is allowed to coagulate for about two days, either around a rod or other device previously inserted in the vessel, or spontaneously in the bottom of the container; the clot at the end of this period may be squeezed free of serum by dropping a weight from the upper part of the vessel. The clot gathers in its meshes the red cells and the white cells of the blood, so that the fluid remaining to be siphoned off is a transparent liquid of a light yellowish brown color. This is called *blood serum.* If the clotting had been prevented by the addition of a citrate or oxalate and the blood cells separated by means of sedimentation, with or without centrifugation, the resulting fluid would be *blood plasma.* If in the third place, the blood had been vigorously agitated by means of rough solid bodies such as pieces of broken glass in the container immediately, upon being withdrawn from the animal, the fibrin or clot would have rapidly formed around these agitating bodies leaving the cells suspended in the fluid; such a fluid is called *defibrinated blood,* it resembles whole blood in appearance, but differs from it in having lost the property of spontaneous coagulation, it differs from serum in containing red blood cells and some white cells. The blood platelets and part of the white cells are destroyed by defibrination. All these operations must be carried out with an aseptic technic more strict than that of the surgical operating room, because blood and the fluids derived from it are excellent culture media for bacteria, and all bacterial contamination, whether pathogenic (disease causing) or not must be excluded. All the instruments and vessels must be sterilized—not by boiling—but in such a manner that even bacterial spores are destroyed. This requires dry heat at 170° C. for an hour and a half. Material such as rubber, which will not withstand this heat, may be sterilized by steam at 15 pounds pressure for half an hour, provided the boiler or autoclave is so arranged that all the air in the interstices of the material to be sterilized is withdrawn and replaced with saturated steam; the usual steam sterilization does not accomplish this.

Even with such precautions, serums are not usually considered safe unless preserved by the addition of some antiseptic, such as 0.5 per cent. phenol or cresol, or chloroform to saturation. As usually administered these quantities of preservative are without serious effect.

The serum of normal animals is used in therapeutics to promote clotting in *hemorrhage* or in hemorrhagic diseases. The other blood fluids described above are not available for this purpose—the plasma on account of its content of citrate or oxalate which prevents clotting, the defibrinated blood and whole blood on account of the red blood cells which they contain; the blood cells of another species might prove harmful to man. It would seem that in blood serum most of the clotting factors have been partially or wholly used up in the production of the clot. Nevertheless, serum has seemed of value in many cases of hemorrhage, though there are other cases in which it is of no value. (See also under *Blood* and *Thromboplastin.*) Fresh serum is apparently more efficacious than old; it is therefore advisable to use serums whose date of production is stated. *Dose,* two and one-half to five fluidrachms (10–20 cc.) hypodermically, or in urgent cases intravenously.

The occurrence of serum sickness and anaphylactic shock after injection of serum or its products has been mentioned under *Antitoxinum Diphtheriæ* (see Part I). The same precautions should be taken in the use of normal serum. Horse serum appears to be less toxic—less likely to cause serum sickness—than the serum of any other alien species, but in cases in which hypersensitiveness to horse serum is feared or proven, serum from the goat or sheep may be used. In hospitals freshly drawn rabbit serum, or whole human blood, is used for similar purposes.

No serum can be sold in interstate commerce except when produced in an establishment licensed by the Secretary of the Treasury. The requirements are those given under *Serum Antidiphthericum* U. S., except those for potency. There is no standard for the potency of normal serum.

Immune Serum. Antitoxins. Antibacterial Serums.—This term includes the serum of animals in whose blood an immunity to any given bacterium or other harmful substance has been produced by the injection of that bacterium or harmful substance. This immunity may show itself in various ways. It is most notable, and most truly an immunity when, as in the case of antitoxic immunity, the serum actually protects another animal from the toxin or poison, or even cures the second animal if injected some time after the toxin. The word *toxin* can only be applied to those poisons which have the property of inciting such an immunity (*i.e.,* producing antitoxin) when injected into an animal in gradually increasing doses. The immunity may be antibacterial instead of antitoxic, that is, attacking the bacteria themselves rather than their soluble poisons or toxins. *Antibacterial immunity* in a serum may be manifest in its bactericidal or bacteriolytic properties; these two modes of action are generally taken as synonymous, but the term bactericidal refers especially to the killing of bacteria by the serum, as shown by tests of the numbers of bacteria present after its action, while bacteriolytic has reference to the gradual breaking up and dissolving of the bacteria as seen under the microscope. Antibacterial immunity is also sometimes demonstrable as a protective action, protecting for example guinea pigs which receive the immune serum against doses of the bacterium in question which kill other guinea pigs of the same weight not receiving the serum. Antibacterial immunity may be bacteriotropic or *opsonic,* which means that the serum in question in some way changes the special bacteria so that they are easily taken up and destroyed by the white blood cells. It is to be noted that immune serums are specific—that is, if antitoxic—they neutralize only the particular toxin which was used in their preparation, and no other; if antibacterial they have an antagonistic affinity for the exact species of bacterium with which the original animal was treated, and no other, or in some cases, only closely related bacteria. This fact of specificity is made of diagnostic use in the agglutinating property of immune serums (see Widal Test for Typhoid Fever, under *Diagnostic Tests*), and in their complement fixing power (see Complement Fixation Reaction for Syphilis, under *Diagnostic Tests*).

In the case of immune serums used for the treatment of disease this specificity is frequently so high as to be detrimental. Thus an antibacterial serum prepared from a given organism may be powerless against the same species of organism arising from other sources. In meningococcus, streptococcus and pneumococcus infection this is particularly true. The organisms from different sources are called strains—and in spite of many different strains being used in the production of these serums, cases of meningitis, sepsis, or pneumonia occur in which the serums can be shown to have no influence against the infecting organism either in the body of the patient or in the laboratory. This is one of the causes of the poor success which has generally attended the use of serums other than diphtheria and tetanus antitoxin. Measures to overcome this difficulty have been taken, notably in anti-meningococcus and partially in anti-pneumococcus serum.

The material which is injected in the production of an immune serum is called the *antigen,* while the substance in the immune serum which gives rise to the different phenomena mentioned above—antitoxic, bactericidal, or bacteriolytic, protective, bacteriotropic or opsonic, agglutinative, complement fixing,—is called an *antibody.* Some workers hold that there is a different antibody for each function, while others take the view that a specific serum has only one antibody, with all these varied functions. It is certain, however, that in different serums these properties are present in different proportions, and consequently it is easier to conceive them as being exercised by different antibodies. Unfortunately, we have little means of knowing in a given case, which properties or which antibodies are the important ones in rendering a serum valuable to cure or prevent the infection in question, therefore we have no means of precisely measuring the worth of a serum.

Immune serums may be prepared against other substances than toxins and bacteria, as against foreign proteins, in which case a seventh property is apparent—that of precipitating the antigen used in its preparation. Blood cells of many other species also act as antigen for another series of immune serums; the antibody most apparent here is *hemolysin,* which dissolves the red corpuscles when added to the immune serum so that the corpuscles disappear and the fluid in which they were suspended takes on a clear red color (see Complement Fixation Reaction for Syphilis, under *Diagnostic Tests*).

All establishments manufacturing serums used in the prevention or treatment of human diseases are required to be licensed by the Secretary of the Treasury if the serums are sold in interstate commerce. Since 1918, The U. S. Treasury Department has required that Anti-dysentery serum, anti-pneumococcic serum and anti-meningococcic serum conform to certain tests for antibodies. It is required that licensed firms submit samples of every lot of those sera to the Hygienic Laboratory for examination before they are dispensed. These requirements are for all purposes potency standards for such sera. There are as yet no approved potency standards for the other sera.

Immune serums commonly contain preservatives and also are prone to cause serum sickness in the same way as diphtheria antitoxin. In this connection it is to be noted that the unofficial serums are in general distinctly less efficacious than the official antitoxins, and further that they are usually to be administered in much larger quantities if any benefit whatever is to be expected; the former consideration would cause one to hesitate if any possible danger were anticipated from their use, and the latter emphasizes the need of extreme caution unless hypersusceptibility to horse serum has been excluded.

Immune serums containing antibodies must be sharply distinguished from Vaccines (p.) which contain antigen and force the human body to manufacture its own antibodies.

All serums lose in potency rapidly at room temperatures, and there is reason to believe that toxic compounds may be found if they become frozen. Therefore they should be kept at a temperature between 4° C. and 15° C. But even with every care they gradually deteriorate and are therefore always dated with an expiration time.

Antianthrax Serum. Serum Antianthracicum. N. N. R. 1924.—This immune serum is prepared by injecting horses with gradually increasing doses of anthrax bacilli. The horses are then bled as described under normal horse serum, and the serum collected. Considerable success has attended the use of this serum in the treatment of *anthrax* in animals, and some in man, if the serum happens to be a potent one and is administered early. *Dose,* 30 cc. to 100 cc. intravenously or subcutaneously.

Antidysentery Serum. Serum Antidysentericum. N. N. R. 1924.—Certain bacilli, or groups of bacilli, have been found to be the cause of some forms of dysentery. These bacilli are classified generically as the dysentery bacillus, and are given various names, as *Shiga-Kruse* type, *Flexner* type, *Strong* type, Y type, according as their characteristics fall into one or another of these fairly well defined groups. Horses have been immunized by the injection of cultures or filtrates of one or several of these types, and the serum used in the treatment of human *dysentery.* The results in many cases have been encouraging, giving a considerable reduction in mortality over similar cases treated without serum; many observers agreeing that the use of a potent serum has reduced the mortality 30 to 50 per cent. below the usual rate. The serum has also been found of value as a prophylactic in localized outbreaks and for those in attendance on cases of the disease. Either a polyvalent serum must be used prepared by immunization with both the Shiga and Flexner types or the infecting strain determined and a corresponding type serum used. *Dose,* two and one-half to eleven fluidrachms (10–50 cc.), subcutaneously or intravenously.

Antigonococcus Serum. Serum Antigonococcicum. N. N. R. 1924.—By injection of animals with gonococci, serum may be prepared which at times shows the properties of bacteriolysis, agglutination and complement fixation. Such serum has been used in the treatment of gonococcal infections, in part with favorable results. The serum seems to have no value in acute *gonorrheal urethritis,* and the lack of complete success in other cases may be due to the failure of antibodies to reach the seat of disease in sufficient concentration.

Antimeningococcus Serum. Antimeningitis Serum. Serum Antimeningococcicum. N. N. R. 1924. —The success attending the use of this serum in cases of *meningitis* caused by the *meningococcus* (*Diplococcus intracellularis meningitidis*) is one of the great triumphs of serum therapy, second only to the success of the antitoxins against diphtheria and tetanus. To immunize the horses used in producing the serum, cultures are injected, freshly killed, living, and partially disintegrated and dissolved. A source of failure of the serum lies in the fact that there are many strains of the meningococcus, and the strain in a given case may be very different from any of those used in producing the serum; the specific antibodies fitting that particular strain would then be lacking and improvement could not be expected from the use of the serum.

A great step in advance, in the use of antimeningococcus serum, is in its application directly to the seat of disease, instead of merely subcutaneously. The injection is made under the dural membrane of the spinal canal, that is, into the meningeal space. As in other successful serum treatment, early diagnosis and early application is necessary. The injection is best done without anesthesia. The patient should be held firmly on his left side, with knees bent up nearly to the face, and with his back resting at the edge of the table or bed. The hands of the operator and the instruments must be sterilized. A stout needle with trocar at least 4 inches long should be used. The skin should be cleansed first, then treated with an antiseptic, such as tincture of iodin. The site for insertion of the needle is preferably the median line just below the fourth lumbar vertebra (on a line with the crests of the ilium). The needle is directed upward at an angle of about 35 degrees along the upper edge of the fifth lumbar spine until the point is felt to penetrate the dura, when the trocar is withdrawn and the spinal fluid allowed to flow out. This should be saved in a sterile container and examined microscopically. A turbid fluid indicates meningitis but in case of doubt it is best to inject the serum. From two to eight fluidrachms (10 to 30 cc.) of serum (previously warmed) is slowly injected by gravity pressure, the amount being best determined by the fall in blood pressure according to Sophian's method. A drop of 20 millimeters is an indication to stop the injection at once. The injection should be repeated daily until the condition of the patient has definitely improved and the spinal fluid has been free from meningococci pus cells. Some observers have reported very good results from the simultaneous intraspinal and intravenous administration of the serum, particularly where meningococci are found in the blood. It must, however, be remembered that the intraspinal injection is the most important.

The amount of preservative in serum for intraspinal administration should not exceed 0.3 per cent. cresol or phenol. If the preservative is too concentrated, or if too much serum is injected, there is danger of collapse and even death. But the danger of the disease itself is much greater and no delay in instituting serum treatment should ensue by reason of fear on this ground.

Antiplague Serum. Yersin Serum.—The horse used for immunization receives killed cultures or living avirulent cultures of *Bacillus pestis* and finally living virulent ones. It is evident that such immunization must be carried out under special precautions in view of the danger involved in working with living plague bacilli. One virulent strain appears to be as effective as another. The resulting serum can be shown to have protective action on animals, but in the treatment of human *plague* only a moderate reduction in mortality is obtained—largely because the serum is not administered at the incipiency of the disease. *Dose,* 100 cc. (three and one-third fluidounces) or more intravenously.

Antipneumococcus Serum. Serum Antipneumococcicum. N. N. R. 1924.—The pneumococcus (*Diplococcus pneumoniæ,* Weichselbaum) is present more often than any other organism as a causative factor in pneumonia. In one or more of its types it is found in about 60 per cent. of normal mouths or throats and is often associated with ordinary colds, severe grip-like infection, middle ear disease, ulcer of the eye, or meningitis. Serums have repeatedly been produced by immunizing animals against the pneumococcus but the results have been variable. Römer, Neufeld, and Cole and others have conducted experimental investigations in serum therapy of pneumonia; it appears to be one requisite for success that the serum be produced by the use of the type of pneumococcus found in the patient to be treated. Certain of these types are more frequent than others and offer more promise. Other desiderata are that the serum be used early —on the first or second day of the disease if possible, and that large amounts—as much as 100 cc. per dose—be injected intravenously. At present the serum treatment of *pneumonia* is practically confined to the type I infection for which alone does the Treasury Department provide a standard. To be of any value the serum must be given early, in large doses intravenously and limited to Type I infections.

Antistreptococcus Serum. Serum Antistreptococcicum. N. N. R. 1924.—Many attempts have been made to produce therapeutically valuable antistreptococcus serum. In many commercial serums some antagonistic influence on streptococci can be demonstrated in the laboratory, but only rarely are authentic series of benefited cases reported. It seems to be necessary to introduce a large amount of the serum (100 cc. or more) intravenously, and in such a serious disease as streptococcus infection the added strain on the eliminative mechanism caused by such quantities of foreign protein may turn the tide in the wrong direction. The Viennese reports of success with streptococcus serum therapy in severe cases of *scarlet fever* have not been confirmed in this country. The strong serum specificity of different strains of the bacterium may account for divergent results. The activity of antistreptococcus serum appears to be largely bacteriotropic.

Antivenomous Serums. Antivenins.—The snake poisons are true toxins and the serums prepared to combat them are true antitoxins. Theoretically, then, we should expect the excellent results of diphtheria and tetanus antitoxin to be duplicated in the serum treatment of *snake bites,* instead of the equivocal results of the antibacterial serums. Certain practical difficulties have interfered with such success. In the first place, the toxins of snake venoms are highly specific. Not only are there present in a given venom several different poisons, such as *hemorrhagins* (causing breaks in the blood-vessels and consequent hemorrhages), *neurotoxin* (poisoning the vital center of the central nervous system), *coagulins* (causing clotting of the circulating blood), *hemolysins* (destroying the red blood cells), *hemoglutinins* (clumping the red blood cells)—but each of these is peculiar to its own species. Therefore to be effective, the serum must be derived from an animal immunized against the particular species of snake to be encountered. In the second place, very potent serums have not as yet been prepared—due largely to the difficulty in securing the antigen, snake venom—in large quantities. Thirdly, the serum must be on hand and used immediately.

In the case of the common North American poisonous snakes,—the rattlesnake, copperhead, and watermoccasin, hemorrhagins are the most important toxins. If antivenomous serums are available they should be carried by the traveller and administered within a few minutes after the bite. Some time may be saved by the ligature cutting off the return flow of blood from the part affected. 100 cc. or more of the antivenomous serum suited to the species of snake concerned should be injected intravenously, and more injected intramuscularly in the vicinity of the wound.

Sesamum. *Sesamum indicum* L. (Fam. *Pedaliaceæ.*)—The *benne* plant is a native of Asia but has become naturalized in our Southern States and is cultivated in all parts of the tropical world. It is an annual, with a branching stem 1 to 2 feet high, and bearing opposite (lower), or alternate (upper), petiolate leaves, varying considerably in their shape. The flowers are pale rose or white, and stand singly upon short peduncles in the axils of the leaves. The fruit is an oblong capsule, with small, oval, yellowish-white, brown, reddish or black seeds.

There are about twenty species referred to the genus *Sesamum,* the majority of which are natives of Africa. In India one or two species occur wild; one of these, *Sesamum indicum* L. (*S. orientale* L.), has been cultivated from time immemorial in various parts of Asia and Africa. From the latter continent it is supposed that seeds were brought by the negroes to the United States, where, as well as in the West Indies, it is now cultivated to a considerable extent. The plant above described will grow as far north as Philadelphia. The seeds are employed as food by the negroes, who parch them over the fire, boil them in broths, make them into puddings, and prepare them in various other modes. By expression they yield a fixed oil, which is recognized by the N. F. (See *Oleum Sesami,* Part I.) Berjot obtained from the seeds 53 per cent. of oil by means of carbon disulphide. Rautenberg reported a series of severe poisonings from the intestinal injection of sesame oil. (*J. A. M. A.*, xlvii, p. 1962.) These accidents, he believes, are due to adulteration of the oil.

Benne Leaves.—These abound in a gummy matter, which they readily impart to water, forming a rich, bland mucilage, much used in the Southern

States as a drink in various complaints to which demulcents are applicable, as in *diarrhea, dysentery, catarrh, acute cystitis, strangury,* etc. One or two fresh leaves of full size, stirred about in half a pint of cool water, will soon render it sufficiently viscid. With dried leaves hot water is used. The leaves also serve for the preparation of emollient cataplasms.

Sethia. *Sethia acuminata* Arn. (now *Erythroxylon lucidum* H. B. K.) (Fam. *Erythroxylaceæ.*)—The juice of this Ceylon plant or the powdered leaves—*dose,* fifteen grains (1.0 Gm.)—are affirmed to be an efficient vermifuge. (*P. J.*, April 7, 1883.)

Sida. *Sida rhombifolia* L. *Mesbé. Queensland-hemp. Jelly-leaf.* (Fam. *Malvaceæ.*)—The leaves of this shrubby plant are largely used in Australia as a demulcent. They contain a large quantity of mucilage. The fluidextract has been asserted to possess expectorant properties and to be especially valuable in the treatment of *pulmonary tuberculosis.* Zink (*M. M. W.*, 1912), however, was unable to obtain evidence of any specific action in *tuberculosis. Sida paniculata* L. (*S. floribunda* H. B. K.), of Peru, which also contains a large quantity of mucilage, is said by Martinet to be an active vermifuge, owing its powers, probably, to the extremely minute but very resisting spines which cover its leaves, the part used.

Siegesbeckia. *Siegesbeckia orientalis* L. (Fam. *Compositæ*).—This plant is used in the Mauritius Islands in *syphilis, leprosy,* and various skin diseases. A white, crystalline principle, *darutine,* has been discovered in it by M. L. Auffray. (*P. J.*, vol. xvi, 1047; also *B. M. J.*, June 25, 1887.)

Sienna. *Terra di Sienna.*—An argillaceous mineral, compact, of a fine texture, very light, smooth, and glossy, of a yellowish-brown or coffee color, leaving a dull orange trace when moistened and drawn over paper. By calcination it assumes a reddish-brown color, and is then called *burnt sienna.* In both the raw and burnt states it is used in painting. The best *sienna* is brought from Italy, but an inferior kind is found in England.

Silene. *Silene virginica* L. (Fam. *Caryophyllaceæ*). *Fire Pink. Catchfly. Wild Pink.*—This perennial herb, native to open woods from Western New York to Minnesota and southward, was considered by the Indians poisonous and by Barton an anthelmintic. It is a slender herb having thin-spatulate or oblong-lanceolate leaves and deep crimson or scarlet flowers in a loose cyme.

Silex, Pulverized. *Silex Contritus* Lond. *Quartz.*—For mechanical purposes, in the making of aromatic waters, etc., the London Pharmacopœia formerly recognized under the name of *Silex Contritus* powdered *quartz;* but at present powdered purified talc, paper pulp and kieselguhr are employed. For details, see 17th edition, *U. S. D.*, p. 1741.

Pulverized silex is a harsh, white, tasteless powder, insoluble in water and most other solvents. Its sp. gr. is 2.66. In composition it is a *silicic oxide,* SiO_2.

Silicon, Si. 28.3, is an electro-negative element, which has been obtained in two allotropic states, called amorphous and crystalline silicon; the first corresponding to amorphous carbon having a sp. gr. of 2.00 and the second to crystallized carbon or the diamond, except that it is steel-gray in color. The second variety is hard enough to scratch glass but not topaz and has the sp. gr. 2.49. It is now made on a large scale as a product of the electric furnace, being used as a deoxidizing agent in the casting of some metals. Pure *silica* is easily prepared by acidulating commercial solution of sodium silicate with hydrochloric acid, heating and evaporating, and washing the precipitated silica. In recent years *silicic acid* and other compounds of silicon have attracted some attention in the treatment of *pulmonary tuberculosis.* Klare and Budde (*M. M. W.*, 1922, lxix, p. 741) used a tetraglycol ester of silicic acid which is marketed under the trade name of *silicitrin.* It is a colorless sweetish fluids representing 18 to 20 per cent. of SiO_2. They gave it in doses of ten drops several times a day.

Silk Peptone.—This is a preparation of peptone derived from silk and standardized to a nearly uniform optical rotatory powder. It is a white to a yellowish non-hygroscopic powder, easily soluble in water and used as a testing agent for peptolytic ferments in tissues or in stomach contents. It has no use in therapy.

Silphium. *Silphium laciniatum* L. *Polar Plant.* (Fam. *Compositæ.*)—The *rosin weed,* or *compass plant,* of Ohio, yields an oleoresin, which is said to be used in making chewing gum. (*A. J. P.*, 1881, 487.)

Silver Acetate. *Argenti Acetas.* $AgC_2H_3O_2$.—*Silver acetate* occurs in white crystals, or a white crystalline powder, soluble in about 90 parts of water at ordinary temperatures, more soluble in hot water. It has been introduced by Zweifel (*Centralbl. f. Gynækologie,* 1900, No. 51) as a substitute for silver nitrate in the treatment of *ophthalmia* of new-born infants. He asserts that the one per cent. solution is in these cases much more effective than the older salt.

Silver Albumoids. *Protein Silver Salts. Silver Proteinates.*—A large number of compounds of silver with various protein derivatives have been brought forward for use in local infections, especially of the mucous membranes. As there is a strong similarity in the chemical properties and therapeutic uses of these compounds it has seemed advisable to consider them in one group. The peculiar properties, both chemical and therapeutic, that characterize this group of compounds have been described under *Argenti Proteinum,* Part I. See also *Silver, Soluble.*

Albargin. Silver Gelatose.—This substance, which is a compound of silver nitrate with gelatose, is a yellowish, shining, sometimes coarse powder which, in either cold or warm water, freely forms neutral dialyzable solutions. It contains 14.8 to 15 per cent. of silver. It is incompatible with tannin and chlorides which precipitate gelatose and silver, respectively. It affects albumin slowly and also precipitates cocaine solutions, but may be used with the alkaloid providing the double solution be freshly prepared at the time of administration. It is not quickly reduced by light, but should be preserved in amber-colored bottles. Another compound of silver and gelatin is known as *Gelargin.*

Albargin was introduced by Bornemann (*Ther. Geg.*, March, 1901) for the treatment of *gonorrhea.* When there is much irritation, the 0.1 per cent. aqueous solution may be injected four or five times a day; in more chronic conditions the solution may be up to 2 per cent.

Argaldin.—This is stated to be a compound of silver, albumin and hexamethylenamin and to contain 8.9 per cent. of silver. It is employed in strengths of 10 per cent.

Argonin. Silver Caseinate. Argentum Casein.—This is a white powder, of neutral reaction, prepared by mixing equivalent quantities of solutions of sodium caseinate and silver nitrate and precipitating with alcohol. It contains 4.28 per cent. of silver and forms opalescent faintly alkaline solutions in water. It is incompatible with acids and acid salts, but is not affected by chlorides. A 10 per cent. solution in warm water is said to be permanent in the dark. (A. Leibrecht, *Th. M.*, vii, 1895.) It has been highly recommended by both German and American clinicians in the treatment of acute and chronic cases of *gonorrhea.* Its 10 per cent. solution causes no pain in acute *gonorrhea.* According, however, to the elaborate study of H. M. Christian, it is not of much service in the treatment of *posterior urethritis.* One hundred and sixty minims (10 cc.) of a 2½ to 3 per cent. solution may, in the acute stages of the disease, be injected into the urethra and allowed to remain there for five minutes. A solution—0.3 ammonia water, 0.6 argonin, 100 of water—is said by R. Mayer to be much more powerful than argonin itself.

Argyn. N. N. R. 1924.—A colloidal form of silver oxide with serum albumin which contains from 25 to 30 per cent. of silver in a form not readily ionizable. It occurs as black, lustrous, hygroscopic granules which readily form colloidal solutions with either water or glycerine but not with alcohol. It is not precipitated by sodium chloride or albumin. It is recommended as a germicide in strengths of 10 to 25 per cent.

Argyrol. Silver Vitellin. Argentic Vitellin. N. N. R. 1917.—This substance is said to be a combination of silver with a protein produced by the electrolysis of serum albumin. It occurs as brownish-black hygroscopic scales, freely soluble in water or glycerine but not in alcohol. It gives a slight cloudiness with sodium chlorides.

Argyrol has been used chiefly in the treatment of *conjunctivitis* and *urethritis*, especially of the gonorrheal type.

Argyrol belongs to the group of silver protein compounds containing very little ionic silver. Although its chemical constitution is not known with certainty, it is generally believed to represent a colloidal silver oxide, the protein acting only as a colloid protective.

Argyrol has been used chiefly in the treatment of infections of the mucous membranes, such as *conjunctivitis, urethritis, rhinitis,* etc. It is practically free from any local irritating or astringent effect. The statements concerning the antiseptic powers of this compound have varied so greatly that one is driven to the conclusion that the substance at present sold under this name is not the same as that originally introduced under this name. The older tests show that its disinfectant powers were very slight; Post and Nicoll (*J. A. M. A.*, 1910, lv) for example, found that a 50 per cent. solution was not certainly germicidal even with thirty minutes' exposure. Culver (*J. Lab. Clin. M.*, 1918, iii, 487) more recently has found that it is an active germicide, one-half of 1 per cent. destroying the gonococcus in 5 minutes' exposure. Lancaster (*B. M. S. J.*, 1920, lxxxiii, 565) finds that 1 per cent. is antiseptic and 10 per cent. slowly germicidal. Some clinicians have attributed its beneficial effect to other than antibacterial properties; it has been suggested that its therapeutic virtue is at least in part owing to the power of dissolving pus and mucus and hence acting as a mechanical cleanser.

Solutions of argyrol, when kept, not only lose their germicidal power, as has been shown by Culver and others, but apparently also develop irritant properties.

It is one of the least irritant of all the silver preparations, and may be used in the urethra in strengths of from 1 to 10 per cent., while in *gonorrheal ophthalmia* it has been employed in concentrations up to 30 per cent.

The stains of argyrol may be readily removed from either skin or clothing by solution of chlorinated soda.

Largin. Silver Protalbin.—This is a compound of silver and protalbin, which occurs as a whitish powder, soluble in water to the extent of 10.5 per cent., freely soluble in glycerin, blood serum, and peptone solution. Not precipitated by chlorides nor yet by albumin, and containing 11.1 per cent. of silver. In brown bottles it keeps unchanged indefinitely. It is astringent as well as germicidal. In male *gonorrhea* the strength of the injection should be one-fourth of one per cent., gradually increased up to two per cent. In women the parts may be irrigated with from a one-half to one per cent. solution, after which a 5 per cent. largin bougie may be held in position by a cotton plug for fifteen minutes and the part again irrigated with a 0.5 per cent. solution of largin. Largin is also largely used in the treatment of infectious *conjunctivitis* and catarrhal *corneal ulcers* in the form of gelatin tablets containing one per cent.

Lunosol. Colloidal Silver Chloride. Argenti Chloridum Colloidale Saccharatum, N. N. R., 1925.—This preparation is claimed to have the advantages of being not only a powerful and penetrating germicide, but especially that it does not stain. It is easily soluble in water, forming dichroic opalescent solutions, and is said to be non-irritant and is used, in strengths of from 3 to 25 per cent., in the treatment of *urethritis, conjunctivitis,* etc.

Novargan. Silver Proteinate.—This occurs as a yellow, amorphous powder, freely soluble in water, yielding a neutral solution. It is asserted that the silver from this solution is not precipitated either by chlorides, sulphides, alkalies, or by any of the substances that ordinarily precipitate silver or its salts from solutions. The compound represents 10 per cent. of silver.

Novargan is actively astringent and also bactericidal. In *gonorrhea* it is used in strengths of from 0.5 to 5 per cent. according to the acuteness of the inflammation. According to Von Hoessle and Grater (*D. M. Ztg.*, 1905, p. 92) it is less irritating to the mucous membranes than protargol and has also the advantage of a deeper penetration. Regenspurger (*Med. Klin.*, 1908, No. 8) has used it for the abortion of *gonorrhea* in the following manner. After washing out the urethra he injects 8 to 12 cc. of a solution containing five parts of novargan and ten parts of glycerin and water to make one hundred which is allowed to remain in the urethra for from five to fifteen minutes. If no inflammatory reaction follows this twenty-four hours later he injects a 10 per cent. solution. He claims that a very considerable number of cases with this treatment are cured within a period of eight days.

Proganol. N. N. R. 1924.—A compound of silver and albumose containing a little over 8 per cent. of silver. It is recommended that in making solutions of this salt a small quantity of cold water be mixed with it and stirred to a thick paste and then the remaining water be added gradually with stirring. It is employed usually in strengths of from 0.25 to 5 per cent.

Protargentum. N. N. R. 1924.—It is a chocolate-colored powder, odorless, freely though slowly soluble in water yielding solutions which are alkaline to litmus but neutral to phenolphthalein. It is insoluble in alcohol. Protargentum contains approximately 8 per cent. of silver. It is usually employed in strengths of from ½ to 5 per cent. solution, which should be freshly prepared.

Protargol. N. N. R. 1924. *Protargolum. Protein Silver Salt.*—A combination of silver and albumin, containing about 8 per cent. of metallic silver. It occurs as a yellow powder, soluble in 1 part of water, the solution not being affected by heat, albumin, hydrochloric acid, weak sodium chloride solution or sodium hydroxide solution. The dry salt as well as the solution should be protected from light.

According to the experiments of Kelly (*B. M. J.*, 1907, ii, p. 1475), silver nitrate is nearly 300 times as powerful a germicide as protargol, and in the experiments of Post and Nicoll (*J. A. M. A.*, 1910, lv, p. 1635) a ten per cent. solution of protargol was inferior to a one-tenth per cent. solution of silver nitrate. On the other hand, Derby (*B. M. S. J.*, cxlv, p. 341) found that *Staphylococcus aureus* was killed by a two to four per cent. solution of protargol in three to five minutes. It is evident that in germicidal power, protargol is far inferior to silver nitrate. It is claimed, however, that it has greater penetrating power, and that it can be used much stronger, because of its relative slight irritant properties. As to the first of these claims, Derby has shown that the presence of blood serum interferes with the activity of protargol, as well as all other preparations of silver, and both Kelly and Marshall and Neave (*B. M. J.*, 1906, ii, p. 350) assert that the penetrating power of silver nitrate into agar-agar is not greatly inferior to the protein compound of silver. As to the second claim that protargol is less irritant in proportion to its germicidal power, the data concerning its antibacterial properties are so contradictory that it is impossible to state categorically whether, in strengths of similar irritation, silver nitrate or protargol is the more efficient germicide.

Protargol has been used very extensively, especially in *gonococcus infections* either of the urethra or conjunctiva. In *acute urethritis* it may be used in strengths of from 0.5 to 2 per cent. for injections, and has been used in 10 per cent. strength for the so-called abortive treatment. In *ophthalmia neonatorum*, Speiro (*M. M. W.*, 1909) drops a 10 per cent. protargol solution into the conjunctival sac, once or twice daily, while, according to Cogwill (*D. M. Ztg.*, 1904) the strength may at times be increased to as high as 30 per cent. in this condition. Protargol has also been used as a germicide for various other conditions. Berliner (*M. M. W.*, 1908) has found it useful in the treatment of *acute tonsillitis*, and it has also been employed as a surgical antiseptic in suppurating *ulcers, carbuncles* and the like.

Silvol. N. N. R. 1924.—This compound, which is said to contain 20 per cent. of silver, resembles argyrol in its physical and, it is asserted also, its therapeutic uses. It is freely soluble in water forming dark-colored solutions with relatively high specific gravity and low viscosity. According to the experiments of Culver (*J. Lab. Clin. Med.*, 1918, iii, 487) silvol is more actively germicidal than argyrol, one part in 3000 killing gonococci in thirty minutes and 0.5 per cent. in less than one minute. The report of the Council on Pharmacy and Chemistry (*J. A. M. A.*, 1918, lxxi, 138) shows that the 10 per cent. solution is non-irritant to the nasal mucous membrane, does not yield a precipitate with the chlorides but, under certain conditions, may yield a precipitate with egg albumin. The claim is made for this preparation in that in addition to its germicidal power it is astringent. It is used in strengths of from 5 to 25 per cent.

Under the name of *Neo-silvol, N. N. R.* 1924, a compound of silvol with an iodide has been introduced. It contains from 18 to 22 per cent. of silver iodide in a colloidal state. The advantage claimed for this preparation is that while it possesses all the therapeutic virtues of its parent it is free from staining properties. It occurs as pale yellow granules which form a milky emulsion when mixed with water. It is used in strengths of from 5 to 40 per cent.

Although solutions of Neo-silvol are actively germicidal they sometimes develop a mold on standing; they therefore should not be kept for more than a few days.

Vargol. N. N. R. 1924.—This contains 20 per cent. of silver combined with albumin. It occurs as greenish-black, lustrous scales, very hygroscopic, easily soluble in water. Its solutions are not affected by sodium chloride, iodide or hydroxide. It is used in strengths of from 10 to 25 per cent., and is said to resemble argyrol in its field of usefulness.

Silver Ammonio-chloride. *Argenti Ammonii-chloridum. Argentum Chlorato-ammoniatum.*—This substance is formed by saturating solution of ammonia, by the aid of heat, with silver chloride and allowing the liquid to cool in a stoppered bottle. It crystallizes in cubes. Silver ammonio-chloride has been used in the treatment of *chorea, epilepsy,* and *syphilis,* and as an anthelmintic, in *doses* of from one-twelfth to one and a half grains (0.005–0.1 Gm.). It is probably of little value.

Silver Arsphenamine. *N. N. R.* 1924. *Silver Salvarsan. Silver Diarsenol.*—The exact molecular formula of this compound has not been established but it is the sodium salt of silver diaminodihydroxy-arseno-benzene containing approximately 20 per cent. of arsenic and 15 per cent. of silver. It is recommended in the treatment of *syphilis* as a substitute for arsphenamine. It has been claimed for it that not only is the spirocheticide effect of the arsenical compound enhanced by the silver but that it is less prone to produce toxic symptoms in the patient. Dyer and Voegtlin (*J. P. Ex. T.*, 1921, xvii, 329) have found, from experiments on the lower animals, that while the tolerated dose is 25 per cent. smaller than that of arsphenamine, the trypanocidal dose is only one-third that of the older compound; in other words, the ratio of therapeutic to toxic dose is much more favorable for the silver salt. Walson (*Am. J. M. S.*, 1921, clxi, 418) from review of the literature and his own employment of the drug in 800 patients comes to the conclusion that it is less dangerous and, at least equally efficacious with arsphenamine. He states that in 100,000 reported injections there has been no deaths attributable to the drug. Strauss (*J. A. M. A.*, 1922, lxxviii,

632) on the other hand finds it decidedly inferior to arsphenamine.

Solutions of silver arsphenamine deteriorate rapidly when exposed to the air and must be freshly prepared at the time of use. The same precautions must be observed as in the use of arsphenamine. The dose recommended is from 0.1 to 0.3 Gm. (one and one-half to five grains) at intervals of one-half to three days.

Silver Atoxylate. *Argenti Atoxylas. Argatoxyl.* $NH_2C_6H_4As.O.AgO.OH$.—*Silver atoxylate* (*atoxylic silver*) is insoluble in water, and is the monosilver salt of para-amino-phenylarsonic acid. According to Blumenthal, atoxylate of silver contains 23 per cent. of arsenic and 33 per cent. of silver. Silver atoxylate has been used chiefly to increase bodily resistance in infectious diseases. According to Rosenstein (*All. M. C.*, 1912) its beneficial effects are due in part to its bactericidal properties and in part to a leukocytosis which it calls forth. It has been used in *puerperal septicemia, rheumatic fever, gonorrheal arthritis, scarlet fever, carbuncles,* and other infections. From five to six grains (0.3–0.4 Gm.) suspended in ten times as much olive oil may be injected intramuscularly at intervals of from one to several days. The injections are often followed by abscess formation but it is stated that the abscesses formed are sterile.

Silver Chloride. *Argenti Chloridum.* AgCl.—This is readily prepared by adding a solution of sodium chloride to one of silver nitrate, as long as it produces a precipitate. As first thrown down, it is a white, curdy substance, but it soon becomes discolored when exposed to the light. It is decomposed by solutions of the caustic alkalies, which convert it into oxide, but not by their carbonates. It is practically insoluble in water but is dissolved by solutions of the cyanides. Silver chloride has been used in *syphilis, epilepsy, chronic dysentery* and *diarrhea,* and other diseases in which silver nitrate has been given, but is probably of no value. The *dose* is from one to two grains or more (0.065–0.13 Gm.), four or five times a day.

Silver Citrate. $Ag_3C_6H_5O_7$. *N. N. R.* 1924. *Itrol.*—An odorless heavy powder which is moderately sensitive to light. It contains not less than 62 per cent. of metallic silver. This salt, which is almost insoluble in water, was introduced by Credé as a dusting powder for wounds. It is powerfully antiseptic and non-irritant. According to Marshall and Neave (*B. M. J.*, 1906, ii) it is a more powerful germicide than silver nitrate. It has been very highly recommended by Werler (*Derm. Zeit.*, vol. cxi) in the treatment of *urethritis,* as being a powerful gonococcocide and non-irritant to the mucous membrane. He employs a solution varying in strength from one part in four thousand to one in eight thousand, which is to be injected four times a day. Von Arlt (*Aerzt. Zentral-Zeit.*, 1905) employs it in various infectious conditions of the eye, such as gonorrheal *ophthalmia, trachoma* and the like. His method of using it is to dust the powder on the previously cleansed conjunctiva, and to rinse off after a few minutes, either with water or borax solution. Warler also commends it as a remedy in the treatment of chronic *cystitis.* Tilger and other surgeons have commended the remedy in the treatment of all forms of infected mucous membrane in saturated solution (1 in 3800). Pfonarlt (*W. M. W.*, 1908, No. 52) recommends the dusting of the conjunctiva with pure itrol in cases of *ophthalmia neonatorum, trachoma,* and other severe infections of the eyes, alleging that it is no more irritant than would be any insoluble foreign body. In using silver citrate, it should be remembered that it is easily decomposed, especially in the presence of organic matter, and should be kept well stoppered and protected from the light.

Silver Cyanide. *Argenti Cyanidum, U. S. VIII.*—This salt was formerly official for the purpose of preparing extemporaneously hydrocyanic acid through decomposition with diluted hydrochloric acid. It is never used as a medicine. Silver cyanide is a white powder insoluble in water or alcohol, but soluble in solution of the cyanides. It is permanent in the air if protected from light, but becomes brownish on exposure to light.

Silver Fluoride. *Tachiol. Argenti Fluoridum.* AgF = 126.88.—Mueller (*D. M. W.*, 1908) recommends this salt as an injection in *gonorrhea* in strengths of from 1 in 10,000 to 1 in 2000. Stronger solutions, he says, are locally irritant. The silver fluoride, as well as the *silver silicofluoride* (*isotachiol*), Ag_2SiF_6, have been suggested for the purpose of sterilizing drinking water. According to the experiments of Hetsch 5 Gm. per 1000 liters will destroy most of the bacteria, but when these were numerous 10 Gm. per 1000 liters are not sufficient, and the agent is therefore not suitable for this purpose.

Silver Iodate. $AgIO_3$.—This is a white insoluble powder. It is used chiefly as antiseptic in various *catarrhs,* especially in *enteritis* and *gastritis.* The *dose* is from one-twelfth to one-sixth of a grain (0.005–0.01 Gm.).

Silver Iodide. *Argenti Iodidum. U. S.* 1890. AgI = 234.80.—This salt may be readily prepared by adding a solution of potassium iodide to one of silver nitrate, and washing and drying the precipitate, which should be kept in dark amber-colored vials, protected from light. This iodide is said to have three allotropic forms and a point of maximum density at about 116° C. (See paper by G. F. Rodwell, in *Chem. News,* xx, 288; xxi, 14.) The U. S. Pharmacopœia, 1890, described it as "a heavy, amorphous, light yellowish powder, unaltered by light, if pure, but generally becoming somewhat greenish-yellow, and having neither odor nor taste. Insoluble in water, alcohol, diluted acids, or in solution of ammonium carbonate, but soluble in about 2500 parts of stronger ammonia water. It is also dissolved by an aqueous solution of potassium cyanide, and by a concentrated solution of potassium iodide, and the resulting solutions yield a black precipitate with hydrogen sulphide test-solution or ammonium sulphide test-solution. When heated to about 400° C., the salt melts to a dark red liquid, which, on cooling, congeals to a soft, yellow, slightly transparent mass. When mixed with ammonia water, it turns white, but regains its yellowish color upon being washed with water. If a small quantity of chlorine water be agitated with an excess of the salt, the filtrate acquires a dark blue color on the addition of starch test-solution." *U. S.*, 1890.

Silver iodide in suspension has been recommended as an injection for gonorrheal *urethritis* by Siter and Uhle. For this purpose, it is generally prepared extemporaneously. The formula recommended by Wilbert (*A. J. P.*, 1906) is 2.2 Gm. of silver nitrate dissolved in 50 cc. of mucilage of acacia and 45 cc. of water and to this is added 2.2 Gm. of potassium iodide which is dissolved in 50 cc. of water and thoroughly shaken. Such a suspension of silver iodide is marketed as *Silvodide.* J. C. and B. L. DeG. Peacock (*Proc. Penna. Pharm. Assn.*, 1916, p. 231) contribute a thorough review of the various methods for preparing this emulsion and conclude that mucilage of chondrus is the best suspending medium when thoroughly purified. For tests of purity, see *U. S. D.*, 19th ed., p. 1647. Silver iodide has been given in *doses* of one or two grains (0.065–0.13 Gm.) three times a day, in *epilepsy* and other chronic nervous diseases, but is devoid of value.

Silver Hexamethylenetetramine.—Two preparations asserted to contain a compound of silver with hexamethylenetetramine are known respectively as *argotropin* and *argaldon* (*D. M. W.*, 1922, xlviii, p. 696). They are used as local antiseptics.

Silver Lactate. *N. N. R.* 1924. *Argenti Lactas. Actol.* $AgC_3H_5O_3 + H_2O$.—*Silver lactate* was introduced by Credé as a surgical germicide. It is affirmed that its injection renders an infected wound rapidly aseptic without much irritation. It is soluble in 20 parts of water, and may be used in very strong, even saturated, solution. D. A. Tilger finds that the application of the pure powder to the curetted infected sore causes only moderate burning pain of short duration and acts most happily. (*M. M. W.*, 1897.) Its therapeutic properties seem to be purely local, since E. Marx found that after injection of very large doses of it into animals it does not prevent the development of pathogenetic germs. It is almost certainly decomposed at the point of injection, but, unlike silver nitrate, it does not form an insoluble compound when brought in contact with tissues, and so is able to find its way through these tissues. Fifteen grains (1 Gm.) of it have been given hypodermically without more serious symptoms than some burning pain at the point of injection. According to Marx, a remarkable rise of temperature follows the use of it in very large doses. Under the proprietary name actol has been used to a considerable extent in dentistry, decayed or decaying pulp being washed with a solution of the strength of 1 in 2000 and then dusted with itrol.

Silver Methylene Blue. *Argochrome.*—This silver salt occurs as a blue powder readily soluble in water and representing 20 per cent. of silver. According to Edelmann (*D. M. W.*, 1913, p. 2292) it is germicidal in strengths of 1 part in 160,000 and contrary to many other antibacterials, exercises a considerable disinfectant power in the blood, 1 part in 80,000 exhibiting a distinctly antiseptic action. Doses of 0.1 Gm. per kilo injected subcutaneously produce no toxic effects in rabbits. It has been used not only as a local application, but as an internal disinfectant in *septicemia, rheumatic fever* and other infectious diseases. (See Leschke, *B. K. W.*, 1920, lvii, 79.) The *dose* recommended is from one to four grains (0.06–0.25 Gm.), either subcutaneously or intramuscularly. Leschke has also reported favorable results in endocarditis streptococcus pneumonia from a *silver trypaflavin* (*argoflavin*), used intravenously in doses of approximately three-quarters of a grain (0.05 Gm.).

Silver Methylene-nucleinate. *Sophol. Silver formo-nucleinate.*—This is a dark yellow, tasteless, odorless powder, readily soluble in water. When heated it gives off formaldehyde, a residue of metallic silver being left behind. Its solutions are not stable. It contains 20 per cent. of silver.

Sophol is asserted to possess a powerful germicidal action without any irritant effect upon mucous membranes. According to Vollert (*Ther. Neu.*, July, 1906), a 0.37 per cent. solution of sophol is bacteriologically equivalent to a 1 per cent. of protargol. It has been used chiefly in ophthalmic conditions, especially *gonorrheal ophthalmia* and also in non-specific cases of *conjunctivitis* in strengths of from 5 to 10 per cent. While apparently of much value for the purpose of destroying bacteria located on the superficies of the conjunctiva, Dreser (*A. J. P.*, xviii) states that it is lacking in penetrating power and is less valuable than silver nitrate after the germs have passed through the epithelium.

The solutions should be freshly prepared, as on standing, formaldehyde is liberated which is likely to prove irritant.

Silver Nitrate Ammonia Albumose. *Hegonon.*—It is asserted to contain approximately 7 per cent. of silver organically combined. It is not precipitated by albumin or sodium chloride.

Hegonon has been employed as an antiseptic in *gonorrhea* by Klingmuller. (*M. M. W.*, 1910.) It may be used in strengths of 1 in 400 to 1 in 3000.

Under the title *Argentamin* there is on the market an 8 per cent. solution of silver nitrate in a 15 per cent. aqueous solution of ethylene diamine. It is a clear, strongly alkaline liquid, sp. gr. 0.97, which does not precipitate albumin or chlorides. On exposure to air it is liable to turn yellow, but can be cleared by filtration. Its use in medicine was proposed in 1894 by Jean Schaeffer. (*Zeitsch., f. Hyg. u. Infektions*, 1894, xvi, Bd. ii.) Hoor used it in a large number of eye cases; he asserts that it causes less pain and irritation than the silver nitrate, and penetrates deeper. He used a 5 per cent. solution in the eye from one to four times a day in the same cases as those in which silver nitrate is useful. According to Aschner (*Orv. hetil.*, 1895), it is well borne by the posterior urethra in as strong solution as 1 to 250; but the anterior urethra will not bear more than 1 to 2000. An aqueous solution containing 10 per cent. of argentamin with 30 per cent. of a 1 per cent. solution potassium bichromate has been used instead of silver nitrate as a stain for histological examination of the nerve tissues. (*Ph. Ztg.*, 1910, No. 43, 436.)

Silver Orthophosphate. *Silver Phosphate. Normal Silver Phosphate. Argenti Phosphas.* $Ag_3(PO_4)$.—This substance is prepared by dissolving silver in concentrated orthophosphoric acid; the vitreous mass which results, while still melted, is dissolved in water acidulated with phosphoric acid, yielding a permanent solution. Normal silver phosphate is a yellow, odorless, powder very sparingly soluble in water but more soluble in the presence of phosphoric acid. Spretzka (*Rév. Med. Pharm.*, v, 292) asserts that it is a valuable remedy in *gonorrhea.* The injection should contain 0.025 to 0.05 per cent. of the salt, increasing gradually to 0.25 or even 0.5 per cent.

Silver Oxide. *Argenti Oxidum. U. S. IX. Argentum Oxydatum, Argentic Oxide; Oxyde d'Argent*, Fr.; *Silberoxyd*, G. $AgO_2 = 231.76$.—Silver oxide was dismissed from the British Pharmacopœia (1914), and from the U. S. P. at the tenth revision.

In the processes for making it, silver nitrate is decomposed by potassium hydroxide or lime, the oxide being precipitated, and potassium nitrate or calcium nitrate, as the case may be, remaining in solution. When thus obtained, the oxide is an olive-brown powder. It was officially described as follows: "Silver Oxide is a heavy, dark brownish-black powder, easily reduced by exposure to light; odorless, and having a metallic taste. Silver Oxide is very slightly soluble in water, to which, however, it imparts an alkaline reaction; insoluble in alcohol; it is dissolved by nitric acid. When heated in a porcelain crucible to about 250° to 300° C., Silver Oxide is rapidly decomposed, with the evolution of oxygen, leaving a residue of metallic silver. Dissolve about 0.2 Gm. of the Oxide in a mixture of 1 cc. of nitric acid and 2 cc. of distilled water, add 10 cc. of ammonia water and dilute the liquid to 60 cc.; 10 cc. of this solution does not immediately become cloudy upon the addition of 1 cc. of nitric acid (*chloride*). A solution of the Oxide in nitric acid is colorless, and responds to the tests for identity and purity under *Argenti Nitras* when the tests are applied to a solution of proportionate strength.

"*Assay.*—Dissolve about 0.5 Gm. of Silver Oxide, previously dried to constant weight at 120° C. and accurately weighed, in 3 cc. of nitric acid and 50 cc. of distilled water in a flask, add 2 cc. of ferric ammonium sulphate T.S. and titrate the mixture with tenth-normal potassium sulphocyanate V.S. It shows, in the dried Silver Oxide, not less than 99.6 per cent. of Ag_2O. Each cc. of tenth-normal potassium sulphocyanate V.S. used corresponds to 0.011588 Gm. of Ag_2O. Each gramme of Silver Oxide, dried to constant weight, corresponds to not less than 86.0 cc. of tenth-normal potassium sulphocyanate V.S." *U. S. VIII.*

When its solution in nitric acid is precipitated by sodium chloride in excess, the supernatant liquid is not discolored by ammonium sulphide. It parts with its oxygen with great facility, being decomposed by many organic substances; in this way it causes sulphur, amorphous phosphorus, or tannin to take fire when rubbed with it, in a mortar. It should be kept in "well-stoppered, dark amber-colored vials. It must not be triturated with readily oxidizable or combustible substances, and must not be brought in contact with ammonia." *U. S. IX.*

If pills are ordered they should not be made with honey, confection of rose, or other excipient containing glucose; and, indeed most organic substances, especially in a moist state, deoxidize the oxide, reviving the silver. A case is recorded in which pills containing it exploded violently in the pocket of the patient. (See Jackson, *P. J.*, xi, 552.) An ointment from five to ten grains to the drachm, has been used as an application to *venereal sores*, and to the urethral membrane in *gonorrhea;* it should be smeared on a bougie.

Dose, one grain (0.065 Gm.).

Silver Phenolsulphonate. *Argenti Phenolsulphonas. Silver Sulphocarbolate. Silberol.* $C_6H_4(OH)SO_3Ag$.—A crystalline powder containing 28 per cent. of metallic silver, soluble in water; proved to undergo spontaneous decomposition, but said to be more permanent than itrol. Originally introduced by Zanardi as having the antiseptic properties without the corrosive action of silver nitrate, silberol has been employed by various practitioners in the treatment of *gonorrhea* and *ophthalmic inflammations*, and as a germicide in ocular surgery. It is asserted that a 2 per cent. solution is well borne as an antiseptic after operations upon the eye; also that when it is used as a substitute for silver nitrate silberol must be employed in twice as concentrated solution.

Silver Picrate. *Silver Tri-nitro-phenylate. Picratol.* $C_6H_2O(NO_2)_3Ag + H_2O$.—This occurs as yellowish crystals and is said to represent 30 per cent. of silver. It is soluble in 50 parts of water. It is used as an antiseptic in *gonorrhea* and other *catarrhs* in strengths of from one-half to two per cent.

Silver Quinaseptolate. *Argenti Quinaseptolas. Argentol.* $C_9H_5N.OHSO_3Ag$.—This substance is a yellow powder, sparingly soluble in water, which was introduced into medicine by Credé on account of its readily splitting up into oxyquinoline and metallic silver. Both septic matters and intestinal juices are said to produce this change. It has been employed either as a dusting powder or in the form of spray, or injection, 1 in 300 to 1000, in *chancres, gonorrheas*, and various other surgical infections. C. Cipriani asserts that it is a valuable intestinal antiseptic of which 15 grains (1 Gm.) may be given safely in the twenty-four hours if necessary. It is said also to be an active non-irritant antiseptic with marked hemostatic properties.

Silver, Soluble. *Argentum Solubile. Argentum Colloidale. Soluble Silver. Colloidal Silver.*—Several allotropic modifications of silver were discovered by Carey Lea in 1891. One of these has been introduced into medicine. "Soluble Silver," so-called, can be prepared by taking a mixture of 30 Gm. ferrous sulphate dissolved in 100 cc. of water and 36 Gm. of crystallized sodium citrate dissolved in 140 cc. of water and pouring this mixture with stirring into 100 cc. of a 10 per cent. silver nitrate solution. After allowing the precipitate to settle, the supernatant liquid is poured off, the precipitate dissolved in water, and again precipitated with absolute alcohol. When dried, the colloidal silver is a bluish or green-colored mass, which dissolves in water with a deep red color, but is precipitated from its solution by the addition of salt solutions. It contains 97.2 per cent. silver. The commercial preparations of colloidal silver usually contain some other protective colloid, such as a protein, and consequently vary considerably in their proportion of silver.

There are at present two forms of so-called colloidal or soluble silver employed in medicine, one of which is prepared by chemical means, and the other by electrolytic methods. The manufacturers of the latter preparations claim that the therapeutic virtues of the electrically prepared colloidal silver are much more clearly established than those of the chemically prepared varieties.

Colloidal silver was introduced into medicine by Credé with the idea that it would possess the germicidal properties of silver, and being non-toxic, might be used internally for the control of various bacterial infections. It has been used very extensively in the treatment of *septicemia, rheumatic fever, gonorrheal arthritis, diphtheria, cerebro-spinal meningitis*, and other infectious diseases. While a large number of clinicians have been enthusiastic in their praises of its efficacy, there is as yet no well-supported theory of its mode of action, and a number of careful observers have denied that it possesses any therapeutic virtues whatsoever. Whatever may be the real value of this remedy, it is evident that it does not act as Credé had expected, as an antiseptic in the blood. In the first place, Brunner has shown that its germicidal action is extremely feeble, and Cohn (*K. T. W.*, 1905) found that within forty-five minutes after its injection the silver had disappeared from the blood entirely. This same observer has stated further that it had neither prophylactic nor curative properties in rabbits, against infection with the staphylococci. On the other hand Dunger (*M. M. W.*, 1907) found that its injection leads to pronounced leukocytosis, and his conclusions have received considerable confirmation.

As has been stated elsewhere (see *Colloids*) the intravenous injection of metallic hydrosols may produce reactions similar to those following the parenteral absorption of foreign proteins and in this way increase the body resistance to bacteria.

While the germicidal power of colloidal silver is too low to explain any possible benefit from its systemic use a number of the preparations of this type are sufficiently active antibacterials to be of use as local agents in the treatment of *rhinitis, conjunctivitis, urethritis,* etc. Their range of usefulness is practically that of the silver proteinates.

The most widely used preparations of colloidal silver are as follows:

Choleval.—In this colloidal silver preparation sodium cholate acts as the protective colloid. Choleval occurs as a brownish-black, lustrous powder, easily soluble in water, containing 10 per cent. of silver. It is asserted to be actively germicidal and is used as a local application in various infectious conditions of strengths of from 0.25 to 1 per cent.

Collargol. N. N. R. 1923. *Collargolum. Argentum Credé.*—A colloidal form of silver and silver oxide stabilized by egg albumen and containing nearly 80 per cent. of metallic silver. This occurs in bluish-black scale-like pieces which, with 20 parts of distilled water, yield a brownish colloidal solution which is permanent if protected from light and heat. It is asserted to represent over 80 per cent. of metallic silver. It may be injected intravenously in solutions of from 2 to 5 per cent. strength, administering an amount of the solution equivalent to one to five grains (0.065–0.32 Gm.) once or twice a day. It is also widely employed in the form of a 15 per cent. ointment, *Unguentum Credé,* of which one-half to one drachm (1.8–3.75 Gm.) is applied at a *dose,* being vigorously rubbed into the skin.

Electrargol is marketed in bottles and in sealed tubes. The *dose* is eighty to one hundred and sixty minims (5–10 cc.) injected intramuscularly or directly into a vein.

Cargentos. N. N. R. 1924.—This is a *colloidal silver oxide,* which is said to represent 50 per cent. of metallic silver.

Lysargin.—A colloidal silver containing 60 per cent. of the metal. It forms steel blue lustrous scales, forming a brilliant brownish solution when dissolved in water. Solutions of *lysargin* are stable in the air, do not stain, are not affected by daylight, but are decomposed in direct sunlight. Possessing antiseptic value it is used as an injection in *gonorrhea* in 0.5 to 1 per cent. solution.

Argoferment is a colloidal silver preparation manufactured by an electrolytic process.

Collene.—This colloidal solution is said to represent 5 milligrammes of silver per cc. Ransohoff (*Am. Med.*, 1921, xvi, 20) has found that it is an active germicide and has used it successfully in a variety of local infections. Another advantage claimed for it is that its solutions are stable.

Dispargen.—In this colloidal preparation a decomposition product of glutin is used as the protective colloid. When dried it contains 30 per cent. of silver. It is injected, for its systemic effect, in doses of 0.04–0.1 Gm. (two-thirds to one and a half grains).

Solargentum. N. N. R. 1924.—A compound of gelatin with silver in the colloidal form containing from 19 to 23 per cent. of silver. It occurs as black, lustrous, non-hygroscopic scales, freely soluble in water, insoluble in oils or alcohol. It is used in strengths of 1 to 25 per cent. in various local inflammations.

Synthargol.—This colloidal silver is asserted to be destructive to both *Staphylococci* and *Streptococci* in 0.5 per cent. strengths in one minute. It is recommended by Gobbi (*Schweiz. Med. Woch.*, 1922, lxii, 617) as a wound disinfectant.

Silver Sodium Thiosulphate. *Sodium and Silver Thiosulphate. Sodii et Argenti Thiosulphas.*—This double salt may be prepared by dissolving freshly precipitated silver oxide in a solution of sodium thiosulphate and evaporating the solution. It is in the form of minute crystals of the formula $2Na_2S_2O_3 + Ag_2S_2O_3$, very soluble in water, but insoluble in alcohol, and possessing a sweet taste. Its solution, protected from the light, undergoes no change, and, when quite pure, does not discolor the skin or linen. Delioux states that this salt acts locally like silver nitrate, but more mildly: for *gonorrhea,* one or two parts in two hundred of water may be used.

Silver Thiohydrocarburo-sulphonate. *Argenti Thiohydrocarburo-sulphonas. Silver Sulphoichthyolate. Silver Ichthyol. Ichthargan.*—This compound of ichthyol-sulphonic acid and silver is a brown amorphous stable powder, freely soluble in water, glycerin and diluted alcohol, insoluble in alcohol, ether, and chloroform. Its aqueous solution blackens with exposure to light, and in concentrated solution it is precipitated by sodium chloride and by albumin, the albuminous precipitate being redissolved by an excess of albumin. It is said to contain about 30 per cent. of silver and 15 per cent. of sulphur.

Wood (*N. Y. M. J.*, 1903, lxxvii) found that, although ichthargan is much less poisonous, its physiological action is the same as that of silver nitrate. The germicidal power of ichthargan is certainly equal, and probably superior, to that of silver nitrate, and it is far less irritant. It is therefore, a very valuable remedy for local application in the treatment of various infectious conditions, especially those involving mucous membranes. In *tonsillitis* and *pharyngitis* it may be applied to the throat with a swab in strengths of from 5 to 10 per cent. In *urethritis* for injections, solutions of 1 to 500 to 1 in 3000 may be used; for irrigations from 1 in 2000, to 1 in 5000.

Unna (*Med. Klin.*, 1913) highly recommends the use of ichthargan in various *skin diseases,* especially *psoriasis* and *chronic eczema.* He uses an ointment varying in strength from 5 to 15 per cent.

In *eczema, ulcerations, phlegmons,* and in *lymphangitis,* the ointment varying from 1 to 15 per cent. is advised, well rubbed into the adjacent healthy skin, previously thoroughly cleansed, and also applied directly to the affected surface, if it be exposed. Ichthargan has also been administered internally with asserted excellent results for the relief of *gastritis* and especially of *gastric ulcer. Dose,* one-twentieth to one-eighth of a grain (0.003–0.008 Gm.) in half a fluidounce (15 cc.) of water, on an empty stomach.

Simaruba. *Orinoco Simaruba. Surinam Simaruba. Ecorce de simarouba,* Fr. *Simarubarinde, Ruhrrinde,* G. *Corteccia di Simaruba,* It. *Corteza de Simaruba,* Sp. (Fam. *Simarubaceæ.*)—The U. S. 1870 recognized the root-bark of the *Simaruba amara* Aubl. (*S. officinalis* DC.). This is a tree of considerable height, having alternate branches, with a bark which in the old tree is black and somewhat furrowed, in the young is smooth, gray, and marked here and there with broad yellow spots. It is a native of French Guiana and the West Indies Islands.

Simaruba bark is in long pieces, from 4 to 12 cm. wide and 2 to 6 mm. thick, folded lengthwise, light, flexible, tenacious, very fibrous, externally of a light brownish-yellow color, rough, warty, and marked with transverse ridges longitudinally rent, inner surface yellowish and longitudinally wrinkled with projecting fibers, internally of a pale yellow. It is without odor, and of a bitter taste. It readily imparts its virtues, at ordinary temperatures, to water and alcohol. The infusion is at least equally bitter with the decoction, which becomes turbid as it cools. Its constituents, according to Morin, are a bitter principle to which Gilling (*P. J.*, 1908, lxxxi) ascribes the formula, $C_{22}H_{30}PO_9$, a resinous matter, a volatile oil having the odor of benzoin, malic acid, gallic acid in very minute proportion, an ammoniacal salt, calcium malate and oxalate, some mineral salts, ferric oxide, silica, ulmin, and lignin.

A closely related species, having, however, diœcious instead of monœcious flowers, flourishes in Jamaica, San Domingo, Bahama Islands, Panama and Guatemala, extending even to Florida; it is called in Jamaica *mountain damson,* and is known as *S. glauca* DC. (*S. officinalis* Macf., not DC.) The two species have probably identical medicinal properties. The bark of the root is the part employed, the wood being nearly tasteless and inert. The middle bark contains much resin. A decoction of the bark and leaves of *S. versicolor* St.-Hil. (*Cortex Paraibæ*), is employed in Brazil as an antidote for snakebites and in the treatment of *syphilis* and *tapeworm;* the powder is used against vermin.

Simaruba possesses the same tonic properties as other simple bitters. In large doses it is said to purge and vomit. On account of its difficult pulverization, it is seldom given in substance. The best mode of administration is by infusion. The *dose* is from twenty grains to a drachm (1.3–3.9 Gm.).

Simulo.—The dried fruit of *Capparis coriacea* Burch., one of the *Capparidaceæ,* has been recommended as a palliative in *epilepsy;* also in *chorea.* (See *T. G.*, 1888, 1889; and *Th. M.*, Aug., 1888.)

Sisymbrium. *Sisymbrium officinale* (L.) Scop. *Hedge Mustard. Herbe aux chantres, Tortelle,* Fr. *Wildersenf, Hederich,* G. (Fam. *Cruciferæ.*)—This small, yellow-flowered annual, growing in Europe and in waste grounds in the United States, is said to be diuretic and expectorant and has been recommended in chronic *coughs, hoarseness,* and ulceration of the mouth and fauces. The juice of the plant may be used mixed with honey or sugar, or the seeds may be taken in substance.

Sisymbrium Sophia L., or the *flax weed,* a plant which grows sparingly in waste places in the United States, was formerly official. It is of a pungent odor when rubbed, and of an acrid, biting taste. W. Zopf attributes its poisonous qualities to a volatile alkaloid. (*Zeit. f. Nat. Pharm. Central.*, 1894, 494.) The herb has been used externally in *indolent ulcers* and the seeds internally in *worms,* calculous complaints, etc.

Diplotaxis muralis DC., (*S. Murale* L.), a plant growing about Atlantic ports, was formerly used in France in *scurvy, scrofula,* and other cachectic affections, especially associated, in the form of a syrup, with potassium iodide. Grazing sheep are said to be killed in Southern France by feeding on *Diplotaxis tenuifolia* DC., and human poisoning has occurred. This species is also sparingly naturalized like *D. muralis.* George Heyl has separated a toxic and apparently uncrystallizable alkaloid. (*Ap. Ztg.*, May 30, 1900.)

Sium.—*Sium cicutæfolium* Schrank. *Water Parsnip* (Fam. *Umbelliferæ*), which grows in British America and the United States, particularly along the water courses of the valleys of the Pacific slope, is asserted to be poisonous. A. R. Porter and N. Rogers (*A. J. P.*, 1876, 348, 483) found in it an active resinous body, toxic to animals. A volatile oil is stated by Rabak to be found in the plant in the proportion of 0.5 per cent. It is yellow and has an odor resembling that of caraway. (*Mid. Druggist,* 1905, 5.) *S. Sisarum* L., or *skirret,* a plant of Chinese origin, cultivated in Europe, has a sweetish, aromatic root. The latter is used in much the same manner as the oyster plant and parsnip. It is supposed to be a useful diet in chest complaints.

Skimmia. *Skimmia japonica* Thunb. *Miramashikimi.* (Fam. *Rutaceæ.*)—From this dwarf-growing, holly-like Japanese shrub, which is cultivated on account of its dark, shining, evergreen leaves and clusters of bright-red berries, Eykman separated a glucoside, *skimmin,* and a decomposition product, *skimmetin.* (*Abhandl. d. Tokyo Diagaku.*, No. 10, Tokyo, 1883.) J. Honda (*A. E. P. P.*, Oct., 1904), however, finds that the activity of the plant depends upon the presence of the crystalline alkaloid, *skimmianine* $C_{32}H_{29}O_9N_3$. It is a muscle poison, producing no primary excitement in the muscle, but an increasing paralysis, the influence of the alkaloid extending to involuntary muscles, such as the heart, so that in mammals arterial pressure is progressively decreased.

Skin Varnishes.—Unna at one time proposed a series of preparations for forming thin coverings on the skin. Among these were, *Bassorin Varnish, Casein Varnish, Castor oil and Shellac Varnish,* etc., Formulas for these and other skin varnishes may be found in the *U. S. D.*, 20th edition, p. 1611.

Smalt. *Smalts. Azure.*—When the impure *cobaltic oxide,* obtained by roasting the native arsenide of that metal, is heated with sand and potassium hydroxide, the mixture melts, and a beautiful blue glass results, which, when reduced to powder, forms smalt or azure. It is used chiefly in painting, and for coloring glass and porcelain.

Sodium Bisulphite. *Sodii Bisulphis. U. S. VIII. Sodium Hydrogen Sulphite. Acid Sodium Sulphite. Leucogen. Sulfite (Bi) de Soude,* Fr. Cod. *Natrium Bisulfurosum. Doppeltschwefligsaures Natron,* G. $NaHSO_3 = 104.08$.—*Sodium bisulphite* is prepared by thoroughly saturating a concentrated solution of sodium carbonate or bicarbonate with sulphurous acid gas, and collecting the crystals which form upon the cooling of the liquid. As found in commerce, it usually contains sodium thiosulphate and sulphate, and is not reliable; even when kept in well-stoppered bottles it will readily lose its crystalline character and the quantity of sulphurous acid gradually diminishes. The bisulphite, under the technical name of leucogen, was formerly largely used in many industries. It served as bleaching agent in washing wool, and in the steeping of grain, and in preserving meats and vegetable juices, because of its reducing and antifermentative character. Its use as a preservative for foods is illegal.

It was officially described as in "opaque, prismatic crystals, or a granular powder, exhaling an odor of sulphur dioxide, and having a disagreeable, sulphurous taste. Exposed to the air, the salt loses sulphur dioxide, and is gradually oxidized to sulphate. Soluble in 3.5 parts of water, and in 70 parts of alcohol at 25° C.; in about 2 parts of boiling water, and in 49 parts of boiling alcohol. When strongly heated, the salt decrepitates, emits vapors of sulphur and of sulphur dioxide, and leaves a residue of sodium sulphate. To a non-luminous flame it imparts an intense yellow color. Its aqueous solution gives an acid reaction with blue litmus paper. On the addition of hydrochloric or sulphuric acid, an aqueous solution of the salt evolves sulphur dioxide, which is recognized by its odor, and by its blackening a strip of paper dipped into mercurous nitrate T.S. and held over the escaping gas." *U. S. VIII.* For further tests for this salt see *U. S. D.*, 20th ed., p. 1612.

This salt possesses germicidal properties, which the neutral salt does not, due to the liberation of sulphurous acid. It is used as an antiseptic in *gastric fermentation* and externally in parasitic *skin diseases. Dose,* five to ten grains (0.32–0.65 Gm.).

An analogous compound employed for similar purposes is *sodium metabisulphite,* $Na_2SO_3.SO_2$.-$Na_2S_2O_5$. It is an acid salt and is also known as *sodium pyrosulphite* and *sodium anhydrosulphite.*

Sodium Boro-Salicylate. *Sodii Boro-salicylas.* —This is made by heating 125 parts of boric acid, 320 parts of sodium salicylate, and 700 parts of water in a flask until a syrupy liquid is produced; this solidifies on cooling, yielding a white product. It dissolves in water. It is used as an antiseptic and preservative.

Sodium Chlorate. *Sodii Chloras. U. S. VIII. Natrium Chloricum. Chlorate de Soude,* Fr. Cod. *Chlorsaures Natron,* G. *Clorato sodico,* Sp. $NaClO_3 = 106.46$.—"It should contain not less than 99 per cent. of pure Sodium Chlorate [ClO_2.-ONa]. This salt should be kept in well-stoppered bottles, and *great caution should be observed* in handling it, as dangerous explosions are liable to occur when it is heated, or subjected to concussion or trituration with organic substances (cork, tannic acid, sugar, etc.), or with sulphur, antimony sulphide, phosphorus, or other easily oxidizable substances." *U. S. VIII.*

It occurs in "colorless, transparent crystals (principally cubes with tetrahedral facets), or a crystalline powder; odorless, and having a cooling, saline taste. Permanent in dry air. Soluble in about 1 part of water, and in about 100 parts of alcohol at 25° C.; in 0.5 part of boiling water, and in about 40 parts of boiling alcohol; also soluble in about 5 parts of glycerin. When heated, the salt melts, then gives off oxygen (about 45 per cent. of its weight), and finally leaves a residue of sodium chloride." *U. S. VIII.*

Sodium chlorate has medicinal properties similar to those of potassium chlorate, while its greater solubility permits the use of stronger solutions. According to Brissaud, when given in daily doses of more than two drachms it is apt to produce albuminuria. In overdose it would probably cause symptoms not distinguishable from those caused by potassium chlorate poisoning. *Dose,* five to fifteen grains (0.32–1.0 Gm.

Sodium Cyanide. *Sodii Cyanidum U. S. IX.*—"It contains not less than 95 per cent. of NaCN (49.01). Preserve it in well-closed containers, protected from light." *U. S. IX.*

This salt, which was dismissed in the tenth revision of the U. S. P., may be made by various processes. One of the most recent methods is by the fusion of calcium cyanide with sodium carbonate, $Ca(CN)_2 + Na_2CO_3 = 2NaCN + CaCO_3$.

It has the advantage over the potassium salt of being somewhat less prone to absorb moisture.

It was officially described as occurring "in the form of white, opaque, amorphous pieces, or as a white, granular powder; odorless when perfectly dry; deliquescent in the air and exhaling the odor of hydrocyanic acid. *Great caution must be used in handling this salt.* It is freely soluble in cold water. An aqueous solution of the salt (1 in 20) is strongly alkaline to litmus and emits the odor of hydrocyanic acid. At a low red heat the salt fuses. To a non-luminous flame it imparts an intensely yellow color. A few drops of a solution of the salt (1 in 20) yield with silver nitrate T.S. a white precipitate, which is soluble in an excess of the solution of Sodium Cyanide, and in ammonia water. Shake 5 mils of a solution of the salt (1 in 20) with a few drops each of ferrous sulphate T.S. and of ferric chloride T.S., and then add a slight excess of hydrochloric acid; a blue precipitate (iron ferrocyanide) is produced. In 5 mils of an aqueous solution of the salt (1 in 10) a drop of ferric chloride T.S., followed by 2 mils of diluted hydrochloric acid produces neither a dark blue color (*ferrocyanide*) nor a red color (*sulphocyanate*).

"*Assay.*—Dissolve about 0.45 Gm. of Sodium Cyanide, accurately weighed, in 25 mils of distilled water, add 4 mils of ammonia water, 3 drops of potassium iodide T.S. and titrate with tenth-normal silver nitrate V.S. to the production of a permanent precipitate. It shows not less than 95 per cent. of NaCN.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.009802 Gm. of NaCN. Each gramme of Sodium Cyanide corresponds to not less than 96.9 mils of tenth-normal silver nitrate V.S." *U. S. IX.*

Sodium cyanide acts upon the system as does prussic acid. (See *Acidum Hydrocyanicum Dilutum.*) It is rarely used as a medicine. Sodium cyanide has the power of dissolving silver oxide and may be used for the removal of silver nitrate stains from clothing. According to Guthrie, a solution of three grains (0.2 Gm.) to the ounce (30 cc.), dropped in the eye every other day, will remove olive colored stains from the conjunctiva caused by silver nitrate. Five grains of it may be regarded as a usual fatal dose (see Venghauss, *A. Pharm.*, clii, p. 138), although smaller doses may occasionally take life.

Owing to the large use of the cyanides for the recovery of gold and other technical purposes, numerous accidental cases of poisoning have occurred. The symptoms and treatment of these are precisely the same as outlined under *Acidum Hydrocyanicum.*

Dose, one-eighth of a grain (0.008 Gm.).

For further tests see *U. S. D.,* 20th ed., p. 1613.

Sodium Dithiosalicylate. $S(C_6H_3(OH)COONa)_2$. *Dithion I* and *II.*—These are two isomeric salts separable by means of sodium chloride solution, the dithion I being insoluble in the latter solution. Dithion I is a yellowish-white, amorphous, soluble powder employed mostly in veterinary practice as a dusting powder of antiseptic value. The dithion II is used like sodium salicylate as an antirheumatic and antipyretic, free, it is said, from secondary action. *Dose,* thirty to sixty grains (2–4 Gm.).

Sodium Ethylate. *Sodii Ethylas. Ethylate of Sodium. Caustic Alcohol.* C_2H_5ONa.—This preparation was introduced by B. W. Richardson of England, as a caustic. He made it by adding sodium in small pieces gradually to absolute alcohol, kept at a temperature of 10° C.; hydrogen is evolved, and when, owing to the formation of the ethylate, the reaction slackens, the liquid is to be carefully heated to 37.7° C. Sodium is then cautiously added until the reaction ceases; the liquid is cooled to 10° C., and the same quantity of absolute alcohol added as was used in the beginning. (*P. J.,* 1878, 485.) *Sodium ethylate* is a white powder, frequently having a brownish tinge, dissolving in water with a hissing sound, having the property of splitting into alcohol and sodium hydroxide upon contact with even a small quantity of water or moist living tissue:

$$C_2H_5ONa + H_2O = C_2H_5OH + NaOH$$

Sodium ethylate does not appear to be of any value as an internal remedy. When, however, it comes in contact with moist tissue, owing to the liberation of its sodium, it acts as a very speedy and powerful caustic. It should always be used in alcoholic solution, and applied by means of a glass rod. It is said to cause very little pain (*L. L.,* Nov., 1878.) A *solution of sodium ethylate* was official in the Br., 1898, under the title *Liquor Sodii Ethylatis.* It was prepared as follows: "Sodium, clean and bright, 22 *grains* (Imperial) or 1 gramme; Absolute Alcohol, 1 *fl. ounce* (Imp. meas.) or 20 cc. Cautiously dissolve the Sodium in the Absolute Alcohol contained in a flask, the latter being kept cool by a stream of cold water." *Br.,* 1898.

It is described as "a colorless liquid of syrupy consistence, becoming brown by keeping. Specific gravity 0.867. When slightly heated it boils and gives off alcoholic vapors, leaving a white residue which, on being strongly heated, becomes charred. If the white residue be mixed with *water* and heated, it yields ethylic alcohol, and the solution, on evaporation, leaves a white residue consisting almost wholly of caustic soda. This solution should be recently prepared. It contains 18 per cent. of the solid substance, C_2H_5ONa." *Br.,* 1898. Gamberini and Monari (*R. T.,* 1892) assert that the 20 per cent. liniment made with olive oil, well rubbed in daily, will usually cure *psoriasis* in twenty days, and that the 10 per cent. aqueous solution is very valuable in the treatment of *lupus erythematosus,* applied after curetting.

Sodium Formate. *Sodii Formas. Ameisensaures Natrium,* G. $HCO_2Na + 2H_2O$.—Prepared by neutralizing formic acid with sodium carbonate. It occurs in colorless, rhombic prisms, which are inodorous, and have a saline, bitter taste. Sodium formate is very deliquescent and dissolves freely in water. For account of therapeutic properties see *Formic Acid. Dose,* one-half to three grains (0.032–0.2 Gm.).

Sodium Lactate. $CH_3CHOHCOONa$.—Prepared by interaction between lactic acid and sodium carbonate. It is so extremely hygroscopic that its preservation in solid form is impossible. It occurs as a colorless or yellowish syrupy liquid, neutral or slightly alkaline and having a mild saline taste, containing about 70 to 75 per cent. of the salt.

According to Curatolo (*Il Policlinico,* 1920, xxvii, 1482) sodium lactate is oxidized in the body with the production of a carbonate, with exceptional readiness. It therefore offers a useful means of alkalizing the system in cases of *acidosis.* He has employed it with especially favorable results in the treatment of acetonemia of *diabetes.* He gives it in doses of from three to eight drachms (10–30 Gm.) in a day.

Sodium Metaborate. *Antipyonin.* $NaBo_2 + H_2O$.—*Sodium metaborate* is made by boiling borax and boric acid in water. It is also erroneously called *sodium tetraborate.* It occurs as a fine, white powder, greasy to the touch, freely soluble in water. This salt is non-poisonous, devoid of caustic action, and markedly antiseptic. It is probably therapeutically equivalent to borax, but has been especially recommended in a 2 to 50 per cent. solution, or blown in as a powder, by Jaenicke and by Kafemann in *acute* and *chronic otorrhea.* Roland attributes extraordinary effects to its insufflation in *keratitis, conjunctivitis,* and other inflammatory eye conditions.

Sodium Methyl Arsenate. *Di-sodium Methyl Arsenate. Sodii Methylarsenas.* ($OAsCH_3O_2Na_2 + 5H_2O$.)—This arsenic preparation occurs as a crystalline powder containing 27.37 per cent. arsenic, easily soluble in water and less so in alcohol. It is precipitated by alkaloids; with mercuric chloride it gives a reddish precipitate, and with copper sulphate a green precipitate. It appears to be about equivalent in its physiological and therapeutic effects to sodium cacodylate (see Part I), over which the advantage is claimed that it does not impart a garlicky odor to the breath that is characteristic of the cacodylates. The *dose* is from one-third to one grain (0.021–0.065 Gm.). It is also sold under various trade names, as *arrhenal, arsynal, neoarsycodile, stenosine,* etc.

Sodium Naphthol. *Naphthol Sodium.—β-Naphthol sodium* (*microcidine*), a white powder easily soluble in water, used as a non-caustic, non-poisonous antiseptic, said to be much stronger than phenol.

Sodium Nitrate. *Sodii Nitras. U. S. VIII. Nitrate of Soda. Soda Nitre. Cubic Nitre. Chili Saltpeter. Nitras (Azotas) Sodicus. Nitrum Cubicum. Azoate de Soude,* Fr. Cod. *Natriumnitrat,* G. *Nitrato di sodio,* It. $NaNO_3 = 85.01$.—This salt is imported from South America, where it is found naturally, especially in the desert of Atacama, forming beds of vast extent. The nitrate deposits have been found uniformly through a zone 250 geographical miles in length north to south, and two geographical miles in width east to west. It was estimated that the nitrate beds contained the enormous quantity of 99,031,525 tons. The salt has been found also largely in

Brazil, in the province of Bahia, near the river San Francisco. For an account of the sodium nitrate deposits of Chili, see *Potassii Nitras.* The crude salt is in saline lumps, rather soft and friable, and damp on the surface. Its varieties are classified, according to their color and state of aggregation.

"*Caliche,*" as the crude mineral is called, contains from 48 to 75 per cent. of sodium nitrate, from 20 to 40 per cent. of sodium chloride, and smaller amounts of sodium sulphate, calcium sulphate, potassium nitrate, and potassium and sodium iodate (from 0.059 to 0.175 per cent. of iodine). Occasionally calcium borate, associated with sodium borate, is found under the beds of the nitrate.

Sodium nitrate, when pure, is in "colorless, transparent, rhombohedral crystals, odorless, and having a cooling, saline, and slightly bitter taste. Hygroscopic in moist air. Soluble in about 1.1 parts of water, and in about 100 parts of alcohol at 25° C.; in 0.6 part of boiling water, and 40 parts of boiling alcohol. When heated to 312° C., the salt melts without decomposition. At a higher temperature it evolves oxygen, and is reduced to nitrite. This salt has been praised as a remedy in *dysentery* (see 15th ed., *U. S. D.*), in the *dose* of from half an ounce to an ounce (15.5–31 Gm.) in the course of the day in dilute solution, but is at present very rarely, if ever, used in practical medicine.

Sodium Nitroferrocyanide. *Sodium Nitroprusside. Sodii Nitroferrocyanidum.* $Na_2Fe(CN)_5NO. + 2H_2O$.—This is one of the interesting series of salts, discovered by Playfair, called *nitroprussides,* which are produced, for the most part, by saturating *nitroferrocyanic acid,* formed by the action of nitric acid in potassium ferrocyanide, with different bases. For method of preparation see *U. S. D.*, 20th ed., p. 1614. The salt is in the form of large, ruby-colored, prismatic crystals, resembling those of potassium ferricyanide. It is soluble in two and a half parts of cold water, and in less quantity of hot water. Its solution, exposed to sunshine, is decomposed, with evolution of nitric oxide gas, and deposition of Prussian blue, at the same time acquiring a green color. Sodium nitroprusside, as well as the other soluble nitroprussides, is a most delicate test for alkaline sulphides, with which it produces a violet color. It is used also as a test for acetone in urine (see *Diagnostic Tests*) and in several tests for the detection of formaldehyde.

Sodium Oleate. *Sodii Oleas. Eunatrol.—Sodium oleate* may be made by dissolving 10 parts of sodium hydroxide in alcohol and adding the solution to 100 parts of oleic acid and carefully evaporating the soap which is formed to dryness. It is a whitish mass or a white powder. It dissolves in about 10 parts of water with partial decomposition, the solution thereby acquiring an alkaline reaction. The so-called *acid sodium oleate* is a mixture of this soap with free oleic acid. Sodium oleate was at one time believed to be useful in cases of *gall stone. Dose,* from fifteen to forty grains (0.9–2.6 Gm.) daily in capsules.

Sodium Phenolsulphonate. *Sodii Phenolsulphonas. U. S. IX. Sodii Sulphocarbolas, Br.,* 1898. *Sodium Sulphocarbolate. Sodium Sulphophenylate. Sodium paraphenol-sulphonate. Sodium Sulphophenate. Sulfophenate de Soude,* Fr.; *Phenolsulfosaures Natrium, Phenylschwefelsaures Natron,* G.—"It contains not less than 83.64 per cent. nor more than 87.82 per cent. of anhydrous sodium phenolsulphonate (sodium paraphenolsulphonate), corresponding to not less than 99 per cent. of the crystallized salt [$NaC_6H_5O.SO_3 + 2H_2O = 232.14$]. Preserve it in well-closed containers." *U. S. IX.*

"Sodium Phenolsulphonate occurs as colorless, transparent, rhombic prisms or crystalline granules; odorless, and having a cooling, saline, bitter taste. It is somewhat efflorescent in dry air. One Gm. of Sodium Phenolsulphonate dissolves in 4.2 mils of water, 140 mils of alcohol and in about 5 mils of glycerin at 25° C.; also in 0.8 mils of boiling water and 13.5 mils of boiling alcohol. An aqueous solution of Sodium Phenolsulphonate (1 in 10) is neutral to litmus. When heated slightly above 100° C. the salt loses all of its water of crystallization and becomes white. At a higher temperature it chars, emits inflammable vapors having the odor of phenol, and finally leaves a residue consisting chiefly of sodium sulphate. To a non-luminous flame it imparts an intensely yellow color. A diluted solution of the salt (1 in 100) is rendered pale violet by ferric chloride T.S., but remains clear; barium chloride T.S. leaves the solution of the original salt clear, but if the salt is ignited, and the residue dissolved in distilled water, the same reagent produces in the filtered solution a copious, white precipitate. Add bromine T.S. to 10 mils of an aqueous solution of the salt (1 in 100); a permanent yellow color but neither turbidity nor precipitation is produced within two minutes (*phenol*). An aqueous solution of the salt does not respond to the Test for heavy metals.

"*Assay.*—Dissolve about 0.25 Gm. of Sodium Phenolsulphonate, accurately weighed, in 50 mils of distilled water, add 50 mils of tenth-normal bromine V.S. and 5 mils of hydrochloric acid. Allow the mixture to stand for fifteen minutes, then add 2 Gm. of potassium iodide dissolved in 5 mils of distilled water, and subject the solution to residual titration with tenth-normal sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 83.64 per cent. nor more than 87.82 per cent. of $NaC_6H_5O_4S$.

"Each mil of tenth-normal bromine V.S. used corresponds to 0.004903 Gm. of $NaC_6H_5O_4S$. Each gramme of Sodium Phenolsulphonate corresponds to not less than 170.6 mils nor more than 179.1 mils of tenth-normal bromine V.S." *U. S. IX.*

The phenol sulphonates, or sulphocarbolates as they are commonly called, were introduced into medicine with the idea of obtaining the antiseptic action of carbolic acid in a non-toxic form, for it is well known that the combination of sulphuric acid with phenol destroys its toxicity. But it has been shown by Withers that the phenol sulphonates are not possessed of any antiseptic power. The claim which has been made that they are decomposed in the intestinal tract with the liberation of phenol is not supported by any scientific evidence and seems *a priori* improbable. There is neither sufficient clinical nor scientific evidence of the value of this drug in medicine. Sodium phenolsulphonate is, however, still employed as an intestinal antiseptic.

Dose, five to ten grains (0.32–0.65 Gm.).

Sodium Pyrophosphate. *Sodii Pyrophosphas. U. S. VIII. Natrium Pyrophosphoricum. Pyrophosphate de Soude,* Fr. Cod. *Pirofosfato sodico,* Sp. $Na_4P_2O_7 + 10H_2O = 446.24$.—This salt which was recognized by the U. S. VIII is prepared by heating sodium phosphate in a suitable vessel to redness. When sodium phosphate is subjected to a temperature of 44° C., it melts in its water of crystallization; if the heat be increased to 100° C., all the water will be expelled, and but 40 per cent. of the original weight remain; at 300° C. it is converted into the tetrabasic phosphate or pyrophosphate. By dissolving this residue in water, filtering and crystallizing, the salt may be obtained.

It occurs in "colorless, transparent, monoclinic prisms, or a crystalline powder; odorless, and having a cooling, saline, and feebly alkaline taste; slightly efflorescent in warm air. Soluble in about 11.5 parts of water at 25° C., and in 1.1 parts of boiling water; insoluble in alcohol. When heated to 100° C., the salt loses its water of crystallization (40.35 per cent.) without previous fusion. At a higher temperature it fuses, forming a transparent liquid, which, on cooling, solidifies to a crystalline mass." *U. S. VIII.* An aqueous solution is feebly alkaline to litmus and to phenolphthalein. It may be distinguished from the orthophosphates by the facts that it gives a precipitate with silver nitrate T.S., and does not with ammonium molybdate even when heated. The action of this salt upon the human economy is probably that of the phosphate. It has been highly recommended for removing some kinds of ink stains from colored cotton fabrics. It is said to remove the stains slowly without affecting the other colors.

Sodium Selenite. *Sodii Selenis.* Na_2SeO_3.—A white powder which freely dissolves in water. The aqueous 2 per cent. solution of *sodium selenite* stains bacteria red by the precipitation of *metallic selenium,* and has been highly recommended for the purpose of microscopic staining.

Sodium Silicate. *Sodii Silicas. Soluble Glass. Water Glass.—Sodium silicate* is made by fusing silica, fine sand, or powdered flint, powdered coal and dried sodium carbonate, mixed in powder, in an earthenware crucible, and pouring out the fused mass on a stone slab to cool. This is pulverized, and treated with boiling water, to dissolve the soluble part. The solution is filtered and concentrated. There are several forms known differing in the degree of hydration and the proportion of silica present. They are Na_2SiO_3-$NaSiO_3.9H_2O$ and $Na_2Si_4O_9$. The commercial solution of sodium silicate usually contains about 20 per cent. of silica and 10 per cent. of soda. In contact with acids the solution undergoes decomposition. It is employed in fixing fresco colors by the process of stereochromy, as a cement in the manufacture of artificial stone, and as an addition to soaps, constituting the so-called *silicate soaps.* It is also used in fireproofing fabrics and in waterproofing paper containers, etc. It is very popular as an egg preserving liquid. The eggs are carefully placed in a crock and covered over with sodium silicate solution of a certain strength. Sodium silicate has been employed as an antiseptic, in the treatment of chronic *urethritis, vaginitis,* etc., but R. Löwenhaupt asserts that when pure it is not antiseptic, any powers which it may seem to have being dependent upon the presence of free alkali in it. Sodium silicate has been suggested as a remedy in *pulmonary tuberculosis,* and Kuehn (*M. M. W.*, 1921, lxviii, p. 1612) believes that the lack of silicic acid is the cause of loss in elasticity of connective tissue, which is characteristic of advancing years, and has used intramuscular injections of sodium silicate with asserted benefit in the treatment of *arterial sclerosis.* He also claims good results in *bronchial asthma* and tuberculosis in the aged. He administered 2 cc. (30 minims) of a 1 per cent. solution intravenously at intervals of 3 or 4 days. Zeller (*M. M. W.*, 1912) recommends the internal use of a mixture of sodium and potassium silicate in the treatment of *external cancers* in conjunction with an arsenical paste. The mixture he employed contains three-quarters of a grain (0.048 Gm.) of each of the silicates, and he gave it three times a day.

Under the name of *Liquor Sodii Silicatis* the U. S. Pharm., 1890, formerly recognized the solution of sodium silicate, describing it as "a semi-transparent, almost colorless, or yellowish, or pale greenish-yellow, viscid liquid, odorless, having a sharp, saline, and alkaline taste, and an alkaline reaction. Specific gravity, 1.300 to 1.400 at 15° C. A drop of the solution, when held in a non-luminous flame, imparts to it an intensely yellow color. If a portion of the solution, largely diluted with water, be supersaturated with nitric acid, a gelatinous or pulverulent, white precipitate of silica hydrate will be produced." The solution is used in the preparation of mechanical dressings by the surgeon in the same class of conditions for which plaster of Paris is employed.

Sodium Silico-Fluoride. *Sodii Silico-fluoridum. Sodium fluosilicate.* Na_2SiF_6.—When gaseous SiF_4, generated by the action of sulphuric acid upon fluorspar in the presence of broken glass, is passed into water, hydrogen silico-fluoride, H_2SiF_6, is formed. This acid, when neutralized by sodium hydroxide or carbonate, will yield the sodium salt. It is a white odorless tasteless powder. It is difficultly soluble in water. A *solution of sodium silico-fluoride,* known as *salufer* has been asserted to be a powerful non-irritant antiseptic. The powder is a strong irritant or a mild caustic. The solution affects steel instruments. Bokenham, in experiments upon bacteria, found that in order to kill them it was necessary for the solution to be at least as strong as one to seven hundred and fifty parts, and that the drug has toxic properties, 0.05 Gm. of it causing prolonged nausea, great slowing of pulse, and reduction of arterial pressure.

Sodium Stearate. *Sodii Stearas.* $NaC_{18}H_{35}O_2$.—Sodium stearate of commerce contains varying proportions of sodium palmitate. It occurs as a white powder, with a fatty odor, soluble in hot water (with partial hydrolysis) or in hot alcohol. Pencils of sodium stearate, which have been recommended by T. G. Unna for use in *sycosis* and other parasitic skin diseases, are made as follows: Sodium stearate, 6 Gm.; glycerin, 2.5 Gm.; alcohol, sufficient to make 100 Gm. The affected part should be rubbed with the pencil five or six times daily.

Sodium Succinate. *Sodii Succinas.* $Na_2C_4H_4O_4 + 6H_2O$.—White crystals freely dissolving in water. Hammett (*J. A. M. A.*, 1917, lxix, p. 31) has found that the hypodermic injection of 1 cc. (grain one-sixtieth) of sodium succinate causes, in both normal and diseased persons, an increase of from 30 to 70 per cent. in the number of leukocytes in the blood which last for several days. *Sodium succinate* has been highly commended by Ch. F. Hope for *catarrhal jaundice. Dose,* fifteen to twenty grains (1.0–1.3 Gm.) every three or four hours.

Sodium Sulphocyanide. *Sodium Sulphocyanate. Sodium Rhodanide. Sodium Thiocyanate.* $NaCNS$.—Colorless deliquescent crystals or a white powder, very soluble in water. Bently and Le Roy have found that this salt has the power of rendering soluble the insoluble salts of calcium and magnesium and have suggested its use in the treatment of *arterial sclerosis* and *urinary calculus.* They administered it in *doses* up to one grain (0.065 Gm.). The remedy has also been suggested as a substitute for the iodides, especially in the treatment of chronic nervous conditions.

Sodium Sulphomethylate. *Sodii Methylsulphonas. Sodium Methylsulphonate.* $CH_2(OH)SO_3Na + H_2O$.—According to Rabuteau, this salt in 240-grain (15.5 Gm.) *doses* produces catharsis without cramp. (*A. J. P.*, 1880, 220.)

Sodium Sulphoricinoleate. *Sodium Sulphoricinate. Oleite.*—This substance may be prepared from castor oil by treating it with sulphuric acid at a low temperature, when a compound of sulphuric and ricinoleic acids is formed. This is known as *Turkey Red Oil* and is used in the textile and leather industries. The free sulphuric acid being removed by washing, and any unchanged oil by ether, the resulting *sulphoricinoleic acid* is then neutralized by sodium hydroxide, the finished product being a brown transparent, jelly-like liquid, with little odor, having an acrid taste, and soluble in water, alcohol, chloroform, and essential oils. It has remarkable solvent powers, dissolving phosphorus, iodine, phenol, resorcinol, naphthalene and many other medicinal substances. It was used as a glycerin substitute in Great Britain during the war. The phenol solution, often incorrectly called *phenol sulphoricinate,* is described below.

According to the experiments of Fred B. Kilmer (*Proc. A. Ph. A.*, 1890; *P. J.*, xx, 1890), its action upon mucous membranes, healthy and diseased skins, *cuts, burns,* etc., is highly soothing, and it may be taken internally or freely absorbed through the skin without danger. It would appear, therefore, to afford an excellent basis for ointments; but as productions made with it are very sticky, and often liable to harden, it is commonly best used by rubbing the substance with oleite, and then adding 50 per cent. of fatty base.

A mixture of sodium sulphoricinate and phenol is sold under the title *Phenolum Natro-sulphoricinicum* (*phenol sulphoricinate*). It is a yellowish, syrupy liquid, containing 25 per cent. of phenol and 75 per cent. of sodium sulphoricinate. The liquid itself mixes in all proportions with water, and has been especially commended as a local application in various *diseases of the skin* and in *tubercular* and other *ulcerations of the mucous membranes.* First, recommended by T. Heryng (*Th. M.*, 1896) as a local caustic application to *papilloma* and *ulcers* in the nasal and laryngeal passages, or diluted in various forms of chronic inflammation of the mucous membrane of the nose and larynx. These statements have been confirmed by various laryngologists. Prezedborski finds it of very great service both in *rhinitis atrophica* and *hypertrophica.* Berlioz (*B. G. T.*, 1890) especially recommends it in *diphtheria.* The 20 per cent. aqueous solution is to be applied locally to the throat four times a day and once or twice in the night. (*S. M.*, 1892.)

Sodium Sulphovinate. *Sodium Ethylsulphate.* $C_2H_4(OH)SO_3Na + H_2O$.—This salt occurs as a white, granular powder or in hexagonal tabular crystals, according to the method of its preparation. Its taste is cooling and rather aromatic, nearly destitute of bitterness. It is very deliquescent, and is soluble in 0.7 part of water.

It is made by the interaction of alcohol and sulphuric acid under carefully controlled conditions. For methods of preparation see *U. S. D.*, 19th ed., p. 1653.

Sodium sulphovinate is said to be a mild although active cathartic. According to Rabuteau, five drachms (19.4 Gm.) of it dissolved in three glasses of water will generally produce in the adult four or five liquid stools without pain. The *dose* for children is from two to three drachms (7.7–11.6 Gm.). The pleasantness of its taste and action would render it a favorite purgative were it not for its high price and the difficulty of preserving it, all of the sulphovinates having a great tendency on exposure to the air to break up into alcohol and a salt of surphuric acid.

Sodium Tartrate. *Sodii Tartras.* $Na_2C_4H_4O_6.2H_2O = 230.06$.—Sodium tartrate was suggested some years ago as an agreeable purgative having the advantage over other saline laxatives of being almost without taste. It occurs in the form of white crystals freely soluble in water. The dose employed was from four to eight drachms (15 to 30 Gm.).

A *solution of sodium tartrate* made by mixing solutions of tartaric acid and sodium bicarbonate and flavoring with lemon syrup has been used as a substitute for solution of magnesium citrate. For formula see *U. S. D.*, 20th ed., p. 1617.

Sodium Thiophene Sulphonate. $NaC_4H_3S_2O_3 + H_2O$.—A white powder containing about 33 per cent. of sulphur. It is soluble in water and is used either in a 5 to 10 per cent. solution or ointment in the treatment of *skin diseases.*

Sodium Valerate. *Sodii Valerianas. Sodii Valeras.* C_4H_9COONa.—This salt was dismissed from the U. S. Pharmacopœia in 1870, and from the British Pharmacopœia in 1898. For a process for preparing it, see *U. S. D.*, 19th ed., p. 1654. *Sodium valerate* is a deliquescent, very soluble salt, in snow-white masses, having the disagreeable odor of valeric acid, and a taste at first styptic but afterwards sweetish. When heated to 140.5° C., it fuses without loss of acid, and upon cooling concretes into a white solid. It is little used medicinally, having been originally introduced into the Dublin Pharmacopœia in 1850 for the sole purpose of forming, by double decomposition, iron, quinine, and zinc valerates. *Dose,* as a nervous stimulant, one to five grains (0.065–0.32 Gm.).

Soja. *Glycine Soja* Sieb. and Zucc. (*Glycine hispida* Maxim.) (*Soja hispida* Moench.) *Soy Bean. Soja* or *Sahuca Bean. Miso. Coffee Bean.* (Fam. *Leguminosæ.*)—*Soja* is an important food plant and forage crop. It is an annual having hairy, trifoliate leaves, inconspicuous, white or purple flowers, and axillary clusters of small, pendulous, hairy legumes containing 2 to 5 seeds. The latter are yellow, green, brown, black or parti-colored. Stingl and Morawski (*Monatsschrift für Chemie,* April, 1886) have determined the presence in this bean of a ferment said to be one of the most powerful known in its action upon starch, two-thirds of which it converts into sugar and one-third into dextrin. Soy beans are an important article of diet in China and Japan, three important products are made from them—namely, soy bean milk, soy bean cheese and soy bean sauce called *shoju* or *shoyu.* In this country they have been used as a coffee substitute. Soja bean has been suggested as a diabetic food, but it contains upwards of 25 per cent. of carbohydrates. Sinclair has highly recommended the soy bean as an infant food in *summer diarrhea* and similar complaints. (*J. A. M. A.*, 1916, lxvi, 841.)

The average composition of soy beans is water 10 per cent., fat 18 per cent., protein 40 per cent., carbohydrates 22 per cent., crude fiber 5 per cent., ash 5 per cent.

The proteids are remarkable for the large proportion soluble in water (over 75 per cent.). The carbohydrates are about equally divided between sucrose and starch with some dextrins and other carbohydrates. No reducing sugar is present. The seeds also contain *urease*, an enzyme which decomposes urea with the formation of ammonium carbonate, and is used for the determination of urea in the urine or other fluids.

Solanine.—A physiologically active substance obtained from the sprouts of *Solanum tuberosum* L. (potato), and other *Solanaceæ.* It is classed both as a glucoside (because of its being decomposable into glucose), and also as an alkaloid (because of its basic properties). *Solanine* is in the form of a white, opaque powder, or of delicate acicular crystals, somewhat like those of quinine sulphate, though finer and shorter. It is inodorous, of a bitter taste. The divergence of formulas which have been given by chemists for solanine suggests very strongly that either the substances investigated were in an impure state or that there are several allied compounds found in this group of plants. Firbas (*Monats. f. Chem.*, 1889, x, 541) reports two alkaloidal glucosides in the potato, *solanine* and *solaneine.* Subsequently Davis (*P. J.*, 1902, xv, 160) reported the same two principles in the dulcamara. The melting point of solanine is variously given from 235° C. (Davis) to 250° C. It is not affected by alkalies but when boiled with dilute acids is hydrolized into a mixture of sugars and *solanidin.* Solanine is practically insoluble in water or ether or chloroform, sparingly soluble in hot ethyl alcohol, but easily in amyl alcohol. It is scarcely alkaline to litmus but is capable of neutralizing acids. It is distinguished by the deep brown or brownish-yellow color which iodine imparts to its solution, and by its reaction with sulphuric acid, which becomes first reddish-yellow, then purplish-violet, then brown, and, lastly, again colorless, with the deposition of a brown powder. This test is said not to be interfered with by the presence of morphine. The salts which solanine forms with acids are mostly amorphous in character. The oxalate, chromate, and phosphate form crystalline crusts. The acid sulphate is said to be very stable, and is not decomposed by water even on heating, in contradistinction to the neutral salt. It is amorphous and very bitter.

The physiological action of solanine is very similar to that of the saponins. Perles (*A. E. P. P.*, 1889, xxvi) found that when mixed with the blood outside of the body it caused rapid coagulation with destruction of the blood corpuscles. In the frog it produced a centric paralysis, with later paralysis of the heart. In mammals it produced excitement, with tremors, followed by central paralysis, collapse, and death in deep coma, preceded by a fall of temperature which is so great as to be almost characteristic. Vomiting and diarrhea were frequently observed, and the urine contained albumin and often hemoglobin. After death inflammation of the gastro-intestinal mucous membranes, and also a parenchymatous and even hemorrhagic nephritis were found. According to Capparoni (*B. G. T.*, May, 1888), minute doses of solanine, while diminishing the rapidity of the heart's action, increase at the same time the arterial pressure.

In the researches of Max Perles, the action of *solanidine* was very similar to that of solanine, the chief difference between the two being that solanine is a violent local irritant, while solanidine seems free from local irritant properties.

Solanine has been used with asserted benefit by Capparoni (*B. G. T.*, May, 1888) and others, as an antispasmodic remedy in *asthma, bronchitis* and *cystitis.* It is also attributed with a sedative action on the central nervous system, and has been used by Capparoni in the treatment of ataxic pains. Waugh (*J. A. M. A.*, 1906) asserts that it is of great service in *epilepsy.*

Schmiedeberg (*A. E. P. P.*, 1899, xxxvi, 361) describes an epidemic of solanine poisoning from sprouted potatoes in which the symptoms were headache, colic, vomiting, diarrhea, dilated pupils, first accelerated, then slowing of the pulse, mental confusion and sometimes unconsciousness. Hansen (*Science*, 1925, lxi, 340) has reported a similar group of poisonings occurring in an Illinois family, two of whom died.

The *dose* of solanine, as given by different writers, varies widely, probably because of varying degrees of purity of the drug employed.

Waugh states that of the pure alkaloid, the proper *dose* is one-twelfth of a grain (0.005 Gm.), but other writers have given much larger amounts.

Solanum.—The genus *Solanum* (Fam. *Solanaceæ*) contains a number of species which are possessed of active physiological properties and some of which have been used to a considerable extent in medicine. The *S. Carolinense* and *S. Dulcamara* are recognized by the N. F. under the titles of *Solanum* and *Dulcamara* respectively, and are described in Part I.

S. aculeatissimum Jacq., known as *Apple of Sodom*, is indigenous to Brazil. It is a spiny undershrub with pinnately 5–7 lobed leaves, white flowers and orange-colored berry-fruits, the latter containing *solanine.*

S. bacciferum (?), of Jamaica, yields the so-called *Susumber berries*, which are habitually used as fruit by the natives, but Manners has recorded in the *Ed. M. J.*, 1867, fatal poisoning by these berries, death being preceded by dilated pupils and collapse. It is probable, however, that the berries were not true susumber berries but were the product of some other species of solanum.

S. Chenopodium F. Muell.—In this plant, which is a native of Queensland, C. E. Sage has found the alkaloid *solanine.* According to E. B. Ormerod the plant is useful in the treatment of *dysentery.* (*P. J.*, lxviii, 1902.)

D. Freire has obtained from the fruit of *S. grandiflorum* Hort., or *wolf fruit*, a twining shrub of Brazil, a toxic alkaloid, *grandiflorine.* (*C. R. A. S.*, cv.)

S. Jacquinii Willd. is used in India as a diaphoretic and expectorant.

S. Lycopersicum L. *Tomato Plant* (formerly termed the *Love Apple*).—The tomato is believed by many practitioners to be an injurious article of diet to gouty persons. The acidity of the juice is due at least in part to citric, malic and oxalic acids. Solanine is said not to be present in the juice but has been found by George W. Kennedy

(*P. J.*, 1873) in the herbaceous part of the plant. It probably also exists in the seeds. (*A. J. P.*, xxxiv.) Tomato is exceptionally rich in vitamines.

S. nigrum L. *Black*, or *Garden*, or *Common Nightshade. Duscle. Hound's Berry. Morelle.*—This is an annual herb in temperate climes although an undershrub in tropical regions. Its leaves are simple, ovate, entire or sinuate-dentate. Its flowers are small and white and its fruits, which are sparingly employed for pies and jams, are globular berries about ¼ inch in diameter. Its occurs widely in shaded and rich open ground throughout the United States. The leaves and tops of this plant have been recently admixed with and substituted for *Belladonnæ Folia.* They may be readily detected by their absence of glandular hairs, by the rotate corolla and by the smaller size of the leaves which are frequently wavy-toothed. The leaves have been used in medicine in the treatment of *scrofulous dyscrasias*, and are said to produce diaphoresis when in overdose; also nausea, purging, and nervous disturbance. The poisonous properties commonly attributed to this plant are, however, to be doubted, since Dunal of Montpellier, states, as the result of numerous experiments, that the berries are not poisonous to man or the inferior animals; and the leaves are said to be consumed in large quantities in the Isles of France and Bourbon and in the Hawaiian Islands by the natives as food, having been previously boiled in water. In the latter case the active principle of the plant may have been extracted by decoction. Introduced by importers under the name of *jurubeba*, this plant was examined by Kobert and found to be inert. According to Peckoldt, however (*Ph. Rund.*, 1889), true jurubeba is *Solanum insidiosum* Mart., from which the results would have been more favorable. It is used in Brazil in *gonorrhea* and *syphilis*.

S. Pseudocapsicum L., *Jerusalem*, or *Winter, Cherry.*—This is a small branching shrub of the tropics and sub-tropics and widely cultivated for greenhouse or house decoration when covered with its bright colored berries. It yields a fruit whose resemblance to the common cherry is said to have led to its being eaten by children with fatal results.

S. rostratum Dunal. *Sand Bur. Buffalo Bur. Beaked Nightshade. Bull Nettle.*—This very prickly plant, which grows on the prairies from Nebraska to Mexico, and is noteworthy as having been the original food of the Colorado bettle or potato bug, has yielded to W. S. Amos an alkaloid. (*Notes on N. R.*, iv.)

S. tuberosum L. *Potato.*—The *common white potato* is a perennial, weak-stemmed herb indigenous to low valleys of Chile, Peru and Bolivia and widely cultivated throughout the world on account of the popularity of its tubers as a food. The herbage appears, at certain stages of growth, to be toxic and several cases of poisoning have been reported from potato sprouts (see under *Solanine*).

Solidago. *Golden-rod. Verge d'Or*, Fr. *Goldruthe*, G. (Fam. *Compositæ.*)—This is a large genus of perennial herbs most of the species of which are native to the Eastern half of North America. Of these *S. odora* Ait., or the *Sweet Golden-rod*, was formerly official. *S. Virgaurea* L. [*S. Randii* (Porter) Britton], or *European Golden-rod* occurs on dry or granitic soil in the northern United States and Europe, and was formerly directed by the Dublin College. It is aromatic, astringent, in hot infusion diaphoretic, and is asserted to be diuretic. (*Rev. Gén. de Clin. et de Thérap.*, 1889.) For an analysis of *S. rugosa* Mill., see *A. J. P.*, 1893, 122.

Species of golden-rod are of medical importance as causative agents of hay-fever (see under *Diagnostic Tests*).

Soluble Mercury of Hahnemann. $NH_2(Hg_2)NO_3$.—This is prepared by adding, drop by drop, a diluted solution of ammonia to an equally diluted solution of mercurous nitrate, until the precipitate begins to be paler than at first. It is a black powder. When it has a gray color, the fact shows that too much ammonia has been employed in its precipitation. In this case $NH_2(Hg_2)NO_3$ yields $NH_2(Hg)NO_3 + Hg$. This preparation was at one time included in the French Codex. It has been used in *syphilitic* diseases.

Solurol. *Hyminic Acid. Nucleotinphosphoric Acid.* $C_{30}H_{46}N_4O_{15}.2P_2O_5$.—A yellow amorphous powder, easily soluble in water. It is used as an uric acid solvent in *gout, rheumatism* and similar affections. *Dose*, four to eight grains (0.25–0.5 Gm.).

Solution of Dialyzed Iron. *Liquor Ferri Dialysatus. Liquor Ferri Oxychlorati*, P. G.—*Dialyzed solution of iron* was formerly recognized by the Br. Ph. It is made by treating a solution of ferric chloride with ammonia, whereby ferric hydroxide is precipitated, which by agitation is dissolved, placing the thick liquid in a dialyzer, and suspendng this in water, which is to be constantly renewed so long as any traces of hydrochloric acid are found in it. The following process has been used in the United States: To one hundred parts of solution of ferric chloride, sp. gr. 1.26, thirty-five parts of ammonia water, sp. gr. 0.923, may be gradually added. The precipitate which almost immediately forms is redissolved, and the solution introduced into the dialyzer, which is then suspended upon the water, contained in a suitable vessel. When the water in the outer vessel ceases to produce a precipitate with silver nitrate, or to show an acid reaction, the preparation in the inner vessel is assayed by evaporating 10 cc. to dryness on a water bath, to ascertain the amount of ferric oxychloride in solution; then the final solution is diluted so that it shall contain 10 per cent. of dry oxychloride.

Dialyzed iron is a colloidal solution of *ferric oxychloride* in water. The solution is of a transparent reddish-brown color, free from the usual astringent, styptic taste of iron preparations. It mixes in all proportions with distilled water, alcohol, syrup, and glycerin, but water containing any saline impurity is apt to cause precipitation. When gelatinization occurs, agitation with a small quantity of solution of ferric chloride will usually restore it to fluidity, care being observed not to add in excess. Contact with the alkalies should be avoided, even in minute quantity, indeed it is best administered without addition of any kind, or simply diluted with distilled water.

The British Pharmacopœia formerly directed that its specific gravity should be 1.047, and "100 grains should afford a precipitate with a solution of ammonia which, washed, dried and ignited, weighs five grains." E. B. Shuttleworth (*Can. Pharm. Journ.*, Dec., 1877) recommends a solution which has the sp. gr. 1.040 and yielding 5 per cent. of residue when well dried on a water bath as the best for medicinal use. The specific gravity test can be relied upon, if the solution does not give a precipitate with silver nitrate or become of a blackish-blue color upon treatment with tannin, showing the absence of free ferric chloride. There is good reason for believing that much of the so-called dialyzed iron formerly found in commerce was made by adding freshly precipitated ferric hydroxide to solution of ferric chloride until it ceased to be dissolved and then filtering the solution. *Ferrum catalyticum*, or *catalytic iron*, used in Europe, is probably made in this way.

Dialyzed iron is also upon the market in the form of scales which enable the solution to be prepared extemporaneously.

Solution of dialyzed iron has been very highly praised as a ferruginous tonic free from astringency. It is capable of acting as an antidote to arsenic by virtue of the readiness with which it yields hydrated ferric oxide, but it is safer to depend upon the official antidote, ferric hydroxide with magnesium oxide (see *Ferri Hydroxidum Cum Magnesii Oxido*). *Dose*, from one-half to one fluidrachm (1.3–3.75 cc.).

Solution of Magnesium Bisulphite. *Liquor Magnesii Bisulphitis.*—George Archibald, having found that magnesium bisulphite is capable of arresting the butyric acid fermentation, proposed a solution of it as a remedy in *heartburn*. He prepared it by treating the magnesium carbonate with sulphurous acid, adding to an ounce of water sixteen grains of the sulphite thus formed, and passing sulphurous acid gas through the mixture until a clear solution is obtained. (*P. J.*, 3d series, ii, 502.)

Solvents for Industrial Purposes.—A surprisingly large number of solvents have made their appearance since the stimulus of chemical research produced during the World War. Liquid organic chemical compounds which had hitherto been purely academic or research interest were produced on a large size manufacturing scale, as for instance ethyl acetate which is now available in tank car lots. Particularly along the lines of research in lacquers, cellulose-derivative varnishes, etc., has the competition been particularly keen to find the solvent with the ideal properties. These ideal qualities are not easy to describe briefly, but among the foremost qualities desired are, freedom from color, freedom from objectionable odor, immiscibility with water, freedom from hygroscopic qualities.

A recent article in the *J. I. E. C.*, 1925, p. 560 enumerates the following solvents in the accompanying classifications; those not italicized are described elsewhere in this volume.

Solvents boiling below 100° C.: Ethyl Acetate (77°); *Methyl Acetate*, CH_3COOCH_3 (56°–57°); *Ethyl Propionyl*, CHCOCH (98°–102°); Ethyl Alcohol (78°); Isopropyl Alcohol (82°); Acetone (57°); Benzene (80°).

Solvents boiling about 125° C.: *Diethyl Carbonate*, $C_2H_5CO_3C_2H_5$ (125°); *Butyl Acetate*, $CH_3COOC_4H_9$ (125°); Amyl Acetate (138°–142°); Ethyl Butyrate (121°); *Butyl Alcohol*, C_4H_9OH (117°); Amyl Alcohol (126°–132°); Toluene (111°).

Solvents boiling between 150° and 200° C.: *Ethyl Lactate*, $CH_3CHOHCOOC_2H_5$ (155°); *Ethyl Acetoacetate*, $CH_3COCH_2COOC_2H_5$ (181°); *Diethyloxalate*, $(CO_2)_2(C_2H_5)_2$ (186°); *Ethyl Benzoate*, $C_6H_5COOC_2H_5$ (212°); Benzyl Alcohol (205°); *Diacetone Alcohol*, $(CH_3)_2COH.CH_2COCH_3$ (164°); Xylene (143°).

Solvents boiling near 300° C., or above: *Tricresyl Phosphate*, $(C_7H_8)_3PO_4$ (below 350°); *Triphenyl Phosphate*, $(C_6H_5)_3PO_4$ (below 325°); *Diethylphthalate* (290°); *Dibutylphthalate*, $C_6H_4(COOC_2H_5)_2$ (below 340°); *Diamylphthalate*, $C_6H_4(COOC_5H_{11})_2$ (340°); *Diethyl Tartrate*, $C_4H_4O_6(C_2H_5)_2$ (below 280°); *Triacetin*, $(C_2H_3O_2)_3C_3H_5$ (267°).

The evaporation time of these solvents is a matter of great practical importance. Some solvents evaporate completely within a reasonably practical time. Ethyl acetate is the speediest in this respect and anhydrous ethyl alcohol next. These facts are of great economic importance in the manufacture of automobile lacquers particularly.

Elasticity of the film in lacquers is produced by the agency of what are known as *plasticizers.* Among the more important plasticizers are: diethylphthalate, diamylphthalate, dibutylphthalate, triphenylphthalate, phosphate, tricresyl phosphate, butyl tartrate, and camphor.

Somatose.—This is an artificially digested meat albumin containing 51.6 per cent. of deutero- and 13.4 per cent. of hetero-albuminoses, 5 per cent. of peptone, 1 per cent. of moisture, and 5 per cent. of nutrient salts. A yellowish, odorless, and almost tasteless powder.

Iron Somatose is a similar preparation containing 2 per cent. of iron in combination.

Milk Somatose is a soluble nutrient prepared by the same digestive process from casein, containing 5 per cent. of tannin. It is a light yellowish powder, readily soluble in water.

Somnoform.—A proprietary anesthetic said to contain ethyl chloride 60 per cent., methyl chloride 35 per cent., ethyl bromide 5 per cent. It was at one time widely used as a general anesthetic specially for dental operations. While it has been stated that it possesses no unpleasant aftereffects when properly administered, the numerous cases where stomachic disturbances have arisen after its use would lead one to doubt this statement. (For a study of its physiological action, see *B. M. J.*, 1903, 1.)

Sonchus. *Sonchus oleraceus* L. *Sow Thistle.* (Fam. *Compositæ.*)—A coarse weed, having runcinate-pinnatifid leaves clasping by a heart-shaped base and producing corymbs of pale yellow flowers in summer and autumn. This European plant is commonly found in waste places around dwellings in the United States. The brownish gum left after the evaporation of the juice of this plant is said to be a powerful hydragogue cathartic, in *doses* of from two to four grains (0.13–0.26 Gm.). Combined with aromatics or belladonna, it may be used instead of elaterium in *dropsy.* (*Med. Bull.*, July, 1888.) It has also been used as a so-called cure for the opium habit. (*Pac. Pharm.*, 1908, 113.)

Soot. *Fuligo Ligni.*—This well-known substance has a peculiar odor, and a bitter, empyreumatic, and disagreeable taste. Its composition varies according to the source and conditions of its formation. When obtained by the combustion of resinous materials it may contain oily distillation products soluble in ether; when obtained by the combustion of wood it may contain pyroligneous (acetic) acid and products peculiar to wood tar, such as creosote, guaiacol, and phenols. Of course mineral substances from the ash of the wood may also be present.

Soot was formerly official with the Edinburgh College, and the Scotch physicians prescribed it as a tonic and antispasmodic. It has also been employed as an external remedy in skin diseases. (See 14th ed., *U. S. D.*)

Sophora. *S. speciosa* Benth. *Coral Bean* (Fam. *Leguminosæ*).—From the poisonous seeds of this Texan tree, H. C. Wood obtained a volatile liquid alkaloid *sophorine*, which, according to P. C. Plugge, is identical with cytisine, $C_{11}H_{14}ON_2$. This same alkaloid probably exists in many species of the genus, as Parsons found a liquid alkaloid in *S. sericea* Nutt., *crazy-weed*, which grows in the prairies of Nebraska and Kansas to Colorado, Texas and Arizona. (*Rep. Commissioner of Agricult.*, 1879, and *N. R.*, 1881, 67.) Greshoff (*P. J.*, xxii) found a poisonous alkaloid in the leaves of *S. tomentosa* L., the seeds and roots of which are used in Ceylon and Java as a remedy for *cholera*. Plugge, however (*A. Pharm.*, 1895) affirms that *matrine*, the alkaloid discovered by Nagai in *S. angustifolia*, is distinct from cytisine. Kondo (*J. Pharm. Soc. Japan*, 1921, p. 1047) finds that is a monoacidic tertiary amine and assigns it the formula $C_{15}H_{24}N_2.CO$.

Sorbus. *Sorbus Aucuparia* L. (Now *Pyrus Aucuparia* (L.) Erhr.) *Mountain Ash. Rowan Tree. Sorbes*, Fr. *Eberesche, Vogelbeere*, G. (Fam. *Rosaceæ.*)—A European tree with odd pinnate leaves having numerous leaflets, compound corymbs of white flowers and small, bright red, pome-fruits. It is extensively cultivated in the United States and becoming naturalized. Its fruit contains a peculiar kind of sugar called *sorbinose*, $C_6H_{12}O_6$, isomeric with levulose. It reduces Fehling's solution, but is not fermentable with yeast. Hoffmann has also discovered two new acids, which he designates as *sorbic* and *parasorbic acids*, $C_6H_8O_2$. Sorbic acid forms colorless needle-like crystals fusing at 134.5° C., while parasorbic acid is a lactone-like body, which, on heating with concentrated acids or solid alkali, changes into sorbic acid. M. J. Boussingault has found in it a crystalline saccharine principle, *sorbitol*, isomeric with mannitol, melting, when anhydrous, at from 110° to 111° C., when hydrated, at 102° C. Its formula is $C_6H_{14}O_6$. It does not undergo the vinous fermentation. (*P. J.*, 1872, 28.) The seeds of the fruit contain 22 per cent. of fixed oil. The fruit has been used in *scurvy*, and in infusion, as a remedy in *hemorrhoids* and *strangury*. All parts of the tree are astringent, and may be employed in tanning and dyeing black. *S. americana* Marsh. (now *Pyrus americana* (Marsh.) DC.), or *American Mountain Ash*, probably has similar virtues to the European species. Edwin Johanson found the fruit to yield from 4.92 to 6.6 per cent. of malic acid. (*Ph. Z. R.*, i, 1882.)

Sorghum.—This is a group of annual fodder-grasses whose outstanding characteristic is their inflorescence which is an open or contracted panicle of spikelets arranged in threes. There are a number of varieties and these are usually distinguished as "saccharine" sorghums and "non-saccharine" sorghums. The former are tall, leafy, contain a sugary sap and are referred to *Andropogon Sorghum* var. *saccharatus* Koern. The latter include the *kafirs, milos, durra* and *broom corn*, all of which are varieties of *Andropogon Sorghum* (L.) Brot. All of our sorghums are believed to have been derived from a wild progenitor, the *Andropogon halepensis* (L.) Pers. or *Johnson Grass*. The saccharine sorghums are cultivated in the United States to some extent as a forage crop. They are not used in the manufacture of sugar, owing to the difficulty of effecting its crystallization. Broom corn has been cultivated in the United States since 1798 and is especially adapted to the manufacturer of brooms and brushes. In some of the semi-arid districts of the West it is reported that cattle have been poisoned from eating of the green sorghum, usually of a second growth. This is apparently due to the production of hydrocyanic acid in the leaves.

The non-saccharine sorghums, *Kaffir corn* and *Durrha*, were used during the war as officially permitted substitutes for wheat.

Sozoiodolic Acid. *Sozoiodol. Diiodoparaphenolsulphonic Acid, Crystalline.* $C_6H_2I_2(SO_3H)OH + 1\frac{1}{2}H_2O$.—This is a white glistening powder, odorless, of slightly acid taste, slightly soluble in cold water, more easily in hot water. It is decomposed on heating to 200° C., giving off violet vapors. It contains about 53 per cent. of iodine. It can be recognized by heating, or by adding sulphuric acid to it in hot solution, when iodine separates. Ferric chloride imparts a dark violet color to the aqueous solution; silver nitrate throws down a white precipitate of silver soziodol completely soluble in diluted nitric or sulphuric acid. For an outline of the process of manufacture, see *Squibb's Ephem.*, Feb., 1893. Soziodol is used as a local remedy, resembling somewhat iodoform in its range of usefulness. According to Langaard, 2 per cent. is sufficient to kill bacteria of pus; for wounds, a 10 per cent. mixture with powdered talc is advocated. Lassar praises it in *eczema*, *herpes tonsurans, impetigo*, etc.; it has also been much used in *otitis* and *rhinitis*. Langaard has found that fifteen-grain doses have no appreciable effect upon rabbits, and Bufalini gave twenty-two grains a day in *phthisis* without unpleasant effect. The soziodolates have also been called by the proprietary name of *Ronozol salts*. The following salts have been used:

Potassium sozoiodol, sparingly soluble; a desiccant indicated in *eczema*. It is usually employed with talc in the proportion of 1:5 or 1:6. *Zinc sozoiodol*, a local irritant in solutions of from 1:20 to 1:50; a caustic, in a solution of 1:5. *Mercury sozoiodol*, a caustic, even in a solution of 1:10. Miller affirms that its solution of 2½ per cent. kills the acarus of *scabies* in twenty-four minutes. It has been used as an antisyphilitic in *doses* of one grain (0.065 Gm.).

Schwarz recommends pills, each containing one-third of a grain of sozoiodol mercury and one-fifteenth of a grain of powdered opium. (*Th. M.*, 1908, 299.)

Sodium Sozoiodolate (*sodium soziodol*) occurs as colorless, inodorous, crystalline needles, soluble in about fifteen parts of water, also soluble in alcohol or glycerin. The finely powdered substance mixed with equal parts of sulphur is employed by insufflation in treating *diphtheria, laryngitis, nasal tuberculosis*, etc. It is also used in a 2 to 5 per cent. solution as an antiseptic douche or wash in *gonorrhea*.

Sozolic Acid. *Acidum Sozolicum. Phenolsulphonic Acid. Aseptol.* $C_6H_4(SO_3H)OH$.—Ortho and paraphenolsulphonic acids are both formed when phenol is dissolved in concentrated sulphuric acid; at medium temperatures the former is far more abundant, but it readily passes into the para compound on the application of heat. Sozolic acid has a very faint odor of phenol. The paraphenolsulphonic acid alone is the basis of the formerly official phenolsulphonate. It is readily soluble in water, alcohol, and glycerin, and is used so diluted as to contain from 3 to 10 per cent. of the active principle. The orthophenolsulphonic acid in 33⅓ per cent. solution has received the trade name of *aseptol*. The ortho acid changes on heating into the isomeric paraphenolsulphonic acid, and this change takes place even in the aqueous solution of the former, a fact which should be remembered in the preparation of aseptol solutions.

E. Riegler (*W. M. Bl.*, xviii, 1895) proposes aseptol as a test for albumin in urine. One part in 20,000 causes coagulation; the precipitate with albumin does not disappear with heat. The solutions of albuminose and peptones are also precipitated, but the precipitates of these disappear with heat. The solution of aseptol undergoes decomposition when exposed to light.

Schiff and Beilstein asserted that phenolsulphonic acid acts like tannic and gallic acids, precipitating albumen and alkaloids, and being capable of replacing gallic acid in the making of leather and in pharmacy. There is, however, no sufficient reason for believing that the substance can be used in medicine in the place of the vegetable acids named. It has also been asserted that phenolsulphonic acid is a powerful antiseptic, but in a careful series of comparative experiments, F. A. Tucker (*Notes on New Remedies*, 1892) found that it had not more than one-third the antiseptic power of phenol.

Sparteine Sulphate. *Sparteinæ Sulphas. U. S. IX.*—The alkaloid sparteine is described in Part I under *Scoparius* from which drug it is obtained. The U. S. IX recognized the sulphate and officially described it as in "colorless, rhombohedral crystals, or as a crystalline powder; odorless, and having a slightly saline and somewhat bitter taste. It is hygroscopic. One Gm. of Sparteine Sulphate dissolves in 1.1 mils of water and in 3 mils of alcohol at 25° C.; insoluble in chloroform or ether. Its aqueous solution (1 in 20) is neutral or acid to litmus. Add 25 mils of ether and a few drops of diluted ammonia water, avoiding an excess, to about 0.1 Gm. of Sparteine Sulphate in a test tube, then add to the mixture an ethereal solution of iodine (1 in 50) until the liquid, when shaken, turns from an orange to a dark reddish-brown color. After a short time, the bottom and sides of the test tube will be coated with minute, dark greenish-brown crystals. Barium chloride T.S. produces a white precipitate insoluble in hydrochloric acid when added to an aqueous solution of Sparteine Sulphate. Incinerate about 1 Gm. of Sparteine Sulphate; not more than 0.1 per cent. of ash remains. A solution of about 0.1 Gm. of the salt in 2 mils of sulphuric acid is colorless (*readily carbonizable organic impurities*). Shake about 0.1 Gm. of Sparteine Sulphate in a test tube with 5 mils of potassium hydroxide T.S., the liquid at first becomes turbid, and small, colorless or nearly colorless drops of sparteine gradually collect on the surface. Suspend a strip of moistened red litmus paper in the mouth of a test tube, and apply a gentle heat; the test paper gradually acquires a blue color, but no odor of ammonia is perceptible (*ammonium salts*). A mixture of about 0.1 Gm. of Sparteine Sulphate, 0.5 mil of chloroform and 0.5 mil of alcoholic half-normal potassium hydroxide V.S. does not emit an odor of phenylisocyanide on heating (*aniline*)." *U. S. IX.*

G. Marque (*J. P. C.*, xxx, 555) states that if a small quantity of sparteine sulphate be mixed with about one-third of its weight of chromium trioxide, and gently heated in a porcelain dish, the mass will soon turn green and emit a strong odor resembling coniine. Moureu and Villier (*Bull. Soc. Chim.*, 1903 (6), 12, 545) confirm Stenhouse's formula for sparteine sulphate, $C_{15}N_{26}N_2.H_2SO_4 + 5H_2O$.

The statements of different investigators both clinical and pharmacological, concerning the effects of sparteine have been so extraordinarily contradictory that they are at present impossible of reconciliation; one is perforce driven to the belief that the different investigators did not have the same principle. It has been variously claimed to accelerate and to slow the pulse rate, to increase and to diminish the contractile power of the heart, to arrest the heart in systole and in diastole, to raise the blood pressure or to lower it, and finally to have no effect on the circulation whatsoever. Again it is claimed by some that it diminishes, and by some that it increases the quantity of urine, and by others that it has no effect upon the kidney. These discrepancies cannot be harmonized on the ground of difference in dosage. For review of the extensive literature upon the subject, the reader is referred to McNider (*Southern Med. Journ.*, 1910, iii, p. 498), and to Pilcher and Sollmann (*J. P. Ex. T.*, 1915, vi, p. 373). It has been used clinically in the treatment of various forms of cardiac disorders, such as *endocarditis*, but especially in such functional derangements as *nervous palpitation*, the *tachycardia of Grave's disease*, etc. It has also been employed as a diuretic in *dropsies*, especially when due to cardiac lesions. The doses recommended by various authors have ranged from one-sixth of a grain to as high as two grains (0.010–0.13 Gm.).

See also *Oxysparteine*.

Spartium. *Spartium junceum* L. *Spanish Broom.* (Fam. *Leguminosæ.*)—A small shrub, indigenous in the south of Europe, and cultivated in our gardens as an ornamental plant. The flowers are large, yellow, and of an agreeable odor. Spanish broom, in its medicinal properties closely resembles *Scoparius*, but appears to be from five to six times more active, 6 Gm. of the dried plant, given in infusion, having produced very violent poisoning; serious results have been produced by the substitution of the Spanish for the true broom. The dried flowers are readily differentiated, those of the *true broom* having a small, bell-shaped calyx with two unequal lobes, the upper of which is bidentate, the lower minutely tridentate, and the style always rolled, while in *Spartium junceum* the calyx is deeply cleft to the base on one side only, and the style is deeply rolled.

The symptoms produced by overdoses are vomiting and purging, with renal irritation. The seeds have been used to a considerable extent in *dropsy* in *doses* of from ten to fifteen grains (0.65–1.0 Gm.) three times a day in the form of tincture.

Sphæranthus. *Sphæranthus indicus* L. (Fam. *Compositæ.*)—An herbaceous plant having winged stems and widely distributed in Africa, Asia and Australia. It is used as a general tonic, deobstruent, alterative, and aphrodisiac, under the names of *Mundi Gorakhmundi*, *Murmuria*, and *Kottakkarandai*. Dymock has found it in a deep cherry-colored essential oil.

Sphagnum. *Peat Moss. Bog Moss.*—The sphagnums (Fam. *Sphagnaceæ*) comprise a group of pale mosses found in swamps and bogs throughout the entire North Temperate Zone. Great masses of these plants accumulate in the areas they inhabit on account of their prolific manner of growth and slow decay. The lower growth is constantly dying away and forming peat, whence the name of *peat moss* assigned to them. They differ from the true *mosses* (*Bryales*) in being paler green in color, in forming taller growths, in possessing no absorptive hairs in their sporophyte generation, as well as in the structure of their reproductive parts. Their stems and leaves possess colorless cells, connected by small perforations, that have the capacity of sucking up and retaining large quantities of liquid.

During the Great European War dried peat moss was largely employed for its absorptive powers as a surgical dressing. The species chiefly employed were the *Sphagnum imbricatum*, *S. palustre*, *S. Magellanicum*, and *S. papillosum*. The moss, after being collected, was spread out and partially dried in the sun and then completely dried by artificial heat and often afterwards treated with some disinfectant as corrosive sublimate. It has been asserted that sphagnum makes a more absorbent dressing than the ordinary absorbent cotton.

Spider Poisons.—The popular belief that certain spiders have the power of poisoning small animals, and even man, has received confirmation, and an active principle, *arachnolysin*, has been separated by Sachs and found to have a powerful hemolytic action upon the blood of rabbits and cats but not to affect dogs and guinea-pigs.

There has been a long standing tradition that the *tarantula* bite was fatal but Baerg (*J. Parasitol*, 1921, viii, p. 86) submitted himself to the bite of the American species (*Eurypelma steindachneri*) several times with no more serious effect than a local inflammation. Kobert had previously reached the conclusion that neither the Italian nor the Russian tarantula bite was dangerous to human beings. (See Kobert, *Giftspinnen*, 1901; also *J. A. M. A.*, 1920, lxxiv, p. 479 and 1922, lxxviii, 1967.)

Spigelia. *U. S. IX. Maryland, Carolina* or *Indian Pink, Worm-grass, Worm-weed, American wormroot, Star-bloom.*—"The dried rhizome and roots of *Spigelia marilandica* Linné (Fam. *Loganiaceæ*), without the presence or admixture of more than 10 per cent. of stems or other foreign matter." *U. S. IX.*

Two species of *spigelia* have attracted attention as anthelmintics—*S. Anthelmia* L., of South America and the West Indies, and *S. marilandica* L., of this country. *Spigelia Anthelmia* L., of South America, is an annual plant, from one or two feet in height, with thin, shortly petioled leaves, those of the lower stem being lanceolate, those above varying from very broadly lanceolate to ovate, with a distinct tendency to a rhomboidal outline and attaining a length of over four inches. It is much used as an anthelmintic in its native country, and its rhizome is said to have appeared in the European markets. The only specimens which we have seen, however, have been the whole dried plant, of which the attached rhizomes are much smaller and the rootlets much finer than in the North American species. It is affirmed that in overdoses this rhizome is a powerful poison, which has caused death not only in the domestic animal but also in man.

The *S. marilandica* is an herbaceous perennial plant. The stems, several of which rise from the same rhizome, are simple, erect, four-sided, nearly smooth, and from twelve to twenty inches high. The leaves are opposite, sessile, ovate-lanceolate, acuminate, entire, and smooth, with the veins and margins slightly pubescent. Each stem terminates in a one-sided spike, and supports from four to twelve flowers with very short pedicels. The calyx is persistent. The corolla is funnel-shaped, and much longer than the calyx, with the tube inflated in the middle, and the border divided into five acute, spreading segments. It is of a rich carmine color externally, paler at the base, and orange-yellow within. The edges of the segments are slightly tinged with green. The capsule is double, consisting of two cohering, globular, one-celled portions, with many seeds.

The plant is a native of our Southern and Southwestern States, being seldom found north of the Potomac. It grows in rich soils on the borders of woods, and flowers from May to July. The commercial supplies being restricted, some attention has been given to the cultivation of the plant. The Bureau of Plant Industry, U. S. Department of Agriculture, Washington, D. C., has grown spigelia under shade, and Miss Henkel states that it is readily cultivated in Georgia. (*D. C.*, lvi, p. 132.)

It was at one time largely substituted by *Ruellia ciliosa* Pursh. Sanders reported examining 57 samples of pink-root which were obtained from various sections of the country and none were genuine. (*Jour. A. Ph. A.*, 1912, p. 502.) To Prof. Greenish (*A. J. P.*, 1891, p. 226) belongs the credit for the first pharmacognostic description of this common substitute, although he incorrectly attributed it to *Phlox carolina* L. (*P. ovata* L.). He pointed out that it was distinguished by the fact that it contained stone cells and cystoliths of calcium carbonate. Greenish's work was confirmed by Holm (*A. J. P.*, 1906, p. 553), and by Stockberger (*Ph. Rev.*, 1907, p. 2). His false identification continued in literature for several years, probably owing to the statements of the large drug houses which make a specialty of collecting American drugs. (*Proc. A. Ph. A.*, 1909, p. 1171.) The presence of *Phlox ovata* L. in commercial lots of spigelia has not been confirmed, and Kraemer illustrates the pharmacognosy of the rhizome and roots of this drug in *A. J. P.*, 1910, p. 470. Moser, however, affirms that *Phlox ovata* and *P. glaberrima* L. are frequently collected and sold as spigelia. (*A. J. P.*, 1909, p. 576.) Among some of the adulterants which have been identified are the rhizomes of goldenseal and caulophyllum, although a large variety of rhizomes are no doubt more or less intermixed.

Pinkroot was officially described as "rhizome horizontal or slightly oblique, more or less flexuous, somewhat branched, from 1.5 to 5 cm. in length and from 2 to 5 mm. in diameter; externally dark brown, slightly annulate, with scars of bud scales, the upper surface knotty from approximate stem-bases, bearing cup-shaped scars; from the lower and lateral portions arise numerous, long, rather coarse, sparingly branched, brittle roots; fracture short, internally differentiated into three nearly equal zones of pith, wood and bark; odor slightly aromatic; taste bitter, pungent. Few if any of the roots exhibit thin, terminal portions with the bark stripped from the slender strands of wood. Stems usually attached to the upper portion of the rhizome, nearly cylindrical, attaining a length of 6 cm. and a diameter of 3 mm., light grayish-brown to purplish-brown, nodes annulate, marked by opposite leaf-scars. Under the microscope, transverse sections of the rhizome of Spigelia show a dark brown, more or less exfoliated epidermal layer; a cortex composed of from 10 to 15 rows of starch-bearing parenchyma; a distinct zone of sieve tissue from 0.075 to 0.15 mm. in width; a compact woody area composed of tracheæ and tracheids which are hardly distinguishable from each other, both kinds of vessels being marked with bordered pores; an internal sieve closely resembling the sieve in the bark; and a pith composed of fairly uniform, nearly polygonal, thin-walled cells, more or less filled with small starch grains. Transverse sections of the root show a large cortex, the cells of which are more or less filled with small starch grains and a central stele of 6 or 8 radial fibrovascular bundles, which in the older roots are united by a strong development of lignified cells. The stem in transverse section is distinguished from the rhizome by a narrower woody zone, the tracheæ having spiral thickenings, and by a nearly uninterrupted circle of non-lignified bast-fibers in the bark. The powder is grayish-brown; when examined under the microscope it exhibits starch grains generally numerous, at times, however, few, spherical or slightly angular, from 0.002 to 0.006 mm. in diameter; fragments of lignified tracheæ and tracheids conspicuous; fragments of tracheæ with spiral thickening relatively few, bast-fibers few, very long, non-lignified; occasional fragments of the reddish-brown epidermal cells. Spigelia yields not more than 10 per cent. of ash." *U. S. IX.*

It contains a volatile alkaloid, *spigeline*, discovered by Dudley in 1881. Spigeline yields a brownish-red precipitate with a solution of iodine in potassium iodide, a white crystalline precipitate with potassio-mercuric iodide, and a white flocculent precipitate with meta-tungstic acid. Boorsma (*P. J.*, 1898, 89) found 0.0005 Gm. of spigeline to be lethal to guinea pigs. It is questionable, however, whether the vermifuge properties of pink-root are to be attributed to spigeline.

The activity of spigelia is somewhat diminished by time. Spigelia is especially esteemed against the *round-worm.* In the ordinary dose it usually produces little sensible effect on the system; more largely given it acts as a cathartic, though unequal and uncertain in its operation; in overdoses it is said to cause vertigo, dimness of vision, dilated pupils, spasms of the facial muscles and of the eye-lids, and even general convulsions. H. A. Hare (*Med. News*, March, 1887) has found that in the lower animals it produces symptoms similar to those just described. The narcotic effects are said to be less likely to occur when the medicine purges, and to be altogether obviated by combining it with cathartics. The danger from its employment cannot be great, as it was formerly largely used in the United States, in both regular and domestic practice, and serious consequences were almost unheard of. Its effects upon the nervous system have been erroneously conjectured to depend on other roots sometimes mixed with the genuine. It is usually combined with senna or some other cathartic, to insure its action on the bowels.

Dose, of the powdered root, for an adult, one or two drachms (3.9–7.7 Gm.), to be repeated, morning and evening for several days successively, and then followed by a brisk cathartic.

Spilanthes. *Spilanthes Oleracea* L. (*S. Acmella* Murr.) *Para Cress. Cresson de Para*, Fr. *Parakresse*, G. (Fam. *Compositæ.*)—A plant of the tropics used as a masticatory for *toothache;* when chewed it produces a copious salivation. (*A. J. P.*, xliv, 323.) It is cultivated both as an ornament and for its pungent leaves which are used as a salad.

Spiracin. *Methyl-carboxyl-salicylic Acid.*—It forms a white crystalline powder, insoluble in water. It is used for the same purposes as the salicylates in *doses* of ten to fifteen grains (0.6–1 Gm.).

Spiræa.—A genus of deciduous shrubs belonging to the *Rosaceæ* which are cultivated for their handsome flowers. Many if not all of the species of this genus contain a colorless volatile oil, very similar to the oil of gaultheria, but composed mainly of salicylic aldehyde, with only smaller amounts of methyl salicylate. The species which have been submitted to actual analysis are the *Spiræa Ulmaria* L. (*Filipendula Ulmaria* (L.) Maxim.), commonly known as *Queen of the Meadow*, or *Meadow-sweet*—a European plant which has been introduced into this country; also the European species *S. lobata* Jacq. and the species *S. Filipendula* L. (*Filipendula vulgaris* Moench.), which grows in Southern Europe and Northern Africa. *Spiræaic acid* (now recognized as salicylic acid) (*J. Pr. Chem.*, xix) was separated from the flowers of *S. Ulmaria* by Löwig and Weidmann, and has been found by Rochebrune in the flowers of *S. Filipendula* L.

The roots of probably most of the species contain tannic acid, gallic acid, and when fresh some of the volatile oils. (*A. J. P.*, 1887.) The root of *Spiræa tomentosa* L. (*Hardhack, Steeplebush*, or *Whitecap*), was formerly recognized in the U. S. Pharmacopœia. It is an indigenous shrub growing in low grounds from New Brunswick and Nova Scotia to the mountains of Georgia and westward. The stems and lower surfaces of the ovate-lanceolate, serrate leaves are whitish and tomentose. The rose-colored flowers are disposed in terminal, compound, crowded racemes.

The flowers of *Spiræa* possess to a very feeble extent the medicinal virtues of salicylic acid, and have been used as diuretic and tonic in the form of decoction. The roots are astringent, and have been used in the treatment of *diarrhea* in *doses* of from five to twenty grains (0.32–1.3 Gm.) of the aqueous extract repeated *pro re nata.*

Spiroform. *Vesipyrin. Acetyl Salol. Acetylphenyl-o-oxybenzoic Acid. Phenyl Acetylsalicylate. Acetyl Salicylic Phenyl Ester.* $C_6H_4(OCH_3CO)$-$COOC_6H_5$.—A tasteless, odorless powder, insoluble in water, readily decomposed by alkalies. This substance acts in the body much like phenyl salicylate; it passes through the stomach unchanged, but is broken up in the intestines, liberating salicylic acid. It was originally introduced as a urinary antiseptic, but has also been employed as an antirheumatic and analgesic. The *dose* is from eight to fifteen grains (0.5–1.0 Gm.).

Sponge. *Spongia. Spongia officinalis. Eponge*, Fr. *Schwamm. Badeschwamm*, G.—Sponges are fixed, flexible, polymorphous, diploblastic, invertebrate animals belonging to the phylum *Porifera.* The majority of sponges are marine, only about thirty species inhabiting fresh water. The sponges of commerce represent skeletons of these animals. Sponges vary greatly in their habit of growth which is responsible for their shape. Some are branched like plants; others are vase-shaped, cup-shaped, fan-shaped, or dome-shaped. Their bodies vary in size from that of a pin-head to over five feet in height, and in color from white or gray to that of every hue in the spectrum. The body-wall is constructed of two layers of cells, *viz.*, the outer or dermal epithelium and the inner or gastral epithelium. Between these is a jelly-like substance containing amœboid cells. In the simplest sponges, such as *Grantia*, a hollow central or gastral cavity opens to the exterior by a single large exhalant opening called the osculum. Numerous water pores or inhalent openings are scattered over the dermal epithelium which communicate with radial canals (a portion of which open into the gastral cavity) and, like the gastral epithelium, are lined with flagellated cells, the flagella of which beat constantly, creating a current of water. Water, containing minute organisms upon which the sponge feeds, is thereby induced to pass through the water pores into the radial canals and thence into the gastral cavity and out through the osculum. Through this system of canals, also, oxygen is distributed, waste matters eliminated and fertilization of eggs effected.

The bodies of sponges collected for commerce represent complex colonies of this simple type. The skeleta of sponges vary from spicules of silicon or carbonate of lime to fibers of a horny substance, chemically allied to silk and called *spongin*. The latter is secreted by cells of the dermal epithelium and makes up entirely the commercial sponge when purchased.

Sponges inhabit the bottom of the sea, where they are fixed to rocks or other solid bodies, and are most abundant within the tropics. They are collected chiefly in the Mediterranean and Red Seas, the West Indies and the coast of Florida and Central America. In the Grecian Archipelago, Crete, Cyprus, on the coast of Asia Minor, Syria, Barbary and the Bahama Islands, sponge fisheries constitute a very important industry.

Most of the sponges used in the United States come from the Bahamas and the coast of Florida but the finest bath sponges are brought from the Mediterranean, especially Turkish waters. The greatest source of the sponges sold in this country is Tarpon Springs, Florida. Key West is the next largest source. The varieties caught there in order of their commercial value are, *sheep's wool*, *yellow*, *grass*, and coarse grades including *boat* and *glove* sponges.

The cultivation of sponges has been undertaken on an extensive scale. Small fragments are cut under water from the live sponge, and fixed upon a sandy bottom by means of skewers. In three years they will have grown sufficiently to be marketable.

Sponge, as found in commerce, is in yellowish-brown masses of various shapes and sizes, light, porous, elastic, and composed of fine, flexible, tenacious fibers, interwoven in the form of cells and meshes. It usually contains numerous minute fragments of coral or stone, or small shells, from which it must be freed before it can be used for ordinary purposes. Sponge is prepared by macerating it for several days in cold water, beating it in order to break up the concretions which it contains, and dissolving what cannot thus be separated of the calcareous matter by hydrochloric acid diluted with thirty parts of water. By this process it is rendered perfectly soft, and fit for surgical use. It may be bleached by steeping it in water impregnated with sulphurous acid, or by exposure in a moist state to the action of chlorine or by alternate treatment first with a weak solution of potassium permanganate and then with an acidulated solution of oxalic acid. It is stated that sponges which have been soaked in pus and infectious matters will recover their primitive condition by soaking in a 4 per cent. solution of potassium permanganate, then in a 25 per cent. solution of official sulphorous acid, and finally thorough washing in an abundance of water. The most important constituent of the sponge is a substance known as *spongin* which is analogous to *fibröin* and *sericin* of silk but which Schlossberger has shown to be a distinct principle.

Sponges are used for mechanical purposes only. *Sponge tent* is employed for dilating sinuses. This is prepared by dipping sponge into melted wax, compressing it between two flat surfaces till the wax hardens, and then cutting it into pieces of a proper form and size. By the heat of the body the wax becomes soft, and the sponge, expanding by the imbibition of moisture, gradually dilates the wound or sinus in which it may be placed. When a conical sponge tent of uniform caliber is required, as for dilating the uterine cavity, a better plan is to cut the sponge into a conical shape while fresh and compress when moist, by winding it carefully with a fine tightly drawn cord, removing the cord when perfectly dry, and dipping the tent into melted wax, so as to get a thick coating. For other modes of preparing sponge tent, as well as of saturating the sponge at the same time with substances calculated to make a remedial impression, as phenol, alum, lead acetate, etc., see *A. J. P.*, 1868, 410; 1869, 446.

Spongia Usta. *Burnt Sponge.*—This was formerly official (*Spongia Usta*, U. S., 1850). Its medicinal value was due chiefly to the iodine content and it has been replaced by more reliable preparations of this element. For method of preparation, analysis, and therapeutic properties, see 16th edition, *U. S. D.*

Statice. *Statice Limonium* (L.) Gray. [Now *Limonium carolinianum* (Walt.) Britt.] *Sea Lavender. Marsh Rosemary. Ink Root. Rosmarin des Marais, Lavande triste*, Fr. *Strandnelke*, G. (Fam. *Plumbaginaceæ.*)—It is an indigenous maritime plant with a perennial, very astringent root, sending up annually tufts of leaves, which are obovate or cuneiform, entire, obtuse, mucronate, smooth, and on long foot-stalks. The small lavender colored flowers appear in panicles of spikes.

Marsh rosemary grows in the salt marshes along the sea coast from Labrador to Texas, and flowers from July to September. The root, which was formerly in the Secondary List of the U. S. Pharmacopœia, is large, spindle-shaped, or branched, fleshy, compact, rough, and of a purplish-brown color. It is bitter and extremely astringent, but odorless. It contains tannic acid (12.4 per cent.), volatile oil, resin, and other substances. *Statice* is powerfully astringent, and in some parts of the United States, particularly in New England, was much employed, especially as a local application, in decoction, to aphthous and ulcerative affections of the mouth and fauces.

In Brazil and Buenos Ayres the roots of *S. brasiliensis* Boiss. are employed under the name of *Buaycura* or *Guaycura*. For a description of the physical and chemical characteristics of the root, see *P. J.*, 1884, xv, 86. In Russia and Spain the very large roots of *S. latifolia* Sm. are used for tanning, and in Morocco the roots of *S. mucronata* L. are stated to be employed, under the name of *safrifa*, as a nervine.

Stibenyl.—Acetyl para-amino phenyl stibinate of sodium, also known as *stibacetin*. This compound is employed in the treatment of *kala-azar*. According to Klippel (*B. Hop. Par.*, 1922, xxxviii, p. 76) it has marked superiority over antimony tartrate and may be given intravenously in doses of 0.05 to 0.2 Gm. one to three grains (0.06–0.2 Gm.) every alternate day.

Sticta. *Lungmoss. Lungwort.*—The lichen *Sticta pulmonaceæ*, a native of Europe, has been used as a folk remedy in the treatment of *pulmonary complaints*. It owes its activity chiefly to *stictic acid*, which is bitter and possesses a powerful astringent action.

Stipa. *Feather Grass.*—According to Gillespie (*B. M. J.*, Oct., 1898), a number of species of this genus of grasses are actively poisonous, and have caused death in horses and other domestic animals. Of such character especially are *Stipa viridula* Trin., *Stipa inebrians* Hance, and *Stipa sibirica* Lam., of the Russian steppes. A few experiments made with *Stipa viridula* Trin., a plant growing in the prairies and meadows from western Minnesota to the Dakotas and southernward, indicated that it acts powerfully upon the brain and spinal cord.

Stipa Vaseyi Scribner.—According to Vernon Bailey this grass, which grows on the mountains of California, is a very active narcotic, producing in animals, which graze upon it, sleep lasting for a week or longer. (See Farwell, *Merck's Rep.*, 1911, p. 271.)

Stipa tenacissima L. *Esparto Grass.*—The leaves of this grass furnish a valuable fiber from which paper, ropes and mats are manufactured.

Stovaine. *N. N. R.* 1924. *Benzoyl-dimethylamino-ethylpropanol Hydrochloride*, $CH_3CH_2C(C_6H_5COO)(CH_3)CH_2N(CH_3)_2HCl$.—It is closely related to alypin. It crystallizes in small, brilliant scales, melting at 175° C., and is very soluble in water. It shows most of the reactions of cocaine, which is also a benzoyl derivative.

This substance which has been advertised by methods approaching that employed by the mountebank has been used as a local anesthetic especially for the production of the so-called *spinal anesthesia* by a very large number of surgeons. In the experiments of LeBrocq (*B. M. J.*, March 27, 1909) it was found that if the toxicity of cocaine represented 1 that of stovaine would be 0.625 and that of eucaine 0.414; in other words it stands midway between cocaine and eucaine in danger. He also found that it was locally irritant, its injection being followed by intense hyperemia and even local sloughing. As confirmatory of this local irritant effect are the changes which have been found in the spinal cord from its lumbar injection. Pauterier and Simon (*Bull. Hop. Par.*, 1907) report a case of meningitis following spinal anesthesia with the agent and Spiller and Leopold (*J. A. M. A.*, 1910, liv, p. 1840) caused intense degeneration of the posterior columns of the cord by repeated injections in the lower animals. In 1907 Chaput (*Press. Med.*, 1907) collected statistics of 3174 spinal anesthesias with stovaine with six deaths, mortality of about one in 530. In the same year, however, Torrance collected 5532 cases with but 3 deaths. Boyd and Young (*J. A. M. A.*, 1917, lxviii, 601) have reported over 6000 cases with three deaths. It is evident that the mortality of spinal anesthesia from stovaine is higher than that of general anesthesia with ether or chloroform. Schwarz (*Cb. C.*, 1907) reported signs of renal irritation in 78 per cent. of cases anesthetized by this method, but Hosemann (*Cb. C.*, 1908, xxxv, 60), in a series of sixty cases, noted mild irritation of the kidney in only ten cases, in none of which was there permanent injury. It has, however, a field of distinct value, not as a routine measure, but in certain conditions where the volatile anesthetics are unusually dangerous.

As a local anesthetic stovaine has the advantage over cocaine of being somewhat less toxic, of not dilating the pupil or causing vascular constriction, and of withstanding boiling temperatures. LeBrocq (*B. M. J.*, 1909, i, 783) found that the toxicity of stovaine was approximately two-thirds that of cocaine which conclusions correspond approximately with those of Eggleston and Hatcher (*J. P. Ex. T.*, 1919, xiii, p. 433) as applied to the intravenous injection, but the latter find that when injected subcutaneously the difference in toxicity was still more favorable for stovaine. Weight for weight, it is one of the most powerful anesthetics of all the cocaine substitutes, according to LeBrocq, surpassing even cocaine itself. For local anesthesia it is generally employed in a 1 per cent. solution of which sixteen to fifty minims (1–3 cc.) may be injected, according to the size of the area it is desired to render insensible. For spinal anesthesia it is recommended to be used in strengths of from 3 to 10 per cent., injecting a quantity of this solution equivalent to from 0.032 to 0.065 Gm. of the drug.

Strontium. Sr. = 87.63.—*Strontium* belongs to the alkaline earth group of metals along with barium and calcium. It is a yellow metal, of the sp. gr. 2.5, somewhat harder than lead, and is sufficiently malleable to be hammered out into thin plates. It oxidizes quickly on exposure to air, and hence must be kept under naphtha, like the alkali metals.

For method of preparing strontium free from barium see *U. S. D.*, 20th ed., p. 1066.

A number of salts of strontium were formerly official but all of them have been dropped from the U. S., but the Br. recognizes the bromide. They impart a bright red color to the non-luminous flame and *strontium nitrate* is largely used for making *red fire* in pyrotechnics.

At one time the strontium salts were deemed to be highly toxic, but in 1890 Laborde (*C. R. S. B.*, 1890, ii) showed that this belief was due to the fact that the earth had been contaminated with barium salts and that pure strontium was no more injurious than potassium. When a salt of strontium is taken by the mouth probably only small amounts of the metal are absorbed. The fact that it is excreted chiefly by the intestinal glands (Mendel and Thatcher, *A. J. Phys.*, 1904, xi, 5) makes it difficult to determine whether the salt found in the feces has been absorbed and re-excreted, or whether it is simply due to non-absorption. Even after hypodermic administration only traces of the metal appear in the urine. Wood and Arnold (*Phila. Monthly Medical Journal*, April, 1899) have shown that when introduced into the blood stream the strontium salts exercise a marked stimulating effect upon both the heart and arterial muscles, which are secondarily depressed by toxic doses. It causes also an increase in the contractions of the voluntary muscles with delay in their relaxation. Taken by the mouth, however, it is so slowly absorbed that it is improbable that enough can be introduced into the system to exercise any influence. According to Mendel and Thatcher, small quantities are stored up in the bones replacing a part of the calcium.

The salts of strontium, especially *strontium lactate*, were at one time extensively employed in the treatment of *chronic Bright's disease.* The remarkable claim was made for them that not only did they have a valuable diuretic effect, but that they exercised a beneficial effect upon the kidney, causing marked diminution in the excretion of albumin. Later experience, however, has not justified the earlier enthusiasm, and the use of the metal, except as a carrier of therapeutically active acids, has almost dropped out of vogue. By some it is believed that the strontium salts are less liable to disturb digestion. Especially has this been urged in regard to the salicylate, but in the experiments of Blankenhorn (*J. A. M. A.*, 1916, lvi, 331), there was no difference in the effects of the strontium and sodium salicylate.

Strontium Acetate. $Sr(C_2H_3O_2)_2 + \frac{1}{2}H_2O$.—This is a white crystalline powder, soluble in water. It is said to possess anthelmintic properties. It is given in *doses* of from ten to thirty grains (0.65–2.0 Gm.) twice a day.

Strontium Arsenite. $Sr(AsO_2)_2 + 4H_2O$.—A white powder soluble in water of somewhat variable composition representing approximately 53 per cent. of arsenic trioxide. It possesses the therapeutic virtues of arsenic, but has no advantages over the official preparation. The *dose* is from one-thirtieth to one-fifteenth of a grain (0.002–0.004 Gm.).

Strontium Carbonate. *Strontii Carbonas.* $SrCO_3 = 147.63$.—This salt has been dropped from the N. F. It was formerly described as follows:

"Strontium Carbonate occurs as a white powder, odorless and tasteless. It is insoluble in water; dissolved with effervescence by diluted hydrochloric, nitric, or acetic acid; the addition of diluted sulphuric acid to these solutions produces a white precipitate.

"*Assay.*—Dissolve about 1.5 Gm. of Strontium Carbonate, dried to constant weight at 100° C. and accurately weighed, in 30 cc. of normal hydrochloric acid V.S. and titrate the excess of acid with normal sodium hydroxide V.S., using methyl orange T.S. as indicator. It shows in the dried salt not less than 99 per cent. of $SrCO_3$.

"Each cc. of normal hydrochloric acid V.S. consumed is equivalent to 0.07381 Gm. of $SrCO_3$. Each gramme of Strontium Carbonate requires not less than 13.4 cc. of normal hydrochloric acid V.S." *N. F. IV.*

It should be free from barium as shown by lack of turbidity when a solution, made by the aid of acetic acid, is treated with potassium dichromate T.S.

It is not used medicinally, but was introduced into the N. F. for the preparation of the compound elixir of formates.

Strontium Iodide. *Strontii Iodidum. U. S. IX. Iodure de Strontium*, Fr.; *Strontiumjodid*, G.—"It contains not less than 99 per cent. of $SrI_2 + 6H_2O$ (449.57). Preserve it in small, amber-colored, glass-stoppered bottles, carefully protected from light." *U. S. IX.*

This salt was dropped at the tenth revision of the U. S. P. It was described as follows:

"Strontium Iodide occurs as colorless, transparent, hexagonal plates, as a white, granular powder, or in crystalline crusts; odorless, and having a bitter, saline taste. It is deliquescent, and is colored yellow by exposure to air and light. One Gm. of Strontium Iodide dissolves in about 0.2 mil of water at 25° C.; soluble in alcohol; slightly soluble in ether. Its aqueous solution (1 in 20) is neutral or slightly alkaline to litmus. When cautiously heated, the crystals melt and gradually lose their water of crystallization. At a red heat, the salt is decomposed, losing iodine and leaving a residue of strontium oxide. To a non-luminous flame it imparts a crimson color." *U. S. IX.* It gives the characteristic tests for strontium and for the iodides. It should not show a turbidity with potassium dichromate T.S. (absence of barium). "Gently heat 5 mils of an aqueous solution of the salt (1 in 10) with 1 drop of ferrous sulphate T.S., 1 drop of ferric chloride T.S., and 0.5 mil of potassium hydroxide T.S.; no blue color appears after acidulating the mixture with hydrochloric acid (*cyanide*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). Dissolve 0.3 Gm. of the salt in 5 mils of distilled water, add an excess of silver nitrate T.S. and a few drops of nitric acid; filter, digest the precipitate with 5 mils of ammonia water and filter. On saturating the filtrate with nitric acid, not more than a slight turbidity is produced (*chloride* or *bromide*).

"*Assay.*—Proceed as directed under the Assay for iodides (see Part III), using about 1 Gm. of Strontium Iodide, accurately weighed. It shows not less than 99 per cent. of $SrI_2 + 6H_2O$.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.022478 Gm. of $SrI_2 + 6H_2O$. Each gramme of Strontium Iodide corresponds to not less than 44 mils of tenth-normal silver nitrate V.S." *U. S. IX.*

Strontium iodide has been brought forward as a means of obtaining the alterative influence of an iodide without irritating the intestinal tract or depressing the general nutrition. It contains about 56.5 per cent. of iodine, and, although its practical advantage is doubtful, may be substituted for potassium iodide in various diseases.

Dose, five to fifteen grains (0.32–1.0 Gm.).

Strontium Lactate. *Strontii Lactas. U. S.* 1890. $Sr(C_3H_5O_3)_2.3H_2O = 319.76$.—This salt may be prepared by the process of Thumann. (See *U. S. D.*, 19th ed., p. 1661.) *Strontium lactate* is "a white, granular powder, or crystalline nodules, odorless, and having a slightly bitter, saline taste; permanent in the air. Soluble in about 4 parts of water at 15° C., and in less than 0.5 part of boiling water. The solution saturated at a boiling heat remains liquid for many hours, even after being cooled to 0° C. Soluble in alcohol. When heated to 110° C., the salt loses its water (16.9 per cent.). At a higher temperature it first fuses, then is decomposed, giving off inflammable vapors, and leaves a residue of strontium carbonate and carbon, which, on the addition of hydrochloric acid, effervesces and communicates an intense, red color to a non-luminous flame. The aqueous solution (1 in 20) is slightly acid to litmus paper." *U. S.*, 1890. It gives the characteristic reactions of the soluble salts of strontium and the lactates. The absence of barium may be shown by potassium dichromate T.S., which should produce no turbidity. For further tests of purity, see *U. S. D.*, 19th ed., p. 1662.

Strontium lactate was originally brought forward by J. V. Laborde, who found it to have a distinct diuretic action. It enjoyed for a period a considerable popularity in the treatment of *nephritis* and chronic *albuminuria*. The experiments, however, of Wood and Arnold (*Phila. Monthly Med. Journ.*, April, 1899) have shown that only infinitesimal amounts of the drug are absorbed from the intestines. Upon the intestinal canal the lactate is asserted to exert a very favorable influence. Strontium lactate has also been tried with alleged good results in the treatment of *rheumatism* and *gout*, it being affirmed that it increases the nitrogenous elimination and causes disappearance of the urates. *Dose*, from ten to thirty grains (0.65–2.0 Gm.) three times a day in solution.

Strontium Phosphate. $Sr_3(PO_4)_2$.—A white, tasteless powder, soluble with decomposition in acids. Nutritive and tonic. It is used in the treatment of *phthisis* and other wasting diseases, as a tissue builder, asserted to be superior to calcium phosphate. (Labordé.) *Dose*, ten to thirty grains (0.6–2.0 Gm.).

Strontium Sulphide. *Strontii Sulphidum.* SrS. —This substance has been used to some extent as a depilatory, in accordance with the following method: A powder of 2 parts strontium sulphide, 3 parts of zinc oxide, and 3 parts of powdered starch, kept dry until used, is formed into a paste with warm water and allowed to remain upon the surface from which the hair is to be removed from one to five minutes, being taken off so soon as pronounced pain or any evidences of caustic action are perceptible. The surface should then be gently but firmly scraped with a blunt edge like that of a paper knife, then washed well with warm water, and treated with an emollient.

Strychnine Salts.—There have been from time to time placed upon the market various salts of strychnine as substitutes for those official. There is no reason, however, to believe that any of these have advantages over the pharmacopœial compounds. The amount of acid radicals represented in such compounds is usually so insignificant that it is impossible to suppose they can modify the action of the alkaloid. There is no reason to suppose that any of these differ materially in their effects from the sulphate. They are used for the same purposes and in the same doses. The following are of sufficient commercial importance to justify a word of mention.

Strychnine Arsenate. Strychninæ Arsenas.—This has been introduced as a means of obtaining the effects of its constituents. It corresponds approximately to 62.25 per cent. of strychnine and 27.75 per cent. of arsenic acid. It has been especially praised by Coriveaud (*K. T. W.*, 1909) in the treatment of bronchial *asthma* and other pectoral complaints. The dose is one-sixtieth of a grain which may be cautiously increased to one-fifteenth (0.001–0.004 Gm.).

Strychnine Formate occurs as white crystalline powder soluble in about five parts of water.

Strychnine Glycerophosphate. *N. F. IV. Strychninæ Glycerophosphas.*—This strychnine salt "occurs in white, rhombic crystals or as a white powder; odorless; having at first a faint, sweet taste, afterward becoming intensely bitter. One gramme dissolves in about 350 cc. of water, the solution being neutral or slightly alkaline to litmus; also in about 310 cc. of alcohol; slightly soluble in chloroform, and very slightly soluble in ether. On incinerating 0.2 Gm. of the salt it yields no weighable residue. The addition of sulphuric acid to the salt produces no color, or at most only a slight yellowish coloration, but on subsequently adding a fragment of potassium dichromate a deep blue color is obtained, which changes to deep violet, then to purplish-red, cherry-red and finally to orange or yellow. Add ammonia water in slight excess to a saturated aqueous solution of the salt; a white precipitate is formed which is readily soluble in chloroform. A saturated aqueous solution of the salt, acidulated with diluted nitric acid, is not rendered more than faintly turbid on the addition of silver nitrate T.S. (*chloride*). A saturated aqueous solution of the salt, acidulated with hydrochloric acid, shows not more than a slight turbidity on the addition of barium chloride T.S. (*sulphate*). Add a slight excess of ammonia water to an aqueous solution of the salt and filter the mixture; the filtrate shows not more than a slight turbidity with magnesia mixture T.S. (*phosphate*)." *N. F. IV.*

It has no advantages medicinally over other strychnine salts.

Strychnine Hypophosphite, a white crystalline powder freely soluble in water.

Strychnine Valerate. Strychninæ Valeras, N. F. IV.—This salt was introduced into the N. F. as an ingredient of an elixir. The proportion of valeric acid present can in no way modify the action of the strychnine and both the salt and elixir have very properly been dropped. It was described as follows:

"Strychnine Valerate occurs as a white crystalline powder, having an odor of valeric acid and an intensely bitter taste. It is sparingly soluble in water, becoming less soluble on keeping, through the loss of valeric acid; soluble in alcohol or chloroform; slightly soluble in ether. Its saturated aqueous solution is neutral or slightly alkaline to litmus. Dissolve about 0.05 Gm. of Strychnine Valerate in 2 cc. of sulphuric acid; no more than a faint yellowish color appears, but on adding a fragment of potassium dichromate a deep violet color is produced which changes to orange or yellow. When sulphuric acid is added to the salt, the odor of valeric acid is evolved. Incinerate 1 Gm. of Strychnine Valerate; the ash does not exceed 0.1 per cent. Ten cc. portions of an aqueous solution of the salt (1 in 100) are not affected at once by barium chloride T.S. when acidulated with hydrochloric acid (*sulphate*) nor by silver nitrate T.S. when acidulated with nitric acid (*chloride*). About 0.02 Gm. of the salt, moistened with nitric acid, may be colored yellow, but not red or reddish (*brucine*)." *N. F. IV.*

The average *dose* of strychnine valerate is given as one-fortieth of a grain (0.0015 Gm.).

Strychnos Potatorum L. fil. *Chilbinj. Clearing Nuts. Indian Gum Nuts.* (Fam. *Loganiaceæ.*) —The nuts of this species of *Strychnos* are very largely used in some parts of India for clearing muddy water. The fruit is also employed by the native practitioners of Hindostan, under the name of *nirmali*, as an emetic and in *dysentery*. They do not contain strychnine. In clearing water, one of the dried nuts is rubbed hard for a short time around the inside of the earthen water pot; on settling, the water is left pure and tasteless. The seeds contain a large quantity of an albuminous principle, upon which their virtues probably depend. They are devoid of bitterness. The tree, which grows to a very large size, produces a shining, black, one-seeded berry (that of the nux vomica being many-seeded). The seeds are broadly lenticular, about half an inch in diameter and a quarter of an inch in thickness, of a dirty whitish-gray color, and covered with a thick coating of delicate appressed hairs. These are so small that the seed to the naked eye looks mealy. Under the microscope the hairs are seen to be agglutinated in groups of from three to six, and to consist each of a single pointed cylindrical cell.

Stylophorum. *Stylophorum diphyllum* (Michx.) Nuttall. (Fam. *Papaveraceæ.*)—This plant, commonly known as "*Celandine Poppy*," is found in damp woods from western Pennsylvania to Wisconsin and Tennessee. In its foliage and flowers it resembles *Chelidonium majus.* According to E. Schmidt, the root contains *chelidonine,* with a second alkaloid closely related to, if not identical with, *chelerythrine.* (*A. J. P.*, 1888.)

Stylosanthes. *Stylosanthes biflora* (L.) B. S. P. (Fam. *Leguminosæ.*)—This low, branching perennial has wiry stems, 3-foliate leaves and small yellow flowers. It is found in the pine barrens and dry soil of the eastern and central United States and it is asserted that it possesses the power of relieving abdominal uterine pains during the latter months of gestation, and is also a uterine tonic during parturition. *Dose,* of the fluidextract, from ten to twenty minims (0.6–1.3 cc.) three times a day.

Styrone. *Cinnamic Alcohol. Styryl Alcohol.* $C_6H_5.CH : CH.CH_2.OH$.—A *beta-phenyl-allyl alcohol* appearing either as an aromatic oily fluid, boiling at 250° C., or a crystalline solid, forming white needles soluble in alcohol and fusing at 25° to 35° C. The fluid is used in *otitis media* and the crystals as a deodorant and antiseptic either in the dry form or in a glycerin solution.

Subcutin.—This compound of paraphenolsulphonic acid with paramido-benzoic acid has been brought forward by Ritsert as non-toxic, distinctly germicidal, and locally anesthetic. It is a white, crystalline powder, soluble to the extent of 1 per cent. in cold water, and two and one-half per cent. in tepid water. For hypodermic use to this solution is added about 1 per cent. of ordinary salt. It is stated that it is especially adapted to the production of infiltration anesthesia but Recke has shown that its anesthetic power is relatively low.

Sublamine. *Hydrargyri Sulphas Æthylenediaminata. Ethylene-diamine-mercury Sulphate. Mercamin.* $HgSO_4.2C_2H_4(NH_2) + 2H_2O$.—This is a white powder, soluble in water, composed of one molecule of mercuric sulphate and two molecules of ethylenediamine, and represents about 43 per cent. of mercury. It was originally brought forward as a non-irritant germicide of exceptional penetrative power, and especially useful for the purpose of disinfecting the hands and skin; used in solution varying from 1 to 1000 up to 1 to 200. It has also been highly commended in 1 to 300 for sterilizing suture silk by boiling.

Sublamine has also been employed to some extent for the hypodermic administration of mercury; it is affirmed by Schuftan, when given hypodermically, to be more active than corrosive sublimate, probably because it does not coagulate albumin. It is incompatible with sodium chloride and should not be exposed to the air.

Succinic Acid. *Acidum Succinicum. Sal Succini Volatile. Acide succinique,* Fr. *Bernsteinsäure,* G. $COOH(CH_2)_2COOH$.—This acid was originally obtained by distilling amber but is now prepared by fermenting ammonium tartrate solution with a specific micro-organism. The product was formerly an aqueous solution of *succinic acid,* associated with empyreumatic oil. (See *Amber.*) By filtering the liquor the solution of the impure acid passes through, while the oil was absorbed by the paper. The acid was purified by boiling the solution with nitric acid, diluted with twice its bulk of water, and then evaporating to crystallize: Succinic acid is made artificially by the action of nitric acid on the fatty acids, and may be produced in a great many ways from various substances. Thus, it is invariably formed in small amount in the alcoholic fermentation of sugar and also in the putrefaction of a variety of fats. For other methods see *U. S. D.*, 20th ed., p. 1627, xxvii.

Succinic acid, when pure, is in white, transparent crystals having no odor and a somewhat acrid taste. It dissolves in five times its weight of cold and twice its weight of boiling water. It is less soluble in alcohol and very sparingly so in ether. Nitric acid is without action on it. It melts at 182° C., and boils without alteration at 235° C. It sublimes, however, at a much lower temperature. According to Wackenroder, it is sometimes adulterated with tartaric acid soaked in oil of amber. Succinic acid, though formerly official, is at present seldom used in medicine. One of its salts, *ammonium succinate,* $(NH_4)_2C_4H_4O_4$, made by supersaturating succinic acid with ammonia, evaporating and crystallizing, has been used with alleged great success in *delirium tremens.* This salt is occasionally used as a precipitant of ferric oxide. See also *Sodium Succinate.*

Sulphaminic Acid. *Amido-sulphonic Acid.* NH_2SO_2OH.—This occurs as colorless crystals, freely soluble in water. Emmerich (*M. M. W.*, 1912), on the theory that the irritant toxin of *cholera* is nitrous acid, recommended the use of *sulphaminic acid* in the treatment of this disease. A tablespoonful of a one per cent. solution may be given every hour.

Sulphanilic Acid. $C_6H_4(NH)_2(HSO_3)$ 1 : 4. *Para-amino-benzene-sulphonic Acid.*—It occurs as colorless crystals, slightly soluble in water, insoluble in alcohol or ether and efflorescent in the air. Internally it has been recommended in the treatment of chronic *catarrh* in *doses* of 10 to 30 grains (0.6–2.0 Gm.), although it is of doubtful value. Its most important use is in Ehrlich's diazo-reaction for typhoid urine. Under the name of *Nizin,* tablets containing 0.13 gramme of sulphanilate of zinc are marketed and asserted to possess both astringent and antiseptic properties.

Sulpharsphenamine. *Sulfarsenol. Disodium-diamino-dihydroxyarsenobenzene-dimethylene Sulphonate. N. N. R.*—Sulpharsphenamine is a light yellow powder freely soluble in water forming solutions ranging from yellow to orange, according to their concentration, and acid to litmus. Solutions of 10 per cent. and over after standing for some days form a yellow jelly, but there is no apparent change takes place in dilute solutions. The average content of arsenic is about 22 per cent. Sulpharsphenamine was brought forward by Voegtlin (*J. P. Ex. T.*, 1920, xvi, 199 and 449) as a substitute for arsphenamine. He claims that its spirocheticidal power is at least equal to arsphenamine and that its toxicity is decidedly less than that of the older drug. He also finds (*U. S. Pub. Health Rep.*, May 11, 1923) that in cases of cerebrospinal *syphilis* it is decidedly more efficient than arsphenamine. While the clinical reports of its use are as yet insufficient to permit of accurate judgment of its relative value, they are numerous enough to hold forth great promise for it.

A great advantage of sulpharsphenamine is its stability in the air. Voegtlin found that solutions allowed to stand for 24 hours were not more toxic than when freshly made.

It may be used either intramuscularly, subcutaneously or intravenously. It is sold in ampules containing 0.06 to 0.6 Gm. (from one to nine grains).

Sulphoform. *Triphenylstibine Sulphide.* $(C_6H_5)_3SbS$.—According to Kaufmann (*Ber. d. Chem. Ges.*, 1908, xli), this compound liberates its sulphur with extreme ease; hydrogen dioxide causes a separation of the sulphur and oxidization to sulphuric acid, and the antimony being oxidized to antimony oxide which combines with the sulphuric acid, this reaction taking place almost quantitatively at a temperature of 36° C. He states that *sulphoform* is more than one hundred times as efficacious as ordinary sulphur as a reducing agent. Joseph (*Derm. Cb.*, 1910, xiv) has found it a very useful remedy for *seborrheic alopecia*, and also of service in *eczema* and other *skin diseases*. He uses an ointment containing from five to twenty per cent. of sulphoform.

Sulpholeic Acid.—Sulpholeic acid is prepared as follows: Castor, almond or other fixed oil is gradually mixed with 30 or 40 parts of concentrated sulphuric acid, the mixture being cooled, if necessary, with ice, to prevent a rise of temperature above 50° C. The reaction, which at first is quite violent, is allowed to go on for from six to twelve hours, after which the mixture of acid and glycerin is decanted, the residue mixed with 100 parts of water, and this, after stirring, is also decanted. A salt is then formed by the addition of a hydroxide or carbonate. From this salt pure sulpholeic acid is obtained by careful decomposition with sulphuric acid, and agitation with purified benzin or ether. (*Ph. Rund.*, 1885, p. 154.) Both the sulpholeic acid and its salts have the power of dissolving a large variety of substances, including the essential oils, sulphur, naphthol, iodoform, etc. These liquid mixtures of sulpholeates and other bodies have the property of forming emulsions or even clear solutions with water. The limit of the miscibility (in form of emulsion) or solubility varies considerably, and depends both on the degree of concentration of the sulpholeate serving as a menstruum, and on certain little understood properties of the substances mixed with it.

This peculiar behavior of the sulpholeates and particularly of the sulpho-ricinoleate of alkalies, (see *Sodium Sulphoricinate*) towards many otherwise insoluble or difficultly soluble substances, as well as their pronounced saponaceous character and the great readiness with which they take up and combine with liquids, is said to render them eminently suitable for various technical and medicinal uses.

The liquid alkaline salt which forms the solvent is termed *polysolve* by A. Mueller Jacobs, who believes that the sulpholeate mixtures will be found excellent solvents or vehicles in place of vaseline, oils, glycerin, etc., in perfumery, soap making or pharmacy. (*Am. Drug.*, 1884, p. 22.)

Sulphopyrine. *Antipyrine para-aminobenzenesulphonate. Antipyrine Sulphanilate.*—It is a white, crystalline powder, without odor, readily soluble in water, insoluble in alcohol. Although originally introduced as a substitute for antipyrine, Neumann (*All. W. M. Z.*, 1906, p. 813) has found that this drug has the power of preventing the appearance of that congery of symptoms commonly known as *iodism.* It is also used in *coryza.* The *dose* he employed was fifteen grains (1 Gm.) three times a day.

Sulphoid. *Sulfidal. Colloidal Sulphur.*—It is made by passing hydrogen sulphide through a solution of sulphurous acid and has been used in the treatment of various *skin diseases* as a substitute for the ordinary form of sulphur. According to Joseph (*Derm. Cb.*, 1907), it is distinctly superior to the insoluble forms of sulphur. In *acne* he employed a paste or ointment containing 10 per cent. of *sulphoid* and 2 per cent. of salicylic acid, in *alopecia seborrheacia* and *eczema squamosum* a 10 per cent. solution in water either with or without glycerin.

Sulphur Iodide. *Sulphuris Iodidum. U. S. VIII, Br.*, 1898. *Sulphur Monoiodide. Sulfur Iodatum. Ioduretum Sulfuris. Iodure de Soufre,* Fr. *Jodschwefel*, G.—This compound is chemically regarded as *iodine disulphide*, I_2S_2, or, as sometimes stated, *sulphur subiodide. Sulphur iodide* is in "brittle masses of a crystalline fracture and a grayish-black, metallic luster, having the odor of iodine and a somewhat acrid taste. Almost insoluble in water; soluble in about 60 parts of glycerin; very soluble in carbon disulphide. Alcohol, ether, and a solution of potassium iodide dissolve the iodine, leaving the sulphur. Continued boiling with water vaporizes all of the iodine, leaving about 20 per cent. of sulphur as residue. On exposing Sulphur Iodide to the air, it gradually loses iodine. On heating it, some iodine sublimes at first; at a somewhat higher temperature a sublimate is formed, containing both iodine and sulphur. At a still higher temperature, the whole is volatilized, leaving only a trace of residue." *U. S. VIII.* For method of preparation see *U. S. D.*, 20th ed.

It is rapidly decomposed, when in a state of powder, upon the addition of several of the volatile oils, violet vapors of iodine being evolved, and the odor of sulphur perceived. Sulphur iodide has been considerably employed as an external remedy in various skin diseases, such as *tinea capitis, lupus, lepra*, etc., applied in the form of ointment. *Ointment of sulphur iodide*, formerly official in the British Pharmacopœia, was made by mixing together 1 part of sulphur iodide, 1 part of glycerin and 23 parts of benzoinated lard. Internally, it has been used with alleged advantage in human *glanders*.

Sulphosalicylic Acid. *Salicyl-sulphonic Acid.* $C_6H_3SO_3H.OH.COOH$.—Made by acting upon salicylic acid with strong sulphuric acid. It is in the form of white acicular crystals, soluble in water and alcohol. *Sulphosalicylic acid* is used, like sodium salicylate, in rheumatism, but its chief value lies in its use as a reagent to detect the presence of proteids of all kinds. Egg-albumin (1 in 12,500) can be detected by this reagent, forming a dense, white precipitate which is not redissolved on boiling. It is used to detect albumin, peptones, globulins and fibrin. Albumoses and peptones redissolve when boiled, but again separate on cooling.

Sweet Pellitory.—The root of *Tanacetum umbelliferum* Boiss. (Fam. *Compositæ*), of India, according to David Hooper, contains pyrethrine in minute proportions with fat and wax, an organic acid which is a pigment, glucose, and inulin. (*P. J.*, xxi, 1890.)

Swietenia. *Swietenia febrifuga* Roxb. (*Soymida febrifuga* Juss.) *Rohan Bark.* (Fam. *Meliaceæ.*)—The bark of this East Indian tree contains a bitter principle and is said to be much used as an antiperiodic in half drachm (2 Gm.) *doses.* The extract is used in *dysentery* like kino.

Swietenia Mahagoni Jacq., or *mahogany tree,* which grows in the West Indies and other parts of tropical America, has also a bitter, astringent bark, containing catechin. (*Bull. Soc. Chim. Paris,* xxiv, 118.) The oil of the seeds is said to be used as a purgative in the West Indies. The bark of *S. senegalensis* Desv. (*Khaya senegalensis* A. Juss.), *Juribali bark,* is used on the coast of Africa in the cure of *intermittents,* and Caventou extracted an alkaloid from it. (*Am. J. M. S.*, N. S., xx, 168.)

Symphytum. *Symphytum officinale* L. *Comfrey. Blackwort. Briussewort. Radix Symphiti. Radix Consolidæ Majoris. Consoude,* Fr. *Schwarzwurz, Beinwurz,* G.—A perennial, European herb often cultivated. Its root is spindle-shaped, branched, often more than 2.5 cm. thick, and 3 dm. long, externally smooth and brownish-black, internally white, fleshy, and juicy. By drying it becomes wrinkled, of a firm, horny texture, and of a dark color within. It is almost inodorous, and has a sweetish mucilaginous, feebly astringent taste. Titherley and Coppin in 1912 found 0.8 per cent. of *allantoin,* $C_4H_6N_4O_3$, in the rhizome. Greimer (*A. Pharm.*, 1900, ccxxxviii, p. 505) found two poisonous alkaloids, *consolidine* and *symphytocynoglossine,* both of which are depressants to the central nervous system. Allantoin is an oxidation product of uric acid and is found normally in the excretions of some animals, but apparently cannot be synthesized by the human organism. It is also widely distributed in the vegetable kingdom.

Comfrey contains mucilage in great abundance (according to Lewis, more than althæa root), and a little tannin. It was formerly highly esteemed as a vulnerary. According to Macalister (*B. M. J.*, Jan. 6, 1912), *allantoin,* in aqueous solution in strengths of 0.3 per cent. has a powerful action in hastening epithelial formation, and is a valuable remedy not only in external ulceration, but also in *ulcers of the stomach* and duodenum. Comfrey is a demulcent, and is used domestically in *chronic catarrhs, consumption,* and other lung diseases.

Symplocos. *Symplocos racemosa* Roxb. (Fam. *Styraceæ.*)—The bark of this East Indian tree is said to be a mild astringent, and especially useful in *menorrhagia.* Hesse reported an alkaloid, *loturine,* which has since been found to be identical with *harman* $C_{12}H_{10}O_2$—a derivative of the indol group. (*P. J.*, Sept. 24, 1881.)

Syringa. *Syringa vulgaris* L. *Common Lilac.* (Fam. *Oleaceæ.*)—A large shrub with simple ovate, sub-cordate, opposite, bright green foliage leaves and thyrsoid panicles of fragrant lilac-purple or white flowers. The leaves and fruit of this common ornamental plant have a bitter and somewhat acrid taste, and have been used as tonics and antiperiodics. Petroz and Robinet found in the fruit a sweet and a bitter principle. The latter was afterwards obtained pure by Meillet, who gave it the name of *lilacïn,* and by Bernays, who called it *syringin.* Kromayer (*A. Pharm.*, (2), cxiii, 19) established its glucosidal character, gave it the formula $C_{17}H_{24}O_9 + H_2O$, and showed its identity with the ligustrin found in privet (see *Ligustrum*). It forms stellate, colorless crystals which are soluble in hot water or alcohol and fuse at 212° C. On heating with dilute acids it breaks up into *syringenin,* $C_{11}H_{14}O_4$ (which has been recognized as *oxymethyl coniferin*) and glucose. Antipyretic and antimalarial properties have been attributed to syringin.

Tacamahac. *Tacamahaca.*—These names are applied to a resinous substance which is sometimes substituted for or admixed with Elemi resin. There are two classes of these products: the West Indian, which have an odor like that of incense, and the East Indian, whose odor resembles Elemi.

The *West Indian tacamahacs* are derived from species of the *Burseraceæ. Cayenne Incense,* also called *Brazilian Elemi,* is obtained from the *Protium heptaphyllum* March (*Icica heptapylla* Aubl.) and related species (see also under *Elemi*). The most important of this group is derived from *Bursera tomentosa* Triana (*Elaphrium tomentosum* Jacq.), a tree of considerable size, of the Fam. *Burseraceæ,* growing in the island of Curaçao and in Venezuela, is in irregularly shaped pieces of various sizes. The color is usually light yellowish or reddish-brown, but in the larger masses is more or less diversified. The pieces are in general translucent, though frequently covered with powder upon their surface, so as to render them apparently opaque. They are heavier than water, brittle, and pulverizable, yielding a pale yellow powder. Their odor is resinous and agreeable, their taste bitter, balsamic, and somewhat acrid. Exposed to heat, they melt and exhale a stronger odor. Tacamahac is partially soluble in alcohol, and completely so in ether and the fixed oils. It consists of resin with a little volatile oil.

The East Indian tacamahac and called *tacamahaca orientale,* or *tacamahaca in testis,* comes into the market in gourd shells covered with rush leaves. It is of a pale yellow color inclining to green, slightly translucent, soft, and adhesive, of an agreeable odor, and an aromatic bitterish taste. It is at present very rare in commerce. The tree which yields this resin produces a drupe, about as large as a plum, from the seeds of which 50 per cent. of a greenish-yellow fixed oil is obtained by expression, which is used in India for lamps, and as a local application in the *itch.* (*J. P. C.*, 1861, 23.) Guibourt described several other varieties of tacamahac, which, however, are little known. Among them is a soft, adhesive, dark, green oleoresin (*J. P. C.*, 3e sér., xxiv, 396), said to be procured from the *Calophyllum Tacamahaca* Willd., growing in the islands of Réunion and Madagascar.

Tacamahac was formerly highly esteemed as an internal remedy, but is now used only in ointments and plasters. Its properties are analogous to those of the turpentines. It is sometimes used as incense. It is known as *Bourbon tacamahac,* also as *Balsamum* (or *Resina*) *Mariæ.*

Tachia. *Tachia guianensis* Aubl.—The root of this tree (Fam. *Gentianaceæ*) has been used under the name of *Caferana,* in Brazil, as an antiperiodic and tonic. According to Peckoldt it contains an organic, crystalline substance, *caferanine.* (See *Merck's Bericht*, 1889; also *B. Chem. G.*, 1899, No. 7.)

Taka Diastase.—This ferment discovered by Takamine is formed by the action of a fungus (*Moyashi; Aspergillus Oryzæ* Cohn., *Eurotium Oryzæ* Ahlburg; for description, see *A. J. P.*, 1898, 137) upon steamed rice, and is used in Japan, where it is known by the name of *koji*, in the preparation of the national intoxicating beverage *sake;* it has also been employed to act upon maize in the making of whisky. Taka-diastase is a yellowish-white, highly hygroscopic powder, almost tasteless, freely soluble in water. It is capable, under proper conditions, of converting one hundred times its weight of starch into glucose in ten minutes. Its action and therapeutic uses are the same as those of diastase from malt. (See *Maltum*, Part I.) It should be given in the middle of the meal, in *doses* of from five to ten grains (0.32–0.65 Gm.), in capsules; or, after the meal, in slightly alkaline solution.

Tamaquare.—A fluid preparation from a Brazilian *Myrospermum*, which is miscible with alcohol, does not dry and possesses an unctuous consistency. It is used in certain diseases of the eye, petrolatum being used as the vehicle. From a three to a ten per cent. ointment is the usual strength.

Tanghinia. *Tanguin. Ordeal Bean of Madagascar.*—The seed of the *Tanghinia venenifera* Poir. (*Cerbera Tanghin* Hook.) (Fam. *Apocynaceæ*) contains a poisonous principle, *tanghinin*, which by some has been considered identical with cerberin. It was found by Quinquaud (*Journ. de l'Anat. et de Phys.*, 1886, xxii) to exert a powerful effect on the nervous system as well as on the circulation.

Tang-kuei or **Man-mu.**—Under the name of *tangkuei* the Chinese have used for a long time a root obtained from *Angelica anomala* var. *chinensis* (Fam. *Umbelliferæ*). A fluid extract of this root has been introduced into European medicine under the name of *eumenol* and is recommended by a number of authors in the treatment of *dysmenorrhea* and other uterine complaints. Read and Schmidt (*Proc. Soc. Exp. Biol. and Med.*, 1923, xx, 395) find that tangkuei produces in the lower animals fall of blood pressure, diuresis, and stimulation of the unstriped muscles, especially the uterus. They separated a crystalline non-nitrogenous, non-glucosidal substance which had the characteristic effect upon the uterus without circulatory depression. The *dose* of this fluidextract is one tablespoonful three times a day.

Tannaphthol.—This is a condensation product of benzonaphthol with tannin albuminate. It is used as a surgical dusting powder, also in the treatment of *diarrhea* in doses of from eight to fifteen grains (0.5 to 1 Gm.).

Tannalum. *Tannal. Basic Aluminum Tannate.* $Al(OH)_2(C_{14}H_9O_9) + 5H_2O$.—This is a brownish-yellow powder, insoluble in water, which has been especially commended by Heymann as a mild, astringent, non-irritant substance, to be used as a dusting powder or by insufflation in diseases of the nasal and laryngeal mucous membranes. By the action of tartaric acid it becomes converted into the so-called *soluble tannal*, $Al(C_4H_4O_6)$-$(C_{14}H_9O_9) + 3H_2O$, also used locally.

Tannocol. *Gelatin-tannate.*—This is a tasteless, odorless powder, containing about 50 per cent. of tannic acid, having the same therapeutic properties and applications as albumin tannate. It is claimed by Rosenheim that it is superior to that substance in being cheaper, of greater constancy of constitution, and less easily affected by the gastric juices. In the intestines it is decomposed by the alkaline secretions and tannic acid is liberated. *Dose*, fifteen to thirty grains (1–2 Gm.).

Tannoform. *Helgotan. Methylene Ditannin.* $CH_2(C_{14}H_9O_9)_2$.—The condensation product of gallotannic acid and formaldehyde, is made by dissolving five grammes of tannin in about fifteen kilogrammes of hot water, adding three kilogrammes of 30 per cent. formaldehyde, and then adding concentrated hydrochloric acid until no further precipitate is thrown down. This requires about twelve to fifteen kilogrammes of acid. The precipitate is then washed with water and dried at a low temperature.

Tannoform occurs as a light, pinkish powder which decomposes at about 230° C. It is dissolved by alcohol and is insoluble in all the other usual organic solvents; but is soluble in diluted ammonia, sodium or potassium hydroxide solutions, giving a brownish-red solution, from which it is again precipitated upon the addition of an acid. When warmed with concentrated sulphuric acid it dissolves with a brown color, turning on further heating to green, and then to blue. This green or blue solution gives a blue color with alcohol, which on standing some time turns to a wine-red, and on dilution with soda solution to a grass-green color. According to Sollmann (*J. P. Ex. T.*, 1921, xvii, 94) there is considerable variation in the composition of specimens of tannoform. He finds that, generally speaking, a considerable proportion is dissolved in neutral or acid aqueous solutions but that they dissolve almost immediately and completely in alkaline solutions.

Tannoform has been used with alleged good results in *enteritis* and other forms of *diarrhea.* It is asserted that the drug is decomposed by the intestines, the tannic acid radical acting as an astringent, and the formaldehyde as an antiseptic. It is, however, more frequently employed as a local remedy in the treatment of *eczema, bed sores*, etc. In *hyperidrosis of the feet*, well rubbed in between the toes over night, it will often give relief of considerable duration, but has the disadvantage of staining the skin brown. It has also been used externally to control *night sweats. Dose*, from five to fifteen grains (0.32–1.0 Gm.), in capsule, from three to six times a day.

Tannon. *Tannopin*, $(CH_2)_6N_4(C_{14}H_{10}O_9)_3$, is a condensation product of tannin and hexamethylenetetramine. It is a light brown, tasteless and odorless, non-hygroscopic powder, insoluble in water, weak acids, spirit, and ether, but dissolving slowly in dilute alkaline solution. It has been used by Schreiber (*D. M. W.*, 1897) in *diarrhea* in *doses* of fifteen grains (1.0 Gm.) from three to four times a day.

Tansy. *Tanacetum. U. S.* 1890.—Under this name the U. S. Pharmacopœia formerly recognized the tops and leaves of the *Tanacetum vulgare* L., a perennial herbaceous plant rising two or three feet in height, which is cultivated in our gardens, although growing wild in the roads and in old fields. It was originally introduced from Europe. It is in flower from July to September.

Tansy was officially described as follows: "Leaves about 15 Cm. long; bipinnatifid, the segments oblong, obtuse, serrate or incised, smooth, dark green, and glandular; flower-heads corymbose, with imbricated involucre, a convex, naked receptacle, and numerous yellow, tubular florets." *U. S.*, 1890. The odor is strong, and characteristic, but much diminished by drying; the taste is warm, bitter, somewhat acrid, and aromatic. These properties are imparted to water and alcohol. Leppig (*Inaug Dis.*, Dorpat, 1882), found in both the flowers and the leaves a peculiar, bitter principle *tanacetin*, to which he gives the formula $C_{11}H_{16}O_4$, and which forms a very hygroscopic, brownish, amorphous mass, easily soluble in alcohol and in water, insoluble in ether. It possesses a taste at first characteristically bitter like willow bark, and then cooling and caustic. The essential oil consists of 70 per cent. of a ketone, *tanaceton*, which appears to be identical with thujone; 26 per cent. of borneol; and 1 per cent. of a terpene, boiling at 155° to 160° C. (See Semmler, *B. Chem. G.*, xxv; see also *Schim. Rep.*, April, 1893, and April, 1897; and Gildemeister and Hoffmann, *Aetherische Oele.*)

Tansy adds to the medicinal properties of the aromatic bitters those of an irritant narcotic. It has been recommended in *intermittents, hysteria,* and *amenorrhea*, but in this country is little employed in regular practice. The seeds are said to be effectual as a vermifuge. Tansy has been used to a considerable extent as a domestic abortifacient, but Macht (*J. P. Ex. T.*, 1913, iv, 547) has shown that it has no stimulating effect on the uterus.

There have been reported several fatal cases of poisoning by it. The symptoms caused by it have been abdominal pain, vomiting, violent epileptic convulsions often followed by profound coma, dilated pupils, great disturbances of respiration, frequent and feeble pulse, and death, which has been said to be from heart failure, but is probably the outcome of a paralytic asphyxia. The minimum fatal dose can scarcely be considered to have been positively ascertained, but a fluidrachm (3.75 cc.) of the oil is said to have caused death, although recovery in one case occurred after taking half a fluidounce. Tansy tea has also caused death. (For cases, see *Am. J. M. S.*, xvi, xxiii, xxiv; *J. P. C.*, April, 1870; *J. A. M. A.*, xlvii, p. 509.) Post-mortems have been reported in which no inflammation of the gastrointestinal mucous membranes could be discovered.

The *dose* of the powder is from thirty grains to a drachm (2.0–3.9 Gm.) two or three times a day; usually in the form of an infusion.

Tapioca.—Under this name the U. S. P. formerly recognized the starch grains obtained from the bitter cassava (*Manihot utilissima* Pohl), and the sweet cassava (*M. Aipi* Pohl) (Fam. *Euphorbiaceæ*). The starch is extracted from the thickened rhizome and is known in commerce by the names of *Cassava, Tapioca* or *Manioca Starch,* and as *Bahia, Rio* or *Para Arrowroot.* These plants are native to Brazil and are cultivated in other tropical or subtropical countries including both the East and West Indies.

The root of the *sweet* cassava may be eaten with impunity; that of the *bitter*, which is the most extensively cultivated, abounds in an acrid, milky juice, which renders it highly poisonous if eaten in the recent state. Henry and Boutron Chalard affirm that the bitter cassava contains hydrocyanic acid (*J. P. C.*, xxii, 119), but Peckoldt claims that its poisonous effects are due to *manihotoxine* (*Ph. Rund.*, iv, 1890). In the production of the starch from the bitter cassava the hydrocyanic acid which is present in fresh fruits is entirely eliminated by the process of washing and drying.

For description of the preparation of tapioca see *U. S. D.*, 20th ed., p. 1632; also *Ph. Era*, 1921, liv, 385.

Tapioca is in irregular, hard, white, rough grains, possessing little taste, partially soluble in cold water, and affording a fine blue color when iodine is added to its filtered solution. The partial solubility in cold water is owing to the rupture of the starch granules by heat. Examined microscopically the starch grains of cassava are rounded or truncated on one side, single or from 2 to 8 compound, 6 to 35 microns in diameter, the hilum central, circular or triangular and frequently with radiating clefts, the lamellæ indistinct, and polarization crosses very prominent.

Tapioca meal, called sometimes *Brazilian arrowroot*, and by the French *moussache*, is the fecula dried without heat. Its granules are identical with those already described. A factitious tapioca is found in commerce, consisting of very small, smooth, spherical grains, and supposed to be prepared from potato starch. It is sold under the name of *pearl tapioca.*

Being nutritious, and the same time easy of digestion and destitute of irritating properties, tapioca forms an excellent diet for the sick and convalescent. It is prepared for use by boiling it in water. Lemon juice and sugar are usually grateful additions, and in low states of disease or cases of *debility* it may be impregnated with wine and nutmeg or other aromatic.

Cassaripe is the thickened gum obtained from the root of the bitter cassava, which is said to be innocuous and so actively antiseptic as to be habitually used in Brazil for the preservation of meat. According to S. D. Risley (*Phila. Med. Journ.*, 1899), the 10 per cent. ointment of cassaripe is useful in *suppurating conjunctivitis* and *ulcers* of the *cornea*, applied with gentle massage three or four times a day.

Taxus. *Taxus baccata* L. *Yew Tree. If commun*, Fr. *Eibe*, G. (Fam. *Taxaceæ.*)—This is a handsome evergreen tree attaining the height of 60 feet, with a short trunk and broad, low crown, reddish, flaky bark, linear to falcate, dark green leaves and scarlet fruits, each of which consists of a globose disk, in which is borne an ellipsoidal brown seed. The fruit appears to be a deadly poison. In a fatal case the child was found semicomatose, with convulsions, a cold and clammy skin, difficult respirations, dilated pupils, and making attempts at vomiting. The poison is probably in the seeds. (See 16th edition, *U. S. D.* For fatal cases in adults, see *M. T. G.*, 1870, ii; also *L. L.*, 1870, 471; also *P. J.*, viii, 361.) W. Marmé obtained from yew seeds and leaves an alkaloid, $C_{37}H_{51}O_{10}N$, to which the name of *taxine* has been given. It was a white, poisonous, crystalline powder, only slightly soluble in water, easily soluble in ether, alcohol, chloroform, benzene and carbon disulphide, but not in petroleum benzin. With concentrated sulphuric acid it gave a red color, but dissolved without color in nitric and phosphoric acids. (*A. J. P.*, 1876, 353.) For Vreven's method of isolating taxine, see *P. J.*, 1896, 215. Taxine has been studied by a number of investigators notably Winterstein (*Zeit. P. C.*, 1921, cxvii, p. 240 and 1923, cxxviii, p. 175). It melts between 105° and 110° C. and is

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dextro-rotatory. Its salts are amorphous, although the base is crystalline. Amato and Capparelli (*Gazz. Chim.*, x, 349) prepared from the leaves a volatile alkaloid, which was soluble in cold sulphuric acid with yellow color, becoming red on heating. They also isolated a nitrogenous crystalline and colorless principle, fusing at from 86° to 87° C., soluble in alcohol, insoluble in water, named *milossin.*

Lefebvre (*A. Pharm.*, ccxlv, 486) has isolated from the twigs of the yew a crystalline glucoside to which he gives the name *taxicatin.* It had the formula of $C_{13}H_{22}O_7 + 2H_2O$ and a melting point of 165° C.

Tayuya.—The root of the *Dermophylla* (*Cayaponia*) *pendulina* Manso (Fam. *Cucurbitaceæ*), is used in Brazil, under the name of *tayuya,* in *syphilis*, etc. (*N. R.*, 1877, 234); also, under the same name, the root of the *Trianosperma ficifolia* Mart. (*Cayaponia Martiana* Cogn.) (*P. J.*, x, 667), and probably various other roots. In *C. ficifolia* Cogn. two alkaloids, *trianospermine* and *trianospermitine,* and a bitter principle, *tayuyin,* have been found by Peckoldt (*P. J.*, x, 667), and in *T. dermophylla* a green resin, bitter extractive, and tannic acid were found by the same investigator. (*B. G. T.*, lxxxiv, xci. See also *Proc. A. Ph. A.*, xxiv.)

Tea. *Thé*, Fr. *Thee*, G.—The plant which furnishes *tea*—*Thea sinensis* L. (*Camelia Thea* Link) (Fam. *Theaceæ*)—is an evergreen shrub. It has numerous alternate branches, furnished with elliptic-lanceolate, or obovate-lanceolate, short-petiolate, acuminate leaves, which are serrate except at the base, smooth on both sides, occasionally pubescent beneath, green, shining, pinnately veined and having a prominent midrib. They are two or three inches long, and from half an inch to an inch in breadth. The flowers are either solitary or supported, two or three together, at the axils of the leaves. They are of considerable size, not unlike those of the myrtle in appearance, consisting of a short green calyx with five or six lobes, of a corolla with from four to nine large unequal snow-white petals, of numerous stamens with yellow anthers and connected at their base, and of a pistil with a three-parted style. The fruit is a three-locular and three-seeded capsule.

There are two principal varieties of *T. sinensis,* viz. *viridis* Pierre (*T. viridis* L.), which is a large spreading shrub, having light green lanceolate leaves from 12 cm. long to 4 cm. wide; and a second variety, *Bohea* Pierre (*T. Bohea* L.), which is an unright shrub with dark-green elliptical leaves 6 cm. long and 3 cm. wide. The flowers of the latter occur in groups of two or three, whereas in *viridis* they are single. There are a great many varieties of tea, on the market, and their trade value is influenced by the peculiarities of mother plant and climate, and the degree of ripeness and preparation of the leaves. As a rule only the youngest leaves are gathered. The so-called black and green teas are due to the method of preparation of leaves. In the first the chlorophyll is destroyed, whereas in the latter it is unaffected. Winton gives the following characters as common to all tea leaves: "The firm, rather thick texture; the glossy upper surface; the short stem into which the base of the leaf tapers; the thick margins, rolled a little towards the inner surface, with cartilaginous teeth; the veins which branch from the midrib at angles usually greater than 45 degrees, and at some distance from the margin form loops uniting adjoining ribs. The teeth on the margin of the leaf are shrunken multicellular glands which break off readily from the old leaves." (For discussion of microscopical characteristics, see Winton and Moeller, *The Microscopy of Vegetable Foods.*

The tea plant is a native of China and India, and is cultivated in both countries, but most abundantly in the former. It is also cultivated in India (Assam), Ceylon, Java and in South Carolina. In Japan it forms hedge rows around the rice and corn fields; in China, whence immense quantities of tea are exported, whole fields are devoted to its culture. It is propagated from the seeds.

(An elaborate article on tea, with methods of cultivation, etc., by Wm. B. Marshall, will be found in *A. J. P.*, 1903, p. 79.)

The odor of the tea leaves themselves is very slight, and it is customary to mix with them the flowers of certain aromatic plants, as those of the orange, different species of jasmine, the rose, *Osmanthus fragrans* Lour. (*Olea fragrans* Thunb.), of the *Oleaceæ,* and *Camellia Sasanqua* Thunb., in order to render them pleasant to the smell. The flowers are afterwards separated by sifting or otherwise. (See *P. J.*, xv, 112.) Under the name of *flowers of tea* was at one time sold a waste product consisting of the hair of young leaves, but the flowers themselves have been used to make a beverage. (*P. J.*, lxxi, p. 453.)

Bush Tea and *Honig Thee*, used at Cape Colony, South Africa, as a substitute for tea, are the dried leaves and tops of several species of *Cyclopia,* among which are *C. subternata* Vog., *C. latifolia* DC., *C. genistoides* Vent. (Fam. *Leguminosæ.*) According to the analysis of Henry G. Greenish, they do not contain theine, but a glucosidal body, *cyclopin*, $C_{25}H_{28}O_{13}$. (*P. J.*, xi, 549.)

The numerous commercial varieties of tea may be divided into two great groups, *Green Tea* and *Black Tea.*

The differences between black tea and green tea are due chiefly to the methods of their preparation. In making green tea, the leaves after being dried for a short time in the sun are heated in open pans with continual agitation, somewhat after the manner of roasting coffee. In the case of *black tea* (formerly called *bohea*), the dried leaves are rolled either between the hands or between two flat surfaces, during which process they acquire their characteristic twisted shape and some of the juice is pressed out; they are then piled on mats and allowed to stand exposed to the air at a temperature of 35 to 40° C. for about twelve hours. During this time they undergo a sort of fermentation, which is signified by a change in the color of the leaf from green to red and finally to the dark brown of commerce. It is believed that this change is due to the effect of an oxydase which is called *thease.* As a result of this treatment some of the aromatic principle of the tea leaf is volatilized and a portion of the tannic acid is destroyed. As a rule, therefore, black tea has a somewhat less fragrant odor and a less astringent taste than green tea. Green tea is sometimes artificially colored by means of Prussian blue or other coloring matter.

A sophisticated tea is largely exported from China, consisting of powdered tea mixed with sand and other earth, and agglutinated with gum;

that which is to pass for black being colored with plumbago, and the green with the coating above referred to. On analysis, these teas were found to afford from 35 to 45 per cent. of ash, while the genuine yields only 5 per cent. A very full account of the adulteration of tea and the methods for the detection of the same may be found in Allen, *Com. Org. Anal.*, 2d edition. See also Rehfous, *Pract. Drug.*, Nov., 1917, 38.

The analyses below[1] by Y. Kozai (*Bulletin No. 7, Imperial College of Agriculture,* Japan) have a special value, owing to the author's knowledge of tea manufacture. Unusual precautions were taken in sampling the leaves, to insure strictly parallel specimens being taken. The figures refer to the moisture-free leaves in each case.

[1] Analyses of Tea (percentage composition).	Unprepared Leaves.	Green Tea.	Black Tea.
Caffeine or Theine	3.30	3.20	3.30
Ether Extract	6.49	5.52	5.82
Hot-water Extract	50.97	53.74	47.23
Tannin (as Gallotannic Acid)	12.91	10.64	4.89

The most important principle in tea is the substance discovered by Oudry and by him called *theine,* but which is now known to be identical with *caffeine* (see *Caffeina*). In 1888 Kossel showed the presence of small amounts of a related principle *theophylline* (dimethylxanthin). Traces of theobromine have also been reported. In 1848 Rochleder isolated a yellowish amorphous substance which he called *boheic acid,* but whose chemical identity seems doubtful.

Tea also contains a notable proportion of tannin (from 5 to 20 per cent.) which is very similar to, if not identical with, that of oak bark. There are present also traces of a volatile oil to which is due the characteristic odor. This oil is of a lemon yellow color and easily resinified on exposure to air.

The proportion of caffeine found in tea varies considerably, the general range being from about 1 to 5 per cent.

Tea is astringent and gently excitant, and exerts a decided influence over the nervous system, evinced by the feelings of comfort and even exhilaration which it produces, and the unnatural wakefulness to which it gives rise when taken in unusual quantities or by those unaccustomed to its use. It is almost exclusively used as a beverage. Taken moderately, and by healthy individuals, it may be considered as practically harmless; but long continued in excessive quantity it is capable of inducing unpleasant nervous and dyspeptic symptoms. Green tea is decidedly more injurious in these respects than black, and should be avoided by dyspeptic individuals, and by those whose nervous systems are peculiarly excitable. It is rarely used as a medicine, but the infusion is popularly employed to relieve neuralgic headaches.

Tea Oil. *Tea-seed Oil.*—The seeds of various species of *Camellia,* especially the *C. drupifera* Lour. (*C. oleifera* Wall.) and the *C. Japonica* L., yield on pressure a pale yellow fixed oil which is used by the Chinese both as fuel and food. It has been used in England as an adulterant of olive oil.

The seeds of the *Camellia Japonica,* which sometimes appears in our gardens as an ornamental shrub, are said to contain a poisonous glucoside *camellin.*

Telfairia Pedata Hook. (Fam. *Cucurbitaceæ.*)—The seeds of this East African climbing shrub yield a deep yellow fragrant oil, of specific gravity 0.918, containing *telfairic acid.* (*Chem. Zeit. R.,* xxiv, 24.)

Tellurium. (Te. Atomic weight, 127.5.)—The metal tellurium is a dark gray powder with a specific gravity of 6.25 and melting point of 450° C. The first physiological investigations as to the action of tellurium were made by Hansen (*Chem. Gaz.,* 1854), who found that the *potassium tellurate* was toxic for both dogs and men. His investigations have been extended and confirmed by William J. Gies (*M. A.,* June, 1901), who found that in doses of one-third of a grain per kilogramme sodium tellurate caused in the dog vomiting, diarrhea, unconsciousness, paralysis, convulsions, and death, with pronounced inflammatory changes in the intestines and kidneys similar to those seen after arsenic. Characteristic was the pigmentation of all parts of the body by metallic tellurium. During life the brown or greenish discoloration of urine and the very pronounced garlicky odor of the breath were almost diagnostic. The continuous administration of minute doses had no effect upon metabolism, but if the amount ingested was increased, gastro-intestinal irritation with restlessness soon appeared. Tellurium was found in the feces, urine, breath, and skin secretions. In man drowsiness, nausea and constipation seemed to result from the remedy, given in doses up to half a grain. There was also a marked anhidrotic action, even in healthy men, appearing fifteen minutes to one hour after the ingestion of the dose. Potassium tellurate is an efficient remedy for the arrest of *colliquative sweating,* but the pronounced alliaceous odor which it imparts to the breath, and even to the perspiration, greatly interferes with its use. *Dose* of potassium or sodium tellurate, one-sixth to one-half of a grain (0.01–0.032 Gm.).

Tellurous acid and its potassium salt have been recommended by Gosio (*Zeit. Hyg. u. Inf.,* 1905, li, 65) as an indicator of the presence of living bacteria, especially in sera. He asserts that it is harmless to the human and is reduced by growing bacteria giving rise to color change.

Sodium Tellurite, Na_2TeO_3, is a white powder sparingly soluble in water. The aqueous 2 per cent. solution of sodium tellurite stains bacteria black by the precipitation of *metallic tellurium,* and has been highly recommended for the purpose of microscopic staining. Cavazutti (*Ann. d'Igiene,* 1921, xxxi, 551) finds that sodium tellurite has marked bactericidal properties.

Tephrosia. *Tephrosia virginiana* (L.) Pers. *Turkey Pea. Wild Sweet Pea. Catgut. Goat's Rue. Hoary Pea. Devil's Shoestring. Tephrosie,* Fr., G. (Fam. *Leguminosæ.*)—Several species of *Tephrosia* are employed in different parts of the world, though unknown in general commerce. They are leguminous plants, shrubby or herbaceous, with odd-pinnate leaves and white, red or purplish racemed flowers. They are generally possessed of cathartic properties, their leaves or roots being employed. Plugge (*Proc. A. Ph. A.*, 1897, 560) examined the root of *T. macropoda* and found a poisonous active principle, not identical with cytisine.

Hanriot isolated from *T. vogellii*, a crystalline principle, *tephrosin*, which occurs in small glistening crystals which are almost insoluble in water, slightly soluble in alcohol or glycerin, more readily soluble in acetone, and freely soluble in chloroform. Its formula is $C_{34}H_{26}O_{10}$. *Tephrosal*, $C_{10}H_{16}O$, is a volatile, aromatic liquid, slightly soluble in water, more readily soluble in alcohol, ether, benzin, and chloroform. (*T. G.*, li, 302.)

According to Holmes (*P. J.*, 1910, lxxxiv) this species is used in Africa as a fish poison. Its toxicity seems to be due to the neutral principle, tephrosin. There is no evidence as to its noxiousness for human beings.

Tephrosia virginiana (L.) Pers. is native to dry sandy soil of the Eastern United States. It is a foot or two high, with pubescent stems and leaves and a handsome terminal raceme or panicle of yellowish-white, purple tinged flowers. The roots, which are slender, long, and matted, are tonic and aperient, and are said to have been used by the Indians as a vermifuge, given in the form of decoction.

The leaflets of *T. apollinea* DC. have been employed as an adulterant for Alexandria senna. They may readily be detected by their obovate-oblong outline with emarginate apex and straight, parallel, lateral veins.

Terpinol.—This is not a simple body, but a mixture of terpenes with variable proportions of an alcohol, *terpineol*, $C_{10}H_{17}OH$. It forms a colorless oily substance with a hyacinthine odor; it is produced by boiling terpin with diluted mineral acids. It is insoluble in water, but readily soluble in alcohol and ether. Terpinol has been used in chronic *bronchial catarrh*, and is especially commended by Lazarus when there is much irritation of the membrane with scanty secretion. Janowsky states that it is a valuable remedy in *hemoptysis*. The *dose* is three to five minims (0.2–0.3 cc.) at intervals of from one to four hours, administered in capsules.

Testa Præparata. *Prepared Oyster-shell.*—Powdered oyster shell was at one time used in the same manner as prepared chalk as an antacid in *diarrhea*, in the *dose* of from ten to forty grains (0.65–2.6 Gm.) or more, frequently repeated. A preparation was introduced into use in this country, under the name of *Castillon's powders*, consisting of sago, salep and tragacanth, each, in powder, *a drachm*, prepared oyster-shell, *a scruple*, and sufficient cochineal to give color to the mixture. A drachm of this is boiled in a pint of milk, and the decoction used *ad libitum* as a diet in chronic bowel affections.

Tetrabromphenolphthalein Sodium. *Tetrabromphenolphthaleini Sodium.*—$NaOOC.C_6H_4.C{:}\text{-}C_6H_2Br_2O.C_6H_2Br_2ONa$.—This salt is a purple powder freely soluble in water, forming slightly alkaline solutions. It is precipitated from its solution by acids.

Tetrabromphenolphthalein sodium has been suggested for use in connection with X-ray examination of the gall-bladder. After the intravenous injection of the salt sufficient of it appears in the gall-bladder to cast a shadow on the Roentgen ray plate (see *Phenoltetrachlorphthalein*). The likelihood of toxic effects from the use of large quantities of the drug is, as yet, not accurately established. The doses which have been employed have been equivalent to about 0.1 Gm. per kilo of body weight which means for the ordinary man from seventy to eighty grains (4.5 to 5 Gm.). It is injected intravenously. Smithies and Oleson (*J. A. M. A.*, 1925, lxxxiv, 1494) report two cases of serious irritative phlebitis produced by the sodium salt and prefer the calcium compound.

Graham and Cole (*J. A. M. A.*, 1925, lxxxiv, 1175) have reported on the use of sodium compound of *tetraiodophenolphthalein* for the same purpose. At the present writing the method must be regarded as in the experimental stage, but seems to hold promise as a diagnostic measure of much value.

Tetrachlorethane. *Acetylene tetrachloride.* $CHCl_2.CHCl_2$.—A colorless liquid, sp. gr. 1.582, boiling point 147° C. Soluble in alcohol and ether, insoluble in water. A solvent for greases and waxes, and also used in cellulose acetate varnishes. A number of cases of poisoning from the use of this compound in industries have been reported. According to Lehmann (*Arch. f. Hyg.*, 1911, lxxiv) it is many times more toxic than either chloroform or carbon tetrachloride. The symptoms observed in industrial poisoning by it have been drowsiness, nausea, destruction of blood corpuscles, jaundice and in fatal cases symptoms resembling those of acute yellow atrophy of the liver. For further information upon this subject see Hamilton (*J. A. M. A.*, 1917, lxix, 2037) and Minot and Smith (*A. I. M.*, 1921, xxviii, 687).

Tetragastris. *Tetragastris panamensis* (Engl.) O. Kuntze. *Bois Cochon*, or *Sucrier de Montagne*, Fr. (Fam. *Burseraceæ.*)—This native of Panama has been examined by Gaucher, Combemale and Marestang (*France Méd.*, October, 1888), who find in it an alkaloid and a resin. The extract of the root and stems produce in the guinea pig rapid and considerable lowering of temperature, progressive paralysis, general convulsions, dilatation of the pupils, respiratory irregularity and cardiac paresis. The alkaloid was found to be a convulsive agent, acting upon the spinal cord. The resin, which seemed much more active than the alkaloid, acted as a paralyzant.

Tetralin.—A name applied to solvents made from *tetrahydronaphthalene*—$C_2(CH_2)_4(CH)_4$—and *dekahydronaphthalene* made by the hydrogenation of naphthalene. They are used in varnishes and shoe polishes. It is used in the preparation of a diagnostic test for tuberculosis devised by Wassermann (*D. M. W.*, 1923, xlix, 303).

Tetronal. *Diethyl-sulphone-diethyl-methane.* $(C_2H_5)_2C(C_2H_5SO_2)_2$.—This occurs as a white crystalline powder, insoluble in water, soluble in alcohol and fusing at 85° C. The effects of this compound are practically the same as the closely allied *Trional.* (See Part I.) Although the introducers of this group of drugs, Baumann and Kast (*A. E. P. P.*, 1892, xxxi), classed tetronal as the most powerful of the group, it has failed to achieve the popularity of the official representatives. The *dose* is from eight to fifteen grains (0.5–1 Gm.).

Teucrium. *Teucrium Chamædrys* L. *Germander Chamædrys. Petit Chêne*, Fr. *Edlar, Gamanderlein, Frauenbiss*, G. (Fam. *Labiatæ.*)—A perennial herb indigenous to Europe which possesses ovate to oblong, incised, crenate leaves and axillary whorls together with terminal racemes of showy reddish-purple or rose colored flowers, with red and white spots on the corolla. It has been employed as a mild corroborant in *uterine, rheumatic, gouty* and *scrofulous affections* and *intermittent fevers.* Germander was an ingredient in the *Portland powder,* noted as a remedy in gout. This powder, according to the original prescription, consisted of equal parts of the roots of *Aristolochia rotunda* L. and *Gentiana lutea* L., of the tops and leaves of *Teucrium Chamædrys* and *Erythræa Centaurium* (L.) Pers. and of the leaves of *Ajuga Chamæpitys* Schreb., or *ground pine.* The *dose* was a drachm every morning before breakfast for three months, then forty grains for three months, afterwards half a drachm for six months, and finally half a drachm every other day for a year. (Parr.)

Two other species of *Teucrium* have been used in medicine,—*T. Marum* L., *cat thyme,* or *Syrian herb mastich,* indigenous in the south of Europe, and *T. Scordium* L., or *water germander,* growing in the higher latitudes of the same continent. The former is a warm, stimulating, aromatic bitter, and has been recommended in *hysteria, amenorrhea* and *nervous debility;* the latter has the odor of garlic and a bitter, somewhat pungent taste, and was formerly highly esteemed as a corroborant in *low forms of disease;* but neither of them is now much employed. *T. Marum* is an errhine, and was formerly an ingredient of the *Pulvis Asari Compositus.*

A plant said to have been used advantageously in *cholera* in the Levant, a specimen of which was sent to Paris, proved to be *Teucrium Polium* L. (*J. P. C.*, xv, 352.) Moorhof (*Ph. Cent.*, 1893, 89) prepared a purified liquid extract from *T. Scordium,* and named it *teucrin,* which he recommends in the treatment of fungoid diseases and abscesses.

The *dose* of either of the three species is about half a drachm (2.0 Gm.).

Tfol is an argillaceous earth, containing free gelatinous silica, which is largely used in northern Africa as a substitute for soap. It has been strongly recommended by Lahache for the purpose of emulsifying tar oil and for disinfecting purposes.

Thalictrum.—This is a genus of perennial herbs belonging to the *Ranunculaceæ* and characterized by possessing alternate, ternately-compound or decompound leaves and small flowers, with petaloid or greenish calyx and no corolla, arranged in panicles or corymbs. It appears probable that many species of this genus have active medicinal or toxic properties. In 1879 Henriot and Doassans asserted that they had separated from the roots of the *Thalictrum macrocarpum* Gren., a shrub of the Pyrenees, a crystalline yellow subtance having very pronounced toxic principles, analogous to those of curare; and subsequently stated (*C. R. S. B.*, 1880) that this substance really consists of two principles,—an alkaloid, *thalictrine,* obtained in the form of prismatic needles, insoluble in water, soluble in alcohol, forming crystalline salts with acids, and *macrocarpin,* a yellow crystalline body, soluble in water, representing the coloring principle of thalictrum. Subsequently *berberine* was found by Doassans and Mousset in *Thalictrum flavum* L., *Fen Rue* or *Monk's Rhubarb,* a shrub widely distributed in Europe and Asia, macrocarpin being, according to this authority, very closely allied to berberine, but differing in that its color is not affected by ammonia. Rochebrune (*Toxicolog. Africaine,* i) has found both thalictrine and macrocarpin in the roots of *Thalictrum glaucum* Desf., of Spain. Thalictrine he states to be a very active cardiac poison, producing loss of power, convulsive movements, irregularity and depression of the heart's beat, and finally death, in some cases with convulsions. According to Rochebrune, thalictrine also exists in the African species *Thalictrum rhynchocarpum* Q. Dillon and A. Rich.

Thalline. *Tetrahydroparaquinanisol* or *Tetrahydroparamethyloxyquinoline.* $C_9H_6H_4N(OCH_3)$.—The term *anisol* is applied to the methyl ether of phenol, and it is therefore methyloxybenzene. Skraup's synthesis of quinoline, C_9H_7N, was effected by heating aniline or amidobenzene with nitrobenzene, glycerin and sulphuric acid. By taking instead paramidoanisol, paranitroanisol, glycerin and sulphuric acid, Skraup obtained paraquinanisol, $C_9H_6N(OCH_3)$. This is then treated with tin and hydrochloric acid, when it takes up four atoms of hydrogen and becomes $C_9H_6H_4N(OCH_3)$. The name *thalline* was given to this base because of the deep green color produced by ferric chloride and other oxidizing agents. The base thalline is obtained in well-formed rhombic crystals, which fuse at 40° C. and recrystallize on cooling. It shows a neutral reaction and has a characteristic aromatic odor resembling that of coumarin. It is soluble in water, alcohol, and ether.

Thalline sulphate is a white crystalline powder which loses its two molecules of water of crystallization at 100° C. and melts at 110° C. It is soluble in five times its weight of cold water and freely soluble in boiling water, soluble in 100 parts of alcohol. Both solutions turn brownish on exposure to air and light. The odor of the sulphate recalls that of anisol. *Thalline tartrate* is a white crystalline powder, fusing at 155° C. and possessing a coumarin-like odor. It is soluble in ten parts of water and hardly soluble in alcohol. Its aqueous solution has an acid reaction.

Thalline tartrate and sulphate are medicinally equivalent. They are powerful antipyretics, acting also, when in sufficient dose, as depressants both upon the vasomotor system and upon the heart, and, according to A. Robin, checking tissue waste in the body and having a very marked tendency to attack the red blood corpuscles. These salts have been used in practical medicine, in *doses* of from four to eight grains (0.26–0.5 Gm.), but are so prone to produce disagreeable symptoms, such as marked cyanosis, vomiting, diarrhea, albuminuria, etc., that their employment has been abandoned. According to Kreis, in from 4 to 4½ per cent. solution they are active germicides, and the frequent use of urethral injections of the 1 to 2 per cent. solution has been found very useful in *chronic gonorrhea.* Moncorvo states that thalline is an active hemostatic.

Thalline Periodide. *Thalline Periodosulphate.*—An iodine addition product of thalline sulphate. It occurs as black crystals soluble in alcohol. It has been used in the treatment of *carcinoma,* three to four grains (0.2–0.25 Gm.) being given in pill form every two or three hours. In cases where functional activity of the epidermal glands has ceased, pilocarpine in slight doses is given at the same time.

Thalline Salicylate. $C_{10}H_{13}NO.C_7H_6O_3$.—This occurs as a reddish, crystalline powder, soluble in alcohol and administered as an antiseptic and antipyretic in the treatment of gonorrhea, typhoid fever, etc. *Dose,* three to eight grains (0.2–0.5 Gm.).

Thallium. (Tl. Atomic weight, 204.0.)—A bluish white lead-like metal. Sp. gr. 11.85, melting point 302° C. Insoluble in water, dissolved by nitric and sulphuric acids. This metal, discovered by spectrum analysis, has been found to occur widely in nature.

Thallium is an active poison, according to Swain and Bateman (*J. Bi. Chem.*, Jan., 1910), only slightly less toxic than arsenic. Moreover, it is distinctly accumulative in its effects, so that small doses repeated over periods of time may produce serious intoxication. The symptoms of acute poisoning in the lower animals by thallium are a disordered muscular action, as shown by tremors, incoördination, gradually increasing paralysis. Often, also, there is evidence of irritation of the intestinal tract, with vomiting and diarrhea. The pupils are dilated, there is salivation, conjunctivitis, with free mucous secretion, diuresis, embarrassment of respiration and more or less weakness of circulation. Death occurs in coma and is due to respiratory failure. After death there may be found some effusion of blood and inflammation of the lungs and intense congestion of the bowels, pericardial effusion and ecchymosis of the heart surface.

Cases of poisoning are uncommon in man, but Ballard (*Reports of the Boston City Hospital,* 1902) has recorded a case in which, after between two to four grains which were taken in the course of a week, there were produced diarrhea, muscular weakness and tenderness over the nerve trunks. As both lead and arsenic were found in the urine, however, it was doubtful how far the symptoms were due to the thallium. Olmer and Tian (*C. R. S. B.*, lxv, p. 742) report a case in which, after application of a paste of acetate of thallium to the chest, there were pains in the extremities, stomatitis, albuminuria and widespread alopecia. The loss of hair has been an almost constant symptom of human poisoning, and also occurs, according to Swain and Bateman, in the lower animals. (See also Buschke and Peiser, *B. K. W.*, 1922, i, 995.)

Sabouraud (*Revue Internationale de Medecin,* 1912) has recommended an ointment containing 1 per cent. of thallium acetate as a depilatory.

That thallium can produce widespread general neuritis is strongly indicated by the violent pains, especially of the legs, which have been noted by Lamy, by Combemale, and other observers, and also by the muscular atrophy which appears to be pronounced in chronic poisoning by the drug in the lower animals. Curci, indeed, claims that thallium is exclusively a muscle poison, and as long ago as 1874 Rabuteau recorded that after death from thallium the muscles did not respond to irritation. (See *Ed. M. J.*, 1874.) Pozzi and Courtade assert that in some cases thallium causes swelling of the gums with a blue line at the junction with the teeth, but this symptom seems not to have been noticed by other observers.

In 1898 Combemale claimed that in *doses* of one and a half grains (0.096 Gm.), given at bedtime, *thallium acetate* is a valuable remedy in the *colliquative sweats* of phthisis; that it is effective has been proved by Huchard and others; but in many cases it has produced severe peripheral pains, loss of hair, abdominal disturbance, and other disagreeable symptoms.

Thapsia. *T. Garganica* L. *Thapsie, Faux Fenouil,* Fr.—An umbelliferous plant, growing in southeastern Europe, and well known to the ancients, named from the isle of Thapsos, where it was obtained. Theophrastus speaks of its root as emetic and purgative. After long neglect this plant has obtained a foothold in the French Codex, which recognizes a *Resina Thapsiæ* prepared by exhausting the bark of the root with alcohol and evaporating to a soft extract. From this extract the Codex further directs that an *Emplastrum Thapsiæ* shall be so prepared as to contain 7 per cent. of the resin combined with yellow wax, turpentine and colophony. The bark of the root and the resin are both objects of commerce. The bark is described by Stanislaus Martin as almost always doubly quilled, unless where altogether in small fragments, exteriorly rugose with the epidermis here and there detached in patches larger or smaller, and of a deep brown color, interiorly smooth and whitish and of a fibrous fracture. The size of the pieces varies, the largest not exceeding 6 dm. in length and 2.5 in width. It is said that great care is necessary, in removing the root from the bales, not to be injured by the powder which escapes, and which causes itching and swelling of the face and hands. By submitting *thapsia* to the successive action of alcohol and ether Pressoir obtained two resins. (*J. P. C.*, 4e sér., xi, 328.) Canzoneri finds that the ethereal extract is an amber-colored syrupy resin possessing vesicating properties. From it he has obtained two acids, *octoic* or *caprylic* acid, and *thapsic* acid, besides a neutral non-nitrogenous vesicating substance. (See *A. J. P.*, vol. xiv, 325.) The French thapsia plaster is an active counter-irritant, producing much inflammation of the skin with an eczematous eruption and intolerable itching and, if the application be maintained, finally an ulcerated and suppurated surface, which on healing leaves behind it pronounced scars. The therapeutic action of the plaster is that of a severe counter-irritant.

The resin from the root of *Thapsia Sylphium* St. Laz., an Algerian plant, which most botanists believe to be a simple variety of *T. Garganica* L., is, according to Herlaut, even more active than the official plant. (*Proc. A. Ph. A.*, xxvi, 250.) Heckel and Schlagdenhauffen (*N. R.*, June and July, 1887) find in the root of *Thapsia villosa* L. a vesicant resin, which acts more slowly and gently than does that of *T. Garganica.*

Theobromine Preparations.—The alkaloid *theobromine* (see Part I), which is itself insoluble in water, unites with several of the earthy metals to form soluble compounds. Advantage of this fact has been taken by manufacturers to place upon the market a large number of soluble preparations of theobromine. The majority of these preparations have the same range of therapeutic usefulness as the official theobromine and sodium salicylate.

Theobromine Acetyl-salicylate. Theocyl. $C_7H_8O_2N_4.C_9H_8O_4$.—A white crystalline powder, soluble in alcohol and insoluble in water. It has been stated that this combination has the advantage over other theobromine preparations of not being irritant to the stomach. *Dose,* five to fifteen grains (0.33–1.0 Gm.).

Theobromine Barium and Sodium Salicylate. Barutin.—This is a white, amorphous powder with a sweetish alkaline taste and soluble in about twenty parts of water. It represents about 25 per cent. of theobromine and 17 per cent. of barium. Carbonic acid causes a precipitation.

The *dose* assigned to it is from three to eight grains (0.2–0.5 Gm.), which should be given well diluted but it would seem that this amount would represent a rather large quantity of barium.

Theobromine Lithium. Theobromose. $C_7H_7O_2N_4Li$.—It occurs as fine needle-like crystals, which are soluble in about one-half their weight of water. The solution is readily decomposed by atmospheric carbonic acid. It is used as a diuretic.

Theobromine and Lithium Benzoate. Uropherin B. $LiC_7H_7O_2N_4 + LiC_7H_5O_2$.—A white powder, soluble in five parts of water, representing 47 per cent. of theobromine. Precipitated by carbonic acid. It is stated to be more actively diuretic than other salts of theobromine. *Dose,* five to fifteen grains (0.3–1 Gm.).

Theobromine and Lithium Salicylate. Uropherin S. $LiC_7H_7O_2N_4 + LiC_7H_5O_3$.—Properties and uses the same as those of *Uropherin B.* but it is somewhat more prone to disturb the stomach.

Theobromine and Sodium Acetate. N. N. R. 1924. *Agurin. Theonacet.* $C_7H_7O_2N_4Na + NaC_2H_3O_2$.—A white, hygroscopic, alkaline powder, representing 60 per cent. of theobromine, readily soluble in water, forming a strongly alkaline solution which is incompatible with most inorganic salts, causes precipitation of alkaloids from solutions of their salt, darkens calomel, reduces potassium permanganate solution and is precipitated by carbon dioxide. The dry substance becomes pasty when triturated with chloral hydrate, phenol or piperazin. It is incompatible with carbonated beverages, acids, saccharin and mucilaginous liquids, alkaloids and alkaloidal reagents generally. Used as a diuretic. *Dose,* five to fifteen grains (0.3–1 Gm.) in solution.

Theobromine Salicylate. $C_7H_8O_2N_4.C_7H_6O_3$.—This forms fine white needle-like crystals of a bitter taste, acid in reaction and fairly soluble in water. *Dose,* five to fifteen grains (0.3–1 Gm.).

Theobromine and Sodium Benzoate.—A white soluble powder, representing 47 per cent. of theobromine. *Dose,* eight to fifteen grains (0.5–1.0 Gm.).

Theobromine and Sodium Citrate. Urocitral.—A white, alkaline powder, moderately soluble in water, representing 45 per cent of theobromine. *Dose,* eight to fifteen grains (0.5–1.0 Gm.) several times a day.

Theobromine Sodium Formate. Thephorin. $NaC_7H_7O_2N_4 + NaCHO_2 + H_2O$.—A white, alkaline, bitterish powder, soluble in 10 parts of water and representing 62.5 per cent. of theobromine. Used as a diuretic. It is asserted to be more irritant to the kidneys than other theobromine salts, and must be used with caution in *nephritis. Dose,* five to eight grains (0.3–0.5 Gm.).

Theobromine and Sodium Iodide. Sodium Iodotheobromate. Eustenin. $C_7H_7O_2N_4Na.NaI$.—This is a white, hygroscopic powder, freely soluble in water, but decomposed with precipitation by carbonic and other acids. It represents 51 per cent. of theobromine and 42.6 per cent. of sodium iodide. It is believed to combine the therapeutic effects of these two drugs and is recommended especially as an antisclerotic in arterial degenerations, *angina pectoris, chronic nephritis* and similar conditions. The *dose* is eight to fifteen grains (0.5–1.0 Gm.) several times a day.

Theobromine and Sodium Lactate.—A white hygroscopic alkaline powder, soluble in sixteen parts of water, readily decomposed by atmospheric carbonic acid.

Theobromine and Sodium Sulphate.—A white powder, soluble in water and containing about 50 per cent. theobromine. It is used like other theobromine salts.

Theobryl. Allyl Theobromine.—Koch and Katzenelbogen (*Schweitz. Med. Woch.*, 1921, li, 1009) find that this preparation has the advantages over other theobromine compounds of free solubility with neutral reaction which makes it suitable not only for oral but for subcutaneous administration. They also assert that it is more actively diuretic. They used it in *doses* of 0.3 to 0.5 Gm. (5 to 8 grains) daily.

Theophylline Compounds.—Although theophylline is now official, it is more frequently employed in the form of one of its soluble compounds. The following are upon the market:

Theophylline Ethylene Diamine. Euphyllin.—This is a white crystalline substance, freely soluble in water and representing 78 per cent. of theophylline. The *dose* recommended is from one and a half to three grains (0.1–0.2 Gm.).

Theophylline Sodium Acetate. Acet-theocin Sodium. N. N. R. 1924. $NaC_7H_7O_2N_4 + NaC_2H_3O_2 + H_2O$.—This is a white, crystalline powder, representing approximately 60 per cent. of theocin, soluble in twenty parts of water. It is used as a diuretic in *doses* of three to five grains (0.2–0.3 Gm.) several times a day.

Theophylline Sodium Salicylate. $C_7H_7O_2N_4Na.C_6H_4.OH.COONa$.—This is soluble in fourteen parts of water. Its doses and uses are the same as the preceding.

Theophylline Sodium Formate. $C_7H_7O_2N_4Na.HCOONa + H_2O$.—This occurs as a white powder, soluble in water and possessing valuable diuretic properties. *Dose,* eight to fifteen grains (0.5–1 Gm.).

Thermin. *Tetrahydro-β-naphthylamine Hydrochloride.* $C_{10}H_7.H_4.NH_2.HCl$.—The tetrahydro addition compound is formed when metallic sodium is caused to act upon naphthylamine in boiling amyl alcohol solution. It is a colorless to reddish-white crystalline powder, soluble in water, alcohol and amylic alcohol. The hydrochloride has been brought forward by Filehne of Breslau, as a local mydriatic of extraordinary power.

Jonescu (*A. E. P. P.*, 1909, lx, p. 345) has shown that tetra-hydronaphthylamin causes dilatation of the pupil by stimulating the sympathetic nerves and that the dilatation follows either the local installation or the subcutaneous injection of the drug; that it causes marked constriction of the blood vessels, chiefly by acting upon the vasomotor centers, although he believes the peripheral nerves to the vessels are also affected. The rise in temperature which it causes he attributes to a direct action upon the heat centers. According to Feri (*A. I. P. T.*, 1911, xxi, p. 27) there is, in poisoning by thermin, an increase in heat production with lessened heat dissipation which differentiates at once the fever it produces from that seen, for example, in infectious diseases. According to Sacharoff (*Z. E. P. T.*, vii, p. 225) the spasm of the blood vessels of the skin is in part responsible for this rise of temperature by preventing the dissipation of the excessive caloric. Thermin appears to cause a non-maximum dilation of the pupil and does not destroy the light reflexes. It is used as a mydriatic in strengths of from 1 to 5 per cent.

Thermodin. *Acetyl Para-ethoxy-phenyl-urethane.* $C_6H_4(OC_2H_5)N(COCH_3)COOC_2H_5$.—A derivative of urethane in the form of a colorless, crystalline powder, fusing at from 86° to 88° C., insoluble in water. It is used as an antipyretic in *doses* of from five to fifteen grains (0.32–1.0 Gm.).

Thermol. *Acetyl-salicyl-phenetidin. A-s-phen.* $C_{17}H_{17}NO_4$.—This substance is a white, crystalline, odorless, tasteless powder, which is claimed to be a harmless and active antipyretic and analgesic and as such has been used to a considerable extent in *typhoid fever, neuralgia, dysmenorrhea, migraine,* etc.; also as an antispasmodic in *whooping cough. Dose,* three to fifteen grains (0.2–1.0 Gm.).

Thevetia. *Yccotli.*—Inhabiting the damp, hot valleys of the Mexican Cordilleras is a large tree belonging to the *Apocynaceæ,* whose fruits are known by the natives as *huesos ó codos de fraile,* or *friar's elbow bones,* and are used as a topical application in *hemorrhoids.* The tree is the *Thevetia Yccotli* A. DC. In the seeds Herrera found a *glucoside, thevetin.* (*A. J. P.,* 1877, 145.) Closely allied to *T. Yccotli* is *T. nereifolia* Juss., a tree which probably grows also in Mexico, but has been found by botanists chiefly, if not solely, in the West Indian Islands, Colombia, Peru and other parts of South America. De Vrij, many years ago, discovered in its seeds a glucoside, *thevetin,* which was at one time believed to be identical with *cerberin* previously discovered in *Cerbera Odallam,* but Plugge (*A. Pharm.,* 1893, 10) reached the conclusion that they were distinct compounds. Under the name, however, of *cerberin* or *cerberid* Merck's index lists the "glucoside from the fruit of the *Thevetia yccotli,*" to which is assigned the formula $C_{25}H_{38}O_{12}$. Herrera (*M. R.,* 1911) found in thevetia a crystalline glucoside, *thevetosin,* which is a cardiac poison. Cerberin, $C_{27}H_{40}O_8$, is decomposed into *cerberetin,* $C_{19}H_{26}O_4$, a citron-yellow amorphous powder melting at 85.5° C., and glucose, while thevetin, $C_{54}H_{84}O_{24}$, is split into *theveresin,* $C_{48}H_{70}O_{17}$, a white powder, and glucose.

A number of cases of poisoning by the seeds of the East Indian thevetia has occurred; the symptoms have been repeated vomiting, a slow, very feeble pulse, delirium, convulsive movements and coma. The physiological action of the thevetin from *T. nereifolia* has been investigated chiefly by König. (*A. E. P. P.,* Bd. v, 228.)

David Cerna finds that the glucoside of *T. Yccotli* (*P. M. T.,* ix, 396) is in moderate doses stimulant both to the circulation and respiration, but finally paralyzes the heart muscle and the respiratory apparatus; that it causes cerebral convulsions and spinal paralysis, abolishing sensation and reflex activity before voluntary movement by an influence upon the sensory nerves or spinal tract. Zotos N. Zotos (*In. Dis.,* Dorpat, 1892) states that *cerberin* belongs physiologically to the digitalin group.

Thiocol. *N. N. R.* 1924. *Potassium Guaiacol Sulphonate. Orthocoll.* $C_6H_3.(OCH_3)OH.SO_3K$.—This is a fine white powder, having a taste at first bitter and afterwards sweetish; readily soluble in water, sparingly so in alcohol; containing about 60 per cent. of guaiacol. It is pleasant to the taste and not irritant to the gastric or other mucous membranes. Its freedom from odor, ready absorption and non-irritant action on the mucous membrane are among its recommendations that have been reported by its introducers. The original commendation of it by C. Schwartz (*K. T. W.,* 1898), in *tuberculosis, chronic bronchitis* and *intestinal catarrh,* has been confirmed by various clinicians. Cole (*Practitioner,* November, 1911) finds its effects about the same as those of creosote, over which it has the great advantage of being practically tasteless and much less likely to irritate the stomach. It occasionally produces a rash which, however, disappears quickly when the remedy is stopped. The *dose* is eight to twenty grains (0.5–1.2 Gm.).

Thionine. *Lauth's Violet.*—The oxidation product of *imidamidoiodiphenylimide,* $C_{12}H_{10}N_3SCl$. A greenish-black powder, having a metallic luster. It dissolves easily in water, imparting to the solution an intense violet color. It is used as a microscopic stain for nuclei and also in metachromatic investigations (for mast cells, mucus, etc.).

Thiophene (C_4H_4S) was recognized by Victor Meyer in 1883 as being an invariable accompaniment of benzene as produced from coal tar, and because of the similarity of properties, adhering very closely to it through all reactions. It can be separated by shaking the benzene with one-tenth of its bulk of concentrated sulphuric acid until the addition of a little isatine no longer produces a blue color (indophenin reaction). Steinkopf obtained a 40 per cent. yield of *thiophene* by passing acetylene over pyrites heated to 300° C. (*Chem. Trade Jour.,* 1911, 394.) Thiophene is a colorless, mobile oil, of faint odor, and boils at 84° C. Just as benzene is accompanied in coal tar by toluene, xylene and higher homologues, so thiophene is accompanied by *thiotolene* (*methyl-thiophene*), $C_4H_3S.CH_3$, and *thioxene* (*dimethyl-thiophene*), $C_4H_2S.(CH_3)_2$. Thiophene and its homologues yield a large number of brilliant dye colors analogous to those derived from benzene. It was first physiologically tested by A. Heffter (*A. G. P.,* xxxix, 420), who found that it appeared in the urine, and lessened the elimination of sulphuric acid in the urine. E. Spiegler (*Th. M.,* Feb., 1892) has employed in *skin diseases*—1, *Sodium thiophene sulphonate,* $C_4H_3S—NaSO_3$; 2, *Thiophenediiodide,* $C_4H_2I_2S$. The first of these compounds is a white crystalline powder, containing 33 per cent. of sulphur, having a feeble, disagreeable odor. It was found in the form of an ointment to act very well in *prurigo* with *eczema.* Thiophenediiodide occurs in tabular crystals, melting at 40.5° C., having a characteristic, not disagreeable odor, insoluble in water, but very feebly soluble in ether, chloroform and warm alcohol, soluble with difficulty in cold alcohol; containing 75.5 per cent. of iodine and 9.5 per cent. of sulphur. It was found to be antiseptic and is one of the compounds suggested as a substitute for iodoform. The *tetrabromide of thiophene,* C_4Br_4S, obtained by the complete bromination of theophene, is recommended as an antiseptic. It occurs as a yellow crystalline powder soluble in alcohol.

Thioresorcin. $C_6H_4(OS)_2$.—A yellowish-gray powder, insoluble in water, made by fusing together one molecule of resorcinol and two molecules of sulphur. It has been recommended as a substitute for iodoform, but has given rise to unpleasant symptoms.

Thiosinamine. *Rhodallin. Allylthio-urea. Allylsulpho-urea. Allylsulphocarbamide.* $(NH_2).CS.NHCH_2.CH : CH_2$.—This occurs in colorless, monoclinic or rhombic crystals, of a bitter taste and feeble garlic-like odor. It is moderately soluble in water, very soluble in alcohol and ether. It possesses no bactericidal properties.

Under the name of *Fibrolysin* a 15 per cent. solution of the double salt of *thiosinamine* and *sodium salicylate* is marketed in the form of ampules, containing 2.3 cc. of the solution. This solution decomposes rapidly on exposure to the air.

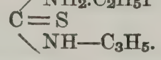
Thiosinamine was introduced into medicine by Von Hebra (*Internat. Klin. Rundschau*, September, 1905) in the treatment of various conditions accompanied with formation of fibrous tissue. He states that after its injection there is a temporary reduction in the number of leukocytes, followed by pronounced hyper-leukocytosis which persists for a considerable period of time. The occurrence of leukocytosis has been pretty generally confirmed by a number of authorities, some of whom have attributed the beneficial effects of the drug to this action. Starkenstein, however (*Th. M.*, 1910), believes that it is due to a power of encouraging the hydrolysis of collagen into gelatin, thereby leading to the softening of the connective tissue. While there is some contradiction of opinion among those who have investigated the action of this drug clinically, there is considerable evidence that it is often a remedy of great service in aiding in the absorption of connective tissue. Among the conditions in which this remedy has received recommendation may be mentioned excessive scarring as from *burns, keloids, urethral* and *œsophageal strictures*, and various other forms of cicatricial formations. Besides these, asserted benefit has been reported in sclerotic conditions of the ear attended with *deafness*, and in sclerosis of the central nervous system as *locomotor ataxia*, and in *arterial fibrosis*. It has also been suggested by Greenbaum (*J. A. M. A.*, 1911, lvi, 835) as a protective against dermatitis after arsphenamine injections.

The remedy, whatever may be said of its efficacy, is not entirely innocuous. A number of instances of excessive reaction, attended with chills and sweating followed by fever, have been reported, and Pritchard reports a case of *purpura hemorrhagica*, which ended fatally, following 18 injections. Tyrode (*A. I. P.*, 1910, xix, 195) has found that relatively small doses may produce in the lower animals severe disturbances of metabolism with degeneration of the internal organs.

Thiosinamine may be administered by the mouth in *doses* of one-half to two grains (0.03–0.12 Gm.) several times a day; for hypodermic use it may be dissolved in alcohol or glycerin. Fibrolysin is marketed only in the form of hermetically sealed vials each of which represents five grains (0.2 Gm.) of thiosinamine. The contents of one of these vials may be injected at one *dose* daily, or on alternate days.

Iodolysin is a compound said to contain 43 per cent. of thiosinamine and 47 per cent. of iodine. The advantage is claimed over other preparations that it is non-irritant and is especially suitable for hypodermic injection. Whitehorn-Cole (*F. Th.*, 1910, p. 69) reports favorably upon its use in *rheumatic arthritis*. The *dose* is from five to eight grains (0.32–0.5 Gm.).

Thiosinamine-ethyl-iodide. *Tiodine.* $C_6H_{13}N_2SI$.—Under the name of *tiodine*, the compound resulting from heating thiosinamine with ethyl-iodide has been introduced into medicine. Its formula is



$$C \begin{cases} \diagup NH_2.C_2H_5I \\ = S \\ \diagdown NH—C_3H_5. \end{cases}$$

It forms colorless crystals readily soluble in water and alcohol. It has been used for the same class of cases as thiosinamine, especially, however, for the relief of lesions of the central nervous system. Its injection is stated to be painless. It may be administered either by mouth or hypodermically. The *dose* is from one and one-half to three grains (0.1–0.2 Gm.), if by the mouth several times a day, if hypodermically, every other day.

Thistle.—Several of the *Compositæ* which are popularly called "thistles" have been attributed with therapeutic properties. The following merit attention.

Cirsium arvense (L.) Scop. (*Cnicus arvensis*, Hoffm.) *Canada Thistle.*—This is a European plant, but widely naturalized in this country. To it have been attributed diaphoretic, emetic, and tonic properties, according to Herman J. Pierce (*A. J. P.*, lxviii, 1896), contains a volatile alkaloid, and also *cnicin*, $C_{42}H_{56}O_{15}$. This is crystallizable, inodorous, very bitter, neutral, scarcely soluble in cold water, more soluble in boiling water, and soluble in all proportions in alcohol. It is analogous to salicin in composition. It is said to possess emetic and emmenagogue properties.

Cnicus benedictus L. (*Centaurea benedicta* L.) *Blessed Thistle. Chardon bénit*, Fr. *Herba Cardui Benedicti*, P. G. *Benedicten Distel*, G. (Fam. *Compositæ.*)—This is an annual herb, common in Europe and occasionally seen on roadsides and waste places in the United States. The leaves were formerly official. They should be gathered when the plant is in flower, quickly dried, and kept in a dry place. The herb has a feeble, unpleasant odor and an intensely bitter taste, more disagreeable in the fresh then in the dried plant.

Water and alcohol extract its virtues. The infusion with cold water is a grateful bitter; the decoction is nauseous, and offensive to the stomach. The active constituents are volatile oil and *cnicin*. It has been used as a bitter tonic, and is, in larger quantities, emetic. Tonic *dose*, from half a drachm to one drachm (2.0–3.9 Gm.) preferably given as an infusion.

Silybum Marianum (L.) Gaertn. (*Mariana Mariana* (L.) Hill, *Carduus Marianus* L.) (*Milk Thistle. Lady's Thistle* (Fam. *Compositæ*) was of old used for the same purpose as *C. benedictus*. Rademacher attributed great value to the seeds in *hemorrhages*, particularly when connected with diseased liver or spleen. A decoction (two ounces to the pint of water), in *doses* of four fluidrachms (15 cc.) every hour, has been used in *amenorrhea* and *menorrhagia*.

Thorium. Th. 232.15.—A gray, heavy, infusible powder. Sp. gr. 11.00, melting point over 1700° C. Soluble in acids. Insoluble in alkalies. One of the radium group of metals which is coming into prominence in medicine through the uses of its salts. The illuminating power of gas mantles is closely dependent upon a particular proportion of thorium oxide in the composition. *Thorium dioxide* has been used as a substitute for bismuth subnitrate in making X-ray pictures of the alimentary tract. According to Kaestle (*M. M. W.*, 1908), it is absolutely inert physiologically, and is very opaque to the X-ray. J. E Burns of Johns Hopkins Hospital recommends for X-ray examination of the ureter and kidney, the soluble *Thorium-sodium citrate* (*N. N. R.* 1924). This is prepared as follows: To prepare it, 10 Gm. of thorium nitrate dissolved in distilled water and heated on the water bath are treated with 30 cc. of a 1:2 solution of sodium citrate, added slowly with constant agitation. The precipitate at first formed is redissolved in the excess of the alkali citrate solution. The liquid is then exactly neutralized with normal sodium hydroxide solution and the volume is made up to 100 cc., when cold, with more water. After filtration, the clear filtrate, sterilized by boiling, is ready for use. That it is quite non-irritant is shown by subsequent cystoscopic examination. The solution is introduced by gravitation, as by the use of the syringe overdistension of the renal pelvis may result. The toxic dose for man, intravenously, would allow more than ten times the quantity required for a pyelogram to be used, or some hundreds of times more than could be absorbed during the procedure. S. Tracey has used the antiseptic action of a current of air passed over heated thorium oxide in the treatment of *tuberculosis* with apparently beneficial results.

Thorium Nitrate. *N. N. R.* 1924. $Th(NO_3)_4 + 4H_2O$.—It forms white, aggregate crystals which are very soluble in water. Depending on the fact, or the belief, that thorium salts are radio-active much attention has been called to this salt as being the most advantageous of the thorium salts for utilization. A solution of the nitrate has been employed in the treatment of parasitic skin diseases and a weak solution has been administered internally in the treatment of *rheumatism.*

Thromboplastin. *N. N. R.* 1924.—The normal coagulation of the blood which occurs after external wounds, according to present theories, is due to the change of a substance *fibrinogen,* normally found in the blood, into fibrin. This change is brought about by union with a substance known as *thrombin,* the elements of which—*prothrombin* and *calcium*—are normally found in the blood but which are prevented from uniting by the presence of a substance called *antithrombin.* The disintegration of tissue cells liberates a substance that neutralizes this antithrombin and thus permits a clotting of the blood. To this material, which is obtained from disintegrating tissue cells of various kinds, a variety of names has been applied as *thrombokinase, zymoplastic* and *thromboplastic* substances, *cytocym,* etc. It corresponds in its physical properties to the lipoid substance found in the brain called *kephalin.* (Howell, *A. J. Phys.,* 1912, xxxi, 1.)

It is probable that most of the animal substances which have been used for the purpose of increasing the coagulability of the blood act by furnishing this thromboplastic substance. It has been known for many years that the hypodermic injection of normal blood serum accelerates clotting and it has been employed as a practical remedy in the treatment of hemorrhage. Normal horse serum is upon the market for this purpose and is given in doses of from 10 to 30 cc. (3 to 8 fluidrachms). (See *Blood.*) More recently, on the theory that thromboplastic substance is identical with *kephalin,* various extracts of the ox brain, which tissue is especially rich in kephalin, have been placed upon the market either under the name of kephalin or thromboplastin. There is much evidence, both clinical and experimental, that these preparations increase the rapidity with which the blood clots, either when applied locally or when administered systemically. According to the researches of Hanzlik and Weidenthal (*J. P. Ex. T.,* 1919, xiv, 157), thromboplastin very greatly accelerates the coagulation either of normal blood or of blood whose clotting has been retarded by the addition of oxalic acid or peptone. These authors find that the solution loses its efficiency on keeping; samples 9 months old possess less than one-half of their original power.

As these preparations contain relatively small amounts of protein, there is little danger of anaphylactic reactions following their use. As there is much difficulty in producing sterile solutions of brain extract manufacturers of these preparations make two grades, one intended for systemic use and which is very carefully sterilized, and the other intended for local application. Thromboplastin occurs as whitish, opalescent fluid of a neutral reaction, with the odor of cresol which has been added as a preservative. It has been used successfully in the treatment of *hemorrhages* of various kinds, either for local application or by hypodermic injection. It is recommended that in external hemorrhages, such as *epistaxis,* cotton or gauze saturated in the solution be applied to the bleeding point. In hemorrhage from the stomach it may be administered by the mouth. In *hemoptysis* and other internal hemorrhages it may be administered subcutaneously in *doses* of 20 cc. (5½ fluidrachms).

Thymoacetol.—This is stated to be a derivative of thymotic acid. *Thymotic acid* bears the analogous relation to thymol that salicylic acid does to phenol.

Thymoacetol is a white crystalline powder insoluble in water but soluble in alcohol with a melting point of 75° C. It has been suggested as a local anesthetic.

Thymol Carbonate. *Thymol Urethane. Thymolcarbonic Ether. Thymotal. Tyratol.* $CO(NH_2)O.C_{10}H_{13}$.—J. F. Pohl, by the same process by which guaiacol is converted into guaiacol carbonate, has produced from thymol a nearly tasteless, colorless, crystalline compound of neutral reaction, fusing at 49° C. It is slightly soluble in water, but is decomposed by the alkaline juices of the intestine, thymol being liberated. It is claimed that this substance is as effective as thymol against the *anchylostoma,* and, owing to its not dissolving in the stomach, is much less apt to produce disagreeable symptoms. (*A. J. P.,* March, 1901, 143.) *Dose,* for adult, thirty grains (2 Gm.) three times a day for four days, followed by brisk purgation.

Thymolphthalein.—This compound, which is analogous in its structure to phenolphthalein, occurs in colorless needles melting at 245° to 246° C. It is readily soluble in alcohol or acetone but practically insoluble in water. In the presence of alkalies, however, it dissolves, forming blue solutions. It is widely employed as an indicator in alkalimetry.

Thyresol. *N. N. R.* 1924. $C_{15}H_{23}O.CH_3$.—The *methyl ether of santalol* is an almost colorless fluid. Sp. gr. 0.93–0.94, boiling point 149°–156° C. at 16 mm. pressure. The preparation is practically insoluble in water, but dissolves to a clear fluid in all proportions in alcohol, ether, and oils. It has a slight sandal-wood odor. It has been used by Knauth (*D. M. W.,* 1909), and others, as a substitute for santalol in the treatment of *urethritis.* According to Knauth it is not split up in the organism but appears in the urine in combination with glycuronic acid.

Tilia. *Basswood. Lime. Linden Tree.*—The dried flowers of *Tilia europæa* L., *T. platyphyllos* Scop. and of other species of *Tilia* (Fam. *Tiliaceæ*), are official in the German Pharmacopœia under the head of *Flores Tiliæ.* This drug consists of long-peduncled, pendulous cymes of small yellowish or greenish-white flowers, the peduncle adnate to a strap-shaped bract for about half of its length. Each flower has 5 sepals and 5 petals. The 5 original stamens, by chorisis have each developed a cluster and at the base occurs in addition, a spatulate petal-like body opposite each of the petals. The pistil has a 5-locular ovary which is surmounted by a single style and a 5-toothed stigma. The flowers contain a colorless, fragrant, volatile oil. The bark has been said to contain a neutral body, *tiliadin*, and a glucoside, *tilicin.* (See *A. J. P.*, 1890; *P. J.*, lxvi, 105.) The infusion is used as a household remedy to relieve hysteria and indigestion.

Timbo.—This name is applied in Brazil to various sapindaceous plants, used as fish poisons. Among these is *Serjania curassavica* Radlk. (*Paullinia pinnata* L.), in which Stanislaus Martin (*B. G. T.*, xcii) has found an alkaloid, *timbonine;* F. Pfaff has obtained from a *timbo* of unknown origin two alkaloids, *timboin* and *anhydrotimboin,* also an oily compound, *timbol.* (*A. J. P.*, Nov., 1891.)

Tin. (Sn. At. wt., 118.1.) *Stannum. Etain,* Fr. *Zinn,* G.—This was recognized in the old Edinburgh and Dublin Pharmacopœias, and in the U. S. of 1850, but is no longer official. It has, however, too long ranked among recognized remedies to be passed without notice. Tin is one of the metals which have been known from the earliest ages. It exists generally as an oxide (in *stone* and *wood tin*), rarely as a sulphide (*tin pyrites*), and is by no means generally diffused. It is found in England, Spain, Germany, Bohemia, and Hungary, in Europe, and sparingly in some parts of the United States; in the island of Banca and the Peninsula of Malacca in Asia; in Bolivia, and at Durango in Mexico. The mines of Banca furnish the purest tin. The metal is extracted from the native oxide. When this occurs in its purest state, in detached roundish grains, called *stream tin,* the reduction is affected by heating with charcoal. When the common oxide, called *mine tin,* is reduced, it requires to be freed, by pounding and washing, from the adhering gangue, after which it is roasted to drive off sulphur, arsenic, and antimony, and finally reduced in furnaces by means of stone coal. The metal, as thus obtained, is called *block tin,* and is not pure. The purest kind of tin known in commerce is called *grain tin.*

Tin is a malleable, rather soft metal, of a silver-white color. It may be beaten out into thin leaves, called *tin foil.* It undergoes a superficial tarnish in the air. Its taste is slight, and when rubbed it exhales a peculiar odor. Its ductility and tenacity are small; when bent to and fro, it emits a cracking noise, which is characteristic. Its sp. gr. is 7.29, melting point 235° C., and it volatilizes at a white heat. If forms two oxides. The *stannous oxide*, SnO, is of a grayish-black color. When perfectly pure it has, according to Roth, a red color. *Stannic oxide*, SnO_2, or *dioxide*, forms two hydrates, both being acids—*stannic acid*, $SnO_2.H_2O$, and *metastannic acid,* $Sn_5O_{10}.5H_2O$, or $(H_2SnO_3)_5$.

The tin of commerce is often impure, being contaminated with other metals, introduced by fraud or present in consequence of the mode of extraction from the ore. A high specific gravity is an indication of impurity. When its color has a bluish or grayish cast, the presence of copper, lead, iron, or antimony may be suspected. Arsenic renders it whiter, but at the same time harder, and lead, copper, and iron cause it to become brittle. Pure tin is converted by nitric acid into a white powder (*metastannic acid*), without being dissolved. Boiled with hydrochloric acid, it forms a solution which yields a white precipitate with potassium ferrocyanide. A blue precipitate with this test indicates iron, a brown one copper, and a violet-blue one both iron and copper. If lead be present, a precipitate will be produced by magnesium sulphate. The Malacca and Banca tin and the English grain tin are the purest kinds found in commerce. Banca tin, from analyses by Mulder, appears to be particularly pure, containing only one twenty-fifth of one per cent. of foreign metals. Block tin and the metal obtained from Germany are usually of inferior quality.

Tin enters into the composition of bronze, bell metal, pewter, and plumber's solder. It is used also in making tin plate, which is sheet iron coated with tin, in making tin amalgam for silvering looking glasses, and in forming the *solution of stannous chloride* (*bichloride of tin*), a combination essential for the dyer's use. Being unaffected by weak acids, it forms a good material for vessels intended for boiling operations in pharmacy. A *false tin foil* is considerably used at present, made by coating lead with tin, and then rolling it out into thin sheets. As tin foil is employed for enclosing medicinal powders and perishable articles of food and medicine, care should be taken not to use this substituted preparation.

Powder of Tin. Stanni Pulvis.—For directions for making, see *U. S. D.*, 16th edition. Powder of tin was used as a mechanical anthelmintic, but has very properly gone out of vogue. The *dose* is half an ounce, mixed with molasses, given for several successive mornings, and then followed by a brisk cathartic purge.

There is strong evidence that the salts of tin are poisonous if they enter the circulation and several cases in which the symptoms have been referred to absorption of tin from canned foods have been reported. While it may be possible that these cases were properly diagnosed the enormous use of tin plated metal and the extreme rarity of any ill effects would seem to demonstrate that the danger is remote. For literature on this subject and report of a case of poisoning see Salzer (*J. A. M. A.*, 1918, lxx, 980).

Frouin (*Press. Méd.*, 1917, xxv, 401) asserts that tin has specific antagonistic properties to the staphylococcus and has used a mixture of tin and its oxide in the treatment of *furunculosis* with gratifying results. *Stannoxyl* is a proprietary preparation of tin oxide intended for medicinal use. *Stannous chloride,* or *chloride of tin,* is a violent irritant and mild caustic. Chemically pure tin, given internally, is probably not absorbed. (See 16th edition, *U. S. D.*)

Tinospora. *Gulancha. Br. Add.* 1900.—"The dried stem of *Tinospora cordifolia* Miers (Fam. *Menispermaceæ*), collected in the hot season." *Br. Add.*, 1900. *Tinosopora* has long been used in India as a medicine and in the preparation of a starch known as *gilœ-ka-sat* or as *palo.* It is said to be a tonic, antiperiodic, and a diuretic. Flückiger obtained from it traces of an alkaloid, probably berberine, and a bitter glucoside. The Br. Add., 1900, recognized an *infusion* (*Infusum Tinosporæ* Br. Add., 1900, two ounces to the pint), *dose,* one-half to one fluidounce (15–30 cc.); a *tincture* (*Tinctura Tinosporæ* Br. Add., 1900, four ounces to the pint), *dose*, one-half to one fluidrachm (1.8–3.75 cc.); and a *concentrated solution* (*Liquor Tinosporæ Concentratus* Br. Add., 1900), *dose*, one-half to one fluidrachm (1.8–3.75 cc.). *Tinospora crispa* Miers, which is abundant in the Philippines, is used freely by the natives under the name of *makabuhay* (that is, "You may live"), as a panacea, especially valuable in *general debility*, in chronic *rheumatism*, and in *malarial fevers*. It may be prepared in the same way and given in the same doses as *Tinospora cordifolia*.

Tissa. *Tissa rubra* (L.) Brit. [now *Spergularia rubra* (L.) J. and C. Presl.] (Fam. *Caryophyllaceæ*), a native of Malta, Sicily, and Algiers, is found growing in dry, sandy soil from Quebec to Virginia. It is a low annual with linear, opposite leaves and small pale red flowers. It has long been used as a popular remedy in diseases of the bladder. It has shown by F. Vigier (*J. P. C.*, 1879, ii, p. 371) to contain a resinous aromatic substance which is probably its active principle. It was strongly recommended by Bertherand in *calculous diseases* and acute and chronic *cystitis*. The aqueous extract may be given in *doses* of thirty grains (2.0 Gm.); or the fluidextract, *dose*, a fluidrachm (3.75 cc.), three or four times a day.

Titanium. Ti = 48.1.—A hard, gray-colored metal in powdery fragments, specific gravity 3.589. It is soluble in warm hydrochloric acid. Pick (*Med. Klin.*, 1911) has used various salts of titanium, especially the sulphate and salicylate, with asserted benefit as local remedies in the treatment of *eczema, lupus, rhinitis* and *conjunctivitis*. On the skin he uses solutions of from one-quarter to one-half per cent. of titanium sulphate, which must be freshly made, as the salt is decomposed by water. For mucous membranes the solution may vary in strength from one-twentieth to one-tenth of one per cent.

Tobacco. *Tabacum. U. S.* 1890. *Nicotiana Tabacum* L. (Fam. *Solanaceæ.*)—This is the commonly cultivated *tobacco* plant of the United States, Cuba and the Philippines. It is an annual in the U. S., but in the tropics becomes bi- or triennial. It has a large, fibrous root, and an erect, round, hairy, viscid stem, which branches near the top, and rises from three to six feet in height. The leaves are numerous, alternate, sessile, and somewhat decurrent, very large, ovate-lanceolate, pointed, entire, slightly viscid, of a pale green color, and have a narcotic odor. The flowers appear in panicles or racemes and vary from pink to red in color.

There is good reason to believe that this plant is a native of tropical America. Columbus, upon landing at St. Domingo in 1492, found the natives smoking cylinders of tobacco leaves. Tobacco is at present cultivated in most parts of the world, and nowhere more abundantly than within the limits of the United States. The young shoots, produced from seeds thickly sown in beds, are transplanted into the fields during the month of May, and set in rows with an interval of three or four feet between the plants. Through the whole period of its growth the crop requires constant attention. The development of the leaves is promoted by removing the top of each plant and thus preventing it from running into flower and seed. The harvest is in August. The ripe plants, having been cut off above their roots, are dried under cover, and then stripped of their leaves, which are tied in bundles and packed in hogsheads. While hung up in the drying houses, they undergo a curing process, consisting in exposure to a considerable degree of heat, through which they become moist, or, in other words, are said to sweat, after which they are dried for packing.

Other species also of *Nicotiana* are cultivated, especially *N. rustica* L., which yields the Turkish tobacco and is said to have been the first introduced into Europe. This species was cultivated by all of the North American Indian tribes from the Mississippi eastward to Atlantic Ocean. It is naturalized near the borders of some of our small northern lakes. The *N. quadrivalvis* of Pursh affords tobacco to the Indians of the Missouri and Columbia Rivers; and *N. fruticosa*, a native of China, was probably cultivated in Asia before the discovery of this continent by Columbus. Besides these there are *N. Persica* Lindl., cultivated in Persia, and is the source of Persian tobacco; *N. repanda* Willd., cultivated in central and southern North America; *N. Bigelovii* Wats., of North America. It is very doubtful, however, whether these plants furnish any large part of the commercial tobacco. Latakia tobacco seems to be the product of the *N. Tabacum*, and Senator Vidal asserts that *N. repanda* is not found in Cuba, *N. Tabacum* being the only species there cultivated. (*P. J.*, viii, 710.) Again, the Persian and Turkish tobacco sold under the name of *tumbeki*, which has been variously attributed to *N. Persica* and to *N. rustica*, is in all probability the product of *N. Tabacum*. (*Kew Bulletin*, April, 1891.)

Tobacco, as it occurs in commerce, is of a yellowish-brown color, a strong narcotic penetrating odor which is wanting in the fresh leaves, and a bitter, nauseous, and acrid taste. These properties are imparted to water and alcohol. They are injured by long boiling, and the extract is, therefore, relatively feeble. The most important constituent is the liquid alkaloid, *nicotine*, discovered by Posselt and Reimann in 1828. This is easily extracted from tobacco by means of alcohol or water as a malate, from which the alkaloid can be separated by shaking it with caustic soda solution and ether. The ether is then expelled by warming the liquid, which finally has to be mixed with slaked lime and distilled in a stream of hydrogen, when the nicotine begins to come over at about 200° C. The percentage of nicotine in tobacco varies considerably—from 1.62 per cent. in Havana tobacco and 2 per cent. in Maryland tobacco to 6 per cent. in Virginia tobacco and 8 per cent. in Kentucky tobacco. For modes of estimating the proportion of nicotine in tobacco, see Harrison and Self, *P. J.*, June 1, 1912 and Thomsen, *Chem. Ztg.*, 1917, xli, 476.

Nicotine (*Nicotina* or *Nicotia.*) $C_{10}H_{14}N_2$. β-pyridyl-*a*-*n*-methyl-pyrrolidine.—This is a colorless, lævorotary, fluid, of the sp. gr. 1.010, boiling at 247° C., and not solidifying at –10° C.; having a faint odor when cold; of an exceedingly acrid, burning taste, even when largely diluted; entirely volatilizable, and, in the state of vapor, very irritant to the nostrils, with an odor recalling that of tobacco; inflammable; very soluble in water, alcohol, ether, the fixed oils, and oil of turpentine; strongly alkaline in its reaction, and capable of forming crystallizable salts with the acids. These salts are deliquescent, having a burning and acrid taste, and, like the salts of ammonia, lose a portion of their base by heat. It has been prepared synthetically by Pictet. On treatment with oxidizing agents, nicotine yields *nicotinic* or *β-pyridinecarboxylic acid*, $C_5H_4N.COOH$. In its action on the animal system it is one of the most virulent poisons known. A drop of it, in the state of concentrated solution, is sufficient to destroy a dog, and small birds perish at the approach of a tube containing it. Tannin forms with it a compound of but slight solubility, and might be employed as an antidote. Nicotine has been found in the seeds, and, in very small proportion, in the root. Nicotine has the remarkable property of resisting decomposition amid the decaying tissues of the body, and was detected by Orfila in the bodies of animals destroyed by it two or three months after their death.

Although Thoms (*A. J. P.*, 1900, p. 227) was unable to detect any nicotine in tobacco smoke, there is no room for doubt that it is present in sufficient amount to be injurious. Lehmann (*P. J.*, Sept. 18, 1909) finds that about 95 per cent. of the nicotine in tobacco passes over into the smoke, and Toth (*Chem. Ztg.*, 1909, p. 866) has shown that the large proportion of nicotine exists in the smoke in uncombined state. Baumberger (*J. P. Ex. T.*, 1923, xxi, p. 23) as a result of his own studies and an extensive review of the literature, reaches the conclusion that in continuous smoking from 27 to 36 milligrammes of nicotine are absorbed per hour.

Nicotimine, isomeric with *nicotine*, *nicoteine* $C_{10}H_{12}N_2$ and *nicotelline* $C_{10}H_8N_2$ are other alkaloids present in tobacco. The bases *pyrrolidine* C_4H_9N and methyl *pyrroline* C_5H_9N are also said to be present.

When distilled at a temperature above that of boiling water, tobacco affords an empyreumatic oil, which was official in the U. S. P., 1870, under the name of *Oleum Tabaci: Oil of Tobacco.* It is highly poisonous, probably from containing nicotine. For further information on the chemistry of nicotine and related alkaloids, see the papers of Pictet and co-workers (*B. Chem. G.*, 1895, xxviii; 1904, xxxvii; *A. Pharm.*, 1906, ccxlix.

It is quite certain that tobacco leaves undergo considerable chemical changes during the processes of curing and preparation for use. Thus, the characteristic odor of ordinary tobacco is entirely different from that of the fresh leaves, and must be owing to the generation of a new volatile principle. The proportion of nicotine is probably slightly diminished by the process of "curing."

Tobacco is locally irritant. Snuffed up the nostrils, it excites violent sneezing, and a copious secretion of mucous; chewed, it irritates the mucous membrane of the mouth and increases the flow of saliva; when injected into the rectum, it sometimes operates as a cathartic; and the alkaloid nicotine injected into the cellular tissue of animals evidently produces much pain. In large doses, or in persons unaccustomed to it, tobacco produces severe nausea, sometimes vomiting, accompanied with profuse perspiration, and great muscular weakness. The alkaloid nicotine is a virulent poison. It primarily excites, and secondarily paralyzes, the ganglia upon the sympathetic nerves, stimulates the intestinal muscles, and, in sufficient quantities, has a paralytic action upon the motor nerves. As a result of its action upon the sympathetic ganglia, it causes contraction of the blood-vessels with marked increase in the blood pressure, followed, after large doses, with vascular dilatation and fall of pressure. The pulse rate is at first decreased, later becomes rapid. There is primary increase in the secretion of the salivary and probably of the other glands, followed, after large doses, by paralysis of secretion.

The use of tobacco was adopted by the Spaniards from the American Indians. In the year 1560 it was introduced into France by the ambassador of that country at the court of Lisbon, whose name —Nicot—has been perpetuated in the generic title of the plant. Sir Walter Raleigh is said to have introduced the practice of smoking into England. In the various modes of smoking, chewing, and snuffing, the drug is now largely consumed in every country on the globe. It must have properties peculiarly adapted to the propensities of our nature to have thus surmounted the first repugnance to its odor and taste and to have become the passion of so many millions. Whether or not nicotine plays any part in the pleasurable effects of tobacco is, despite considerable research and discussion, unsettled, but it is generally agreed that the evil effects of excessive indulgence are due to this alkaloid. The most important disturbances produced are in the digestive and circulatory organs. As a result of the disturbed innervation of the heart, palpitation and cardiac irregularities are common, and the vascular contraction is generally regarded as one of the causes of arterial degenerations.

Formerly much used as a relaxant, tobacco has been superseded by safer and more efficacious remedies, so that it is at present never employed in medicine, except occasionally in *chronic asthma.* It should always be borne in mind that its active principle is absorbed readily by the skin, and that serious or even fatal poisoning may result from its too free application to the surface of the body. A case of death is on record, occurring in a child eight years old, in consequence of the application of the expressed juice of the leaves to the head, for the cure of *tinea capitis.* Death has also been produced by the inhalation of the smoke.

From five to six grains (0.32–0.4 Gm.) of powdered tobacco will generally act as an emetic; but should never be used for this purpose.

Toddalia. *Br. Add.* 1900.—"The dried root-bark of *Toddalia aculeata* Lam." (Fam. *Rutaceæ.*) This climbing shrub, known also as *Lopez root*, growing in East Africa, Madagascar, the subtropical Himalayas, Ceylon, and the Philippines, is a tonic stomachic, containing berberine, a resin and a volatile oil, which may be readily obtained from the leaves by distillation. This oil has the odor of citron peel, and a bitter, aromatic taste. See also *Schim. Rep.*, 1906, 82, and 1912, 121. The British Addendum recognized an *infusion* (*Infusum Toddaliæ*, two ounces to a pint), *dose*, one to two fluidounces (30–60 cc.); also a *concentrated solution* (*Liquor Toddaliæ Concentratus*, Br. Add., 1900), *dose*, from one-half to one fluidrachm (1.8–3.75 cc.).

Tonka Bean. *Tonco Bean. Tonquin Bean. Semina Tonco. Fève Tonka*, Fr. *Tonka-bohnen*, G.—The seeds of *Coumarouna odorata* of Aublet, a large tree native to Guiana which yields the Dutch Tonka Bean; and of *C. oppositifolia* (Aubl.) Taub (*Dipteryx oppositifolia* Willd.) (Fam. *Leguminosæ*), a tree indigenous to Brazil, which is the source of the English tonka bean. The fruit is an oblong-ovate pod, enclosing a single seed, from 3 to 4 cm. long and about 1 cm. wide, usually somewhat compressed, with a dark brown, wrinkled, shining, thin, and brittle skin, and a light brown, oily kernel. The seed has a strong, agreeable, aromatic odor, and a bitterish, aromatic taste. Its active constituent is a crystallizable, odorous substance, called *coumarin* or *cumarin*, $C_9H_6O_2$ (see Part I). It is sometimes found in a crystalline state, between the two lobes of the kernel. For methods of obtaining coumarin from tonka bean see *U. S. D.*, 20th ed., p. 1646. One pound of the beans yields about 108 grains of coumarin. Tonka bean is used to adulterate tincture and extract of vanilla and to flavor snuff, being either mixed with it in the state of powder or put entire into the snuff box. *Tonquin butter* is an article of commerce in Holland. It is the fatty substance of tonka beans; it was analyzed by M. Duyk, it has the sp. gr. of 0.888, melting point is 28° C., saponification number 25.7. (*Rep. de Pharm.*, 1908.)

The fluidextract of the bean has been used with asserted advantage in *whooping cough* in *doses* equivalent to from five to eight grains (0.32–0.5 Gm.) for children five years old. (*A. J. P.*, 1869, 27.)

Toramin is the ammonium salt of malonic acid trichlorbutyl ester. $CH_2.COONH_4.COOC.CCl_3$-$(CH_3)_2$. It occurs in pearly scales, melting point 116° C. It is used as a cough sedative in *bronchitis*, especially in conjunction with expectorant drugs, in doses of 0.1 to 0.2 Gm. (1.5 to 3 grains).

Tormentil. *Rhizoma Tormentillæ*, P. G. *Tormentille*, Fr. *Tormentillwurzel*, G. *Tormentilla*, It. *Tormentila*, Sp.—Various species of the rosaceous genus *Potentilla* have been employed in medicine. (See *A. J. P.*, 1875, 109.) It is asserted that our common *P. canadensis* L. is a valuable sudorific and diuretic.

Potentilla Tormentilla Neck. (*Tormentilla erecta* L., *T. officinalis* Curt.)—The *tormentil*, or *septfoil*, which was formerly in the Secondary List of the U. S. Pharmacopœia, is a small perennial plant of Europe and Asia. All parts of the plant are astringent, especially the rhizome, which is the part employed. The rhizome of *tormentil* is cylindrical, somewhat fusiform, branching and more or less curved, from 2.5 to 8 cm. long, and from 0.5 to 1.5 cm. thick, brown or blackish externally, and reddish within. It has a slight aromatic odor and a very astringent taste. It contains a red coloring principle, soluble in alcohol, but insoluble in water, which appears to be identical with rhatany-red (see *Krameria*) and considerable quantities of a peculiar tannin (*tormentil-tannic acid*, $C_{26}H_{22}O_{11}$). *Kinovic acid*, $C_{24}H_{38}O_4$, and small quantities of *ellagic acid*, $C_{14}H_6O_8$ are also present. The root is said to be used for tanning leather in the Orkneys and Western Islands of Scotland, and for staining leather red by the Laplanders. Tormentil is a simple and powerful astringent, applicable to all cases of disease in which this class of medicines is indicated. It may be given in substance, decoction, or extract. The *dose* of the powder is from thirty grains to a drachm (2.0–3.9 Gm.).

Toxicodendron Capense Thunb. (*Hyænanche capensis* Pers.) *Hyena Poison.* (Fam. *Euphorbiaceæ.*)—The fruits of this small South African tree are said to be used for the poisoning of hyenas. They have been investigated by von Engelhardt (*Kobert's Arbeiten*, 1892), who finds in them a neutral, bitter principle, *hyananchin*, which is a powerful poison, resembling strychnine in its physiological action, from which, however, it differs in that it powerfully affects the cerebrum. The convulsions which it produces are of central origin, the poison having no action upon the nerve trunks or the muscles.

Tradescantia Erecta Jacq. (Now *Tinantia fugax* Scheidw.) (Fam. *Commelinaceæ.*)—The natives of South America used an extract of this herb as a hemostatic in cock-fights and it has lately been introduced into medicine, being especially recommended in *hemorrhages* of the ear and the upper air passages. Nothing definite is known of its actual composition and its styptic virtue has been ascribed, by some, to its tannin content. For description of *Commelina communis*, a perennial herb of the United States, see Preston, *A. J. P.*, 1898, p. 321.

Tragoponic Acid.—This was found by Rademaker and Fisher in the seeds of *Tragopogon porrifolius* L. (Fam. *Compositæ.*) This plant, commonly called *Salsify, oyster plant*, furnishes an edible root. (See *Nat. Drug.*, July 23, 1886, 47.)

Traumatol. *Iodocresine. Iodocresol.* $C_6H_3I.$-$(CH_3)OH$.—This occurs as a purplish-red or yellow powder; it is obtained by acting on cresol with iodine, and is used as a substitute for iodoform.

Tribrom Beta-naphthol. $C_{10}H_4Br_3OH$.—This occurs as a grayish crystalline powder, readily soluble in alcohol, ether and the alkalies. Lehmann (*Beitr. Klin. Chir.*, 1911, xlvii) has used it for the purpose of disinfecting the hands of the surgeon. He uses an alcoholic solution containing 0.5 per cent.

Tribromhydrin. *Tribromhydrinum. Allyl Tribromide. Tribromallyl. Tribrompropane. Propargyl Tribromide.* $CH_2Br.CHBr.CH_2Br$.—This substance is a colorless or faintly yellowish liquid at the ordinary temperature, but solidifying when cooled below 10° C. to a mass having a specific gravity of 2.430 at 15° C. Its boiling point is about 220° C. and is soluble in alcohol or ether. It has been recommended by De Fleury as a nerve sedative in *hysteria, asthma, whooping cough*, and other nervous disorders. It may be administered by mouth in capsules containing each five drops (0.25 cc.), of which one or two may be given several times a day. It has also been employed subcutaneously in two to three minim (0.12–0.2 cc.) doses in 20 minims of ether. (*Ph. Post*, Dec., 1888.)

Tribromphenol. $C_6H_2Br._3.OH$. *Bromol.*—This is prepared by shaking a solution of phenol with bromine water. It occurs in the form of soft, white, colorless needles, melting at 95° C., and subliming undecomposed at a higher temperature. It is practically insoluble in water but soluble in alcohol, ether or chloroform. In caustic alkaline solutions it is readily soluble, and from them it is separated unaltered by acids. The odor is disagreeable, like that of bromine, but more penetrating; the taste is sweet and astringent.

Bechold and Ehrlich (*Cb. C.*, 1906, xlvii) have found that tribromphenol will inhibit the growth of bacteria when present in 1 part in 10,000. Grimm, who recommends tribromphenol as a surgical antiseptic, states that a half per cent. solution will kill the bacteria of putrefaction in an hour. According to Grimm and Rademacher, tribromophenol, when in concentrated form, acts as a caustic, and is especially valuable in the treatment of *tuberculous ulcers* and *gangrene*. Grimm considered the remedy too caustic to be used upon the mucous membrane of the upper air-passages, but Rademacher has used it in the solution of olive oil (2 to 30) with asserted excellent results in *diphtheria.* It is said to be very slowly acted upon by the intestinal juices, and has been used as an intestinal disinfectant in *doses* of from three to eight grains (0.2–0.5 Gm.) a day. That it is absorbed in some form is shown by the fact of its excretion in the urine in the form of *tribromophenol-sulphonic acid.*

Triferrin, or *paranucleinate of iron,* contains about 22 per cent. of iron as well as 2.5 per cent. of organically combined phosphorus and is prepared from casein of cow's milk by digestion and precipitation by means of ferric salts. *Triferrin* is freely and completely soluble in a weak solution of sodium hydroxide, but it is insoluble in diluted hydrochloric acid having the acid strength of normal gastric juice. *Dose,* five grains (0.32 Gm.).

Trigemin. *Dimethyl-amido-antipyrin-butyl-chloral Hydrate.* $C_{17}H_{24}N_3O_3Cl_3$.—A product of the action of butyl chloral hydrate on pyramidon, forming long white needles, fusing at 85° C. and possessing a delicate aromatic odor and a mild taste. It has been used as an analgesic in all those forms of pain for which the coal-tar derivatives are valuable. It is incompatible with spirit of nitrous ether, acacia and most of the chemicals that are so with antipyrin. The *dose* is from three to fifteen grains (0.2–1.0 Gm.).

Trigonella. *Greek Hay Seed. Fenugreek. Semen Fœnugræci. Bockshornsamen,* G. *T. Fœnum-græcum* L. (Fam. *Leguminosæ.*)—A low European annual herb with pinnately 3-foliate leaves, obscurely dentate, obovate, leaflets and white flowers, cultivated in southern Europe, northern Africa and India for its seeds. These are oblong-quadrangular, somewhat compressed, obliquely truncated at each extremity, 3 to 5 mm. in length and 2 mm. broad, brownish-yellow externally, internally yellow, and marked with an oblique furrow running half their length. They have a strong peculiar odor resembling that of elm bark, and an oily, bitter, farinaceous taste, and contain fixed and volatile oils, mucilage, bitter extractive and a yellow coloring substance. E. Jahns (*B. Chem. G.,* 1886, xviii and 1887, xx, p. 2840) has obtained choline, and *trigonelline,* $C_7H_7O_2N$. The yield of the former was 0.05 per cent., and of the latter 0.13 per cent. Trigonelline is a betäine of nicotinic acid. It is found in several other plants and appears to be the same as caffearine found in coffee (Gorter, *Ann. Chem.,* 1910, ccclxxii, 237).

An ounce of the seeds, boiled in a pint of water, renders it thick and slimy. They yield the whole of their odor and taste to alcohol. On the continent of Europe they are employed in the preparation of emollient cataplasms, enemata, ointments and plasters. They are never used internally for human beings, but the ground seeds are used to an enormous extent in the manufacture of cattle powders or condition powders and the decoction or fluidextract for making *imitation maple flavor.*

Trimethol. *Trimethyl-methoxyphenol.* $C_6H(CH_3)_3OCH_3OH$.—This compound is asserted to be an extremely powerful disinfectant having a phenol coefficient of 40. It is recommended as an intestinal antiseptic in *doses* of 1 to 2 grains (0.06 to 0.12 Gm.). It is on the market in the form of capsules and as a syrup.

Trimethylamine. *Secaline.* $CH_3CH_3CH_3N$.—This substance which has been so often confused with propylamine (see p.) is a colorless liquefiable gas of a fishy ammoniacal odor, soluble in water and alcohol and having at 0° C. specific gravity of 0.673, boiling at 9° to 10° C. and possessing extremely toxic properties. It was first prepared by Wertheim in 1850 from narcotine and was given the name *metacetamine.* The common method of preparing this substance at the present time is by the action of ammonia gas on methyl iodide. The aqueous solution of *trimethylamine* is often miscalled "propylamine," which is a primary compound of ammonia (*monamine*), whereas the trimethylamine is a tertiary compound ammonia (triamine). It is not used medicinally.

The hydrochloride, $(CH_3)_3NHCl$, is used as an odorous addition to bait, to lure fish.

Trinitrotoluene. *T.N.T.*—This substance which is used as an explosive has the formula of $C_6H_2(NO)_3CH_3$. To explode it it is necessary to have a certain degree of heat combined with concussion. Heat alone causes it to burn like camphor. Workers in munition plants who are exposed to the inhalation of T.N.T. dust or fumes suffer with severe, and often fatal poisoning. The symptoms are divisible into two groups, those due to local irritation, as lachrymation, dry cough, with a yellow bitter sputum and occasionally epistaxis; there is also irritation of the skin with eczematous eruptions. In this group of cases there are also often digestive disturbances, cramp-like pains in the abdomen, constipation followed by diarrhea and sometimes vomiting. The second group of toxic symptoms were due to the action of the drug upon the liver and consist of nausea, vomiting and jaundice, mental disturbance, blurred vision and sometimes peripheral neuritis. A fatal case reported by Maitland (*J. A. M. A.,* 1917, lxviii, p. 835) showed a small contracted liver with cloudy swelling and fatty degeneration of the parenchyma followed by necrosis of the cells. Panton (*L. L.,* 1917, ii, p. 77) has found the blood, even of apparently healthy workers in T.N.T. factories frequently to be bile tinged. Finding also that many of these patients were anemic he believes that the poison may exercise a destructive action on the bone marrow. He divides types of T.N.T. poisoning into three groups: (1) Severe gastric disturbance without jaundice or anemia, (2) anemia of the aplastic type, and (3) jaundice.

Minot (*J. A. M. A.,* Aug. 30, 1919) as the result of an examination of over 200 unselected workers in T.N.T. finds frequent evidence of destruction of the red blood cells such as the presence of fragmented cells in the blood or various forms of abnormal cells.

The skin and hair of T.N.T. workers become stained a characteristic yellowish-orange color which may be removed by oils or various organic solvents.

Triosteum. *T. perfoliatum* L. *Horse Gentian. Bastard Ipecac. Tinker's Weed. Wild Coffee. Fever Root. Feverwort. Wild Ipecac. Racine de Trioste,* Fr. *Dreisteinwurzel,* G. (Fam. *Caprifoliaceæ.*)—This coarse perennial herb is found in rich woods from Massachusetts to Alabama and westward to Nebraska, preferring a limestone soil and shady situations. The rhizome and roots represent the drug. The rhizome is of horizontal growth, subcylindrical and knotty, 15 cm. long about 15 mm. thick; externally yellowish-brown, showing prominent cup-shaped stem scars on its upper surface and numerous rootlets about 5 mm. thick on its lower surface; internally with thin bark and broad whitish wood and pith. When dry it is brittle and easily pulverized. It has a sickening odor, and a bitter, nauseous taste. It is said to contain an alkaloid which Andree believed to be identical with emetine, but which Hartwich has shown to be different. It yields its active properties of both water and alcohol. Triosteum is cathartic, and is large doses emetic and perhaps diuretic. The bark of the root may be given in *doses* of twenty to thirty grains (1.3–2.0 Gm.), or the extract in half the quantity. For uses, see *A. J. P.*, 1891, 326.

Tripoli. *Terra Tripolitana.*—An earthy mineral, of a whitish, yellowish, or pale straw color, sometimes inclining to red or brown, usually friable, often adhesive to the tongue, and presenting the aspect of argillaceous earth, though differing from clay by the roughness and hardness of its particles, and by not forming a paste with water. The *Venice tripoli* is said to come from Corfu. Tripoli is sometimes artificially prepared by calcining certain argillites. It is used for cleaning and polishing metals.

Trompatila.—This is the stem and branches of *Bouvardia triphylla* Salisb. (Fam. *Rubiaceæ*), a Mexican plant used by the natives for *hydrophobia.* (*A. J. P.*, 1874, 51.)

Tropacocaine. *Benzoyl-pseudotropeine.* $C_8H_{14}ON.C_7H_5O$.—This compound, belonging chemically to the class of *Tropeines* (see *Atropine*), was isolated by Geisel from a narrow-leaved coca plant from Java. (*Ber. d. Chem. Ges.*, xxiv, p. 2336.) It is obtained as an oil, which when quite dry solidifies in radiating crystals, melting at 49° C. It has a strong alkaline reaction, and is easily soluble in alcohol, ether, chloroform, benzene, and petroleum benzin. The *hydrochloride*, being freely soluble in water, is usually preferred to the base. It is decomposed by heating with hydrochloric acid into benzoic acid and pseudotropine, $C_8H_{15}ON$.

Tropacocaine resembles cocaine in its stimulant action upon the nerve centers, and also in its local anesthetic action. It differs from cocaine, however, in that it does not cause local constriction of the blood vessels, and that it has very little influence upon the pupil. Sollmann (*J. A. M. A.*, 1918, lxx, 216) has shown that it is approximately equal to cocaine in its anesthetic power and Eggleston and Hatcher that it is distinctly less toxic. It has been used chiefly in the so-called spinal anesthesia and a large number of surgeons have reported favorably upon it. A *dose* of one grain (0.06 Gm.) is ordinarily recommended, although a number of authors have used larger quantities without evil effects. Tropacocaine has been used also as a local anesthetic in ophthalmic and pharyngological practice. It possesses an advantage over cocaine in being more stable in solution and easily sterilizable.

Trypan Blue. *Diamine blue. Congo blue. Azidin blue. Niagara blue. Sodium salt of tolidin-disazo-bi-l-amido-8-naphthol-3-6-disulphonic acid.* $C_{34}H_{24}O_{14}N_6S_4Na$.—It has been used as a dyestuff. Recently a purified form of this dye has been brought forward as a therapeutic remedy in various protozoan infections. It occurs as a bluish-gray powder which forms in water a deep violet-blue solution. It is almost insoluble in alcohol and quite so in ether. We do not know of any reports of its use in human beings, but Evers, Zengel (*B. Thier W.*, 1913) and others have reported rapid cures of both *malaria* and *trypanosomiasis* in the lower animals.

Trypan Red. *Sodium salt of ortho-benzidine-mono-sulpho-acid-disazo-bi-2-naphthylamine-3.6-sulpho-acid.* $C_{10}H_4(NaSO_3)_2NH_2N.N(C_6H_4)(C_6H_3)NaSO_3N.NC_{10}H_4(NaSO_3)_2NH_2$.—By *trypan red* is meant a coloring matter allied to *benzopurpurin B.* or to *Brilliant Congo R.* It is a reddish-brown powder, soluble in water. The aqueous solution is not altered by the addition of acetic acid, but on the addition of a sufficient quantity of hydrochloric acid, the free sulpho-acid is eliminated in blue flakes.

This was brought forward by Ehrlich and Shiga (*B. K. W.*, 1904) as a useful remedy in experimental, and a hopeful remedy in human, *trypanosomiasis.* Jaboulay and one or two other French writers (*Lyons Medicale*, 1905) have used it hypodermically in the treatment of *cancers* with asserted extraordinary benefit, but the remedy has failed to come into general use. Eight grains (0.5 Gm.) of the remedy may be injected hypodermically, dissolved in 40 cc. of physiological salt solution, at intervals of from two to ten days.

Tryparsamide.—The sodium salt of N-phenylglycineamide-*p*-arsonic acid, $C_6H_4(NHCH_2CONH_2).(AsO.OH.ONa)$.—The dried salt contains 25.32 per cent. of arsenic, in the pentavalent form. This compound, which was developed in the Rockefeller Institute for Medical Research, is a colorless crystalline solid freely soluble in water and without odor, taste or local irritant action. It is in its chemical structure more nearly related to atoxyl than to arsphenamine.

Tryparsamide was brought forward as a remedy for *trypanosomiasis* and *syphilis.* Brown and Pierce (*J. Ex. M.*, 1919, xxx, 417 et seq.) find that it has a well marked effect upon the trypanosomes but that its spirocheticidal action is less potent. In a discussion before the American Medical Association (*J. A. M. A.*, 1924, lxxxiii, p. 888 et seq.) the consensus of opinion developed was that in ordinary cases of syphilis the drug was far inferior to arsphenamine but that in those tertiary manifestations involving the central nervous system such as *general paresis, tabes,* etc., it gave better results than any other treatment. A number of cases of disturbance of vision, some with permanent blindness, similar to those caused by atoxyl have been reported. At present the drug is distributed for experimental purposes only. The doses employed have been usually in the neighborhood of 45 grains (3 Gm.) given intravenously at intervals of about one week.

Tulipine.—An alkaloid extracted from the garden tulip, *Tulipa,* and of which there are a number of classes depending upon the order of their flowering. It is said to be a cardiac poison, with remarkable sialagogue properties. (*Nouv. Rem.*, 1886.) Under the name of *chielin* there has been put upon the market a brownish thick extract-like substance of an agreeable odor, easily soluble in water, said to be derived from the bulb of the tulip and to be non-poisonous. It has been highly recommended by H. Heyman as a soothing application in various forms of inflammatory skin diseases. (*D. M. W.*, August, 1902.)

Tussol. *Antipyrine Mandelate. Phenyl-glycolate.* $C_{11}H_{12}N_2O.C_6H_5CH(OH)COOH$.—It forms a white powder, fusing at 52° to 53° C., is soluble in water and incompatible with most of the substances that are incompatible with antipyrine. It is recommended in the treatment of *whooping cough* in the following *doses:* for children under one year, from three-fourths to one and a half grains (0.048–0.096 Gm.); from two to four years, four to six grains (0.26–0.4 Gm.).

Tutty. *Tutia. Impure Oxide of Zinc.*—This oxide is formed during the smelting of lead ores containing zinc. It is deposited in the chimneys of the furnaces, in the form of incrustations, moderately hard and heavy, and studded over with small protuberances of a brownish color on the outside and yellowish within. As it occurs in commerce, the pieces occasionally present a bluish cast, from the presence of small particles of metallic zinc. Sometimes a spurious substance is sold for *tutty,* consisting of a mixture of blue clay and copper filings, made into a paste with water and dried on an iron rod. It is distinguished from the genuine tutty by its diffusing in water and exhaling an earthy odor, and by its greater friability. Tutty was formerly used as an external desiccant. To fit it for medicinal use it must be reduced to fine powder, which is dusted over the affected part, or applied in the form of an ointment. It is used as a metal polish, also as a finger-nail polish.

Tylophora Leaves. *Tylophoræ Folia. Br. Add.,* 1900. (Fam. *Asclepiadaceæ.*)—The dried leaves of *Tylophora asthmatica* (L.) Wight and Arnott, are used in certain parts of India as a poison for vermin, and have been used with fatal results as a poison. This plant, which grows in Bengal, Burma and Ceylon, has been known in Indian medicine since 1780, and has been largely used in both the civil and the military medical service of Madras. It was officially described as "petiolate, entire, from two to five inches (five to twelve and a half centimeters) long and from three-quarters of an inch to two and one-half inches (eighteen to sixty-five millimeters) broad, lanceolate-ovate or ovate or subrotund in outline, somewhat cordate at the base, abruptly acuminated; rather leathery in texture, glabrous on the upper surface, and finely downy on the lower; of a brownish-green color, which is paler on the lower surface. Odor slightly aromatic; almost devoid of taste." *Br. Add.*

David Hooper (*P. J.,* 1891, xxi, 6) has separated from this drug an alkaloid, *tylophorine,* soluble in ether and alcohol, but scarcely so in water; forming crystalline salts, and striking with nitric acid a purplish-red color, with Fröhde's reagents a deep sap-green, and with potassium dichromate and sulphuric acid a dirty violet. Tylophora resembles in its activity ipecac, and is used as a substitute for that drug in *bronchitis* and in *dysentery.* In *doses* of from twenty to thirty grains (1.3–2.0 Gm.) it is used as an emetic. The expectorant *dose* is from one-half to two grains (0.032–0.13 Gm.).

Tyramine. *N. N. R.* 1924.—One of the active bases which was found in ergot by Barger and Dale was *para-hydroxy-phenyl-ethylamine,* $OH.C_6H_4CH_2CH_2NH_2$, which had previously been found by Barger and Walpole as one of the decomposition products in putrid meat infusion. This base is now prepared synthetically, and the hydrochloride is marketed under the trade-name of "*tyramine.*" In a general way the physiological action of tyramine is similar to that of epinephrine, but it is very much less powerful, and produces practically no effect when applied locally to the mucous membranes. Hewlett and Kay (*J. A. M. A.,* 1918, lxx, 1810) have shown that the subcutaneous injection of one grain (0.06 Gm.) of tyramin causes in normal men a marked rise in the blood pressure with increase in the volume of the pulse which lasts for fifteen to thirty minutes. From their clinical experience they conclude that in ordinary circulatory failure, because of the transitoriness of its action, tyramin is not likely to prove a clinically useful remedy, but that in sudden emergencies such as surgical *shock* or circulatory failure occurring during general *anesthesia* the drug may be of practical value. In such cases, from one to one and one-third grains (0.06–0.08 Gm.) may be injected hypodermically and repeated several times at intervals of twenty to thirty minutes as conditions may indicate. Barbour (*J. A. M. A.,* 1917, lxviii, 882) has shown that tyramin is a stimulant to respiration and suggests its combination with morphine to antagonize the depressant influence of the latter on the respiratory center. There is not sufficient clinical evidence to justify a conclusion as to its practical usefulness. The *dose* is from one-third to one grain (0.02 to 0.065 Gm.).

Ulex.—*Ulex europœus* L. (Fam. *Leguminosæ*) is the common *furze, gorse,* or *whin* so conspicuous in the waste places and by the roadsides of Great Britain, from its spiny branches and bright yellow flowers situated on the spines, either solitary or in pairs. The young tops are fed to cattle and horses, but the food value has been questioned. The leaf buds have been used as a substitute for tea and the flowers yield a beautiful yellow dye. In the seeds of this plant, A. W. Gerrard has found an alkaloid, *ulexine.* In 1890 Kobert (*D. M. W.,* 1890), as the result of an elaborate physiological study, came to the conclusion that ulexine is identical with cytisine. The suggestion has given rise to a considerable chemico-physiological discussion, a brief abstract of which may be found in *P. J.,* Feb., 1891. Kobert found indications of a second alkaloid in ulex. Partheil (*A. Pharm.,* 1892, 448; 1894, 486) and Plugge (*A. Pharm.,* 1894, 444) are in accord as to the identity of ulexine and cytisine. Ulexine has been used in cardiac *dropsy* *Dose,* from one-fifteenth to one-twentieth of a grain (0.004–0.003 Gm.).

Ulmaren is the name given by Bourcet to a mixture of the salicylic acid esters of the higher aliphatic alcohols. It has been stated to contain 75 per cent. of salicylic acid. *Ulmaren* is described as a heavy, pale yellowish-red, refractive, neutral, or weakly acid liquid, of pleasant, faint odor recalling salol, and burning taste. Its sp. gr. at 15° C. is 1.06; and its boiling point lies between 237° C. and 242° C. It crystallizes from an equal volume of petroleum benzin, and is almost insoluble in water, but is soluble in alcohol, ether and chloroform. Animal experimentation (*Th. M.,* 1903, xvii) showed that in moderate doses it is well taken, but if given in large doses by the mouth causes in the dog vomiting and purging, and in the rabbit a dose of 0.07 Gm. per kilogramme intraperitoneally injected, caused death from asphyxia. It is recommended to be used as an external application in *rheumatic* and *neuralgic* diseases, as well as in *gout,* either to be painted on the part and covered with waxed paper or used in the form of an ointment made up with lanolin, in which case it should be present in the proportion of 30 per cent. After epidermatic application the salicylic acid reaction may be demonstrated in the urine in three hours and lasts for three days. It is affirmed to have marked analgesic, antipyretic and antirheumatic powers. (*B. G. T.,* June, 1903.) *Dose,* fifteen to forty-five grains (1–3 Gm.); externally thirty to sixty grains (2–3.9 Gm.).

Ultramarine. *Outremer*, Fr. *Ultramarin*, G.—This fine blue pigment was formerly obtained from *lapis lazuli*, or *lazulite*, a mineral of Siberia. It is now prepared artificially on a very large scale. In preparing it, a mixture of soft clay with sodium sulphate, charcoal, caustic soda and sulphur is heated in crucibles. In this way a colorless compound is first produced, termed white ultramarine. This, however, soon becomes of a green color. The green ultramarine thus obtained, which is also used as a color, is then mixed with sulphur and heated. The sulphur takes fire and is allowed to burn in the air, when the product becomes of a fine blue color. (*Roscoe and Schlorlemmer*, vol. ii, 459.) It is thought to be a compound of aluminum and sodium silicates with sodium polysulphide, although the sulphur present is retained in two conditions, part being deposited when ultramarine is treated with acids and part escaping as hydrogen sulphide.

Umbellularia. *Umbellularia californica* (Arn.) Nutt. *California Laurel. California Sassafras. Spice Tree.* (Fam. *Lauraceæ.*)—This is a handsome, evergreen shade tree of California, up to 90 feet in height with alternate, lanceolate, aromatic leaves, axillary umbels of small greenish flowers and purple drupes. The leaves are employed in *neuralgic headaches*, and in *intestinal colic* and *atonic diarrhea;* also externally as a mild counterirritant. Stillman and O'Neill (*N. R.*, 1883) obtained from the seeds a new acid, *umbellulic acid.* The leaves are said also to contain about 4 per cent. of a volatile oil, having a specific gravity of 0.936, a warm camphoraceous taste, and a strong pungent odor. Burse has separated from the oil by fractional distillation *umbillol*, an oil having the formula $C_8H_{12}O$, which dissolves in concentrated sulphuric acid with red color, and is narcotic. (*Ap. Ztg.*, xi.) According to Schimmel & Co. (*Schim. Rep.*, April, 1897), it also contained cineol. It is probable that the volatile oil is a strong local anesthetic, as it has been found to act rapidly when brought in contact with exposed pulp or sensitive dentine. The fluidextract has been used in *doses* of from ten to thirty minims (0.6–1.8 cc.).

Umber. *Terra Umbra.*—A mineral of a fine compact texture, light, dry to the touch, shining when rubbed by the nail, and of a fine pale brown color, which changes to a peculiar beautiful deep brown by heat. According to Klaproth, it contains 13 parts of silica, 5 of alumina, 48 of ferric oxide, 20 of manganese, and 14 of water in 100. *Burnt umber*, as well as the mineral in its unaltered state, is used in painting. The umber of commerce is said to be brought chiefly from the island of Cyprus.

Uranium. $U = 238.5$.—A heavy metal of the radium group, sp. gr. 18.68 melting point 800° C. The salts of uranium are obtained from the mineral *uraninite* or *pitchblende*, which is noteworthy from the fact that it is the mineral in which Becquerel discovered radio-active properties in 1896, which led to further investigation and the subsequent discovery of radium by the Curies about four years later (see *Radium*). Pitchblende consists of mixed oxides of uranium and has the formula $UO_2.2UO_3$. The salts of uranium are really not true salts of the element but are compounds of the lower oxide UO_2, and are usually called uranyl salts. Upon treating solutions of these uranyl salts with sodium hydroxide solution a yellow precipitate of sodium uranate $Na_2U_2O_7$ is produced which is of technical use in producing a variety of glass, with a peculiar yellow fluorescence, known as uranium glass. The salts of the metal uranium are violent poisons, producing not only severe *gastro-enteritis* and *nephritis*, but also acting specifically on the hemoglobin of the blood, affecting its oxygenating powers. (See *P. J.*, Sept., 1890; Oct. 30, 1897.) They have been carefully investigated by Jacob Woroschilsky (*Arbeiten d. Pharm. Inst.*, Dorpat, v, 1890), who finds that they are violent poisons, though acting slowly, especially when given subcutaneously, small toxic doses producing death almost as rapidly as larger ones. In the lower animals, 1 milligramme of the oxide per kilogramme will produce an intense parenchymatous nephritis, followed by violent inflammation of the intestines. There is marked elevation of the blood pressure and widspread degeneration of the tissues, especially of the blood vessels. In mild cases of poisoning a transient glycosuria is a primary symptom.

Uranium calcium phosphate, according to Churchward (*L. L.*, 1911, i, p. 660), is radioactive and may be used instead of radium in the treatment of *rodent ulcers*.

Jackson (*A. J. Phys.*, 1910, xxvi, p. 381) finds that *sodium-uranium tartrate* causes a slight rise in the blood pressure and some increase in the respiration; it destroys the coagulability of the blood, but does not affect its oxygen carrying power.

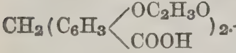
Uranium Nitrate. *Uranii Nitras, U. S. IX. Uranyl Nitrate.* $UO_2(NO_3)_2 + 6H_20 = 502.62$.—Uranium nitrate was dismissed at the tenth revision of the U. S. P. It was formerly described as follows: "Uranium Nitrate occurs in the form of light yellow prisms; odorless and having a bitter, astringent taste; somewhat efflorescent; radioactive. One Gm. of Uranium Nitrate dissolves in 1.2 mils of water at 25° C.; freely soluble in alcohol or ether. Aqueous solutions of Uranium Nitrate are yellow and acid to litmus. Separate portions of an aqueous solution of the salt (1 in 20) yield, with sodium hydroxide T.S. or ammonia water, a yellow precipitate insoluble in an excess of the reagent but soluble in ammonium carbonate T.S.; with ammonium sulphide T.S. a dark brown precipitate; and with sodium phosphate T.S. a yellow precipitate. Mix 2 mils of the aqueous solution with an equal volume of sulphuric acid, cool the mixture, and add a crystal of ferrous sulphate; a dark brown color appears around the crystal. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III). An aqueous solution of the salt (1 in 20) remains clear after the addition of an equal volume of ammonium carbonate T.S. (*alkaline earths*). Dilute 3 mils of this mixture to 10 mils with distilled water and add 10 mils of hydrogen sulphide T.S.; no color or precipitate is produced (*iron, manganese*, or *zinc*). A solution of 1 Gm. of Uranium Nitrate in 20 mils of distilled water, acidulated with 1 mil of diluted sulphuric acid, does not completely decolorize 0.1 mil of tenth-normal potassium permanganate V.S. (*uranous compounds*). An aqueous solution of the salt (1 in 100) does not at once produce a turbidity with barium chloride T.S. (*Sulphate*).

"*Assay.*—Dissolve about 0.4 Gm. of the salt, accurately weighed, in 100 mils of distilled water, heat the solution to boiling, add ammonia water until no further precipitate is produced, and allow the precipitate to settle. Then wash the precipitate well on a filter with an aqueous solution of ammonium nitrate (1 in 100), and afterwards moderately ignite it in a platinum crucible, with free access of air, until the weight is constant. The urano-uranic oxide (U_3O_8) so obtained corresponds to not less than 54.8 per cent. of the weight of the salt taken, which is equivalent to not less than 98 per cent. of $UO_2(NO_3)_2 + 6H_2O$." *U. S. IX.*

Uranium nitrate has been used in the treatment of *diabetes mellitus.* There is, however, no sufficient reason to believe that it can influence the metabolism and any diminution which has followed its exhibition may be attributed to injury to the kidney. It is used as an indicator in the estimation of the urinary phosphates, as well as for other chemical purposes. It is incompatible with the alkaloids, chloral hydrate, salts of arsenous and phosphoric acids and changes the color of cochineal and its derivatives.

Dose, from one to two grains (0.065 to 0.13 Gm.).

Urasol. *Acetyl-methylene-disalicylic Acid. Afsal.*



$CH_2(C_6H_3\left\langle{OC_2H_3O \atop COOH}\right.)_2$.—This substance is said to be formed from about 75 per cent. of salicylic acid, 16 per cent. of acetic acid, and 8 per cent. of formaldehyde. It occurs as a yellowish-white powder, insoluble in water, soluble in ether and alcohol, and is incompatible with acids and with iron compounds. It has been used in *doses* of five to eight grains (0.32–0.5 Gm.), given in capsules, in *muscular rheumatism,* irregular *gout,* and as an antiseptic in *cystitis* and other inflammations of the genito-urinary tract.

Urea. *N. N. R.* 1924. *Carbamide. Urée,* Fr. *Harnstoff,* G. $CO(NH_2)_2$.—For an account of the physical and chemical properties of urea, the reader is referred to treatises upon physiology. Urea has been employed in practical medicine as a hydragogue diuretic in the treatment of *dropsies* and as a tonic alterative in *phthisis.* (*L. L.,* December, 1901.) *Dose,* ten grains (0.65 Gm.) every six hours; increase *pro re nata.* Urea is incompatible with chloral hydrate and lead acetate.

Thio-urea is a substance in which one atom of oxygen in a molecule of urea is replaced by an atom of sulphur,

$CS\left\langle{NH_2 \atop NH_2}\right.$ or C_4N_2S. According to Paul Binet (*Rev. Méd. de la Suisse Rom.,* 1893), it is a very active poison, paralyzing the nerve centers, but leaving intact the peripheral nerves and the muscles. It is used commercially as a photo fixing agent and to remove stains from negatives.

Ureabromine. *Bromo-calcium Urea.* $CaBr_2 \cdot 4CO(NH_2)_2$.—This occurs as colorless, odorless crystals, freely soluble in both water and alcohol, with a melting point of 186° C. and representing 36 per cent. of bromine. It is incompatible with chloral hydrate, potassium iodide and acids. It has been used by Fischer and Hoppe (*B. K. W.,* 1911) with asserted remarkable results in spasmodic conditions of children, especially in *epilepsy.* He attributes this effect not only to the bromine, but also to the readily absorbable calcium it contains. The *dose* for the adult is from thirty to sixty grains (2–4 Gm.).

Urechites. *Urechites suberecta* Muell. *Savannah Flower. Yellow-flowered Nightshade.* (Fam. *Apocynaceæ.*)—This is a woody plant with ovate leaves and yellow flowers, indigenous to Colombia. It grows abundantly in the West Indian Islands and to some extent in Florida. It is said to be used in Jamaica by the negroes as a poison. The symptoms which it produces are violent vomiting and purging, with convulsions. J. J. Bowrey (*J. Chem. S.,* June, 1878) has isolated from it two glucosides, *urechitin* and *urechitoxin,* having respectively the formula $C_{28}H_{42}O_8$ and $C_{13}H_{20}O_5$. Isaac Ott (*T. G.,* 1880) finds the plant to be a powerful cardiac poison, first increasing and then depressing the arterial pressure, and finally, if the dose be large enough, killing by producing cardiac arrest. The results reached by Ott are in accord with those of Ralph Stockman (*Laborat. Rep., Royal College of Physicians,* Edinburgh, vol. iv, 1892), who finds that both of the glucosides are very active poisons belonging to the digitalis group. On the other hand, Vowinkie came to the conclusion that even small doses of the plant depress the heart, and experiments made upon man by Bowrey show that in large doses the drug produces nausea, vomiting, general depression, great perspiration, and slight swelling of the pulse. Stockman (*Rev. de Clin. et de Thér.,* June 29, 1892) found that the leaves contain a toxic alkaloid, which he calls *urechitine,* $C_{28}H_{42}O_8 + H_2O$, and a glucoside, *urechitonin,* which is less toxic. In Jamaica the drug is said to have been used in the treatment of *intermittent* and other *sthenic fevers.* The *dose* of the fluidextract is from two to ten minims (0.12–0.6 cc.).

Uretrol. *Sodium Dimethylaminoazobenzene Meta-sulphonate.* $C_6H_5N = NC_6H_3N(CH_3)_2CH_2 \cdot SO_3Na$.—This substance is asserted to be the product of the reaction of dimethyl amidoazobenzene with formaldehyde and sodium bi-sulphite. It occurs in orange-yellow crystals, melting at 113° C. It is said to be actively antiseptic and non-irritant. It has been used by Italian physicians as an injection in urethritis.

Ursal.—A compound of urea and salicylic acid, used as a substitute for sodium salicylate for the treatment of *rheumatism* in doses of ten to thirty grains (0.6–2.0 Gm.).

Urtica. *Nettle. Ortie brûlante,* Fr. *Brennessel,* G.—Various species of this genus (Fam. *Urticaceæ*) are furnished with poisonous stinging hairs. *Urtica gigas* A. Cunn (now *Laportea gigas* Wedd.), of Eastern Australia is said frequently to kill horses, and to produce in man a sting whose impression lasts for months. (*N. R.,* 1875.) Stinging hairs are known to occur in the following genera of *Urticaceæ: Urtica, Laportea, Hesperocnide, Fleurya, Urera, Girardinia,* and *Scepocarpus.* Under the microscopic those of *Urtica* and *Laportea* are long, conical and unicellular, the apex bearing a small spherical or ovoid head which is attached obliquely and readily breaks off upon contact, when the irritating fluid contents are discharged. It has generally been thought that the virulence of the hairs is due to the presence of free formic acid (*A. J. P.,* xxii), and David Hooper (*P. J.,* April, 1887) has demonstrated the presence of formic acid, or a substance very closely allied to it, in the hairs of the *Nilgri nettle* (*Girardinia palmata* Gaudich.). Nevertheless, it does not seem probable that formic acid is the poison. G. Haberlandt believes it to be a non-volatile albuminoid, and L. Reuter has obtained from several nettles a glucoside. (*A. J. P.,* Jan., 1890.) Oddi and Lomonaco (*Rif. Med.,* April, 1892) isolated from the common nettle a crystalline alkaloid, and found that in mammals the extract acts powerfully upon the vasomotor system, and in frogs causes centric paralysis with diastolic cardiac arrest.

U. dioica L., or *common nettle,* and *U. urens* L., or *dwarf nettle,* European plants naturalized in waste places to some extent in the United States, have been used in medicine as local irritants, as diuretics (*A. J. P.*, 1866), and especially for the purpose of arresting *uterine hemorrhage.* The fluidextract may be given in *doses* of half a fluidrachm (1.8 cc.) or a decoction of the strength of an ounce to a pint in teacupful doses. Under the name of *brandol* is marketed a preparation used in the treatment of *burns* and *wounds;* it is a liquid consisting of 93 per cent. infusion of urtica, 2 per cent. picric acid and 5 per cent. glycerin.

Ustilago. *U. S.* 1880. *Corn Smut.*—The genus *Ustilago* belongs to the *Ustilaginaceæ,* a family of protobasidiomycete fungi whose members are parasites living in their vegetative (mycelial) stage, within the intercellular spaces of the host and frequently developing haustoria which penetrate the host-cells and absorb nutriment from them. Their conspicuous reproductive stage is usually evident as spore masses upon the flowers but occasionally on other parts of the host plant. Each spore mass first appears as a shiny tumor that later matures to form a sooty mass of spores. They produce the *smut* in cereals. *Ustilago Maydis* (DC.) Tul. is produced on the stems, the pistils (corn grains), and the male inflorescence (tassel) of the Indian corn. It is specifically characterized by its minute spheroidal spores, averagely 7 to 10 microns in diameter, the outer walls of which are marked with blunt echinulations. It is abundant in the United States. Upon the corn the smut appears in masses, varying in size from a cherry to a child's head. These masses are smooth, irregularly globose, or sometimes lobulated, having at first a livid, bluish tint, and then becoming blackish, and finally bursting and emitting the black contents, consisting of innumerable globose very minute spores, each of which is covered with beautiful little pointed processes. In a dried state the masses are blackish and covered with a black powder.

C. H. Cressler found in ustilago an alleged alkaloid, *secaline,* besides a thick, viscid, fixed oil and a resin soluble in ether, but not in alcohol. (*A. J. P.*, 1861, 306.) Rademaker and Fischer (*Nat. Drug.*, 1887, 296) believed that they had discovered a white, bitter alkaloid, *ustilagine,* soluble in ether, while H. B. Parsons decided that the fixed oil contained an acid which he provisionally named *sclerotic acid;* also an amine-like volatile substance extracted by ether. (*N. R.*, March, 1882; also *West. Drug.*, 1894.) A. W. Balch (*Journ. Boston Soc. Med. Sci.*, March, 1901) was not able to find any active substance in the smut.

The belief that corn smut is an abortifacient to the lower animals (*A. J. P.*, Sept., 1861) appears to be without foundation, as in the experiments made by the United States Department of Agriculture in 1898 (*Farmers' Bulletin*, No. 69) no effect was produced by corn smut given to pregnant cows. The experiments of James Mitchell (*T. G.*, ii, 223) that ustilago abolishes sensation, reflex action, and later general motor power in the frog, is contradicted by the results of Balch, who also found that enormous doses of the substance have no effect upon the color of the cock's comb. In *doses* of one to two drachms (3.9–7.7 Gm.) it has been claimed by W. A. N. Dorland that the fluidextract markedly increases the severity and frequency of the uterine pains in human labor. The whole drift of our present evidence is to show that ustilago is probably inert.

Uzara. *Uzaron.*—Under this name the root of an undetermined African plant, probably belonging to the *Asclepiadaceæ,* has been used both by the natives and European physicians in the treatment of *dysentery,* especially of the amebic variety. Guerber and Frey (*A. E. P. P.*, 1913, lxxv, p. 75) have determined that it contains neither alkaloid nor tannin, but does contain non-nitrogenous glucosides which have a digitalis-like action upon the heart and diminish peristalsis of the intestines. It appears to owe its virtues in part to its amebicidal action, but in part also to its effect upon the intestinal muscles.

Vaccines. *Bacterins.*—Efficient vaccine therapy is much older than serum therapy. The word vaccine takes its origin from the Latin *vacca,* cow, and Jenner's publication of 1798, "*An Inquiry into the Causes and Effects of Variola Vaccinæ.*" (See Part I, *Virus Vaccinicum,* U. S. *Vaccine Virus,* p. 1203.) Vaccination against smallpox is still our most reliable method of immunization against an infectious disease. Pasteur later applied the term vaccine to his attenuated anthrax virus, and Sir Almroth Wright has still further extended it in his "*bacterial vaccines*" to cover killed cultures of micro-organisms injected into man for the cure as well as the prevention of disease. Strictly, vaccine should mean only one thing, the virus of vaccinia or cow pox.

The various products treated below have this in common, that they are disease producers so modified as to be comparatively harmless, and are used to immunize against the disease which in their virulent form they cause.

This immunization may be either to prevent infection or to ameliorate, or cure, an already existing infection. Vaccines, then, are classed as *antigens,* while serums represent *antibodies.* In receiving a vaccine, the patient is called upon to manufacture his own antibodies. This fact is not to be lost sight of, particularly in serious illness. By vaccine treatment there is being introduced into the body material more or less similar to those invaders which the body forces are already striving to overcome. The balance in the struggle may be a narrow one, and such a load, though well intended, may turn the battle in the wrong direction. On the other hand, for preventive immunization, vaccine therapy has the advantage that the antibodies produced in the patient's own serum are more stable than when introduced in foreign serum and, furthermore, that the cells of the body as well as the blood fluid may be brought into the defensive line.

The greater part of these vaccines are bacterial vaccines. These are suspensions of killed bacteria in physiological saline solution, with 0.25 to 0.5 per cent. phenol or cresol as preservative. The bacteria are usually grown on a solid medium, such as agar, are washed off with the saline solution, and the killing is usually accomplished by heating one hour at 53° to 60° C., though strong antiseptics may be used for this purpose.

The number of organisms per cc. is estimated by direct counting in a microscopic chamber, by comparison with the number of blood cells in normal human blood, or by relative density; saline solution is then added to reduce the suspension to the desired strength. When in the final containers tests are made to insure sterility.

"*Stock vaccines*" are prepared from strains of the different organisms carried in stock by the producer. "*Autogenous vaccines*" are made up from the actual cultures obtained from the patient to be treated and are usually preferred (see remarks on specificity, under *Immune Serum.* Nevertheless, on account of the delay and expense of obtaining and isolating the patient's own strain, stock vaccines are often used. For prophylactic immunization, of course, stock vaccines are necessary. Many of the reported instances of benefit from the use of stock vaccines are to be attributed not so much to the formation of specific antibodies, for the organism in consideration as to the general increase in the bodily resistance against bacterial invasion which is brought about by the introduction of a foreign protein. (See *Protein Therapy.*)

Aside from prophylaxis (*typhoid fever, cholera*) the success in bacterial vaccine therapy seems to have been attained in chronic, sluggish, localized infections.

Bacterial vaccines deteriorate with age—how much we are unable to tell until we have a measure of their potency. They should, however, be kept at 4° to 15° C. and be used within a short time—probably three or four months—of their preparation.

Rabies Vaccine. N. N. R. 1917. *Antirabic Virus. Pasteur Treatment.*—The prevention of *hydrophobia* in persons bitten by rabid animals is one of the debts owed by the world to Pasteur. While formerly 15 per cent. of such unfortunate people contracted rabies and died, the mortality now in treated cases is less than 1 per cent. usually and in some institutes almost zero. The treatment is in a sense a preventive one. It is instituted after the bite, but before symptoms have developed. On account of the long incubation period in rabies there is then opportunity to acquire immunity in most cases.

The dried cord method of Pasteur, which is still the most used on account of its long successful history, consists in daily hypodermic injections of portions of the dried spinal cord of rabid rabbits. The rabbits have been inoculated intradurally with "fixed virus," that is, a virus whose incubation period has been shortened and fixed at five to seven days by passage from rabbit to rabbit through a long series. The usual incubation period of "street virus," or rabies as it occurs naturally, is from 12 to 90 days. In this process of fixation the virus gradually loses its virulence for man. The cords of the rabbits are dried for various lengths of time over caustic potash in an aseptic manner; if dried for 6 days, the cord is called a "6-day cord." The treatment is begun with cords dried the longest time; originally Pasteur began with a 14-day cord, but the tendency has been to use cords dried fewer and fewer days, as the fixed virus has been found practically innocuous for man. The treatment lasts about 21 days, a piece of cord 5 millimeters long is emulsified in 2.5 cc. salt solution and injected each time. Other modifications of the Pasteur treatment are the injection of weak dilutions of the fresh fixed virus (Högyes), the carbolization of the virus (Fermi), attenuation by dialysis (Cumming) or by drying while frozen (Harris). The emulsion of the virus should be prepared as few hours as possible before its use.

Acne Bacillus Vaccine. Vaccinum Acne. N. N. R. 1924.—The acne bacillus is a short rod, not decolorized by Gram's stain, growing only in the absence of oxygen, and even sluggishly then. The vaccine prepared from it is used in cases of *acne* in which the bacillus is found and which do not improve under the usual staphylococcus vaccine. The usual *dose* is about 5,000,000 killed bacteria.

Cholera Vaccine. Vaccinum Choleræ. N. N. R. 1924.—The cholera vibrio is the cause of *Asiatic cholera.* It is a curved rod, decolorized by Gram's stain, a rapid grower, and prefers an alkaline medium. Cholera vaccine has given favorable results in India and Japan, and during the World War was used extensively in the Balkans with reduction in the incidence and mortality among the vaccinated.

Gonococcus Vaccine. N. N. R. 1924.—The gonococcus is a thick, coffee-bean shaped organism occurring in pairs. It is decolorized by Gram's stain and is difficult to grow, even on media which contain one of the body fluids. In *gonorrheal urethritis, vaginitis,* and *ophthalmia* no benefit is to be expected from vaccine treatment. There are probably different strains or types of gonococci, and this together with the low antigenic power of the organism may explain the not very satisfactory results with gonococcus vaccine in chronic infections such as *arthritis* and deep urethritis. The *doses* used are 5,000,000 (freshly isolated cultures) to 1,000,000,000 (old strains).

Pertussis Bacillus Vaccine. N. N. R. 1924.—The pertussis bacillus, or bacillus of Bordet-Gengou, is the cause of *whooping-cough.* It is a very small Gram-negative rod, growing at first only on special media. The vaccine prepared from this organism is used both as a preventive and in the treatment of whooping-cough. In the former case three doses of 50,000,000 to 2,000,000,000 are given a week apart. For treatment, the *doses* range from 50,000,000 to 2,000,000,000 every two to four days. It is reported that the vaccine treatment makes the attack milder and in particular shortens the course of the disease. Apparently a freshly prepared vaccine gives better results than an old vaccine. In many institutions for children, the vaccine is given to all new admissions with a claimed reduction in the number of cases developing after admission.

Plague Bacillus Vaccine. Vaccinum Pestis. N. N. R. 1924. *Haffkine Prophylactic.*—The bacillus of *bubonic plague,* or *Bacillus pestis,* is a short, Gram-negative rod which has a tendency to take up the stain more intensely at the ends, leaving a relatively light staining central portion. It grows fairly well on ordinary laboratory media and is one of the most virulent bacteria known, since it will easily cause a fatal infection by mere contact with the abraded skin. The vaccine is used with fair success as a preventive—those inoculated being less prone to the disease than the uninoculated in the same community and having relatively milder attacks if not entirely protected. Though the prophylactic is useful for travellers through badly infected territory, reliance in a plague outbreak is to be placed in eradicative measures rather than in Haffkinization of the population.

Staphylococcus Vaccines. N. N. R. 1924.—There are three species of varieties of staphylococci concerned in human disease, the *Staphylococcus albus,* which produces a white growth on solid media; the *Staphylococcus aureus,* which produces golden yellow, and the *Staphylococcus citreus*, giving a lemon yellow. The first of these is the usual cause of the relatively mild skin pimples and boils; the second is more likely to be encountered in more severe abscesses and carbuncles, while the third is relatively rare. All are large round organisms, Gram positive and tending to a tesselated arrangement; rapid growth is obtained on all ordinary media. It is with these organisms that the most striking successes of vaccine therapy have been made, particularly in *furunculosis*. If possible, the vaccine should be autogenous, but cure is frequent with stock vaccines. Some cases will not respond even to autogenous vaccines. The initial dose should be 500,000 to 1,000,000 and subsequent doses should be increased by 500,000 until a dose of 2,000,000 is reached. The injections should not be given more frequently than 5 days, and usually 6 to 10 injections are advisable. Reactions following the use of staphylococcus vaccine are usually slight. As with other methods of treating this affection, relapses are not infrequent; more intensive and prolonged treatment is then indicated. *Sycosis vulgaris, pustular acne, carbuncles, abscesses* are all amenable to vaccine therapy to a greater or less degree, but, especially in the two latter, surgical measures should not be neglected.

Streptococcus Vaccine. N. N. R. 1924.—There are two general types of streptococci, one known as *Streptococcus hemolyticus*, and the other as *streptococcus non-hemolyticus*, and there are a number of different types or strains in each of these two main divisions. The usual *Streptococcus pyogenes* is a round or oval organism. Gram positive, tending to be arranged in chains, and to divide with the line of division at right angles with the chain; the cocci often appear in pairs. This organism grows less readily and in smaller colonies than the staphylococcus. The streptococci forming long chains (*Streptococcus longus*) are thought to be more pathogenic than those with short chains (*Streptococcus brevis*). On blood agar the colonies have a clear halo, due to hemolysis (*Streptococcus hemolyticus*). Other strains (called *Streptococcus viridans*) produce greenish colonies under like conditions; these latter are found in infections such as *endocarditis* and *arthritis*, while the hemolytic strains occur in the virulent, pyogenic *phlegmons* and fatal *septicemias*. Another form, *Streptococcus mucosus*, produces a mucoid growth, and has a capsule like the pneumococcus.

The name *Streptococcus rheumaticus* is given to the streptococci found in *rheumatism*, *Streptococcus erysipelatus* to those of *erysipelas*. Recent work by Dick and Dick, Dochez and others (see *J. A. M. A.*, 1924, lxxxviii, p. 542, 712, 1246) has apparently proved that *scarlet fever* is caused by a particular strain of the streptococcus of the hemolytic group to which has been given the name of scarlet fever streptococcus. This strain produces a toxin which has been used to produce an antitoxin against scarlet fever. The toxin has been used in the performance of the Dick test to determine susceptibility to scarlet fever in the same way that the Schick test is used for diphtheria.

On account of our inability to treat the greater part of the streptococcal infections directly, this has been a favorite field for vaccine therapy, but the results are far from convincing. Occasional favorable results are obtained in the treatment of one or another conditions of streptococcal invasions, especially if attention is paid to strain specificity and the tendency of the organisms to decrease in pathogenicity and immunizing power under artificial cultivation.

Streptococcus and Prodigiosus Vaccine. N. N. R. 1924. *Toxins of Erysipelas and Prodigiosus. Coley's Fluid.*—This suspension, used in the treatment of inoperable *sarcoma*, is practically a bacterial vaccine prepared from *Streptococcus pyogenes* and *Bacillus prodigiosus*. Due to the latter, the fluid has a reddish tint. An analysis of the reported cases in which it has been used indicates that it is probably of some value in the field for which it is recommended.

Typhoid Bacillus Vaccine. Vaccinum Typhosus. N. N. R. 1924. *Typhoid Vaccine. Typhoid Prophylactic.*—The typhoid bacillus, or *bacillus of Eberth*, is an actively motile rod, sometimes very short, sometimes by the end-to-end arrangement of several individuals, long and filamentous, Gram-negative and growing readily on ordinary media. It is the cause of *typhoid fever*—in German *typhus*, but to be distinguished from true typhus fever, or *typhus exanthematicus*. As the staphylococcus vaccines are the best examples of vaccine therapy, so typhoid vaccine is the best example of prophylaxis by bacterial vaccine. Treatment of *typhoid fever* by vaccines, while yielding some slightly encouraging results, is often dangerous on account of the severity of the general infection. Attempts to rid typhoid carriers of their bacilli by vaccine therapy are occasionally successful, usually not.

In 1896 Pfeiffer and Kolle in Germany and Wright in England began work on typhoid immunization. The German vaccine was grown on solid medium-agar—the English in broth and heated to 60° C. Later Leishman found that heating to 53° to 54° C. was sufficient and gave better immunization. The English used one injection at first, then two, eight days apart. Kolle advised three. The method of the American army, instituted by Russell, followed the agar cultures and the triple dose of Kolle, but used Leishman's strain and temperature. The results in the United States Army are well known and striking; together with improved sanitation, the compulsory vaccination has practically eliminated typhoid. The results from the use of typhoid vaccine both in civil and army practice have been so overwhelmingly favorable that it is not necessary to give statistics of these results. The value of typhoid vaccination is universally recognized and its practice is general. It should be given in a course of three injections seven days apart. A certain number of persons develop a local and sometimes general reaction after taking typhoid vaccine. The reaction is milder and less frequent in young children than in adults.

Reactions both local and febrile are often seen within forty-eight hours, more frequently with some lots of vaccine than with others. The vaccine produces agglutinins (positive Widal test) in men and animals injected, also bacteriotropism or opsonin against the typhoid bacillus. Typhoid vaccine probably becomes more or less inactive after a few months and should be kept at a temperature between 4° and 15° C. in the dark.

The protection given by the vaccine is not absolute nor life-long, but for three years it is usually sufficient to resist all ordinary intensities of infection, and some immunity doubtless persists through life. Even when the vaccinated do chance to contract the disease, their attack is generally much milder than in the unvaccinated. As it has been found that vaccination with the typhoid vaccine does not give protection against infection with the *B. paratyphosus A.* and *B. paratyphosus B.*, practically all typhoid vaccine now used is prepared from the three organisms in the proportion of 1,000,000 of typhoid bacilli and 500,000 each of the two paratyphoids in each cc.

Pollen Extract. N. N. R. 1924. *Hay Fever Vaccine.*—This product is included with the vaccines because it depends on an immunological response on the part of the person receiving treatment. Hay fever and rose cold are probably caused by the irritant action of the pollen of certain plants on the ocular and respiratory mucous membranes of especially sensitive individuals. By skin inoculation it is often possible to determine to what pollens a person is sensitive. The administration of pollen extract is an attempt to decrease their sensitiveness, in other words, to immunize the patient against the pollen. The Gramineæ or grasses are chiefly concerned in the production of rose cold (June cold), and the Compositæ in that of *hay fever* or autumnal catarrh. Pollen extracts have been prepared from each of these two great classes and favorable reports from treatment are not uncommon. The extract is usually given in a long series of injections, preferably before the symptoms of the year appear. The extract is unstable and should be used when freshly prepared. Severe reactions may also occur with potent extract unless the symptoms are watched and the increase in dosage made gradually.

Vaccinium. *Vaccinium crassifolium* Andr. *Blueberry.* (Fam. *Vacciniaceæ.*)—The leaves of this slender trailing shrub, found growing in sandy most pine woods from North Carolina to Georgia, are said to be astringent and diuretic, and capable of replacing uva ursi. *Dose*, of the fluidextract, from a half to one fluidrachm (1.8–3.75 cc.).

Valeric Acid. *Valerianic Acid. Acidum Valericum. Acidum Valerianicum. U. S.*, 1870. *Isopropylacetic Acid. Acide valérique*, Fr. *Valeriansäure, Baldriansäure*, G. *Acido valerianico*, It., Sp. $HC_5H_9O_2$. Mol. wt., 102.08.

Valeric acid (originally valerianic acid) received its name from having been found in the oil distilled from valerian. It was first obtained in 1817 by Chevreul from the oil of the dolphin, and received the name of *delphinic acid*, which, however, upon the discovery of its identity with the acid afterwards obtained by Pentz from valerian, was superseded by its present title. It has been obtained also from the bark and fruit of *Viburnum Opulus* L. and other species of *Viburnum* (Fam. *Caprifoliaceæ*), the sap wood of the European elder (*Sambucus nigra* L.) (Fam. *Caprifoliaceæ*), the root of *Angelica Archangelica* L. (*Archangelica officinalis* Hoffm.) (Fam. *Umbelliferæ*), and from various organic products of the vegetable and animal kingdom. At present it is chiefly made synthetically from amyl alcohol.

Valeric acid is a colorless liquid, of an oily consistence, a repulsive odor, resembling that of valerian, and a pungent, sour, acrid, disagreeable taste. Its sp. gr. is 0.955, melting point 36° C., boiling point 177° C. It is soluble in thirty parts of cold water. Alcohol and ether mix with it in all proportions. It is very soluble in strong acetic acid and dissolves camphor and some resins. It forms salts with the alkalies and reddens litmus paper strongly, but the blue color gradually returns in a warm place. For tests of purity by Mossler, see *P. J.*, 1911, 175.

The virtues of valerian have been attributed to valeric acid and the latter has therefore been used as a nerve sedative, but it is probably inert. The customary *dose* is from three to ten minims (0.2–0.6 cc.).

Valeridin. *Valerydin. Sedatin. Iso-valeryl-p-phenetidin.* $C_6H_4\left\{\begin{matrix}NHCOC_4H_9\\OC_2H_5\end{matrix}\right.$.—This substance occurs as white, glistening needles, which are readily soluble in alcohol or chloroform, difficultly soluble in ether, and almost insoluble in water. It is obtained by heating isovaleric acid with p-phenetidin. C. Erdmann (*Ph. Ztg.*, xliii) commends this substance in *doses* of from eight to fifteen grains (0.5–1.0 Gm.) a day, as a succedaneum for valeric acid, and as being serviceable in *migraine, neuralgia* and *hysteria.*

Validol. *Menthyl Valerate.* $CH_3.CH_2.CH_2.COO.(C_{10}H_{19})$.—*Validol* is a clear, colorless liquid, of a mild, pleasant odor, and slightly bitter taste, said to contain 30 per cent. of menthol combined chemically with 70 per cent. of valeric acid. It was originally proposed by Schwersenski (*Th. M.*, 1897) as being locally non-irritant and affording a means of exhibiting menthol for its local action in *pruritus, gastralgia, coryza,* various mucous inflammations, and as an antispasmodic in *migraine, neurasthenia, hysteria* and other neuroses. Validol has also been used as an antemetic, for the relief of *sea-sickness* and in other forms of *nausea.* It is stated to be specially eliminated through the urine, to which it imparts a peculiar odor. *Dose,* five to twenty minims (0.3–1.3 cc.); locally 10 to 15 per cent. ointment is recommended.

Validolum Camphoratum is a 10 per cent. solution of camphor in validol.

Valonia. *Acorn Cups. Valloné, Vélanède, Gallon,* Fr. *Knoppern, Walonen,* G.—The great cups of the acorns of the *Quercus Aegilops* L. (Fam. *Cupuliferæ*), an evergreen tree, native to Bosnia, contain a very large percentage of tannin. They are extensively exported for dyeing and tanning, and have been employed as an astringent in *diarrhea.*

Valyl. *Valeric Acid Diethylamide,* $C_4H_9.CO.N(C_2H_5)_2$.—It occurs as a colorless liquid having a characteristic odor and burning taste, and boiling at 210° C. According to Kionka (*D. M. W.*, xxvii, 1901), valyl produces cerebral excitement, attended with convulsions, probably of cerebral origin, as there is no increased reflex activity. It is said primarily to increase the blood pressure and to have little action upon the heart or respiration. It is somewhat irritant, but may be given in four per cent. aqueous solution, and has been used as a substitute for valerian in *hysterical* and allied *neuroses. Dose,* four to fifteen grains (0.26–1.0 Gm.) three times a day, preferably administered with an equal amount of tallow in gelatin capsules.

Vanadic Acid. *Acidum Vanadicum. Metavanadic Acid.* HVO_3.—Forms golden-yellow scales, which are only slightly soluble. According to Le Blond and C. David, *vanadic acid* is actively antiseptic, and very useful in solutions for the skin, 0.05 in 1000; for gynecological use, 0.17 in 1000.

The meta-vanadates are used in preference to the ortho, pyro, etc., due to their stability in solutions. They are incompatible with acids, the latter imparting to their solutions a yellowish-red color.

In the arts vanadic acid is used in various oxidizing processes as a carrier of oxygen, effecting by its presence the more efficient action of other oxidants, as in the aniline black formation, where a small amount of ammonium vanadate is capable of taking the place of large amounts of chlorates and similar oxidizing agents. It is also used in vanadium inks.

The vanadium compounds are prepared from the element *vanadium,* a light gray crystalline metal. The principal source of vanadium is the mineral natronite, an impure vanadium sulphide mined in Peru. The element is used in iron alloys to give hardness.

According to Jackson (*J. P. Ex. T.*, 1912, iv, p. 1) *sodium orthovanadate,* when injected in large doses, produces a slight rise in the general blood pressure, which is due to constriction of the vessels of the abdominal region, increased peristalis of the intestinal tract, salivation, vomiting and diarrhea, more or less spasm of the bronchial muscles, and death from respiratory failure.

According to Dutton (*J. A. M. A.*, June 3, 1911), workers in industries in which vanadium is used, suffer from a form of chronic poisoning, the most important results of which are congestion of the lungs and of the kidneys, and sometimes hemorrhagic nephritis and also irritation of the gastro-intestinal tract. Anemia is an early symptom, and there is usually a dry cough, loss of appetite, emancipation and albuminuria.

The vanadates have been used in *anemia, tuberculosis* and a host of other chronic diseases, but are probably without therapeutic virtue. The usual *dose* of *sodium* or *lithium metavanadate* is from one-sixtieth to one-fifteenth of a grain (0.001–0.004 Gm.).

Under various names, as *vanadiol, oxylasine,* etc., various proprietary preparations containing vanadium have been introduced for which extraordinary therapeutic properties were claimed. The evidence in support of these claims, however, is extremely unsatisfactory.

Verbena. *N. F. IV. Blue Vervain.*—"The dried overground portion of *Verbena hastata* Linné (Fam. *Verbenaceæ*), collected when flowering." The plant is a tall shrub growing in damp situations throughout the United States. "In broken or cut pieces; stem stout, obtusely quadrangular, rough, pubescent; leaves opposite, petioles from 12 to 25 mm. in length, blades from 6 to 12 cm. in length, lanceolate, acuminate, acute, coarsely and sharply serrate or the lower hastate lobed, deep green above, paler beneath, conspicuously veined; flowers in terminal interrupted panicles of spikes, spikes erect cylindraceous, densely flowered, each flower subtended by a lanceolate acute bract; calyx adherent, little more than half the length of the corolla, tubular, five-lobed, the mouth slightly oblique; corolla small, bright blue, salver-form tube externally pubescent, subequally five-lobed; stamens adnate to the corolla tube, included, didynamous, fruit dividing at maturity into four one-seeded parts. Odor heavy, especially if dampened; taste bitter and disagreeable. Verbena yields not more than 10 per cent. of ash." *N. F. IV.* The *fluidextract of verbena* was official in the N. F. IV. There is no reason to suspect it of medicinal virtue. The *dose* is fifteen minims (1 cc.).

Verditer.—Two compounds of copper, employed as pigments, are known by this name in commerce, and are distinguished by the epithets of blue and green. *Blue verditer* is a blue *cupric carbonate,* $2CnCO_3Cn(OH)_2$. *Green verditer* is a green cupric carbonate, $CnCO_3Cn(OH)_2$, also known by the names *Bremen green, Brunswick green, mountain green* and *artificial malachite green.*

Vernonia. *Vernonia anthelmintica* Willd. (Fam. *Compositæ.*)—This is an East Indian plant, whose black, bitter, and nauseous seeds have a high reputation in Ceylon as an anthelmintic in *doses* of sixty grains (3.9 Gm.). (*P. J.*, April, 1883; also *Ph. Rev.*, 1896, 274.)

Veronica. *Veronica officinalis* L. *Speedwell. Veronique mâle,* Fr. *Ehrenpreis,* G. (Fam. *Scrophulariaceæ.*)—Several species of *veronica,* common to Europe and this country, have been medicinally employed. Of these, *V. officinalis* L., and *V. Beccabunga* L., or European *brooklime,* are the most conspicuous. *V. officinalis* has a bitterish, warm, and somewhat astringent taste.

Vintilesco found a glucoside in *V. officinalis* and *V. Chamædrys* L. (*J. P. C.*, 1910, No. 4.) The plant has been considered diaphoretic, diuretic, expectorant, tonic, etc., and was formerly employed in *pectoral* and *nephritic complaints, hemorrhages, diseases of the skin,* and in the treatment of *wounds. V. Beccabunga* was used in the fresh state in *scurvy.*

Vieirine.—This substance is obtained from the bark of the *Remijia Vellozii* DC. (Fam. *Rubiaceæ*), of Brazil. It is used in Brazil in *doses* of from one to four grains (0.065–0.26 Gm.) repeated *pro re nata,* as a tonic and as an antiperiodic in place of quinine.

Vilca Bark.—The bark of *Piptadenia macrocarpa* Benth. (Fam. *Leguminosæ*), a timber tree indigenous to Bolivia and adjacent parts of South America which is characterized by its warty bark, bipinnate leaves, mimasaceous flowers and pod-fruits. The natives of Bolivia are said by Rusby to make an aqueous extract from this bark which is added to cane juice to hasten fermentation, the process resulting in an increased yield of sugar. According to Fanchon Hart (*J. A. Ph. A.*, 1922, p. 906) who has first described the structure of the drug, it contains a large percentage of tannin, resin and calcium oxalate.

Vinca.—Under this name are included *V. major* L., *Greater Periwinkle,* and *V. minor* L., *Lesser Periwinkle* (Fam. *Apocynaceæ*). It was, at one time, used in arresting *menorrhagic* and other *hemorrhages.* (*A. J. P.*, 1872.)

Vincetoxicum. *V. officinale* Moench. (now more properly *Cynanchum Vincetoxicum* (L.) Pers. *White Swallow-wort. Vincetoxicum. Asclépiade, Dompte-venin, Hirundinaire,* Fr. *Schwalbenwurz, Giftwende,* G. (Fam. *Asclepiadaceæ.*)—A perennial, herbaceous European plant, the root of which was formerly esteemed a counterpoison, and hence the botanical name. It has a bitterish, acrid taste, and, when fresh, a disagreeable odor, which is diminished by drying. Kubler found a glucoside, *vincetoxin,* $C_{50}H_{82}O_{20}$, which he states differs from *condurangin* which other investigators asserted to be identical. (*A. Pharm.*, 1908, 659.) Taken internally, especially in the recent state, it excites vomiting, and is capable, in larger quantities, of producing dangerous, if not fatal, inflammation of the stomach. Feneulle found in the root a principle analogous to emetine. It has been used in *skin diseases* and *scrofula.*

Vinegar. *Acetum.*—*Vinegar* is produced by the acetous fermentation in infusion of mixed malted and unmalted grain, or of various fruit juices. Any substance which is capable of undergoing the alcohol fermentation is further liable under the influence of a microscopic plant, *Mycoderma aceti*, first described by Pasteur, and exposure to the air at a temperature between 24° C. and 35° C., to undergo further change with oxidation, which converts the alcohol into acetic acid. Practically for success there should not be more than 12 per cent. of alcohol in the original fluid. There are a number of other organisms which oxidize alcohol into acetic acid, viz., *Bacterium aceti*, *B. Pasteurianum*, *B. Kuetzingianum*, *B. Oxydans*, and *B. Industrium*.

In the quick *German process* for making vinegar a mixture of one part of 80 per cent. alcohol, four or six parts of water, and one-thousandth of honey or extract of malt, at a temperature of 24° C. to 35° C., is allowed to percolate through beech shavings, previously steeped in vinegar, and contained in a deep oaken tub, in which is a wooden diaphragm perforated with numerous small holes, loosely filled with packthread about six inches long. It is essential to the success of the process that a current of air shall pass through the tub. In order to establish this current, eight equidistant holes are pierced near the bottom of the tub, forming a horizontal row, and four glass tubes are inserted vertically in the diaphragm, of sufficient length to project above and below it. The air enters by the holes below, and passes out by the tubes. Although the air is necessary for the furnishing of oxygen, acetification consisting chiefly in the oxidation of the alcohol, the beech shavings and similar articles chiefly aid in the process by affording surface upon which the mycoderms can grow. During the process the temperature rises to 37° C. or 40° C., and remains nearly stationary while the process is going on favorably. The liquid is drawn off by a discharge pipe near the bottom, and must be passed three or four times through the tub before the acetification is completed, which generally occupies from twenty-four to thirty-six hours. According to Wimmer, pieces of purified charcoal, about the size of a walnut, may be advantageously substituted for the beech shavings in the process.

In 1862, Pasteur substituted for the German process the sowing of the mycoderm upon the surface of a mixture of wine and vinegar, or of water, alcohol (2 per cent.), and acetic acid (1 per cent.) adding alcohol daily in small quantities after about half that contained in the original liquid had been converted into acetic acid, until a vinegar of sufficient strength was produced. The *French process* was improved in 1869 by Laugier, and it was subsequently further elaborated by Emanuel Wurm. (For details, see *P. J.*, xi, 133.)

In England, vinegar is made from the infusion of malt. The fermented wort is caused to fall in a shower upon a mass of fagots of birch twigs occupying the upper part of a large vat, and, after trickling down to the bottom, is pumped up repeatedly to the top, to be again allowed to fall, until the acetification is completed. This mode of oxidizing the alcohol in the fermented wort has the advantage of rendering insoluble certain glutinous and albuminous principles, which, if not removed, would cause a muddiness in the vinegar and make it liable to spoil.

In the United States, vinegar is largely made by the German method of oxidizing very diluted alcohol, and is called *white vinegar;* it is often prepared from cider—*cider vinegar.* The cider is placed in barrels (with their bung holes open) which are exposed during the summer to the heat of the sun. The acetification is completed in the course of about two years. The process of the fermentation, however, must be watched, and as soon as perfect vinegar is formed, it should be racked off into clean barrels. Without this precaution, the acetous fermentation would run into the putrefactive, and the vinegar spoil. Cider vinegar contains no aldehyde. It contains malic acid, and therefore yields a precipitate with lead acetate. The absence of such a precipitate indicates that the alleged cider vinegar is a manufactured substitute, although a fictitious article might yield a similar precipitate.

Cider or apple vinegar is also made by the quick process described above. Much commercial vinegar is made from the apple cores, skins and other waste from the dried apple and pectin industry. Vinegar may be clarified, without impairing its aroma, by throwing about a tumblerful of boiling milk into from fifty to sixty gallons of the liquid, and stirring the mixture. This operation also makes red vinegar pale.

The series of changes which occur during the *acetous fermentation* is called acetification. The following equations represent this change:

$$C_2H_6O + O = C_2H_4O + H_2O$$
$$C_2H_4O + O = C_2H_4O_2$$

Vinegar, when good, is of an agreeable, penetrating odor, and a pleasant acid taste. According to Magnes-Lahens, wine vinegar always contains a little aldehyde. The better sorts of vinegar have a grateful aroma, probably due to the presence of an ethereal substance, perhaps acetic ether. The color of vinegar varies from water white to deep red. When long kept, especially if exposed to the air, it becomes ropy, acquires an unpleasant odor, putrefies, and loses its acidity.

The essential ingredients of vinegar are acetic acid and water; but, besides these, it contains various other substances, derived from the particular vinous liquor from which it may have been prepared.

Malt Vinegar (*Acetum Britannicum*) has a brown color, and a sp. gr. from 1.006 to 1.019. The strongest kind, called *proof vinegar,* contains from 4.6 to 5 per cent. of acetic acid. That of British manufacture usualy contains sulphuric acid, which the manufacturer is allowed by law to add in a proportion not exceeding one part in a thousand; but if the vinegar be properly made it does not require to be thus protected.

Malt Vinegar is "a liquid of a brown color and peculiar odor. Specific gravity 1.017 to 1.019. 445.4 grains by weight (1 fluidounce) of it require about 402 grain-measures of the volumetric solution of soda for their neutralization, corresponding to 5.41 per cent. of real acetic acid, $HC_2H_3O_2$. If ten minims of solution of barium chloride be added to a fluidounce of the vinegar, and the precipitate, if any, be separated by filtration, a further addition of the test should give no precipitate. Sulphuretted hydrogen causes no change of color." *Br.*, 1885.

Wine Vinegar (*Acetum Gallicum*) is nearly one-sixth stronger than pure malt vinegar. It is of two sorts, the white and the red, according as it has been prepared from white or from red wine. *White wine vinegar* is usually preferred. *Red* *wine vinegar* may be deprived of its color, and rendered limpid, by being passed through animal charcoal. Under the name of wine vinegar or white wine vinegar the so-called distilled vinegar is sometimes sold. This is made, not by distillation of vinegar as the name indicates, but by the distillation of a weak alcoholic liquid produced by the fermentation of molasses with yeast and the subsequent acetification of the weak alcohol by percolation through beechwood shavings impregnated with mycoderma aceti.

The best test for the detection of free inorganic acids is a weak solution of methyl violet which turns green in the presence of free inorganic acids, but remains unaffected by organic acids.

Distilled Vinegar (*Acetum Destillatum; Vinaigre distillé, Oxéolat simple,* Fr.; *Destillirter Essig,* G.) was official in the U. S. Pharmacopœia, 1870, and was prepared by obtaining seven pints of distillate from eight pints of vinegar placed in a glass retort, the one pint left in the retort retaining the fixed impurities, salts, etc. One hundred grains should saturate not less than seven and six-tenths grains of potassium bicarbonate.

The principal foreign substances which vinegar is liable to contain are sulphuric and sulphurous acids, and copper and lead, derived from improper vessels used in its manufacture. Tin has been found in it after standing a short time in tin vessels. The testing of vinegar for genuineness and purity involves so many complex factors that a work on food analysis, such as that of Leach, should be consulted.

Vinegar is at present used as a medicine only for its local astringent properties, and in the form of an enema diluted with three times its bulk of water to kill *seat worms.* In the *dermatitis* produced by exposure to the sun, made into a paste with glycerin, bismuth, and starch, it is very effective. In *hematemesis* one ounce to a tumbler of water often acts very advantageously, and may be taken freely. At one time vinegar was largely used in pharmacy as a menstruum, but on account of its tendency to undergo decomposition it has been replaced by diluted acetic acid in both the American and British Pharmacopœias.

Vioform. *Nioform.* $C_9H_3NOHICI$.—*Iodo-chloroxyquinoline* was introduced as a substitute for iodoform in surgery. It is a greenish-yellow, almost odorless, bulky, insoluble powder. According to the researches of E. Tavel, it is less toxic than iodoform, especially when brought in local contact with wounds, and is also more actively germicidal than is iodoform. Locally it is not at all irritant. (See *S. Jb.*, Bd. 267, p. 133; Bd. 272, p. 163.)

Viola. *Violet.*—The genus *Viola* (Fam. *Violaceæ*) includes numerous species, many, perhaps all, of which are possessed of analogous medicinal properties. *Viola tricolor* L., the *Heart's-ease, Pansy,* or *Johnny-jump-up* of the gardens, was formerly recognized by the U. S. Pharmacopœia; while *V. odorata* L., and *V. pedata* L., have held places in both the British and the United States Pharmacopœias.

V. odorata L. *Sweet Violet, Violette, Violette odorante,* Fr.; *Wohlriechendes Veilchen, Veilchen,* G.; *Violetta,* It.; *Violeta,* Sp.—This is the common violet of Europe and also the parent of the florists' violets. It resembles very closely the American blue violet, *V. cucullata* Ait., from which, however, it is at once distinguished by its greater fragrance. It is the *sweet violet* of our gardens. *V. pedata* L., or *Bird's Foot Violet* is an indigenous, stemless violet, characterized by its large blue or variegated beardless flowers, and its deeply three- to five-divided, pointed pedate leaves.

The flowers of *V. odorata* yield their odor and their slightly bitter taste to boiling water. Their infusion affords a delicate test for acids and alkalies, being reddened by the former and rendered green by the latter. Their odor is destroyed by desiccation, and the degree to which they retain their fine color depends upon the care used in collecting and drying them. They should be gathered before being fully blown, deprived of their calyx, and rapidly dried, either in a heated room or by exposing them to a current of very dry air. The flowers of other species are often mingled with them, and, if of the same color, are equally useful as a chemical test.

In the root, leaves, flowers, and seeds of *Viola odorata,* Boullay discovered an alkaloid, *violine,* allied to emetine, but possessing distinct properties. It exists in the plant combined with malic acid. Orfila asserts that it is exceedingly active and even poisonous. Linde, however (*Chem. Abstr.*, 1919, xiii, 2963) says that the amount of alkaloid in the violet roots is so small that one can scarcely attribute any toxic effect of these roots to their alkaloidal content. Mandelin (*Jahresb.*, 1883) obtained a glucoside analogous to quercitrin, which he names *violaquercitrin.* It crystallizes out of hot water in fine yellow needles. When boiled with diluted acids, it is decomposed into *quercetin, isodulcite* and a fermentable glucose,

$$C_{27}H_{30}O_{16} + 3H_2O =$$
$$C_6H_{14}O_6 + C_6H_{12}O_6 + C_{15}H_{10}O_7$$

he also obtained salicylic acid from several species of viola. (*A. J. P.*, 1882, 10.) Kraemer (*Inaug. Diss.*, Marking, 1896) detected methyl salicylate and this was later confirmed by Schimmel & Co. See also Gadd's article, *Y. B. P.*, 1905, 466.

The herbaceous parts of various species of violets are mucilaginous, emollient, and slightly laxative, and have been used in *pectoral, nephritic,* and *cutaneous diseases.* In Europe a syrup prepared from the fresh flowers of *Viola odorata* is employed as an addition to demulcent drinks, and as a laxative for infants. The root, which has a bitter, nauseous, slightly acrid taste, acts in the *dose* of from thirty grains to a drachm (2.0–3.9 Gm.) as an emetic and cathartic. It is probable that the same property is possessed by the roots of all the violets, as it is known to be by several species of *Ionidium,* which belongs to the same family. The existence in small proportion of the emetic principle in the leaves and flowers accounts for their expectorant properties.

Virginia Creeper. *Ampelopsis quinquefolia* Michx. *Psedera quinquefolia* (L.) Greene. *Parthenocissus quinquefolia* (L.) Planch. *American Ivy. Vigne vierge,* Fr. *Wilder Wein, Amerikanischer Epheu,* G. (Fam. *Vitaceæ.*)—The bark and twigs of this indigenous, woody creeper have been used by the eclectics as an alterative, tonic, and expectorant. They contain tartaric acid and potassium and calcium tartrates, albumen, sugar, pyrocatechin, and some other principles. In two cases of poisoning reported by Bernays, the symptoms were violent vomiting and purging, collapse, and deep sleep, with dilated pupils. (*P. J.*, vii.)

Viscum. *Viscum album* L. *Mistletoe. European Mistletoe. Gui de Chéne, Gillon,* Fr. *Mistel,* G. (Fam. *Loranthaceæ.*)—A yellowish-green, glabrous, evergreen, parasitic shrub with much branched and jointed stems, opposite or 3-whorled obovate-lanceolate leaves and 1-seeded, viscid, white berries growing on various trees, particularly the apple and other rosaceous fruit trees, and forming a pendent bush from two to five feet in diameter. The plant is famous in the history of Druidical superstition. In the religious rites of the Druids, the mistletoe of the oak was employed, and hence was afterwards preferred when the plant came to be used as a remedy; but it is in fact identical in all respects with those which grow upon other trees. (*P. J.*, 1897, 289.) The fresh bark and leaves have a peculiar, disagreeable odor, and a nauseous, sweetish, slightly acrid and bitterish taste. *Viscin*, which forms the glutinous constituent in the berries, leaves, and stalks of the mistletoe, is the principal constituent of *birdlime.* Crude viscin may be obtained by kneading the finely bruised mistletoe bark with water, as long as anything is dissolved, and removing the ligneous impurities mechanically. A purer product may be obtained by boiling the crude product in strong alcohol, macerating the residue with ether, evaporating the ethereal extracts, purifying these extracts by kneading first with alcohol and then with water. The formula $C_{20}H_{48}O_8$($C_{20}H_{32}$ + $8H_2O$) has been given to it by Reinsch. Pawlevsky (*Bull. Soc. Chim.* (2), 34, 348) obtained from mistletoe a crystallizable acid, slightly soluble in water, insoluble in alcohol and ether, fusing at from 101° to 103° C., to which he gave the formula $CH_3O_3.OH$. The berries, which are white, and about the size of a pea, abound in the peculiar viscid principle, and are sometimes used in the preparation of birdlime, of which this principle is the basis. Mistletoe is said to be productive of vomiting and purging when largely taken. The berries caused in a child three years old vomiting and prostration, coma, a fixed and somewhat contracted pupil, and convulsive movements. (*Ann. Thér.*, 1859, 36.) A fatal case is recorded. (*M. T. G.*, 1867, 26.) The plant was formerly looked upon as a powerful nervine, but it is now out of use. The leaves and wood were given in the *dose* of a drachm (3.9 Gm.) in substance. *Viscum* has been recommended by Gaultier (*S. M.*, 1907) for the reduction of high blood pressure in *arteriosclerosis* and other conditions of excessive arterial tension. But Dossin (*A. I. P. T.*, 1911, xxi, p. 432) finds that the lowering of blood pressure is of but short duration and is preceded by a rise and concludes, therefore, that the drug is not clinically useful for this purpose. Gaultier employed a watery extract in *doses* of 3 grains (0.2 Gm.) daily. According to P. Riehl (*D. M. W.*, xxvi, 1900), viscin affords an excellent basis for the making of applications to the skin, a benzene viscin solution mixed with starch affording an excellent plaster mass.

The *American Mistletoe* is the *Phoradendron flavescens* (Pursh.) Nutt. (*Viscum flavescens* Pursh.) It is a yellowish-green, woody parasite with jointed, branched stems, thick, obovate, persistent leaves and one-seeded berries. It grows upon the branches of deciduous trees from New Jersey to Florida and westward. Henry Dye (*Memphis Med. Recorder*, iv, 344) reported cases of poisoning from what was probably the berries of this plant. In the western part of the United States *Arceuthobium Americanum* Nutt., and *Phoradendron juniperinum* Englm., are also known under the name of mistletoe. Crawford (*J. A. M. A.*, 1911, lvii) has found that the extract of *P. flavescens* or the *P. juniperinum*, when injected into the blood stream, produces a sharp rise in the blood pressure similar to that produced by epinephrine. He also succeeded in isolating an active base, the composition of which, however, he did not satisfactorily determine, but suggests that it may be phenylethylamine. The *P. flavescens* has been more closely studied by Hanzlik and French, who find that it is a powerful stimulant to involuntary muscle, causing a rise in blood pressure and an increase in the contractions of intestine and uterus, and believe that the drug may be found clinically useful as a circulatory and uterine stimulant. It was recommended many years ago by Dr. W. H. Long as an oxytocic of great value in *post-partum hemorrhage* and *menorrhagia.* His statements have received some confirmation by other clinicians. It has also been clinically recommended as a cardiac stimulent. Dalassus proposes a formula for an aqueous *extract of mistletoe.* Five hundred parts of the ground, dry, young twigs and leaves are infused for 12 hours in 3000 parts of boiling water, expressed and the residue treated with 1500 parts of boiling water. The united liquids are then evaporated to the consistence of an extract. *Syrup of mistletoe* is made by dissolving 1 part by weight of the above extract in 10 parts by weight of boiling water and adding 990 parts of simple syrup.

Vitamins.—As far back as 1896 it was suggested that the disease known as *beri-beri*, which was then widely endemic in Asiatic countries, was associated with the predominance of rice in the diet of the Oriental peoples. Later it was shown that beri-beri occurred only on an almost exclusive diet of polished rice, that if the whole grain were employed the disease did not occur. In 1910 Frazer and Stanton (*L. L.*, 1910, i, p. 733) showed that the disease could be cured by the administration of an extract of the rice polishings. From this starting-point the work of a large number of investigators, including Funk, Hopkins, Osborne and Mendel, McCollum, etc., has developed the present vitamin theory. (For literature see Emmett, *J. A. Ph. A.*, 1921, x, p. 176.)

Without going into details of the history of the development of this hypothesis or the evidence in its support, the present accepted views may be briefly stated as follows: An animal fed on a diet calorically sufficient, composed of chemically pure carbohydrates, fats and proteins, plus the necessary mineral constituents, will not maintain its health. The failure of such a diet is due to the absence of certain elements, whose chemistry is unknown and whose mode of action is still in the realm of speculation. It was at first believed that these elements belonged among the group of amins and the word "vitamin" was coined to describe them. Although there is considerable evidence today that some of them at least are not of basic character, this word is still in current use as the name for this class of essential food stuffs. Although the term *vitaliment* has been suggested as a substitute it has not come into common use. The group of diseases which are brought about by this dietetic deficiency is known collectively as *avitaminosis.*

The amount of vitamin necessary to maintain health or even to restore health to an animal suffering from the lack of this element is so small that it is impossible to consider that their action in any way depends upon the energy which might be derived from their oxidation. Among the theories of their mode of action which have been suggested is that of Voegtlin and Myers (*A. J. Phys.*, 1919, xlix, p. 124) that they act as hormones stimulating the secretions of certain bodily glands which are essential for complete metabolism, and that of Dutcher (*J. Bi. Chem.*, 1918, xxxvi, p. 63) that their action is essentially similar to that of the catalytic agents.

While our knowledge of the chemistry of the vitamins is as yet rather hazy, Funk (*Science*, 1925, lxii, 157) believes that it is sufficient to allow us to divide them into two groups. The first of these, to which Funk would limit the term vitamin, are nitrogenous compounds easily destroyed by alkalies; the second group, which he terms *vitasterols*, are non-nitrogenous, alkali resistant and seem to belong to the sterols. They are usually denominated by the letters of the alphabet often preceded by descriptive adjectives, as *fat-soluble A*, *water-soluble B*, etc.

Vitamin A. Fat-soluble A.—This vitamin was discovered independently by Osborne and Mendel and by McCollum, in 1913. Young rats fed on a diet lacking in fat-soluble A at first grow normally then begin to lose weight and develop a characteristic disease of the eye known as *xerophthalmia* which eventually leads to complete blindness. A similar disease occurs in human beings due to similar dietetic deficiency.

Mellanby (*L. L.*, 1919, i, p. 407) and others believe that rickets is due to a deficiency of a fat-soluble vitamin but if this view be correct it is probably not the same as vitamin A. (See Hess, *J. A. M. A.*, 1921, lxxvii, 693.)

The fat-soluble vitamin is found in egg yolk, butter-fat, certain animal fats, carrots, green leaves, etc. Steenbock (*J. Bi. Chem.*, 1920, xli and 1922, li, p. 63) has noted a peculiar relation between the occurrence of the yellow pigment, carotin, and this vitamin which suggests some chemical relationship. This view, however, has not been definitely established. It resists saponification and therefore is probably not itself a fat. It withstands a temperature of boiling water for some time and is not destroyed in the process of desiccation.

Vitamin B. Water-soluble B. Anti-neuritic Vitamin.—This is found in a large number of green vegetables such as asparagus tops, bamboo sprouts, etc., probably in all growing parts of plants. It is also found in the outer layer of the cereal foods; highly-milled grains such as are used in making white bread and polished rice do not contain it. According to Daniels, Byfield and Loughlin (*Amer. Jour. of Dis. of Children*, 1919, xvi, p. 546) it is present in relatively small proportion in cow's milk as compared to human milk. It is also found abundantly in yeast and in many fruit juices. Voegtlin (*U. S. Pub. Health Rep.*, 1916) has noted that, although it is not demonstrated that phosphorus is a part of the vitamin molecule, practical experience has shown that the percentage of P_2O_5 in cereal foods runs parallel to their content of vitamin B.

Vitamin B is absorbed by Fuller's Earth (see Seidell, *A. J. P.*, 1922, xciv, p. 440). It is destroyed by alkalies and hence is not found in bread made with unneutralized baking soda, even if whole wheat be used. In slightly acid solutions it will withstand temperature of boiling water for a short period of time.

Vitamin C. Anti-scorbutic Vitamin.—It has long been known that the absence of certain foods leads to the occurrence of *scurvy* and it has also been known that the administration of lemon juice, raw potatoes and other vegetable foods will prevent or cure this disease. This disease is now believed to be due to the absence of an essential element which is ordinarily known as *water-soluble C.* This vitamin, in some ways, is the most unstable of all the known vitamins. It is so easily destroyed by heat and oxidation that few of the canned or desiccated foods contain any large proportions. Eckman (*J. A. M. A.*, 1922, lxxviii, p. 635) tested 7 kinds of desiccated fruits and found that the only one of these which contained sufficient antiscorbutic vitamin to maintain life, in the guinea pig, was dried peaches, and even this was not successful for an indefinite period of time. It is found most abundantly in lemons, tomatoes and in other raw fruits including bananas, apples, etc. Curiously, it is present in relatively small proportion in limes. (The lime juice which was formerly provided to the British Navy as a protective against scurvy was the juice of the lemon, not of the fruit known in this country as the lime.) It is found also abundantly in certain root foods, as turnips and potatoes, and to a lesser extent in some green vegetables. The fact that this vitamin is so often associated with fruit acids led at one time to the theory that itself was an acid. This old view has been thoroughly disproven. The vitamin, however, is destroyed by alkalies.

As most of the methods for the preservation of foods that are at present in commercial use have destructive action on water-soluble vitamin C, the use of raw foods is essential in the treatment or prevention of scury.

There are a number of other diseases which have been attributed to lack of similar elements in the diet but which have not been so firmly established as deficiency diseases. Among these may be mentioned especially *pellagra* and *rickets.* There is considerable evidence that the latter disease is dependent on the lack of a fat-soluble vitamin, which some identify with vitamin A described above but others believe it to be a separate fat-soluble vitamin (see McCollum and Simmonds, *J. Bi. Chem.*, 1922, liii, 293) while still other authorities maintain that rickets is not a dietetic disease. One reason which has been advanced for the opinion that rickets is not a deficiency disease is based upon the fact that therapeutic results in this disorder are produced by sunlight, similar to those brought about by the administration of cod liver oil whose efficacy has been believed to demonstrate the presence of a vitamin. Curiously enough it has recently been shown that cod liver oil is radioactive and that certain other oils which are ordinarily not beneficial in rickets may be endowed with curative properties by exposing them to ultra-violet radiation.

While it may be regarded as well established that certain disorders may be attributed to vitamin deficiency there has been an extraordinary amount of popular misconception and consequent mulcting of the public by manufacturers of various proprietary preparations. In the first place, it should be remembered that on an ordinary mixed diet such as is commonly employed by American and European peoples there is practically no danger of avitaminosis; raw milk contains in itself all the necessary vitamins and even in those cases where it is necessary to boil the milk—which may destroy the antiscorbutic vitamin—the addition of a small quantity of lemon juice or orange juice makes up for this deficiency. Even when milk is not part of the diet the man who uses a certain modicum of butter and some raw vegetable food, as lettuce or celery or parsley, with a fairly variegated diet need have no fear of vitamin deficiency. In the second place, while a lack of vitamin is deleterious to the health there is no evidence that an excess of vitamin is beneficial. Various assertions have been made concerning the therapeutic value of vitamin excess but they are not scientifically confirmed. In the third place, if there be need of an increase in one or the other of the vitamins this can be met much more economically by the use of some food known to contain large amounts of that vitamin than by the administration of any medicinal product. Finally many of the proprietary vitamin preparations on the market are rank frauds. McCollum and Simmonds (*J. A. M. A.*, 1922, lxxviii, p. 1953) investigated seven of these supposed vitamin concentrations and found that none of them would protect against avitaminosis even although given in 20 times the recommended dose. For references to the literature on vitamins, see paper by Emmett (*J. A. Ph. A.*, 1921, p. 176).

Warburg's Tincture.—This famous remedy, at first a proprietary medicine, afterwards by the voluntary act of its inventor had its formula revealed. A simplified form of it is recognized by the N. F. There is so much testimony as to its extraordinary virtues in the severe *remittent* and *pernicious malarial fevers* of India that its powers can scarcely be questioned. After the bowels of the patient in the acutest stage of the disorder have been freely opened, a half ounce of the tincture is given undiluted, all drink being withheld, and at the end of three hours a second half ounce is given in a similar manner. Soon after the second dose a violent, aromatic perspiration comes on, and the fever is usually broken. The remedy is also commended in *collapse* without organic disease. The formula given by Warburg is as follows: Socotrine aloes 1 lb.; rhubarb, angelica fruit, confection of Damocratis, each 4 oz. troy; elecampane, saffron, fennel, prepared chalk, each 2 oz. troy; gentian, zedoary, cubebs, myrrh, camphor, agaric, each 1 oz., troy. Digest the whole with 500 oz. proof spirit in a water bath for 12 hours, express, add 10 oz. sulphate of quinia, dissolve by the aid of a water bath, cool, and filter.

It is evident that *Warburg's tincture* contains various substances which are inert, but the practical difficulty is to determine as to what its extraordinary value anti-malarial powers are really due. The formula used in the U. S. Army, with asserted excellent results in Cuba, has the advantage of yielding a product in tablets, which is as follows: Aqueous extract aloes, 224 grains; rhubarb, 448 grains; angelica seed, 448 grains; elecampane, 224 grains; saffron (Spanish), 224 grains; fennel, 224 grains; gentian, 112 grains; zedoary root, 112 grains; cubeb, 112 grains; myrrh, 112 grains; white agaric, 112 grains; camphor, 112 grains; quinine sulphate, 1280 grains. Exhaust with eight pints of diluted alcohol, or divide into 1024 tablets.

The confection of Damocratis, in the original, which was a combination of thirty aromatic substances mostly obsolete, may be found in the 19th ed., *U. S. D.*, p. 1695. It is contained in the formula in such small amount that it is hardly possible that it could have any effect. (See also *Tinctura Antiperiodica*, N. F., Part III.)

The National Formulary has revised the formula of Warburg's tincture and there are two tinctures, one with and one without aloes.

Dose.—The dosage of Warburg's tincture depends on the kind used—whether with aloes or without—and the intended purpose, and varies from 4 cc. (1 fluidrachm) to 15 cc. (4 fluidrachms). The larger quantity is given when Doctor Warburg's original directions are followed for administering the remedy in remittent fevers. These directions were as follows: "One-half ounce to be given alone, without dilution, after the bowels have been evacuated by any convenient purgative, all liquids being withheld. After three hours another half ounce is to be given."

Watercress. *Cresson de fontaine*, Fr. *Brunnenkresse*, G.—*Radicula Nasturtium aquaticum* (L.) Britten et Rendle. (*Nasturtium officinale* R. Br.) (*Roripa Nasturtium* Rusby) (Fam. *Cruciferæ.*) In sensible and medicinal properties watercress bears some resemblance to scurvy grass, though milder, and on this account is preferred for the table. It is useful in *scorbutic affections.* It contains a volatile oil, which according to A. W. Hofmann, contains as its chief constituent a body boiling at 253° C., which he considers to be the nitrile of *phenyl-propionic acid*, and therefore has the formula $C_9H_{10}N$. Greenish states that the chief constituent is phenyl-ethyl iso-thiocyanate. The expressed juice is sometimes given in the *dose* of one or two fluidounces (30–60 cc.); but the herb is more frequently used in the form of a salad.

Other species of *Radicula* grow in similar situations with the *R. Nasturtium*, and act similarly.

Water Melon.—This popular fruit, *Citrullus vulgaris* Schrad., is a native of Asia but is largely cultivated all over the world. Both the pulp and the seeds have been attributed with diuretic properties. Power and Salway (*P. J.*, lxxxiv, p. 760) found in the seeds a fixed oil similar to that of pumpkin seeds. There is no convincing evidence that this fruit contains any medicinally active ingredient.

White Ash Bark. *Fraxinus.*—The N. F. formerly recognized "the dried bark of *Fraxinus americana* Linné (Fam. *Oleaceæ*) and probably of other species of *Fraxinus*, deprived of the corky layer." *N. F. IV.*

The white ash is a large tree of the northern United States and Canada. The bark occurs "in flat pieces of varying length and width, from 3 to 6 mm. in thickness, externally yellowish or pale brown, sometimes with ridges of a warty nature and fissures of a grayish-brown color with markings of lichens; inner surface, pale brown to yellowish, longitudinally striate; fracture very uneven, fibrous. Odor faintly aromatic; taste bitter, weakly acrid. Fraxinus yields not more than 10 per cent. of ash." *N. F. IV.* It contains a volatile oil, an alkaloid and several resins. The bark has been used in *dysmenorrhea* by Charles P. Turner and others.

Fraxinus excelsior L. *Frêne*, Fr. *Esche*, G. *Fresco*, Sp. (Fam. *Oleaceæ.*)—The bark of the *Common European Ash* occurs in quills and is of a grayish or grayish-green color. It is bitter and astringent, and at one time was employed in the treatment of *intermittent fever.* It contains a crystalline glucoside and a bitter principle, and a fixed oil obtained from the seeds. (*Chem. Ztg.*, 1911, 478.) The leaves were formerly used in *rheumatic affections* and *gout*. *Dose*, an ounce (30 Gm.), usually in infusion.

Whiting.—This is essentially the same as prepared chalk, being made by the pulverization and elutriation of crude chalk. It is used as a coarse paint, and for various purposes in the arts, for which calcium carbonate is requisite. *Paris white* is a variety of the same material.

Winter's Bark. *Wintera.*—The bark of *Drimys Winteri* Forst. *Cortex Winteranus. Ecorce de Winter, Cannelle de Magellan*, Fr. *Winter's Zimmt*, G. (Fam. *Magnoliaceæ.*)—For descriptions of tree, see *U. S. D.*, 16th edition. The tree is a native of the southern part of South America, growing along the Strait of Magellan, and extending as far north as Chile. The commercial supply now comes chiefly from Colombia. This bark was brought to England, in the latter part of the sixteenth century, by Captain Winter, who attended Drake on his voyage round the world, and while in the Strait had learned its aromatic and medicinal properties. Since this period, from time to time various barks have appeared in European commerce as *Winter's bark*. Among these are the bark of *Cinnamodendron corticosum* Miers. (Fam. *Canellaceæ*), of Jamaica, which is pungent like true Winter's bark, but is of a much paler brown color, and resembles canella bark except in the absence of the chalky-white inner surface, and the bark of *Croton Malambo* Karst. (Fam. *Euphorbiaceæ*), which resembles in color and thickness the bark of the *Cinnamodendron*, but has a bitter taste and a calamus-like flavor. P. N. Arata and F. Canzonri (*P. J.*, June 14, 1890) describe a bark which they assert to be a genuine Winter's bark from the Strait of Magellan. From this they separated a volatile oil by distilling the bark with water, exhausting the distillate with petroleum, and distilling off the solvent. The crude oil, amounting to 0.64 per cent. of the weight of the bark employed, was a mixture of several substances. *Winterene*, $C_{15}H_{24}$, is the essential oil separated from this by fractional distillation. It is readily oxidized on exposure to the air, becoming yellow. The formula $C_{25}H_{40}$ was calculated from the ultimate analysis and vapor density, but the authors consider that the ready oxidizability of winterene and its analogy to similar essences point rather to the formula $C_{15}H_{24}$, which would place it in the group of sesquiterpenes, such as cedrene, cubebene, etc. The presence of tannic acid and ferric oxide, according to Henry, serves to distinguish Winter's bark from *Canella alba*, with which it has often been confounded. The bark above described as commercial Winter's bark is destitute of both tannic acid and ferric oxide, and cannot therefore be the bark examined by Henry.

The bark of the *Drimys granatensis* L. f. (now regarded as identical with *D. Winteri* Forst.), has been imported into London under the name of *Merida coto*, and it has been stated that it contains *cotoin*. It occurs in short pieces of a yellowish-gray color, traversed longitudinally by hard cellular layers, which distinguish it at once from coto and paracoto bark. Its odor resembles that of true coto, but is more feeble. A careful chemical study of it by O. Hesse (*P. J.*, vol. iv) shows that it contains no cotoin, but a crystalline substance, $C_{13}H_{14}O_4$, to which the name of *drimin* was given. From the leaves Hesse obtained a wax alcohol, *drimol*, $C_{28}H_{58}O_2$. As *Drimys granatensis* L. f., is recognized as *D. Winteri* Forst., it is plain that Merida coto must be looked upon as a form of Winter's bark coming from Venezuela.

Winter's bark is a stimulant aromatic tonic, and was employed by Winter as a remedy for *scurvy*. It may be used in half-drachm (2.0 Gm.) *doses* for similar purposes with cinnamon or canella alba, but is scarcely known in the medical practice of this country. *Drimys chilensis* of De Candolle, growing in Chile, yields a bark having similar properties (Carson, *A. J. P.*, xix, 81) also *D. aromatica* F. Muell., of Australia. (*P. J.*, xxi.)

Wistaria. *Wisteria sinensis* Sweet (*W. chinensis* DC.) (*Krauhnia sinensis* Makino.) *Wisteria. Chinese Wisteria.* (Fam. *Leguminosæ.*)—Ottow (*P. J.*, Oct., 1886) has obtained from this ornamental woody climber a crystalline poisonous glucoside, *wistarin*.

Withania. *Withania coagulans* Dun. (Stocks.) *Vegetable Rennet.* (Fam. *Solanaceæ.*)—This shrub, common in Afghanistan and East India, has the property of coagulating milk, and has been used for preparing a vegetable rennet ferment for making cheese. Sheridan Lea found upon examination that the substance which possesses the coagulating power is a ferment closely resembling animal rennet. The active principle is soluble in glycerin, and can be extracted from the seeds by this solvent; the extract possesses strong coagulating powers even in small amounts. Alcohol precipitates the ferment body from its solutions, and the precipitate, after washing with alcohol, may be dissolved again without having lost its coagulating powers. The active principle of the seeds will cause the coagulation of milk when present in very small quantities, the addition of more of the ferment simply increasing the rapidity of the change. The coagulation is not due to the formation of acid by the ferment. If some of the active extract be made neutral or alkaline, and added to neutral milk, a normal clot is formed, and the reaction of the clot remains neutral or faintly alkaline. The clot formed by the action of the ferment is a true clot, resembling in appearance and properties that formed by the animal rennet, and not a mere precipitate. Lea prepared an active extract, applicable for cheese making purposes, by grinding the dry seeds very finely in a mill, and extracting them for twenty-four hours with such a volume of 5 per cent. sodium chloride solution that the mass is still fluid after the absorption of water by the fragments of the seeds as they swell up. From this mass the fluid part may be readily separated by centrifugation. Forty grammes of the seeds treated as above, with 150 cc. of 5 per cent. sodium chloride solution, gave an extract of which 0.25 cc. clotted 20 cc. of milk in twenty-five minutes, and 0.1 cc. clotted a similar portion of milk in one hour. When added in these proportions the curd formed is quite white. The presence of the coloring matter is, however, perhaps on the whole unimportant, since even if a larger quantity of the ferment extract is added in order to obtain a very rapid coagulation, the coloring matter is obtained chiefly in the whey, the curd being white; by adding sufficient common salt to make the percentage up to 15 per cent., and alcohol up to 4 per cent., the preparation would retain its activity very well. (*P. J.*, 1884, 606.)

Wurrus.—Under the name of *Vars, Wars*, or *Warrus*, a powder somewhat similar to kamala has been used as an anthelmintic in Southern Arabia, and exported into commerce from Aden. It is obtained from the fruits of *Flemingia congesta* Roxb. (Fam. *Leguminosæ.*) (*P. J.*, Sept., 1887.) It has a dull purplish color and under the microscope is observed to consist of simple non-glandular hairs and glandular hairs, the latter characterized by large oblong resinous heads with 3 or 4 tiers of elongated cells. It contains *flemingin, homoflemingin* and resins.

Xanthium. *Cocklebur. Clotbur.* (Fam. *Compositæ.*)—This is a genus of coarse annual weeds having branched stems bearing alternate toothed or lobed, often cordate, leaves and burs clothed with characteristically hooked prickles. Guichard believes that he has found an alkaloid in the *X. spinosum* L. (*P. J.*, vii, 249.) In the *Xanthium Strumarium* L., which is common both in Europe and in America, A. Zander believes that he has found a glucoside, *xanthostrumarin.* M. V. Cheatham thinks that there is a second active principle. (See *A. J. P.*, vol. xi, 271; vol. xiv, 134.) Clotbur is stated to be an active styptic, both local and general. *Dose,* of the fluidextract, from one to two fluidrachms (3.75–7.5 cc.).

Xanthorrhiza. *Yellow-root. Shrub Yellow-root. Zanthorhiza apiifolia* L'Her. (*Xanthorrhiza apiifolia* L'Her.) (Fam. *Ranunculaceæ.*)—This is a low shrub, with a horizontal rhizome, which sends off numerous suckers. The stem is simple, about 5 mm. thick, with a smooth bark and bright yellow wood. The leaves are compound, consisting of several ovate-lanceolate, acute, doubly serrate leaflets, sessile upon a long petiole, which embraces the stem at its base. The flowers are small, purple, and disposed in long, drooping, divided racemes, placed immediately below the first leaves. Yellow-root grows from southern New York to Georgia and west to Kentucky. It flowers in April. The root was formerly in the Secondary List of the U. S. Pharmacopœia, but the bark of the stem possesses the same virtues. The root is from 7 cm. to 1 dm. in length, and about 12 mm. thick near the stem. It shrinks somewhat in drying, and, as found in commerce, is in slender pieces of various lengths, wrinkled longitudinally, with a light yellowish-brown, easily separable epidermis, a thick, hard, bright yellow woody portion, and a very slender central pith. It is inodorous, and of a simple but extremely bitter taste. It imparts its color and taste to water. The infusion is not affected by ferric salts. J. Dyson Perrins found *berberine* in it. (*P. J.*, May, 1862.) Samuel S. Jones believed that he had proved the existence in the drug of a second alkaloid. (*A. J. P.*, vol. xvi, 1861.) *Xanthorrhiza* possesses properties closely analogous to those of calumba, quassia, and other simple tonic bitters, and may be used for the same purposes and in the same manner. Woodhouse employed it in the *dose* of forty grains (2.6 Gm.).

Xanthorrhœa Resin. *Gum Accroides. Yacca Gum. Accroides Resin. Earth Shellac. Grass-tree Gum. Botany Bay Gum.*—Yellow and reddish resinous substances, the products of *Xanthorrhœa hastilis* R. Br. and *X. australis* R. Br. (Fam. *Liliaceæ*), have been introduced into England from Australia. They are obtained by spontaneous exudation from the stems of the plants, which are usually shrubs. The *yellow resin* (from *X. hastilis*) is in tears, in flattish pieces having on one side the mark of the stem, or in masses of various size and irregular shape. It has a reddish-yellow color, resembling gamboge when broken, and when heated emits a fragrant odor like that of Tolu balsam. It contains resin, cinnamic and benzoic acids, and a trace of volatile oil, and may therefore be ranked among the balsams. When heated with nitric acid, it yields a large proportion of picric acid. In medicinal properties it is said to bear a close resemblance to storax and the balsam of Tolu. The natives and early settlers employed it as a medicine in *diarrhea.* It is said to be used extensively, instead of shellac, as a resinous glaze for confectionery and also in cabinet work, but to be distinctly inferior. For much interesting information concerning it and other resinous products of the genus *Xanthorrhœa,* see paper by J. H. Maiden, *P. J.*, 1891, xxi. A tincture, made in the proportion of two ounces to a pint of alcohol, may be given in the *dose* of one or two fluidrachms. The *red variety* (from *X. australis* R. Br.) resembles dragon's blood in color, and appears to be analogous to the other variety in properties. Enormous quantities of this resin were imported into Germany before the war, although for what purpose is unknown, perhaps as a source of picric acid. It is now widely used in making varnishes and also linoleum. (See *Ph. Era,* 1921, liv, 366; also *D. C.*, 1895, p. 83.)

Xylene. *Xylol. Xylène,* Fr. *Xylol,* G. $C_6H_4(CH_3)_2$.—There are three isomeric hydrocarbons of this name, the ortho-, meta-, and para-xylene respectively, all contained in coal tar. A mixture of them was first extracted from naphtha by Hugo Müller, and was brought forward by Zuelzer as a specific in *smallpox,* but is useless. (*P. J.*, 1872, 623.) Volpino (*P. J.*, 1920, civ, 171) on the basis of experiments on guinea-pigs and some clinical observations has suggested its use in *tuberculosis.* It is largely used as a solvent.

Yadil. *Trimethenal-allyl-carbide.*—This preparation has been used in the treatment of *influenza.* The doses employed have varied enormously but it has been mostly employed in doses of about one fluidrachm (4 cc.) several times a day.

Yohimbe.—This is the bark of *Corynanthe Johimbi* Schum. (*Pansinystalia Yohimbe* (Schum.) Pierre), a rubiaceous tree growing in the southern Cameroons district in Africa. The bark comes into commerce in flattened or slightly quilled pieces 75 cm. long to 4 to 8 mm. thick, with an external corky layer of a gray-brown color covered with isolated lichens. It shows numerous longitudinal and transverse fissures like some old specimens of cinchona bark. The transverse fracture is of a uniform yellowish-brown color, and presents short, soft fibers like rough velvet. The taste is bitter. For a history of Yohimbe bark consult *Pharm. Zentralh.*, 1921, p. 169.

This bark contains at least three alkaloids, Siedler (*Ph. Ztg.*, 1902) says five. The most important of these is *yohimbine,* discovered by Spiegel in 1896; it is asserted by Fourneau and Page (*B. Sc. Pharm.*, 1914, xxi, 7) to be identical with quebrachine (see *Aspidosperma*), but there is some difference of opinion as to its chemical composition. *Mesoyohimbine* is isomeric with it; *yohimbinine,* also present, seems to be physiologically inert. For further data on the chemistry of these substances which is at present in an unsettled state, see Spiegel (*B. Chem. G.*, 1915 and 1916), Ewins (*Tr. Chem. Soc.*, 1914, cv) and Barger and Field (*Tr. Chem. Soc.*, 1923, cxxiii).

The salt of this base that is ordinarily used is the hydrochloride, being preferable on account of its solubility and high percentage of the alkaloid.

Yohimbine was physiologically studied by Oberwarth and Loewy (*V. A. P. A.*, cliii, and *B. K. W.*, No. 42, 1900), who found it to be in animals and also in man a very active excitant to the sexual organs and functions. On the other hand, Kravkoff, as the result of experiments upon the lower animals and upon man, concluded that it has no aphrodisiac effects and frequently produces nausea, salivation, irritability, and other disagreeable results.

Müller (*A. I. P. T.*, 1907, p. 65) found that yohimbine in small doses stimulated, and in large doses depressed, the respiratory center. If lethal doses are given the heart continues beating after the respiration has ceased. Small doses have little effect upon the blood pressure, but moderate-sized doses caused a slight rise in the blood pressure with local dilatation of the vessels of the pelvic organs. He believes that its aphrodisiac action is due to an increase in the excitability of the lower centers in the spinal cord. On the other hand, many authors believe that its effect is due to the hyperemia produced. Toff (*D. M. W.*, 1904) has found it useful because of this effect in scanty or *irregular menstruation.*

It has been used by numerous clinicians in *neurasthenic impotence*, with reports which are generally favorable to its influence. (For literature, see *M. R.*, 1901, 1902.) It is said to be of no value when the impotence depends upon organic nerve trouble, and to be harmful when it is caused by chronic inflammatory disease of the sexual organs or of the prostate gland. It has also been employed in *angina pectoris* and arteriosclerosis (Staehelin, *Th. M.*, Sept., 1910). *Dose*, of the hydrochloride, 0.005 Gm. (one-twelfth grain), either in tablet or solution, three or four times a day. Yohimbine has also been employed in a 1 per cent. solution hypodermically.

Zerumbet. *Cassumuniar.*—Under these names an East Indian root was formerly used, having some analogy in sensible and medicinal properties to ginger, and ascribed to the *Zingiber Zerumbet* of Roscoe. By some authors the zerumbet has been erroneously confounded with the round zedoary. Geiger describes it as in pieces of the size of a fig or larger, externally grayish-brown and wrinkled, internally yellowish, hard and tough, of a biting, aromatic taste and a spicy odor.

Zinc Borate. *Zinci Boras.* $ZnB_4O_7 + 7H_2O$.—Prepared by mixing an aqueous solution of zinc sulphate (1 in 10) with one of borax (1 in 25), and collecting the precipitate. Used as an antiseptic dusting powder.

Zinc Bromide. *Zinci Bromidum. U. S. VIII. Zincum Bromatum. Bromure de Zinc,* Fr. *Bromzink, Zinkbromid,* G. *Bromuro zincico*, Sp. $ZnBr_2 = 225.21$.—"It should contain, when anhydrous, at least 97 per cent. of pure Zinc Bromide, and should be kept in small, glass-stoppered bottles." *U. S. VIII.*

It is "a white, or nearly white, granular powder; odorless, having, even in dilute solutions, a sharp, saline and metallic taste. Very deliquescent. Readily soluble in water and alcohol. When heated to 394° C., the salt fuses, and, with a careful increase of heat, may be sublimed in the form of needle-shaped prisms. Its aqueous solution gives a slightly acid reaction with blue litmus-paper." *U. S. VIII.*

Zinc bromide is capable in excessive doses of acting as an irritant poison. It has been commended in *epilepsy*, but is of no value.

Dose, one to two grains (0.065–0.13 Gm.).

Zinc Cyanide. *Zinci Cyanidum.* $Zn(Cn)_2$.—This cyanide is precipitated as a white insoluble powder, by adding cautiously, until it ceases to produce a precipitate, a recently filtered solution of potassium cyanide to a solution of zinc sulphate. It is used in Germany as a substitute for hydrocyanic acid, and is said to be anthelmintic. It has been recommended by Lashkevich in *cardiac neuroses* in doses of from one-tenth to one-eighth grains (0.006–0.008 Gm.) three times a day. It has been employed in *epilepsy, chorea* and *neuralgia,* in several *painful affections of the stomach* and in the *colics* attendant on *difficult menstruation.* The *dose* is a quarter of a grain (0.016 Gm.), gradually increased to one grain (0.06 Gm.), given in mixture.

Zinc Ferrocyanide. *Zinci Ferrocyanidum.* $Zn_2Fe(Cn)_6 + 3H_2O$.—Formed by double decomposition between hot solutions of potassium ferrocyanide and zinc sulphate. It is precipitated as a white powder. It has similar medicinal properties to those of the cyanide, and is used in the same diseases. The *dose* is from one to four grains (0.065–0.26 Gm.), given in pill.

Zinc Iodide. *Zinci Iodidum. U. S. VIII. Zincum Iodatum. Iodure de Zinc,* Fr. *Zinkjodid, Jodzink,* G. $ZnI_2 = 319.21$.—"It should contain, when anhydrous, not less than 98 per cent. of pure Zinc Iodide, and should be kept in small, glass-stoppered bottles protected from light." *U. S. VIII.*

It is "a white, or nearly white, granular powder; odorless, and having a sharp, saline and metallic taste. Very deliquescent, and, upon exposure to air and light, becoming brown from liberated iodine. Readily soluble in water, alcohol, or ether. When heated to about 446° C., the salt fuses to a colorless liquid, and at a higher temperature sublimes, forming quadratic needles, while a small part is decomposed and leaves a residue of zinc oxide. Its aqueous solution reddens blue litmus paper." *U. S. VIII.* For further tests see *U. S. D.*, 20th ed., p. 1672.

Zinc iodide was proposed many years ago as an alterative remedy in *chorea, scrofula* and *hysteria* but is no longer employed. The best form of administration is in *syrup*, to protect it from change. (See p. 1353, *U. S. D.*, 19th ed.) A solution containing from one to two grains (0.065–0.13 Gm.) to the fluidounce (30 cc.) of water has been used as an astringent injection in *gonorrhea.*

Dose, one-half to two grains (0.032–0.13 Gm.).

Zinc Lactate. *Zinci Lactas.* $Zn(C_3H_5O_3)_2 + 3H_2O$.—This salt was used by Herpin in *doses* of two grains (0.13 Gm.), three times a day, gradually increased to ten grains (0.65 Gm.) a day, as a substitute for zinc oxide in *epilepsy.* For its physical properties and methods of preparation see 16th edition, *U. S. D.*

Zinc Permanganate. *N. N. R.* 1924. *Zinci Permanganas. Zinkpermanganat, Uebermangansaures Zink,* G. $Zn(MnO_4)_2 + 2H_2O$.—Made by precipitating barium permanganate with zinc sulphate, using exact molecular proportions. It forms dark brown, almost black, deliquescent crystals, giving off oxygen even more readily than does potassium permanganate. It dissolves in about 3 parts of water, usually with a slight residue. The solution decomposes if exposed to the air. It is incompatible with peroxides, acids, ammonia and hypophosphites, and must not be triturated with organic substances. Zinc permanganate possesses the disinfectant powers of the other permanganates but is more astringent. It is used chiefly as an injection in *urethritis* in strengths of about 1 to 4000 as an astringent and antiseptic application.

Zinc Phenolsulphonate. *Zinci Phenolsulphonas, U. S. IX. Zinci Sulphocarbolas*, Br. 1898; *Zincum Sulphophenolicum; Zinc Paraphenolsulphonate.*—" It contains not less than 73.7 per cent. nor more than 77.4 per cent. of anhydrous zinc phenolsulphonate, corresponding to not less than 99.5 per cent. of the crystallized salt $[(C_6H_5O.SO_3)_2Zn + 8H_2O = 555.72]$. Preserve it in small, well-closed containers." *U. S. IX.*

This salt, which was dropped at the tenth revision of the *U. S. P.* was officially described as in " colorless, transparent, rhombic prisms or tabular crystals or in granular form; odorless, and having an astringent, metallic taste. When exposed to the air the salt effloresces, and upon exposure to light and air may become slightly pink. One Gm. of Zink Phenolsulphonate dissolves in 1.6 mils of water, and in 1.8 mils of alcohol at 25° C.; also in 0.4 mil of boiling water. Its aqueous solution (1 in 10) is acid to litmus. When heated to 125° C., the salt loses all of its water of crystallization. At a higher temperature it chars, emitting inflammable vapors having the odor of phenol, and finally leaves an incombustible residue. An aqueous solution of the salt (1 in 20) yields a white, gelatinous precipitate with potassium ferrocyanide T.S., and a white precipitate with ammonium sulphide T.S. Ammonium carbonate T.S., when added in small portions to an aqueous solution of the salt (1 in 20), produces a white precipitate which redissolves completely upon the addition of an excess of the reagent. A dilute solution of the salt (1 in 100) is colored pale violet by ferric chloride T.S. The addition of a few drops of barium chloride T.S. to 10 mils of an aqueous solution of the salt (1 in 20), previously acidulated with 3 drops of hydrochloric acid, produces not more than a slight turbidity (*sulphate*). Ten mils of an aqueous solution of the salt (1 in 50), to which 1 mil of diluted hydrochloric acid has been added, does not respond to the Test for heavy metals. An aqueous solution of the salt meets the requirements of the Test for arsenic.

"*Assay.*—Dissolve about 1 Gm. of Zinc Phenolsulphonate, accurately weighed, in 100 mils of distilled water and proceed as directed in the assay under *Zinci Acetas.* The amount of zinc oxide obtained corresponds to not less than 73.7 per cent. nor more than 77.4 per cent. of $Zn(C_6H_5O_4S_2)_2$.

" Each gramme of Zinc Phenolsulphonate corresponds to not less than 0.146 Gm. nor more than 0.153 Gm. of ZnO.

" Zinc Phenolsulphonate may also be assayed by the Electrolytic method." *U. S. IX.*

Zinc phenolsulphonate has been employed as an antiseptic and astringent application to indolent or foul *ulcers,* and in subacute inflammations of the mucous membrane. The solutions used may be a little stronger than those of zinc sulphate employed for similar purposes. It has also been used as an intestinal antiseptic.

Dose, one to three grains (0.065–0.2 Gm.).

Zinc Phosphate. *Zinci Phosphas. Trizincic Orthophosphate.* $Zn_2(PO_4)_2 + 4H_2O$.—Zinc phosphate may be prepared by the mutual reaction of zinc sulphate and an alkaline phosphate. Zinc phosphate is a white powder, insoluble in water but soluble in acids. It was at one time used in the treatment of various nervous diseases. It is largely used in dental cements.

Zinc Phosphide. *Zinci Phosphidum. U. S.* 1890. $Zn_3P_2 = 258.19$.—According to Hager, *zinc phosphide* was first prepared by Marggraf in 1740. It was formerly made by fusing, in a bath of iron filings, 74 parts of pure zinc, and adding gradually, in small pieces, 26 parts of dry phosphorus. This process gives good results only in small quantities (10 to 20 Gm.). A more recent process is to pass vapors of phosphorus in a current of dry hydrogen over fused zinc. The product is a spongy, gray mass, of metallic appearance, containing rhomboidal crystals, and when powdered resembling somewhat reduced iron. The particles of metallic zinc should be separated. Its sp. gr. is 4.72. " Zinc phosphide should be kept in small, glass-stoppered vials." *U. S.*, 1890.

It occurs as " a gritty powder of a dark gray color, or crystalline fragments of a dark, metallic luster, and having a faint odor and taste of phosphorus. In contact with the air it slowly emits phosphorous vapor. Insoluble in water or alcohol. Soluble in diluted hydrochloric or sulphuric acid with evolution of hydrogen phosphide. When strongly heated, with exclusion of air, it melts and finally sublimes. When heated in air, it becomes oxidized to zinc phosphate." *U. S. VIII.* For a method of assay of zinc phosphide, see *N. R.*, June, 1879.

It has been proved by direct experiment upon animals, as well as by clinical experience, that zinc phosphide affects the system physiologically and therapeutically in exactly the same manner as does phosphorus, and it is employed in medicine as a substitute for that element. Theoretically, each grain of the phosphide contains nearly a quarter of a grain of phosphorus. It is asserted in the journals to have been administered in doses of one or even two grains; but of the pure salt such amounts would be extremely dangerous; the commencing *dose* is one-twentieth of a grain (0.003 Gm.).

Zinc Salicylate. *Zinci salicylas. Zinksalicylat,* G. $Zn(C_6H_4.OH.COO)_2 + 3H_2O$.—Made by boiling together molecular proportions of sodium salicylate and zinc sulphate, cooling, washing the crystals and recrystallizing from hot water. In the form of long satiny needle-like crystals, having a sweet but astringent and bitter taste. It is soluble in about 20 parts of cold water. Zinc salicylate is an astringent and antiseptic, a solution (one-fifth to one per cent.) is used in *ophthalmia* and *gonorrhea.* It is incompatible with iron compounds and with mineral acids.

Zinc Subgallate. *Zinci Subgallas.*—An odorless powder containing 44 per cent. of zinc oxide and 56 per cent. of gallic acid. Internally it is used in intestinal disorders as an antiferment in *doses* of from one-half to four grains (0.032–0.26 Gm.). It is incompatible with iron compounds and with alkaloidal salts. Externally it has been used in *skin diseases.*

Zinc Sulphite. *Zinci Sulphis.* $ZnSO_3 + 2H_2O$. —Made by precipitating a solution of zinc sulphate with sodium sulphite, collecting, washing and drying the precipitate. A white crystalline powder, soluble in about 600 parts of water.

Zirconium. $Zr = 90.6$.—*Zirconium dioxide* is a heavy white insoluble powder which has been used by Kaestle (*M. M. W.*, 1909) for making X-ray examinations of internal organs. According to this author it is the most opaque substance available except thorium oxide and has the advantage of being much cheaper.

Zizyphus. *Zizyphus sativa* Gaertn. (*Z. vulgaris* Lamarck.) *Common Jujube, Jujube,* Fr. *Brusthbeeren, Judendornbeeren,* G.—A shrub, or small tree, of the Fam. *Rhamnaceæ*, growing on the shores of the Mediterranean, and cultivated in Italy, Spain, and Southern France. It has become naturalized in Alabama. The fruit is the part used. This consists of oval drupes, of the size of a large olive, with a thin, coriaceous, red or reddish-brown skin, a yellowish, sweet, acidulous pulp, and an oblong, pointed stone in the center. These have the name of *jujubæ.* By drying, their pulp becomes softer and sweeter, and acquires a vinous taste, evincing the commencement of fermentation. They are nutritive and demulcent, and are used in the form of decoction in *pectoral complaints. Jujube paste* consists properly of gum arabic and sugar, dissolved in a decoction of this fruit and evaporated to the proper consistence. As a demulcent it is in no respect superior to a paste made with gum arabic and sugar alone, and the preparation formerly sold in this country under the name contains in fact none of the fruit. The fruits of two other species, *Z. Lotus* Lam., growing in the north of Africa, and *Z. Jujuba* Lam., a native of Syria, possess properties similar to those of the *Z. sativa* and are used as food by the inhabitants of the countries where they grow. The *Zizyphus Jujuba* is stated by Rixford (*Stand. Cycl. Hort.*, 1922, p. 3548) to produce the best fruits. It has been cultivated in Northern China for many centuries and is now under cultivation in Mediterranean countries, California and neighboring states. The fruits which are subglobose to oblong, orange-red drupes, have been esteemed for throat troubles in the form of pastes, tablets and syrups. It is also one of the sources of *lac.*

Zygadenus. *Death Camas.*—At least nine species of this liliaceous genus, found in the Western United States, are highly toxic to grazing animals, notably to sheep. *Zygadenus venenosus* Watson, probably the most extensively studied of these, is a perennial herb having a tunicated bulb from which arise a rosette of very narrow dark green basal leaves and a scape 1 to 2 feet high which bears a spike of yellowish-white flowers. During May and June, the period of foliage, it is considered most dangerous to stock. H. S. Goodell affirms that he has seen violent convulsions produced by the juice of *Z. venenosus.* Slade (*A. J. P.*, 1905, p. 262) obtained an alkaloid *zygadenine* $C_{39}H_{63}O_{10}N$ from *Z. venenosus,* which resembled veratalbine. Heyle and others (*J. A. C. S.*, 1911 and 1913) obtained an alkaloid from the leaves of *Z. intermedius, zygadenine,* which resembled veratrine.

PART III

SECTION I

In this section are considered those matters included in the "General Tests, Processes and Apparatus" of the U. S. Pharmacopœia and the "Appendix" of the British Pharmacopœia which are not given elsewhere in this volume. There has also been inserted a collection of formulas for reagents used in the examination of urine, blood, etc., which is an amplification of the "Diagnostical Agents and Clinical Tests" of the U. S. IX.

Acid Number

(U. S.)

The acid number is the number of milligrammes of potassium hydroxide required to neutralize the free acid in 1 Gm. of oils, fats, waxes, resins, balsams, and similar organic substances of complex composition. It is determined as follows: Shake about 2 Gm. of the substance, accurately weighed, with from 30 to 50 cc. of neutral alcohol or with a neutral mixture of equal volumes of alcohol and ether, and titrate with half-normal potassium hydroxide, using 1 cc. of phenolphthalein T.S. as indicator.

When the quantity of free acid is small, tenth-normal potassium hydroxide should be used. In place of potassium hydroxide, half-normal or tenth-normal sodium hydroxide may be used for this test, but should be calculated to the equivalent of potassium hydroxide.

Alcohol Determination

(U. S.)

Place 25 cc. of the preparation, measured at any definite temperature between 15° and 30° C., in a distilling flask of about 200 cc. capacity, provided with a high side tube connected with a suitable condenser; add 50 cc. of distilled water, distil into a 50 cc. graduated flask, at such a rate that about 48 cc. of distillate will be received in a half hour; if volatile products other than alcohol are known to be absent, bring to the original temperature and dilute to 50 cc. with water of the same temperature.

Determine the specific gravity of the distillate at any definite temperature between 15° and 30° C. by means of a pycnometer, and find the per cent. of absolute alcohol by volume by reference to the alcoholometric table (page 1616), and multiply by the dilution factor to find the per cent. of alcohol in the original preparation.

If the preparation is thought to contain less than 25 per cent. of alcohol, 50 cc. should be used for analysis; if it is believed to contain over 50 per cent. of alcohol, 10 cc. should be taken. In either case, the volume of the distillate should be made up to 50 cc. as directed above.

If the preparation contains iodine, treat it with zinc dust before distilling. (Sodium thiosulphate may be used instead of zinc dust, in which case several drops of sodium hydroxide T.S. should be added to prevent sulphur compounds from distilling over.) If volatile acids are present, neutralize with sodium hydroxide T.S.; if volatile bases are present, neutralize with diluted sulphuric acid; if both volatile acids and volatile bases are present, neutralize with diluted sulphuric acid and distil about 50 cc., neutralize this distillate with sodium hydroxide T.S., add 25 cc. of distilled water, and distil once more in the manner directed above and dilute to 50 cc.

If camphor, chloroform, ether, volatile oils, or other volatile products are known or believed to be present, transfer the first distillate to a separatory funnel and saturate it with sodium chloride, add 15 cc. of petroleum benzin and shake the mixture for one or two minutes.

If glycerin is present, dilute the liquid with sufficient distilled water to insure not more than 50 per cent. of glycerin remaining in the liquid left in the flask after distilling. After the liquids have completely separated, draw off the lower alcoholic salt solution into a second separator, and repeat the extraction with 15 cc. of petroleum benzin; draw off the lower alcoholic salt solution into a distilling flask of about 200 cc. capacity, wash the combined petroleum benzin solutions with about 25 cc. of saturated sodium chloride solution, and add the washings to the distilling flask. Distil into a 50 cc. graduated flask at such a rate that about 45 to 48 cc. of distillate are received within a half hour. Bring to the original temperature, dilute with water of the same temperature to 50 cc., and determine the specific gravity and alcoholic per cent. as directed above.

Arsenic Test

(U. S.)

Test Apparatus.—Prepare several generators, equipped with tubes, etc., as described below. Select as a generator a bottle of about 50 cc. capacity, having a mouth about 2.5 cm. in diameter and provide a well-fitting rubber stopper, suitably perforated. Through the perforation insert a vertical exit tube about 13 cm. in total length and 1 cm. in diameter throughout the upper portion (for about 10 cm.) and constricted at its lower extremity to a tube of about 3 cm. in length and about 5 mm. in diameter. This latter tube should extend but slightly below the stopper. In the lower part of the wider exit tube insert a small pledget of dry glass wool (page 1557) and then a strip of freshly prepared but dry lead acetate test paper (page 1564) rolled into a coil, and above this a plug of moist (not wet) lead acetate glass wool (page 1564). In the upper extremity of this tube insert, through a perforated cork stopper, a glass tube 12 cm. in length, having an internal diameter of about 3 mm. Place a strip of mercuric bromide test paper in this tube, bending or creasing the upper portion of the strip so that it will retain its position. The strip should extend within about 2 cm. of the perforated cork stopper and must not be introduced into the tube until the test is ready to start. This tube should be thoroughly cleaned and dried each time it is used.

Standard Arsenic Test Solution.—Dissolve 0.1 Gm. of arsenic trioxide (page 186) which has been finely pulverized, dried over sulphuric acid, and accurately weighed, in about 5 cc. of a 20 per cent. solution of sodium hydroxide (free from arsenic). Neutralize the solution with diluted sulphuric acid (free from arsenic), add 10 cc. of the same acid and sufficient recently boiled distilled water to bring the volume of the solution to exactly 1000 cc. at 25° C. Accurately measure 10 cc. of this solution, transfer it to a 1000 cc. flask, add 10 cc. of diluted sulphuric acid (free from arsenic) and make up the volume with recently boiled distilled water to exactly 1000 cc. at 25° C. Employ this solution, which contains 0.001 milligramme of arsenic trioxide in each cc. (at 25° C.), in preparing the standard stain. Keep this solution in a glass-stoppered bottle. It is advisable to make fresh solutions when new standard stains are to be prepared.

Preparation of the Chemical to be Tested.—Add 1 cc. of a mixture of equal volumes of concentrated sulphuric acid and distilled water, to 5 cc. of an aqueous solution of the chemical (1 in 25) or to a solution in 5 cc. of distilled water of the residue remaining after any special treatment that may be directed. This acidulation is not necessary in the case of inorganic acids. Now, unless specially directed, add 10 cc. of sulphurous acid. Evaporate this liquid in a small beaker, on a water bath, until it is free from sulphurous acid and has been reduced to about 2 cc. in volume. Dilute this evaporated liquid to about 5 cc. with distilled water.

Preparation of the Standard Stain.—Introduce into the generator from 8 to 10 Gm. of reagent zinc, followed by 25 cc. of dilute sulphuric acid, prepared by mixing 1 part of concentrated sulphuric acid, free from arsenic (page 1561), with 4 parts of distilled water, and 5 drops of acid stannous chloride T.S. Add at once 2 cc. (accurately measured at 25° C.) of the standard arsenic T.S., and immediately insert the stopper containing the exit tube, into which have been placed the glass wool pledget, the dry lead acetate test paper, the moist lead acetate glass wool, and the mercuric bromide test paper, as described under *Test Apparatus* (page 1533). Should the evolution of the gas be violent at first, check the reaction by immersing the bottle in cold water. Should the reaction subside, increase it by placing the bottle in warm water. If the reaction is too violent, the stain will spread and not form a distinctive band, thus making the comparisons of color intensity difficult. After the test has continued for forty-five minutes, remove the mercuric bromide test paper and place it in a clean, dry tube for comparison. This stain represents 0.002 milligramme of arsenic trioxide in addition to any stain produced by the reagents. The stain produced by the reagents in a blank test should be scarcely perceptible. Since light, heat, and moisture cause the stain to fade rapidly, comparison should be made as soon as possible. The stained test papers may be preserved by dipping in hot, melted paraffin or by keeping them over phosphoric anhydride, protected from light.

Testing the Chemical.—Introduce into another generator from 8 to 10 Gm. of the zinc, followed by 25 cc. of the dilute sulphuric acid (1 to 4) and 5 drops of acid stannous chloride T.S. Insert the stopper containing the exit tube in which have been placed the test papers and glass wool, as just described. Then add 5 cc. of the solution to be tested, previously treated as directed under *Preparation of the Chemical to be Tested*, and immediately insert the stopper containing the exit tube. When the evolution of hydrogen has proceeded actively for forty-five minutes, remove the mercuric bromide test paper and carefully compare it with the standard stain prepared as described above. The stain produced by the chemicals tested does not exceed in length or intensity of color that prepared as the standard, indicating not more than 1 part of arsenic trioxide in 100,000 parts of the substance tested.

Interfering Chemicals.—*Antimony*, if present in the substance tested, will produce a gray stain. *Sulphites, sulphides, thiosulphates*, and other compounds which liberate hydrogen sulphide or sulphurous acid when treated with sulphuric acid, must be oxidized by means of nitric acid and then reduced by means of sulphurous acid as directed under *Preparation of the Chemical to be Tested*, before introducing them into the apparatus. *Sulphur compounds* as well as *hydrogen phosphide* give a bright yellow band on the test paper. If sulphur compounds are present, a simultaneous darkening of the lead acetate test paper and glass wool will occur. If such is the case, the operation as directed under *Preparation of the Chemical to be Tested* must be repeated upon a fresh portion of the solution being tested, using greater care in effecting the complete removal of the sulphurous acid. In testing hypophosphites special care should be observed to oxidize completely the solution being tested as directed, otherwise a yellow stain may be produced through the evolution of hydrogen phosphide, which might be confused with the orange-yellow color produced by arsenic. The stain produced by hydrogen phosphide is differentiated from that given by arsenic by moistening it with ammonia T.S. A stain caused by arsenic will become dark, but if produced by hydrogen phosphide it will not materially change in color. The test apparatus should be thoroughly cleaned and dried immediately before and after use.

Compounds containing antimony should be tested for arsenic by Bettendorf's Test (see below).

Arsenic Test, Bettendorf's

(U. S.)

This test for the presence of *arsenic* is employed only in testing salts of bismuth and compounds containing antimony.

To a solution of the prescribed quantity of the substance to be tested in 5 cc. of concentrated hydrochloric acid (page 1557) contained in a clean test tube, add 10 cc. of acid stannous chloride T.S. which has been freshly prepared, and set it aside for thirty minutes. If arsenic is present in non-permissible amounts, a brownish tint or precipitate will be seen when the tube is placed over a white surface and the solution viewed from above, comparison being made with a mixture of 5 cc. of concentrated hydrochloric acid (page 1557) and 10 cc. of concentrated stannous chloride T.S., prepared as directed above.

NOTE: It is absolutely necessary that for this test the solution of stannous chloride be freshly prepared, and that nitrates, sulphates, sulphides, sulphites, and compounds of mercury, gold, and selenium be absent from the reagents, and the chemicals being tested.

Ash or Non-Volatile Matter in Chemicals

(U. S.)

Weigh accurately from 1 to 2 Gm., or the amount of the chemical directed in the text, and place it in a tared platinum or porcelain crucible. Ignite it, at first very gently, then gradually raise the temperature until any carbon which may be formed is completely burned off. Conduct the ignition in a place protected from air currents and use as low a temperature as possible to effect the combustion of the carbon. When the carbon has completely disappeared, transfer the crucible while still hot to a desiccator, and weigh it when cold. In the case of substances which increase in volume on ignition, or where it is very difficult to burn off the carbon, the determination is facilitated by using a platinum dish of suitable size, or by igniting the weighed quantity of the substance, in the manner described above, in several separate portions.

To test for non-volatile matter in volatile inorganic chemicals, proceed as directed above, using as low a temperature as possible.

Assay for Acids (Alkalimetric)

(U. S.)

In assaying acids the quantity of acid to be taken should be such that about 30 to 40 cc. of the alkali solution will be consumed. As a general principle it is recommended that the normality of the acid to be titrated should be approximately the same as that of the titrating medium. Except when otherwise directed the liquid to be titrated is to be brought to room temperature before titration, as many indicators give different values at different temperatures. For most of the inorganic acids, methyl orange, methyl red, phenolphthalein, or litmus can be used as indicators, but the alkali must be standardized with the particular indicator used. For organic acids, phenolphthalein is always used.

Tare a glass-stoppered flask of about 150 to 200 cc. capacity, pour into it approximately the quantity of acid directed in the text, stopper immediately, and reweigh: the difference represents the quantity of acid taken. Dilute with distilled water to about 40 cc. and titrate with normal sodium hydroxide, using the indicator specified in the text.

In assaying acids which evolve fumes on exposure to air, such as hydrochloric, nitric, and glacial acetic acids, the flask is tared with 10 cc. of distilled water, then the specified quantity of acid is added, the flask immediately stoppered, allowed to cool, and reweighed. Solid acids are weighed either in a tared glass-stoppered flask or in another suitable container, dissolved in about 40 cc. of distilled water, and titrated.

Assay for Alkali Benzoates and Salicylates

(U. S.)

Dry about 2 Gm. of the salt to constant weight at from 100° to 110° C., weigh accurately in a platinum or porcelain crucible, and heat at first gently, then gradually raise the temperature until the salt is thoroughly carbonized. The final temperature must not exceed a dull red heat and the flame of the burner must not come into contact with the carbonized mass. Allow the carbonized mass to cool, disintegrate it well with a stout glass rod or powder carefully, and transfer with the crucible to a beaker or casserole. Add 50 cc. of distilled water and 50 cc. of half-normal sulphuric acid, cover the beaker or casserole with a watch glass, and boil for thirty minutes. Filter and wash the residue with hot distilled water until the washings cease to redden blue litmus paper. Dry the residue and filter paper, and ignite as described above. Transfer the ignited residue to the filtrate, and determine the excess of acid in the cooled filtrate by titration with half-normal sodium hydroxide, using methyl orange T.S. as indicator. The volume of half-normal sulphuric acid consumed, multiplied by the proper equivalent of the salt, represents the amount of the salt present in the quantity taken.

Assay for Alkali Salts of Organic Acids

(U. S.)

Heat about 2 Gm. of the salt, accurately weighed, in a platinum or porcelain crucible, heating at first very gently, then gradually raising the temperature until the salt is thoroughly carbonized. (*Caution*—Do not use platinum crucibles for lithium salts.) The final temperature must not exceed a dull red heat and the flame of the burner must not come in contact with the carbonized mass. After allowing the carbonized mass to cool, moisten with distilled water, ignite again, and repeat the moistening and igniting until a white residue is obtained. Then disintegrate the ignited mass with the aid of a stout glass rod and transfer the mass and crucible to a beaker. Add 50 cc. of distilled water and titrate with half-normal sulphuric acid, using methyl orange T.S. as indicator. The number of cc. of half-normal sulphuric acid used, multiplied by the proper equivalent of the salt, represents the amount of salt present in the quantity taken.

Assay for Chlorides, Bromides, and Iodides

(U. S.)

Chlorides.—Dissolve about 0.2 Gm. of the salt to be assayed, accurately weighed, (corresponding to from 30 to 40 cc. of tenth-normal silver nitrate), in 25 cc. of distilled water in a 200 cc. graduated flask. Add 50 cc. of tenth-normal silver nitrate to the solution, and 5 cc. of nitric acid, then add sufficient distilled water to make 200 cc., and mix well. Filter the mixture through a dry filter into a dry flask, and reject the first 20 cc. of the filtrate. To 100 cc. of the filtrate add 2 cc. of ferric ammonium sulphate T.S. and titrate with tenth-normal potassium thiocyanate until the supernatant liquid remains reddish after it is well shaken. Multiply by 2 the number of cc. of tenth-normal potassium thiocyanate required, and subtract this figure from the number of cc. of tenth-normal silver nitrate added. The difference, multiplied by the equivalent of the respective chloride, represents the amount of chloride present in the weight of the salt or solution taken.

Bromides and Iodides.—Dissolve about 0.4 Gm. of the salt if a bromide, or 0.5 Gm. of the salt if an iodide, accurately weighed, in 25 cc. of distilled water in a glass-stoppered flask. Add 50 cc. of tenth-normal silver nitrate to the solution, then 2 cc. of ferric ammonium sulphate T.S. and 2 cc. of nitric acid and determine the excess of silver nitrate by titrating with tenth-normal potassium thiocyanate until the supernatant liquid remains reddish after it is well shaken. The difference between the number of cc. of tenth-normal silver nitrate added and the number of cc. of tenth-normal potassium thiocyanate used, multiplied by the equivalent of the respective bromide or iodide being assayed, represents the amount of the bromide or iodide present in the weight of the salt taken. This difference, divided by the weight of the salt taken, represents the number of cc. of tenth-normal silver nitrate required by 1 Gm. of the salt.

Boiling and Distilling Points

(U. S.)

Method I.—For the purpose of the Pharmacopœia the boiling point is defined as that range of temperature within which at least 95 per cent., by volume, of the substance distils, when treated as directed below.

Apparatus Required.—A distilling bulb of from 50 to 60 cc. capacity to the lower part of the neck; the length of the neck is from 10 to 12 cm. and its internal diameter from 14 to 16 mm. The outlet tube of from 4 to 5 mm. internal diameter is to be attached to the neck at approximately its midpoint, forming an angle of from 70° to 75° with the lower end of the neck.

A straight glass condenser with a water jacket from 40 to 60 cm. in length; the distance from the upper end of the water jacket to the neck of the bulb being from 18 to 25 cm.

Thermometer.—In order to avoid the necessity for an emergent stem correction, it is advisable that an accurately standardized thermometer of the Anschütz type be used. If such a thermometer is not available, a thermometer used for melting points may be employed, applying the emergent stem correction as described under *Melting Points*, the length of emergent stem being measured, in degrees, from the lower end of the stopper to the highest point of the boiling temperature. When placed in position, the lower end of the thermometer is from 2 to 3.5 cm. below the center of the orifice of the outlet tube.

An asbestos board of from 12 to 15 cm. square and from 3 to 5 mm. in thickness, having a circular perforation, located centrally, for the reception of the bulb. The edge of the asbestos around the perforation should fit closely to the bulb when the latter is set into it. The size of the perforation should be such that when the bulb is set into it the portion of the bulb below the upper surface of the asbestos will have a capacity of from 3 to 4 cc.

Procedure.—Place the asbestos board on a tripod or other suitable support. Introduce into the distilling bulb 25 cc. of the liquid to be tested, insert the thermometer, stand the bulb in an upright position in the perforation of the asbestos board and connect it with the condenser. Then distil the liquid at the rate of 1 cc. for each fifteen to twenty seconds, noting the temperature as soon as 5 drops of the liquid have distilled into the receiver and when 95 per cent. of the original volume has distilled. Correct the reading for any variation in the barometric pressure from the normal (760 mm.) by allowing 0.1° C. for each 2.7 mm., adding if the pressure is lower, and subtracting if higher.

Note: In order to have the entire volatile portion distil over at the prescribed rate, it is best to make a preliminary distillation of a separate portion of 25 cc. of the liquid, during which the source of heat (a Bunsen burner) is regulated so that the distillation proceeds at the prescribed rate. Having thus regulated the burner, temporarily remove it, clean the bulb, recharge it with a fresh portion of 25 cc. of the liquid, and conduct a new distillation as described above.

Method II.—This method is to be used with liquids for which the permissible range in boiling temperature exceeds 5° C.

Apparatus Required.—A 200 cc. distilling bulb with an outlet tube at approximately the center of the neck, forming an angle of from 70° to 75°, with the lower end of the neck. The length of the neck is from 10 to 12 cm. and its inside diameter is from 18 to 24 mm. The length of the outlet tube is from 10 to 12 cm. and its inside diameter is from 5 to 6 mm. A straight glass condenser, a thermometer, and an asbestos board as in Method I. The diameter of the perforation in the asbestos board is 25 mm.

Procedure.—Place the distilling bulb in an upright position in the perforation in the asbestos board and connect it with the condenser. The outlet tube is to extend from 25 to 35 mm. into the condenser beyond the connecting stopper. Measure 100 cc. of the liquid[1] to be tested, using a cylinder having 1 cc. graduations. Note the temperature of the liquid and transfer it as completely as possible to the distilling bulb. Use this cylinder as the receiver for the distillate without rinsing out any of the adhering liquid. Insert the thermometer through a stopper in the position described in Method I and heat with a Bunsen burner protected from drafts until the liquid begins to boil, then distil at the rate of from 4 to 5 cc. per minute. The temperature when 5 drops of the liquid have distilled into the receiver is the minimum distillation temperature and, unless otherwise specified, the maximum distillation temperature is the temperature at which 95 per cent. of the liquid has distilled over. Bring the distillate to the same temperature at which the liquid was originally measured, and note the volume. Correct the temperature reading for barometric pressure and apply the emergent stem correction as described in Method I.

Liquids which begin to distil below 80° C. are cooled to 10° or 15° C. before measuring the 100 cc. for the test. The end of the condensing tube is fitted with an adapter bent at a suitable angle and the end of the adapter is passed through a cork inserted into the receiving cylinder. The cork has a small perforation to permit the exit of air. The receiving cylinder is kept immersed in ice to within 2.5 cm. of its height during the distillation.

Congealing Points

(U. S.)

Unless otherwise directed, about 10 cc. of the liquid to be tested is introduced into a dry test tube of from 18 to 20 mm. internal diameter, which is then cooled in water or a suitable freezing mixture, the temperature of which should be about 5° lower than the supposed congealing point of the liquid. To induce crystallization, rub the walls of the tube with a standard thermometer (page1549), or add a small crystal of the substance being tested. By alternated immersion of the tube in the bath, or removal from the bath and constant stirring with the thermometer, the temperature is so adjusted that the greater part of the liquid gradually congeals. The highest temperature remaining constant for a short time during the congelation is defined as the congealing point.

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[1] For the determination of the distillation range of the creosote from creosote carbonate and of the cresol from compound solution of cresol, use the volume of the creosote or of the cresol obtained as described under the respective monographs.

Electrolytic Determinations

(U. S.)

Copper, Mercury, Silver, and Zinc.—The electrolytic apparatus consists principally of an ammeter, voltmeter, and rheostat, properly connected with the source of the current, a platinum spiral or disc anode, and a device for rotating the anode. Other suitable apparatus adapted to the use of rotating electrodes may also be employed. The source of the current may be either storage batteries or any other system of direct current which permits regulation of the voltage and amperage. Copper and silver are determined in a platinum dish of about 100 cc. capacity which serves as the cathode. Mercury is determined in a mercury cathode cup, or in a platinum dish which serves as the cathode. The mercury cathode cup consists of a glass cylinder about 6.5 cm. in height and 3.5 cm. in diameter, into which is fused a platinum wire near the bottom, and containing from 50 to 60 Gm. of mercury. The platinum wire must be in contact with the mercury. For the determination of zinc, a nickel dish of about 175 cc. capacity is used. A platinum dish upon which a thin layer of silver or copper has been previously deposited may also be used.

Cupric Sulphate.—Dissolve from 0.75 to 1.0 Gm. of the salt, accurately weighed, in about 100 cc. of distilled water in a weighed platinum dish, add 1 cc. of diluted sulphuric acid, rotate the anode about 500 revolutions per minute and pass the current, gradually increasing it to 2.5 amperes and from 5 to 7 volts. Occasionally add a little distilled water to the electrolyte to keep the deposit of copper covered. When the copper is all deposited (usually in about twenty minutes, to be ascertained by withdrawing a little of the electrolyte and testing it with hydrogen sulphide T.S.), stop the rotation, and wash the deposit with distilled water by means of a siphon without interrupting the current, until the current drops to nearly zero. Remove the dish, wash again with distilled water by decantation, followed by a little alcohol and ether, successively, dry for a few minutes only, at from 80° to 100° C., and weigh.

One gramme of Copper is the equivalent of:

	Gramme
Cupric Sulphate, $CuSO_4.5H_2O$	3.9281
Cupric Sulphate, anhydrous, $CuSO_4$	2.5112

Corrosive Mercuric Chloride.—Dissolve from 0.3 to 0.4 Gm. of the salt, accurately weighed, in 10 cc. of distilled water and transfer the solution to the cathode cup, which has been previously weighed with its metallic mercury. Dilute the liquid to about 20 cc. with distilled water, add 1 cc. of nitric acid, which has been diluted with an equal volume of distilled water, and 10 cc. of toluene, and pass through the solution a current of from 1 to 3 amperes and from 8 to 12 volts, stirring the solution by rotating the anode from 500 to 600 revolutions per minute. After twenty minutes, when the mercury is all removed from solution, (to be ascertained by removing a few drops of the solution and testing with hydrogen sulphide T.S.), wash with distilled water, with the aid of a siphon and without interrupting the current, until the current drops to nearly zero. Remove the cathode cup, wash the mercury with alcohol, then with ether, remove most of theremaining ether with filter paper, dry over sulphuric acid, and weigh. The increase in weight of the cathode cup represents the amount of mercury present in the quantity of the salt taken.

Mercury (Metallic), Mercuric Oxide (Red or Yellow), Mercury with Chalk, and Solution of Mercuric Nitrate.—Dissolve an accurately weighed quantity of the substance in a mixture of equal volumes of nitric acid and distilled water (metallic mercury or mercuric oxide from 0.2 to 0.3 Gm. in 1 cc.; mercury with chalk from 0.6 to 0.8 Gm. in 2.5 cc.), transfer the solution to the cathode cup, which has previously been weighed with its metallic mercury, and dilute with distilled water to about 30 cc. Electrolyze the solution and proceed further as described under *Corrosive Mercuric Chloride* using a current of from 1.5 to 2 amperes and from 7 to 10 volts.

Ammoniated Mercury, Mild Mercurous Chloride, Mercuric Salicylate, Red Mercuric Iodide, Yellow Mercurous Iodide.—Introduce the accurately weighed substance (from 0.5 to 0.6 Gm. of ammoniated mercury or mild mercurous chloride; from 0.7 to 0.8 Gm. of mercuric salicylate or yellow mercurous iodide; from 1.0 to 1.2 Gm. of red mercuric iodide) into the cathode cup, previously weighed with its metallic mercury, add 10 cc. of solution of sodium sulphide (made by dissolving 50 Gm. of crystallized sodium sulphide in sufficient distilled water to measure 100 cc.), and dissolve as completely as possible by agitation. Dilute the mixture to about 30 cc. with distilled water and pass through the solution a current of from 2 to 3 amperes and from 7 to 10 volts for thirty minutes (or until a few drops of the liquid do not give a black precipitate or coloration when gently warmed with a few drops of concentrated ammonium chloride solution), stirring the solution by rotating the anode about 500 revolutions per minute. Wash the mercury, and proceed as described under *Corrosive Mercuric Chloride*, except that before washing with alcohol allow it to stand with about 20 cc. of dilute acetic acid (from 2 to 3 per cent.) until bubbles cease to be evolved.

One gramme of Mercury is the equivalent of:

	Gramme
Ammoniated Mercury, $HgNH_2Cl$	1.2566
Mercuric Chloride, Corrosive, $HgCl_2$	1.3535
Mercurous Chloride, Mild, HgCl	1.1768
Mercuric Iodide, Red, HgI_2	2.2654
Mercurous Iodide, Yellow, HgI	1.6327
Mercuric Nitrate, $Hg(NO_3)_2$	1.6182
Mercuric Oxide (Red or Yellow), HgO	1.0798
Mercuric Salicylate, $HgC_7H_4O_3$	1.1798

Silver Nitrate.—Powder the salt, dry it to constant weight over sulphuric acid in the dark, dissolve from 0.3 to 0.5 Gm., accurately weighed, in about 35 cc. of distilled water in a tared platinum dish, add a solution of 2 Gm. of sodium cyanide in 10 cc. of distilled water, rotate the anode about 500 revolutions per minute, and pass a current, gradually increased to 2.5 amperes and from 5 to 7 volts. After the silver is all deposited (usually from twenty to thirty minutes, to be ascertained by withdrawing a small quantity of the electrolyte and testing it with hydrochloric acid), interrupt the current, wash the deposit of silver several times with distilled water, rinse with a little alcohol, then with ether, dry the dish at from 80° to 100° C. for a few minutes, and weigh.

Moulded Silver Nitrate.—Dissolve from 0.3 to 0.5 Gm., accurately weighed, in 10 cc. of distilled water, filter through a small filter paper, wash the paper with distilled water until free from silver nitrate, bring the combined filtrate and washings to a volume of about 35 cc. in a tared platinum dish, add a solution of 2 Gm. of sodium cyanide in 10 cc. of distilled water, and proceed with the determination as under *Silver Nitrate.*

One gramme of Silver is the equivalent of:

	Gramme
Silver Nitrate, $AgNO_3$	1.5748
Silver Oxide, Ag_2O	1.0742

Zinc (Metallic), Zinc Acetate, Zinc Carbonate, Zinc Chloride, Zinc Oxide, Zinc Phenolsulphonate, Zinc Sulphate.—Introduce into a tared nickel dish, an accurately weighed quantity of the salt, equivalent to about 0.15 Gm. of metallic zinc (zinc acetate, 0.5 Gm., zinc carbonate, 0.25 Gm.; zinc chloride, 0.3 Gm., zinc oxide, 0.2 Gm.; zinc phenolsulphonate, 1.2 Gm.; zinc sulphate, 0.6 Gm.); dissolve it in distilled water or in 10 cc. of diluted sulphuric acid (zinc carbonate, zinc oxide), add from 30 to 35 cc. of sodium hydroxide solution (20 per cent.), and dilute with distilled water to about 120 cc. Heat the mixture nearly to boiling and electrolyze for thirty minutes with a current of from 4 to 5 amperes and from 5 to 6 volts, stirring the solution by rotating the anode from 500 to 600 revolutions per minute. Without interrupting the current, wash the deposited zinc with distilled water with the aid of a siphon until the current drops to zero or nearly so. Remove the dish, wash the zinc first with alcohol then with ether, dry over sulphuric acid, and weigh. The increase in weight of the dish represents the amount of zinc present in the weight of the salt taken.

To determine zinc in metallic zinc, weigh accurately about 1.5 Gm. of the metal, dissolve it by warming with 40 cc. of diluted sulphuric acid, filter the solution, if necessary, wash the filter well with distilled water, and make up the volume of the solution and washings to 100 cc. Measure 10 cc. of this liquid into the weighed dish and proceed as directed above.

One gramme of Zinc is the equivalent of:

	Gramme
Zinc Acetate, $Zn(C_2H_3O_2)_2.2H_2O$	3.3570
Zinc Chloride, $ZnCl_2$	2.0849
Zinc Oxide, ZnO	1.2448
Zinc Phenolsulphonate, $Zn(C_6H_5SO_4)_2.8H_2O$	8.5011
Zinc Sulphate, $ZnSO_4.7H_2O$	4.3988
Zinc Sulphate, anhydrous, $ZnSO_4$	2.4695

Ester Number

(U. S.)

The ester number is the number of milligrammes of potassium hydroxide required to saponify the esters in 1 Gm. of oils, fats, waxes, resins, balsams, and similar organic substances of complex composition. If the saponification value and the acid number have been determined, the difference between these two represents the ester number.

The ester number is also determined directly as follows: Shake from 1.5 to 2 Gm. of the substance, accurately weighed in a 200 to 250 cc. tared flask, with from 20 to 30 cc. of alcohol, add 1 cc. of phenolphthalein T.S., and titrate with half-normal alcoholic potassium hydroxide until the free acid is neutralized. Add exactly 25 cc. of half-normal alcoholic potassium hydroxide, and proceed as directed under *Saponification Value*, beginning with "Insert in the neck of the flask" and omitting the further addition of phenolphthalein T.S. The difference in the number of cc. of half-normal hydrochloric acid consumed in the actual test and in the blank, multiplied by 28.06 and divided by the weight of the substance taken, gives the ester number.

Gasometric Estimations

(U. S.)

In certain cases the Pharmacopœia directs the strength of a product or chemical substance to be determined by the volume of gas (nitrogen dioxide) given off during a definite reaction. This volume is to be determined by the use of a nitrometer in the following manner:

By means of clamps attached to a stand, arrange a nitrometer consisting of a measuring tube (having a capacity of at least 50 cc. and graduated into one-tenth cc.) connected by stout rubber tubing with an open equilibrium tube (both tubes, preferably, provided with a globular expansion near the lower end) in such a manner, that either tube may be readily adjusted and quickly clamped at a higher or lower level. The stop-cock of the measuring tube having been opened, and the open equilibrium tube having been raised to a higher level, pour into the latter a saturated aqueous solution of sodium chloride, until the measuring tube, including the bore of the stop-cock, is completely filled. Then close the latter and adjust the equilibrium tube at a low level. Having ascertained that the stop-cock is closed and is air tight, and having, if necessary, wiped out the graduated tube of the nitrometer, introduce into it the prescribed quantity of the liquid to be tested, and allow this to flow slowly into the measuring tube, being careful not to admit any air. Follow it successively, with the prescribed quantities of potassium iodide T.S. and normal sulphuric acid. When the reaction moderates, remove the measuring tube from its clamp, and, being careful to hold it constantly so that the liquid contained in it stands at a higher level than that in the equilibrium tube, shake its contents without permitting any gas to pass into the open tube. When the reaction has completely ceased and the volume of gas has become constant, which usually requires from thirty to sixty minutes, restore the tube to its fastening and allow the apparatus and contents to acquire the ordinary temperature of the room, which is assumed to be close to 25° C. Then adjust the two tubes so that the liquid columns are at exactly the same level, and read the volume of gas in the measuring tube. Multiply this figure by the weight of the liquid being assayed which is the equivalent of 1 cc. of nitrogen dioxide (see below). The result will be the weight of the absolute substance (ethyl, amyl, or sodium nitrite) contained in the quantity taken for the assay.

For pharmacopœial purposes, the determination will be sufficiently exact if the evolved gas is measured within 3° above or below 25° C.

Since temperature and barometric pressure affect the volume of the gas, the following correction factors must be used to obtain exact results when the temperature and pressure vary from the normal. The barometric correction is important at any locality more than 250 meters above sea level:

FACTORS FOR TEMPERATURE CORRECTIONS
(Normal Temperature, 25° C.)

Temperature	Factor	Temperature	Factor	Temperature	Factor
15° C.	1.035	22° C.	1.010	29° C.	0.987
16° C.	1.031	23° C.	1.007	30° C.	0.983
17° C.	1.028	24° C.	1.003	31° C.	0.980
18° C.	1.024	25° C.	1.000	32° C.	0.977
19° C.	1.021	26° C.	0.997	33° C.	0.974
20° C.	1.017	27° C.	0.993	34° C.	0.971
21° C.	1.014	28° C.	0.990	35° C.	0.968

Example: Assuming that the volume of gas read off was 44.5 cc. at 32° C., and it is desired to ascertain the corresponding volume at 25° C., barometric pressure not being taken into consideration, then the 44.5 cc. must be reduced in the proportion of 1 to 0.977 (see temperature correction factors above), or 44.5 must be multiplied by 0.977. The result will be 43.48 cc. as the equivalent volume of gas at 25° C.

FACTORS FOR CORRECTION FOR BAROMETRIC PRESSURE
(Normal Barometer, 760 mm.)

Barometer Reading		Factor	Barometer Reading		Factor
Millimeters	Inches		Millimeters	Inches	
790	31.10	1.039	660	25.98	0.868
780	30.71	1.026	650	25.59	0.855
770	30.31	1.013	640	25.20	0.842
760	29.92	1.000	630	24.80	0.829
750	29.53	0.987	620	24.41	0.816
740	29.13	0.974	610	24.02	0.803
730	28.74	0.961	600	23.62	0.789
720	28.35	0.947	590	23.23	0.776
710	27.95	0.934	580	22.83	0.763
700	27.56	0.921	570	22.44	0.750
690	27.17	0.908	560	22.05	0.737
680	26.77	0.895	550	21.65	0.724
670	26.38	0.882	540	21.26	0.711

Example: Assuming that the volume of gas read off was 43.48 cc. at 590 mm. barometric pressure, and it is desired to ascertain the corresponding volume at normal barometric pressure (760 mm.), temperature not being taken into consideration, then the 43.48 cc. must be reduced in the proportion of 1 to 0.776 (see barometric correction factors above), or 43.48 must be multiplied by 0.776. The result will be 33.74 cc. as the equivalent volume of gas at normal barometric pressure.

FACTORS FOR DETERMINING NITRITES

$$NO = 30.01;\ 1\text{ Liter} \begin{cases} \text{at } 0^\circ\text{ C. and 760 mm.} = 1.3406\text{ Gm.} \\ \text{at } 25^\circ\text{ C. and 760 mm.} = 1.2281\text{ Gm.} \end{cases}$$

One cubic centimeter of Nitrogen Dioxide is the equivalent of:

		At 0° C. and 760 mm. Gramme	At 25° C. and 760 mm. Gramme
Nitrogen Dioxide, NO	= 30.01	0.0013406	0.0012281
Amyl Nitrite, $C_5H_{11}NO_2$	= 117.10	0.0052310	0.0047920
Ethyl Nitrite, $C_2H_5NO_2$	= 75.05	0.0033528	0.0030713
Sodium Nitrite, $NaNO_2$	= 69.01	0.0030828	0.0028241

Heavy Metals Test

(U. S.)

Chemicals.—This test is to be used to detect the presence of undesirable metallic impurities in official chemical substances or their solutions. Acidulate 10 cc. of a solution of the substance in distilled water (1 in 50), contained in a test tube of about 25 cc. capacity and about 2 cm. in diameter, with 1 cc. of diluted hydrochloric acid (unless otherwise directed),[1] warm it to about 50° C., add an equal volume of freshly prepared hydrogen sulphide T.S., stopper, and allow the mixture to stand at 35° C. for half an hour. At the end of this time the mixture should still possess the odor of hydrogen sulphide; if not, it should be thoroughly saturated with the gas and again set aside for half an hour. The color produced, if any, is not greater than that observed in a blank test made in the same manner and with the same quantities of the reagents (omitting the solution to be tested), the solutions being viewed crosswise by reflected light while held against a white surface. A slight turbidity due to separation of sulphur from the hydrogen sulphide may occur. Filter the solution if necessary and render it alkaline by the addition of ammonia T.S.: a greenish color may be produced but no precipitate is formed within one minute. The addition of ammonia T.S. is omitted in testing salts which produce precipitates when ammonia is added to their solutions.

Volatile Oils.—Shake 10 cc. of the oil with an equal volume of distilled water to which a drop of hydrochloric acid has been added, and pass hydrogen sulphide through the mixture until it is saturated: no darkening in color is produced in either the oil or the water (*lead* or *copper*).

Identification Tests for Chemicals

(U. S.)

Under this head are placed tests which are frequently referred to throughout the Pharmacopœia. In order to save space they are here grouped together and in the text are referred to by title and page number.

These tests are to be used for the identification of official chemicals. They are not intended to be applicable to mixtures of substances unless specific directions are given for such use.

Acetates.—When warmed with concentrated sulphuric acid, acetates evolve acetic acid. If acetic acid or an acetate is warmed with sulphuric acid and alcohol, the characteristic fragrant odor of ethyl acetate is evolved. With neutral solutions of acetates, ferric chloride T.S. produces a deep red color which is destroyed by the addition of mineral acids.

Aluminum.—Solutions of aluminum salts yield with ammonia T.S. a white precipitate which is insoluble in a moderate excess of ammonium hydroxide. Sodium hydroxide T.S. or sodium sulphide T.S. produces a similar precipitate which dissolves in an excess of either of these reagents.

Ammonium.—Ammonium salts are decomposed by the addition of an excess of sodium hydroxide T.S., with the evolution of ammonia, recognizable by its odor and by its alkaline effect upon moistened red litmus paper, exposed to the vapor.

Arsenates.—Soluble arsenates yield with silver nitrate T.S. a dark red precipitate which is soluble in diluted nitric acid. When hydrogen sulphide is passed into a solution of an arsenate containing hydrochloric acid, a yellow precipitate is slowly formed. This precipitate is soluble in ammonium sulphide T.S. Soluble arsenates yield a white precipitate with magnesia mixture T.S.

Arsenous Compounds.—Solutions of arsenous compounds, to which hydrochloric acid has been added, yield with hydrogen sulphide a yellow precipitate which is insoluble in strong hydrochloric acid but soluble in ammonium carbonate T.S.

Barium.—Solutions of barium salts yield a white precipitate with diluted sulphuric acid. This precipitate is insoluble in hydrochloric or nitric acid. Barium salts impart a green color to a non-luminous flame.

Benzoates.—In neutral solutions, benzoates yield a salmon-colored precipitate with ferric chloride T.S. In moderately concentrated aqueous solutions, benzoates yield a precipitate of benzoic acid upon acidulation with diluted sulphuric acid. This precipitate is readily soluble in ether.

Bicarbonates.—(See *Carbonates*).

Bismuth.—When dissolved in a slight excess of nitric or hydrochloric acid, bismuth salts yield a white precipitate upon dilution with water. This precipitate is blackened by hydrogen sulphide, and the resulting compound dissolves in a warm mixture of equal parts of nitric acid and water.

Bisulphites.—(See *Sulphites*).

Borates.—Solutions of borates, acidulated with hydrochloric acid, turn turmeric paper brownish-red, the color changing to greenish-black by moistening with ammonia T.S. When a borate is treated with sulphuric acid, alcohol added, and the mixture ignited, it burns with a green bordered flame.

Bromates.—Sulphurous acid added drop by drop to a solution of a bromate produces a yellow color, which disappears upon the addition of an excess of sulphurous acid. Bromates, when gently ignited with charcoal, yield bromides which may be recognized by the characteristic reactions.

Bromides.—In solutions of bromides, the addition of chlorine T.S., drop by drop, liberates bromine which is dissolved by shaking with chloroform, coloring the chloroform red to reddish-brown. Silver nitrate T.S. produces in solutions of bromides a yellowish precipitate which is insoluble in nitric acid, and only slightly soluble in dilute ammonia T.S.

Cadmium.—Neutral, alkaline, or moderately acid solutions of cadmium salts yield a yellow precipitate with hydrogen sulphide. This precipitate is insoluble in alkali hydroxides, in alkali sulphides, and in cold dilute acids, but it is soluble in cold, moderately dilute nitric acid, in hot dilute hydrochloric acid, or in hot moderately dilute sulphuric acid.

Calcium.—In neutral or alkaline solutions, or in solutions of calcium salts free from mineral acid, ammonium oxalate T.S. produces a white precipitate. This precipitate is insoluble in acetic acid, but dissolves in hydrochloric acid. Calcium salts moistened with hydrochloric acid impart a yellowish-red color to a non-luminous flame.

Carbonates.—Carbonates or bicarbonates effervesce with acids, yielding a colorless gas, which when passed into calcium hydroxide T.S. produces a white precipitate. Carbonates in solution produce a reddish-brown precipitate with mercuric chloride T.S., while bicarbonates produce a white precipitate with the same reagent. A cold aqueous solution of a carbonate is reddened by phenolphthalein T.S., while a similar solution of a bicarbonate remains unchanged or is only slightly reddened.

Chlorates.—Solutions of chlorates yield no precipitate with silver nitrate T.S. The addition of sulphurous acid to this mixture produces a white precipitate which is insoluble in nitric acid but soluble in ammonia T.S. Upon ignition, chlorates yield chlorides, recognizable by appropriate tests. When concentrated sulphuric acid is added to a dry chlorate, decrepitation occurs and a greenish-yellow gas is evolved. *Caution.*—Only a small amount of chlorate should be used for this test and extreme caution must be exercised in performing it.

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[1] Acids are first carefully neutralized by the addition of ammonia T.S. and then acidified as directed above.

Chlorides.—Solutions of chlorides yield a white, curdy precipitate with silver nitrate T.S. This precipitate is insoluble in nitric acid, but is easily and completely dissolved by a slight excess of ammonia T.S.

Chromates.—Solutions of chromates or dichromates, free from mineral acids, yield with lead acetate T.S. a yellow precipitate, which is insoluble in acetic acid. When a chromate or a dichromate is acidulated with diluted sulphuric acid and hydrogen dioxide T.S. added, a blue color is produced. Upon shaking with ether, the blue color passes into the ethereal layer.

Citrates.—Neutral solutions of citrates are not affected in the cold by the addition of an excess of calcium chloride T.S., but, upon heating the mixture, a white precipitate is produced. When to a hot solution of a citrate, to which has been added one-tenth of its volume of mercuric sulphate T.S., potassium permanganate T.S. is added, a white precipitate is produced.

Cobalt.—Solutions of cobaltous compounds yield a blue precipitate with sodium hydroxide T.S. This precipitate rapidly changes color, becoming olive-green, and, if boiled soon after its formation, becomes rose-red. Solutions of cobalt salts, when treated with an excess of potassium nitrite and acetic acid, yield a yellow precipitate.

Copper.—Solutions of copper compounds, acidulated with hydrochloric acid, deposit a red film of metallic copper upon a bright untarnished surface of metallic iron. An excess of ammonia T.S., added to a solution of a copper salt, produces a blue color. With potassium ferrocyanide T.S., solutions of cupric salts yield a red precipitate.

Cyanides.—Solutions of cyanides yield a white, curdy precipitate with an excess of silver nitrate T.S. This precipitate is soluble in an excess of a solution of a soluble cyanide, or ammonia T.S., also soluble in boiling nitric acid. To 10 cc. of a weak solution of a cyanide, add a few drops of freshly prepared ferrous sulphate T.S., 1 cc. of sodium hydroxide T.S., a few drops of ferric chloride T.S., warm, and finally add an excess of diluted sulphuric acid: a blue precipitate is produced.

Dichromates.—(See *Chromates*).

Ferricyanides.—Solutions of ferricyanides yield a blue precipitate with ferrous sulphate T.S. This precipitate is insoluble in diluted hydrochloric acid, but is decomposed by sodium hydroxide T.S.

Ferrocyanides.—Solutions of ferrocyanides yield a blue precipitate with ferric chloride T.S. With copper sulphate T.S., ferrocyanides yield a red precipitate.

Glycerophosphates.—Solutions of glycerophosphates yield no precipitate in the cold with ammonium molybdate T.S., but upon boiling, an abundant yellow precipitate is formed. Moderately diluted solutions of glycerophosphates, when treated with calcium chloride T.S., remain unaffected in the cold, but on boiling, a precipitate is produced which redissolves on cooling.

Gold.—Solutions of gold salts yield a purple coloration or precipitate with stannous chloride T.S.

Hypophosphites.—When strongly heated, hypophosphites evolve spontaneously inflammable hydrogen phosphide. Hypophosphites in solution yield a white precipitate with mercuric chloride T.S. This precipitate becomes gray when an excess of hypophosphite is present. Solutions of hypophosphites, acidulated with sulphuric acid and warmed with copper sulphate T.S., yield a red precipitate.

Iodides.—In solutions of iodides, the addition of chlorine T.S., drop by drop, liberates free iodine which colors the solution yellow to red, and on shaking with chloroform the latter is colored violet. The iodine thus liberated gives a blue color with starch. Silver nitrate T.S. produces in solutions of iodides a yellow, curdy precipitate which is insoluble in nitric acid and in ammonia T.S.

Iron.—Ferrous or ferric compounds in solution yield a black precipitate with ammonium sulphide T.S. This precipitate is dissolved by cold diluted hydrochloric acid with the evolution of hydrogen sulphide.

Ferric salts in solution yield a dark blue precipitate with potassium ferrocyanide T.S. With an excess of sodium hydroxide T.S., a reddish-brown precipitate is formed. Solutions of ferric salts produce with potassium thiocyanate T.S. a deep red color which is not destroyed by diluted mineral acids.

Ferrous salts in solution yield a dark blue precipitate with potassium ferricyanide T.S. This precipitate is insoluble in diluted hydrochloric acid, but is decomposed by sodium hydroxide T.S. Solutions of ferrous salts yield with sodium hydroxide T.S. a white precipitate, the color rapidly changing to green.

Lactates.—Solutions of lactates, when acidulated with sulphuric acid, potassium permanganate T.S. added, and the mixture heated, evolve acetaldehyde which is recognizable by its odor.

Lead.—Solutions of lead salts yield with diluted sulphuric acid a white precipitate which is slightly soluble in diluted hydrochloric or nitric acid, but completely soluble in warm sodium hydroxide T.S. With potassium chromate T.S. solutions of lead salts, free or nearly free from mineral acids, yield a yellow precipitate which is insoluble in acetic acid but soluble in sodium hydroxide T.S.

Lithium.—Lithium salts moistened with hydrochloric acid impart an intense crimson color to a non-luminous flame. Solutions of lithium salts are not precipitated by diluted sulphuric acid or soluble sulphates (*difference from Strontium*).

Magnesium.—Solutions of magnesium salts in the presence of ammonium chloride yield no precipitate with ammonium carbonate T.S., but on the subsequent addition of sodium phosphate T.S. a white precipitate is produced which is insoluble in ammonia T.S.

Manganous Compounds.—When in solution manganous compounds yield a salmon-colored precipitate with ammonium sulphide T.S. This precipitate is dissolved by acetic acid.

Mercury.—Solutions of mercury salts free from excess of nitric acid, when applied to bright copper foil, yield a deposit, which, upon rubbing, becomes bright and silvery in appearance. With an excess of hydrogen sulphide, mercury compounds yield a black precipitate which is insoluble in ammonium sulphide T.S., or in boiling diluted nitric acid.

Mercuric compounds in solution yield a yellow precipitate with sodium hydroxide T.S. They also yield in neutral solutions a scarlet precipitate with potassium iodide T.S. This precipitate is very soluble in an excess of potassium iodide T.S.

Mercurous compounds are blackened by ammonia T.S. or sodium hydroxide T.S. Solutions of mercurous salts yield with hydrocc ihlroacid a white precipitate which is blackened by ammonia T.S. With potassium iodide T.S., a yellow precipitate is produced.

Molybdates.—When a dry molybdenum compound is covered with sulphuric acid and heated until the acid is almost all driven off, a blue residue remains. Solutions of molybdates acidulated with nitric acid, yield a yellow precipitate on warming with sodium phosphate T.S. This precipitate is soluble in ammonia T.S.

Nitrates.—When a solution of a nitrate is mixed with an equal volume of sulphuric acid, the mixture cooled, and a solution of ferrous sulphate superimposed, a brown color is produced at the junction of the two liquids. When a nitrate is heated with sulphuric acid and metallic copper, brownish-red fumes are evolved.

Nitrites.—When treated with diluted mineral acids or with acetic acid, nitrites yield brownish-red fumes. On adding a few drops of potassium iodide T.S. and a few drops of dilute sulphuric acid to a solution of a nitrite, iodine is liberated which colors starch T.S. blue.

Nitroprussides.—The addition of a dilute solution of a soluble sulphide to a solution of a nitroprusside produces a transient purple to deep violet color, the intensity and shade of color depending upon the concentration of the solutions.

Oxalates.—Neutral or alkaline solutions of oxalates yield a white precipitate with calcium chloride T.S. This precipitate is insoluble in acetic acid but is dissolved by hydrochloric acid.

Palladium.—When in solution palladous salts yield with ammonia T.S. a salmon-colored precipitate, which is soluble in an excess of the reagent. Hydrochloric acid added to this solution produces a yellow precipitate.

Permanganates.—Solutions of permanganates acidulated with sulphuric acid are decolorized by hydrogen dioxide T.S., sodium bisulphite T.S., or oxalic acid T.S.

Peroxides.—Solutions of peroxides slightly acidulated with sulphuric acid yield a deep blue color upon the addition of potassium dichromate T.S. On shaking the liquid with an equal volume of ether, the blue color passes into the ethereal layer.

Phosphates.—Neutral solutions of orthophosphates yield with silver nitrate T.S. a yellow precipitate, which is soluble in diluted nitric acid or in ammonia T.S. With ammonium molybdate T.S., a yellow precipitate is produced which is soluble in ammonia T.S.

Phosphotungstates.—(See *Tungstates*).

Potassium.—Potassium compounds impart a violet color to a non-luminous flame, but the presence of small quantities of sodium masks the color. In neutral, concentrated or moderately concentrated solutions of potassium salts (depending upon the solubility and the potassium content of the salt), sodium bitartrate T.S. produces a white crystalline precipitate which is soluble in ammonia T.S., alkali hydroxides or carbonates. The formation of the precipitate, which is usually slow, is accelerated by stirring or rubbing the sides of the test tube with a glass rod. The addition of a little glacial acetic acid also promotes the formation of the precipitate.

Salicylates.—In moderately dilute solutions of salicylates, ferric chloride T.S. produces a violet color. The addition of acids to moderately concentrated solutions of salicylates produces a precipitate of salicylic acid.

Selenium.—Stannous chloride T.S. produces a red color in solutions of *selenates*. Solutions of *selenites* yield a red color with sodium bisulphite.

Silver.—Solutions of silver salts yield with hydrochloric acid a white, curdy precipitate which is insoluble in nitric acid but is easily soluble in ammonia T.S.

Sodium.—Sodium compounds impart an intense yellow color to a non-luminous flame.

Strontium.—Strontium compounds, moistened with hydrochloric acid, impart a crimson color to a non-luminous flame. Calcium sulphate T.S. produces a white precipitate with solutions of strontium salts.

Sulphates.—Solutions of sulphates yield with barium chloride T.S. a white precipitate, which is insoluble in hydrochloric or nitric acid.

Sulphides.—When treated with an acid, many sulphides yield hydrogen sulphide, recognizable by its characteristic odor and by its blackening moist lead acetate test paper.

Sulphites.—When treated with hydrochloric acid, sulphites, and bisulphites yield colorless sulphur dioxide, recognizable by its pungent odor which resembles burning sulphur. This gas blackens filter paper moistened with mercurous nitrate T.S.

Tartrates.—With neutral solutions of tartrates, silver nitrate T.S. produces a white precipitate. Upon dissolving this precipitate in just sufficient ammonia T.S. and warming, metallic silver is deposited on the sides of the test tube, forming a mirror. When a drop of ferrous sulphate T.S., then a few drops of hydrogen dioxide T.S., and finally an excess of sodium hydroxide T.S. are added to a solution of tartaric acid or of a tartrate, acidified with acetic acid, a purple or violet color is produced.

Thiocyanates.—Solutions of thiocyanates yield a red color with ferric chloride T.S. which is not destroyed by moderately concentrated mineral acids.

Thiosulphates.—Solutions of thiosulphates yield with hydrochloric acid a white precipitate of sulphur which soon turns yellow, sulphur dioxide being liberated, recognizable by its odor. The addition of ferric chloride T.S. to solutions of thiosulphates, produces a dark violet color which quickly disappears.

Tin.—When metallic zinc is placed in a solution of a salt of tin acidified with hydrochloric acid, the tin is precipitated in metallic form. The precipitated metal is soluble in boiling hydrochloric acid and the resulting solution yields a white or gray precipitate with mercuric chloride T.S.

Tungstates.—Solutions of tungstates or phosphotungstates yield with stannous chloride T.S. a yellow precipitate, which, upon heating with hydrochloric acid, changes to blue. Solutions of tungstates, when evaporated to dryness with hydrochloric acid, leave a yellow residue of tungstic oxide which is soluble in ammonia T.S.

Vanadates.—Solutions of vanadates yield a yellow precipitate with potassium ferrocyanide T.S.

Zinc.—In alkaline solutions, zinc salts yield a white precipitate with hydrogen sulphide. This precipitate is insoluble in acetic acid but is dissolved by diluted hydrochloric acid. Ammonium sulphide produces a similar precipitate in neutral or alkaline solutions. Zinc salts in solution yield with potassium ferrocyanide T.S. a white precipitate which is insoluble in diluted hydrochloric acid.

Iodine Value

(U. S.)

The iodine value or number of a fat or oil indicates the proportion of iodine absorbed under specified conditions. It is determined as follows: Introduce about 0.8 Gm. of a solid fat or about 0.3 Gm.[1] of an oil, accurately weighed, into a glass-stoppered bottle of 250 cc. capacity, dissolve it in 10 cc. of chloroform, add 25 cc. of iodobromide T.S., accurately measured from a burette or pipette, stopper the bottle securely, and allow the mixture to stand for half an hour[2] in a cool place protected from light. After this time it must still retain a brown color; if the color is not brown a new test should be started, using a smaller quantity of the fat or oil. Then add in the order named 30 cc. of potassium iodide T.S., 100 cc. of distilled water, and tenth-normal sodium thiosulphate in small, successive portions, shaking thoroughly after each addition, until the color of the mixture becomes quite pale. Now add a few drops of starch T.S. and continue the addition of tenth-normal sodium thiosulphate until the blue color is discharged. While this test is being carried out, make a blank test by mixing exactly the same quantities of reagents and titrate the free iodine with tenth-normal sodium thiosulphate as directed above. The difference in the number of cc. of tenth-normal sodium thiosulphate consumed by the blank test and the actual test, multiplied by 1.269 and divided by the weight of the fat or oil taken, gives the iodine value.

Melting Points

(U. S.)

For the purpose of the Pharmacopœia the melting point is defined as that interval of temperature within which the substance is observed to melt when treated as directed below.

For the determination of the melting point, Pharmacopœial substances are divided into two classes:

Class I.—Substances readily reduced to a powder; *Class II.*—Substances not readily reduced to a powder, such as fats, fat acids, paraffin, petrolatum, and waxes.

Apparatus required (see illustration):

1. *A round-bottom, glass tube* of from 30 mm. to 40 mm. internal diameter and about 10 cm. long, flaring slightly at the top like an ordinary test tube. The walls of the tube are not more than 1.5 mm. thick at any point. The tube is made of glass which will permit heating over an open Bunsen flame.
2. *A stirring device,* which can be made from a glass rod of about 2 mm. external diameter. It is made circular at the end to fit the container (1) and is bent twice at right angles above the top of the container to bring its outer end within reach for convenient manipulation.
3. *A standard thermometer* covering the desired range of temperature (page 1549).
4. *An auxiliary thermometer* (page 1550).
5. *A capillary glass tube* about 6 cm. long and from 0.8 to 1.2 mm. internal diameter, the walls from 0.2 to 0.3 mm. thick and the tube closed at one end.

Procedure for Class I:

Reduce the substance to a very fine powder and, unless otherwise stated, render it anhydrous, when it contains water of crystallization, by drying it at the temperature given in the text, or, when the substance contains no water of crystallization, by drying it for twenty-four hours over sulphuric acid.

Select a bath suitable for the melting temperature to be determined, and fill the container to a depth which will permit of such immersion of the thermometer that the upper end of the bulb will be from 2 to 3 cm. below the surface of the bath and the lower end of the bulb about equally distant from the bottom of the container.

Charge the capillary glass tube with sufficient of the dry powder to form a column in the bottom of the tube from 2.5 to 3.5 mm. high when packed down as closely as possible by moderate tapping on a solid surface. Attach the capillary tube to the thermometer by wetting both with the liquid of the bath or by means of a piece of platinum wire and adjust it so that the substance is centrally located by the side of the thermometer bulb. Heat the bath by means of a free Bunsen flame until a temperature 25° C. below the supposed melting point is reached, then carefully regulate the rate of rise in temperature to about 3° per minute until the substance begins to melt (the temperature at which the column of the substance is observed to collapse definitely against the sides of the tube at any point is defined as the beginning of melting), and from that time carefully regulate the rise in temperature to about 0.5° per minute until the melting is complete. (The temperature at which the substance becomes liquid throughout is defined as the end of melting). The bath must be stirred constantly throughout the heating.

The result thus obtained as the melting interval must be adjusted by applying the calibration correction and that for the emergent stem, as follows:

Attach the auxiliary thermometer, as shown in the illustration, so that the center of its bulb is as close as possible to the stem of the main thermometer at a point midway between the surface of the bath and the supposed melting point. In order to prevent the heat from the burner or currents of cold air from affecting the temperature of the auxiliary thermometer, it is advisable to adjust to the stem of the main thermometer a movable platform made of stiff paper, having its edges folded so as to form a box-like shield surrounding the bulb of the auxiliary thermometer. Note the temperature registered by the auxiliary thermometer at the end of the melting of the substance and calculate the emergent stem correction by the following formula:

$$\text{correction} = 0.00015 \times N\ (T - t)$$

in which N represents the number of degrees of emergent stem from the bath, T the temperature at the end of melting, and t the temperature registered by the auxiliary thermometer; the correction to be added to the observed reading of the main thermometer.

To avoid the necessity of determining the emergent stem correction each time a melting point is taken, the corrections for intervals of 10° C. may be determined (at about 25° C. room temperature) and the results plotted on cross-section paper, the temperature of the bath represented by the abscissæ and the amount of correction by the ordinates. The correction for any intermediate temperature can then be interpolated.

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[1] 0.15 to 0.18 Gm. for linseed oil, 0.18 to 0.2 Gm. for cod liver oil, and 0.8 to 1.0 Gm. for oil of theobroma.

[2] One hour is required for castor oil and linseed oil.

NOTE: Suggestions regarding liquids to be used for baths in Class I:

For temperatures up to 200° C., a purified, concentrated sulphuric acid is a suitable bath. For higher temperatures, up to about 350° C., a pure grade of cotton-seed oil (almost colorless) will serve for a limited number of determinations. Other, though less desirable, substitutes for sulphuric acid at high temperatures are: (1) a pure grade of paraffin which has been freshly distilled; (2) clean, white, artificial (cotton seed) lard. A very satisfactory bath is prepared by cautiously boiling together, for five to ten minutes under a hood, a mixture of 70 parts of sulphuric acid and 30 parts of potassium sulphate, stirring constantly until the potassium sulphate is completely dissolved.

Procedure for Class II:

Carefully melt the substance to be tested at as low a temperature as possible and draw it into a capillary tube, which is open at both ends, to a depth of about 10 mm. Cool the charged tube at 10° C., or lower, for twenty-four hours, or in contact with ice for at least two hours. Then attach the tube to a standard thermometer by means of a rubber band, adjust and heat it in a water bath, as directed in Class I, except that, within 5° of the assumed melting temperature, the rate of rise of temperature is carefully regulated to about 0.5° per minute.

The temperature at which the substance is observed to rise in the capillary tube is taken as the melting point.

Optical Rotation

(U. S.)

In a ray of ordinary light the transverse vibrations take place indifferently in any plane about the line of propagation. When these waves are limited to a single plane, they are termed polarized and the phenomenon is known as polarization.

Many organic substances, either liquid or in solution in suitable solvents, when examined in a specially constructed optical apparatus called a polariscope, are capable of rotating the plane of polarization of a ray of light either to the right or to the left. Such substances are termed "optically active," and when rotating to the right are designated as "dextrorotatory" and when rotating to the left, as "lævorotatory." Substances which do not possess this property of optical rotation are termed "optically inactive." Optical activity in many instances is intimately connected with the chemical constitution of a substance, frequently becoming a specific property, and its determination is of considerable value.

Among the substances recognized in the Pharmacopœia, there are a number, particularly certain essential or volatile oils and related bodies, for which the determination of the angle of rotation of a ray of polarized light, or, in some cases, the proof of their optical inactivity, affords the most simple and positive evidence of their identity or purity.

The instruments used for polariscopic tests, vary in their construction and are classified as polarimeters (measuring angular rotation) and saccharimeters (measuring percentage of sucrose). Those which are most generally adapted for the examination of the substances mentioned above are the penumbral or so-called "half-shadow" instruments of Laurent and of Schmidt and Hansch in which the two sides of the field of vision are capable of becoming unequally illuminated. Polarimeters permit the angle of rotation to be read off in degrees or fractions of a degree of a circle. Saccharimeters, set to measure percentage of sucrose, give readings in terms of divisions of the sugar scale.

These determinations are best made in a dark room, and by means of monochromatic light, the latter being obtained by introducing into a non-luminous flame, on a loop of platinum wire, a small bead of fused sodium chloride. The light thus radiated corresponds with the line D of the solar spectrum.

The following factors are employed for converting readings of a saccharimeter into readings of a polarimeter: 1 division Laurent sugar scale equals 0.2167° angular rotation D.; 1 division Schmidt and Hansch sugar scale equals 0.346° angular rotation D.

Since the deviation of the plane of polarization either to the right or to the left of the zero point is directly proportional to the length of the column of liquid, it is essential that the observations should be made with tubes of a definite length, such as 200, 100, 50, or 25 mm. The selection of the length of the tube to be employed is, however, usually dependent upon the depth of color of the liquid and the magnitude of its optical rotation.

The rotatory power of an optically active, liquid substance, observed with sodium light, and referred to the ideal density 1, and in a tube having a length of 1 decimeter (100 mm.), is designated as its *specific rotatory power*. This is usually expressed by the term $[a]_D$. Since, however, not only the density of an optically active liquid, but also its rotation, is influenced by the temperature, the specific rotation varies with the latter. In stating the specific rotation it is, therefore, necessary to indicate at what temperature the rotation and the density of the liquid have been determined. But for the same temperature the specific rotation of a pure, optically active liquid is always a constant number. The temperature used in the text of the Pharmacopœia is 25° C., except when otherwise indicated. For saccharimeters the temperature is fixed at 20° C. by international agreement.

For calculating the specific rotatory power of an optically active liquid substance, or solution of an optically active solid, the following formulas are of general application:

I. For liquid substances $$[a]_D = \frac{100 \times a}{L \times d}$$

II. For solutions of solids $$\left\{ \begin{array}{l} [a]_D = \dfrac{10000 \times a}{L \times p \times d} \\[2ex] \text{or} \quad [a]_D = \dfrac{10000 \times a}{L \times c} \end{array} \right.$$

For calculating these formulas, the determination of the following factors is necessary:

a = the angle of rotation of the liquid or solid observed with sodium light.
L = the length of the tube in millimeters.
d = the density of the active liquid or solution.
p = the amount of active substance in 100 parts by weight of the solution.
c = the number of grammes of active substance in 100 cc. of solution.

Proximate Assays

(U. S)

General Directions for Alkaloidal Assays

Fineness of Powders.—The portion to be assayed, which must represent the entire drug, is to be in powder of specified fineness. This is interpreted to mean that the drug powder must not be coarser than the size specified, but finer powders may be used.

Extraction of the Alkaloids. **Extraction with Immiscible Solvents.**—For the extraction of alkaloids from an ethereal or chloroformic solution, use dilute acid. The strength of the acid and the quantity employed are left to the discretion of the operator, but it is advisable to use as small quantities as can be conveniently handled. Shaking should not be violent, but should be sufficient to mix the liquids thoroughly without forming an emulsion. The extraction with acid must be repeated until the alkaloid is completely removed from the ethereal or chloroformic liquids. Each portion of acid solution as drawn off should be filtered through cotton or filter paper. If preferred, the combined acid solutions may be washed with a little chloroform or ether, this in turn washed with distilled water and the water added to the acid solution.

In shaking out an alkaline aqueous solution with an immiscible solvent, the process must be repeated until the extraction of the alkaloid is complete. Each portion of solvent as drawn off should be filtered through cotton or filter paper.

Care must be taken to avoid loss of alkaloidal solutions through imperfect separation, creeping, or other similar conditions.

Ether-Chloroform Mixture.—When a mixture of ether and chloroform is employed, the proportion of the mixture is to be three volumes of ether and one volume of chloroform, cooled to working temperature after being mixed.

Evaporation of Solvents.—The evaporation of the final alkaloidal solution may be conducted by distillation, by evaporation on a water bath, or by means of a current of warm air. In evaporating chloroform solutions, the residue should be treated with ether or alcohol which is in turn evaporated to carry off the last traces of chloroform.

As the alkaloids from hyoscyamus are very sensitive to heat, a solution of these alkaloids should not be evaporated to dryness on a water bath. After the last trace of chloroform has evaporated spontaneously, 1 or 2 cc. of neutral alcohol should be added and warmed but not entirely evaporated, then cooled and titrated immediately.

Titration of the Alkaloids.—When the alkaloid is to be estimated by titration, the residue is dissolved in neutralized alcohol, the volumetric acid, accurately measured, is added, and followed by a convenient quantity of distilled water. The excess of acid is immediately determined by titration with fiftieth-normal sodium hydroxide. If preferred, the residue is dissolved in ether or chloroform, the volumetric acid and distilled water added, and the ether or chloroform expelled by gentle heat before titrating.

Indicators.—The indicators to be employed in the titration of alkaloids are cochineal T.S. and methyl red T.S. These are interchangeable and either may be used at the discretion of the operator.

Gravimetric Determination.—When the alkaloid is to be estimated gravimetrically, the solvent is evaporated, as above directed, in a tared flask or beaker. The residue is dried to constant weight at 100° C. and weighed.

Type Processes for Alkaloidal Assays

(U. S.)

Type Process A for Drugs—Aliquot Part Method. **Extraction of the Drug.**—Place the accurately weighed drug in a dry flask or bottle of suitable capacity, add the required volume of solvent, accurately measured, stopper securely with a well-fitting cork stopper, and shake. Allow to stand for at least five minutes, add 10 cc. of ammonia T.S., stopper tightly, and shake for one hour in a mechanical shaker, or intermittently during two hours. In case of intermittent shaking agitation must be vigorous for at least one minute and be repeated at intervals of not more than fifteen minutes. Allow the mixture to stand over night, again shake intermittently during one-half hour, and then allow the drug to settle. If the supernatant liquid is not clear, add a few cc. of distilled water, shake vigorously, and again allow to settle.

Decant an aliquot part of the liquid, accurately measured at approximately the same temperature at which the original solvent was measured. Transfer the liquid to a separator, rinsing the measuring container with a small quantity of the solvent and adding the rinsing to the separator.

Shaking out with Acid.—Completely extract the alkaloid from the ethereal or chloroformic solution by shaking with successive portions of dilute sulphuric acid, and filtering each portion drawn off or washing with ether or chloroform if preferred. After extracting with several portions of acid, test a few drops of the last portion used for the presence of alkaloid. Extraction must be continued until not more than a very faint cloudiness results upon the addition of a drop of mercuric potassium iodide T.S. or, in the case of hydrastis or colchicum, upon the addition of a drop of iodine T.S.

Shaking out with Immiscible Solvent.—Add a portion of the specified solvent to the combined acid solutions and make the mixture alkaline with ammonia T.S. Completely extract the alkaloid from the aqueous liquid with successive portions of the solvent, filtering each portion as drawn off. After extracting with several portions of the solvent, evaporate about 1 cc. of the last portion used, dissolve the residue in a few drops of dilute acid, and test for the presence of alkaloid. Extraction must be continued until not more than a very faint cloudiness results upon the addition of a drop of mercuric potassium iodide T.S. or, in the case of hydrastis or colchicum, upon the addition of a drop of iodine T.S.

Determination of Alkaloidal Content.—Determine the alkaloid volumetrically or gravimetrically as directed.

TYPE PROCESS B FOR DRUGS—TOTAL EXTRACTION METHOD. **Extraction of the Drug.**—Place an accurately weighed quantity of the ground drug in a small cylindrical percolator (see illustration), previously prepared by packing the outlet with cotton. Add a sufficient amount of the solvent to saturate the drug completely and mix thoroughly. Cover the percolator and allow it to stand at least five minutes, then add 5 cc. of ammonia T.S., and mix this thoroughly with the drug. After macerating for one hour, pack the drug firmly, place a pledget of cotton above it and percolate slowly with the solvent until the drug is completely extracted. The percolation must be continued until, upon evaporating 3 or 4 cc. of the percolate,dissolving the residue in a few drops of dilute acid, and adding a drop of mercuric potassium iodide T.S., only a very faint cloudiness results.

Any suitable percolator may be used, but one similar in form and size to that illustrated is recommended.

From this point proceed as directed under *Type Process A*, beginning with the words "Transfer the liquid to a separator."

TYPE PROCESS C FOR GALENICAL PREPARATIONS—ALIQUOT PART METHOD.—**Preparation of the Sample.** *Powdered Extracts.*—When powdered extracts are assayed by the aliquot part method, they are to be treated as directed under the powdered drug. If the extract has a tendency to form lumps in the solvent, mix it with an equal bulk of clean sand or powdered pumice. If lumps form after the addition of the ammonia, they should be disintegrated by the addition of a little water.

Pilular Extracts.—Liquefy an amount of extract, accurately weighed, approximating the quantity directed, by warming with sufficient diluted alcohol, or with the menstruum used in making the extract, stirring with a glass rod. To the thoroughly liquefied extract, contained in a small evaporating dish, add sufficient sawdust or other suitable material (see below) to absorb the liquid, and dry at a temperature not exceeding 60° C. Transfer the dry mixture to a flask or bottle containing the specified quantity of solvent and remove any traces of material adhering to the dish by rinsing with successive small portions of ammonia T.S., using a total of 10 cc. and adding the ammoniacal rinsings to the solvent. Continue as directed under Type Process A, beginning with the words "stopper tightly and shake for one hour."

Fluidextracts.—Pipette fluidextracts directly upon the sawdust, or other suitable material (see below), contained in a small evaporating dish, dry at a temperature not exceeding 60° C., and transfer as directed under *Pilular Extracts* to a flask or bottle containing the specified quantity of solvent. Proceed as directed under Type Process A, beginning with the words "stopper tightly and shake for one hour."

Tinctures.—Concentrate the specified quantity of tincture, by evaporation at a temperature not exceeding 60° C., to a volume of about 10 to 15 cc., add sufficient sawdust or other suitable material (see below) to absorb the liquid, and continue the heat until dry. Transfer the dry mixture, as directed under *Pilular Extracts,* to a flask or bottle containing the specified quantity of solvent. Then proceed as directed under Type Process A, beginning with the words "stopper tightly and shake for one hour."

Absorbents.—The absorbents employed may be sawdust, gauze, cheesecloth, paper pulp, asbestos fiber, absorbent cotton or any similar suitable substance. Sawdust should be clean, not resinous, and must not show the presence of alkaloids when tested as follows: Macerate 5 Gm. in 50 cc. of ether-chloroform mixture and 10 cc. of ammonia T.S., shaking frequently during two hours. Decant 10 cc. of the clear ethereal liquid, evaporate to dryness, and treat the residue with 1 cc. of diluted sulphuric acid. Test portions of the acid liquid for alkaloids with mercuric potassium iodide T.S. and with iodine T.S. If necessary, sawdust may be purified for use in assays by extracting it in a percolator, first with a 1 per cent. solution of sodium hydroxide, then with a 1 per cent. solution of hydrochloric acid, finally washing with distilled water until free from acid and soluble salts, and drying. The last portions of the acid percolate must give no test for alkaloid with mercuric potassium iodide T.S. or with iodine T.S.

TYPE PROCESS D FOR GALENICAL PREPARATIONS—TOTAL EXTRACTION METHOD. **Preparation of the Sample.** *Powdered and Pilular Extracts.*—Liquefy an amount of extract, accurately weighed, approximating the quantity directed, by digesting in about 10 cc. of diluted alcohol, or in the menstruum used in making the extract. Transfer the liquid to a separator containing a portion of the specified solvent, and rinse all traces of the extract from the dish, using small portions of diluted alcohol, or menstruum, and adding the rinsings to the separator. Dilute the alcoholic liquid with an equal quantity of distilled water, add sufficient ammonia T.S. to make it decidedly alkaline, and completely extract the alkaloids by shaking with successive portions of the solvent. Complete the assay as directed under Type Process A, beginning with the words "shaking out with acid."

Fluidextracts.—Pipette fluidextracts directly into a separator containing a portion of the specified solvent, add a volume of distilled water about equal to that of the fluidextract taken, render the liquid alkaline by the addition of ammonia T.S., and completely extract the alkaloids by shaking out with successive portions of the solvent. Complete the assay as directed under Type Process A, beginning with the words "shaking out with acid."

Tinctures.—Concentrate the specified quantity of tincture, by evaporation at a temperature not exceeding 60° C., to a volume of about 10 to 20 cc. Transfer the concentrated liquid to a separator containing a portion of the specified solvent, and rinse all traces of the liquid from the dish, using small portions of diluted alcohol, and adding the rinsings to the separator. Add a volume of distilled water equal to that of the alcoholic liquid, render the liquid alkaline by the addition of ammonia T.S., and completely extract the alkaloids by shaking out with successive portions of the solvent. Complete the assay as directed under Type Process A, beginning with the words "shaking out with acid."

Refractive Index

(U. S.)

When a ray of light passes from one transparent substance into another of different density, it is deflected, except when it enters perpendicularly to the surface of contact. The direction of the deviation is dependent upon the difference of density of the two substances; the extent is also influenced by this difference.

This deviation is termed "refraction." When the ray passes from a substance of given density to one of greater density (*e.g.*, from air into glass) the refraction is towards the perpendicular meeting the surface at the point of contact; when passing from a substance of greater density to one of less (*e.g.*, from water into air) the ray deviates from the perpendicular at the point of contact.

Quantitative measurements of refraction are expressed as "indices of refraction," the index being the figure obtained by dividing the sine of the angle that the incident ray makes with the perpendicular, by the sine of the angle that the refracted ray makes with the same perpendicular; that is, it is the ratio between these sines. Thus, the ratio for a ray of light passing from air into water at standard temperature is about 4:3 or, expressing it decimally and with greater exactness, 1.336. This is, therefore, the index of refraction of water. The determination of the refractive index is accomplished by means of optical instruments known generally as *refractometers*, which are of several types. Some of these give figures on an arbitrary scale, the actual refractive index being ascertained by consulting a table.

As the exact temperature at which the examination is made is of great importance, all of the instruments are provided with attachments for circulating water of the proper temperature about the prisms or about the vessel containing the liquid to be observed, and are also equipped with thermometers for observing the temperature very closely.

The principal instruments in use are as follows:

Pulfrich refractometer.—This instrument is used chiefly for purely scientific investigations. It is adapted for use with liquids and solids of all degrees of refractive power. When a liquid is to be examined, it is placed in a small cylindrical glass vessel immediately above the observation prism. When solids are to be examined, the glass cylinder is removed and the solid (previously polished) is placed in direct contact with the observation prism. The reading of this instrument is made by noting a boundary line between a light and a dark field in its position with reference to a graduated scale upon which the refractive index is directly expressed.

The Abbe refractometer.—This is an instrument of wide utility, designed primarily for the examination of liquids. Only a few drops of the liquid are required for an observation. This is spread in a thin film between the two observation prisms. The index of refraction is also read off directly upon the scale of this instrument, in which, as in the Pulfrich refractometer, a boundary line between a light and a dark field is the observation line.

The Zeiss butyro-refractometer.—This instrument is especially designed for the examination of fixed oils and fats. It is not applicable to aqueous or alcoholic liquids. The distinctive line for observation in this instrument is the border line of total reflection which is a narrow line capable usually of being accurately read to within a tenth of a unit of the arbitrary scale used. Sometimes this observation line is accompanied by a blue and a red fringe or haze which interferes with the accuracy of the reading. Should a close reading be mpossible on this account it will be found necessary to use the monochromatic sodium flame for the observation (see under *Optical Rotation*).

Zeiss immersion refractometer.—This is adapted for the examination of aqueous, oily, or alcoholic liquids. The distinctive line for observation is as described under the preceding instrument, the border line of total reflection in this case being much sharper and capable of being more accurately read.

For making observations of the entire range of pharmacopœial substances, the Abbe instrument is the one generally selected, the Pulfrich instrument not being in common use, and the Zeiss butyro- and immersion refractometers not covering the entire range necessary.

Rosin Test

(U. S.)

For testing for rosin as an adulterant in resins, gum resins and balsams, place in a small mortar 1 Gm. of the substance, powdered or crushed if necessary, and add 10 cc. of purified petroleum benzin unless the substance contains free cinnamic or benzoic acid, in which case the petroleum benzin should be replaced by xylene. Triturate well for one or two minutes, filter into a test tube, and add to the filtrate 10 cc. of a fresh aqueous solution of copper acetate (1 in 200). Shake well and allow the liquids to separate: the benzin or xylene layer should not show a green color (*rosin*).

Saponification Value

(U. S.)

The saponification value is the number of milligrammes of potassium hydroxide required to neutralize the free fatty acids and saponify the esters of 1 Gm. of a fat, oil, wax, etc. It is determined as follows: Place from 1.5 to 2 Gm. of the filtered fat or oil, accurately weighed, in a flask of from 200 to 250 cc. capacity, and add to it exactly 25 cc. of alcoholic half-normal potassium hydroxide (page 1571). Insert into the neck of the flask, by means of a perforated stopper, a glass tube from 70 to 80 cm. in length and from 5 to 8 mm. in diameter, and heat the flask on a water bath for half an hour, frequently rotating the contents. Then add 1 cc. of phenolphthalein T.S. and titrate the excess of potassium hydroxide with half-normal hydrochloric acid. Make a blank test at the same time, using exactly the same amount of alcoholic half-normal potassium hydroxide. The difference in the number of cc. of half-normal hydrochloric acid consumed in the actual test and in the blank, multiplied by 28.06 and divided by the weight of the fat or oil taken, gives the saponification value.

Solubilities

The statements concerning solubilities quoted in this Pharmacopœia are not intended as physical constants in the strict sense of this term, but primarily as information required by physicians and pharmacists in connection with the preparation and dispensing of medicines.

The solubility of Pharmacopœial compounds in given solvents is considered to be of minor importance as a means for their identification or determination of purity, as the other tests contained in the description of each article in the text cover both identity and purity.

The following points must be observed in the accurate determination of solubilities: 1. Purity of both the dissolved substance and the solvent is essential since impurities in either affect the solubility to a greater or less extent. 2. Constancy of temperature must be accurately maintained during the course of the determination. 3. Complete saturation must be secured. 4. Accurate analysis of the saturated solution and correct expression of the results are imperative. In connection with the above named essential features of a correct solubility determination, attention must be given to the varying rates of solution of different compounds, and to the marked effect of the degree of fineness of the particles upon the time required for the saturation of the solution. In general, it may be said that an equipment comprising a thermo-regulator and a constant agitation device is indispensable for accurate solubility determinations.

The solubility data given throughout this volume have for the most part been determined under the above described conditions, and will, therefore, frequently show a somewhat greater solubility than would be found in the daily experience of most pharmacists.

When in Pharmacopœial texts it has not been possible, or in some instances not desirable, to indicate exact solubility, a descriptive term has been used. The following table indicates the meaning of such terms:

	Solvent
"Very soluble"	Less than 1 part.
"Freely soluble"	From 1 to 10 parts.
"Soluble"	From 10 to 30 parts.
"Sparingly soluble"	From 30 to 100 parts.
"Slightly soluble"	From 100 to 1000 parts.
"Very slightly soluble"	From 1000 to 10,000 parts.
"Practically insoluble"	More than 10,000 parts.

Method for Determining Solubilities.—In brief, this consists in preparing a saturated solution of the given substance and ascertaining, by analysis, the amount present in a definite quantity of the solution. Complete saturation can be attained most readily by constant stirring or agitation by means of a suitable mechanical contrivance. A simple apparatus for this purpose consists of a test tube of medium size fastened upright in a water bath maintained at constant temperature. The solvent and excess of solids are placed in the tube and stirred by means of a motor-driven rotating glass spiral. After a given period of stirring, a definite weight of the clear solution is analyzed and the stirring continued for an additional period of several hours. If analysis shows no increase of dissolved substance after the second period of stirring, the result is to be taken as the solubility at the particular temperature. Minute details of methods for determining solubilities are described in Bulletin No. 67 of the Hygienic Laboratory, U. S. Public Health Service.

Sterilization

(U. S.)

The term "sterilization" as employed in the practice of medicine and pharmacy means the destruction or removal of bacteria or their spores and other living organisms. This may be accomplished in various ways, depending upon the nature of the material to be sterilized.

A sterile condition can be maintained only so long as the substance or material is kept from contact with air or other media which may carry micro-organisms.

The important subject of sterilization cannot be treated exhaustively, nor can the details of scientific technique be fully described in this chapter.

Two of the chief reasons for failure in attempted sterilization are (*a*) lack of penetration of the maximum degree of heat to all parts of the substances to be sterilized, due to insufficient time, too close packing, or a source of heat not sufficiently powerful to secure and maintain the desired temperature throughout the entire contents of the sterilizer, and (*b*) in the case of moist sterilization, incomplete saturation of the materials and surfaces to be sterilized. Temperatures necessary for dry sterilization are much higher than those needed for moist sterilization, so that if the steam is superheated or mixed with dry air, the sterilization may be insufficient.

Suggested methods for the sterilization of different classes of material are as follows:

Glass and Metal Utensils.—These may be sterilized by heating at a temperature of 170° C. maintained for two hours in a hot-air sterilizing oven, or in a closed vessel (autoclave) under steam pressure at a temperature of 115° C. maintained for thirty minutes. In steam sterilization, thorough saturation may be provided by arranging the utensils in the sterilizer with unstoppered openings down so that there will be no dead horizontal air spaces, or by the use of a preliminary vacuum to allow the steam to displace the air in all parts, or by insuring that all utensils contain at least one-eighth of one per cent. of their volume of water when placed in the autoclave. As the presence of even a minute quantity of alkali is objectionable in glass containers in certain cases, the process of sterilization should in such instances be preceded by a thorough cleansing of the bottle, ampule, or other receptacle with 1 per cent. hydrochloric acid, followed by a thorough rinsing with distilled water. Relatively insoluble glass should be used and sterilization should be by dry heat rather than by steam.

Cork stoppers should not be used for containers to be sterilized. Cotton stoppers may be employed, and when used may be wrapped in a layer of gauze and covered with stout paper or tinfoil as described under *Aqua Destillata Sterilisata.* Rubber stoppers should be wrapped and should be sterilized separately or attached to the outside of the necks of the containers. These stoppers should be long enough so that they may be inserted and removed without touching the lip of the container with the fingers. The sterilized wrapper of the stopper may be used as a cap. Glass-stoppered containers are sterilized preferably by dry heat, capped, and the stopper separated from tight contact with the neck of the container by a strip of paper.

The flame from a Bunsen burner applied directly to a surface for ten seconds may be used for sterilizing surfaces which are not adversely affected by such application.

Heating in a current of steam for thirty minutes, or boiling for five minutes in water, or in an aqueous 0.1 per cent. solution of sodium bicarbonate (to prevent rusting), will kill all non-spore-bearing organisms and some spore-bearing organisms.

Articles Made of Rubber.—Rubber tubing and rubber stoppers should not be sterilized by hot air, but by steam under pressure, with the precautions indicated above, or by boiling for thirty minutes in a 2 per cent. aqueous solution of cresol or phenol.

Medicinal Substances Not Easily Decomposed by Heat.—If in aqueous solution, these substances should be sterilized by steam under pressure, as described under *Glass and Metal Utensils.* In order that the exposure to heat may be the shortest which will effect thorough sterilization, the container should not be of thick glass and should be of as small a capacity as can conveniently be used. The preliminary heating before the temperature of 115° C. is reached may be shortened by admitting the steam to the autoclave under pressure from a separate generating plant, delivering a pressure constantly above eighteen pounds. The stoppers should be of cotton, as above described, and a wrapped rubber stopper should be attached to each container unless the contents are for immediate use.

If the substances are dry or oily, they should be sterilized by dry heat, preferably in glass-stoppered containers, as described under *Glass and Metal Utensils.* Cap the utensil or container with parchment paper before sterilization for protection against contamination and do not remove the paper until the substance is to be used.

Medicinal Substances Which Are Decomposed by Heat Above 100° *C. and in Which Bacteria May Multiply.*—These substances may be rendered approximately sterile by *fractional sterilization* on three successive days at 100° C. in boiling water or in streaming steam. If boiling water is used, the substances should be contained in glass-sealed ampules and be kept entirely immersed in the water by means of a metal screen or other weight; the water is then boiled at 100° C. for fifteen minutes and this is repeated on each of the three days. After completion of the sterilization, the ampules are tested for permeability and any showing permeability to liquid are discarded. If streaming steam is used, the substances should be in containers of thin, heat-resistant glass of not over 100 cc. capacity each, stoppered with cotton as above described, and the heating chamber should be double-walled; steam is admitted continuously to the heating chamber in sufficient volume to maintain a temperature of 100° C. for thirty minutes, as indicated by a thermometer with the bulb placed close to the containers, and this is repeated on each of the three successive days. In both methods of fractional sterilization, by boiling water and by streaming steam, the containers should be kept at 35° to 40° C. during the two days between the successive heatings.

Medicinal Substances Readily Decomposed or Damaged by Heat.—Substances of solutions which are decomposed when subjected to heat as directed in the preceding section (this includes solutions of many alkaloids) may be prepared in an approximately sterile condition as directed below:

METHOD I.—Filter the liquid through a sterilized stone or porcelain filter (which has previously been tested to prove its efficiency in removing bacteria) into a sterile container protected by a sterile cover. Sterile rubber or glass tubing may be used to connect the filter with the container.

METHOD II.—Sterilize all utensils which will come in contact with the substance, such as scale-pans, or paper, spatulas, funnels, etc., either by steam, followed by drying, or by hot air, or by the Bunsen flame. After weighing out the required amount of substance, dissolve it in the required amount of sterile distilled water in a sterile, glass-stoppered container. Should the solution require filtration, use a sterilized funnel and filter paper and collect the filtrate in a sterilized container, closing it with a sterilized rubber stopper. The filtration must be conducted under a cover and in such a manner that no contamination will result.

Emulsions in Glycerin or Oil.—Approximately sterile solutions or emulsions in glycerin or oil may be prepared in the following manner: Heat glycerin or oil in flasks of thin glass containing not over 50 cc. each, for two hours at from 120° to 130° C. in a dry air sterilizer, then introduce the sterile or approximately sterile medicinal substances after the liquid has cooled. The desired medicament may be incorporated by triturating it with a sterilized pestle and mortar containing the previously sterilized medium (glycerin or oil) and the solution or emulsion should then be quickly transferred to a sterilized glass container.

Surgical Dressings.—Cotton, gauze, and ligatures (except catgut and other absorbable material) may be rendered sterile by steam under pressure or by hot air under the conditions and precautions previously indicated. It should be remembered that all surgical materials are not amenable to such thorough treatment without more or less deterioration taking place. Surgical dressings must be wrapped and packed in such a manner as to permit the penetration of steam or dry heat and at the same time so as to prevent all subsequent contamination with bacteria when removed from the sterilizer. The wrappers should be so folded that the packages may be unwrapped at the time of use without touching the contents.

Thermometers

(U. S.)

General Requirements.—The bulbs are to be of normal Corning thermometer glass, or of Jena 16III normal glass. The stems may be made of other white enamel back glass tubing having a circular cross section; the diameter of the capillary must not be greater than 0.1 mm. The diameter of the stem is to be 5.5 mm. (to within ∓ 0.3 mm.), and the maximum diameter of the bulb must not be greater than the diameter of the stem. The thermometers are to have a pear-shaped reservoir at the upper end of the capillary having a volume at least equal to the volume of the entire graduated portion of the stem. The upper end of the stem is to have a small glass ring.

Graduation.—The thermometers are all to be graduated in 0.5° (one-half degree) intervals. The 1° graduation marks are to be longer than those for the half degrees, the longer graduations preferably extending equally to the right and left of the shorter marks. The graduation marks are to be clean cut and fine, and to be uniformly well-filled with insoluble colored pigment.

Numbering.—The 100° graduations (the 0°, 100°, 200°, 300° graduations on the different thermometers) are to be numbered in full and the intermediate 5° and 10° graduations are to be numbered 5, 10, 15, etc. ..... 95, 100, 5, 10, 15, ... 95, 200, 5, 10, etc. The numbers must be distinct and easily legible, preferably in such position that they will be upright when the thermometer is vertical. The figures should not be unduly large. It is suggested that the figures opposite the 0°, 100°, 200°, 300° graduations be made about 2 mm. in height and the intermediate numbers 5, 10, 15, etc., somewhat less (about 1.4 mm.).

Annealing.—The thermometers should be so thoroughly annealed that there will be no appreciable change in their indications after long continued exposure to the highest temperature on the scale.

Error of Scale.—The maximum error at any temperature below 100° C. must not exceed 0.5°, nor exceed 1.0° in the interval 100° to 300° C.

Standardization.—The thermometers should be submitted to the Bureau of Standards for standardization, or carefully compared with thermometers actually standardized by the Bureau of Standards.

Filling Under Pressure.—Thermometers reading over 200° C. must be filled under sufficient pressure to prevent the mercury column from boiling or breaking up into small pieces.

Thermometer No. 1.—The thermometer is to be graduated from –10° to 150° C. in half degrees, the length of a 1° interval being 1.5 to 2 mm.

Thermometer No. 2.—The thermometer is to be graduated from 95° or 98° to 300° C. in half degrees, the length of a 1° interval being 1.5 to 2 mm. The length of the thermometer between the lower graduation and the lower end of the bulb should not exceed 50 mm.

Auxiliary Thermometer.—This thermometer is for emergent stem corrections. Use a standard thermometer from 15 to 20 cm. in length and graduated from 20° to 100° C., in degrees.

Thermometers for Boiling Points.—In order to avoid the necessity for an emergent stem correction, it is advisable that an accurately standardized thermometer for the Anschütz type be used for boiling points. If such a thermometer is not available, a thermometer such as is specified above (see Nos. 1 and 2) may be employed, applying the emergent stem correction as described under *Melting Points*, the length of emergent stem being measured, in degrees, from the lower end of the stopper to the highest point of the boiling temperature.

Turbidimetric Tests

(U. S.)

These tests are applied to certain official chemicals, to insure the absence of excessive amounts of chloride or sulphate.

In carrying out these turbidimetric tests, the following points are to be observed: The same quantities of the same reagents must be used in the test of the substance under examination and in the control test. The glass cylinders in which the tests are made must be of the same diameter and match in all other respects as closely as possible. The precipitating reagent must be added to both in immediate sequence.

Chloride.—The prescribed quantity of the substance to be tested is dissolved in from 30 to 40 cc. of distilled water, and the solution neutralized, if necessary, with nitric acid, using litmus paper as indicator. One cc. of nitric acid and 1 cc. of silver nitrate T.S. are added and then sufficient distilled water to make 50 cc. After mixing well and allowing to stand five minutes protected from direct sunlight, the turbidity, if any, is compared with that produced in a control test made with the specified volume of fiftieth-normal hydrochloric acid.

Bismuth Salts are first dissolved in a few cc. of distilled water and 2 cc. of nitric acid, then diluted with distilled water to 50 cc.

Sulphate.—The specified quantity of the substance to be tested is dissolved in from 30 to 40 cc. of distilled water, and the solution neutralized if necessary, with hydrochloric acid, using litmus paper as indicator. One cc. of diluted hydrochloric acid and 1 cc. of barium chloride T.S. are added and then sufficient distilled water to make 50 cc. After mixing well, it is allowed to stand for ten minutes and the turbidity, if any, is compared with that produced in a control test made with the specified volume of fiftieth-normal sulphuric acid.

If the solution, after the addition of acid, is not perfectly clear, it is filtered through a filter paper free from chloride or sulphate, then the silver nitrate or the barium chloride is added.

In applying the turbidimetric tests to salts of heavy metals, which normally show an acid reaction, their aqueous solutions prepared for the test are not to be neutralized.

When the tests for chloride or sulphate are to be applied to a specified volume of a solution of a substance prepared as directed in the text, and the permissible limit for these impurities corresponds to 0.2 cc. or less of fiftieth-normal hydrochloric or sulphuric acid, the solution is not to be further diluted. The control test is also made with the same volume of water (or other specified solvent) as in the test.

Unsaponifiable Matter

(U. S.)

The term "unsaponifiable matter" is understood to mean substances present in oils or fats that are not saponifiable by caustic alkali and are insoluble in water. It is determined as follows: Heat 5 Gm. of the oil or fat under a reflux condenser with a solution of about 2 Gm. of potassium hydroxide in 40 cc. of alcohol for an hour or until completely saponified. Evaporate most of the alcohol, dissolve the residue in 50 cc. of hot distilled water, and transfer the solution to a separator, rinsing the flask with 25 or 50 cc. of hot distilled water. Cool, and shake with two successive portions of 50 cc. each of ether, adding a few cc. of alcohol to facilitate the separation of the two liquids. Wash the combined ether extracts with small portions of distilled water until the water is not reddened by phenolphthalein T.S. Transfer the ether solution to a tared dish or beaker, evaporate the ether on a water bath, dry the residue at a temperature not exceeding 100° C., and weigh.

Vegetable Drugs, Sampling and Analysis

(U. S.)

SAMPLING FROM ORIGINAL CONTAINERS.—I. It is recommended that gross samples of vegetable drugs in which the component parts are 1 cm. or less in any dimension, and all powdered or ground drugs, be taken by means of a sampler which removes a core from the top to the bottom of the container, not less that two cores being taken in opposite directions; that when the total weight of the drug to be sampled is less than 100 kilos (200 pounds), at least 250 Gm. shall constitute an *official sample*; that when the total weight of the drug to be sampled is in excess of 100 kilos, repeated samples shall be taken by the above method, and according to the schedule given below, mixed and quartered, two of the diagonal quarters being rejected, the remaining two quarters being combined and carefully mixed, and again subjected to a quartering process in the same manner until two of the quarters weigh at least 250 Gm., which latter quarters shall constitute an *official sample.*

II. It is recommended that gross samples of vegetable drugs in which the component parts are over 1 cm. in any dimension be taken by hand; that when the total weight of the drug to be sampled is less than 100 kilos, at least 500 Gm. shall constitute an *official sample,* and this shall be taken from different parts of the container or containers; that when the total weight of the drug to be sampled is in excess of 100 kilos, repeated samples shall be taken by the above method and according to the schedule below, mixed and quartered, two of the diagonal quarters being rejected, and the remaining two quarters being combined and carefully mixed, and again subjected to a quartering process in the same manner until two of the quarters weigh not less than 500 Gm., which latter quarters shall constitute an *official sample.*

SCHEDULE RECOMMENDED FOR SAMPLING

Number of packages in shipment	*Number of packages to be sampled*
1 to 10	1 to 3
10 to 25	2 to 4
25 to 50	3 to 6
50 to 75	6 to 8
75 to 100	8 to 10

When over 100, the total number sampled should not be less than 10.

III. When the total weight of a drug to be sampled is less than 10 kilos it is recommended that the above methods be followed but that somewhat smaller quantities be withdrawn, and in no case should the final *official sample* weigh less than 125 Gm.

IV. In addition to the withdrawing of *official samples* according to methods I, II, and III, the *official sample* may consist of the total amount of a direct purchase made by Federal, State or Municipal Food and Drugs' Act enforcement officials.

Foreign Organic Matter in Whole Vegetable Drugs.—V. Withdraw from 25 to 500 Gm. from the *official sample,* spread out in a thin layer, and separate the foreign organic matter by hand as completely as possible. Weigh and determine the per cent. of foreign organic matter, calculated upon the weight of drug taken. The maximum quantity should be used for coarse or bulky drugs.

Preparation of Vegetable Drugs for Analysis.—VI. The following method is to be used where specific directions are not otherwise given in the text: Withdraw as much as may be necessary of the *official sample* by quartering, taking pains to see that the portion is representative of the gross sample. In the case of unground or unpowdered drugs, grind the withdrawn sample so that it will pass through a No. 20 standard-mesh sieve. If the sample cannot be ground reduce it to as fine a state as possible. Mix by rolling it on paper or sampling cloth, spread it out in a thin layer and withdraw the portion for analysis.

Total Ash in Vegetable Drugs.—VII. Accurately weigh a quantity of the ground drug, representing from 2 to 4 Gm. of the air-dried material, in a tared crucible and incinerate at a low temperature, not to exceed very dull redness, until free from carbon, and determine the weight of the ash. If a carbon-free ash cannot be obtained in this way, exhaust the charred mass with hot distilled water, collect the insoluble residue on an ashless filter paper, incinerate the residue and filter paper until the ash is white or nearly so, then add the filtrate, evaporate it to dryness and heat the whole to a low redness. If a carbon-free ash cannot be obtained in this way, cool the crucible, add 15 cc. of alcohol, break up the ash with a glass rod, burn off the alcohol, and again heat the whole to a low redness. Finally determine the weight of the ash. Calculate the percentage of total ash from the weight of the drug taken.

Acid-insoluble Ash in Vegetable Drugs.—VIII. Boil the ash obtained under paragraph VII with 25 cc. of diluted hydrochloric acid for five minutes, collect the insoluble matter in a Gooch crucible or on an ashless filter, wash with hot distilled water, ignite and weigh. Determine the per cent. of acid-insoluble ash calculated from the weight of drug taken.

Moisture in Vegetable Drugs.—IX. Preparation of Sample. In the case of unground or unpowdered drugs, prepare about 10 Gm. of the *official sample* by cutting, granulating, or shredding, so that the parts are about 3 mm. in thickness. Seeds or fruits smaller than 3 mm. should be cracked. High-speed mills should not be used for preparing the sample and care should be taken that no appreciable amount of moisture is lost during the preparation, and that the portion taken is representative of the *official sample.*

Moisture Method for Drugs Containing no Constituents Volatile at 100° C.—X. Accurately weigh about 10 Gm. of the drug as prepared under paragraph IX in a tared evaporating dish. Dry at a temperature of 100° C. for five hours, and weigh. Continue the drying and weighing at one hour intervals until the loss is not more than 0.25 per cent. in one hour's drying.

Moisture Method for Drugs Containing Ether-soluble Constituents Volatile at 100° C.—XI. Proceed as under paragraph X. Determine the volatile ether-soluble extractive (paragraph XIII) and subtract the percentage of volatile ether-soluble extractive from the percentage lost during drying. The difference represents the percentage of moisture.

Crude Fiber.—XII. Exhaust a weighed quantity of the prepared drug (paragraph VI), representing about 2 Gm. of the drug, with ether or use the residue from the determination of the volatile ether-soluble extractive (paragraph XIII). Add 200 cc. of boiling sulphuric acid solution, adjusted to exactly 1.25 per cent. by titration, to the ether-exhausted drug, in a 500 cc. flask, and connect the flask with a reflux condenser, the tube of which passes only a short distance below the rubber stopper, into the flask. Heat the mixture to boiling and continue the boiling exactly thirty minutes. Then filter the mixture through a filter and wash the residue on the filter with boiling distilled water until the washings are no longer acid. Rinse the residue back into the flask with 200 cc. of boiling sodium hydroxide solution, adjusted to exactly 1.25 per cent. by titration and free from sodium carbonate. Again heat the mixture to boiling and continue the boiling exactly thirty minutes under the reflux condenser as described under the treatment with acid, then rapidly filter through a tared filter, wash the residue with boiling distilled water until the washings are neutral, dry it at 110° C. until of constant weight, and note the weight. Now completely incinerate the dried residue and weigh the ash: the loss of weight is considered to be the weight of the crude fiber.

NOTE: The boiling with acid and alkali should continue *exactly* thirty minutes from the time that the liquid (which is cooled below the boiling point by adding it to the cold flask) again boils. After the solution has been brought to boiling, the flame should be turned low enough just to maintain boiling. During the boiling the flask should be gently rotated from time to time to catch any particles which may adhere to the walls of the flask. A slow current of air introduced into the flask during the boiling operation will be very helpful to keep down excessive frothing.

Volatile Ether-Soluble Extractive.—XIII. Extract completely 2 Gm. of the prepared drug (paragraph VI), dried over sulphuric acid for not less than twelve hours, by subjecting it, during twenty hours, to the action of dehydrated ether in continuous extraction apparatus. Transfer the ethereal solution to a tared porcelain dish and allow it to evaporate spontaneously. Then dry it over sulphuric acid during eighteen hours and weigh the total ether extract. Now heat the extract gradually up to 110° C. until the weight becomes constant: the loss in weight during the heating represents the volatile portion of the extract.

Non-volatile Ether-soluble Extractive.—XIV. Proceed as directed under *Volatile Ether-soluble Extractive* (paragraph XIII). The weight of the extract after drying in a desiccator and then at 110° C. until of constant weight represents the non-volatile portion of the extract.

Alcohol-soluble Extractive.—XV. Macerate about 2 Gm. of the prepared drug (paragraph VI), accurately weighed, in about 70 cc. of alcohol in a suitable flask. Shake during eight hours at thirty minute intervals and allow to stand for sixteen hours without shaking. Filter and wash the flask and residue with small portions of alcohol until the filtrate measures 100 cc. Evaporate a 50 cc. aliquot portion to dryness in a suitable tared dish on a water bath and dry to constant weight at 110° C. Calculate the percentage of anhydrous extractive from the weight of drug taken.

Diluted Alcohol-soluble Extractive.—XVI. Proceed as directed under paragraph XV, using diluted alcohol instead of alcohol.

Water-soluble Extractive.—XVII. Proceed as directed under paragraph XV, using distilled water instead of alcohol.

Extractive, Soluble in Purified Petroleum Benzin.—XVIII. Extract completely about 2 Gm. of the prepared drug (paragraph VI), accurately weighed, by subjecting it during twenty hours to the action of purified petroleum benzin in a continuous extraction apparatus. Transfer the benzin solution to a tared porcelain dish and allow it to evaporate spontaneously. Then dry it over sulphuric acid for eighteen hours and weigh. Calculate the percentage of anhydrous extractive from the weight of drug taken.

Viscosity

(U. S.)

Viscosity is a term used to denote the relative degree of fluidity of a liquid. Scientifically, viscosity may be defined as the force which will move a unit area of plane surface, with unit speed relative to another parallel plane surface, from which it is separated by a layer of the liquid of unit thickness. The viscosity of a liquid varies with the temperature, the higher the temperature the lower the viscosity and *vice versa*.

Several methods of expressing viscosity are in use. The method adopted in this Pharmacopœia is "kinematic viscosity" which is based on absolute viscosity. The kinematic viscosity is the ratio of the absolute viscosity expressed in poises over the density $\left(\frac{\mu}{\gamma}\right)$. The poise is the unit of absolute viscosity and is equivalent to the force of one "dyne-second per square centimeter."

As a poise is rather large, one-hundredth of a poise, or a centipoise (cp.), is now generally accepted as a more convenient unit for absolute viscosity. The centipoise is almost exactly the viscosity of water at 20° C.

Methods of determining absolute or kinematic viscosity are described in the U. S. Bureau of Standards papers S–298, T–100, and T–112. Instead of the direct determination of absolute or kinematic viscosity which is rather difficult, the viscosity may be determined with either the Engler or Saybolt viscosimeters and the results obtained with these instruments converted into the kinematic viscosity with the aid of the conversion tables given below.

In the Engler instrument, viscosity is expressed in "Engler degrees." These are obtained by dividing the time of discharge for the liquid being tested by the time of discharge for water at 20° C.

With the Saybolt Universal Viscosimeter, results are expressed as the time of discharge, in seconds, of the liquid being tested. In the United States the Saybolt Universal Viscosimeter is generally used for the determination of viscosity of lubricating oils. This instrument, in brief, consists of a metallic cylinder to contain the liquid under examination and having an outlet in the bottom closed with a cork stopper. It is surrounded with a jacket which serves as a bath to heat the liquid under examination to the specified temperature, the jacket being provided with facilities for stirring and heating the bath. Thermometers, a flask graduated at 60 cc., and a stop watch accompany the apparatus.

To determine the viscosity, the bath is first filled with a suitable liquid, and heated to a few degrees above the temperature at which the test is to be made, then the cylinder is filled with the liquid under examination, and when the liquid in the cylinder registers the specified temperature, adjust the volume, place the flask, graduated at 60 cc., under the outlet, and quickly remove the cork, immediately starting the stop watch. When the oil in the flask reaches the 60 cc. mark, stop the watch. The time, in seconds, required to fill the flask to the 60 cc. mark represents the viscosity of the liquid. A fuller description of the apparatus and the details of manipulation are given in the U. S. Bureau of Mines, Technical Paper, 323 A.

Table for Conversion of Saybolt or Engler Viscosity into Kinematic Viscosity

(U. S.)

Column 1 = Viscosity, Saybolt Universal, sec.
Column 2 = Kinematic viscosity, poises divided by Gm. per cc.
Column 3 = Viscosity, Engler degrees.

1	2	3	1	2	3	1	2	3	1	2	3
50	0.074	1.59	128	0.273	3.86	196	0.429	5.85	274	0.601	8.09
52	0.080	1.65	130	0.278	3.93	198	0.433	5.90	276	0.605	8.14
54	0.086	1.71	132	0.282	3.98	200	0.437	5.96	278	0.609	8.18
56	0.092	1.77	134	0.287	4.04	202	0.442	6.02	280	0.614	8.25
58	0.097	1.82	136	0.292	4.10	204	0.446	6.08	282	0.618	8.29
60	0.103	1.88	138	0.297	4.16	206	0.450	6.13	284	0.622	8.35
62	0.109	1.94	140	0.301	4.22	208	0.455	6.19	286	0.627	8.42
64	0.114	2.00	142	0.306	4.27	210	0.460	6.26	288	0.631	8.48
66	0.120	2.05	144	0.310	4.32	212	0.464	6.31	290	0.636	8.55
68	0.125	2.11	146	0.315	4.39	214	0.468	6.36	292	0.640	8.61
70	0.130	2.17	148	0.320	4.45	216	0.473	6.42	294	0.645	8.68
72	0.136	2.23	150	0.324	4.50	218	0.477	6.47	296	0.649	8.72
74	0.141	2.29	152	0.328	4.55	220	0.482	6.54	298	0.654	8.78
76	0.146	2.35	154	0.333	4.61	222	0.487	6.60	300	0.659	8.85
78	0.151	2.40	156	0.338	4.68	224	0.491	6.66	302	0.663	8.90
80	0.156	2.46	158	0.342	4.74	226	0.495	6.71	304	0.667	8.95
82	0.161	2.52	160	0.347	4.81	228	0.499	6.76	306	0.672	9.02
84	0.166	2.58	162	0.352	4.87	230	0.503	6.81	308	0.676	9.07
86	0.171	2.64	164	0.356	4.92	232	0.508	6.87	310	0.680	9.12
88	0.176	2.70	166	0.361	4.98	234	0.512	6.93	312	0.685	9.19
90	0.182	2.76	168	0.365	5.03	236	0.517	6.99	314	0.689	9.24
92	0.186	2.81	169	0.368	5.06	238	0.521	7.04	316	0.693	9.30
94	0.191	2.87	170	0.370	5.09	240	0.526	7.10	318	0.698	9.36
96	0.196	2.93	171	0.372	5.12	242	0.530	7.16	320	0.702	9.41
98	0.201	2.98	172	0.374	5.14	244	0.535	7.21	322	0.707	9.48
100	0.206	3.04	173	0.376	5.17	246	0.539	7.27	324	0.711	9.54
102	0.211	3.10	174	0.379	5.20	248	0.543	7.32	326	0.716	9.59
104	0.215	3.16	175	0.381	5.23	250	0.548	7.38	328	0.720	9.64
106	0.221	3.22	176	0.383	5.26	252	0.552	7.44	330	0.724	9.70
108	0.225	3.27	177	0.385	5.28	254	0.557	7.50	332	0.729	9.77
110	0.230	3.33	178	0.388	5.31	256	0.561	7.56	334	0.733	9.82
112	0.235	3.39	180	0.392	5.37	258	0.566	7.62	336	0.738	9.89
114	0.240	3.45	182	0.397	5.43	260	0.570	7.68	338	0.742	9.94
116	0.244	3.51	184	0.402	5.49	262	0.574	7.73	340	0.746	10.00
118	0.249	3.57	186	0.406	5.55	264	0.579	7.79	342	0.751	10.05
120	0.254	3.63	188	0.410	5.61	266	0.584	7.86	344	0.755	10.10
122	0.259	3.69	190	0.415	5.66	268	0.588	7.91	346	0.759	10.16
124	0.263	3.74	192	0.420	5.73	270	0.592	7.96	348	0.764	10.22
126	0.268	3.80	194	0.424	5.79	272	0.597	8.03	350	0.768	10.28

Vitamine A Assay for Cod Liver Oil

(U. S.)

Cod Liver Oil may be assayed by the following process. When so assayed the Oil should contain at least 50 units per Gm. and must be labelled "This unit is not a measure of the antirachitic activity of Cod Liver Oil." This assay is based upon the estimation of the minimum amount of Cod Liver Oil necessary to meet specific growth-promoting requirements in a standard test animal. The test animals shall be albino rats from a constant source and bred preferably under the control of the experimenter. The vitamine A potency of Cod Liver Oil shall be expressed in units per gramme of oil, the unit to be the minimum daily amount of Cod Liver Oil required to cure induced symptoms of vitamine A starvation in young albino rats, and to cause a gain in weight of from 10 to 20 Gm. within a period of thirty-five days under the conditions of growth and diet specified in this assay.

Place on a vitamine A free diet, rats not less than twenty-five days and not more than twenty-nine days old, and weighing not less than 35 Gm., and not more than 45 Gm. The basal diet is to be composed as follows:

Casein, or desiccated fresh meat, rendered free from vitamine A, ...	18 per cent.
Salt mixture, such as that of Osborne and Mendel[1] or McCollum and Davis,[2].....	4 per cent.
Starch, sufficient to make, ...	100 per cent.

Use sufficient dried brewer's yeast to meet the vitamine B requirements of the animal, mixing it with the basal diet during the vitamine A free period.

The rats shall begin receiving the Cod Liver Oil to be tested after not less than seven days of stationary or declining weight, and from the time of feeding the test oil, they shall be kept in separate cages. The test period shall continue for thirty-five days and the potency of the oil shall be judged from the rat or rats showing a gain on the thirty-fifth day of between 10 and 20 Gm. over the weight at the beginning of the test, and the cure of the induced symptoms of vitamine A starvation.

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[1] See *J. Bi. Chem.*, 1913, xv, page 317.

[2] See *J. Bi. Chem.*, 1918, xxxiii, page 55.

Each test shall be controlled by at least two standard rats which have received no Cod Liver Oil. These animals may serve as controls for any number of concurrent tests on which the same basal diet is used.

No oil shall be labelled as assayed by the U. S. P. method unless it contains at least 50 units per Gm. of Oil.

The diet for rats used as breeders shall be composed as follows:

Finely ground whole wheat,	66 per cent.
Whole milk powder,	33 per cent.
Sodium chloride,	1 per cent.

The antirachitic requirements of the breeders shall be assured.

Reagents, Test Solutions, Indicators, and Volumetric Solutions

(U. S.)

Reagents are substances used in chemical testing or in microscopic examinations.

Test Solutions, abbreviated "T.S.," are solutions of prescribed strength of reagents in appropriate solvents for use in applying tests.

Indicators are reagents or test solutions employed for the purpose of determining the completion of reactions.

Volumetric Solutions are solutions of reagents of accurately determined strength. The strength is usually related to the molecular weight. These solutions are primarily intended for quantitative estimations.

Some official substances are satisfactory for use as reagents or test solutions if they comply with the tests for purity given in the monographs of the Pharmacopœia. Space is conserved by simply referring to these where such is the case. When a substance is not official or when a greater degree of purity is required than is provided for in the monograph, the substance will be found in the following list, with such description and tests as will insure its suitability for the purpose intended.

Reagents, test solutions, volumetric solutions, and indicators should be preserved in bottles or other containers made of glass of a minimum solubility and low alkalinity, and approximately free from lead or arsenic. The bottles must be capable of being tightly closed with appropriate stoppers. When ground glass stoppers are directed for bottles and apparatus which are to contain substances capable of attacking such surfaces, the ground glass surfaces are to be coated with a thin film of petrolatum. Certain reagents and their solutions are affected by light. In such cases, the direction to keep the substances in amber-colored glass bottles should be carefully observed.

Water, wherever mentioned in carrying out tests or as a solvent in preparing test solutions, etc., is always meant to be distilled water.

The chemical formulas when definitely known, immediately follow the titles of the reagents. This is for convenience and is not to be interpreted as meaning that the reagents are of absolute purity and strength.

Amounts of Substances to be Used in Applying Tests.—When not otherwise stated, it is to be understood that a volume of 10 cc. of an aqueous solution of the designated strength is to be used for a test.

Reagents

Acetic Acid, $CH_3.COOH$.—Use *Acidum Aceticum.*

Acetic Acid, Diluted.—Use *Acidum Aceticum Dilutum.*

Acetic Acid, Glacial, $CH_3.COOH$.—Use *Acidum Aceticum Glaciale.*

Acetic Anhydride, $(CH_3CO)_2O$.—A colorless liquid having a pungent odor. Boiling point, about 137° C. Specific gravity, about 1.075 at 25° C. Non-volatile residue at 110° C. not over 0.005 per cent. An aqueous solution (1 in 50) gives no reaction for *chloride.* One Gm., when dissolved in 50 cc. of distilled water and allowed to stand for one hour in a stoppered flask, requires not less than 19.3 cc. of normal sodium hydroxide for neutralization, using phenolphthalein T.S. as indicator, corresponding to at least 90 per cent. of $(CH_3CO)_2O$.

Preserve in glass-stoppered bottles in a cool, dry place. The stoppers should be sealed with paraffin.

Acetone, CH_3COCH_3.—Use *Acetonum.*

Alcohol, C_2H_5OH.—Use *Alcohol.*

Alcohol, Dehydrated (*Absolute Alcohol*), C_2H_5OH.—Use *Alcohol Dehydratum.*

Alcohol, Neutralized.—To a suitable quantity of alcohol, add 2 or 3 drops of phenolphthalein T.S. and just sufficient fiftieth-normal or tenth-normal sodium hydroxide to produce a slight pink color. Neutralized alcohol should be prepared immediately before using.

Aluminum Metallic, Al.—Aluminum in the form of wire.

Ammonium Carbonate, $NH_4HCO_3.NH_4NH_2CO_2$.—In addition to the description and tests for *Ammonii Carbonas*, it must conform to the following tests: Residue upon incineration not over 0.01 per cent. An aqueous solution (1 in 10) gives no reaction for *chloride, phosphate, sulphate, thiocyanate*, or *heavy metals.*

Ammonium Chloride, NH_4Cl.—In addition to the description and tests for *Ammonii Chloridum*, it must conform to the following tests: Residue upon incineration not over 0.03 per cent. An aqueous solution (1 in 10) gives no reaction for *phosphate, sulphate, thiocyanate*, or *heavy metals.* Ammonium chloride employed in the test for lead under citric and tartaric acids and their salts, must also comply with the following special test. Dissolve 3 Gm. in 10 cc. of distilled water, acidified with 1 drop of reagent hydrochloric acid, in a test tube having an internal diameter of about 20 mm., add 10 cc. of clear, colorless hydrogen sulphide T.S., and mix well. The liquid must show no color when viewed downward against a white background.

Ammonium Nitrate, NH_4NO_3.—Colorless crystals, or white granules, very soluble in water, slightly soluble in alcohol. Residue upon incineration not over 0.03 per cent. An aqueous solution (1 in 10) gives no reaction for *chloride, phosphate, sulphate, thiocyanate*, or *heavy metals.* An aqueous solution (1 in 20) gives no reaction for *nitrite* when tested as follows: To a solution of 1 Gm. of ammonium nitrate in 20 cc. of distilled water add 2 cc. of diluted sulphuric acid and 1 cc. of metaphenylenediamine hydrochloride T.S.: no yellow or yellowish-brown color develops.

Ammonium Oxalate, $(NH_4)_2C_2O_4.H_2O$.—Colorless crystals, soluble in water. Residue, upon incineration, not over 0.03 per cent. An aqueous solution (1 in 25) gives no reaction for *chloride, phosphate, sulphate,* or *heavy metals.*

Ammonium Sulphate, $(NH_4)_2SO_4$.—Colorless crystals or white granules, very soluble in water. Residue upon incineration not over 0.05 per cent. An aqueous solution (1 in 10) gives no reaction for *chloride, phosphate, thiocyanate,* or *heavy metals.*

Ammonium Vanadate, (*Ammonium Metavanadate*), NH_4VO_3.—A white crystalline powder, slightly soluble in water. Easily decomposed upon heating either dry or in solution.

Amyl Alcohol, $C_5H_{11}OH$.—Colorless, oily liquid. Boiling point, 128° to 132° C. Specific gravity, about 0.812 at 25° C. Miscible with alcohol, ether, chloroform, carbon disulphide, petroleum benzin, benzene, and fixed or volatile oils. Slightly soluble in water. Non-volatile residue at 100° C., not over 0.005 per cent.

Aniline, $C_6H_5NH_2$.—A colorless or nearly colorless, strongly refractive, oily liquid. Boiling point, 182° to 184° C. Specific gravity, about 1.020 at 25° C. Soluble in water; miscible with alcohol, ether, and fixed or volatile oils. Five cc. of aniline dissolved in 10 cc. of hydrochloric acid, produces a clear solution. Upon diluting this solution with 15 cc. of distilled water and cooling to 15° C., the liquid does not become more than slightly cloudy.

Preserve in amber-colored bottles. Upon keeping, it often assumes a yellow or brown color, and should then be distilled before using.

Aniline Sulphate, $(C_6H_5NH_2)_2H_2SO_4$.—White or nearly white crystals, very soluble in water, slightly soluble in alcohol.

Arsenic Trioxide, As_2O_3.—Use *Arseni Trioxidum.*

Asbestos.—The silky, well-matted variety of long-fiber asbestos. When moistened and rolled between the thumb and finger, it forms a compact mass. For use as a filtering medium for the Gooch crucible, boil the asbestos for one hour with diluted hydrochloric acid, and wash it with boiling distilled water until free from all acid.

Barium Chloride, $BaCl_2.2H_2O$.—Colorless crystals, freely soluble in water, slightly soluble in alcohol and in concentrated hydrochloric acid. An aqueous solution (1 in 20) is neutral and gives no reaction for *nitrate, chlorate,* or *heavy metals.* Dissolve 2 Gm. of barium chloride in 100 cc. of distilled water, add a few drops of hydrochloric acid, heat to boiling, then add 20 cc. of diluted sulphuric acid, and set aside for at least twelve hours. Filter, evaporate the filtrate, and ignite. The weight of the residue does not exceed 0.002 Gm. (*other fixed bases*). Shake 1 Gm. of finely powdered barium chloride with 20 cc. of dehydrated alcohol during five minutes, filter, evaporate the filtrate, and ignite. The weight of the residue does not exceed 0.002 Gm. (*strontium and calcium*).

Barium Hydroxide, $Ba(OH)_2.8H_2O$.—Colorless crystals, soluble in water, very soluble in boiling water. An aqueous solution (1 in 20) gives no reaction for *chloride* or *heavy metals.* Dissolve 2 Gm. of barium hydroxide in 100 cc. of distilled water, add 5 cc. of hydrochloric acid, heat to boiling, then add 15 cc. of diluted sulphuric acid, and set aside for at least twelve hours. Filter, evaporate the filtrate, and ignite. The weight of the residue does not exceed 0.003 Gm. (*other fixed bases*).

Assay.—One Gm. dissolved in distilled water, and titrated with normal hydrochloric acid, using methyl orange T.S. as indicator, shows not less than 99 per cent. of $Ba(OH)_2.8H_2O$.

Preserve in tightly-stoppered containers to prevent access of carbon dioxide.

Barium Nitrate, $Ba(NO_3)_2$.—Colorless crystals, soluble in water, freely soluble in boiling water. An aqueous solution (1 in 20) gives no reaction for *heavy metals* and meets the requirements of the test for *other fixed bases* under *barium chloride.* Converted into chloride by twice evaporating to dryness with hydrochloric acid, it meets the requirements of the tests for *strontium* and *calcium* under *barium chloride.*

Benzene (*Benzol*), C_6H_6.—A colorless, transparent liquid. Boiling point, 79° to 81° C. Congealing point, about 5° C. Specific gravity, about 0.876 at 25° C. Insoluble in water, miscible with alcohol, ether, and with fixed or volatile oils. When equal volumes of benzene and sulphuric acid are shaken together in a glass cylinder during fifteen minutes, the acid upon separation is not colored. Add a few mgm. of isatin, shake well, and allow to stand for thirty minutes. The acid does not acquire a blue or green color (*thiophene*). Non-volatile residue at 100° C., not over 0.01 per cent.

Benzidine (*Paradiaminodiphenyl*), $(C_6H_4NH_2)_2$.—A white or slightly reddish crystalline powder. Sparingly soluble in cold water, slightly soluble in boiling water, alcohol, and ether. Melting point, about 128° C. A solution (1 in 50) in 2 per cent. hydrochloric acid gives no reaction for *sulphate.* Residue upon incineration not over 0.05 per cent.

Benzin, Petroleum.—Use *Benzinum Purificatum.*

Betanaphthol, $C_{10}H_7OH$.—Use *Betanaphthol.*

Bromine, Br.—A dark reddish-brown fuming, corrosive volatile liquid containing not less than 99 per cent. of Br and not more than 1 per cent. of Cl. Specific gravity, about 3.1 at 25° C. Soluble in about 30 parts of water, soluble in alcohol and in ether (with gradual decomposition of the solvents). Dissolve about 1 cc. of bromine in 50 cc. of sodium hydroxide T.S. and allow to stand for six hours: the solution remains clear (*organic bromine compounds*). Agitate 10 cc. of a saturated aqueous solution of bromine with 1 Gm. of reduced iron until the solution is nearly colorless. Filter and add 1 cc. of starch T.S. and 1 cc. of ferric chloride T.S.: no blue color develops (*iodine*). Non-volatile residue at 100° C., not over 0.01 per cent.

Assay.—Dissolve 10 Gm. of potassium iodide in 25 cc. of distilled water, introduce the solution into a 100 cc. measuring flask, stopper, and determine accurately the weight of the flask and its contents. Add about 1 Gm. of bromine to the contents of the flask, determine its exact weight, then fill the flask to the mark with distilled water, and titrate 25 cc. of this solution with tenth-normal sodium thiosulphate, using starch T.S. as indicator. Each Gm. of bromine (containing not more than 1 per cent. of chlorine) corresponds to not more than 126.7 cc. of tenth-normal sodium thiosulphate. Preserve in glass-stoppered bottles, in a cool place, the bottles being enclosed in larger vessels with the space between filled with some substance, capable of absorbing bromine.

Cadmium and Potassium Iodide.—A mixture of equal weights of cadmium iodide and potassium iodide. An aqueous solution (1 in 20) shows no *free iodine.*

Cadmium Chloride, $CdCl_2.2H_2O$.—Small, colorless crystals, efflorescent in dry air. Very soluble in water, soluble in alcohol.

Cadmium Iodide, CdI_2.—Colorless crystals, becoming yellow upon exposure to light and air. Very soluble in water and in alcohol, sparingly soluble in ether and acetone.

Calcium Carbonate, $CaCO_3$.—Use *Calcii Carbonas Præcipitatus.*

Calcium Chloride, $CaCl_2.2H_2O$.—In addition to the description and tests for *Calcii Chloridum*, page 252, it must conform to the following tests: One Gm. dissolves completely in 10 cc. of alcohol. An aqueous solution (1 in 20) is neutral to litmus paper, does not respond to the test for *heavy metals*, and yields no precipitate with an equal volume of calcium sulphate T.S. (*barium*). One Gm. of calcium chloride shows no *ammonia* when warmed with sodium hydroxide, and 0.5 Gm. meets the requirements of the test for *arsenic.* Precipitate the calcium from 1 Gm. of the salt dissolved in 50 cc. of distilled water by ammonium oxalate T.S., evaporate and ignite the filtrate: the residue does not exceed 0.3 per cent. (*alkali* and *magnesium salts*).

Calcium Chloride, Fused, $CaCl_2$.—Deliquescent lumps or granules. It complies with the test for identity and purity under *Calcii Chloridum*, and when assayed by the method given under that substance shows not less than 98 per cent. of $CaCl_2$.

Calcium Sulphate, $CaSO_4.2H_2O$.—Transparent crystals, crystalline masses or a white powder. Slightly soluble in water.

Canada Turpentine.—A liquid oleoresin from *Abies balsamea* (Linné) Miller (Fam. *Pinaceæ*). A pale yellow or greenish, viscid, transparent liquid. Completely soluble in ether, chloroform, and benzene. When exposed to the air, Canada turpentine gradually dries and remains transparent. Canada turpentine solidifies when mixed with 20 per cent. of its weight of magnesium oxide, previously moistened with water.

Carbon Disulphide, CS_2.—A clear, colorless, very volatile, inflammable liquid. Boiling point, about 46° C. Specific gravity, about 1.26 at 25° C. Slightly soluble in water, very soluble in alcohol, ether, chloroform and fixed or volatile oils. Carbon disulphide does not affect the color of blue litmus paper moistened with water (*sulphur dioxide*). Agitate 10 cc. of carbon disulphide with 0.5 Gm. of lead carbonate: the latter should not acquire a brown color (*foreign sulphur compounds*). Non-volatile residue at 100° C., not over 0.004 per cent.

Carbon Tetrachloride, CCl_4.—Use *Carbon Tetrachloridum.*

Casein.—A white or slightly yellow, odorless, granular powder. Insoluble in water and other neutral solvents, but readily dissolved by ammonia T.S. and by solutions of alkali hydroxides, forming a cloudy solution. Ash: not more than 1 per cent. Loss on drying at 100° C., not more than 10 per cent. Shake 1 Gm. of casein with 20 cc. of distilled water for ten minutes and filter: the filtrate is not alkaline to litmus paper, and on evaporating to dryness and drying at 100° C., the residue does not exceed 0.1 per cent (*soluble substances*). Dissolve 1 Gm. of casein in 10 cc. of distilled water, with 5 cc. of alcoholic ammonia T.S., and shake out with two successive portions of 20 cc. each of purified petroleum benzin. Evaporate the benzin extract at a low temperature and dry at 70° C. The weight of the residue does not exceed 0.5 per cent. (*fats*). Anhydrous casein contains from 15.2 to 16 per cent. of nitrogen, using the Kjeldahl method.

Charcoal.—Use *Carbo Ligni.*

Chloral Hydrate, $CCl_3CHO.H_2O$.—Use *Chloralis Hydras.*

Chlorinated Lime.—Use *Calx Chlorinata.*

Chloroform, $CHCl_3$.—Use *Chloroformum.*

Chromium Trioxide, CrO_3.—Use *Chromii Trioxidum.*

Cobaltous Chloride, (*Cobalt Chloride*) $CoCl_2.6H_2O$.—Red crystals or a red, crystalline powder. Very soluble in water and in alcohol, soluble in acetone and in glycerin. Dissolve 2 Gm. of cobaltous chloride in 100 cc. of distilled water. Completely precipitate the cobalt by the addition of an excess of ammonia T.S., followed by ammonium sulphide T.S., and filter. The filtrate, after evaporation and ignition, leaves not more than 0.008 Gm. of residue (*salts of alkalies* and *alkali earths*). Dissolve 1 Gm. of cobaltous chloride in 20 cc. of distilled water, add 3 Gm. of sodium cyanide, and boil until the solution acquires a yellow color. Filter, add 1 cc. of bromine and sufficient sodium hydroxide T.S. to render strongly alkaline: no brown color develops (*nickel*). A solution of cobaltous chloride (1 in 20) strongly acidulated with hydrochloric acid, yields no dark precipitate with hydrogen sulphide (*lead* or *copper*).

Copper, Cu.—Copper in the form of wire, foil, turnings, filings, or granules. It should give no reaction for *antimony, lead, silver,* or *tin.* It should contain not more than 0.03 per cent. of *iron* and not more than 0.0001 per cent. of *arsenic.*

Cupric Acetate, $Cu(C_2H_3O_2)_2.H_2O$.—Bluish-green crystals, or powder, having an acetous odor. Soluble in water, slightly soluble in alcohol. It should contain not more than 0.01 per cent. of *sulphate* or *chloride.* Dissolve 1 Gm. of cupric acetate in 100 cc. of distilled water, add 1 cc. of hydrochloric acid, completely precipitate the copper with hydrogen sulphide, filter, evaporate the filtrate to dryness, and gently ignite: the residue does not exceed 0.5 per cent.

Cupric Sulphate, $CuSO_4.5H_2O$.—Use *Cupri Sulphas.*

Cupric Sulphate, Anhydrous, $CuSO_4$.—A white or grayish-white powder, free from a blue tinge. Upon adding a small quantity of water, it becomes blue. It is soluble in water and responds to the reactions characteristic of copper and sulphates. An aqueous solution (1 in 50) yields no immediate reaction for *chloride.* Precipitate the copper from a solution of 2 Gm. in 100 cc. of distilled water, acidulated with 2 cc. of hydrochloric acid, with hydrogen sulphide and filter. Evaporate the filtrate to dryness and gently ignite: the residue does not exceed 0.1 per cent.

Curare.—The composition of curare is not definitely known, and different specimens vary, depending upon the special variety of plant used in its manufacture. The most important source of curare is the bark of several varieties of *Strychnos*, the species most commonly employed being *S. Castelnæi* Wedd., *S. Toxifera* Benth., or *S. Crevauxii* G. Planch. (Fam. *Loganiaceæ*). Commercial curare is a brownish or black, shining resinoid mass. About 75 per cent. is soluble in cold water and it is almost completely soluble in diluted alcohol.

Dextrose, $C_6H_{12}O_6.H_2O$.—Use *Dextrosum.*

Dichloramine, $C_7H_7O_2NSCl_2$.—Use *Dichloramina.*

Diphenylamine, $(C_6H_5)_2NH$.—Grayish-white or colorless crystals. Melting point, about 54° C. Slightly soluble in water and in alcohol. A solution of 0.2 Gm. in 20 cc. of sulphuric acid, is colorless (*nitrates*). No violet color results when 1 Gm. of powdered diphenylamine is added to 20 cc. of a saturated aqueous solution of chlorinated lime (*aniline*).

Epinephrine, $C_9H_{13}O_3N$.—Use *Epinephrina.*

Ether, Dehydrated, $(C_2H_5)_2O$.—It conforms to the description and tests for *aldehyde* and *peroxide,* page 80, and to the following: Specific gravity, not over 0.711 at 25° C. Boiling point, from 34° to 36° C. To 10 cc. of ether, contained in a dry, clean, glass cylinder, add 0.1 Gm. of rosaniline acetate: no coloration results (*water* or *alcohol.*) Non-volatile residue at 100° C., not more than 0.002 per cent.

Ethyl Acetate, $CH_3COOC_2H_5$.—A transparent, colorless, inflammable liquid. Soluble in water, miscible with alcohol, ether, and fixed or volatile oils. Boiling point, 75° to 77° C. Specific gravity: 0.893 to 0.898 at 25° C. Ethyl acetate does not redden moistened blue litmus paper. Evaporate 5 cc. of ethyl acetate from clean, odorless, unsized paper. The final odor is not different in character from that observed at the beginning of the test. Superimpose 5 cc. of ethyl acetate upon 5 cc. of sulphuric acid: no dark coloration is produced at the zone of contact (*readily carbonizable substances*). Non-volatile residue at 100° C., not more than 0.005 per cent.

Ferric Ammonium Sulphate, $FeNH_4(SO_4)_2.12H_2O$.—Pale violet crystals. Efflorescent on exposure to air. Very soluble in water, insoluble in alcohol. An aqueous solution (1 in 20) gives no reaction for *chloride* or *ferrous salts.*

Ferric Chloride, $FeCL_3.6H_2O$.—Use *Ferri Chloridum.*

Ferrous Sulphate, $FeSO_4.7H_2O$.—Use *Ferri Sulphas.*

Ferrous Sulphide, FeS.—Dark gray or grayish-black lumps, fragments, sticks, granules, or globules. It is insoluble in water but is dissolved by diluted sulphuric or diluted hydrochloric acid with copious evolution of hydrogen sulphide.

Filter Paper, Quantitative.—For the Mercuric Bromide Test Paper of the Arsenic Test, use Schleicher and Schull's No. 589 (Blue Ribbon), or Swedish O. filter paper, or other makes of like surface, quality and ash (see *Arsenic Test*).

Fluorescein (*Resorcinolphthalein*), $C_{20}H_{12}O_5$.—A yellowish-red to dark red powder. Sparingly soluble in water and in ether, soluble in alcohol. Fluorescein dissolves in solutions of the alkali hydroxides or carbonates, forming a solution which has a bright green fluorescence. Ash, not over 0.25 per cent. Agitate about 1 Gm. of fluorescein with 20 cc. of distilled water and filter. One drop of tenth-normal sodium hydroxide imparts to 10 cc. of the filtrate a bright green fluorescence. The addition of a drop of ferric chloride T.S. to the remaining portion of the filtrate does not produce a bluish coloration (*resorcinol* or *other phenolic compounds*).

Fuchsin, Basic (*Basic Fuchsin, Rosaniline, Rosaniline Acetate, Rosaniline Hydrochloride*).—Crystals or crystalline fragments with a glossy, greenish-bronze luster. Soluble in water, alcohol, and amyl alcohol, An aqueous solution (1 in 500) yields a red precipitate upon the addition of tannic acid T.S. To 10 cc. of an aqueous solution (1 in 500), add 10 cc. of ammonia T.S. and 0.5 Gm. of zinc dust, and agitate. Decolorization of the solution results. Place a few drops of this decolorized solution upon filter paper, then place near by, on the paper, a few drops of hydrochloric acid. The zone of contact assumes a red color. Ash: not over 0.25 per cent.

Gallic Acid, $HC_7H_5O_5.H_2O$.—White or nearly white crystals. A cold, saturated aqueous solution of gallic acid neither colors nor precipitates solutions of pure ferrous salts, and does not produce a precipitate with gelatin T.S. (*tannic acid*).

Gelatin.—Use *Gelatinum.*

Glass Wool.—Fine threads of glass. Glass wool should yield not more than 0.5 per cent. of soluble matter when boiled for one-half hour with diluted hydrochloric acid. Boil 1 Gm. of glass wool for five minutes with a mixture of 25 cc. each of diluted nitric acid and distilled water, filter, evaporate the filtrate to dryness, treat the residue with 10 cc. of distilled water, and again filter. This latter filtrate is not colored by the addition of an equal volume of hydrogen sulphide T.S. (*lead*).

Gold Chloride (*Chlorauric Acid*), $HAuCl_4.4H_2O$.—Yellow, hygroscopic crystals. Very soluble in water, soluble in alcohol and in ether. An accurately weighed portion of about 0.1 Gm., when moistened with a slight excess of ammonium oxalate T.S., evaporated to dryness, ignited, and weighed, yields a residue of about 48 per cent. of metallic gold. Heat the metallic gold thus obtained with diluted hydrochloric acid and filter. The filtrate gives no appreciable coloration with either hydrogen sulphide T.S. or ammonium sulphide T.S. (*other metals*).

Hematein, $C_{16}H_{12}O_6$.—A product of the oxidation of hematoxylin. Reddish-brown crystalline plates of a greenish metallic luster. Sparingly soluble in water, alcohol and in ether, insoluble in chloroform. It is dissolved by ammonia T.S. with a brownish-violet color and by dilute solutions of caustic alkalies with a bright red color.

Hydrochloric Acid, HCl.—Use *Acidum Hydrochloricum.*

Hydrochloric Acid, Concentrated, HCl.—In addition to the description and identity tests for *Acidum Hydrochloricum,* it must conform to the following tests: Specific gravity, between 1.170 and 1.184 at 25° C., corresponding to from 35 to 38 per cent. of HCl. Non-volatile residue, upon evaporation and ignition with a drop of sulphuric acid, not more than 0.002 per cent. Evaporate 100 cc. of concentrated hydrochloric acid to about 5 cc., dilute with 10 cc. of distilled water, and add 5 drops of barium chloride T.S.: no precipitate occurs within twelve hours (*sulphate*). Add 5 cc. of concentrated hydrochloric acid, diluted with 50 cc. of distilled water, to a solution of 1 drop of tenth-normal iodine in 50 cc. of distilled water to which a few drops of starch T.S. have been added: no decolorization occurs (*sulphur dioxide*). Dilute 10 cc. of the acid with about 100 cc. of distilled water at a temperature of about 50° C. and thoroughly saturate it with hydrogen sulphide: no dark coloration or precipitate forms either before or after rendering alkaline with ammonia T.S. and adding 5 drops of ammonium sulphide T.S. (*heavy metals*). Two cc. of concentrated hydrochloric acid, diluted with 10 cc. of distilled water, when subjected to the arsenic test, page 1533, produces a stain not greater than that produced by the zinc alone.

Hydrochloric Acid, Diluted.—Use *Acidum Hydrochloricum Dilutum.*

Hydrogen Sulphide, H_2S.—A gas generated by treating ferrous sulphide with diluted sulphuric or hydrochloric acid.

Indicators.—See page 1566.

Indigo Carmine, $C_{16}H_8O_2N_2(SO_3Na)_2$.—Use *Sodii Indigotindisulphonas.*

Iodine, Purified, I.—Prepared from *Iodum,* page 584, as follows: Powder a suitable quantity of iodine and place it in a porcelain dish. Heat it over a water bath for twenty minutes, stirring constantly with a glass rod to vaporize moisture and other impurities. Then transfer the iodine to a glass, porcelain, or wedgewood mortar and triturate with about 5 per cent. of its weight of potassium iodide. Return the mixture to the dish, cover it with a glass funnel, and heat carefully on a sand bath to sublime the iodine. When the operation is completed, detach the sublimed iodine, powder it, and dry it over calcium chloride in a desiccator for twenty-four hours: the ash from 2 Gm. is negligible.

Preserve in well-closed, glass-stoppered bottles, in a cool place.

Iron, Fe.—Bright, clean iron in the form of wire, sheet, filings, or powder. In the test for copper, use bright pieces of sheet iron or steel knitting needles.

Preserve iron in well-closed glass containers to protect it from moist air, acid fumes, etc.

Isatin, $C_8H_5NO_2$.—Small yellowish-red crystals; slightly soluble in water, soluble in alcohol, and in ether. Melting point about 200° C. Aqueous alcoholic or ethereal solutions of isatin are reddish-brown in color.

When isatin is dissolved in a solution of an alkali hydroxide, it yields a violet colored solution which upon heating or upon long standing becomes yellow.

Kerosene.—A mixture of hydrocarbons, chiefly of the methane and naphthene series. It is a clear, colorless, or only slightly colored liquid, having a characteristic but not disagreeable odor. Specific gravity about 0.80 at 25° C. Boils between 180° and 300° C. Prepare purified kerosene by shaking a convenient volume of kerosene twice with about one-tenth its volume of 15 per cent. sodium hydroxide solution, then wash with distilled water until free from alkali.

Lead Acetate, $Pb(C_2H_3O_2)_2.3H_2O$.—Use *Plumbi Acetas.*

Lead Carbonate, $(PbCO_3)_2.Pb(OH)_2$.—A white, heavy powder. Insoluble in water and in alcohol. It is dissolved by acetic or diluted nitric acid with effervescence, the resulting solutions responding to the identity tests for lead.

Lead Monoxide, PbO.—Use *Plumbi Monoxidum.*

Lead Nitrate, $Pb(NO_3)_2$.—Colorless or white crystals or a white crystalline powder. Very soluble in water, almost insoluble in alcohol. Lead nitrate responds to the identity tests for lead, and nitrates, and meets the requirements of the tests for *foreign metals* under *Plumbi Acetas.*

Lead Peroxide (*Lead Dioxide*), PbO_2.—A dark brown powder containing not less than 90 per cent. of PbO_2. Insoluble in water and in alcohol. It is unaffected by nitric acid, but is decomposed by hydrochloric acid with the evolution of chlorine, and by hot sulphuric acid with the evolution of oxygen. It is dissolved by concentrated solutions of alkali hydroxides. Boil 2 Gm. of lead peroxide with 50 cc. of distilled water for fifteen minutes, filter, evaporate the filtrate to dryness and ignite. The residue does not exceed 0.5 per cent. (*soluble salts*).

Assay.—Dissolve about 0.5 Gm. of finely powdered lead peroxide, previously dried to constant weight at 100° C. and accurately weighed, in a solution made by mixing 1.5 Gm. of potassium iodide, 12 Gm. of sodium acetate, 8 cc. of glacial acetic acid, and 8 cc. of distilled water. Clear the solution if necessary by the further addition of sodium acetate, and then determine the liberated iodine by titration with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.01195 Gm. of PbO_2.

Lime, Freshly Slaked, $Ca(OH)_2$.—To prepare freshly slaked lime, drop upon a convenient quantity of lime, page 263, one-third of its weight of water, cover and allow it to stand until it has been converted to a pulverulent mass and is cool. Freshly slaked lime, after drying and igniting, yields not more than 0.1 per cent. of residue insoluble in hydrochloric acid and should show practically no effervescence when dissolved.

Magnesium Chloride, $MgCl_2.6H_2O$.—White, deliquescent crystals, very soluble in water. An aqueous solution is neutral to litmus paper. Two Gm. of magnesium chloride should completely dissolve in 10 cc. of 85 per cent. alcohol. Magnesium chloride also complies with the tests for *barium, calcium, heavy metals,* and *sulphate,* under reagent sodium chloride.

Magnesium Oxide, MgO.—Use *Magnesii Oxidum.*

Magnesium Sulphate, $MgSO_4.7H_2O$.—Use *Magnesii Sulphas.*

Manganese Dioxide, MnO_2.—A fine heavy black powder, containing not less than 85 per cent. of MnO_2. It is insoluble in water, but is dissolved by hydrochloric acid with the evolution of chlorine.

Assay.—Dissolve about 0.2 Gm. of manganese dioxide, accurately weighed, in a mixture of 50 cc. of tenth-normal oxalic acid and 3 cc. of sulphuric acid, heat to about 80° C., and titrate the excess of oxalic acid with tenth-normal potassium permanganate. Each cc. of tenth-normal oxalic acid represents 0.0043465 Gm. of MnO_2.

Manganese Sulphate, $MnSO_4.4H_2O$ or $MnSO_4.5H_2O$.—Pink crystals. Very soluble in water, insoluble in alcohol. An aqueous solution (1 in 50) gives no reaction for *chloride* or *iron.* Dissolve 1 Gm. of manganese sulphate in 50 cc. of distilled water, add 10 cc. of ammonium chloride T.S., heat to boiling, and precipitate the manganese with a slight excess of ammonium sulphide T.S. Continue the heating until the precipitate assumes a greenish color, then filter, evaporate the filtrate to dryness, and ignite; not more than 0.5 per cent. of residue remains (*salts of foreign metals*).

Mercuric Bromide, $HgBr_2$.—White needles, prisms, lustrous scales, or a granular, crystalline powder. Slightly soluble in cold water, soluble in boiling water and in alcohol. Mercuric bromide should be completely soluble in hot water. Residue upon incineration, not more than 0.05 per cent.

Mercuric Chloride, $HgCl_2$.—Use *Hydrargyri Chloridum Corrosivum.*

Mercuric Oxide, Red, HgO.—An orange-red crystalline powder. Insoluble in water but dissolved by dilute nitric or dilute hydrochloric acid. A solution (1 in 50) in diluted nitric acid gives no reaction for *chloride* or *sulphate.* One Gm. mixed with 10 cc. of diluted sulphuric acid should give no reaction for nitrate with ferrous sulphate. Residue upon incineration, not more than 0.2 per cent. When dried to constant weight at 100° C. and assayed electrolytically or by titration with tenth-normal potassium thiocyanate, it should show not less than 99.5 per cent. of HgO.

Mercurous Chloride, Mild, HgCl.—Use *Hydrargyri Chloridum Mite.*

Mercury, Hg.—Use *Hydrargyrum.*

Metaphenylenediamine Hydrochloride, $C_6H_4(NH_2)_2.2HCl$.—A white or slightly reddish-white, crystalline powder, easily soluble in water. An aqueous solution (1 in 200) should be colorless.

Molybdic Acid.—A white or yellowish-white powder of somewhat variable composition, containing, when assayed by the lead molybdate method, not less than 83 per cent. of MoO_3. It is insoluble in water, soluble in solutions of alkali hydroxides. No insoluble residue should remain when 1 Gm. of molybdic acid is dissolved in 10 cc. of ammonia T.S. The addition of 10 cc. of hydrogen sulphide T.S. produces a greenish-yellow color but no brownish-yellow color or precipitate (*heavy metals*). Dissolve 10 Gm. of molybdic acid in 25 cc. of ammonia T.S., pour this solution gradually and with constant stirring into a mixture of 75 cc. of nitric acid and 75 cc. of distilled water, and set the solution aside for at least twelve hours at 40° C.: no yellow precipitate should appear (*phosphate*).

Naphthylamine (Alpha) Hydrochloride, $C_{10}H_7NH_2.HCl$.—A white, crystalline powder which turns bluish upon exposure to light and air. Insoluble in water, soluble in alcohol and in ether. An aqueous solution (1 in 100) in diluted acetic acid gives a violet color with 5 drops of ferric chloride T.S. An aqueous solutiod (1 in 40) in diluted acetic acid should be colorless and not more than slightly opalescent from undissolven matter. Non-volatile residue upon incineration, not more than 0.05 per cent.

Naphthylamine (Beta) Acetate, $C_{10}H_7NH_2.C_2H_4O_2$.—White to yellowish-white, crystalline scales or flakes. Slightly soluble in water, soluble in alcohol. An aqueous solution (1 in 100) does not give a violet color with 5 drops of ferric chloride T.S. (*alpha naphthylamine.*

Nitric Acid, HNO_3.—Use *Acidum Nitricum.*

Nitric Acid, Diluted.—Use a 10 per cent. aqueous solution of HNO_3.

Nitric Acid, Fuming.—A yellowish-red to brownish-red fuming liquid. Specific gravity, about 1.50 at 25° C. It conforms to the tests for purity under *Acidum Nitricum,* page 42, omitting the assay.

Preserve carefully in glass-stoppered bottles, in a cool place.

Oil of Cedar Wood.—For clearing microscopic sections, a selected commercial distilled oil from the wood of the red cedar, *Juniperus virginiana* Linné (Fam. *Pinaceæ*), should be used. Refractive index, about 1.504 at 20° C. For use with homogeneous immersion lenses, a specially prepared oil is required, having a refractive index of exactly 1.515 at 18° C.

Ouabain, $C_{30}H_{46}O_{12}.xH_2O$.—Ouabain, crystallized from a mixture of alcohol and ether, contains approximately 12½ per cent. of water, and requires a temperature of 130° C. for rapid and complete dehydration. The optical properties are as follows: In ordinary light—colorless rods. In parallel polarized light with crossed nicols extinction is parallel. The double refraction is strong. The sign of elongation is +. Refractive indices $\left(\frac{20^\circ}{D}\right)$: $\alpha = 1.540$ (crosswise), $\gamma = 1.580$ (lengthwise), both ± 0.002.

The specific rotation of anhydrous ouabain: $\left(\alpha\right)^{20}_{D} = -31.3^\circ$ to -31.9°.

Ouabain is stable at 130° C. Anhydrous ouabain, whether originally crystallized from alcohol and ether or from water at room temperature, begins to soften at about 180° C.

Oxalic Acid, $H_2C_2O_4.2H_2O$.—Colorless, uneffloresced crystals. Soluble in water, very soluble in boiling water and in alcohol. Dissolve 2 Gm. of oxalic acid in 30 cc. of distilled water, add 2 Gm. of sodium hydroxide, and treat with 1 cc. of Nessler's reagent: it shows no darker coloration than a blank test from which the oxalic acid has been omitted (*ammonium compounds*). An aqueous solution (1 in 20) gives no reaction for *chloride, sulphate, nitrate,* or *heavy metals.* Residue upon incineration, not over 0.05 per cent. Preserve in well-stoppered bottles.

Palladous Chloride, $PdCl_2$.—A dark brown, hygroscopic powder, yielding a turbid solution with water in consequence of the formation of a basic salt.

Phenol, C_6H_5OH.—Use *Phenol.*

Phenylhydrazine, $C_6H_5.NH.NH_2$.—A colorless or slightly yellowish, highly refractive liquid. Boiling point, about 242° C., congealing when cold to crystalline plates which melt at 19° C. Slightly soluble in water, soluble in alcohol and in ether. Its aqueous solution soon becomes dark from oxidation. Shake 2 cc. of phenylhydrazine with 20 cc. of 5 per cent. acetic acid: a clear liquid results.

Phloroglucinol, $C_6H_3(OH)_3.2H_2O$.—White or yellowish-white crystals or a crystalline powder. Slightly soluble in water, soluble in alcohol and in ether. When rapidly heated, it melts between 217° and 219° C. When slowly heated, it melts at a much lower temperature. Add 0.1 Gm. of phloroglucinol to 1 cc. of acetic anhydride and 1 cc. of sulphuric acid in a test tube, and heat in a bath of boiling water for ten minutes: no blue color develops (*diresorcinol*).

Phosphoric Acid, H_3PO_4.—Use *Acidum Phosphoricum.*

Phosphotungstic Acid, approximately $P_2O_5.24WO_3.xH_2O$.—White or yellowish-green crystals or a crystalline powder. Soluble in water and in alcohol. Slightly soluble in ether. To a solution of 1 Gm. of phosphotungstic acid in 10 cc. of distilled water, add 0.1 Gm. of sodium chloride and 3 drops of indigo carmine T.S., then cautiously add 10 cc. of sulphuric acid, and allow the liquid to stand for ten minutes: the blue color does not disappear (*nitrate*). An aqueous solution (1 in 10) gives no reation for *ammonium salts.*

Picric Acid, $C_6H_2(OH)(NO_2)_3$.—Use *Trinitrophenol.*

Platinic Chloride (*Chloroplatinic Acid*), $H_2PtCl_6.6H_2O$.—A brownish-red, very hygroscopic, crystalline mass. Very soluble in water, soluble in alcohol and in ether. It dissolves completely in 10 parts of water or alcohol, forming yellow solutions. The residue, upon incineration in a porcelain crucible, is not less than 37.6 per cent. When this residue is treated with 50 times its weight of diluted nitric acid for fifteen minutes on a water bath, the acid solution, upon filtration, evaporation to dryness and incineration, yields a residue not exceeding 0.15 per cent. of the platinic chloride taken.

Potassium and Sodium Tartrate, $KNaC_4H_4O_6.4H_2O$.—Use *Potassii et Sodii Tartras.*

Potassium Acetate, $KC_2H_3O_2$.—Use *Potassii Acetas.*

Potassium Bicarbonate, $KHCO_3$.—Use *Potassii Bicarbonas.*

Potassium Bisulphate, $KHSO_4$.—Fused white, deliquescent masses or granules. Reaction acid. Freely soluble in water. It responds to the identity tests for potassium and for sulphates.

Potassium Bitartrate, $KHC_4H_4O_6$.—In addition to the tests described under *Potassii Bitartras,* page

876, it gives no reaction for *chloride, sulphate, calcium, ammonium compounds,* or *heavy metals.* Heat 5 Gm. of potassium bitartrate at 100° C. for thirty minutes: no loss of weight should result. Dissolve 5 Gm. of potassium bitartrate, accurately weighed, in 250 cc. of hot distilled water, heat to boiling, and titrate with normal sodium hydroxide, phenolphthalein T.S. being used as indicator: it shows not less than 99.9 per cent. and not more than 100 per cent. of $KHC_4H_4O_6$.

Potassium Bromate, $KBrO_3$.—White crystals or a granular powder. Soluble in water, slightly soluble in alcohol. An aqueous solution (1 in 20) is neutral and should not at once acquire a yellow color upon the addition of 3 drops of diluted sulphuric acid (*bromide*).

Assay.—When dried to constant weight at 100° C. and assayed by titration with tenth-normal sodium thiosulphate, after adding potassium iodide and hydrochloric acid, it shows not less than 99.8 per cent. of $KBrO_3$. Each cc. of tenth-normal sodium thiosulphate corresponds to 0.002784 Gm. of $KBrO_3$.

Potassium Carbonate, $K_2CO_3.xH_2O$.—Use *Potassii Carbonas.*

Potassium Carbonate, Anhydrous, K_2CO_3.—White granules or powder, very hygroscopic. Very soluble in water with the evolution of heat. When heated to redness, it should not lose more than 1 per cent. of its weight (*water*). It meets the requirements of the tests for identity and purity under *Potassii Carbonas,* making allowance for the difference in water content.

Potassium Chlorate, $KClO_3$.—Use *Potassii Chloras.*

Potassium Chloride, KCl.—Colorless crystals or a white, granular powder. It is odorless. Freely soluble in water, slightly soluble in alcohol. Its aqueous solution (1 in 10) is neutral to litmus paper, and imparts to a non-luminous flame not more than a slight transient yellow color (*sodium*). To a solution of 1 Gm. of the salt in 5 cc. of distilled water, add an equal volume of sulphuric acid and 1 drop of indigo T.S.: the blue color does not disappear (*nitrate*). Potassium chloride also complies with the tests for *barium, sulphate, magnesium, calcium, heavy metals,* and *ammonia* under *Reagent Sodium Chloride.*

Potassium Chromate, K_2CrO_4.—Yellow crystals, very soluble in water, insoluble in alcohol. An aqueous solution (1 in 20) is not reddened by phenolphthalein T.S. An aqueous solution (1 in 20) gives no reaction for *aluminum* or *calcium.* Ten cc. portions of an aqueous solution (1 in 20), acidulated respectively with 5 cc. of nitric acid and 3 cc. of hydrochloric acid, give no reaction for *chloride* or *sulphate.*

Potassium Citrate, $K_3C_6H_5O_7.H_2O$.—Use *Potassii Citras.*

Potassium Dichromate, $K_2Cr_2O_7$.—Dark yellowish-red crystals or crystalline granules. Soluble in water. An aqueous solution (1 in 20) should give no reaction for *aluminum* or *calcium.* Twenty cc. portions of an aqueous solution (1 in 20), treated respectively with 5 cc. of nitric acid and 2 cc. of hydrochloric acid, should give no reaction for *chloride* and no reaction for *sulphate* within eighteen hours after adding 1 cc. of barium chloride T.S.

Assay.—When dried to constant weight at 100° C. and assayed by titration with tenth-normal sodium thiosulphate, after adding potassium iodide, and diluted sulphuric acid, it shows not less than 99.9 per cent. of K_2CrO_7.

Potassium Ferricyanide, $K_3Fe(CN)_6$.—Dark red crystals. Very soluble in water. An aqueous solution (1 in 20) gives no reaction for sulphate. An aqueous solution (1 in 50), to which 2 drops of ferric chloride T.S. have been added, forms a clear, brown solution free from any green or blue coloration (*ferrocyanide*).

Potassium Ferrocyanide, $K_4Fe(CN)_6.3H_2O$.—Yellow, transparent, soft crystals very soluble in water. An aqueous solution (1 in 20) is neutral to litmus paper and gives no reaction for *sulphate.*

Potassium Hydroxide, KOH.—Use *Potassii Hydroxidum.*

Potassium Iodide, KI.—Use *Potassii Iodidum.*

Potassium Nitrate, KNO_3.—In addition to the description and tests given under *Potassii Nitras,* page 891, it should conform to the following tests: An aqueous solution (1 in 20) gives no reaction for *sulphate.* Gently ignite 1 Gm. of potassium nitrate and dissolve the residue in 10 cc. of distilled water: it gives no reaction for *chloride.*

Potassium Nitrite, KNO_2.—White or nearly white, deliquescent sticks. It responds to the identity tests for potassium and for nitrites.

Potassium Permanganate, $KMnO_4$.—Use *Potassii Permanganas.*

Potassium Sulphate, K_2SO_4.—Hard, colorless crystals or a white powder, soluble in water. An aqueous solution (1 in 20) is neutral to litmus paper, and gives no reaction for *heavy metals, chloride, iron, calcium, magnesium, ammonia,* or *nitrate.* An aqueous solution (1 in 30) meets the requirements of the test for *arsenic.*

Potassium Thiocyanate (*Potassium Sulphocyanate*), $KSCN$.—Colorless, hygroscopic crystals. Very soluble in water, completely soluble in eight parts of warm alcohol without coloration. An aqueous solution (1 in 20) gives no reaction for *sulphate, heavy metals,* or *ammonia.*

Pyrogallol, $C_6H_3(OH)_3$.—Use *Pyrogallol.*

Resorcinol, $C_6H_4(OH)_2$.—Use *Resorcinol.*

Salicylic Acid, $HC_7H_5O_3$.—Use *Acidum Salicylicum.*

Selenous Acid, H_2SeO_3.—Colorless crystals. Efflorescent in dry air and hygroscopic in moist air. Soluble in water and in alcohol.

Silver, Ag.—Silver in foil or wire containing not more than 0.025 per cent. of *foreign metals.*

Silver Nitrate, $AgNO_3$.—Use *Argenti Nitras.*

Silver Sulphate, Ag_2SO_4.—Small, white, lustrous crystals or a white powder. Slightly soluble in water and dissolved by nitric acid, or by ammonia T.S.

Preserve in amber-colored bottles.

Sodium Acetate, $NaC_2H_3O_2.3H_2O$.—Use *Sodii Acetas.*

Sodium Acetate, Anhydrous, $NaC_2H_3O_2$.—Made from sodium acetate by heating it carefully until all water of crystallization is driven off and a dry powder results. It contains not more than 3 per cent. of *water.*

Sodium Bicarbonate, $NaHCO_3$.—Use *Sodii Bicarbonas.*

Sodium Bisulphite (*Sodium Acid Sulphite*), $NaHSO_3$.—White crystals or a white granular powder, having the odor of sulphur dioxide. Freely soluble in water, slightly soluble in alcohol. An aqueous solution (1 in 50), boiled with a slight excess of hydrochloric acid to expel sulphur dioxide, gives no reaction for *heavy metals* and 0.2 Gm., oxidized with nitric acid, meets the requirements of the test for *arsenic.*

Assay.—Dissolve a weighed amount of sodium bisulphate in distilled water, add a measured excess of tenth-normal iodine, and titrate the excess of iodine with tenth-normal sodium thiosulphate. Each cc. of tenth-normal iodine corresponds to 0.005204 Gm. of $NaHSO_3$. It shows not less than 90 per cent of $NaHSO_3$. Preserve in well-filled, well-stoppered bottles, in a cool place.

Sodium Bitartrate, $NaHC_4H_4O_6.H_2O$.—White crystals or crystalline powder. Soluble in cold water. An aqueous solution (1 in 10) is clear and colorless and gives no reaction for *sulphate* or *heavy metals.* An aqueous solution (1 in 40) gives no reaction for *chloride.*

Sodium Borate, $Na_2B_4O_7.10H_2O$.—Use *Sodii Boras.*

Sodium Bromide, NaBr.—Use *Sodii Bromidum.*

Sodium Carbonate, Anhydrous, Na_2CO_3.—A white, hygroscopic powder, soluble in water. An aqueous solution (1 in 10) should be clear and colorless and gives no reaction for *sulphate, silicate, nitrate, phosphate, calcium, magnesium, iron, ammonia, heavy metals,* contains not more than 0.005 per cent. of *chloride* and meets the requirements of the test for *arsenic.* Not more than traces of potassium should be shown by the flame test, using cobalt glass. Titrate about 1.5 Gm. of anhydrous sodium carbonate, accurately weighed, with normal sulphuric acid, methyl orange T.S. being used as indicator. It shows not less than 99 per cent. of Na_2CO_3.

Sodium Carbonate, Monohydrated, $Na_2CO_3.H_2O$.—Use *Sodii Carbonas Monohydratus.*

Sodium Chloride, NaCl.—In addition to the requirements and the tests prescribed under *Sodii Chloridum,* page 995, it is required to conform to the following additional tests. An aqueous solution of sodium chloride (1 in 20) shows no turbidity or precipitation in the addition of dilute sulphuric acid (*barium*). To a solution of 3 Gm. of sodium chloride in 80 cc. of distilled water, add 1 cc. of concentrated hydrochloric acid (page 1557), heat to boiling, and add about 5 cc. of barium chloride T.S. No precipitation takes place within twenty-four hours (*sulphate*). To a solution of 3 Gm. of sodium chloride in about 10 cc. of distilled water, add 5 cc. of ammonia T.S., and 5 cc. of sodium phosphate T.S.: no precipitation takes place within twelve hours (*magnesium salts*). Dissolve 5 Gm. of the salt in 80 cc. of distilled water, heat the solution to boiling, and add 5 cc. of ammonium oxalate T.S.: no precipitate is produced within twelve hours (*calcium*); nor is this solution affected by the addition of sodium carbonate T.S.; nor is a freshly prepared solution of the same concentration affected by the addition of ammonium sulphide T.S. (*alkali earths* and *heavy metals*). To a solution of 1 Gm. of sodium chloride in 10 cc. of distilled water, add 5 cc. of sodium cobaltic nitrite T.S.: no precipitation occurs after twenty-four hours (*potassium*). The addition of Nessler's Reagent to a solution of 3 Gm. of sodium chloride produces no yellow coloration (*ammonium salts*).

Sodium Cyanide, NaCN.—White, opaque, amorphous fragments, or a white, granular powder. Very soluble in water. An aqueous solution (1 in 10) gives no reaction for *ferrocyanides* or *thiocyanates.*

Assay.—Dissolve about 0.45 Gm. of sodium cyanide accurately weighed, in 25 cc. of distilled water, add 4 cc. of ammonia T.S., 3 drops of potassium iodide T.S., and titrate with tenth-normal silver nitrite to the production of a permanent turbidity: it shows not less than 95 per cent. of NaCN. Each cc. of tenth-normal silver nitrate represents 0.009802 Gm. of NaCN.

Sodium Hydroxide, NaOH.—Use *Sodii Hydroxidum.*

Sodium Nitrite, $NaNO_2$.—Use *Sodii Nitris.*

Sodium Nitroprusside (*Sodium Nitroferricyanide*), $Na_2Fe(NO)(CN)_5.2H_2O$.—Transparent, dark-red crystals, very soluble in water. An aqueous solution (1 in 50) gives no reaction for *sulphate.*

Sodium Oxalate, $Na_2C_2O_4$.—A white, crystalline powder, slightly soluble in water. The loss on drying at 105° C. does not exceed 0.01 per cent. The residue insoluble in water does not exceed 0.01 per cent. *Sulphate,* not over 0.001 per cent. *Chloride,* not over 0.002 per cent. *Iron,* not over 0.002 per cent. *Sodium bicarbonate,* not over 0.03 per cent. *Sodium binoxalate,* not over 0.02 per cent.

Sodium Phosphate, $Na_2HPO_4.12H_2O$.—Use *Sodii Phosphas.*

Sodium Sulphide, $Na_2S.9H_2O$.—Clear, colorless, deliquescent crystals. Very soluble in water. An aqueous solution (1 in 10) is alkaline to litmus paper and has an odor of hydrogen sulphide.

Assay.—Transfer about 0.3 Gm. of sodium sulphide, accurately weighed, to a flask containing 40 cc. of tenth-normal iodine. Allow it to stand until the sulphide is completely decomposed, add 2 cc. of hydrochloric acid and titrate with tenth-normal sodium thiosulphate. It shows not less than 95 per cent. of $Na_2S.9H_2O$. Each cc. of tenth-normal iodine represents 0.01201 Gm. of $Na_2S.9H_2O$.

Sodium Sulphite, Exsiccated, Na_2SO_3.—A white powder, freely soluble in water, slightly soluble in alcohol. An aqueous solution (1 in 50), boiled with a slight excess of hydrochloric acid to expel sulphur dioxide, gives no reaction for *heavy metals.*

Assay.—Dissolve 0.5 Gm. of exsiccated sodium sulphite in sufficient freshly boiled distilled water to make 100 cc. Run this solution gradually from a burette into a mixture of 30 cc. of tenth-normal iodine and 5 cc. of hydrochloric acid, until complete decolorization results, using starch T.S. as indicator. It shows not less than 85 per cent. of Na_2SO_3. Each cc. of tenth-normal iodine represents 0.006308 Gm. of Na_2SO_3.

Sodium Tartrate, Neutral, $Na_2C_4H_4O_6.2H_2O$.—Transparent crystals, very soluble in water, insoluble in alcohol. An aqueous solution (1 in 20) gives no reaction for *ammonia, sulphate,* or *heavy metals.* An aqueous solution (1 in 40) gives no reaction for *chloride.*

Sodium Thiosulphate, $Na_2S_2O_3.5H_2O$.—Use *Sodii Thiosulphas.*

Sodium Tungstate, $Na_2WO_4.2H_2O$.—Colorless crystals or crystalline lumps, or a white, crystalline powder. An aqueous solution (1 in 40) gives no reaction for *chloride* or *sulphate.* The loss in weight after gentle ignition does not exceed 12 per cent.

Stannous Chloride, $SnCl_2.2H_2O$.—Colorless crystals, very soluble in water, the aqueous solutions requiring a slight excess of hydrochloric acid to prevent the formation of basic chloride. An aqueous solution (1 in 50) gives no reaction for *sulphate.* When tested for *arsenic* (page 1533), 0.3 Gm. of stannous chloride produces no stain. A solution of 0.2 Gm. in 1 cc. of distilled water and 0.5 cc. of hydrochloric acid does not become opalescent upon diluting with 20 cc. of distilled water (*lead*).

Starch, Potato.—The starch separated from the tubers of *Solanum tuberosum* Linné (Fam. *Solanaceæ*). A more or less finely granular powder, consisting of starch grains of characteristic shape and appearance when examined microscopically.

Sucrose, $C_{12}H_{22}O_{11}$.—Use *Sucrosum.*

Sulphanilic Acid, $C_6H_4NH_2(SO_3H)2H_2O$.—Colorless, acicular, efflorescent crystals. Slightly soluble in water. Residue upon incineration, not over 0.05 per cent. A hot, aqueous solution (1 in 25) gives no reaction for *sulphate.*

Sulphosalicylic Acid, $C_6H_3(OH)(SO_3H).COOH$.—Colorless needles, soluble in water and in alcohol. Melting point, about 120° C.

Sulphur, S.—Use *Sulphur Præcipitatum.*

Sulphuric Acid, H_2SO_4.—Use *Acidum Sulphuricum.*

Sulphuric Acid, Concentrated, H_2SO_4.—In addition to the description and tests under *Acidum Sulphuricum,* page 55, it complies with the following tests: It contains not less than 94 per cent. and not more than 97 per cent. of H_2SO_4. Residue upon ignition not to exceed 0.001 per cent. Dilute 1 volume of the acid with 4 volumes of distilled water: no stain is produced by 25 cc. of this dilute acid when subjected to the test for *arsenic.* An aqueous solution (1 in 10) gives no reaction for *nitrate* when tested with diphenylamine.

Sulphuric Acid, Diluted.—Use *Acidum Sulphuricum Dilutum.*

Sulphuric Acid, Fuming, $H_2SO_4.SO_3$.—A heavy, fuming, colorless, oily liquid. It contains at least 84.5 per cent. of total SO_3, corresponding to about 15 per cent. of free SO_3. Specific gravity about 1.870 at 25° C. Residue upon ignition, not over 0.01 per cent. An aqueous solution (1 in 10) gives no reaction for *nitrate.*

Assay.—Cautiously add about 1 cc. of fuming sulphuric acid, accurately weighed, to 100 cc. of distilled water, and titrate with normal sodium hydroxide, methyl orange T.S. being used as indicator. Each cc. of normal sodium hydroxide corresponds to 0.040035 Gm. of SO_3.

Sulphurous Acid, H_2SO_3.—An aqueous solution having the odor of sulphur dioxide. A 10 cc. portion of sulphurous acid gives no reaction when subjected to the test for *arsenic.*

Assay.—Add about 2 Gm. of sulphurous acid, accurately weighed, to 50 cc. of tenth-normal iodine and allow it to stand for five minutes. Then titrate with tenth-normal sodium thiosulphate, starch T.S. being used as indicator. Each cc. of tenth-normal iodine corresponds to 0.003203 Gm. of SO_2. It shows not less than 6 per cent. of SO_2.

Tannic Acid.—Use *Acidum Tannicum.*

Tartaric Acid, $C_2H_2(OH)_2(COOH)_2$.—Use *Acidum Tartaricum.*

Tin, Sn.—Tin, in the form of granules or irregular fragments. Digest 5 Gm. of tin with 40 cc. of nitric acid until entirely converted into the oxide, then evaporate to dryness. Stir the residue with 25 cc. of distilled water and filter. To the filtrate add 1 cc. of diluted sulphuric acid, evaporate on a water bath as completely as possible, and add 10 cc. of distilled water. No weighable residue remains undissolved (*lead*). When converted into stannous chloride by the action of hydrochloric acid, it complies with the tests under that salt.

Toluene (*Toluol*), $C_6H_5.CH_3$.—A colorless, highly refractive, inflammable liquid. Insoluble in water, miscible with alcohol, ether, chloroform, carbon disulphide, and petroleum benzin. Specific gravity, about 0.865 at 25° C. Boiling point, about 111° C.

Trinitrophenol, $C_6H_2(OH)(NO_2)_3$.—Use *Trinitrophenol.*

Turmeric.—The dried root of *Curcuma longa* Linné, Fam. *Scitaminaceæ,* reduced to a fine powder.

Xylene, C_8H_{10}.—A colorless, transparent liquid. Boiling point, 137° to 140° C. Specific gravity, about 0.85 at 25° C.

Yeast, Compressed.—The moist, living cells of *Saccharomyces cerevisiæ* Meyen (Fam. *Saccharomycetaceæ*) or of other species of *Saccharomyces,* combined with a starchy or absorbent base. White or yellowish-white, soft and easily broken masses, having a characteristic, slightly sour odor, and not more than a faintly acid reaction to litmus paper. When examined under the microscope, numerous saccharomyces, and also oidium and mycoderma cells and starch grains are visible. Compressed yeast must not be used unless fresh, and free from mildew and musty or foul odors.

Zinc, Zn.—Zinc in the form of globules, irregular fragments, granules, or a fine powder, the latter being known as zinc dust. The stain from 10 Gm. of zinc, when determined by a blank experiment as directed under the test for *arsenic,* is barely perceptible. It contains not more than 0.08 per cent. of *iron.*

Zin cOxide, ZnO.—In addition to the description and tests under *Zinci Oxidum,* page **1170,** it should contain not more than 0.003 per cent. of *chloride.*

Test Solutions

(U. S.)

Wherever convenient or possible the strength of the following test solutions has been adjusted approximately to normality basis, which signifies that 1 liter of the solution contains a quantity of the reacting substance chemically equivalent to 1 Gm. of hydrogen.

N. or **1 N.** indicates that the quantity of the substance contained in 1 liter of the test solution is approximately equivalent to 1 Gm. of hydrogen. Multiples or subdivisions of this ratio are expressed by appropriate numerals, fractions or decimals as **4 N., N/10, 0.5 N.,** etc.

Albumen Test Solution.—Carefully separate the white from the yolk of a hen's egg, strictly fresh, having a specific gravity of not less than 1.07. Shake the white thoroughly with 100 cc. of distilled water until thoroughly mixed and all but the chalaza has undergone solution; then filter. This solution must be freshly made when required.

Ammonia Test Solution.—Use *Aqua Ammoniæ.*

Ammonia Test Solution, Alcoholic.—A solution of ammonia gas in alcohol. A clear, colorless liquid having a strong odor of ammonia. Specific gravity, about 0.80 at 25° C. When assayed by the method directed under *Aqua Ammoniæ,* it shows not less than 9 per cent. and not more than 11 per cent. by weight of NH_3.

Preserve in glass-stoppered bottles in a cool place.

Ammonia Test Solution, Stronger.—Use *Aqua Ammoniæ Fortior.*

Ammonium Carbonate Test Solution.—Dissolve 20 Gm. of reagent ammonium carbonate and 20 cc. of ammonia T.S. in sufficient distilled water to make 100 cc.

Ammonium Chloride Test Solution (2 N.).—Dissolve 10.5 Gm. of reagent ammonium chloride, in sufficient distilled water to make 100 cc.

Ammonium Molybdate Test Solution.—Dissolve 6.5 Gm. of finely powdered molybdic acid in a mixture of 14 cc. of distilled water and 14.5 cc. of stronger ammonia T.S. Cool the solution and add it slowly to a well-cooled mixture of 32 cc. of nitric acid, and 40 cc. of distilled water. Allow the solution to stand for twenty-four hours and then filter through asbestos. The reagent deteriorates upon standing and it must be rejected if, upon the addition of 2 cc. of sodium phosphate T.S. to 5 cc. of the solution, an abundant yellow precipitate does not form at once or after slight warming. Preserve in the dark; if a precipitate forms, use only the clear decanted solution.

Ammonium Oxalate Test Solution (0.5 N.).—Dissolve 3.5 Gm. of ammonium oxalate in sufficient distilled water to make 100 cc.

Ammonium Polysulphide Test Solution.—A yellow liquid, made by saturating ammonium sulphide T.S. with sulphur.

Ammonium Sulphide Test Solution.—Saturate 3 volumes of ammonia T.S. with hydrogen sulphide and add to it 2 additional volumes of ammonia T.S. Residue upon ignition, not over 0.05 per cent. The solution is not rendered turbid by either magnesium sulphate T.S. (*free ammonia*) or by calcium chloride T.S. (*carbonate*). It must be rejected when it shows an abundant precipitate of sulphur. Sodium sulphide T.S. may be used when ammonium sulphide T.S. is directed.

Preserve in small, well-filled, dark amber-colored bottles, in a cool, dark place.

Aniline Sulphate Test Solution.—Dissolve 5 cc. of aniline sulphate in 51 cc. of diluted alcohol and add sufficient distilled water to make 100 cc.

Barium Chloride Test Solution (1 N.).—Dissolve 12 Gm. of barium chloride in sufficient distilled water to make 100 cc.

Barium Hydroxide Test Solution (0.5 N.).—A saturated solution (about 8 per cent.) of barium hydroxide in recently boiled distilled water. This solution must be freshly made when required for use.

Barium Nitrate Test Solution (0.5 N.).—Dissolve 6.5 Gm. of barium nitrate in sufficient distilled water to make 100 cc.

Bromine Test Solution (*Bromine Water*).—An approximately saturated aqueous solution of bromine, prepared by agitating 2 cc. of bromine with 100 cc. of cold distilled water in a glass-stoppered bottle, the stopper of which should be lubricated with petrolatum. Preserve in a cool place, protected from light.

Cadmium Chloride Test Solution (1 N.).—Dissolve 11 Gm. of cadmium chloride in sufficient distilled water to make 100 cc.

Calcium Chloride Test Solution (1 N.).—Dissolve 7.5 Gm. of calcium chloride in sufficient distilled water to make 100 cc.

Calcium Hydroxide Test Solution (0.04 N.).—Use *Liquor Calcii Hydroxidi*, page 627.

Calcium Sulphate Test Solution (0.03 N.).—A saturated solution (about 0.25 per cent.) of calcium sulphate in distilled water.

Chloral Test Solution.—Dissolve 50 Gm. of chloral hydrate in 15 cc. of distilled water and 10 cc. of glycerin.

Chlorinated Soda Test Solution.—Use *Liquor Sodæ Chlorinatæ*.

Chlorine Test Solution (*Chlorine Water*).—Place 10 Gm. of manganese dioxide in a 500 cc. flask connected by a suitable tube with a small wash bottle containing 50 cc. of distilled water, and connect this by a delivery tube leading to the bottom of a bottle having a capacity of 1000 cc. and containing 400 cc. of distilled water, which has previously been boiled and allowed to cool. Add to the dioxide in the generating flask 25 cc. of hydrochloric acid, previously diluted with 25 cc. of distilled water, stopper the generating flask, and apply a gentle heat by means of a sand bath. Conduct the generated chlorine through the water contained in the wash bottle into the bottle containing the water, which should be loosely stoppered with purified cotton and kept, during the operation, at a temperature of about 10° C. When the air has been entirely displaced by the gas, disconnect the bottle from the apparatus and, having inserted the stopper, shake the bottle, loosening the stopper from time to time, until the gas ceases to be absorbed. If necessary, reconnect the bottle with the apparatus, and continue passing the gas and agitating, until the water is saturated. Finally, pour the chlorine water into small, dark amber-colored, glass-stoppered bottles, which should be completely filled. Chlorine T.S., even when kept from light and air, is apt to deteriorate. When required of full strength, it must be freshly prepared.

Preserve in a dark, cool place.

Cobaltous Chloride Test Solution (0.16 N.).—Dissolve 2 Gm. of cobaltous chloride in 1 cc. of hydrochloric acid and sufficient distilled water to make 100 cc.

Cupric Acetate Test Solution.—Dissolve 0.1 Gm. of cupric acetate in sufficient distilled water to make 100 cc., adding a few drops of acetic acid, if necessary, to make a clear solution.

Cupric Ammonium Sulphate Test Solution.—To cupric sulphate T.S., add ammonia T.S., drop by drop, until the precipitate at first formed is nearly but not completely redissolved, then allow to settle and decant the clear solution. This solution must be freshly made when required.

Cupric Oxide, Test Solution, Ammoniated (*Schweitzer's Reagent*).—Dissolve 10 Gm. of cupric sulphate, in 100 cc. of distilled water, add just sufficient 20 per cent. sodium hydroxide solution to precipitate the copper hydroxide, collect the latter on a filter, and wash free from sulphate. Then dissolve the purified, moist precipitate in the minimum quantity of ammonia T.S. necessary for complete solution.

Cupric Sulphate Test Solution (1 N.).—Dissolve 12.5 Gm. of cupric sulphate in sufficient distilled water to make 100 cc.

Denigè's Reagent.—Use *Mercuric Sulphate T.S.*

Diphenylamine Test Solution.—Dissolve 0.5 Gm. of diphenylamine in 100 cc. of reagent sulphuric acid, diluted with 20 cc. of distilled water. The solution should be colorless.

Ferric Ammonium Sulphate Test Solution (0.5 N.).—Dissolve 8 Gm. of reagent ferric ammonium sulphate in sufficient distilled water to make 100 cc.

Ferric Chloride Test Solution (1 N.).—Dissolve 9 Gm. of ferric chloride in sufficient distilled water to make 100 cc.

Ferrous Sulphate Test Solution.—Dissolve 8 Gm. of clear crystals of ferrous sulphate in about 100 cc. of distilled water, which has been freshly boiled. This solution must be freshly prepared when required.

Ferrous Sulphate Test Solution, Acid (0.5 N.).—Dissolve 7 Gm. of ferrous sulphate in crystals in 90 cc. of distilled water, which has been freshly boiled and cooled, and then add sufficient sulphuric acid to make 100 cc. This solution must be freshly prepared when required.

Formaldehyde Test Solution.—Use *Liquor Formaldehydi.*

Fuchsin-Sulphurous Acid Test Solution.—Dissolve 0.2 Gm. of fuchsin in 120 cc. of hot distilled water, cool the solution, add a solution of 2 Gm. of anhydrous sodium sulphite in 20 cc. of distilled water, and follow by 2 cc. of concentrated hydrochloric acid. Then dilute the solution with distilled water to 200 cc. and allow to stand for one hour before use. This solution must be frequently prepared.

Gelatin Test Solution.—Dissolve 1 Gm. of gelatin in 50 cc. of distilled water, with the aid of gentle heat and filter, if necessary. Prepare freshly when required.

Gold Chloride Test Solution (0.2 N.).—Dissolve 1 Gm. of reagent gold chloride in 35 cc. of distilled water.

Hydrogen Dioxide Test Solution.—Use *Liquor Hydrogenii Dioxidi.* This reagent must contain at least 3 per cent., by weight, of H_2O_2 when used.

Hydrogen Sulphide Test Solution.—A saturated aqueous solution of hydrogen sulphide, made by passing H_2S into cold distilled water. Keep the solution in small, dark amber-colored bottles, filled nearly to the top. Do not use unless it retains a strong odor of H_2S, and, when added to an equal volume of ferric chloride T.S., it produces at once a copious precipitate of sulphur. Preserve in a cool, dark place.

Hypophosphorous Acid Test Solution.—Use *Acidum Hypophosphorosum.*

Indigo Carmine Test Solution.—Dissolve 1 Gm. of sodium indigotindisulphonate in 150 cc. of distilled water.

Iodine and Potassium Iodide Test Solution.—Dissolve 0.5 Gm. of iodine and 1.5 Gm. of potassium iodide in 25 cc. of distilled water.

Iodine Test Solution.—Use the tenth-normal iodine volumetric solution.

Iodobromide Test Solution.—(For use in determining iodine absorption value). Dissolve 13.2 Gm. of reagent iodine in 1000 cc. of glacial acetic acid, with the aid of a gentle heat if necessary. Cool the solution to 25° C. and determine the iodine content in 20 cc. by titration with tenth-normal sodium thiosulphate, then add to the remainder of the solution a quantity of bromine chemically equivalent to that of the iodine present. Preserve in glass-stoppered bottles, protected from light.

Lead Acetate Glass Wool.—Immerse glass wool in a mixture of equal parts of lead acetate T.S. and distilled water, and remove the excess of liquid by pressing it between folds of filter paper. It should be freshly prepared when required for a test.

Lead Acetate Test Paper.—Immerse strips of heavy white filter paper, 6 mm. in width and 8 cm. in length, in a mixture of equal parts of lead acetate T.S. and distilled water, drain off the excess of liquid and dry the paper on glass in an oven at 100° C., avoiding contact with metal.

Lead Acetate Test Solution (0.5 N.).—Dissolve 9.5 Gm. of clear, transparent crystals of lead acetate, in sufficient freshly boiled distilled water to make 100 cc. Preserve in well-stoppered bottles.

Lead Acetate Test Solution, Alcoholic (0.1 N.).—Dissolve 2 Gm. of clear, transparent crystals of lead acetate in sufficient alcohol to measure 100 cc.

Preserve in well-stoppered bottles.

Lead Acetate Test Solution, Basic.—Dilute 4 Gm. of solution of lead subacetate (page 648) with enough distilled water, previously boiled and cooled, to make the product weigh 100 Gm. Preserve in small, well filled, and tightly-stoppered bottles.

Locke-Ringer's Solution:

Reagent Sodium Chloride	9.000 Gm.
Reagent Potassium Chloride	0.420 Gm.
Reagent Calcium Chloride, crystals	0.240 Gm.
Reagent Magnesium Chloride	0.005 Gm.
Sodium Bicarbonate	0.500 Gm.
Dextrose	0.500 Gm.
Water, freshly distilled from a hard glass flask	
To make	1000 cc.

The solution must be made up each day. The constituents (except the dextrose) may be made up in more concentrated stock solutions and diluted as needed.

Magnesia Mixture Test Solution.—Dissolve 5.5 Gm. of magnesium chloride and 7 Gm. of reagent ammonium chloride in 65 cc. of distilled water, add 35 cc. of ammonia T.S., set the mixture aside for a few days in a well-soppered bottle, and then filter. If not perfectly clear, filter the solution before using.

Magnesium Sulphate Test Solution (1 N.).—Dissolve 12 Gm. of magnesium sulphate in sufficient distilled water to make 100 cc.

Manganese Sulphate Test Solution (1 N.).—Dissolve 11 Gm. of manganese sulphate in 50 cc. of distilled water and add sufficient sulphuric acid to make 100 cc.

Mayer's Reagent.—See *Mercuric Potassium Iodide T.S.*

Mercuric Bromide Test Paper.—Cut stiff, heavy quantitative filter paper (see *Filter Paper, Quantitative*) into strips 3 mm. in width and about 12 cm. in length. Immerse these strips for five minutes in alcoholic mercuric bromide T.S. (see below). Remove the excess of solution by pressing the strips between filter paper and then dry them quickly on glass in an oven heated to 100° C. Place at once in a glass-stoppered, wide-mouthed bottle, and protect from light.

Mercuric Bromide Test Solution, Alcoholic (0.3 N.).—Dissolve 5 Gm. of mercuric bromide in 100 cc. of alcohol, employing a gentle heat to facilitate solution.

Preserve in glass-stoppered bottles, and protect from light.

Mercuric Chloride Test Solution (0.5 N.).—Dissolve 6.5 Gm. of mercuric chloride in sufficient distilled water to make 100 cc.

Mercuric Nitrate Test Solution (4 N.).—Dissolve 40 Gm. of red mercuric oxide in a mixture of 32 cc. of nitric acid and 15 cc. of distilled water.

Preserve in glass-stoppered bottles, protected from light.

Mercuric Potassium Iodide Test Solution (*Mayer's Reagent*).—Dissolve 1.358 Gm. of mercuric chloride in 60 cc. of distilled water, and 5 Gm. of potassium iodide in 10 cc. of distilled water. Mix the two solutions and then add sufficient distilled water to make 100 cc.

Mercuric Potassium Iodide Test Solution, Alkaline (*Nessler's Reagent*).—Dissolve 10 Gm. of potassium iodide in 10 cc. of distilled water, and add gradually, in portions, a saturated aqueous solution of mercuric chloride, with constant agitation until a slight red precipitate remains undissolved. To this mixture add 30 Gm. of potassium hydroxide, and, after solution has taken place, add 1 cc. additional of the saturated aqueous solution of mercuric chloride. Dilute this solution with distilled water until it measures 200 cc. Allow the precipitate to subside and draw off the clear liquid. A 2 cc. portion of this reagent, when added to 50 cc. of distilled water containing 0.05 mgm. of ammonia, produces at once a yellowish-brown coloration.

Mercuric Sulphate Test Solution (*Denigè's Reagent*).—Mix 5 Gm. of yellow mercuric oxide with 40 cc. of distilled water and while stirring add 20 cc. of sulphuric acid, then add 40 cc. additional distilled water, and stir until completely dissolved.

Mercurous Nitrate Test Solution (0.5 N.).—Mix 20 Gm. of mercury with 10 cc. of nitric acid and 10 cc. of distilled water, in a porcelain dish and set it aside for twenty-four hours in a cool, dark place. Separate and drain the crystals of mercurous nitrate and dissolve 15 Gm. of the crystals in a mixture of 90 cc. of distilled water and 10 cc. of diluted nitric acid.

Preserve in a dark amber-colored bottle in which a small globule of mercury is placed.

Metaphenylenediamine Hydrochloride Test Solution.—Dissolve 1 Gm. of metaphenylenediamine hydrochloride in 200 cc. of distilled water: the solution is colorless. If necessary, decolorize by heating with freshly carbonized animal charcoal.

Naphthylamine Acetate Test Solution.—Dissolve 0.5 Gm. of reagent naphthylamine acetate in 100 cc. of 30 per cent. acetic acid and filter quickly through purified cotton.

Preserve in well-stoppered bottles, protected from light.

Nessler's Reagent.—Use *Mercuric Potassium Iodide T.S., Alkaline* (see above).

Oxalic Acid Test Solution (1 N.).—Dissolve 6.8 Gm. of oxalic acid in sufficient distilled water to measure 100 cc.

Palladous Chloride Test Solution.—Dissolve 0.5 Gm. of palladous chloride in sufficient distilled water to measure 10 cc.

Preserve in glass-stoppered bottles.

Phenol Disulphonic Acid Test Solution.—Dissolve 2.5 Gm. of colorless phenol in 15 cc. of reagent concentrated sulphuric acid in a flask of suitable capacity. Add 7.5 cc. of fuming sulphuric acid, stir well, and heat for two hours at 100° C. Transfer the product, while still fluid, to a glass-stoppered bottle, and, when desired for use, warm in a water bath until liquefied.

Phloroglucinol Test Solution.—Dissolve 0.5 Gm. of phloroglucinol in 25 cc. of alcohol.

Preserve in a tightly-stoppered bottle, protected from light.

Picric Acid Test Solution (*Trinitrophenol Test Solution*).—Dissolve 1 Gm. of picric acid in 100 cc. of hot distilled water. Cool the solution and filter, if necessary.

Platinic Chloride Test Solution (0.5 N.).—Dissolve 2.6 Gm. of platinic chloride in sufficient distilled water to make 20 cc.

Potassium Acetate Test Solution.—Dissolve 10 Gm. of potassium acetate in sufficient distilled water to make 100 cc.

Potassium Carbonate Test Solution (1 N.).—Dissolve 7 Gm. of reagent anhydrous potassium carbonate in sufficient distilled water to make 100 cc.

Potassium Chromate Test Solution.—Dissolve 10 Gm. of potassium chromate in sufficient distilled water to make 100 cc.

Potassium Dichromate Test Solution (1 N., based on the basicity of CrO_3.).—Dissolve 7.5 Gm. of potassium dichromate in sufficient distilled water to make 100 cc.

Potassium Ferricyanide Test Solution (1 N.).—Dissolve 1 Gm. of potassium ferricyanide in 10 cc. of distilled water. The solution must be freshly prepared when required.

Potassium Ferrocyanide Test Solution (1 N.).—Dissolve 10 Gm. of potassium ferrocyanide in sufficient distilled water to make 100 cc.

Potassium Hydroxide Test Solution (1 N.).—Dissolve 6.5 Gm. of potassium hydroxide in sufficient distilled water to make 100 cc.

Potassium Hydroxide Test Solution, Alcoholic.—Use half-normal alcoholic potassium hydroxide.

Potassium Iodide Test Solution (1 N.).—Dissolve 16.5 Gm. of potassium iodide in sufficient distilled water to make 100 cc.

Preserve in dark amber-colored, well-stoppered bottles.

Potassium Permanganate Test Solution.—Use tenth-normal potassium permanganate.

Potassium Sulphate Test Solution.—Dissolve 1 Gm. of potassium sulphate in sufficient distilled water to make 100 cc.

Potassium Thiocyanate Test Solution (*Potassium Sulphocyanate Test Solution*).—Use tenth-normal potassium thiocyanate.

Pyrogallol Test Solution, Alkaline.—Dissolve 0.5 Gm. of pyrogallol in 2 cc. of distilled water, and 12 Gm. of potassium hydroxide in 8 cc. of distilled water. The solutions should be freshly prepared and mixed immediately before using.

Resorcinol Test Solution.—Dissolve 1 Gm. of resorcinol in sufficient reagent concentrated hydrochloric acid to make 100 cc.

Silver Ammonium Nitrate Test Solution.—Dissolve 1 Gm. of silver nitrate in 20 cc. of distilled water and add ammonia T.S., drop by drop, agitating the mixture until the precipitate at first produced is almost but not entirely redissolved, and filter.

Preserve in dark amber-colored, well-stoppered bottles.

Silver Nitrate Test Solution.—Use tenth-normal silver nitrate.

Silver Sulphate Test Solution.—Mix 1 Gm. of silver sulphate with 100 cc. of distilled water in a glass-stoppered bottle and shake the mixture thoroughly. Decant the clear solution when required for use.

Sodium Acetate Test Solution (1 N.).—Dissolve 13.6 Gm. of sodium acetate in sufficient distilled water to make 100 cc.

Sodium Bisulphite Test Solution.—Dissolve 30 Gm. of sodium bisulphite in sufficient distilled water to make 100 cc. Should the solution possess a strong odor of sulphur dioxide, add sodium hydroxide T.S., drop by drop, until the odor becomes barely perceptible. The solution must be freshly prepared when required.

Sodium Bitartrate Test Solution (1 N.).—Dissolve 9 Gm. of sodium bitartrate in 100 cc. of distilled water. The solution must be freshly prepared when required.

Sodium Carbonate Test Solution (2 N.).—Dissolve 12.5 Gm. of monohydrated sodium carbonate in sufficient distilled water to make 100 cc.

Sodium Cobaltic Nitrite Test Solution.—Dissolve 4 Gm. of cobaltous chloride and 10 Gm. of sodium nitrite in about 50 cc. of distilled water, add 2 cc. of acetic acid, and dilute with sufficient distilled water to make 100 cc. This reagent must not be kept longer than three months. It may be preserved for this length of time by the occasional addition of a few drops of acetic acid.

Sodium Cyanide Test Solution (2 N.).—Dissolve 1 Gm. of sodium cyanide in sufficient distilled water to make 10 cc. The solution must be freshly prepared when required.

Sodium Hydroxide Test Solution (1 N.).—Dissolve 4.3 Gm. of sodium hydroxide in sufficient distilled water to make 100 cc.

Sodium Hydroxide Test Solution, Special.—This solution is to be prepared of the same strength as *Liquor Sodii Hydroxidi*, employing sodium hydroxide, which, in addition to the tests prescribed under *Sodii Hydroxidum*, should show not more than 0.005 per cent. of *chloride* determined by the turbidimetric test, page 1550.

Sodium Hypobromite Test Solution.—To a solution of 40 Gm. of sodium hydroxide in 150 cc. of distilled water, add 10 cc. of bromine, and, after solution has taken place, add sufficient distilled water to make 200 cc. The solution must be freshly prepared when required.

Sodium Nitroprusside Test Solution.—Dissolve 1 Gm. sodium nitroprusside in sufficient distilled water to make 20 cc. This solution must be freshly prepared when required.

Sodium Phosphate Test Solution (1 N.).—Dissolve 12 Gm. of clear crystals of sodium phosphate in sufficient distilled water to make 100 cc.

Sodium Phosphotungstate Test Solution.—To a solution of 20 Gm. of sodium tungstate in 100 cc. of distilled water, add sufficient phosphoric acid to impart a strongly acid reaction to litmus paper, and filter. When required for use, decant the clear solution from any sediment that may be present.

Preserve the solution in amber-colored, glass-stoppered bottles.

Sodium Sulphide Test Solution (1 N.).—Dissolve 12 Gm. of sodium sulphide in sufficient distilled water to make 100 cc.

NOTE: Sodium sulphide T.S. may be used in all cases when ammonium sulphide T.S. is directed. The solution must be freshly prepared when required for use.

Sodium Tartrate Test Solution (1 N.).—Dissolve 11.5 Gm. of sodium tartrate in sufficient distilled water to make 100 cc.

Sodium Thiosulphate Test Solution.—Use tenth-normal sodium thiosulphate.

Stannous Chloride Test Solution.—Dissolve 1.5 Gm. of stannous chloride in 10 cc. of distilled water containing a few drops of hydrochloric acid.

Preserve the solution in a glass-stoppered bottle in which a fragment of reagent tin has been placed. The solution must be renewed at frequent intervals.

Stannous Chloride Test Solution, Acid.—Dissolve 40 Gm. of stannous chloride in 60 cc. of reagent concentrated hydrochloric acid.

Preserve in a glass-stoppered bottle.

Starch Test Solution.—Triturate 1 Gm. of reagent starch with 10 cc. of cold distilled water, add sufficient boiling distilled water, with constant stirring, to make 200 cc., then boil the mixture until a thin, translucent fluid is obtained. The solution must be freshly prepared and filtered, if necessary.

Starch-Potassium Iodide Test Solution.—Dissolve 0.5 Gm. of potassium iodide in 100 cc. of freshly prepared starch T.S. This solution should be made not longer than twenty-four hours before use.

Sulphanilic Acid Test Solution.—Dissolve 0.8 Gm. of sulphanilic acid in 100 cc. of a 30 per cent. solution of acetic acid. Preserve in well-stoppered bottles.

Sulphuric Acid Test Solution.—Use *Acidum Sulphuricum Dilutum*, page 1559.

Tannic Acid Test Solution.—Dissolve 1 Gm. of tannic acid in 1 cc. of alcohol, and add sufficient distilled water to measure 10 cc. This solution should be freshly prepared when required for use.

Tartaric Acid Test Solution (4 N.).—Dissolve 6 Gm. of tartaric acid in sufficient distilled water to measure 20 cc. This solution should be freshly prepared.

Trinitrophenol Test Solution.—See *Picric Acid T.S.*

Turmeric Test Paper.—Impregnate sheets of white filter paper with turmeric T.S., dry, and cut into strips of a suitable size. Preserve in well-stoppered bottles.

Turmeric Test Solution.—Digest 20 Gm. of powdered turmeric with 4 successive portions of 100 cc. each of cold distilled water, decanting the clear liquid portion each time and discarding it. Then dry the residue at a temperature not over 100° C., and digest it with 100 cc. of alcohol for several days, and filter. Turmeric turns yellow with acids, and brown with alkalies. It is unsuitable for ordinary titrations, being used for special tests.

Indicators

(U. S.)

An indicator is a substance used in volumetric analysis, usually in solution, which shows by a change of color the exact point at which a reaction is complete.

Each indicator test solution used in acidimetric or alkalimetric tests must be examined for its sensitiveness. The indicator test solution, unless otherwise directed, should be so adjusted that when 0.15 cc. of the indicator is added to 25 cc. of distilled water, 0.5 cc. of hundredth-normal acid or alkali, respectively, will distinctly develop the characteristic color changes. Indicator test solutions are injured by exposure to light and should be preserved in dark amber-colored vials. Test papers should be kept in dark bottles.

[Further information on indicators is contained in the article on *Hydrogen Ion Concentration*, Part II of this volume.]

Brom Cresol Purple (*Dibromo-orthocresol-sulphonphthalein*)—$(OH.C_6H_2BrCH_3)_2CO.C_6H_4SO_2$.—Light pink to yellowish crystals (melting point from 241° to 242° C. uncorrected), soluble in alcohol, water, and in solutions of alkali hydroxides and carbonates. Alkaline solutions of brom cresol purple are colored deep purple and exhibit dichromatism, *i. e.*, predominance of red in thick layers and of blue in thin layers. The color is changed to yellow on the addition of acids.

Brom Cresol Purple Test Solution.—In an agate mortar, grind 0.1 Gm. of the dry powder with 9.5 cc. of fiftieth-normal sodium hydroxide. When solution is complete, dilute to 250 cc. with boiled-out and cooled distilled water.

This test solution should be deep orange to wine-red in color. If it is purple, the addition of not more than 0.5 cc. of fiftieth-normal acid (to the 250 cc.) should make it wine-red; and if it is yellow, the addition of not more than 0.5 cc. of fiftieth-normal alkali should produce the wine-red coloration. The pH range is from yellow, 5.2 to 6.8, purple. Preserve in glass-stoppered bottles.

Cochineal Test Solution.—Macerate 1 Gm. of unbroken cochineal (page 357) during four days with 20 cc. of alcohol and 60 cc. of distilled water, then filter. The color of this test solution is turned violet by alkalies, and yellowish-red by acids. Cochineal T.S. is used in titrating alkaloids.

Litmus.—A blue pigment prepared from various species of *Roccella* DeCandolle. In blue cubes, masses, fragments or granules, partly soluble in water and in alcohol.

Litmus Paper.—For blue litmus paper, impregnate sheets of white filter paper with litmus T.S. and dry by suspending them on clean cord in a neutral atmosphere.

For red litmus paper, add to litmus T.S. just sufficient of a highly diluted solution of hydrochloric acid to impart to it a faint red tint, impregnate, and dry sheets of filter paper as directed above. The impregnated sheets after drying may be cut into strips as desired. Litmus test papers should respond quickly to one drop of two-hundred-and-fiftieth-normal acid or alkali, respectively. Preserve in well-stoppered bottles.

Litmus Test Solution.—Exhaust 25 Gm. of powdered litmus with three successive portions of 100 cc. each of boiling alcohol, continuing each extraction for about one hour. Filter, wash with alcohol, and discard the alcoholic filtrate. Digest the residue with about 25 cc. of cold distilled water and filter. Discard this filtrate also. Finally extract the residue with 125 cc. of boiling distilled water and, after thoroughly cooling, filter. Litmus turns red with acids and blue with alkalies. The pH range is from red, 4.5 to 8.3, blue. Litmus is unsuitable for determining alkaloids, carbonates, or bicarbonates. Preserve the filtrate in wide-mouthed bottles, stoppered with loose plugs of purified cotton.

Methyl Orange (*Tropæolin D., Dimethylaniline Orange*).—The sodium salt of paradimethylaminoazobenzene sulphonic acid, $(CH_3)_2\text{–}N\text{–}C_6H_4\text{–}N=N\text{–}C_6H_4.SO_3Na$. An orange-yellow powder, slightly soluble in cold water, insoluble in alcohol.

Methyl Orange Test Solution.—Dissolve 0.1 Gm. of methyl orange in 100 cc. of distilled water. Methyl orange turns from orange to rose-red with acids, and to yellow with alkalies. This indicator is not suitable for determining organic acids or alkaloids, nor should it be used in alcoholic or in very hot solutions. The pH range is from orange red, 3.1 to 4.4, yellow.

Methyl Red (*Paradimethylaminoazobenzeneorthocarboxylic Acid*) $(CH_3)_2\text{–}N\text{–}C_6H_4\text{–}N=N\text{–}C_6H_4.COOH$.—Violet crystals sparingly soluble in cold water, soluble in alcohol.

Methyl Red Test Solution.—Dissolve 0.2 Gm. of methyl red in 100 cc. of alcohol. Methyl red turns from red with acids to yellow with alkalies. This solution is unsatisfactory for the determination of carbonates or bicarbonates. It is very satisfactory for many alkaloids. The pH range is from red, 4.2 to 6.3, yellow.

Phenol Red (*Phenolsulphonphthalein*).—Use *Phenolsulphonphthaleinum*, page 834.

Phenol Red Test Solution.—In an agate mortar, grind 0.1 Gm. of the dry powder with 14.5 cc. of fiftieth-normal sodium hydroxide. When solution is complete, dilute to 250 cc. with boiled-out and cooled distilled water. Filter off the insoluble residue. The zone of color transformation of this indicator is from yellow, pH 6.8 to 8.4, red. Preserve in a glass-stoppered bottle.

Phenolphthalein.—Use *Phenolphthaleinum*, page 833.

Phenolphthalein Test Solution.—Dissolve 1 Gm. of phenolphthalein in 100 cc. of alcohol. Phenolphthalein is colorless with acids and turns red with alkalies. This test solution is not satisfactory for determining alkaloids, ammonia, carbonates, or bicarbonates in cold solutions. The pH range is from colorless, 8.3 to 10.0, red.

Phenolphthalein Test Paper.—Impregnate sheets of white unsized paper with phenolphthalein T.S., dry, and cut into strips of a suitable size. Preserve as directed under litmus paper.

Volumetric Solutions

(U. S.)

It is absolutely necessary that the measuring vessels employed in the operations of volumetric analysis (burettes, flasks, mixing cylinders, pipettes, etc.) shall agree accurately among themselves in their graduation at the standard temperature selected. All volumetric solutions, if practicable, should be prepared at the standard temperature of 25° C. and used in titrations at that standard temperature. If a titration is made at a markedly different temperature, a volumetric solution should be used which has been standardized for such temperature. In case graduated apparatus calibrated at 25° C. is not procurable, volumetric solutions may be prepared at the temperature for which the apparatus in hand was graduated (*e.g.*, 15° C. or 20° C.), and all such volumetric solutions should be marked to indicate the temperature at which they have been standardized. Such solutions must be used as above stated at the temperature at which the apparatus is standardized, care being taken that all graduated apparatus used be standardized at the same temperature.

Units of Capacity.—The units of volume employed by this Pharmacopœia must accord with its standard liter at 25° C., which represents the volume occupied by 996.04 Gm. of distilled water, weighed in air with brass weights, at a temperature of 25° C.[1] and barometer at 760 mm. To secure uniformity among the various forms of apparatus employed, the standard specifications of the U. S. Bureau of Standards should be adhered to as closely as possible, except that the temperature adopted is 25° C. The tables for calibrating graduated apparatus will be found on page 1632.

Measuring Flasks.—Standard measuring flasks are calibrated to contain, when filled to the mark, 1000, 500, 250, 200, or 100 cc., at 25° C. The necks must be of uniform caliber, and measure in diameter not less than 14 mm. and not more than 20 mm. for 1000 cc. capacity; from 12 mm. to 18 mm. for 500 cc. capacity; from 10 mm. to 15 mm. for 250 cc. capacity, and from 8 mm. to 12 mm. for 100 cc. capacity. The capacity mark on any of these flasks should be not less than 6 cm. distant from the mouth and not less than 2 cm. from the base of the neck.

Cylinders.—These should be graduated to contain their respective volumes at the standard temperature. Their inside diameter must not be more than one-fifth the graduated length.

Transfer Pipettes.—These should be graduated to deliver at standard temperature the exact volume of fluid indicated. The suction stem should be at least 16 cm. long, and the delivery tube not less than 3 cm. and not more than 25 cm. long. The inside diameter at the capacity mark must not be less than 2 mm. and must not exceed 4 mm. for those of 25 cc. capacity. The capacity mark should not be more than 6 cm. from the bulb. The outlet of any transfer pipette should be of such size that the free outflow for water shall last not more than one minute, and not less than fifteen seconds for 5 cc., twenty seconds for 10 cc., and thirty seconds for 50 cc. After filling, the fluid adhering to the outside should be wiped from the stem; then when draining the contents, the pipette should be held in a vertical position; finally, to complete the emptying, the tip of the pipette should be held against the side of the vessel, permitting the last portions of the fluid to flow out by gravity. Pipettes should never be drained by blowing into them, except the Oswald pipettes which are especially graduated for use in this way.

Burettes.—These must be provided with glass stop-cocks and be graduated for use at the standard temperature. Burettes provided with rubber tubes and pinch-cocks in place of glass stop-cocks may be used for potassium and sodium hydroxide V.S. The tips should be gradually tapered from 2 to 3 cm. in length and slightly bent. The rate of outflow should be regulated so that not less than 2 seconds should be consumed for each cc. delivered. When completing titration, the tip of the delivery tube should be touched with the wet surface of the receiving vessel to complete the emptying.

GENERAL DIRECTIONS.—All bottles in which volumetric solutions are to be kept, as well as the burettes or pipettes in which they are to be measured, should be thoroughly cleaned prior to use, and rinsed first with distilled water, and then with two or three small portions of the solution that they are to contain. In all apparatus where the surface of the fluid is limited by a meniscus, the reading must be made from the lowest point of the meniscus unless the liquid is too opaque to permit exact observation of that point. It is of the utmost importance that the inner surface of all measuring apparatus shall be free from any suggestion of greasiness.

Normal Volumetric Solutions $\left(\frac{N}{1}\right)$ are those which contain in 1000 cc., in any stated reaction, the chemical equivalent of 1.008 Gm. of hydrogen. If the molecule of the reagent is univalent, one liter will contain a weight in grammes equal to the molecular weight of the reagent; if bivalent, a weight in grammes equal to one-half its molecular weight; if trivalent, a weight in grammes equal to one-third its molecular weight. Thus, hydrochloric acid, $HCl = 36.47$, having but one H atom replaceable by a basic element, has 36.47 Gm. of HCl in 1000 cc. of the normal volumetric solution; while sulphuric acid, $H_2SO_4 = 98.09$, having two replaceable H atoms, contains only one-half this number, or 49.045 Gm. of H_2SO_4 in 1000 cc. of its normal solution. Potassium hydroxide, $KOH = 56.11$, has but one K to replace one H in acids, hence its normal solution contains 56.11 Gm. of KOH in one liter. Again, one molecule of potassium dichromate ($K_2Cr_2O_7 = 294.20$) in oxidation liberates three atoms of oxygen which are capable of combining with six atoms of hydrogen. Therefore, each molecule of the dichromate, yielding three atoms of oxygen, is equivalent to six atoms of hydrogen. Hence, the normal solution should contain $\frac{294.20}{6}$ or 49.0333 Gm. in 1000 cc. Two molecules of potassium permanganate, $2KMnO_4 = 316.06$, in oxidation, give off five atoms of O, which are equivalent to ten atoms of H; hence its normal solution should contain $\frac{316.06}{10}$ or 31.606 in 1000 cc. Solutions containing in 1000 cc. one-tenth of the quantity of the active reagent in the normal solution are called tenth-normal (decinormal) $\left(\frac{N}{10}\right)$ (normality = 0.1); those containing one one-hundredth, hundredth-normal (centinormal) $\left(\frac{N}{100}\right)$ (normality = 0.01); those containing one-fiftieth, fiftieth-normal $\left(\frac{N}{50}\right)$ (normality = 0.02); those containing twice the amount, double-normal $\left(\frac{2N}{1}\right)$ (normality = 2); half the amount, half-normal $\left(\frac{N}{2}\right)$ (normality = 0.5). Solutions containing quantities of the active reagent having no simple relation to the molecular weight are called empirical. The general policy has been followed to limit the factors of volumetric solutions to four significant figures.

Use of Empirical Solutions.—As it is difficult to maintain the theoretical standard strength with many volumetric solutions, it is not absolutely necessary that such standard strength be maintained, or even attained originally. A solution of approximately the desired normality is prepared and its strength accurately determined. The correction factor of the normality is applied in all calculations where the empirical solution is employed. As many volumetric solutions are subject to alteration in strength on keeping, their strength should frequently be ascertained.

When the same kind of volumetric solution of several normalities is used, the details of the preparation and standardization are given for the strength most frequently required. Stronger or weaker solutions are prepared and standardized in the same manner as the solutions described, using proportionate amounts of material. Whenever convenient, it is preferable to prepare tenth or lower normality solutions by properly diluting the stronger volumetric solutions, but in preparing any alkali hydroxide volumetric solution by dilution, its exact strength must be ascertained by the same method of titration as described under the stronger solution.

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[1] 500 cc. would weigh 498.02 Gm.; 250 cc., 249.01 Gm.; 100 cc., 99.604 Gm.

Alkaline Cupric Tartrate Volumetric Solution

FEHLING'S SOLUTION

A. The Copper Solution.—Dissolve 34.66 Gm. of carefully selected, small crystals of cupric sulphate, showing no trace of efflorescence or of adhering moisture, in a sufficient quantity of distilled water to make the solution measure exactly 500 cc. at standard temperature. Keep this solution in small, well-stoppered bottles.

B. The Alkaline Tartrate Solution.—Dissolve 173 Gm. of crystallized potassium and sodium tartrate and 50 Gm. of sodium hydroxide in a sufficient quantity of distilled water to make the solution measure exactly 500 cc. at standard temperature. Keep the solution in small, rubber-stoppered bottles.

For use, mix exactly equal volumes of the two solutions at the time required.

NOTE: In this Pharmacopœia Fehling's Solution is not used as a volumetric reagent, but is used qualitatively. The correct formula is given for the volumetric solution, because of its extensive use in this manner. It must always be used under carefully standardized conditions in quantitative work, and in connection with tables which will be found in "Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists."

Barium Hydroxide, Tenth-Normal

$Ba(OH)_2.8H_2O = 315.51$ 15.776 Gm. in 1000 cc.

Dissolve about 18 Gm. of reagent barium hydroxide in 1000 cc. of recently boiled and cooled distilled water, and, if necessary, filter the solution quickly.

Ascertain the exact strength by titration against tenth-normal hydrochloric acid, phenolphthalein T.S. being used as indicator, and adjust to exact normality or to a known strength of approximate normality. This solution deteriorates rapidly and should be standardized before using.

Preserve the solution in rubber-stoppered bottles provided with soda-lime tube as directed under normal sodium hydroxide.

One cubic centimeter of Tenth-Normal Barium Hydroxide is the equivalent of:

	Gramme
Barium Hydroxide, $Ba(OH)_2.8H_2O$	0.01578
Ammonium Benzoate, $NH_4C_7H_5O_2$	0.01391
Ammonium Salicylate, $NH_4C_7H_5O_3$	0.01551
Benzoic Acid, $HC_7H_5O_2$	0.01221
Hydrochloric Acid, HCl	0.03647
Salicylic Acid, $HC_7H_5O_3$	0.01381
Sodium Benzoate, $NaC_7H_5O_2$	0.01441
Sulphuric Acid, H_2SO_4	0.004904

Bromine, Tenth-Normal

KOPPESCHAAR'S SOLUTION

Br = 79.92 7.992 Gm. in 1000 cc.

Dissolve 3 Gm. of potassium bromate and 50 Gm. of potassium bromide in sufficient distilled water to make 1000 cc.

Ascertain its exact strength by titration against tenth-normal sodium thiosulphate after the addition of potassium iodide and a slight excess of hydrochloric acid, and adjust to exact normality or to a known strength of approximate normality. Preserve in dark amber-colored, glass-stoppered bottles.

One cubic centimeter of Tenth-Normal Bromine is the equivalent of:

	Gramme
Bromine, Br	0.007992
Phenol, C_6H_5OH	0.001568
Resorcinol, $C_6H_4(OH)_2$	0.001835
Sodium Phenolsulphonate, anhydrous, $NaC_6H_5O_4S$	0.004903
Sodium Phenolsulphonate, crystallized, $NaC_6H_5O_4S.2H_2O$	0.005804

Hydrochloric Acid, Normal

HCl = 36.47 36.47 Gm. in 1000 cc.

Mix 95 cc. of hydrochloric acid with sufficient distilled water to measure 1000 cc.

Ascertain its exact strength by titration against freshly standardized sodium carbonate or normal sodium hydroxide, methyl orange T.S. being used as indicator; or gravimetrically by precipitation as silver chloride, and adjust to exact normality or to a known strength of approximate normality.

One cubic centimeter of Normal Hydrochloric Acid is the equivalent of:

	Gramme
Hydrochloric Acid, HCl	0.03647
Barium Hydroxide, $Ba(OH)_2.8H_2O$	0.1578
Calcium Carbonate, $CaCO_3$	0.05004
Calcium Hydroxide, $Ca(OH)_2$	0.03705

	Gramme
Calcium Oxide, CaO	0.02804
Potassium Hydroxide, KOH	0.05611
Sodium Borate, anhydrous, $Na_2B_4O_7$	0.1008
Sodium Borate, crystallized, $Na_2B_4O_7.10H_2O$	0.1909
Sodium Cacodylate, anhydrous, $Na(CH_3)_2.AsO_2$	0.16002
Sodium Hydroxide, $NaOH$	0.04001

NOTE: Normal hydrochloric acid is in every aspect equivalent in neutralizing power to normal sulphuric acid and may be employed, except in special cases, for the same purposes.

Hydrochloric Acid, Half-Normal

$HCl = 36.47$ 18.235 Gm. in 1000 cc.

One cubic centimeter of Half-Normal Hydrochloric Acid is the equivalent of:

	Gramme
Hydrochloric Acid, HCl	0.01824

Other factors are identical with those under Half-Normal Sulphuric Acid.

Hydrochloric Acid, Fiftieth-Normal

$HCl = 36.47$ 0.7294 Gm. in 1000 cc.

One cubic centimeter of Fiftieth-Normal Hydrochloric Acid is the equivalent of:

	Gramme
Hydrochloric Acid, HCl	0.0007294

This volumetric solution is not used officially for titration but is employed in connection with the special Turbidimetric Test.

Iodine, Tenth-Normal

$I = 126.92$ 12.692 Gm. in 1000 cc.

METHOD I.—Dissolve 12.692 Gm. of reagent iodine in a solution of 18 Gm. of potassium iodide in 100 cc. of distilled water. Then add sufficient distilled water to make the solution measure exactly 1000 cc. at 25° C. Unless freshly prepared its normality should always be redetermined before use. Preserve in glass-stoppered bottles.

METHOD II.—Tenth-normal iodine may also be prepared as follows:

Dissolve about 14 Gm. of reagent iodine in a solution of 18 Gm. of potassium iodide in about 100 cc. of distilled water, diluting finally to 1000 cc. Carefully measure from a burette 25 cc. of this solution (which is too concentrated), into a flask, then add gradually and cautiously from a burette tenth-normal sodium thiosulphate, shaking constantly, until the color of the solution is but slightly yellow, then add a few drops of starch T.S. and continue the addition of the tenth-normal sodium thiosulphate until the blue color is just discharged. Note the number of cc. of the tenth-normal sodium thiosulphate consumed and then dilute the iodine solution so that 25 cc. will require for decolorization exactly 25 cc. of the tenth-normal sodium thiosulphate at standard temperature.

One cubic centimeter of Tenth-Normal Iodine is the equivalent of:

	Gramme
Iodine, I	0.01269
Acetone, $(CH_3)_2CO$	0.0009677
Antimony and Potassium Tartrate, crystallized, $K(SbO)C_4H_4O_6.\frac{1}{2}H_2O$	0.01662
Arsenic, in arsenous compounds, As	0.003748
Arsenous Iodide, AsI_3	0.02279
Arsenic Trioxide (Arsenous Acid), As_2O_3	0.004948
Calcium Sulphide, CaS	0.003607
Iron, Fe	0.002792
Mercurous Chloride, $HgCl$	0.02361
Mercurous Iodide, HgI	0.03275
Mercury (in mercurous compounds), Hg	0.02006
Sodium Bisulphite, $NaHSO_3$	0.005204
Sodium Sulphite, anhydrous, Na_2SO_3	0.006303
Sodium Thiosulphate, anhydrous, $Na_2S_2O_3$	0.01581
Sodium Thiosulphite, crystallized, $Na_2S_2O_3.5H_2O$	0.02482
Sulphur Dioxide, SO_2	0.003203

Oxalic Acid, Tenth-Normal

$H_2C_2O_4.2H_2O = 126.06$ 6.303 Gm. in 1000 cc.

Dissolve 6.45 Gm. of reagent oxalic acid in sufficient distilled water to measure 1000 cc. Ascertain its exact strength by titration against freshly standardized tenth-normal sodium hydroxide, phenolphthalein T.S. being used as indicator, and adjust to exact normality or to a known strength of approximate normality.

One cubic centimeter of Tenth-Normal Oxalic Acid is the equivalent of:

	Gramme
Oxalic Acid, crystallized, $H_2C_2O_4.2H_2O$	0.006303
Ammonia Gas, NH_3	0.001703
Calcium Carbonate, $CaCO_3$	0.005004

	Gramme
Calcium Hydroxide, $Ca(OH)_2$	0.003705
Calcium Oxide, CaO	0.002804
Lead, Pb	0.01036
Lead Acetate, anhydrous, $Pb(C_2H_3O_2)_2$	0.01626
Lead Acetate, crystallized, $Pb(C_2H_3O_2)_2.3H_2O$	0.01897
Lead Oxide, PbO	0.01116
Lead Peroxide, PbO_2	0.01196
Lead Subacetate, approximately, $Pb_2O(C_2H_3O_2)_2$	0.01371
Manganese Dioxide, MnO_2	0.004347
Potassium Hydroxide, KOH	0.005611
Potassium Permanganate, $KMnO_4$	0.003161
Sodium Hydroxide, $NaOH$	0.004001

Potassium Dichromate, Tenth-Normal

$K_2Cr_2O_7 = 294.20$ 4.9033 Gm. in 1000 cc.

Method I.—Dissolve 4.9033 Gm. of potassium dichromate, which has been pulverized and dried to constant weight at 120° C., in sufficient distilled water to measure exactly 1000 cc. at standard temperature.

Method II.—Tenth-normal potassium dichromate may also be prepared as follows:

Dissolve about 5 Gm. of potassium dichromate in 1000 cc. of distilled water, transfer exactly 25 cc. of this solution to a 500 cc. glass-stoppered flask, add 2 Gm. of potassium iodide (free from iodate), dilute with 200 cc. of distilled water, add 5 cc. of hydrochloric acid, allow to stand for ten minutes in a dark place, and titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch T.S. at the end of the titration as indicator. Adjust to exact normality or to a known strength of approximate normality.

For estimating ferrous iron, it is used in the following manner. Introduce an acidulated aqueous solution of the ferrous compound into a flask. Gradually add the tenth-normal potassium dichromate from a burette with agitation until a drop placed upon a white porcelain surface no longer becomes blue when mixed with a drop of freshly prepared potassium ferricyanide T.S. Several closely agreeing determinations should be made before finally calculating the result.

One cubic centimeter of Tenth-Normal Potassium Dichromate is the equivalent of:

	Gramme
Potassium Dichromate, $K_2Cr_2O_7$	0.004903
Ferrous Carbonate, $FeCO_3$	0.01159
Ferrous Sulphate, anhydrous, $FeSO_4$	0.01519
Ferrous Sulphate, crystallized, $FeSO_4.7H_2O$	0.02780
Iron, in ferrous compounds, Fe	0.005584
Sodium Thiosulphate, $Na_2S_2O_3.5H_2O$	0.02482

Potassium Hydroxide, Dekanormal

$KOH = 56.11$ 561.1 Gm. in 1000 cc.

Prepare and preserve as directed under normal potassium hydroxide.

Note: This solution is intended specifically for the ready measurement of definite amounts of absolute potassium hydroxide, hence it is not necessary to adjust the solution to exact strength, but the factor of strength must be accurately known and the solution used accordingly. The use of barium hydroxide in this solution is unnecessary, provided the solution be allowed to settle before standardizing and only the clear liquid employed.

Potassium Hydroxide, Normal

$KOH = 56.11$ 56.11 Gm. in 1000 cc.

Normal Potassium Hydroxide is used only as an alternative solution. It is prepared and standardized in exactly the same manner as normal sodium hydroxide, using an equivalent quantity of the base for preparing the solution.

The factors for this solution are the same as for normal sodium hydroxide which is preferred on account of its economy.

Potassium Hydroxide Alcoholic, Half-Normal

$KOH = 56.11$ 28.055 Gm. in 1000 cc.

Dissolve 2.5 Gm. of silver nitrate in 5 cc. of distilled water and add the solution to 1200 cc. of alcohol in a glass-stoppered bottle, and mix thoroughly. Dissolve 5 Gm. of potassium hydroxide in 25 cc. of warm alcohol, cool the solution, and pour it slowly, without stirring, into the alcoholic solution of silver nitrate. Let the mixture stand until the precipitated silver oxide has settled, filter, and distil. Dissolve about 35 Gm. of potassium hydroxide in 20 cc. of distilled water and add sufficient alcohol, purified as above, to make 1000 cc. Allow the solution to stand in a tightly stoppered bottle (using either a glass or rubber stopper) for twenty-four hours, then quickly decant the clear supernatant liquid into a bottle provided with a well-fitting rubber stopper. Ascertain the strength by titration against a hot solution of reagent potassium bitartrate, phenolphthalein T.S. being used as indicator, and adjust to exact normality or to a known strength of approximate normality. The strength may also be ascertained and adjusted after titration against half-normal hydrochloric acid.

Note: This solution should be kept in bottles provided with well-fitting stoppers of rubber, or of cork which have been well coated with paraffin, and it should be protected from light. It should be restandardized whenever it is used. It is very important that this solution should be used at the same temperature at which it was standardized.

One cubic centimeter of Half-Normal Alcoholic Potassium Hydroxide is the equivalent of:

	Gramme
Potassium Hydroxide, KOH	0.02806
Borneol, $C_{10}H_{17}OH$	0.07710
Bornyl Acetate, $C_{10}H_{17}.C_2H_3O_2$	0.09811
Linalyl Acetate, $C_{10}H_{17}.C_2H_3O_2$	0.09811
Menthol, $C_{10}H_{19}OH$	0.07811
Menthyl Acetate, $C_{10}H_{19}.C_2H_3O_2$	0.09912
Menthyl Salicylate, $CH_3.C_7H_5O_3$	0.07605
Potassium Bitartrate, $KHC_4H_4O_6$	0.09408
Santalol, $C_{15}H_{24}O$	0.1101

Potassium Permanganate, Tenth-Normal

$KMnO_4 = 158.03$ 3.1606 Gm. in 1000 cc.

Dissolve about 3.3 Gm. of potassium permanganate in 1000 cc. of distilled water in a flask and boil for about five minutes. Close the flask with absorbent cotton and allow it to stand for at least two days, then pour off the clear portion of the solution or filter through asbestos. The water for preparing and diluting this solution should be freshly distilled after adding about 1 Gm. of potassium permanganate to each liter of water in the retort before beginning the distillation. Ascertain its exact strength by titration against reagent sodium oxalate, and adjust to exact normality or to a known strength of approximate normality.

The strength may also be determined and adjusted by titrating against tenth-normal sodium thiosulphate after the addition of diluted sulphuric acid and an excess of potassium iodide.

Burettes provided with glass stop-cocks must be employed when titrating with this solution. It should be frequently restandardized. Preserve in glass-stoppered bottles.

One cubic centimeter of Tenth-Normal Potassium Permanganate is the equivalent of:

	Gramme
Potassium Permanganate, $KMnO_4$	0.003161
Calcium Oxide, CaO (as oxalate)	0.002804
Ferrous Carbonate, $FeCO_3$	0.01159
Ferrous Oxide, FeO	0.007184
Ferrous Sulphate, anhydrous, $FeSO_4$	0.01519
Ferrous Sulphate, crystals, $FeSO_4.7H_2O$	0.02780
Hydrogen Dioxide, H_2O_2	0.001701
Iron, in ferrous compounds, Fe	0.005584
Oxalic Acid, crystallized, $H_2C_2O_4.2H_2O$	0.006303
Oxygen, O	0.0008
Potassium Chlorate, $KClO_3$	0.002043
Sodium Chlorate, $NaClO_3$	0.001774
Sodium Nitrate, $NaNO_2$	0.003451
Sodium Oxalate, $Na_2C_2O_4$	0.006701

Potassium Thiocyanate, Tenth-Normal

$KSCN = 97.173$ 9.7173 Gm. in 1000 cc.

Dissolve 11 Gm. of reagent potassium thiocyanate in 1000 cc. of distilled water. Ascertain its exact strength by titration against tenth-normal silver nitrate, and adjust to exact normality or to a known strength of approximate normality.

One cubic centimeter of Tenth-Normal Potassium Thiocyanate is the equivalent of:

	Gramme
Potassium Thiocyanate, $KSCN$	0.009717
Mercuric Iodide, HgI_2	0.02272
Mercuric Nitrate, $Hg(NO_3)_2$	0.01623
Mercuric Oxide, HgO	0.01083
Mercury, Hg	0.01003
Silver, Ag	0.01079
Silver Nitrate, $AgNO_3$	0.01699
Silver Oxide, Ag_2O	0.01159

Silver Nitrate, Tenth-Normal

$AgNO_3 = 169.89$ 16.989 Gm. in 1000 cc.

METHOD I.—In a flask containing 10.788 Gm. of silver and provided with a small funnel inserted into the neck to prevent loss by spurting, introduce gradually about 30 cc. of nitric acid, or sufficient for complete solution. After thoroughly rinsing the funnel, transfer the clear solution, with the rinsings, to a beaker or porcelain dish, and evaporate to dryness on a water bath, carefully protecting the vessel from dust. Then dry in an oven at about 120° C. for ten minutes, cool the residue, and dissolve it in 1000 cc. of distilled water at 25° C.

METHOD II.—The solution may also be made by dissolving 17.006 Gm. of thoroughly dried silver nitrate in enough distilled water to make 1000 cc.

One cubic centimeter of Tenth-Normal Silver Nitrate is the equivalent of:

	Gramme
Silver Nitrate, $AgNO_3$	0.01699
Allyl Iso-thiocyanate, C_3H_5NCS	0.004957
Ammonium Bromide, NH_4Br	0.009796
Ammonium Chloride, NH_4Cl	0.005350
Ammonium Iodide, NH_4I	0.01450
Arsenous Iodide, AsI_3	0.01519
Bromine, Br	0.007992
Calcium Bromide, anhydrous, $CaBr_2$	0.009996
Calcium Bromide, $CaBr_2.2H_2O$	0.01180
Calcium Chloride, anhydrous, $CaCl_2$	0.005550
Calcium Chloride, $CaCl_2.2H_2O$	0.007351
Calcium Hypophosphite, $Ca(PH_2O_2)_2$	0.002836
Chlorine, Cl	0.003546
Ferrous Bromide, anhydrous, $FeBr_2$	0.01078
Ferrous Iodide, FeI_2	0.01548
Hydriodic Acid, HI	0.01279
Hydrobromic Acid, HBr	0.008093
Hydrochloric Acid, HCl	0.003647
Hydrocyanic Acid, HCN, to first formation of precipitate	0.005404
Hydrocyanic Acid, HCN, potassium chromate as indicator	0.002702
Iodine, I	0.01269
Lithium Bromide, LiBr	0.008686
Lithium Chloride, LiCl	0.004240
Phosphoric Acid, H_3PO_4	0.003269
Potassium Bromide, KBr	0.01190
Potassium Chloride, KCl	0.007456
Potassium Cyanide, KCN, to first formation of precipitate	0.01302
Potassium Hypophosphite, KPH_2O_2	0.003472
Potassium Iodide, KI	0.01660
Potassium Nitrate, KNO_3	0.01011
Potassium Thiocyanate, KSCN	0.009717
Sodium Biphosphate, $NaH_2PO_4.H_2O$	0.004602
Sodium Biphosphate, anhydrous, NaH_2PO_4	0.004002
Sodium Bromide, NaBr	0.01029
Sodium Chloride, NaCl	0.005846
Sodium Cyanide, NaCN, to first formation of precipitate,	0.009802
Sodium Hypophosphite, $NaPH_2O_2.H_2O$	0.003536
Sodium Iodide, NaI	0.01499
Sodium Nitrate, $NaNO_3$	0.008501
Sodium Phosphate, anhydrous, Na_2HPO_4	0.004735
Sodium Phosphate, crystallized, $Na_2HPO_4.12H_2O$	0.01194
Strontium Bromide, anhydrous, $SrBr_2$	0.01237
Strontium Bromide, crystallized, $SrBr_2.6H_2O$	0.01778
Strontium Chloride, $SrCl_2.6H_2O$	0.01333
Strontium Iodide, anhydrous, SrI_2	0.01707
Strontium Iodide, crystallized, $SrI_2.6H_2O$	0.02248
Zinc Chloride, $ZnCl_2$	0.006815

Sodium Hydroxide, Dekanormal

NaOH = 40.01 400.1 Gm. in 1000 cc.

Prepare and preserve as directed under normal sodium hydroxide.

NOTE: This solution is intended specifically for the ready measurement of definite amounts of absolute sodium hydroxide, hence it is not necessary to adjust the solution to exact strength, but the factor of strength must be accurately known and the solution used accordingly. The use of barium hydroxide in this solution is unnecessary, provided the solution be allowed to settle before standardizing and only the clear liquid employed.

Sodium Hydroxide, Double-Normal

NaOH = 40.01 80.02 Gm. in 1000 cc.

Preserve the solution as directed under normal sodium hydroxide (see below). This solution should be frequently restandardized.

Sodium Hydroxide, Normal

NaOH = 40.01 40.01 Gm. in 1000 cc.

Dissolve 45 Gm. of sodium hydroxide in about 950 cc. of distilled water and add a freshly prepared saturated solution of reagent barium hydroxide until no more precipitate forms. Allow the precipitate to subside, decant the clear liquid or filter the solution, and determine its strength by titration against a hot solution of an accurately weighed quantity of reagent potassium bitartrate, or against normal hydrochloric or sulphuric acid, and adjust to exact normality or to a known strength of approximate normality.

NOTE: Solutions of alkali hydroxides absorb carbon dioxide when exposed to the atmosphere. They should therefore be preserved in bottles with well-fitting rubber stoppers, provided with tubes filled with a mixture of sodium hydroxide and lime (soda-lime tubes) so that air in entering the container must pass through such tubes which will absorb the carbon dioxide.

The solution should be frequently restandardized.

One cubic centimeter of Normal Sodium Hydroxide is the equivalent of:

	Gramme
Sodium Hydroxide, $NaOH$	0.04001
Acetic Acid, $HC_2H_3O_2$	0.06004
Acetic Anhydride, $(CH_3CO)_2O$	0.05104
Ammonia Gas, NH_3	0.01703
Boric Acid, H_3BO_3	0.06192
Chloral Hydrate, $CCl_3CHO.H_2O$	0.1654
Citric Acid, crystallized, $H_3C_6H_5O_7.H_2O$	0.07004
Formaldehyde, $HCHO$	0.03002
Hydriodic Acid, HI	0.1279
Hydrobromic Acid, HBr	0.08093
Hydrochloric Acid, HCl	0.03647
Hypophosphorous Acid, HPH_2O_2	0.06606
Lactic Acid, $HC_3H_5O_3$	0.09006
Nitric Acid, HNO_3	0.06302
Oxalic Acid, crystallized, $H_2C_2O_4.2H_2O$	0.06303
Paraformaldehyde, $(HCHO)_3$	0.03002
Phosphoric Acid, H_3PO_4 (to form Na_2HPO_4; with phenolphthalein)	0.04903
Potassium Bitartrate, $KHC_4H_4O_6$	0.1882
Potassium Hydroxide, KOH	0.05611
Sodium Bisulphate, $NaH_2PO_4.H_2O$	0.1381
Sodium Biphosphate, anhydrous, NaH_2PO_4	0.1201
Sodium Bitartrate, $NaHC_4H_4O_6.H_2O$	0.1901
Sulphuric Acid, H_2SO_4	0.04904
Sulphuric Anhydride, SO_3	0.04003
Tartaric Acid, $H_2C_4H_4O_6$	0.07504
Trichloracetic Acid, $CCl_3.COOH$	0.1634

Sodium Hydroxide, Half-Normal

$NaOH = 40.01$ 20.005 Gm. in 1000 cc.

Preserve as directed under normal sodium hydroxide. This solution should be frequently restandardized.

One cubic centimeter of Half-Normal Sodium Hydroxide is the equivalent of:

	Gramme
Sodium Hydroxide, $NaOH$	0.02001
Acetic Acid, $HC_2H_3O_2$	0.03002
Acetylsalicylic Acid, $C_6H_4.O(C_2H_3O).COOH$	0.04503
Benzyl Benzoate, $C_6H_5CO_2.CH_2C_6H_5$	0.1061
Boric Acid, H_3BO_3	0.03100
Citric Acid, crystallized, $H_3C_6H_5O_7.H_2O$	0.03502
Hydriodic Acid, HI	0.06397
Hydrobromic Acid, HBr	0.04047
Hydrochloric Acid, HCl	0.01824
Hypophosphorous Acid, HPH_2O_2	0.03303
Lactic Acid, $HC_3H_5O_3$	0.04503
Nitric Acid, HNO_3	0.03151
Oxalic Acid, crystallized, $H_2C_2O_4.2H_2O$	0.03152
Phosphoric Acid, H_3PO_4 (to form Na_2HPO_4; with phenolphthalein)	0.02452
Potassium Bitartrate, $KHC_4H_4O_6$	0.09408
Potassium Hydroxide, KOH	0.02806
Sodium Bitartrate, $NaHC_4H_4O_6.H_2O$	0.09504
Sulphuric Acid, H_2SO_4	0.02452
Sulphuric Anhydride, SO_3	0.02002
Tartaric Acid, crystallized, $H_2C_4H_4O_6$	0.03752
Trichloracetic Acid, $CCl_3.COOH$	0.08170

Sodium Hydroxide, Tenth-Normal

$NaOH = 40.01$ 4.001 Gm. in 1000 cc.

Preserve as directed under normal sodium hydroxide. This solution should be frequently restandardized.

One cubic centimeter of Tenth-Normal Sodium Hydroxide is the equivalent of:

	Gramme
Sodium Hydroxide, $NaOH$	0.004001
Cinchophen, $C_6H_5.C_9H_5N.COOH$	0.02492
Eucaine Hydrochloride, $C_{15}H_{21}O_2N.HCl$	0.02837
Lactic Acid, $HC_3H_5O_3$	0.009006
Potassium Bitartrate, $KHC_4H_4O_6$	0.01882
Potassium Hydroxide, KOH	0.005611
Sulphuric Acid, H_2SO_4	0.004904

Sodium Hydroxide, Fiftieth-Normal

$NaOH = 40.01$ 0.800 Gm. in 1000 cc.

Preserve as directed under normal sodium hydroxide. This solution should be frequently restandardized.

One cubic centimeter of Fiftieth-Normal Sodium Hydroxide is the equivalent of:

	Gramme
Sodium Hydroxide, $NaOH$	0.0008002
Potassium Bitartrate, $KHC_4H_4O_6$	0.003763
Sulphuric Acid, H_2SO_4	0.0009808

Sodium Hydroxide, Hundredth-Normal

$NaOH = 40.01$ 0.400 Gm. in 1000 cc.

Preserve as directed under normal sodium hydroxide. This solution should be frequently restandardized.

One cubic centimeter of Hundredth-Normal Sodium Hydroxide is the equivalent of:

	Gramme
Sodium Hydroxide, $NaOH$	0.0004001
Potassium Bitartrate, $KHC_4H_4O_6$	0.001882
Sulphuric Acid, H_2SO_4	0.0004904

Sodium Thiosulphate, Tenth-Normal

$Na_2S_2O_3.5H_2O = 248.20$ 24.820 Gm. in 1000 cc.

Dissolve 30 Gm. of sodium thiosulphate in sufficient distilled water, previously boiled for twenty minutes in a flask of hard glass and quickly cooled, to measure 1000 cc. Ascertain its exact strength by titration against tenth-normal potassium dichromate, in the presence of an excess of potassium iodide and a small amount of sulphuric acid, and adjust to exact normality, or to a known strength of approximate normality. The strength may also be ascertained and adjusted after titration against tenth-normal iodine. This solution should be frequently restandardized.

One cubic centimeter of Tenth-Normal Sodium Thiosulphate is the equivalent of:

	Gramme
Sodium Thiosulphate, $Na_2S_2O_3.5H_2O$	0.02482
Arsenic, As (in Arsphenamine and Neoarsphenamine)	0.003748
Bromine, Br	0.007992
Chlorine, Cl	0.003546
Chlorine, Cl (in Chloramine and Dichloramine)	0.001773
Chromium Trioxide, CrO_3	0.003333
Cupric Sulphate, anhydrous, $CuSO_4$	0.01596
Cupric Sulphate, crystallized, $CuSO_4.5H_2O$	0.02497
Iodine, I	0.01269
Iodine, I (in Thymol Iodide and Calcium Iodobehenate)	0.002115
Iron, Fe, in ferric salts	0.005584
Lead Peroxide, PbO_2	0.01196
Potassium Bromate, $KBrO_3$	0.002784
Potassium Dichromate, $K_2Cr_2O_7$	0.004903
Sodium Arsenate, anhydrous, Na_2HAsO_4	0.009299
Sodium Arsenate, crystallized, $Na_2HAsO_4.7H_2O$	0.01560
Sodium Hypochlorite, $NaOCl$	0.003723

Sodium Thiosulphate, Two-Hundredth-Normal

$Na_2S_2O_3.5H_2O = 248.20$ 1.241 Gm. in 1000 cc.

This solution should be frequently restandardized.

One cubic centimeter of Two-Hundredth-Normal Sodium Thiosulphate is the equivalent of:

	Gramme
Sodium Thiosulphate, $Na_2S_2O_3.5H_2O$	0.001241
Iodine, I	0.0006346
Iodine, I (from Thyroxin and Thyroid Glands)	0.0001058

Sulphuric Acid, Normal

$H_2SO_4 = 98.076$ 49.038 Gm. in 1000 cc.

Add slowly, with constant stirring, 30 cc. of sulphuric acid to 1020 cc. of distilled water and allow the solution to cool to 25° C. Ascertain its exact strength by titration against freshly standardized normal sodium hydroxide, methyl orange T.S. being used as indicator, and adjust to exact normality or to a known strength of approximate normality.

The strength may also be ascertained and adjusted after titration against an accurately weighed amount of reagent anhydrous sodium carbonate. It may also be standardized gravimetrically by precipitation and weighing as barium sulphate.

One cubic centimeter of Normal Sulphuric Acid is the equivalent of:

	Gramme
Sulphuric Acid, H_2SO_4	0.04904
Ammonia Gas, NH_3	0.01703
Ammonium Acetate, $NH_4C_2H_3O_2$	0.07707
Calcium Hydroxide, $Ca(OH)_2$	0.03705
Calcium Oxide, CaO	0.02804
Lithium Carbonate, Li_2CO_3	0.03695
Lithium Salicylate, $LiC_7H_5O_3$	0.1440
Magnesium Carbonate, $(MgCO_3)_4Mg(OH)_2.5H_2O$	0.04857
Magnesium Hydroxide, $Mg(OH)_2$	0.02917
Magnesium Oxide, MgO	0.02016
Methenamine, $(CH_2)_6N_4$	0.03504
Potassium Acetate, $KC_2H_3O_2$	0.09813
Potassium Bicarbonate, $KHCO_3$	0.1001
Potassium Bitartrate, $KHC_4H_4O_6$	0.1882
Potassium Carbonate, anhydrous, K_2CO_3	0.06911
Potassium Citrate, crystallized, $K_3C_6H_5O_7.H_2O$	0.1081
Potassium Hydroxide, KOH	0.05611
Potassium and Sodium Tartrate, $KNaC_4H_4O_6.4H_2O$	0.1411
Sodium Acetate, $NaC_2H_3O_2.3H_2O$	0.1361
Sodium Bicarbonate, $NaHCO_3$	0.08401
Sodium Borate, crystallized, $Na_2B_4O_7.10H_2O$	0.1909
Sodium Carbonate, anhydrous, Na_2CO_3	0.05301
Sodium Carbonate, monohydrated, $Na_2CO_3.H_2O$	0.06201
Sodium Hydroxide, NaOH	0.04001
Sodium Salicylate, $NaC_7H_5O_3$	0.16008
Zinc Oxide, ZnO	0.04069

Sulphuric Acid, Half-Normal

$H_2SO_4=98.076$ 24.519 Gm. in 1000 cc.

One cubic centimeter of Half-Normal Sulphuric Acid is the equivalent of:

	Gramme
Sulphuric Acid, H_2SO_4	0.02452
Ammonia Gas, NH_3	0.008520
Benzaldehyde, C_7H_6O	0.05304
Calcium Glycerophosphate, $CaC_3H_7PO_6$	0.10509
Calcium Lactate, anhydrous $Ca(C_3H_5O_3)_2$	0.05455
Cinnamic Aldehyde, C_9H_8O	0.03303
Citrol, $C_{10}H_{16}O$	0.07609
Lithium Citrate, anhydrous, $Li_3C_6H_5O_7$	0.03498
Lithium Citrate, crystallized, $Li_3C_6H_5O_7.4H_2O$	0.04699
Lithium Salicylate, $LiC_7H_5O_3$	0.07201
Magnesium Hydroxide, $Mg(OH)_2$	0.01459
Potassium Acetate, $KC_2H_3O_2$	0.04907
Potassium and Sodium Tartrate, anhydrous, $KNaC_4H_4O_6$	0.05254
Potassium and Sodium Tartrate, crystallized, $KNaC_4H_4O_6.4H_2O$	0.07056
Potassium Bicarbonate, $KHCO_3$	0.05006
Potassium Bitartrate, $KHC_4H_4O_6$	0.09408
Potassium Carbonate, anhydrous, K_2CO_3	0.03455
Potassium Citrate, anhydrous, $K_3C_6H_5O_7$	0.05106
Potassium Citrate, crystallized, $K_3C_6H_5O_7.H_2O$	0.05407
Potassium Hydroxide, KOH	0.02806
Sodium Acetate, anhydrous, $NaC_2H_3O_2$	0.04102
Sodium Acetate, crystallized, $NaC_2H_3O_2.3H_2O$	0.06804
Sodium Benzoate, $NaC_7H_5O_2$	0.07204
Sodium Bicarbonate, $NaHCO_3$	0.04201
Sodium Carbonate, anhydrous, Na_2CO_3	0.02650
Sodium Carbonate, monohydrated, $Na_2CO_3.H_2O$	0.03101
Sodium Citrate, anhydrous, $Na_3C_6H_5O_7$	0.04301
Sodium Citrate, crystallized, $Na_3C_6H_5O_7.2H_2O$	0.04902
Sodium Hydroxide, NaOH	0.02001
Sodium Salicylate, $NaC_7H_5O_3$	0.08004
Sodium Tartrate, neutral, $Na_2C_4H_4O_6.2H_2O$	0.05752
Strontium Salicylate, anhydrous, $Sr(C_7H_5O_3)_2$	0.09045
Strontium Salicylate, crystallized, $Sr(C_7H_5O_3)_2.2H_2O$	0.09945

Sulphuric Acid, Tenth-Normal

$H_2SO_4=98.076$ 4.9038 Gm. in 1000 cc.

One cubic centimeter of Tenth-Normal Sulphuric Acid is the equivalent of:

	Gramme
Sulphuric Acid, H_2SO_4	0.004904
Atropine, $C_{17}H_{23}O_3N$	0.02893
Belladonna, combined alkaloids	0.02893

	Gramme
Brucine, $C_{23}H_{26}O_4N_2$	0.03943
Calcium Hydroxide, $Ca(OH)_2$	0.003705
Cephaëline, $C_{14}H_{19}O_2N$	0.02332
Cinchona, combined alkaloids	0.0309
Cinchonidine, $C_{19}H_{22}ON_2$	0.02943
Cinchonine, $C_{19}H_{22}ON_2$	0.02943
Cocaine, $C_{17}H_{21}O_4N$	0.03033
Codeine, $C_{18}H_{21}O_3N$	0.02993
Coniine, $C_8H_{17}N$	0.01272
Emetine, $C_{15}H_{21}O_2N$	0.02483
Hydrastine, $C_{21}H_{21}O_6N$	0.03833
Hyoscyamus, combined alkaloids	0.02893
Ipecac, ether-soluble alkaloids	0.0240
Morphine, anhydrous, $C_{17}H_{19}O_3N$	0.02853
Morphine, crystallized, $C_{17}H_{19}O_3N.H_2O$	0.03033
Nux Vomica, combined alkaloids	0.0364
Physostigmine, $C_{15}H_{21}O_2N_3$	0.02753
Pilocarpine, $C_{11}H_{16}O_2N_2$	0.02082
Potassium Hydroxide, KOH	0.005611
Quinidine, anhydrous, $C_{20}H_{24}O_2N_2$	0.03243
Quinine, anhydrous, $C_{20}H_{24}O_2N_2$	0.03243
Sodium Carbonate, anhydrous, Na_2CO_3	0.005301
Stramonium, combined alkaloids	0.02893
Strychnine, $C_{21}H_{22}O_2N_2$	0.03343
Zinc Oxide, ZnO	0.004069

Sulphuric Acid, Fiftieth-Normal

$H_2SO_4 = 98.076$ 0.98076 Gm. in 1000 cc.

One cubic centimeter of Fiftieth-Normal Sulphuric Acid is the equivalent of:

	Gramme
Sulphuric Acid, H_2SO_4	0.0009808
Atropine, $C_{17}H_{23}O_3N$	0.005786
Cinchonidine, $C_{19}H_{22}ON_2$	0.005886
Cinchonine, $C_{19}H_{22}ON_2$	0.005886
Cocaine, $C_{17}H_{21}O_4N$	0.006065
Coniine, $C_8H_{17}N$	0.002544
Hydrastine, $C_{21}H_{21}O_6N$	0.007666
Ipecac, combined alkaloids	0.00480
Morphine, anhydrous, $C_{17}H_{19}O_3N$	0.005705
Morphine, crystallized, $C_{17}H_{19}O_3N.H_2O$	0.006065
Physostigmine, $C_{15}H_{21}O_2N_3$	0.005505
Pilocarpine, $C_{11}H_{16}O_2N_2$	0.004164
Quinine, anhydrous, $C_{20}H_{24}O_2N_2$	0.006486
Strychnine, $C_{21}H_{22}O_2N_2$	0.006686

Atomic Weights

(U. S.)

Adopted by the International Committee on Chemical Elements (1921)

Oxygen = 16

Name	Symbol	Atomic Weight	Name	Symbol	Atomic Weight
Aluminum	Al	27.0	Molybdenum	Mo	96.0
Antimony	Sb	120.2	Neodymium	Nd	144.3
Argon	A	39.9	Neon	Ne	20.2
Arsenic	As	74.96	Nickel	Ni	58.68
Barium	Ba	137.37	Niton (Radon)	Nt	222.4
Bismuth	Bi	209.0	Nitrogen	N	14.008
Boron	B	10.9	Osmium	Os	190.9
Bromine	Br	79.92	Oxygen	O	16.00
Cadmium	Cd	112.40	Palladium	Pd	106.7
Calcium	Ca	40.07	Phosphorus	P	31.04
Carbon	C	12.005	Platinum	Pt	195.2
Cerium	Ce	140.25	Potassium	K	39.10
Cesium	Cs	132.81	Praseodymium	Pr	140.9
Chlorine	Cl	35.46	Radium	Ra	226.0
Chromium	Cr	52.0	Rhodium	Rh	102.9
Cobalt	Co	58.97	Rubidium	Rb	85.45
Columbium	Cb	93.1	Ruthenium	Ru	101.7
Copper	Cu	63.57	Samarium	Sa	150.4
Dysprosium	Dy	162.5	Scandium	Sc	45.1
Erbium	Er	167.7	Selenium	Se	79.2
Europium	Eu	152.0	Silicon	Si	28.1
Fluorine	F	19.0	Silver	Ag	107.88
Gadolinium	Gd	157.3	Sodium	Na	23.00
Gallium	Ga	70.1	Strontium	Sr	87.63
Germanium	Ge	72.5	Sulphur	S	32.06
Glucinum	Gl	9.1	Tantalum	Ta	181.5
Gold	Au	197.2	Tellurium	Te	127.5
Helium	He	4.00	Terbium	Tb	159.2
Holmium	Ho	163.5	Thallium	Tl	204.0
Hydrogen	H	1.008	Thorium	Th	232.15
Indium	In	114.8	Thulium	Tm	169.8
Iodine	I	126.92	Tin	Sn	118.7
Iridium	Ir	193.1	Titanium	Ti	48.1
Iron	Fe	55.84	Tungsten	W	184.0
Krypton	Kr	82.92	Uranium	U	238.2
Lanthanum	La	139.0	Vanadium	V	51.0
Lead	Pb	207.20	Xenon	Xe	130.2
Lithium	Li	6.94	Ytterbium	Yb	173.5
Lutecium	Lu	175.0	Yttrium	Yt	89.33
Magnesium	Mg	24.32	Zinc	Zn	65.37
Manganese	Mn	54.93	Zirconium	Zr	90.6
Mercury	Hg	200.6			

Articles Employed in Chemical Testing and Reagents of the British Pharmacopœia

APPENDIX I. Br.

The British test-solutions here given are used for determining the character of particular substances, whether isolated or in composition; thus enabling us to ascertain the identity of medicines, their purity or impurity, and the character of the foreign ingredients, which may be mixed with them accidentally, or with a view to adulteration.

Acetic Acid, of the British Pharmacopœia.
Acetic Acid, Diluted, of the British Pharmacopœia.
Acetic Acid, Glacial, of the British Pharmacopœia.
Acetic Anhydride, $C_4H_6O_3$, of commerce, pure.
Acetone, of the British Pharmacopœia.
Albumen, the liquid white of fresh eggs.
Alcohol, Absolute, of the British Pharmacopœia.
Alcohol (90 per cent.). **Alcohol** (70 per cent.). **Alcohol** (20 per cent.), of the British Pharmacopœia.
Alum, Purified, of the British Pharmacopœia.
Ammonium Chloride, of the British Pharmacopœia.
Ammonium Molybdate, $(NH_4)_2MoO_4$, of commerce, pure.

Ammonium Oxalate, $(NH_4)_2C_2O_4,H_2O$, of commerce, pure.

Ammonium Persulphate, NH_4SO_4, of commerce, pure.

Ammonium Thiocyanate, NH_4SCN, of commerce, pure.

Amylic Alcohol is a liquid consisting principally of iso-primary amylic alcohol, $C_5H_{11}OH$, and may be prepared by shaking commercial fusel oil with a saturated solution of common salt, separating the oily layer, submitting it to distillation, and collecting and reserving the fraction which distils between 125° and 143° C.

Aniline, of commerce, redistilled.

Animal Charcoal, of commerce, purified.

Auric Chloride, of commerce, pure.

Barium Chloride, $BaCl_2,2H_2O$, of commerce, pure.

Barium Hydroxide, $Ba(OH)_2,8H_2O$, of commerce, pure.

Benzene, of the British Pharmacopœia.

Benzolated Amylic Alcohol, benzene, 3 parts by volume; Amylic Alcohol, 1 part by volume; mix; decant from any deposited water.

Bismuth Oxynitrate, of the British Pharmacopœia.

Borax, Purified, of the British Pharmacopœia.

Bromine, of commerce, pure.

Cadmium Iodide, CdI_2, of commerce, pure.

Calcium Carbonate, the pure white marble, or calc spar, of commerce.

Calcium Hydroxide, of the British Pharmacopœia.

Calcium Oxide, the Lime of the British Pharmacopœia.

Calcium Sulphate, $CaSO_4,H_2O$, native, pure.

Carbon Disulphide, of the British Pharmacopœia.

Carbon Tetrachloride, CCl_4, of commerce, pure.

Chlorine, a gas prepared by the interaction of hydrochloric acid and manganese peroxide, and purified by passing through a small quantity of water contained in a wash bottle.

Chloroform, of the British Pharmacopœia.

Chloroform Water, of the British Pharmacopœia.

Citric Acid, of the British Pharmacopœia.

Collodion, of the British Pharmacopœia.

Copper, Copper in foil, wire, or turnings.

Copper Acetate, $Cu(C_2H_3O_2)_2,H_2O$, of commerce, crystalline, pure.

Copper Carbonate, precipitated, of commerce.

Copper Sulphate, of the British Pharmacopœia.

Ether, of the British Pharmacopœia.

Ferric Ammonium Sulphate, $Fe_2(SO_4)_3,(NH_4)_2SO_4,24H_2O$, of commerce, pure.

Ferric Chloride, of commerce, pure, anhydrous.

Ferrous Sulphate, of the British Pharmacopœia.

Fuchsin, of commerce, pure.

Glycerin, of the British Pharmacopœia.

Hydrochloric Acid, of the British Pharmacopœia.

Hydrochloric Acid, Diluted, of the British Pharmacopœia.

Hydrochloric Acid, Gaseous, HCl, dry, prepared by the interaction of sulphuric acid and common salt.

Hydrogen Sulphide, Synonym, *Sulphuretted Hydrogen*, a gas prepared by the action of hydrochloric acid on commercial ferrous sulphide. It will be sufficiently pure after passing through two wash-bottles containing water. A solution of the gas in water may also be employed, but only if it smells strongly of the gas, and yields an abundant black precipitate with solution of lead acetate.

Hydroxylamine Hydrochloride, NH_2OH,HCl, of commerce, pure.

Hypophosphorous Acid, of commerce, specific gravity 1.137.

Indigo, a blue pigment prepared from various species of Indigofera, Linn.

Iodic Acid, HIO_3, of commerce, pure.

Iodine, of the British Pharmacopœia.

Iron, of the British Pharmacopœia.

Isinglass, the swimming bladder or sound of various species of Acipenser, Linn., prepared, and cut into shreds.

Lead Acetate, of the British Pharmacopœia.

Lead Nitrate, $Pb(NO_3)_2$, of commerce, pure.

Lead Oxide, of the British Pharmacopœia.

Lead Peroxide, PbO_2, of commerce, pure.

Lime, of the British Pharmacopœia.

Litmus, a blue pigment prepared from various species of Roccella, D.C. Litmus is used in several forms; for example, Solution of Litmus (Appendix II); Blue Litmus Paper, made by impregnating unglazed white paper with a solution of litmus; and Red Litmus Paper, made by impregnating the paper with the solution reddened by the previous addition of a very minute quantity of sulphuric acid. Litmus may also be employed in the solid form.

Magnesia, Heavy, of the British Pharmacopœia.

Manganese Peroxide, MNO_2, the powdered native pyrolusite.

Mercurous Chloride, of the British Pharmacopœia.

Methyl Orange, pure sodium dimethyl-amido-azo-benzene-sulphonate, $NaC_{14}H_{14}N_3SO_3$, of commerce.

Milk of Lime, lime, 100 grammes; distilled water, 200 millilitres; mix.

Morphinated Water, prepared by digesting pure Morphine in Chloroform Water for seven days at a temperature of 15.5° C., shaking occasionally so as to obtain a saturated solution of the alkaloid, and filtering from the undissolved morphine.

Morphine, the precipitate obtained on adding solution of ammonia, in slight excess, to the solution of a pure morphine salt in *water*, the precipitate being washed with water until free from ammonium, salt.

Mucilage of Gum Acacia, of the British Pharmacopœia.

Mucilage of Starch.—Triturate 1 gramme of Starch with a small quantity of Distilled Water to form a smooth paste; add more Distilled Water, gradually, to produce 50 millilitres of mixture; boil for a few minutes, constantly stirring; cool. Mucilage of starch must be recently prepared.

Nitric Acid, of the British Pharmacopœia.

Nitric Acid, Diluted, of the British Pharmacopœia.

Nitric Acid, Fuming, of commerce, specific gravity 1.5.

Oil of Turpentine, of the British Pharmacopœia.

Olive Oil, of the British Pharmacopœia.

Oxalic Acid, $H_2C_2O_4,2H_2O$, of commerce, pure.

Paraffin, Soft, of the British Pharmacopœia.

Petroleum Spirit, Synonym, *Petroleum Ether*, a colorless very volatile and highly inflammable liquid obtained from petroleum, and consisting of a mixture of the lower members of the paraffin series of hydrocarbon. Boiling point 50–60. Specific gravity 0.670 to 0.700.

Phenol, of the British Pharmacopœia.

Phenol-Disulphonic Acid.—Heat 3 grammes of Phenol with 20 millilitres of Sulphuric Acid on a water bath for six hours. Transfer the resulting liquid to a stoppered bottle.

Phenolphthalein, of the British Pharmacopœia.

Phosphoric Acid, Concentrated, of the British Pharmacopoeia.

Phosphoric Acid, Syrupy, of commerce, specific gravity 1.750.

Picric Acid, of the British Pharmacopœia.

Platinic Chloride, of commerce, pure.

Potassium Bichromate, of the British Pharmacopœia.

Potassium Chlorate, of the British Pharmacopœia.

Potassium Chromate, K_2CrO_4, of commerce, pure.

Potassium Cyanide, of commerce. Contains not less than 90 per cent. of pure potassium cyanide, KCN.

Potassium Ferricyanide, $K_6Fe_2C_{12}N_{12}$, of commerce, pure.

Potassium Ferrocyanide, $K_4FeC_6N_6,3H_2O$, of commerce, pure.

Potassium Hydrogen Sulphite.—Synonym—*Acid Potassium Sulphite*, $KHSO_3$, of commerce, pure.

Potassium Hydroxide of the British Pharmacopœia.

Potassium Iodide of the British Pharmacopœia.

Potassium Nitrate of the British Pharmacopœia.

Potassium Permanganate of the British Pharmacopœia.

Potassium Sulphate of the British Pharmacopœia.

Resorcin of the British Pharmacopœia

Salicylic Acid of the British Pharmacopœia.

Sodium Acetate, $NaC_2H_3O_2,3H_2O$, of commerce, pure.

Sodium Acetate, Anhydrous, $NaC_2H_3O_2$, of commerce, pure.

Sodium Arsenate, Anhydrous of the British Pharmacopœia.

Sodium Bicarbonate of the British Pharmacopœia.

Sodium Carbonate of the British Pharmacopœia.

Sodium Carbonate, Exsiccated of the British Pharmacopœia.

Sodium Chloride of the British Pharmacopœia.

Sodium Hydrogen Sulphite.—Synonym—*Acid Sodium Sulphite*, $NaHSO_3$, of commerce, pure.

Sodium Hydroxide of commerce, purified by means of alcohol.

Sodium Nitrite of the British Pharmacopœia.

Sodium Potassium Tartrate of the British Pharmacopœia.

Sodium Sulphate of the British Pharmacopœia.

Sodium Sulphate, Anhydrous, The Sodium Sulphate of the British Pharmacopœia, rendered anhydrous by heat.

Sodium Sulphide, $Na_2S,9H_2O$, of commerce, pure.

Sodium Sulphite of the British Pharmacopœia.

Sodium Thiosulphate, $Na_2S_2O_3,5H_2O$, of commerce, pure.

Sugar, Refined of the British Pharmacopœia.

Sulphur, Precipitated of the British Pharmacopœia.

Sulphuric Acid of the British Pharmacopœia.

Sulphuric Acid, Diluted, of the British Pharmacopœia.

Talc, Powdered, a natural magnesium silicate, powdered and purified by boiling with dilute hydrochloric acid, washing with distilled water until neutral to litmus, and drying.

Tartaric Acid of the British Pharmacopœia.

Tin, granulated by letting drops of the metal in the molten state fall into water. Yields no characteristic reactions for lead, copper, iron, or zinc.

Turmeric, the dried rhizome of Curcuma, Longa, *Linn.* It is usually employed in the form of a tincture prepared by the process of maceration, from the bruised rhizome, in the proportion of 1 gramme to 6 millilitres of Alcohol (90 per cent.), or in the form of paper prepared by steeping unglazed white paper in the tincture and drying.

Water, the Distilled Water of the British Pharmacopœia.

Zinc, the laminated or granulated metal. Completely dissolved by diluted hydrochloric acid, the solution yielding no characteristic reactions for lead, copper, cadmium, arsenic, tin or iron.

Zinc Carbonate of the British Pharmacopœia.

APPENDIX II. Br.

Solutions Employed in Chemical Testing.

(*Br.*)

Solution of Albumen.—Albumen, 20 millilitres; Distilled Water, 80 millilitres. Mix by trituration in a mortar, and filter through clean tow previously moistened with Distilled Water. Solution of Albumen must be recently prepared. The strength of the Solution may be adjusted to suit particular requirements.

Solution of Ammonia, of the British Pharmacopœia.

Solution of Ammonia, Strong, of the British Pharmacopœia.

Solution of Ammonium Acetate, of the British Pharmacopœia.

Solution of Ammonium Carbonate.—Ammonium Carbonate, 5.0 grammes; Solution of Ammonia, 7.5 millilitres; Distilled Water, sufficient to produce 100.0 millilitres; dissolve; filter if necessary.

Solution of Ammonium Chloride.—Ammonium Chloride, 10 grammes; Distilled Water sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Ammonium Chloride (Nessler's).—Ammonium Chloride, 3.15 grammes; Distilled Water, free from ammonia, sufficient to produce 1000.00 millilitres; dissolve.

Solution of Ammonium Chloride, Dilute, (Nessler's) .—Solution of Ammonium Chloride, (Nessler's) 10 millilitres; Distilled Water, free from ammonia, sufficient to produce 1000 millilitres; Mix.

Solution of Ammonium Citrate, of the British Pharmacopœia.

Solution of Ammonium Hydrosulphide.—Saturate one hundred and twenty millilitres of Solution of Ammonia with washed Hydrogen Sulphide; add eighty millilitres of Solution of Ammonia. This solution must be recently prepared.

Solution of Ammonium Molybdate.—Ammonium Molybdate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Ammonium Oxalate.—Ammonium Oxalate, 2.5 grammes; Distilled Water sufficient to produce 100.0 millilitres; dissolve; filter if necessary.

Solution of Auric Chloride.—Auric Chloride, 2 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Barium Chloride.—Barium Chloride, in crystals, 10 grammes; Distilled Water sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Barium Hydroxide.—Barium Hydroxide, 3 grammes; Distilled Water, recently boiled, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Boric Acid.—Boric Acid, 2.5 grammes; Alcohol (90 per cent.) sufficient to produce 100.0 millilitres; dissolve; filter if necessary.

Solution of Bromine.—A saturated solution of Bromine in Distilled Water.

Solution of Cadmium Iodide.—Cadmium Iodide, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Calcium Chloride.—Calcium Chloride 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessory.

Solution of Calcium Sulphate.—A saturated solution of Calcium Sulphate in Distilled Water.

Solution of Chlorinated Soda.—Solution of Chlorinated Soda of the British Pharmacopœia.

Solution of Chlorine.—A saturated solution of Chlorine in Distilled Water. This Solution must be recently prepared.

Solution of Chromic Acid, of the British Pharmacopœia.

Solution of Copper Acetate.—Copper Acetate, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Copper Acetate, Diluted.—Solution of Copper Acetate, 1 millilitre; Distilled Water sufficient to produce 100 millilitres. Mix.

Solution of Copper Ammonio-Sulphate.—Copper Sulphate, in crystals, 5 grammes; Solution of Ammonia, a sufficient quantity; Distilled Water sufficient to repoduce 100 millilitres. Dissolve the Copper Sulphate in one hundred and sixty millilitres of the Distilled Water, and cautiously add the Solution of Ammonia to the liquid until the precipitate first formed is nearly dissolved; filter the product; finally add to the filtrate sufficient of the Distilled Water to produce the required volume.

Solution of Copper Oxide, Ammoniacal.—Copper Carbonate, 5 grammes; Strong Solution of Ammonia, 100 millilitres. Shake together occasionally during twelve hours; set aside for twenty-four hours, and pour off the clear liquid. This solution must be recently prepared.

Solution of Copper Sulphate.—Copper Sulphate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Ferric Sulphate.—Solution of Ferric Sulphate of the British Pharmacopœia.

Solution of Ferrous Sulphate.—Ferrous Sulphate, 2 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary. This Solution must be recently prepared.

Solution of Formaldehyde, of the British Pharmacopœia.

Solution of Fuchsin, Decolorized.—Dissolve one gramme of Fuchsin in five hundred millilitres of hot Distilled Water; add slowly twenty millilitres of a saturated aqueous solution of Acid Sodium Sulphite and then, also slowly, ten millilitres of Hydrochloric Acid, the mixture being kept well shaken. Cool and add sufficient Distilled Water to produce one thousand millilitres.

Solution of Hydrogen Peroxide of the British Pharmacopœia.

Solution of Indigo Sulphate.—Indigo dry and in fine powder, 0.1 gramme; Sulphuric Acid 100.0 millilitres. Mix the Indigo with one millilitre of the Sulphuric Acid in a small test-tube, and heat in boiling water for an hour; pour the product into the remainder of the Sulphuric Acid; shake the mixture; decant the clear liquid.

Solution of Isinglass.—Isinglass, 2 grammes; Distilled Water, sufficient to produce 100 millilitres. Mix, and digest for half an hour on a water-bath with repeated shaking; filter through clean tow previously moistened with Distilled Water. This Solution must be recently prepared.

Solution of Lead Acetate.—Lead Acetate, 10 grammes; Distilled Water, recently boiled, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Lead Subacetate.—The Strong Solution of Lead Subacetate of the British Pharmacopœia diluted, if necessary, with Distilled Water.

Solution of Lime.—Synonym—*Solution of Calcium Hydroxide;* of the British Pharmacopœia.

Solution of Litmus.—Litmus in powder, 10 grammes; Alcohol (90 per cent.), 100 millilitres; Distilled Water, 100 millilitres. Boil the Litmus with forty millilitres of the Alcohol for one hour; pour away the clear liquid; repeat this operation with thirty millilitres of the Alcohol, and a third time with the remainder of the Alcohol. Digest the washed Litmus in the Distilled Water, and filter.

Solution of Magnesium Ammonio-Sulphate.—Magnesium Sulphate, 10 grammes; Ammonium Chloride 20 grammes; Solution of Ammonia, 42 millilitres; Distilled Water, 80 millilitres. Dissolve the Magnesium Sulphate and Ammonium Chloride in the Distilled Water; add the Solution of Ammonia, and set the mixture aside for a few days in a well-closed bottle; decant and filter.

Solution of Magnesium Sulphate.—Magnesium Sulphate, 10 grammes; Distilled Water sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Mercurous Nitrate.—Mercury, 2 grammes; Nitric Acid, 1 millilitre: Distilled Water, a sufficient quantity. To the Mercury, in a small dish, add one millilitre of Distilled Water and the Nitric Acid, and set the whole aside for twenty-four hours in a cool dark place; drain the resulting crystals; dissolve them in two hundred nillilitres of Distilled Water.

Solution of Mercury Nitrate.—Synonym—*Millon's Reagent.* Mercury, 3 millilitres; Fuming Nitric Acid, 27 millilitres; Distilled Water, a sufficient quantity. Dissolve the Mercury in the Fuming Nitric Acid without heat; dilute the solution with an equal volume of Distilled Water. This solution must be recently prepared.

Solution of Methyl Orange.—Methyl Orange, 0.2 gramme; Alcohol (90 per cent.), 25.0 millilitres; Distilled Water, sufficient to produce 100.0 millilitres; dissolve.

Solution of Phenolphthalein.—Phenolphthalein, 0.2 gramme; Alcohol (90 per cent.), 60.0 millilitres; Distilled Water, sufficient to produce 100.0 millilitres; dissolve.

Solution of Picric Acid.—Picric Acid, 0.66 gramme; Distilled Water, sufficient to produce 100.00 millilitres; dissolve.

Solution of Platinic Chloride.—Platinic Chloride, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve.

Solution of Potassio-Cupric Tartrate.—Synonym—*Fehling's Solution.*

No. 1. Copper Sulphate, in crystals, 34.64 grammes; Sulphuric Acid, 0.50 millilitre; Distilled Water, sufficient to produce 500.00 millilitres; dissolve.

No. 2. Sodium Potassium Tartrate, 176 grammes; Sodium Hydroxide, 77 grammes; Distilled Water sufficient to produce 500 millilitres; dissolve. Mix equal volumes of the solutions No. 1 and No. 2 at the time of using.

Solution of Potassio-Mercuric Iodide.—Synonym—*Mayer's Reagent.* Mercuric Chloride, 1.355 grammes; Potassium Iodide, 5.000 grammes; Distilled Water, sufficient to produce 100.000 millilitres. Dissolve the Mercuric Chloride in sixty millilitres of the Distilled Water; dissolve the Potassium Iodide in twenty millilitres of the Distilled Water; mix the two solutions, and add sufficient Distilled Water to produce the required volume.

Solution of Potassio-Mercuric Iodide, Alkaline.—Synonym—*Nessler's Reagent.* Potassium Iodide, 3.5 grammes; Mercuric Chloride, sufficient quantity; Sodium Hydroxide, 12.0 grammes; Distilled Water sufficient to produce 100.0 millilitres. Dissolve the Potassium Iodide and one and a quarter grammes, of Mercuric Chloride in eighty millilitres of Distilled Water; to this liquid add a cold saturated aqueous solution of Mercuric Chloride, with constant stirring, until a slight red precipitate remains; add the Sodium Hydroxide and dissolve; then add a little more of the aqueous solution of Mercuric Chloride, and sufficient Distilled Water to produce the required volume.

Solution of Potassium Acetate.—Potassium Acetate, 10 grammes; Distilled Water sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Acid Potassium Tartrate.—A saturated solution of Acid Potassium Tartrate in Distilled Water.

Solution of Potassium Carbonate.—Potassium Carbonate, 10 grammes; Distilled Water sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Potassium Chromate.—Potassium Chromate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Potassium Cyanide.—Potassium Cyanide, 10 grammes; Distilled Water, 100 millilitres; dissolve; filter if necessary.

Solution of Potassium Ferricyanide.—Potassium Ferricyanide, in crystals, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary. This Solution must be recently prepared.

Solution of Potassium Ferrocyanide.—Potassium Ferrocyanide in crystals, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Potassium Hydroxide, of the British Pharmacopœia.

Solution of Potassium Hydroxide, Alcoholic.—Potassium Hydroxide, 10 grammes; Alcohol (90 per cent.), sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Potassium Iodide.—Potassium Iodide, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Potassium Permanganate of the British Pharmacopœia.

Solution of Pyroxylin, the Collodion of the British Pharmacopœia.

Solution of Silver Ammonio-Nitrate.—Silver Nitrate, in crystals, 2.5 grammes; Solution of Ammonia, 10.0 millilitres, or a sufficient quantity; Distilled Water, sufficient to produce 100.0 millilitres. Dissolve the Silver Nitrate in eighty millilitres of the Distilled Water, and cautiously add the Solution of Ammonia to the liquid until the precipitate first formed is nearly dissolved; set aside; decant; finally add sufficient Distilled Water to produce the required volume.

Solution of Silver Nitrate.—Silver Nitrate, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve.

Solution of Sodium Acetate.—Sodium Acetate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Sodium Carbonate.—Sodium Carbonate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Sodium Hydroxide.—Sodium Hydroxide, 20 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Sodium Phosphate.—Sodium phosphate in crystals, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Sodium Sulphate.—Sodium Sulphate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Sodium Sulphide.—Sodium Sulphide, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Stannous Chloride.—Tin, granulated, 20 grammes; Hydrochloric Acid, 60 millilitres; Distilled Water, sufficient to produce 100 millilitres. Dilute the hydrochloric Acid with twenty millilitres of the Distilled Water, and having the added Tin, apply heat gently until gas ceases to be evolved; add sufficient Distilled Water to produce the required volume, allowing the dissolved Tin to remain in the Solution.

Solution of Sulphurous Acid, of the British Pharmacopœia.

Solution of Tannic Acid.—Tannic Acid, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve. This Solution must be recently prepared.

Solution of Tartarated Antimony.—Tartarated Antimony, 5 grammes; Distilled Water, boiling, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Solution of Tartaric Acid.—Tartaric Acid, in crystals, 12.5 grammes; Alcohol (90 per cent.), 25.0 millilitres; Distilled Water, sufficient to produce 100.0 millilitres. Dissolve the Tartaric Acid in sixty millilitres of the Distilled Water; add the Alcohol; add sufficient Distilled Water to produce the required volume.

Test-Solution of Ferric Chloride (T. Sol.).—Ferric Chloride, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

Test-Solution of Mercuric Chloride (T. Sol.).—Mercuric Chloride, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary.

APPENDIX III. Br.

Solutions Employed in Volumetric Determinations.

(Br.)

Solution of Ammonium Thiocyanate, N/10.—Ammonium Thiocyanate dissolved in Distilled Water to contain in 1000 millilitres 7.612 grammes of ammonium thiocyanate, NH_4SCN.

Solution of Hydrochloric Acid, N/1, N/10.—Hydrochloric Acid diluted with Distilled Water to contain in 1000 millilitres the following quantities of hydrochloric acid, HCl: for N/1, 36.468 grammes HCl: for N/10, 3.646 grammes HCl.

Solution of Hydroxylamine Hydrochloride, N/2.—Hydroxylamine Hydrochloride dissolved in a mixture of equal volumes of Alcohol (90 per cent.) and Alcohol (70 per cent.) to contain in 1000 millilitres 34.751 grammes of hydroxylamine hydrochloride, NH_2OH,HC.

Solution of Iodine, N/10.—Iodine and Potassium Iodide dissolved in Distilled Water to contain in 1000 millilitres 12.692 grammes of iodine, I, and 18 grammes of Potassium Iodide.

Solution of Oxalic Acid, N/1, N/10.—Oxalic Acid dissolved in Distilled Water to contain in 1000 millilitres the following quantities of oxalic acid, $H_2C_2O_4,2H_2O$: for N/1, 63.024 grammes $H_2C_2O_4,2H_2O$: for N/10, 6.302 grammes $H_2C_2O_4$, $2H_2O$.

Solution of Potassium Bichromate, N/1, N/10.—Potassium Bichromate dissolved in Distilled Water to contain in 1000 millilitres the following quantities of potassium bichromate, $K_2Cr_2O_7$: for N/1, 49.033 grammes $K_2Cr_2O_7$; for N/10, 4.903 grammes $K_2Cr_2O_7$.

Solution of Potassium Hydroxide, Alcoholic, N/1, N/2, N/10.—Potassium Hydroxide dissolved in Alcohol (90 per cent.) to contain in 1000 millilitres the following quantities of potassium hydroxide, KOH: for N/1, 56.108 grammes KOH; for N/2, 28.054 grammes KOH; for N/10, 5.610 grammes KOH. These Solutions are colourless, or not more than faintly yellow.

Solution of Potassium Permanganate, N/10.—Potassium Permanganate dissolved in Distilled Water to contain in 1000 millilitres 3.161 grammes of potassium permanganate, $KMnO_4$.

Solution of Silver Nitrate, N/10.—Silver Nitrate dissolved in Distilled Water to contain in 1000 millilitres 16.989 grammes of silver nitrate, $AgNO_3$.

Solution of Sodium Hydroxide, N/1, N/2, N/5, N/10, N/20.—Sodium Hydroxide dissolved in Distilled Water to contain in 1000 millilitres the following quantities of sodium hydroxide, $NaOH$: for N/1, 40.008 grammes $NaOH$; for N/2, 20.004 grammes $NaOH$; for N/5, 8.001 grammes $NaOH$; for N/10, 4.000 grammes $NaOH$; for N/20, 2.000 grammes $NaOH$.

Solution of Sodium Thiosulphate, N/10.—Sodium Thiosulphate dissolved in Distilled Water to contain in 1000 millilitres 24.822 grammes of sodium thiosulphate, $Na_2S_2O_3,5H_2O$.

Solution of Sulphuric Acid, N/1, N/2, N/10, N/20, N/100.—Sulphuric Acid diluted with Distilled Water to contain in 1000 millilitres the following quantities of sulphuric acid, H_2SO_4: for N/1, 49.043 grammes H_2SO_4; for N/2, 24.521 grammes H_2SO_4; for N/10, 4.904 grammes H_2SO_4; for N/20, 2.452 grammes H_2SO_4; for N/100, 0.490 gramme H_2SO_4.

Indicators of the Termination of Reactions in Volumetric Determinations.

(Br.)

Mucilage of Starch.—It gives an intensely blue colour with iodine, at ordinary temperatures.

Solution of Ferric Sulphate, of the British Pharmacopœia, gives a deep red colour with ammonium thiocyanate.

Solution of Litmus.—It gives a red colour with acids and a blue colour with alkalies. Carbon dioxide, if present in the solution, must be previously expelled by boiling.

Solution of Methyl Orange.—It gives a pink colour with mineral acids and a yellow colour with alkalies.

Solution of Phenolphthalein, gives with alkalies a red colour, which is discharged by acids.

Solution of Potassium Ferricyanide, gives an intensely blue precipitate or coloration with ferrous salts, but none with ferric salts.

Tincture of Cochineal, of the British Pharmacopœia, gives a purple colour with alkalies and a brownish-yellow colour with acids.

APPENDIX IV. Br.

Reactions and Tests for Substances Mentioned in the Text of the British Pharmacopœia.

(*Br.*)

Acetates.—Neutral acetates are decomposed by heat, yielding vapours which possess a characteristic acetous odour. Hydrogen acetate and ethyl acetate have characteristic odours. Acetates when warmed with *sulphuric acid* yield vapours of hydrogen acetate; or, when warmed with *sulphuric acid* and a small quantity of *alcohol* (90 per cent.), yield ethyl acetate. *T. Sol. of ferric chloride* produces a deep-red coloration with neutral or faintly acid acetates, and the resulting liquid on boiling yields a reddish-brown precipitate. On adding *hydrochloric acid* the red solution turns yellow.

Aluminium.—*Solution of ammonia* or *solution of ammonium hydrosulphide* produces a white gelatinous precipitate, soluble in *hydrochloric acid*, in *acetic acid*, and in *solution of sodium hydroxide*, but nearly insoluble in *solution of ammonia* and in solutions of ammonium salts, and quite insoluble when the solutions are boiled.

Ammonium Salts.—Ammonium salts volatilise when strongly heated, generally without residue. When heated with *solution of sodium hydroxide*, ammonia is evolved, recognisable by its odour. *Solution of platinic chloride* produces with ammonium salts acidified with *hydrochloric acid* a yellow crystalline precipitate, especially in the presence of alcohol. On ignition, this precipitate leaves a residue of platinum only.

Antimony.—*Hydrogen sulphide* produces, in slightly acid solutions, an orange-coloured precipitate, soluble in *solution of sodium hydroxide*, and *of ammonium hydrosulphide*, and in warm *hydrochloric acid* with evolution of hydrogen sulphide, but almost insoluble in solution of Ammonium Carbonate. Nascent hydrogen, generated by the interaction of *zinc* and *diluted sulphuric acid*, partially converts antimony compounds into hydrogen antimonide. A cold porcelain tile held in the flame of this gas acquires a dark metallic deposit which is not appreciably dissolved by *solution of chlorinated soda*. Nascent hydrogen, generated by the interaction of *zinc* and *solution of sodium hydroxide*, does not convert antimony into hydrogen antimonide. If one end of a strip or rod of *zinc* be allowed to rest on a platinum capsule containing an acidified solution of an antimony compound, the other end being in the solution, the antimony is precipitated on the platinum as a black, adherent, non-granular stain, insoluble in *hydrochloric acid*. Bright *copper* foil precipitates antimony from solutions, and the antimony may be volatilised by heat in an open tube, condensing as a white amorphous sublimate of oxides of antimony near to the copper.

Arsenic.—*Hydrogen sulphide* produces in solutions containing *hydrochloric acid* a yellow precipitate, soluble in *solution of sodium hydroxide*, and *of ammonium hydrosulphide*, and in solution of Ammonium Carbonate, but reprecipitated on addition of *hydrochloric acid*. The precipitate is insoluble in *hydrochloric acid*. Nascent hydrogen, generated by the interaction of *zinc* and *diluted sulphuric acid*, converts arsenic compounds into hydrogen arsenide. A cold porcelain tile held in the flame of this gas acquires a dark metallic deposit, which is readily dissolved by *solution of chlorinated soda*. Nascent hydrogen, generated by the interaction of *zinc* and *solution of sodium hydroxide*, converts arsenic compounds into hydrogen arsenide. This gas gives a black stain to filter-paper soaked with *solution of silver nitrate* and placed as a cap over the tube in which the test is being performed. Bright *copper* foil precipitates arsenic from solutions acidified by *hydrochloric acid*, and the arsenic may be volatilised by heat in an open tube, and condenses, at some distance from the copper, as a white sublimate of characteristic octahedral crystals of arsenious oxide.

ARSENITES.—Solutions of arsenites yield a yellow precipitate with *solution of silver ammonio-nitrate*.

ARSENATES.—Solutions of arsenates yield a reddish-chocolate precipitate with *solution of silver ammonio-nitrate. Solution of magnesium ammonio-sulphate* produces a white crystalline precipitate.

Bicarbonates. *See* **Carbonates.**

Bismuth.—*Hydrogen sulphide* produces a brownish-black precipitate, insoluble in *solution of sodium hydroxide*, in *diluted hydrochloric acid* and in *solution of ammonium hydrosulphide*, but soluble in warm *nitric acid. Solution of sodium hydroxide*, or of *ammonia*, except in the presence of citrates, produces a white precipitate insoluble in excess of the precipitant. Dilute solution of *sodium chloride* in large excess produces in solutions which are not too acid a white precipitate, insoluble in *solution of tartaric acid*.

Bromates.—From bromates *solution of sulphurous acid* liberates bromine, recognisable by its odour and appearance. After ignition with charcoal bromates are converted into bromides, and the latter yield their characteristic reactions.

Bromides.—*Solution of silver nitrate* produces a yellowish curdy precipitate, somewhat soluble in strong but almost insoluble in diluted *solution of ammonia*, and insoluble in *nitric acid. Solution of chlorine* liberates bromine, soluble in two or three drops of *carbon disulphide* or of *chloroform*, and forming a reddish solution. Bromine is liberated when a bromide is heated with *sulphuric acid* and *manganese peroxide*, or *potassium bichromate*, the vapour giving an orange-yellow colour to filter-paper soaked in *mucilage of starch*. In testing for bromides in the presence of iodides, all iodine should first be removed by boiling the aqueous solution with excess of *lead peroxide*.

Cadmium.—*Hydrogen sulphide* produces a yellow precipitate, insoluble in cold *diluted hydrochloric acid*, in *solution of ammonium hydrosulphide* and in *solution of sodium hydroxide*, but soluble in *nitric acid*, in hot *diluted hydrochloric acid*, and in hot *diluted sulphuric acid. Solution of sodium hydroxide* produces a white precipitate insoluble in excess. *Solution of ammonia* produces a white precipitate readily soluble in excess.

Calcium.—*Solution of ammonium carbonate* produces a white precipitate which, after well boiling and allowing to cool, is insoluble in *solution of ammonium chloride. Solution of ammonium oxalate* produces a white precipitate, soluble in *hydrochloric acid* but insoluble in *acetic acid. Solution of potassium chromate* produces no precipitate.

Carbonates and Bicarbonates.—Dilute acids liberate carbonic acid; the escaping gas is odourless, and produces a white precipitate in *solution* of lime. Soluble carbonates produce a brownish-red precipitate with *T. Sol. of mercuric chloride,* bicarbonates a whitish precipitate; the former produce a white precipitate with cold *solution of magnesium sulphate,* the latter do not.

Chlorides.—*Solution of silver nitrate* produces a white curdy precipitate, soluble in *solution of ammonia,* but insoluble in *nitric acid.* A solid chloride or hydrochloride when subjected to distillation with *sulphuric acid* and *potassium bichromate,* yields a reddish-brown distillate which is decomposed by *water.* The resulting solution when nearly neutralized produces a yellow precipitate with *solution of lead acetate,* Heated with *manganese peroxide* and *sulphuric acid,* chlorides yield chlorine, recognisable by its odour and by giving a blue colour with *solution of potassium iodide* and *mucilage of starch.*

Citrates.—Citrates become charred when heated. *Solution of Calcium Chloride* added in excess produces, when boiled with a neutral solution of a citrate, a white precipitate in solutions of neutral citrates a white precipitate soluble in *solution of amonia.* A mirror is not formed on the sides of the tube when the ammoniacal solution is warmed.

Copper.—*Hydrogen sulphide* produces a brownish-black precipitate, insoluble in *diluted hydrochloric acid* and in *solution of sodium hydroxide,* almost insoluble in *solution of ammonium hydrosulphide,* but decomposed and dissolved by boiling *nitric acid. Solution of sodium hydroxide* produces a bulky light-blue precipitate which becomes brownish-black on boiling. *Solution of ammonia* added in small quantity to a neutral solution of a copper salt produces a greenish-blue precipitate which readily dissolves in excess of the precipitant, forming a deep- blue solution. *Solution of potassium ferrocyanide* produces a reddish-brown precipitate, or in very dilute solutions a reddish-brown coloration.

Cyanides.—*Solution of silver nitrate* produces a white curdy precipitate, soluble in *solution of potassium cyanide,* in *solution of ammonia,* and in boiling *nitric acid.* When to a soluble cyanide there are added a few drops of a mixed solution of ferrous and ferric salts, then of *solution of sodium hydroxide,* and lastly excess of *hydrochloric acid,* a blue precipitate is produced. Mercury cyanide and silver cyanide decompose when heated, evolving (highly poisonous) cyanogen, which burns with a pink flame.

Iodates.—*Solution of silver nitrate* produces a white precipitate sparingly soluble in *water* and in *diluted nitric acid,* but readily dissolved by *solution of ammonia. Solution of sulphurous acid* when added to the ammoniacal solution produces a pale yellow precipitate. A mixed *solution of potassium iodide* and *tartaric acid* added to a solution of an iodate liberates iodine, which produces a blue colour with *mucilage of starch. Solution of barium chloride* produces a white precipitate nearly insoluble in *water* and soluble with difficulty in *diluted nitric acid.* On the addition of *mucilage of starch* and *solution of sulphurous acid* a blue colour is produced.

Iodides.—*Solution of silver nitrate* produces a curdy yellow precipitate, insoluble in *nitric acid* and almost insoluble in *solution of ammonia. T. Sol. of mercuric chloride* produces a scarlet precipitate, slightly soluble in excess of this reagent, and very soluble in *solution of potassium iodide.* A small quantity of *solution of chlorine* added to a solution of an iodide liberates iodine, which colours *carbon disulphide* violet and *mucilage of starch* deep blue. Heated with *sulphuric acid* and *manganese peroxide* or *potassium bichromate* violet vapours of iodine are evolved.

Iron.—Reaction common to Ferrous and Ferric salts: *Solution of ammonia hydrosulphide* produces, in neutral solutions, a black precipitate soluble in cold *diluted hydrochloric acid* with evolution of hydrogen sulphide. Reactions characteristic of Ferrous salts: *Solution of potassium ferrocyanide* produces a white precipitate, rapidly turning blue, insoluble in *diluted hydrochloric acid. Solution of potassium ferrocyanide* produces a dark-blue precipitate, insoluble in *diluted hydrochloric acid;* decomposed by *solution of sodium hydroxide. Solution of sodium hydroxide* produces a dull-green precipitate. Reactions characteristic of Ferric salts: *Solution of ammonium thiocyanate* produces a blood-red coloration which is discharged on the addition of *T. Sol. of mercuric chloride. Solution of potassium ferricyanide* produces a reddish-brown coloration but no precipitate. *Solution of potassium ferrocyanide* produces a dark-blue precipitate, insoluble in *diluted hydrochloric acid. Solution of sodium hydroxide* produces a reddish-brown precipitate, soluble in solution of *citric acid* or *tartaric acid,* and not formed in the presence of citrates or tartrates.

Lead.—*Hydrochloric acid* produces except in very weak solutions, a white precipitate, soluble in boiling *water,* but re-deposited in crystals on cooling. *Hydrogen sulphide,* in not very strongly acid solutions, produces a black precipitate insoluble in *diluted hydrochloric acid, solution of potassium hydroxide,* and *solution of ammonium hydrosulphide,* but soluble in hot *diluted nitric acid. Diluted sulphuric acid* produces a white precipitate almost insoluble in *water,* and still less soluble in *diluted sulphuric acid* or in *alcohol* (96 per cent.), but soluble in *solution of ammonium acetate. Solution of potassium chromate* produces a yellow precipitate readily soluble in *solution of sodium hydroxide,* in hot *nitric acid,* sparingly soluble in *diluted nitric acid,* insoluble in *acetic acid.*

Magnesium.—*Solution of ammonium carbonate,* in the presence of *solution of ammonium chloride,* produces no precipitate. *Solution of sodium phosphate* in the presence of ammonium salts and *solution of ammonia,* produces a white crystalline precipitate. *Solution of sodium hydroxide* produces a white precipitate, insoluble in excess of the reagent, but soluble in *solution of ammonium chloride.*

Mercury.—Reactions common to Mercurous and Mercuric salts: *Hydrogen sulphide* produces a black precipitate, insoluble in *solution of ammonium hydrosulphide* and in boiling *diluted nitric acid.* Bright *copper* foil immersed in a solution free from excess of nitric acid becomes coated with a deposit of mercury which on rubbing becomes bright; the mercury may be volatilised from the foil by heat and obtained in globules. Reaction characteristic of Mercurous salts: *Hydrochloric acid* produces a white precipitate insoluble in *water,* and blackened by *solution of ammonia.* Reactions characteristic of Mercuric salts: *Solution of sodium hydroxide* produces a yellow precipitate. *Solution of potassium iodide* produces in neutral solutions a scarlet precipitate soluble in excess of the preciptant, and in a considerable excess of the solution of the mercuric salt.

Nitrates.—*Ferrous sulphate* and *sulphuric acid,* when added to a solution of a nitrate in such a way that the acid forms a stratum below the aqueous solution, produce a brown coloration at the junction of the two liquids. Nitrates liberate red fumes when warmed with *sulphuric acid* and *copper*.

Nitrites.—On the addition to a solution of a nitrite, of a few drops of diluted sulphuric acid, solution of potassium iodide and mucilage of starch, a blue colour is produced. Diluted sulphuric acid produces red fumes. Solution of ferrous sulphate produces a deep brown colour.

Oxalates.—*Solution of calcium chloride* produces a white precipitate soluble in *hydrochloric acid* but insoluble in *acetic acid. Solution of silver nitrate* produces a white precipitate, soluble in *solution of ammonia* and in diluted nitric acid. Oxalates do not char when heated with sulphuric acid but yield carbon monoxide and carbon dioxide.

Phosphates.—*Solution of silver ammonio-nitrate* produces in salt solutions of ortho-phosphates a light-yellow precipitate readily soluble in *solution of ammonia* and in cold *diluted nitric acid. Solution of magnesium ammonio-sulphate* produces a white crystalline precipitate. Excess of *solution of ammonium molybdate* containing much *nitric acid,* produces on warming, a yellow precipitate.

Potassium.—*Solution of platinic chloride* produces with moderately strong solutions of potassium chloride (or with other potassium salts if hydrochloric acid be present) a yellow crystalline precipitate, which, upon ignition, leaves a residue of potassium chloride and platinum. Potassium compounds moistened with *hydrochloric acid* when introduced, on platinum wire, into the flame of a Bunsen burner, communicate to the flame a violet coloration.

Selenium and Tellurium.—Selenium and Tellurium may occur in compounds of bismuth. To detect these elements, dissolve the compound in *nitric acid,* add solution of *sodium chloride* or *solution of ammonium chloride,* and dilute freely with *water.* The filtrate from the precipitate, mixed with excess of an aqueous solution of *sodium sulphite,* produces no precipitate or coloration even after twelve hours.

Silica.—Silica after exposure to a red heat, is insoluble in acids, and is not dissolved in a bead of *purified borax* when heated to fusion in the blowpipe flame. The result of its fusion with *sodium carbonate* is soluble in water, the solution yielding a gelatinous precipitate on the addition of *hydrochloric acid.*

Silver.—*Hydrochloric acid* and other chlorides produce a white curdy precipitate, soluble in *solution of ammonia* but insoluble in *nitric acid. Solution of Potassium chromate* produces a red precipitate, soluble in *nitric acid.*

Sodium.—Sodium compounds, moistened with *hydrochloric acid,* when introduced on platinum wire, into the flame of a Bunsen burner, communicate to the flame a yellow coloration.

Strontium.—*Solution of ammonium carbonate* produces a white precipitate, insoluble in *solution of ammonium chloride. Solution of ammonium oxalate* produces a white precipitate, insoluble in *acetic acid* but soluble in *hydrochloric acid. Solution of potassium chromate* produces a light-yellow precipitate, soluble in *acetic acid. Solution of calcium sulphate* produces a white precipitate.

Sulphates.—*Solution of barium chloride* produces a white precipitate insoluble in *hydrochloric acid.*

Sulphides.—The official sulphides, hydrosulphides, and sulphurated compounds evolve hydrogen sulphide when boiled with *hydrochloric acid.*

Sulphites.—*Hydrochloric acid* liberates sulphur dioxide, a colourless gas with a pungent small of burning sulphur. *Solution of barium chloride* produces a white precipitate soluble in *hydrochloric acid.* Sulphites decolorise *N/10 solution of iodine.*

Tartrates.—Tartrates become charred when heated. *Solution of calcium, chloride* added in excess to a solution of a neutral tartrate produces, even when cold, a white franular precipitate, soluble in *acetic acid. Solution of silver nitrate* produces a white precipitate, soluble in *solution of ammonia* and in *nitric acid.* The ammoniacal solution, on heating, deposits metallic silver as a mirror on the sides of the test-tube. When to a solution of tartaric acid in *water,* or of a tartrate acidified with *acetic acid,* a drop of *solution of ferrous sulphate,* then a few drops of *solution of hydrogen peroxide,* and finally an excess of *solution of sodium hydroxide* are added, a purple or violet colour is produced.

Tellurium. *See* **Selenium.**

Thiosulphates.—*Hydrochloric acid* produces a yellow precipitate and liberates sulphur dioxide recognisable by its odour. *Solution of barium chloride* produces no precipitate in dilute solutions; on the further addition of *solution of bromine* a white precipitate is produced. Thiosulphates decolorise *N/10 solution of iodine.*

Tin.—Metallic *zinc* placed in a solution of any tin salt acidified with *hydrochloric acid* precipitates the tin in metallic scales or as a grey sponge. The metal separated from the liquid, is soluble, in boiling *hydrochloric acid,* and the solution, which then contains stannous chloride, produces with *T. Sol. of mercuric chloride* a white precipitate which becomes grey if excess of the tin salt is present.

Zinc.—*Solution of Ammonium hydrosulphide* produces in neutral, and *hydrogen sulphide* in alkaline solutions, a white precipitate, soluble in *hydrochloric acid* but insoluble in *acetic acid. Solution of sodium hydroxide* or *solution of ammonia* produces a white precipitate, soluble in excess of either reagent. *Solution of potassium ferrocyanide* produces a white precipitate, insoluble in *diluted hydrochloric acid.*

APPENDIX V. Br.

Quantitative Limit-test For Lead.

(*Br.*)

APPARATUS

(All glass apparatus used must be lead-free.)

Nessler Glasses—Thin, and of lead-free glass. About 150 millilitres long, and of such diameter that the mark indicating a content of 50 millilitres is at the height of 100 millilimetres from the base.

SOLUTIONS AND REAGENTS

The special solutions and reagents for the Quantitative Limit-test for lead are distinguished by the letters "Pb T".

Strong Solution of Lead Pb T.—Dissolve 0.16 gramme of Lead Nitrate in Distilled Water, adding 50 millilitres of Nitric Acid and dilute with Distilled Water to 1000 millilitres. This solution contains 0.001 gramme of lead in 1 millilitre.

Dilute Solution of Lead Pb T. —Dilute 1 millilitre of the Strong Solution of Lead Pb T., measured from a burette, with Distilled Water so that the resulting solution measured 100 millilitres. This solution contains 0.00001 gramme of lead in 1 millilitre.

Solution of Potassium Cyanide Pb T.—Dissolve 10 grammes of Potassium Cyanide in Distilled Water, add 2 millilitres of Solution of Hydrogen Peroxide and make up to 100 millilitres with Distilled Water. This solution after being allowed to stand, when tested by the quantitative limit-test for lead, gives no colour with the Dilute Solution of Lead Pb T.

Solution of Sodium Sulphide Pb T.—Dissolve 10 grammes of Sodium Sulphide in Distilled Water and make up to 100 millilitres with Distilled Water.

MODE OF TESTING (GENERAL)

Br.

Two solutions of the substance under examination are made in hot Distilled Water: (1) The primary solution containing 12 grammes of the substance. (2) The auxiliary solution containing 2 grammes of the substance. Each solution is filtered (if necessary), made alkaline with *solution of ammonia*, and treated with 1 millilitre of the solution of potassium cyanide Pb T. If the colours of the solutions differ much, the difference may be rectified by the cautious addition of a highly diluted solution of burnt sugar. Then, by the method of trial and error (well known in water analysis as "Nesslerizing"), is determined quantity of the dilute solution of lead Pb T. which must be added to the auxiliary solution, in order that there may be equal colorations produced upon the addition of 2 drops of the solution of sodium sulphide Pb T. to both the primary and the auxiliary solution after dilution to the 50 millilitre mark. In these circumstances, each millilitre of the dilute solution of lead Pb T. required corresponds to 1 part per million of lead in the substance examined. The colorations may be viewed by light reflected from a horizontal white tile through the Nessler glasses inclined at an angle to the observer.

Note.—In some cases, 7 or 4 grammes only are used in the primary solution. In these cases each millilitre of the dilute solution of lead Pb T. required will represent 2 or 5 parts per million of lead respectively.

Substance.	Primary Solution of Substance: Grammes employed.	Auxiliary Solution of Substance Grammes employed.	Dilute Solution of Lead Pb T.: Millimetres employed.	Limit of Lead: Parts per Million.
Acidum Acetylsalicylicum	7[a]	2[a]	5	10
Acidum Boricum	7[a]	2[a]	12.5	25
Acidum Citricum	7	2	10	20
Acidum Hydriodicum Dilutum	7	2	5	10
Acidum Hydrobromicum	12	2	5	5
Acidum Hydrochloricum	12	2	10	10
Acidum Lacticum	7	2	5	10
Acidum Nitricum	7	2	10	20
Acidum Phosphoricum Concentratum	12	2	10	10
Acidum Sulphuricum	7	2	10	20
Acidum Sulphurosum	12	2	10	10
Acidum Tartaricum	7	2	10	20
Ammonii Benzoas	7	2	5	10
Ammonii Bromidum	12	2	10	10
Ammonii Carbonas	12[b]	2	5	5
Ammonii Chloridum	12	2	5	5
Borax Purificatus	7	2	2.5	5
Calcii Carbonas Præcipitatus	7[c]	2[c]	5	10
Calcii Chloridum	7[d]	2[d]	10	20
Calcii Hydras	7[c]	2[c]	10	20
Calcii Hypophosphis	7[d]	2[d]	5	10
Calcii Lactas	7[d]	2[d]	5	10
Liquor Magnesii Bicarbonatis	Special	process	5	0.5
Lithii Carbonas	7[c]	2[c]	5	10
Lithii Citras	12	2	5	5
Magnesia Levis	4[c]	2[c]	4	20
Magnesia Ponderosa	4[c]	2[c]	4	20
Magnesii Carbonas Levis	7[c]	2[c]	10	20
Magnesii Carbonas Ponderosus	7[c]	2[c]	10	20
Magnesii Sulphas	12	2	5	5
Potassii Acetas	12	2	10	10
Potassii Bicarbonas	12	2	5	5
Potassii Bromidum	12	2	10	10
Potassii Carbonas	12	2	5	5
Potassii Chloras	7	2	5	10

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[a] Solution effected by the addition of *solution of ammonia*.

[b] Primary solution boiled down to measure 50 millilitres.

[c] Solutions prepared by dissolviwg in excess of *acetic acid*, boiling to expel any carbon dioxide present, then making alkaline with *solution of ammonia* and adding solution of potassium cyanide Pb T.

[d] *Acetic acid* added to each solution before making alkaline with *solution of ammonia*.

[e] Primary solution prepared by treating 200 millilitres with excess of *acetic acid* and concentrating so that the solution (after being made alkaline with *solution of ammonia* and treated with solution of potassium cyanide Pb T.) measures 50 millilitres. Auxiliary solution—100 millilitres similarly treated.

Substance.	Primary Solution of Substance: Grammes employed.	Auxiliary Solution of Substance Grammes employed.	Dilute Solution of Lead Pb T.: Millimetres employed.	Limit of Lead: Parts per Million.
Potassii Citras	12	2	10	10
Potassii Iodidum	12	2	10	10
Potassii Nitras	12	2	10	10
Potassii Sulphas	7	2	10	20
Potassii Tartras	7	2	10	20
Potassii Tartras Acidus	7[a]	2[a]	10	20
Sodii Benzoas	7	2	5	10
Sodii Bicarbonas	7[f]	2	2.5	5
Sodii Bromidum	12	2	10	10
Sodii Carbonas	12	2	10	10
Sodii Carbonas Exsiccatus	7	2	12.5	25
Sodii Chloridum	12	2	10	10
Sodii et Potassii Tartras	7	2	10	20
Sodii Hypophosphis	7	2	5	10
Sodii Iodidum	12	2	10	10
Sodii Phosphas	12	2	5	5
Sodii Phosphas Acidus	12	2	5	5
Sodii Salicylas	12	2	10	10
Sodii Sulphas	12	2	5	5
Strontii Bromidum	7[d]	2[d]	10	20

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[a] Solution effected by the addition of *solution of ammonia.*
[d] *Acetic Acid* added to each solution before making alkaline with *solution of ammonia.*
[f] Solution effected by boiling.

APPENDIX VI. Br.

Quantitative Limit-test for Arsenic.

(*Br.*)

Note.—In the quantitative limit-test for arsenic the amount of arsenic present per million is calculated as arsenious oxide, As_4O_6.

APPARATUS.—A wide-mouthed bottle capable of holding about 120 millilitres and fitted with a rubber cork through which passes a glass tube. The latter, made from ordinary soft glass tubing, has a total length of 200 millimetres and an internal diameter of 5 millimetres (external diameter 7 millimetres) and is open at both ends. The upper end is slightly widened to a diameter of 8 millimetres, while the lower end is drawn out to about 1 millimetre in diameter, and a hole about 2 millimetres in diameter blown in the side of the tube where it is constricted.

LEAD PAPERS.—Lead papers are pieces of thin white filter paper 100 millimetres x 40 millimetres, soaked in *solution of lead acetate* and dried.

MERCURIC CHLORIDE PAPERS.—Mercuric chloride papers are circles of smooth white filter paper 5.5 centimetres in diameter soaked in a saturated aqueous solution of mercuric chloride and dried.

Note.—The mercuric chloride papers should be stored in a stoppered bottle in the dark. Mercuric chloride papers that have been exposed to sunlight afford a lighter-coloured stain when employed in an arsenic test.

REAGENTS (*Br.*)

The special reagents for the quantitative limit-test for arsenic are distinguished by the letters "As T."

Brominated Hydrochloric Acid As T.—Solution of Bromine As T., 1 millilitre; Hydrochloric Acid As T. sufficient to produce 100 millilitres. Mix.

Calcium Hydroxide As T.—10 grammes tested as described under "Calcii Hydras," page 1742, give no visible stain.

Citric Acid As T.—10 grammes tested as described under "Acidum Aceticum," page 1740, give no visible stain.

Hydrochloric Acid As T.—Contains not more than 0.1 part per million of arsenic, as shown by the *Control Test*, and is free from iron.

Nitric Acid As T.—10 millilitres treated as described under "Acidum Nitricum," page 1741, give no visible stain.

Potassium Chlorate As T.—Five grammes tested as described under "Potassii Chloras," page 1744. give no visible stain.

Solution of Arsenic As T.—Hydrochloric Solution of Arsenic, 1 millilitre; Distilled Water sufficient to produce 1000 millilitres. Mix. This solution must be freshly prepared. 1 millilitre contains 0.00001 gramme (one-hundredth of one milligram) of arsenic.

Solution of Bromine As T.—Bromine 30 grammes; Potassium Bromide, 30 grammes; Distilled Water sufficient to produce 100 millilitres. Dissolve. It contains not more than 1 part per million of arsenic as shown by the *Control Test.*

Solution of Stannous Chloride As T.—It is prepared from the Solution of Stannous Chloride, Appendix II, page 1734, by adding an equal volume of Hydrochloric Acid, boiling down to the original bulk and filtering. It contains not more than 1 part per million of arsenic, as shown by the *Control Test.*

Stannated Hydrochloric Acid As T.—Solution of Stannous Chloride As T., 1 millilitre; Hydrochloric Acid As T. sufficient to produce 100 millilitres. Mix.

Sulphuric Acid As T.—Ten grammes, tested as described under "Acidum Sulphuricum," page 1741, but omitting the stannated hydrochloric acid As T. and adding 0.2 millilitre of solution of stannous chloride As T., give no visible stain.

Zinc As T.—Zinc As T. is granulated zinc which conforms to the arsenic requirement involved in the *Control Test*, and is free from iron.

METHOD OF PERFORMING THE QUANTITATIVE TEST FOR ARSENIC

By a variable method of procedure suitable to the particular needs of each case there is prepared from the substance to be tested a solution, which may or may not contain the substance to be treated, but in every case contains the whole of the arsenic (if any) originally in that substance. It is this solution—hereinafter referred to as "the solution to be examined"—which is introduced into the actual test.

General Test.—A strip of lead paper is rolled up and placed in the glass tube so that the upper end is not less than 2 centimetres below the top of the tube. A piece of the mercuric chloride paper is now placed over the top of the tube and secured by means of a rubber ring. The tube is inserted in the rubber cork. The solution to be examined, prepared as specified, is placed in the wide-mouthed bottle and 10 grammes zinc As T. added. The rubber cork with glass tube attached is quickly placed in position so that the lower end of the tube is clear above the surface of the liquid, and the hole is the constricted portion of the tube is clear below the bottom of the cork. The action should be allowed to proceed for thirty to forty minutes the mercuric chloride paper not being exposed to strong sunlight. The yellow stain which is produced on the mercuric chloride paper if arsenic be present is compared, by daylight, with stains produced by operating in a similar manner with known quantities of the solution of arsenic As T. The comparison of the stains should be made at the completion of the test and those used for comparison should be freshly prepared. The stains fade upon keeping.

Note.—The action may be accelarated by standing the apparatus on a hot plate, care being taken that the mercuric chloride paper remains quite dry throughout the duration of the test.

Standard Stain.—Prepare a solution by adding to 50 millilitres of hot *water*, 10 millilitres of stannated hydrochloric acid As T. and 1 millilitre of solution of arsenic As T. The resulting solution when treated as described in the "General Test" will yield a stain on the mercuric chloride paper hereinafter referred to as the "Standard Stain".

CONTROL TESTS FOR REAGENTS AS T.

Hydrochloric Acid As T.—To 50 millilitres of the hydrochloric acid to be tested add 0.2 millilitre of solution of bromine As T., evaporate on a water-bath until reduced to 16 millilitres, add 50 millilitres of hot *water* and 5 drops of solution of stannous chloride As T. and with this solution carry out the "General Test" described above. The stain produced on the mercuric chloride paper is not deeper that that given by 10 millilitres of the same hydrochloric acid with 5 drops of solution of stannous chloride As T., 0.4 millilitre of solution of arsenic As T. and 50 millilitres of hot *water*, showing that the proportion of arsenic present does not exceed 0.1 part per million.

Solution of Bromine As T.—Evaporate 10 millilitres of the solution of bromine on water-bath nearly to dryness, add 50 millilitres of hot *water*, 10 millilitres of hydrochloric acid As T., and sufficient solution of stannous chloride As T. to reduce the remaining bromine, and with this solution carry out the "General Test," described above. The stain produced on the mercuric chloride paper is not deeper than the Standard Stain, showing that the proportion of arsenic present does not exceed 1 part per million.

Solution of Stannous Chloride As T.—To 10 millilitres of the solution of stannous chloride add 6 millilitres of water and 10 millilitres of hydrochloric acid As T., and distill 16 millilitres. To the distillate add 50 millilitres of hot *water* and a few drops of solution of stannous chloride As T. and with this solution carry out the "General Test" described above. The stain produced on the mercuric chloride paper is not deeper than the Standard Stain, showing that the proportion of arsenic present does not exceed 1 part per million.

Zinc As T.—Add 10 millilitres of stannated hydrochloric acid As T., to 50 millilitres of hot *water*, and with this solution of 10 grammes of zinc As T. proceed as with the "General Test," but allow the action to continue for one hour. No visible stain is produced on the mercuric chloride paper (limit of arsenic in the zinc).

The following Table shows the varying methods of preparing the "solution to be examined." The quantities are so arranged that, when tested according to the "General Test" described above, the stain produced on the mercuric chloride paper is not deeper than the Standard Stain, showing that the proportion of arsenic present does not exceed the permissible limit.

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Acidum Aceticum	5 grammes in 50 millilitres of hot *water*, adding 10 millilitres of stannated hydrochloric acid As T.	2
Acidum Acetylsalicylicum	5 grammes made into a paste in a porcelain dish with 2 grammes of calcium hydroxide As T. and 5 millilitres of *water*, drying and gently igniting, dissolving residue in 16 millilitres of brominated hydrochloric acid As T. and 45 millilitres of hot *water*, and finally removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Acidum Benzoicum	5 grammes treated as described under "Acidum Acetylsalicylicum."	2
Acidum Boricum	2 grammes with 4 grammes of citric acid As T. in 50 millilitres of hot *water*, adding 10 millilitres of stannated hydrochloric acid As T.	5

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Acidum Citricum	7 grammes treated as described under "Acidum Aceticum."	1.4
Acidum Hydriodicum Dilutum	2 grammes with 50 millilitres of hot *water*, adding 0.5 millilitre of solution of bromine As T. and 10 millilitres of hydrochloric acid As T., allowing it to stand for five minutes, and removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Acidum Hydrobromicum Dilutum	2 grammes treated as described under "Acidum Aceticum."	5
Acidum Hydrochloricum	2 grammes with 50 millilitres of hot *water* and 8 millilitres of stannated hydrochloric acid As T.	5
Acidum Lacticum	2 grammes treated as described under "Acidum Aceticum."	5
Acidum Nitricum	2 grammes heated in a porcelain dish with 2 millilitres of sulphuric acid As T. until white fumes are evolved then cooling, adding 2 millilitres of *water*, again heating until white fumes are evolved again cooling and adding to the residue 50 millilitres of hot *water* and 10 millilitres of stannated hydrochloric acid As T.	5
Acidum Phosphoricum Concentratum	2 grammes treated as described under "Acidum Aceticum."	5
Acidum Salicylicum	5 grammes treated as described under "Acidum Acetylsalicylicum."	2
Acidum Sulphuricum	2 grammes mixed with 10 millilitres of *water*, adding 40 millilitres of hot *water* and 8 millilitres of stannated hydrochloric acid As T.	5
Acidum Sulphurosum	2 grammes mixed in the cold with 0.5 gramme of potassium chlorate As T. and 11 millilitres of hydrochloric acid As T., warming to expel excess of chlorine, then adding 50 millilitres of hot *water* and a few drops of solution of stannous chloride As T.	5
Acidum Tartaricum	7 grammes treated as described under "Acidum Aceticum."	1.4
Alumen Purificatum	2 grammes treated as described under "Acidum Aceticum."	5
Ammonii Benzoas	5 grammes treated as described under "Acidum Acetylsalicylicem."	2
Ammonii Bromidum	2 grammes in 50 millilitres of hot *water*, adding 12 millilitres of stannated hydrochloric acid As T.	5
Ammonii Carbonas	5 grammes in 50 millilitres of hot *water*, boiled gently until the greater part of the ammonium carbonate is volatilised, then adding 15 millilitres of brominated hydrochloric acid As T. and removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Ammonii Chloridum	2 grammes treated as described under "Acidum Aceticum."	5
Antimonium Sulphuratum	0.01 gramme dissolved by boiling in a small flask with 0.2 gramme of clacium hydroxide As T. and 5 millilitres of *water*, then adding 2 millilitres of solution of bromine As T. and again gently boiling then adding 17 millilitres of hydrochloric acid As T. and 5 millilitres of *water* and boiling until most of the bromine is volatilised, the last traces being removed by adding a slight excess of solution of stannous chloride As T., connecting to a condenser and distilling 20 millilitres, then washing the condenser and flask, returning the distillate to the flask, adding 1 drop of solution of stannous chloride As T. and redistilling 16 millilitres, then adding to the distillate 45 millilitres of hot *water* and a few drops of solution of stannous chloride As T.	1000
Bismuthi Carbonas	5 grammes dissolved in a small flask in 5 millilitres of *water* and 20 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T., connecting to a condenser and distilling 18 millilitres, then adding to the distillate 40 millilitres of hot *water* and 3 drops of solution of stannous chloride As T.	2

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Bismuthi Salicylas	5 grammes made into a paste in a porcelain dish with 1 gramme of calcium hydroxide As T. and 5 millilitres of *water*, drying and gently igniting, dissolving the residue in 20 millilitres of brominated hydrochloric acid As T. and 10 millilitres of *water*, transferring to a small flask and adding sufficient solution of stannous chloride As T. to remove the excess of bromine, connecting to a condenser and distilling 20 millilitres, then adding to the distillate 40 millilitres of hot *water* and 3 drops of solution of stannous chloride As T.	2
Bismuthi Subnitras	5 grammes heated in a porcelain dish with 2 millilitres of sulphuric acid As T. until white fumes are evolved, cooling, adding 5 millilitres of *water* and again heating until white fumes are evolved, dissolving the residue when cold in 20 millilitres of *water* and 10 millilitres of stannated hydrochloric acid As T., transferring to a small flask, connecting to a condenser and distilling 20 millilitres, adding to the distillate a little solution of bromine As T. to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride As T., and adding 40 millilitres of hot *water*.	2
Borax Purificatus	2 grammes with 4 grammes of citric acid As T. in 50 millilitres of hot *water*, adding 12 millilitres of stannated hydrochloric acid As T.	5
Calcii Carbonas Præcipitatus	2 grammes in 14 millilitres of brominated hydrochloric acid As T. and 45 millilitres of hot *water*, removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Calcii Chloridum	2 grammes treated as described under "Acidum Aceticum."	5
Calcii Hydras	2 grammes in 16 millilitres of brominated hydrochloric acid As T. and 45 millilitres of hot *water*, removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Calcii Hypophosphis	2 grammes mixed in the cold with 2 grammes of potassium chlorate and 18 millilitres of hydrochloric acid As T., then warming to expel excess of chlorine, adding 40 millilitres of hot *water* and a few drops of solution of stannous chloride As T.	5
Calcii Lactas	2 grammes treated as described under "Ammonii Bromidum."	5
Calcii Phosphas	2 grammes in 50 millilitres of hot *water* and 14 millilitres of stannated hydrochloric acid As T.	5
Calx	2 grammes in 18 millilitres of brominated hydrochloric acid As T. and 40 millilitres of *water*, removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Creta Præparata	2 grammes treated as described under "Calcii Carbonas Præcipitatus."	5
Cupri Sulphas	1 gramme dissolved in a small flask, with 10 millilitres of *water* and 15 millilitres of hydrochloric acid As T., adding 5 drops of solution of stannous chloride As T., connecting to a condenser and distilling 20 millilitres, adding a little solution of bromine As T. to the distillate to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride As T., finally adding 40 millilitres of hot *water*.	10
Ferri Carbonas Saccharatus	2 grammes made into a paste with 1 gramme of calcium hydroxide As T. and 2 millilitres of *water* in a porcelain dish, drying and gently igniting, dissolving the residue in 20 millilitres of brominated hydrochloric acid As T. and 10 millilitres of *water*, transferring to a small flask, adding solution of stannous chloride As T. until the yellow colour disappears, then connecting to a condenser and distilling 24 millilitres, finally adding to the distillate 35 millilitres of hot *water* and 3 drops of solution of stannous chloride As T.	5
Ferri et Ammonii Citras	2 grammes treated as described under "Ferri Carbonas Saccharatus."	5

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Ferri et Potassii Tartras	2 grammes treated as described under "Ferri Carbonas Saccharatus."	5
Ferri et Quininæ Citras	2 grammes treated as described under "Ferri Carbonas Saccharatus."	5
Ferri Phosphas Saccharatus	2 grammes treated as described under "Ferri Carbonas Saccharatus."	5
Ferri Sulphas	5 grammes dissolved in a small flask, with 10 millilitres of *water* and 15 millilitres of hydrochloric acid As T., adding solution of stannous chloride As T. until the yellow colour disappears, connecting to a condenser and distilling 20 millilitres, adding a a little solution of bromine As T. to the distillate to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride As T., and finally adding 40 millilitres of hot *water*.	2
Ferri Sulphas Exsiccatus	2 grammes treated as described under "Ferri Sulphas."	5
Ferrum	0.05 gramme mixed in a small flask with 0.1 gramme of potassium chlorate As T. and 7 millilitres of *water*, adding 11 millilitres of hydrochloric acid As T. and, when the reaction has ceased and all the iron is dissolved, boiling gently to expel chlorine, then adding solution of stannous chloride As T. until the yellow colour disappears, connecting to a condenser and distilling 14 millilitres, finally adding to the distillate 50 millilitres of hot *water* and a few drops of solution of stannous chloride As T.	200
Ferrum Redactum	0.05 gramme treated as described under "Ferrum."	200
Glucosum	5 grammes treated as described under "Acidum Hydriodicum Dilutum."	2
Glycerinum	2.5 grammes treated as described under "Acidum Aceticum."	4
Liquor Ammoniæ Fortis	20 grammes evaporated on a water-bath until reduced to 5 millilitres, adding 40 millilitres of *water* and 15 millilitres of brominated hydrochloric acid As T., and removing excess of bromine by a few drops of solution of stannous chloride As T.	0.5
Liquor Ferri Perchloridi Fortis	1 gramme heated in a porcelain dish with 1 millilitre of sulphuric acid As T. until white fumes are evolved, cooling, adding an equal volume of *water* and again heating until white fumes are evolved, dissolving the residue in 10 millilitres of water and 15 millilitres of hydrochloric acid As T., transferring to a small flask, adding solution of stannous chloride As T. until the yellow colour disappears, connecting to a condenser and distilling 20 millilitres, adding to the distillate a little solution of bromine As T. to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride As T. and then adding 40 millilitres of hot *water*.	10
Liquor Ferri Persulphatis	2 grammes treated as described under "Liquor Ferri Perchloridi Fortis."	5
Liquor Magnesii Bicarbonatis	50 millilitres with 13 millilitres of bromated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	0.2
Lithii Carbonas	2 grammes treated as described under "Calcii Hydras."	5
Lithii Citras	5 grammes in 45 millilitres of hot *water*, adding 15 millilitres of stannated hydrochloric acid As T.	2
Magnesia Levis	2 grammes with 40 millilitres of *water* and 20 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Magnesia Ponderosa	2 grammes treated as described under "Magnesia Levis."	5

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Magnesii Carbonas Levis	2 grammes in 45 millilitres of hot *water* and 15 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Magnesii Carbonas Ponderosus	2 grammes treated as described under "Magnesii Carbonas Levis."	5
Magnesii Sulphas	2 grammes treated as described under "Acidum Aceticum."	5
Potassii Acetas	2 grammes treated as described under "Ammonii Bromidum."	5
Potassii Bicarbonas	2 grammes in 50 millilitres of hot *water*, adding 12 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Potassii Bromidum	2 grammes treated as described under "Ammonii Bromidum."	5
Potassii Carbonas	5 grammes in 50 millilitres of hot *water*, adding 16 millilitres of bromated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Potassii Chloras	2 grammes mixed in the cold with 10 millilitres of *water* and 20 millilitres of hydrochloric acid As T. and, when the reaction is complete, warming to expel chlorine, then adding a few drops of solution of stannous chloride As T. and 30 millilitres of hot *water*.	5
Potassii Citras	5 grammes treated as described under "Lithii Citras."	2
Potassii Iodidum	2 grammes treated as described under "Ammonii Bromidum."	5
Potassii Nitras	2 grammes heated in a porcelain dish with 2 millilitres of sulphuric acid As T. and 5 millilitres of *water* until white fumes are evolved, cooling, adding 3 millilitres of *water* and again heating until white fumes are evolved, finally cooling and adding to the residue 50 millilitres of hot *water* and 10 millilitres of stannated hydrochloric acid As T.	5
Potassii Sulphas	2 grammes treated as described under "Acidum Aceticum."	5
Potassii Tartras	5 grammes treated as described under "Calcii Phosphas."	2
Potassii Tartras Acidus	5 grammes in 50 millilitres of hot *water* and 13 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Sodii Benzoas	5 grammes gently heated in a porcelain dish, until inflammable vapours cease to be evolved, dissolving the residue (ignoring any carbon) in 14 millilitres of brominated hydrochloric acid As T. and 50 millilitres of hot *water* and removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Sodii Bicarbonas	5 grammes treated as described under "Potassii Carbonas."	2
Sodii Bromidum	2 grammes treated as described under "Ammonii Bromidum."	5
Sodii Carbonas	5 grammes in 50 millilitres of hot *water*, adding 14 millilitres of brominated hydrochloric acid As T. and removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Sodii Carbonas Exsiccatus	2 grammes treated as described under "Sodii Carbonas."	5
Sodii Chloridum	5 grammes treated as described under "Acidum Aceticum."	2
Sodii et Potassii Tartras	5 grammes treated as described under "Calcii Phosphas."	2
Sodii Hypophosphis	2 grammes treated as described under "Calcii Hypophosphis."	5
Sodii Iodidum	2 grammes in 50 millilitres of hot *water*, adding 11 millilitres of stannated hydrochloric acid As T.	5
Sodii Nitris	2 grammes treated as described under "Potassii Nitras."	5

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Sodii Phosphas	2 grammes treated as described under "Acidum Aceticum."	5
Sodii Phosphas Acidus	5 grammes treated as described under "Acidum Aceticum."	2
Sodii Salicylas	5 grammes treated as described under "Sodii Benzoas."	2
Sodii Sulphas	5 grammes treated as described under "Acidum Aceticum."	2
Sodii Sulphis	2 grammes with 0.5 gramme of potassium chlorate As T. in 5 millilitres of warm *water*, adding 12 millilitres of hydrochloric acid, As T. then warming to expel excess of chlorine and adding 45 millilitres of hot *water* and a few drops of solution of stannous chloride As T.	5
Strontii Bromidum	2 grammes treated as described under "Ammonii Bromidum."	5
Sulphur Præcipitatum	2 grammes digested for one hour on a water bath with 50 millilitres of *water* and 5 millilitres of solution of ammonia, filtering and evaporating the filtrate to low bulk, adding 10 millilitres of nitric acid As T. and boiling to oxidise any sulphur then adding 2 millilitres of sulphuric acid As T. and heating until white fumes are evolved, cooling, adding 2 millilitres of *water*, and again heating until white fumes are evolved, finally adding 50 millilitres of hot *water* and 10 millilitres of stannated hydrochloric acid As T.	
Sulphur Sublimatum	2 grammes treated as described under "Sulphur Præcipitatum."	5
Zinci Acetas	2 grammes treated as described under "Ammonii Bromidum."	5
Zinci Carbonas	1 gramme treated as described under "Potassii Carbonas."	10
Zinci Chloridum	2 grammes treated as described under "Acidum Aceticum."	5
Zinci Oxidum	1 gramme treated as described under "Potassii Carbonas."	10
Zinci Sulphas	2 grammes treated as described under "Acidum Aceticum."	5
Zinci Valerianas	2 grammes made into a paste in a porcelain dish with 2 grammes of calcium hydroxide As T. and 5 millilitres of *water*, drying and gently igniting, then dissolving the residue in 18 millilitres of brominated hydrochloric acid As T. and 40 millilitres of hot *water* and removing excess of bromine by a few drops of solution of stannous chloride As T.	5

APPENDIX VII. Br.

Determination of the Acid Value of Fixed Oils, Fats, Waxes, and Resins.

(*Br.*)

The acid value of a fixed oil, fat, or wax (the number of milligrams of potassium hydroxide required to neutralize the free acid in 1 gramme of the substance) is determined as follows:—Mix 10 grammes of the substance with 50 millilitres of *alcohol* (90 per cent.), previously neutralised with *solution of potassium hydroxide*, add 1 millilitre of *solution of phenolphthalein*, heat until the fat or wax is melted and titrate with *N/10 solution of potassium hydroxide*, shaking constantly. Note the number of millilitres required (*a*). Calculate the acid value from the following formula:—

$$\textbf{Acid value} = \frac{a \times 0.0056 \times 1000}{\text{weight (in grammes) of substance taken}}$$

The acid value of a resin is determined by dissolving from 1 to 5 grammes of the substance in 50 millilitres of *alcohol* (90 per cent.), previously neutralized, and titrating and calculating as above directed.

Determination of the Saponification Value of Fixed Oils, Fats, Waxes, and Resins.

(*Br.*)

The saponification value of a fixed oil, fat, wax, or resin (the number of milligrams of potassium hydroxide required for the complete saponification of 1 gramme of the substance) is determined as follows:—Dissolve 40 grammes of *potassium hydroxide* in 1000 millilitres of *alcohol* (90 per cent.), previously neutralised; allow the solution to stand for twenty-four hours and filter. Weigh from 1.5 to 2 grammes of the substance in a flask having a capacity of about 200 millilitres; add 25 millilitres of the alcoholic solution of potassium hydroxide, attach a reflex condenser and heat on a water-bath for thirty minutes: add 1 millilitre of *solution of phenolphthalein* and titrate the excess of alkali with *N/2 solution of hydrochloric acid.* Note the number of millilitres required (*a*). At the same time treat 25 millilitres of the alcoholic solution of potassium hydroxide in a similar manner. Note the number of millilitres required (*b*). Calculate the saponification value from the following formula:—

$$\textbf{Saponification value} = \frac{(b-a) \times 0.028 \times 1000}{\text{weight (in grammes) of substance taken}}$$

Determination of the Iodine Value of Fixed Oils and Fats.

(*Br.*)

The iodine value of a fixed oil or fat (the proportional weight of iodine absorbed by 100 parts by weight of the oil or fat under the conditions specified) is determined as follows:—

Solution to be Prepared.—Iodine Solution.—Dissolve 13 grammes of iodine in 1000 millilitres of *glacial acetic acid.* Titrate the solution with *N/10 solution of sodium thiosulphate,* note the proportion required and pass *chlorine,* washed and dried, through the remainder of the iodine solution until this proportion is exactly doubled. Keep the solution in a stoppered amber bottle in a cool, dark place.

Weight of Substance to be Taken.—Lard, Suet, and Oil of Theobroma 0.8 to 1.0 gramme; Almond Oil, Castor Oil, and Olive Oil, 0.3 to 0.4 gramme; Cod-liver Oil, and Linseed Oil, 0.15 to 0.18 gramme.

Time to be Allowed for Absorption.—Lard, Suet, and Oil of Theobroma, Almond Oil, Castor Oil, and Olive Oil, 1 hour; Cod-liver Oil and Linseed Oil, 2 hours.

Method of Procedure.—Place the specified weight of oil or fat in a stoppered bottle having a capacity of 800 millilitres, add 10 millilitres of *carbon tetrachloride* and dissolve. Add 25 millilitres of the iodine solution, insert the stopper, previously moistened with *solution of potassium iodide,* and keep in a dark place at a temperature of about 17° for the specified time. Then add 20 millilitres of *solution of potassium iodide* and 500 millilitres of *water.* Shake, and titrate with *N/10 solution of sodium thiosulphate,* using *mucilage of starch* as indicator. Note the number of millilitres required (*a*). At the same time treat 25 millilitres of the solution of iodine in a similar manner and note the number of millilitres of *N/10 solution of sodium thiosulphate* required (*b*). Calculate the iodine value from the following formula:—

$$\textbf{Iodine value} = \frac{(b-a) \times 0.01269 \times 100}{\text{weight (in grammes) of oil or fat taken}}$$

Determination of the Unsaponifiable Matter in Fixed Oils and Fats.

(*Br.*)

The percentage of unsaponifiable matter in a fixed oil or fat is determined as follows:—Boil 5 grammes of the oil or fat with 50 millilitres of *N/1 alcoholic solution of potassium hydroxide* in a flask provided with a reflux condenser on a water-bath for thirty minutes. Transfer the contents of the flask to a porcelain dish and evaporate the alcohol on a water-bath. Dissolve the resulting soap in about 100 millilitres of hot water, cool and transfer to a separator. Add 50 millilitres of *ether,* mix thoroughly and allow to separate. Transfer the soap solution to another separator and again extract with 50 millilitres of *ether.* Mix the ethereal solutions, wash with three portions each of 20 millilitres, of *water,* transfer to a tared flask, evaporate the ether, dry the residue at 100° C. (212° F.) and weigh. The weight (in grammes) of the residue multiplied by 20 gives the percentage of unsaponifiable matter.

Determination of the Esters in Volatile Oils.

(*Br.*)

The percentage of esters present in a volatile oil is determined as follows:—Dissolve from 2 to 5 grammes of the oil in 25 millilitres of alcohol (90 per cent.) and neutralize the solution, if necessary, with *N/1 alcoholic solution of potassium hydroxide.* Then add 25 millilitres of *N/1 alcoholic solution of potassium hydroxide,* boil in a flask provided with a reflux condenser on a water-bath for one hour and titrate the excess of alkali with *N/1 solution of sulphuric acid.* Note the number of millilitres required (*a*). At the same time treat 25 millilitres of *alcohol* (90 per cent.) in a similar manner and note the number of millilitres of acid required (*b*). Calculate the percentage of esters in the oil from the following formula:—

$$\textbf{Percentage of Esters} = \frac{(b-a) \times \text{molecule weight of esters}}{\text{weight (in grammes) of oil taken} \times 10}$$

Determination of the Alcohols in Volatile Oils.

(*Br.*)

The percentage of alcohols present in a volatile oil is determined as follows:—Heat 10 millilitres of the oil with 10 millilitres of *acetic anhydride* and 2 grammes of *anhydrous sodium acetate* in an acetylation flask for two hours; add 100 millilitres of *water,* transfer to a separator and, after separation, remove the aqueous layer and wash the oily layer free from acidity with successive quantities, each of 100 millilitres of *water,* thoroughly shaking and allowing to separate each time. Dry the acetylated oil with *anhydrous sodium sulphate* and filter. Then treat from 2 to 5 grammes of the acetylated oil according to the process for the determinations of the esters present in volatile oils. Calculate the percentage of alcohols present in the oil from the following formula:—

$$\textbf{Percentage of alcohols} = \frac{\frac{1}{10} \times (b-a) \times \text{molecule weight of the alcohol}}{\text{weight (in grammes) of acetylated oil taken—0.042 } (b-a)}$$

Alkaloidal Assays: Limit of Error.

(*Br.*)

Successive assays of the same substance may yield numerical results varying within narrow limits, which are taken to be the range of "error". When an average of successive assays shows a deviation from the prescribed standard greater or less than the "limit of error," the preparation examined does not conform to the requirements of the British Pharmacopœia.

APPENDIX VIII. Br.

Determination of Melting Points.

(*Br.*)

Prepare some thin-walled glass tubes having an internal diameter of about one millilitre by heating thick-walled, soft glass tubing in a blow-pipe flame, drawing out the heated portion until it has the required diameter, then allowing a small flame to play against the middle of this tube so as to make and seal two tubes which are finally to be cut off to suitable lengths; these tubes should be freshly made; if stored they should be carefully protected from moisture.

Dry a very small quantity of the powdered substance at 100° C. (212° F.) for fifteen minutes; transfer a portion to one of these tubes, shaking the powder down to the sealed extremity. Attach the tube to a thermometer so that the substance is near the middle of the bulb. Heat a suitable liquid, such as *sulphuric acid*, to which *nitric acid* in the proportion of about 4 drops to 100 millilitres has been added, in a beaker or boiling tube about 3 centimetres in diameter, to about 5° below the expected melting point of the substance; this point if not known, being determined by a preliminary experiment. Then introduce the thermometer with the attached tube, and slowly heat, efficiently stirring, and note the temperature at which the substance first shows visible change; this temperature is regarded as the uncorrected melting point of the substance. The whole of the mercury column of the thermometer should be immersed in the liquid, but as this is seldom practicable the following correction is to be applied:—

To the thermometer attach a second thermometer in such a position that its bulb is near the middle of the emergent column of mercury, and observe thereby the mean temperature of the column. Calculate the corrected melting point of the substance from the following formula:—

Corrected melting point $= T + 0.000143$ (T-t N, in which $T =$ the uncorrected melting point; $t =$ the mean temperature of the emergent column; $N =$ the number of scale degrees in the emergent column.

The melting point of solid fats, fatty acids and waxes is determined by running a small quantity of the melted substance into an unsealed melting point tube, allowing it to cool for twenty-four hours, and then, using *water* in the place of sulphuric acid, determining in the manner described the temperature at which the substance becomes a clear liquid; this temperature is to be taken as the uncorrected melting point.

Determination of Boiling Points.

(*Br.*)

Place the liquid under examination in a distillation flask having a side tube for conveying the vapour to a condenser, while a thermometer passes through a cork inserted in the neck. The bulb of the thermometer should be opposite the entrance of the side tube, and not immersed in the liquid or exposed to splashes of it, and the whole of the column of mercury should, if possible, be surrounded by the vapour; the temperature is read off as soon as the liquid is distilling freely. If any considerable length of the column of mercury is not surrounded by the vapour, the mean temperature of the emergent column should be ascertained as directed under the "Determination of Melting Points," and the like correction applied.

Determination of Refractive Indices.

(*Br.*)

The refractive index of a substance should be determined in a suitable apparatus as nearly as possible at the temperature specified. Should the temperature be either above or below the specified temperature, the following correction is to be applied:—For each degree below the specified temperature subtract 0.00038 from the observed refractive index; for each degree above the specified temperature add 0.00038.

Determination of Optical Rotation.

(*Br.*)

The optical rotation unless otherwise specified, is the angle through which the plane of polarisation is turned when a layer of the liquid substance one decimetre in thickness and at a temperature of 20° C is examined by polarised sodium light.

The specific rotation of a substance in solution may be calculated from the formula $\frac{a \times 100}{l \times c}$, where a is the observed optical rotation, l the thickness in decimetres of the layer examined, and c the number of grammes of substance contained in 100 millilitres of the solution.

Determination of Specific Gravity.

(*Br.*)

The specific gravity of a substance is the weight of a given volume of that substance at 15.5° C. (59.9° F.) as compared with the weight of an equal volume of distilled water, at the same temperature unless otherwise specified.

APPENDIX IX. Br.

Process of Percolation.

(*Br.*)

Moisten the solid materials with the prescribed quantity of menstruum, set aside for four hours in a well-closed vessel, pack in a percolator and add sufficient of the menstruum to saturate the materials and leave a layer of liquid above. Macerate for twenty-four hours; then allow percolation to proceed slowly until the percolate measures about three-fourths of the volume required for the finished tincture. Press the marc, mix the expressed liquid with the percolate, and add sufficient of the menstruum to produce the required volume. Clarify by subsidence or filtration, if necessary.

Process of Repercolation.

(*Br.*)

Take one hundred parts by weight of the drug and divide it into five equal portions. Moisten the first portion with the menstruum, set aside in a closed vessel for four hours and pack in a percolator. Add sufficient of the menstruum to saturate the drug and leave a layer of liquid above. Macerate for twenty-four hours, then allow percolation to proceed slowly, collecting the percolate in fractions of twenty parts.

Moisten the second portion of the drug with the first fraction of the percolate collected. Set aside, pack in a percolator, macerate and percolate, as before, using as menstruum the successive fractions of percolate collected from the portion first treated. Again collect the percolate in fractions of twenty parts.

In turn, treat in the manner described above the third, fourth, and fifth portions of the drug with the fractions of percolate obtained in the percolation of the portion immediately preceding using the successive fractions of percolate in order, until a liquid extract is obtained of the required strength.

Process of Maceration.

Place the solid materials with the whole of the menstruum in a closed vessel; shake occasionally during seven days; strain; press the marc; mix the liquids obtained. Clarify by subsidence or filtration if necessary.

APPENDIX X. Br.

Process for Preparation of Discs (Lamellæ).

(*Br.*)

Discs are prepared by the following process:—Gelatin, 18 grammes; Glycerin, 2 grammes; Distilled Water, 88 grammes. Mix the Glycerin with the Distilled Water, allow the Gelatin to soak in the mixture till soft, and then dissolve by a gentle heat; cool the basis so produced. Take the prescribed quantity of the above basis, melt it by a gentle heat, add the prescribed quantity of medicament, dissolve and mix. Pour the melted and medicated basis upon a sheet of plate glass 10 centimetres square, previously thinly coated with White Beeswax, in such a manner that the solution is evenly distributed. Dry at a temperature not exceeding 36° C. (96.8° F.), and from the film thus obtained cut discs 3 millimetres nearly (⅛ inch) in diameter.

APPENDIX XI. Br.

Processes for Preparation of Lozenges (Trochisci).

(*Br.*)

With Fruit Basis.—Take five hundred times the quantity of the drug ordered for one lozenge. Mix with it 6.5 grammes of Tragacanth and 26 grammes of Refined Sugar, both in fine powder. Add sufficient of the black-currant paste of commerce to produce 650 grammes, beat into a uniform mass, divide into 500 equal lozenges and dry in a hot air chamber at a moderate temperature.

With Rose Basis.—Take five hundred times the quantity of the drug ordered for one lozenge. Treat it as described under "Preparation with Simple Basis," previously mixing with the Refined Sugar 0.025 millilitre of oil of Rose.

With Simple Basis.—Take five hundred times the quantity of the drug ordered for one lozenge, mix it with 496 grammes of Refined Sugar and 19.5 grammes of Gum Acacia, both in fine powder. Make the mixture into a paste with 35 millilitres of Mucilage of Gum Acacia and a sufficient quantity of Distilled Water, divide into 500 equal lozenges and dry in a hot air chamber at a moderate temperature.

With Tolu Basis.—Take five hundred times the quantity of the drug ordered for one lozenge; dissolve such salts of alkaloids as may be ordered in 10 millilitres of Distilled Water; mix the solution with 482 grammes of Refined Suger and 19.5 grammes of Gum Acacia, both in fine powder. Incorporate 10 millilitres of Tincture of Balsam of Tolu, and any other drugs ordered for the lozenges. Make into a paste with 35.5 millilitres of Mucilage of Gum Acacia and a sufficient quantity of Distilled Water; divide into 500 equal lozenges and dry in a hot-air chamber at a moderate temperature.

APPENDIX XII. Br.

Alternative Preparations Sanctioned for Use in Tropical, Subtropical, and Other Parts of the British Empire.

(*Br.*)

Aquæ Olei Anethi, Anisi, Carui, Cinnamomi, Fœniculi, Menthæ Piperitæ, Menthæ Viridis.—Each of these Waters may be prepared by tirturating the corresponding Oil with twice its weight of Calcium Phosphate and five hundred times its volume of Distilled Water and filtering the mixture. In tropical and subtropical parts of the Empire these Aquæ Olei may be used in place of the corresponding Aquæ of the Text of the Pharmacopœia.

Emplastra.—In tropical and subtropical parts of the Empire, more or less Hard Soap, Resin, or Yellow Beeswax, may be employed in the preparation of the Plasters of the Text of the Pharmacopœia, when prevailing high temperatures otherwise render the basis too soft for convenient use; but the official proportion of the active ingredient must in all cases be maintained.

Extracta Liquida.—Any Liquid Extract, defined in the Text of the Pharmacopœia, containing less than one-fourth of its weight of Alcohol (90 per cent.), may have the proportion of Alcohol (90 per cent.) increased to an amount not exceeding one-fourth of the weight of the Extract in tropical and subtropical parts of the Empire where otherwise the preparation would be liable to ferment.

Limonis Cortex Siccatus—In tropical and subtropical parts of the Empire, when fresh Lemon Peel cannot be obtained, Dried Lemon Peel may be used in preparing Compound Infusion of Orange Peel, Compound Infusion of Gentian, Syrup of Lemon, and Tincture of Lemon.

Oleum Olivæ.—In India, and in the Eastern, African, Australasian, and North American Divisions of the Empire, Arachis Oil or Sesame Oil, but no other oil or fat, may be employed in making the official Liniments, Plasters, Ointments, and Soaps for which Olive Oil is directed to be used.

Suppositoria.—More or less White Beeswax, according to prevailing temperatures, may be used in place of an equivalent amount of Oil of Theobroma in tropical and subtropical parts of the Empire, when otherwise the Suppositories of the Text of the Pharmacopœia would be too soft for convenient use.

Syrupus Rhœados.—In tropical and subtropical parts of the Empire, when prevailing high temperatures render this preparation liable to ferment, the proportion of Alcohol (90 per cent.) may be increased, but not to more than double the proportion stated in the Text of the Pharmacopœia and equivalent quantity of Distilled Water being omitted.

Unguenta.—In tropical and subtropical parts of the Empire or more less Benzoated Lard, Prepared Lard, Benzoated Suet, Prepared Suet, Yellow Beeswax, or White Beeswax, may be employed in the preparation of the Ointments of the Text of the Pharmacopœia when prevailing high temperatures otherwise render the basis too soft for convenient use; but the official proportion of the active ingredient must in all cases be maintained.

APPENDIX XIII. Br.

Table of Proportions Relating to the Preparation of Diluted Alcohols.

(Br.)

Volume of Alcohol (90 per cent.) to be diluted with Distilled Water to 1000 millilitres at 15.5° C. (59.9° F.) in order to give the Diluted Alcohols of the British Pharmacopœia.

Alcohol Required.	Specific Gravity.	Volume of Alcohol (90 per cent.)
70 per cent.	0.8899	777.8 millilitres
60 per cent.	0.9134	666.7 millilitres
45 per cent.	0.9435	500.0 millilitres
20 per cent.	0.9760	222.2 millilitres

Diagnostic Reagents and Chemical Tests.

(Not Official)

In the following pages of Diagnostical Reagents and Clinical Tests it is understood that the standard for official substances like Iodine, Potassium Iodide, Gelatin, Sodium Chloride, etc., are those of the U. S. P. Where other substances not so described are used, a description will be found elsewhere in this volume.

REAGENTS FOR EXAMINATION OF URINE.

For Acetone.—*Lange's Test. Le Noble's Test. Legal's Test.*

Sodium Nitroprusside (see Sodium Nitroferrocyanide) one part in 20 of distilled water. Must be freshly prepared.

Lieben's Iodine Potassium Iodide Solution:

Potassium Iodide	6 Gm.
Iodine	4 Gm.
Distilled Water, a sufficient quantity, to make	100 cc.

Dissolve the potassium iodide in the distilled water, add the iodine and shake the mixture frequently until a solution is obtained.

Gunning's Test.—Use a freshly prepared 10 per cent. solution of iodine in aclohol.

For Albumin.—*Glacial Acetic Test* (U. S. P.), *Acetic Acid* (U. S. P.), *Trichloracetic Acid* (U. S. P.) and *Nitric Acid* (U. S. P.) are used for various tests.

Esbach's Reagent:

Trinitrophenol	1 Gm.
Citric Acid	2 Gm.
Distilled water, a sufficient quantity	
To make a solution measuring	100 cc.

Spiegler-Jolles' Reagent:

Corrosive Mercuric Chloride	2 Gm.
Succinic Acid	4 Gm.
Sodium Chloride	4 Gm.
Distilled Water, a sufficient quantity	
To make	100 cc.

Mix the several ingredients and dissolve them in the distilled water.

For Albumose.—*Salkowski's Test.* Use a 4 per cent. aqueous solution of phospho-tungstic acid.

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For Bile Reactions.—*Urobilin.*
Amyl Alcohol (see page 000).
Solution of Zinc Chloride (10 per cent. in distilled water).
Mixture of Zinc Acetate:

Zinc Acetate	10 Gm.
Dehydrated Alcohol, a sufficient quantity	
To make	100 cc.

Finely powder the zinc acetate and intimately mix with the alcohol. Dispense the mixture with directions "to be well shaken before using."

Urobilinogen.—*Ehrlich's Solution:*

Paradimethylamidobenzaldehyde	2 Gm.
Hydrochloric Acid	50 cc.
Distilled Water, a sufficient quantity	
To make a solution measuring	100 cc.

Biliary Color Reactions.—*Nitric Acid* (containing a trace of nitrous acid). This may be prepared by adding a few drops of formaldehyde to nitric acid.

Hupert's Test.—Use a 10 per cent. aqueous solution of calcium chloride.

Alcoholic Solution of Iodine (about 1 per cent.):

Iodine	1 Gm.
Alcohol, a sufficient quantity	
To make a solution measuring	100 cc.

For Blood Reaction.—*Benzidine Hydrochloride.* A freshly prepared saturated solution of benzidine hydrochloride in glacial acetic acid.

Solution of Guaiac.—A 2 per cent. solution of guaiac in dehydrated alcohol.

Ether and Solution of Hydrogen Dioxide of full strength are used in the benzidine test.

For Diacetic Acid Reaction.—*Gerhardt's Test.* A 2 per cent. freshly prepared aqueous solution of ferric chloride.

For Diazo Reaction, Ehrlich:

1. Sodium Nitrite	1 Gm.
Distilled Water, a sufficient quantity	
To make	200 cc.
2. Sulphanilic Acid	5 Gm.
Hydrochloric Acid	50 cc.
Distilled Water, a sufficient quantity	
To make	1000 cc.

Dissolve the sulphanilic acid in about 700 cc. of distilled water to which the hydrochloric acid has been added and follow with enough distilled water to make the product measure 1000 cc.

For use, 1 cc. of the sodium nitrite solution should be mixed with 50 cc. of the sulphanilic acid solution.

For Indican Reaction.—*Solution of Chlorinated Lime.* A saturated solution of chlorinated lime diluted with an equal volume of distilled water and filtered.

Obermeyer's Solution:

Ferric Chloride	0.4 Gm.
Hydrochloric Acid, U. S. P., a sufficient quantity	
To make a solution measuring	100 cc.

Solution of Lead Acetate.—A 25 per cent. filtered, aqueous solution.

For Pentose Reactions.—*Bial's Reagent:*

Orcin	1 Gm.
Hydrochloric Acid	500 cc.
Solution of Ferric Chloride	25 drops

Dissolve the orcin in the hydrochloric acid and add the solution of ferric chloride.

Phloroglucinol T.S.—A 3 per cent. alcoholic solution.

For the Estimation of Urea.—*Solution of Sodium Hypobromite:*

1. Bromine	125 Gm.
Sodium Bromide	125 Gm.
Distilled Water, a sufficient quantity	
To make a solution measuring	1000 cc.
2. Sodium Hydroxide	225 Gm.
Distilled Water, a sufficient quantity	
To make a solution measuring	1000 cc.

The reagent should be freshly prepared by mixing equal volumes of solutions 1 to 2 and diluting the resulting mixture with one and a half volumes of distilled water.

For Sugar Reactions.—*Solution of Sodium Hydroxide.* A 10 per cent. aqueous solution of sodium hydroxide.

Solution of Copper Sulphate.—A 10 per cent. aqueous solution of uneffloresced crystals of copper sulphate.

Nylander's Reagent:

Potassium and Sodium Tartrate	4 Gm.
Sodium Hydroxide	10 Gm.
Bismuth Subnitrate	2 Gm.
Distilled Water, a sufficient quantity	
To make	100 cc.

Dissolve the potassium and sodium tartrate in 90 cc. of distilled water. Add the bismuth subnitrate to the solution, shake the mixture thoroughly and then filter through glass wool. Preserve and dispense this solution in amber-colored bottles.

Benedict's Solution:(Qualitative)

Sodium (or potassium) Citrate	173	Gm.
Sodium Carbonate, Anhydrous	100	Gm.
Distilled Water	700	cc.

Dissolve with the aid of heat.

Copper Sulphate Crystals	17.3	Gm.
Distilled Water	100	cc.

Dissolve with the aid of heat.

Cool both solutions to room temperature, pour the copper solution into the other slowly and with constant stirring, and make up to 1000 cc. with distilled water.

Benedict's Solution: (Quantitative)

Copper Sulphate (Cryst)	18 Gm.
Sodium Carbonate (Cryst) (½ the weight of the anhydrous salt may be used)	200 Gm.
Potassium Sulphocyanate	125 Gm.
Sodium Citrate	200 Gm.
Potassium Ferrocyanide, 5 per cent. solution	5 cc.
Distilled Water to measure	1000 cc.

With the aid of heat dissolve the citrate, carbonate and sulphocyanate in enough water to make about 800 cc. of the mixture, and filter. Dissolve the copper sulphate in about 100 cc. of water and pour the solution slowly into the other liquid with constant stirring. Add the ferrocyanide solution cool, and dilute to exactly one litre. Of the various constituents, only the copper need to be *weighed with exactness.* 25 cc. of the reagent are reduced by 0.050 Gms. of glucose, or by 0.055 Gms. of levulose.

Fehling's Solution: (See Alkaline Cuptric Tartrate V.S.)

Pavy's Solution:

1.	Copper Sulphate	4.158 Gm.
	Distilled Water, a sufficient quantity	
	To make a solution measuring	500 cc.
2.	Potassium and Sodium Tartrate	20.4 Gm.
	Potassium Hydroxide	20.4 Gm.
	Stronger Ammonia Water	300.0 cc.
	Distilled Water, a sufficient quantity	
	To make a solution measuring	500.0 cc.

For use, mix equal quantities of the two solutions.

REAGENTS FOR THE EXAMINATION OF KIDNEY FUNCTION.

Phenolsulphonphthalein.—An aqueous solution containing in each cc. 6 mgm. of the dye in the form of a mono-sodium salt. (See *Phenol Sulphonphthaleinum,* Part I.)

Indigo-Carmine Reagent.—An aqueous solution containing 10 per cent. of sodium indigotindisulphonate (U.S.). (See Part I.)

REAGENTS FOR THE EXAMINATION OF GASTRIC CONTENTS.

Congo Red Test Paper.—Saturate filter paper with an aqueous solution of Congo Red (1 in 1000). Dry and cut the paper into strips and preserve them in well-stoppered glass vials.

Topfer's Reagent.—*(Alcoholic Solution of Dimethylaminoazobenzene.)* Dissolve 5 Gm. of the dye in 100 cc. of alcohol.

Gunzburg's Reagent:

Phloroglucinol	2 Gm.
Vanillin	1 Gm.
Alcohol	30 cc.

Dissolve the ingredients in the alcohol.

REAGENTS FOR THE EXAMINATION OF BLOOD.

For Red Blood Corpuscles.—*Hayem's Solution:*

Sodium Sulphate	5	Gm.
Sodium Chloride	1	Gm.
Corrosive Mercuric Chloride	0.5	Gm.
Distilled Water	200	cc.

Dissolve the salts in the distilled water and filter.

Toisson's Solution:

Methyl Violet 6B	0.025 Gm.
Sodium Chloride	1.000 Gm.
Sodium Sulphate	8.000 Gm.
Glycerin (Neutral)	30.000 cc.
Distilled water	300.000 cc.

Dissolve the salts in the distilled water and add the methyl violet and the glycerin.

For White Corpuscles:

Acetic Acid (U. S. P.)	1 cc.
Distilled Water	99 cc.

Mix them.

Jenner's Stain:

1. Eosin	0.5 Gm.
Methanol, a sufficient quantity	
To make a solution measuring	100 cc.
2. Methylene Blue	0.5 Gm.
Methanol, a sufficient quantity to make a solution measuring	100 cc.

For use mix 25 cc. of eosin solution with 20 cc. of methylene blue solution.

Ehrlich's Triacid Stain:

Saturated Aqueous Solution of Orange-G	120–125 cc.
Satruated Aqueous Solution of Acid Fuchsin	80 –165 cc.
Saturated Aqueous Solution of Methylene Green	125 cc.
Distilled Water	300 cc.
Dehydrated Alcohol	200 cc.
Glycerin	100 cc.

Mix.

Wright's Stain:

Wright's Stain (dried powder)	0.1 Gm.
Methanol (Rectified)	60.0 cc.

Giemsa's Stain:

Azur II–Eosin	0.3 Gm.
Azur II	0.8 Gm.
Glycerin	250.0 cc.
Methanol (Rectified)	250.0 cc.

Dissolve the dyes in the methanol and add the glycerin and filter.

STAINS FOR USE IN THE STUDY OF MICRO-ORGANISMS.

The amounts of distilled water and absolute alcohol respectively required to produce saturated solutions of the common stains are indicated in the following table:

	Gram of Dye	Water cc.	Alcohol cc.
Bismarck Brown, pure	1	70	70
Fuchsine (Basic)	1	100	25
Gentian violet	1	70	70
Hematoxylin	1	20	10
Methyl violet	1	50	10
Methylene blue	1	70	70
Thionin blue	1	50	100

Alum-hematoxylin Solution:

Hematoxylin, crystals	1.0 Gm.
Saturated Aqueous Solution of Ammonium Alum	100.0 cc.
Distilled Water	300.0 cc.
Thymol	0.5 Gm.

Dissolve the hematoxylin in a little distilled water by the aid of heat, add the other ingredients and expose the combined solution to the light, in a bottle loosely stoppered, until it has assumed a dark red colour, then filter. The thymol is added as a preservative.

Hematoxylin Solution (Delafield):

Hematoxylin crystals	1.0 Gm.
Alcohol	6.0 cc.

To this solution add

Saturated aqueous solutions of ammonium alum	100 cc.

Expose to light for one week, when the colour will change to a deep purple.

Add to this ripened stain

Glycerin	25 cc.
Methanol	25 cc.

Let stand 2 days and filter.

This makes a stock solution which should be diluted with 10 parts of water when staining.

Mayer's Hemalum:

Hematein or its ammonium salt	1.0 Gm.
Alcohol, 90 per cent	50.0 cc.
Alum	50.0 Gm.
Distilled Water	1000.0 cc.
Thymol	0.5 Gm.

Dissolve the hematein in the alcohol by the aid of heat, add the thymol, and then this solution to the alum dissolved in the distilled water, and then filter. The thymol is added as a preservative.

Alcoholic Solution of Eosin:

Eosin, S. F. Yellowish	0.5 Gm.
Alcohol diluted	100 cc.

Alcoholic Solution of Methyl Violet 6B:

Methyl Violet 6B	10 Gm.
Alcohol, a sufficient quantity	
To make a solution measuring	100 cc.

Borax-Methylene Blue Solution:

Methylene blue	2 Gm.

Dissolve in 100 cc. of a boiling-hot 5 per cent. aqueous solution of sodium borate.

Loeffler's Methylene Blue Solution:

Methylene Blue	0.5 Gm.
Alcohol	30.0 cc.
Tenth-normal Potassium Hydroxide V.S.	2.0 cc.
Distilled Water	98.0 cc.

Dissolve the methylene blue in alcohol, add the potassium hydroxide and distilled water. Filter.

Solution of Carbol Methyl Violet:

Alcoholic Solution of Methyl Violet 6B	10 cc.
Aqueous solution of Phenol (1 in 20), a sufficient quantity	
To make a solution measuring	100 cc.

Solution of Carbolfuchsin (Ziehl-Neelsen's Solution):

Fuchsin	1 Gm.
Dehydrated Alcohol	10 cc.

Dissolve and add 100 cc. of a 5 per cent. aqueous solution of phenol.

For Tubercle Bacilli.—*Solution of Carbolfuchsin (Ziehl-Neelsen's Solution).*

For Decolorizing.—*Ebner's Fluid:*

Hydrochloric Acid	2.5 cc.
Sodium Chloride	2.5 Gm.
Distilled Water	100.0 cc.
Alcohol	500.0 cc.

Prepare a solution.

Nitric Acid Decolorizing Solution: (Acid Alcohol)

Nitric Acid	30.0 cc.
Distilled Water, a sufficient quantity	
To make	100.0 cc.

Diluted Lugol's Solution: (Gram's Iodine Solution)

Iodine	1 Gm.
Potassium Iodide	2 Gm.
Distilled Water, a sufficient quantity	
To make	200 cc.

For Diphtheria Bacilli.—*Solution of Methylene Blue (Neisser's):*

Methylene Blue	0.5 Gm.
Alcohol	10.0 cc.
Diluted Acetic Acid (U. S. P.)	500.0 cc.

Ponder's Stain:

Toluidin Blue	0.02 Gm.
Glacial Acetic Acid	1.0 cc.
Dehydrated Alcohol	2.0 cc.
Distilled Water, a sufficient quantity	
To make	100.0 cc.

For Counter Staining.—*Loeffler's Methylene Blue Solution* (see page Gram's Stain) (*Aniline Water—Methyl Violet 6B Blue Solution*):

Aniline Oil	15 cc.
Saturated Alcoholic Solution of Methyl Violet 6B	7 cc.
Dehydrated Alcohol	10 cc.
Distilled Water, a sufficient quantity	
To make	100 cc.

Shake the aniline oil with 65 cc. of distilled water for several minutes; filter the resulting opalescent aniline water through a moistened filter, pour the filtrate into a solution prepared by mixing the other liquids and add sufficient distilled water to make 100 cc.

Diluted Carbolfuchsin Solution:

Solution of Carbolfuchsin	1 cc.
Distilled Water	4 cc.

Prepare a solution.

Bismarck Brown Solution:

Bismarck Brown	0.2 Gm.
Distilled Water	100.0 cc.

Prepare a solution.

CULTURE MEDIA.

Culture media require titration and subsequent adjustment to certain hydrogen ion concentration in order to insure constant and reliable results. For this purpose phenolphthalein has been generally adopted as the indicator.

Titration is made as follows.—In a white glazed porcelain dish put 5 cc. of the medium to be tested, add 45 cc. of recently boiled distilled water. Boil briskly for one minute. Add 1 cc. of phenolphthalein reagent (twice the strength of the official indicator solution). Titrate at once with a N/10 solution of sodium hydroxide. A faint but distinct pink colour indicates the true end point (neutrality).

The media listed herewith, are to be made neutral to phenolphthalein and adjustment is made to the reaction indicated in the text. (Plus 1 reaction requires the addition of 1 per cent. of N/1 acid to the medium at the neutral point).

Sterilization is preferably done in the autoclave (120° C.) for 15 minutes after the pressure reaches 15 pounds.

All glassware shall be sterilized in the dry oven at 170° C. for at least 1½ hours.

Bouillon Stock:

Lean Beef	500 Gm.
Or Extract of Beef	3 Gm.
Distilled water, a sufficient quantity	
To make	1000 cc.

Mix thoroughly 500 Gm. of finely minced lean beef with 1000 cc. of cold distilled water, heat it to boiling in a closely covered dish or flask and keep it at that temperature for one hour. If extract of beef is used to make bouillon stock, boil the solution for one-half hour. Filter the resulting bouillon through a well-wetted filter, until clear and use it as the basis for the following combinations:

Plain Bouillon:

Peptone	10 Gm.
Sodium Chloride	5 Gm.
Tenth-normal Sodium Hydroxide V.S.	
Bouillon stock each a sufficient quantity	
To make	1000 cc.

Dissolve the peptone and sodium chloride in the bouillon stock by means of heat and add sufficient deci-normal sodium hydroxide V.S. to bring the reaction to plus 1. Then filter the product through wetted filter, fill it into suitable containers and sterilize.

Glucose Bouillon:

Glucose (dry)	10 Gm.
Peptone	10 Gm.
Sodium Chloride	5 Gm.
Tenth-normal Dosium Hydroxide V.S.	
Bouillon Stock, each a sufficient quantity	
To make	1000 cc.

Dissolve the glucose, peptone, and sodium chloride in the bouillon stock by means of heat and add sufficient deci-normal sodium hydroxide V.S. to bring the reaction to the neutral point with phenolphthalein. Then filter the product through a well-wetted filter, fill it into suitable containers and sterilize by the discontinuous method.

Plain Gelatin:

Gelatin	100 Gm.
Peptone	10 Gm.
Sodium Chloride	5 Gm.
Tenth-normal Sodium Hydroxide V.S.	
Bouillon Stock, each a sufficient quantity	
To make	1000 cc.

Dissolve the gelatine, peptone, and sodium chloride in the bouillon stock by means of heat and add sufficient deci-normal sodium hydroxide V.S. to bring the reaction to plus 1. Filter the warmed product through filter paper, fill it into suitable containers and sterilize by the discontinuous method.

Glucose Gelatin:

Dextrose	10 Gm.
Gelatin	100 Gm.
Peptone	10 Gm.
Sodium Chloride	5 Gm.
Tenth-normal Sodium Hydroxide V.S.	
Bouillon stock, each a sufficient quantity	
To make	1000 cc.

Dissolve the glucose, gelatine, peptone, and sodium chloride in the bouillon stock by means of heat and add sufficient deci-normal sodium hydroxide V.S. to neutralize the resulting mixture to phenolphthalein. Then filter the product through paper, fill it into suitable containers and sterilize by the discontinuous method.

Plain Agar-Agar:

Agar, washed and dried for ½ hour at 105° C. before weighing	15 Gm.
Peptone	10 Gm.
Sodium Chloride	5 Gm.
Tenth-normal Sodium Hydroxide V.S.	
Bouillon stock, each a sufficient quantity	
To make	1000 cc.

Dissolve the agar, peptone, and sodium chloride in the bouillon stock by means of heat and add a sufficient quantity of deci-normal sodium hydroxide V.S. to bring the reaction of the mixture to plus 1. Then filter the warmed product through paper, fill it into suitable containers and sterilize.

Glucose Agar-Agar:

Dextrose	10 Gm.
Agar, washed and dried for one-half hour at 105 C. before weighing	15 Gm.
Peptone	10 Gm.
Sodium Chloride	5 Gm.
Tenth-normal Sodium Hydroxide V.S.	
Bouillon Stock, each a sufficient quantity	
To make	1000 cc.

Dissolve the glucose, peptone and sodium chloride in the bouillon stock by means of heat, and add sufficient quantity of the deci-normal sodium hydroxide V.S. to neutralize the resulting mixture to phenolphthalein. Then filter the warmed product through paper, fill it into suitable containers and sterilize by the discontinuous method.

Glycerin, Agar-Agar:

Glycerin	60 cc.
Agar, washed and dried for one-half hour at 105 C. before weighing	15 Gm.
Peptone	10 Gm.
Sodium Chloride	5 Gm.
Tenth-normal Sodium Hydroxide V.S.	
Bouillon Stock, each a sufficient quantity	
To make	1000 cc.

Dissolve the glycerin, agar, peptone, and sodium chloride in the bouillon stock by means of heat, and add a sufficient quantity of tenth-normal sodium hydroxide V.S. to neutralize the resulting mixture to phenolphthalein. Then filter the warmed product through paper to fill into suitable containers and sterilize.

Lactose-litmus Agar-Agar:

Sugar of milk	10 Gm.
Agar, washed and dried for one-half hour at 105 C. before weighing	15 Gm.
Peptone	10 Gm.
Sodium Chloride	15 Gm.
Tenth-normal Sodium Hydroxide V.S.	
Azolitmin Test Solution (see page 000)	
Bouillon Stock, each a sufficient quantity	
To make	1000 cc.

Dissolve the sugar of milk, agar, peptone, and sodium chloride in the bouillon stock by means of heat and add a sufficient quantity of deci-normal sodium hydroxide V.S. to neutralize the resulting mixture to phenolphthalein. Then filter the warmed product through paper, add a sufficient quantity of azolitmin solution to impart to the resulting mixture a pale blue colour, fill into suitable containers and sterilize by the discontinuous method.

Blood Serum Loeffler's Mixture.

Glucose Bouillon	150 cc.
Horse or Beef Blood Serum	750 cc.

Run the mixture of glucose bouillon and beef or horse blood serum into properly sterilized test tubles and coagulate it by means of heat so as to form a slanting surface for culture purposes.

Endo's Medium:

Beef Extract	5 Gm.
Peptone	10 Gm.
Agar, washed and dried for one-half hour at 105 C. before weighing	30 Gm.
Distilled Water to	1000 cc.

Dissolve with the aid of the water bath. Adjust to a neutral reaction to phenolphthalein. Filter the warmed product through cloth and cotton until clear. Sterilize.

When ready to make plates, prepare a 10 per cent. solution of anhydrous sodium sulphite. To 10 cc. of the sodium sulphite solution add 2 cc. of the fuchsin stock solution (basic fuchsin 10 Gm., alcohol 100 cc.), and steam five minutes in the Arnold or on a water bath. To each 100 cc. of the agar mixture, add 1 gram of lactose, dissolve on a water bath and add one-half cc. of the fuchsin sulphite solution.

TABLES OF THE U. S. P. X.

Atomic and Molecular Weights.

(U.S.)

This list contains the official chemicals and reagents of a definite conposition, and also some that are not official but which are likely to be required in stoichiometrical calculations. The figures in the list given below are based upon the Table of International Atomic Weights (1921), with Oxygen taken as 16. The elementary substances are also given in a separate list. In the case of a few salts, for which this Pharmacopœia has given no formula on account of the difficulty of securing an obsolutely uniform composition, the theoretical formula has been inserted merely for information. In the case of many hydrated compounds the formula and molecular weight of the corresponding anhydrous salt have also been given to save time in making calculations.

		O=16
Acetaldehyde (Acetic Aldehyde)	CH_3CHO	44.04
Acetanilid (Phenylacetamide)	$C_6H_5NH.CH_3CO$	135.12
Acetic Anhydride	$(CH_3CO)_2O$	102.07
Acetone	$(CH_3)_2CO$	58.06
Acetphenetidin (Acetophenetide)	$C_{10}H_{13}O_2N$	179.16

		$0=16$
Acid, Acetic	$HC_2H_3O_2$	60.04
“ “ Anhydride	$(CH_3CO)_2O$	102.07
“ Acetylsalicylic	$HC_7H_4O_2C_2H_3O_2$	180.11
“ Arsenic	$H_3AsO_4.\frac{1}{2}H_2O$	150.99
“ Aurochloric (Chlorauric Acid)	$HAuCl_4.4H_2O$	412.11
“ Benzoic	$HC_7H_5O_2$	122.08
“ Boric	H_3BO_3	61.92
“ Bromauric (Aurobromhydric Acid)	$HAuBr_4.5H_2O$	607.97
“ Camphoric	$H_2C_{10}H_{14}O_4$	200.18
“ Carbolic (see Phenol)		
“ Chlorauric (see Aurochloric Acid)		
“ Chloroplatinic	$H_2PtCl_6.6H_2O$	518.07
“ Cinnamic (Cinnamylic Acid)	$HC_9H_7O_2$	148.11
“ Citric	$H_3C_6H_5O_7.H_2O$	210.11
“ “ anhydrous	$H_3C_6H_5O_7$	192.09
“ Diethyl-barbituric (see Barbital)		
“ Formic	$HCHO_2$	46.02
“ Gallic	$HC_7H_5O_5.H_2O$	188.10
“ “ anhydrous	$HC_7H_5O_5$	170.08
“ Glycerophosphoric	$H_2C_3H_5(OH)_2PO_4$	172.13
“ Hydriodic	HI	127.93
“ Hydrobromic	HBr	80.93
“ Hydrochloric	HCl	36.47
“ Hydrocyanic	HCN	27.02
“ Hydrofluoric	HF	20.01
“ Hydrosulphuric (see Hydrogen Sulphide)		
“ Hypophosphorous	HPH_2O_2	66.06
“ Lactic	$HC_3H_5O_3$	90.06
“ Molybdic	H_2MoO_4	162.02
“ Nitric	HNO_3	63.02
“ Nitrous	HNO_2	47.02
“ Oleic	$HC_{18}H_{33}O_2$	282.36
“ Oxalic	$H_2C_2O_4.2H_2O$	126.06
“ “ anhydrous	$H_2C_2O_4$	90.03
“ Phenolsulphonic (Phenoldisulphonic Acid)	$H_2C_6H_3(SO_3)_2OH$	254.20
“ Phenylcinchoninic (see Cinchophen)		
“ Phosphoric	H_3PO_4	98.06
“ Phosphorous	H_2PHO_3	82.06
“ Picric (see Trinitrophenol)		
“ Pyroboric (Tetraboric Acid)	$H_2B_4O_7$	157.62
“ Pyrogallic (see Pyrogallol)		
“ Rosolic (see Methylaurin)		
“ Salicylic	$HC_7H_5O_3$	138.08
“ Selenous	H_2SeO_3	129.22
“ Stearic	$HC_{18}H_{35}O_2$	284.38
“ Succinic	$H_2C_4H_4O_4$	118.07
“ Sulphanilic	$HC_6H_4(NH_2)SO_3.2H_2O$	209.19
“ “ anhydrous	$HC_6H_4(NH_2)SO_3$	173.15
“ Sulphuric	H_2SO_4	98.08
“ Sulphurous	H_2SO_3	82.08
“ Tannic (variable)	$HC_{14}H_9O_9$	322.15
“ Tartaric	$H_2C_4H_4O_6$	150.07
“ Tetraboric (see Pyroboric Acid)		
“ Trichloracetic	$CCl_3.COOH$	163.40
“ Tungstic	H_2WO_4	250.02
“ Valeric (Valerianic Acid)	$HC_5H_9O_2$	102.11
Aconitine	$C_{34}H_{47}O_{11}N$	645.55
Alcohol, Amyl (Amyl Hydroxide)	$C_5H_{11}OH$	88.12
“ Ethyl (Ethyl Hydroxide)	C_2H_5OH	46.06
“ Methyl (Methyl Hydroxide), Methanol	CH_3OH	32.04
Aldehyde, Acetic (see Acetaldehyde)		
“ Benzoic (see Benzaldehyde)		
“ Cinnamic (see Cinnamic Aldehyde)		
“ Formic (see Formaldehyde)		
Allyl-isothiocyanate	C_3H_5NCS	99.13
Allyl-sulphocarbamide (Thiosinamine)	$C_3H_5NCS_2H_3$	116.16
Alum (see Aluminum and Potassium Sulphate and Aluminum and Ammonium Sulphate)		
Aluminum	Al	27.0
Aluminum and Ammonium Sulphate (Alum)	$AlNH_4(SO_4)_2.12H_2O$	453.35
“ “ “ anhydrous	$AlNH_4(SO_4)_2$	237.16
“ “ Potassium Sulphate (Alum)	$AlK(SO_4)_2.12H_2O$	474.41
“ “ “ “ anhydrous	$AlK(SO_4)_2$	258.22
Hydroxide	$Al(OH)_3$	78.02

		0=16
Aluminum Oxide	Al_2O_3	102.00
“ Sulphate	$Al_2(SO_4)_3.18H_2O$	666.47
“ “ anhydrous	$Al_2(SO_4)_3$	342.18
Aminopyrine	$C_{13}H_{17}ON_3$	231.23
Ammonia	NH_3	17.03
Ammonium Acetate	$NH_4C_2H_3O_2$	77.07
“ Arsenite (Metarsenite)	NH_4AsO_2	125.00
“ Benzoate	$NH_4C_7H_5O_2$	139.12
“ Bromide	NH_4Br	97.96
“ Carbomate	$NH_4NH_2CO_2$	78.07
“ Carbonate (Acid)	NH_4HCO_3	79.05
“ “ (Normal)	$(NH_4)_2CO_3$	96.09
“ “ (U. S. P.) (approximately)	$NH_4HCO_3NH_4NH_2CO_2$	157.12
“ Chloride	NH_4Cl	53.50
“ Chloroplatinate	$(NH_4)_2PtCl_6$	444.04
“ Citrate	$(NH_4)_3C_6H_5O_7$	243.19
“ Hydrogen Fluoride	NH_4HF_2	57.05
“ Hydrogen Sulphide	NH_4HS	51.11
“ Hypophosphite	$NH_4PH_2O_2$	83.10
“ Iodide	NH_4I	144.96
“ Molybdate	$(NH_4)_6Mo_7O_{24}.4H_2O$	1236.30
“ Nitrate	NH_4NO_3	80.05
“ Oxalate	$(NH_4)_2C_2O_4.H_2O$	142.11
“ Oxalate, anhydrous	$(NH_4)_2C_2O_4$	124.09
“ Phosphate	$(NH_4)_2HPO_4$	132.13
“ Salicylate	$NH_4C_7H_5O_3$	155.12
“ and Sodium Phosphate	$NH_4NaHPO_4.4H_2O$	209.15
“ Sulphate	$(NH_4)_2SO_4$	132.14
“ Sulphide	$(NH_4)_2S$	68.14
“ Tartrate	$(NH_4)_2C_4H_4O_6$	184.13
“ Valerate (not U. S. P.)	$NH_4C_5H_9O_2$	119.14
“ Vanadate (Metavanadate)	NH_4VO_3	117.04
Amyl Nitrate	$C_5H_{11}NO_2$	117.12
Amylene Hydrate	$C_5H_{11}OH$	88.12
Anethol	$C_{10}H_{12}O$	148.15
Aniline (Phenylamine)	$C_6H_5NH_2$	93.09
“ Sulphate	$(C_6H_5NH_2)_2H_2SO_4$	284.26
Antimonic Sulphide	Sb_2S_5	400.70
Antimonous Oxide	Sb_2O_3	288.40
“ Sulphide	Sb_2S_3	336.58
Antimony	**Sb**	**120.2**
Antimony and Potassium Tartrate	$K(SbO)C_4H_4O_6.\frac{1}{2}H_2O$	332.36
“ “ “ anhydrous	$K(SbO)C_4H_4O_6$	323.35
Antipyrine	$C_{11}H_{12}ON_2$	188.17
Apomorphine Hydrochloride	$C_{17}H_{17}O_2NHCl.\frac{1}{2}H_2O$	312.71
Argon	**A**	**39.9**
Arsenic	**As**	**74.96**
Arsenic Sulphide	As_2S_5	310.22
“ Trioxide (see Arsenous Oxide)		
Arsenous Iodide (Arsenous Triiodide)	AsI_3	455.72
“ Oxide (Arsenic Trioxide)	As_2O_3	197.92
“ Sulphide	As_2S_3	246.10
Arsphenamine	$C_{12}H_{12}O_2N_2As_2.2HCl.2H_2O$	475.06
Ascaridol	$C_{10}H_{16}O_2$	168.18
Aspidospermine	$C_{22}H_{30}O_2N_2$	354.37
Atropine	$C_{17}H_{23}O_3N$	289.28
“ Sulphate	$(C_{17}H_{23}O_3N)_2H_2SO_4.H_2O$	694.65
Auric Chloride	$AuCl_3$	303.58
Barbital	$C_8H_{12}O_3N_2$	184.15
“ Soluble	$C_8H_{11}O_3N_2Na$	206.14
Barium	**Ba**	**137.37**
Barium Carbonate	$BaCO_3$	197.38
“ Chloride	$BaCl_2.2H_2O$	244.32
“ “ anhydrous	$BaCl_2$	208.29
“ Chromate	$BaCrO_4$	253.37
“ Dioxide	BaO_2	169.37
“ Hydroxide	$Ba(OH)_2.8H_2O$	315.51
“ Nitrate	$Ba(NO_3)_2$	261.39
“ Sulphate	$BaSO_4$	233.43
“ Sulphide	BaS	169.43
Benzaldehyde (Benzoic Aldehyde)	C_6H_5CHO	106.08
Benzene (Benzol)	C_6H_6	76.08
Benzidine (Paradiaminodiphenyl)	$(C_6H_4)_2(NH_2)_2$	184.17

		0=16
Benzocaine	$C_9H_{11}O_2N$	165.14
Benzosulphinide (see Gluside)		
Benzyl Benzoate	$C_6H_5CO_2.CH_2C_6H_5$	212.16
Betaeucaine Hydrochloride (see Eucaine Hydrochloride)		
Betanaphthol (Naphthol)	$C_{10}H_7OH$	144.11
Bismuth	**Bi**	**209.0**
Bismuth Betanaphthol (approximately)	$(BiO)_2OHC_{10}H_7O$	610.11
" Citrate	$BiC_6H_5O_7$	398.07
" Nitrate (normal)	$Bi(NO_3)_3.5H_2O$	485.10
" Subcarbonate (approximately)	$[(BiO)_2CO_3]_2.H_2O$	1038.03
" Subgallate (approximately)	$Bi(OH)_2C_7H_5O_5$	412.09
" Subnitrate (approximately)	$Bi(OH)_2NO_3$	305.02
" Subsalicylate (approximately)	$Bi(OH)_2C_7H_5O_3$	380.09
" Sulphide	Bi_2S_3	514.18
" Trioxide	Bi_2O_3	466.00
Borax (see Sodium Borate)		
Borneol	$C_{10}H_{17}OH$	154.19
Bornyl Acetate	$C_{10}H_{17}C_2H_3O_2$	196.22
Boron	**B**	**10.9**
Boron Trioxide	B_2O_3	69.80
Bromine	**Br**	**79.92**
Bromoform	$CHBr_3$	252.77
Brucine	$C_{23}H_{26}O_4N_2.4H_2O$	466.40
" anhydrous	$C_{23}H_{26}O_4N_2$	394.34
Cadmium	**Cd**	**112.40**
Cadmium Chloride	$CdCl_2.2H_2O$	219.35
" " anhydrous	$CdCl_2$	183.32
" Iodide	CdI_2	366.24
" Sulphate	$3CdSO_4.8H_2O$	769.51
" " anhydrous	$CdSO_4$	208.46
Sulphide	CdS	144.46
Caffeine	$C_8H_{10}O_2N_4.H_2O$	212.17
anhydrous	$C_8H_{10}O_2N_4$	194.15
Citrated	$C_8H_{10}O_2N_4C_6H_8O_7$	386.25
Calcium	**Ca**	**40.07**
Calcium Bromide	$CaBr_2.2H_2O$	235.94
" " anhydrous	$CaBr_2$	199.91
" Carbonate	$CaCO_{31}$	100.08
Chloride	$CaCl_2.2H_2O$	147.02
" " anhydrous	$CaCl_2$	110.99
" Fluoride	CaF_2	78.07
" Glycerophosphate	$CaC_3H_7PO_6.H_2O$	228.20
" " anhydrous	$CaC_3H_7PO_6$	210.18
Hydroxide	$Ca(OH)_2$	74.09
Hypophosphite	$Ca(PH_2O_2)_2$	170.18
Iodobehenate	$(C_{21}H_{42}ICO_2)_2Ca$	970.80
" Lactate	$Ca(C_3H_5O_3)_2.5H_2O$	308.26
" " anhydrous	$Ca(C_3H_5O_3)_2$	218.18
" Oxalate	$CaC_2O_4.H_2O$	146.10
" Oxide (Lime, Quick Lime)	CaO	56.07
" Phosphate	$Ca_3(PO_4)_2$	310.29
" Pyrophosphate	$Ca_2P_2O_7$	254.22
" Sulphate	$CaSO_4.2H_2O$	172.16
" " anhydrous	$CaSO_4$	136.13
" Sulphide (Monosulphide)	CaS	72.13
Camphor	$C_{10}H_{16}O$	152.18
" Monobromated	$C_{10}H_{15}OBr$	231.09
Carbon	**C**	**12.005**
Carbon Dioxide	CO_2	44.01
Disulphide	CS_2	76.13
" Tetrachloride	CCl_4	153.85
Carbromal	$C_7H_{13}O_2N_2Br$	237.08
Carvone	$C_{10}H_{14}O$	150.16
Cephaëline	$C_{14}H_{19}O_2N$	233.23
Cerium	**Ce**	**140.25**
Cerium Oxalate (not U. S. P.)	$Ce_2(C_2O_4)_3.10H_2O$	724.69
" " anhydrous	$Ce_2(C_2O_4)_3$	544.53
Cesium	**Cs**	**132.81**
Chloral, anhydrous	CCl_3CHO	147.40
" Hydrate	$CCl_3CHO.H_2O$	165.41
Chloralformamide	$C_3H_4Cl_3O_2N$	192.44
Chloramine	$C_7H_7O_2NSClNa.3H_2O$	281.67
Chlorine	**Cl**	**35.46**
Chloroform	$CHCl_3$	119.39

		O=16
Chlormium	Cr	52.0
Chromium Oxide	Cr_2O_3	152.00
“ Trioxide (Chromic Anhydride)	CrO_3	100.00
Cinchonidine	$C_{19}H_{22}ON_2$	294.29
“ Salicylate	$C_{19}H_{22}ON_2C_7H_6O_3$	432.37
“ Sulphate	$(C_{19}H_{22}ON_2)_2H_2SO_4.3H_2O$	740.70
“ “ anhydrous	$(C_{19}H_{22}ON_2)_2H_2SO_4$	686.65
Cinchonine	$C_{19}H_{22}ON_2$	294.29
“ Sulphate	$(C_{19}H_{22}ON_2)_2H_2SO_4.2H_2O$	722.68
“ “ anhydrous	$(C_{19}H_{22}ON_2)_2H_2SO_4$	686.65
Cinchophen (Phenylcinchopinic Acid)	$HC_{16}H_{10}O_2N$	249.18
Cineol (Eucalyptol)	$C_{10}H_{18}O$	154.19
Cinnamic Aldehyde	C_9H_8O	132.11
Citral	$C_{10}H_{16}O$	152.18
Cobalt	Co	58.97
Cobaltous Chloride	$CoCl_2.6H_2O$	237.99
“ “ anhydrous	$CoCl_2$	129.89
“ Nitrate	$Co(NO_3)_2.6H_2O$	291.08
“ “ anhydrous	$Co(NO_3)_2$	182.99
“ Sulphate	$CoSO_4.7H_2O$	281.14
“ “ anhydrous	$CoSO_4$	155.03
Cocaine	$C_{17}H_{21}O_4N$	303.26
“ Hydrochloride	$C_{17}H_{21}O_4NHCl$	339.73
Codeine (Methyl Morphine)	$C_{18}H_{21}O_3N.H_2O$	317.28
“ anhydrous	$C_{18}H_{21}O_3N$	299.27
“ Phosphate	$C_{18}H_{21}O_3NH_3PO_4.2H_2O$	433.36
“ “ anhydrous	$C_{18}H_{21}O_3NH_3PO_4$	397.33
“ Sulphate	$(C_{18}H_{21}O_3N)_2H_2SO_4.5H_2O$	786.69
“ “ anhydrous	$(C_{18}H_{21}O_3N)_2H_2SO_4$	696.61
Colchicine	$C_{22}H_{25}O_6N$	399.32
Columbium	Cb	93.1
Coniine	$C_8H_{17}N$	127.18
Copper	Cu	63.57
Cotarnine	$C_{12}H_{14}O_3N$	220.18
“ Chloride	$C_{12}H_{14}O_3NCl.H_2O$	273.66
Creosol	$C_6H_3(CH_3)\ (OCH_3)OH$	138.12
Cresol	$C_6H_4(CH_3)OH$	108.10
Cupric Acetate	$Cu(C_2H_3O_2)_2.H_2O$	199.65
Cupric-Ammonium Sulphate	$Cu(NH_3)_4SO_4.H_2O$	245.77
“ Sulphate	$CuSO_4.5H_2O$	249.71
“ “ anhydrous	$CuSO_4$	159.63
“ Sulphide	CuS	95.63
“ Tartrate	$CuC_4H_4O_6.3H_2O$	265.67
“ “ anhydrous	$CuC_4H_4O_6$	211.62
Dextrose	$C_6H_{12}O_6$	180.13
Diacetylmorphine	$C_{21}H_{23}O_5N$	369.30
Diacetylmorphine Hydrochloride	$C_{21}H_{23}O_5NHCl.H_2O$	423.78
“ “ “ anhydrous	$C_{21}H_{23}O_5NHCl$	405.77
Dichloramine	$C_7H_7O_2NSCl_2$	240.08
Diethylsulphon-dimethylmethane (see Sulphonmethane)		
Diethylsulphon-methylethylmethane (see Sulphonethylmethane)		
Dipentine	$C_{10}H_{16}$	136.18
Diphenylamine	$(C_6H_5)_2NH$	169.16
Dithymol Diiodide (see Thymol Iodide)		
Dysprosium	Dy	162.5
Emetine	$C_{15}H_{22}O_2N$	248.26
“ Hydrochloride, anhydrous	$C_{15}H_{22}O_2NHCl$	284.73
Epinephrine, anhydrous	$C_9H_{13}O_3N$	183.16
“ Hydrated	$C_9H_{13}O_3N.\frac{1}{2}H_2O$	192.17
Erbium	Er	167.7
Erythrol Tetranitrate	$C_4H_6(NO_3)_4$	302.10
Ether (Ethyl Oxide)	$(C_2H_5)_2O$	74.10
Ethyl Acetate	$C_2H_5C_2H_3O_2$	88.08
Ethyl Aminobenzoate	$C_9H_{11}O_2N$	165.14
“ Carbamate	$CO(OC_2H_5)NH_2$	89.08
“ Chloride	C_2H_5Cl	64.51
“ Hydroxide (see Alcohol, Ethyl)		
Ethylmorphine Hydrochloride	$C_{19}H_{23}O_3NHCl.2H_2O$	385.79
“ “ anhydrous	$C_{19}H_{23}O_3NHCl$	349.76
Ethyl Nitrite	$C_2H_5NO_2$	75.06
“ Oxide (see Ether)		
Eucaine Hydrochloride (Beta)	$C_{15}H_{21}O_2NHCl.H_2O$	301.74
“ “ (Beta) anhydrous	$C_{15}H_{21}O_2NHCl$	283.72
Eucalyptol (see Cineol)		

		O=16
Eugenol	$C_{10}H_{12}O_2$	164.15
Europium	**Eu**	**152.0**
Ferric acetate	$Fe(C_2H_3O_2)_3$	232.94
“ Ammonium Sulphate	$FeNH_4(SO_4)_2.12H_2O$	482.19
“ “ “ anhydrous	$FeNH_4(SO_4)_2$	266.00
“ Chloride	$FeCl_3.6H_2O$	270.32
“ “ anhydrous	$FeCl_3$	162.22
“ Hydroxide	$Fe(OH)_3$	106.86
“ Hypophosphite	$Fe(PH_2O_2)_3$	251.01
“ Nitrate	$Fe(NO_3)_3$	241.86
“ Oxide	Fe_2O_3	159.68
“ Phosphate (normal, not U. S. P.)	$FePO_4$	150.88
“ Pyrophosphate (normal, not U. S. P.)	$Fe_4(P_2O_7)_3$	745.60
“ Sulphate (Tersulphate)	$Fe_2(SO_4)_3$	399.86
Ferrous Bromide	$FeBr_2.6H_2O$	323.78
“ “ anhydrous	$FeBr_2$	215.68
“ Carbonate	$FeCO_3$	115.85
“ Iodide	FeI_2	309.68
“ Lactate	$Fe(C_3H_5O_3)_2.3H_2O$	288.00
“ “ anhydrous	$Fe(C_3H_5O_3)_2$	233.95
“ Oxide	FeO	71.84
“ Sulphate	$FeSO_4.7H_2O$	278.01
“ “ anhydrous	$FeSO_4$	151.90
“ “ Exsiccated (approximately)	$2FeSO_4.3H_2O$	357.85
“ Sulphide	FeS	87.90
Ferrum	**Fe**	**55.84**
Fluorescein (Resorcinolphthalein)	$C_{20}H_{12}O_5$	332.20
Fluorine	**F**	**19.0**
Formaldehyde	$HCHO$	30.02
Fuchsin	$C_{20}H_{19}N_3HCl$	337.74
Gadolinium	**Gd**	**157.3**
Gallium	**Ga**	**70.1**
Germanium	**Ge**	**72.5**
Glucinum	**Gl**	**9.1**
Glucose (Grape Sugar)	$C_6H_{12}O_6$	180.13
Gluside (Benzosulphinide, Saccharin)	$C_7H_5O_3.NS$	183.14
Gluside, Soluble (Soluble Saccharin)	$NaC_7H_4SNO_3.2H_2O$	241.17
Glycerin (Glycerol)	$C_3H_5(OH)_3$	92.08
Glyceryl Trinitrate (Nitroglycerin)	$C_3H_5(NO_3)_3$	227.08
Gold	**Au**	**197.2**
Gold Chloride (Chlorauric Acid)	$HAuCl_4.4H_2O$	412.11
Gold Trichloride, anhydrous	$AuCl_3$	303.58
Guaiacol	$C_7H_8O_2$	124.10
“ Carbonate	$(C_7H_7O)_2CO_3$	274.19
Helium	**He**	**4.00**
Hematein	$C_{16}H_{12}O_6$	300.18
Hematoxylin	$C_{16}H_{14}O_6.3H_2O$	356.24
Hexamethylemanine (see Methenamine)		
Holmium	**Ho**	**163.5**
Holocaine	$C_{18}H_{22}O_2N_2$	298.28
“ Hydrochloride	$C_{18}H_{22}O_2N_2HCl$	334.75
Homotropine	$C_{16}H_{21}O_3N$	275.26
“ Hydrobromide	$C_{16}H_{21}O_3NHBr$	356.18
Hydrastine	$C_{21}H_{21}O_6N$	383.28
“ Hydrochloride	$C_{21}H_{21}O_6NHCl$	419.75
Hydrastinine Hydrochloride	$C_{11}H_{11}O_2NHCl$	225.62
Hydrogen	**H**	**1.008**
Hydrogen Dioxide	H_2O_2	34.02
“ Sulphide (Hydrosulphuric Acid)	H_2S	34.08
Hyoscine (see Scopolamine)		
Hyoscyamine	$C_{17}H_{23}O_3N$	289.28
“ Hydrobromide	$C_{17}H_{23}O_3NHBr$	370.21
“ Sulphate	$(C_{17}H_{23}O_3N)_2H_2SO_4$	676.63
Indigo Carmine (see Sodium Indigotindisulphonate)		
Indium	**In**	**114.8**
Iodeosin (Tetraiodo-fluorescein)	$C_{20}H_8O_5I_4$	835.84
Iodine	**I**	**126.92**
Iodoform	CHI_3	393.77
Iodol (Tetraiodopyrrol)	C_4NHI_4	570.72
Iridium	**Ir**	**193.1**
Iron	**Fe**	**55.84**
Iron Salts (see under Ferric and Ferrous)		
Krypton	**Kr**	**82.92**
Lactose (Sugar of Milk)	$C_{12}H_{22}O_{11}.H_2O$	360.25

		0=16
Lanthanum	**La**	**139.0**
Lead	**Pb**	**207.20**
Lead Acetate	$Pb(C_2H_3O_2)_2.3H_2O$	379.32
“ “ anhydrous	$Pb(C_2H_3O_2)_2$	325.27
“ “ Basic (see Lead Subacetate)		
“ Carbonate, Basic	$(PbCO_3)_2Pb(OH)_2$	775.63
“ Chloride	$PbCl_2$	278.12
“ Chromate	$PbCrO_4$	323.20
“ Dioxide	PbO_2	239.20
“ Iodide	PbI_2	461.04
“ Nitrate	$Pb(NO_3)_2$	331.22
“ Monoxide (Lead Oxide)	PbO	223.20
“ Subacetate (approximately)	$Pb_2O(C_2H_3O_2)_2$	548.47
“ Sulphate	$PbSO_4$	303.26
“ Sulphide	PbS	239.26
Lime (see Calcium Oxide)		
Limonene	$C_{10}H_{16}$	136.18
Linalyl Acetate	$C_{10}H_{17}C_2H_3O_2$	196.22
Lithium	**Li**	**6.94**
Lithium Benzoate	$LiC_7H_5O_2$	128.02
“ Bromide	$LiBr$	86.86
“ Carbomate	Li_2CO_3	73.89
“ Chloride	$LiCl$	42.40
“ Citrate	$Li_3C_6H_5O_7.4H_2O$	281.95
“ “ anhydrous	$Li_3C_6H_5O_7$	209.89
“ Phosphate, anhydrous	Li_3PO_4	115.86
“ Salicylate	$LiC_7H_5O_3$	144.02
“ Sulphate, anhydrous	Li_2SO_4	109.94
Lutecium	**Lu**	**175.0**
Magnesia (see Magnesium Oxide)		
Magnesium	**Mg**	**24.32**
Magnesium Carbomate, Basic (approximately)	$(MgCO_3)_4Mg(OH)_2.5H_2O$	485.72
“ Chloride	$MgCl_2.6H_2O$	203.34
“ “ anhydrous	$MgCl_2$	95.24
“ Hydroxide	$Mg(OH)_2$	58.34
“ Oxide (Magnesia)	MgO	40.32
“ Pyroarsenate	$Mg_2As_2O_7$	310.56
“ Pyrophosphate	$Mg_2P_2O_7$	222.72
“ Sulphate	$MgSO_4.7H_2O$	246.49
“ “ anhydrous	$MgSO_4$	120.38
Manganese	**Mn**	**54.93**
Manganese Dioxide	MnO_2	86.93
“ Hypophosphite	$Mn(Ph_2O_2)_2.H_2O$	203.06
“ “ anhydrous	$Mn(PH_2O_2)_2$	185.04
Manganous Oxide	MnO	70.93
“ Sulphate	$MnSO_4.4H_2O$	223.05
“ “ anhydrous	$MnSO_4$	150.99
Mannitol Hexanitrate	$C_6H_8(NO_3)_6$	452.14
Menthol	$C_{10}H_{19}OH$	156.21
Menthyl Acetate	$C_{10}H_{19}C_2H_3O_2$	198.24
Mercurammonium Chloride (see Mercury, Ammoniated)		
Mercuric Bromide	$HgVr_2$	360.44
“ Chloride	$HgCl_2$	271.52
“ Cyanide	$Hg(CN)_2$	252.63
“ Iodide	HgI_2	454.44
“ Nitrate	$Hg(NO_3)_2.4H_2O$	396.68
“ “ anhydrous	$Hg(NO_3)_2$	324.62
“ Oxide	HgO	216.60
“ Potassium Iodide	$HgI_2.2KI$	786.48
“ Salicylate	$HgC_7H_4O_3$	336.67
“ Subsulphate	$Hg(HgO)_2SO_4$	729.86
“ Sulphate	$HgSO_4$	296.66
“ Sulphide	HgS	232.66
Mercurous Chloride	$HgCl$	236.06
“ Iodide	HgI	327.52
“ Nitrate	$HgNO_3.H_2O$	280.62
“ “ anhydrous	$HgNO_3$	262.61
“ Sulphate	Hg_2SO_4	497.26
Mercury	**Hg**	**200.6**
Mercury, Ammoniated	$HgNH_2Cl$	252.08
Metaphenylenediamine Hydrochloride	$C_6H_4(NH_2)_22HCl$	181.05
Methanamine (Hexamethylemamine)	$C_6H_{12}N_4$	140.16
Methylacetanilid	$C_6H_5N(CH_3)C_2H_3O$	149.14

		0=16
Methylaurin (Rosolic Acid)	$C_{20}H_{16}O_3$	304.23
Methylene Blue (see Methylthionine Chloride)		
Methyl Hydroxide (see Alcohol, Methyl)		
" Morphine (see Codeine)		
" Orange (Sodium Dimethylaminoazobenzene-sulphonate)	$NaC_{14}H_{14}N_3SO_3$	327.27
Methyl Red	$C_{14}H_{14}N_3CO_2H$	269.22
" Salicylate	$CH_3C_7H_5O_3$	152.10
Methylthionine Chloride (Methylene Blue)	$C_{16}H_{18}N_3ClS.3H_2O$	373.82
Molybdenum	**Mo**	**96.0**
Morphine	$C_{17}H_{19}O_3N.H_2O$	303.26
" anhydrous	$C_{17}H_{19}O_3N$	285.25
" Acetate (variable)	$C_{17}H_{19}O_3NC_2H_4O_2.3H_2O$	399.34
" Hydrochloride	$C_{17}H_{19}O_3NHCl.3H_2O$	375.76
" " anhydrous	$C_{17}H_{19}O_3NHCl$	321.71
" Sulphate	$(C_{17}H_{19}O_3N)_2H_2SO_4.5H_2O$	758.65
" " anhydrous	$(C_{17}H_{19}O_3N)_2H_2SO_4$	668.57
Naphthalene	$C_{10}H_8$	128.11
Naphthol (see Betanaphthol)		
Naphthylamine Acetate	$C_{10}H_7NH_2HC_2H_3O_2$	203.17
Naphthylamine Hydrochloride	$C_{10}H_7NH_2HCl$	179.60
Neoarsphenamine (approximately)	$C_{13}H_{13}O_4N_2SAs_2Na$	466.17
Neodymium	**Nd**	**144.3**
Neon	**Ne**	**20.2**
Nickel	**Ni**	**58.68**
Nickelous Oxide	NiO	74.68
" Sulphate	$NiSO_4.7H_2O$	280.85
" " anhydrous	$NiSO_4$	154.74
Niton (radium emanation) (Radon)	**Nt**	**222.4**
Nitric Oxide	No	30.01
Nitrogen	**N**	**14.008**
Nitrogen Monoxide	N_2O	44.02
Nitroglycerin (see Glyceryl Trinitrate)		
Nitrous Oxide (see Nitrogen Monoxide)		
Orthoform	$C_8H_9O_3N$	167.12
Osmium	**Os**	**190.9**
Ouabain	$C_{30}H_{46}O_{12}.9H_2O$	760.66
" anhydrous	$C_{30}H_{46}O_{12}$	598.52
Oxygen	**O**	**16.00**
Palladium	**Pd**	**106.7**
Palladous Chloride	$PdCl_2$	177.62
Paradiaminodiphenyl (see Benzidine)		
Paraformaldehyde (Trioxymethylene)	$(CH_2O)_3$	90.06
Paraldehyde	$C_6H_{12}O_3$	132.13
Phenobarbital	$C_{12}H_{12}O_3N_2$	232.17
Phenol (Carbolic Acid)	C_6H_5OH	94.08
Phenolphthalein	$C_{20}H_{14}O_4$	318.21
Phenolsulphonphthalein	$C_{19}H_{14}O_5S$	354.27
Phenylacetamide (see Acetanilid)		
Phenylamine (see Aniline)		
Phenylhydrazine	$C_6H_5NHNH_2$	108.11
" Hydrochloride	$C_6H_5NHNH_2HCl$	144.58
Phenyl Salicylate (Salol)	$C_6H_5C_7H_5O_3$	214.15
Phloroglucinol	$C_6H_3(OH)_3$	126.08
Phosphorus	**P**	**31.04**
Physostigmine	$C_{15}H_{21}O_2N_3$	275.27
" Salicylate	$C_{15}H_{21}O_2N_3C_7H_6O_3$	413.35
" Sulphate	$(C_{15}H_{21}O_2N_3)_2H_2SO_4$	648.61
Picrotoxin	$C_{30}H_{34}O_{13}$	602.42
Pilocarpine	$C_{11}H_{16}O_2N_2$	208.20
" Hydrochloride	$C_{11}H_{16}O_2N_2HCl$	244.67
" Nitrate	$C_{11}H_{16}O_2N_2HNO_3$	271.22
Piperine	$C_{17}H_{19}O_3N$	285.25
Platinic Chloride (in solution)	$PtCl_4$	337.04
" " (see Acid Chloroplatinic)		
Platinum	**Pt**	**195.2**
Potassium	**K**	**39.10**
Potassium Acetate	$KC_2H_3O_2$	98.13
" Arsenite (Metarsenite)	$KAsO_2$	146.06
" Benzoate	$KC_7H_5O_2.3H_2O$	214.22
" Benzoate, anhydrous	$KC_7H_5O_2$	160.18
" Bicarbonate	$KHCO_3$	100.11
" Bichromate (see Potassium Dichromate)		

		0=16
Potassium Bisulphate	$KHSO_4$	136.17
“ Bitartrate	$KHC_4H_4O_6$	188.16
“ Bromate	$KBrO_3$	167.02
“ Bromide	KBr	119.02
“ Carbonate	K_2CO_3	138.21
“ Chlorate	$KClO_3$	122.56
“ Chloride	KCl	74.56
“ Chlorophatinate	K_2PtCl_6	486.16
“ Chromate	K_2tCO_4	194.20
“ Citrate	$K_3C_6H_5O_7.H_2O$	324.39
“ “ anhydrous	$K_3C_6H_5O_7$	306.37
“ Cyanide	KCN	65.11
“ Dichromate (Bichromate)	$K_2Cr_2O_7$	294.20
“ Ferricyanide	$K_3Fe(CN)_6$	329.22
“ Ferrocyanide	$K_4Fe(CN)_6.3H_2O$	422.37
“ “ anhydrous	$K_4Fe(CN)_6$	368.32
“ Hydroxide	KOH	56.11
“ Hypophosphite	KPH_2O_2	104.16
“ Iodide	KI	166.02
“ Lactate	$KC_3H_5O_3$	128.16
“ Nitrate	KNO_3	101.11
“ Permanganate	$KMnO_4$	158.03
“ Phosphate, Dibasic	K_2HPO_4	174.25
“ Salicylate	$KC_7H_5O_3$	176.18
“ Sodium Tartrate	$KNaC_4H_4O_6.4H_2O$	282.22
“ “ “ anhydrous	$KNaC_4H_4O_6$	210.15
“ Sulphate	K_2SO_4	174.26
“ Sulphite	$K_2SO_3.2H_2O$	194.29
“ “ anhydrous	K_2SO_3	158.26
“ Tartrate	$K_2C_4H_4O_6.\frac{1}{2}H_2O$	235.26
“ “ anhydrous	$K_2C_4H_4O_6$	226.25
“ Thiocyanate (Sulphocyanide)	$KSCN$	97.17
Praseodymium	**Pr**	**140.9**
Procaine Hydrochloride	$C_{13}H_{18}O_2N_2.HCl$	272.71
Pyrogallol (Pyrogallic Acid)	$C_6H_3(OH)_3$	126.08
Quinidine	$C_{20}H_{24}O_2N_2$	324.31
“ Sulphate	$(C_{20}H_{24}O_2N_2)_2H_2SO_4.2H_2O$	782.72
“ “ anhydrous	$(C_{20}H_{24}O_2N_2)_2H_2SO_4$	746.69
Quinine	$C_{20}H_{24}O_2N_23H_2O$	378.36
“ anhydrous	$C_{20}H_{24}O_2N_2$	324.31
“ Bisulphate	$C_{20}H_{24}O_2N_2H_2SO_4.7H_2O$	548.50
“ Bisulphate, anhydrous	$C_{20}H_{24}O_2N_2H_2SO_4$	422.38
“ Dihydrochloride	$C_{20}H_{24}O_2N_2.2HCl$	397.24
“ Ethyl Carbonate	$C_{20}H_{23}O_2N_2.CO_2.C_2H_5$	396.36
“ Hydrobromide	$C_{20}H_{24}O_2N_2HBr.H_2O$	423.25
“ “ anhydrous	$C_{20}H_{24}O_2N_2HBr$	405.24
“ Hydrochloride	$C_{20}H_{24}O_2N_2HCl.2H_2O$	396.81
“ “ anhydrous	$C_{20}H_{24}O_2N_2HCl$	360.78
“ Salicylate	$C_{20}H_{24}O_2N_2C_7H_6O_3.H_2O$	480.41
“ “ anhydrous	$C_{20}H_{24}O_2N_2C_7H_6O_3$	462.39
“ Sulphate	$(C_{20}H_{24}O_2N_2)_2H_2SO_4.7H_2O$	872.80
“ “ anhydrous	$(C_{20}H_{24}O_2N_2)_2H_2SO_4$	746.69
“ and Urea Hydrochloride	$C_{20}H_{24}O_2N_2HCl.CO(NH_2)_2HCl.5H_2O$	547.38
Radium	**Ra**	**226.00**
Radon (see **Niton**)		
Resorcinol (Resorcin)	$C_6H_4(OH)_2$	110.08
Resorcinolphthalein (see Fluorescein)		
Rhodium	**Rh**	**102.9**
Rosaniline Acetate	$C_{19}H_{18}N_3C_2H_4O_2$	348.31
Rubidium	**Rb**	**85.45**
Ruthenium	**Ru**	**101.7**
Saccharin (see Gluside)		
Safrol	$C_{10}H_{10}O_2$	162.13
Salicin	$C_{13}H_{18}O_7$	286.21
Salol (see Phenyl Salicylate)		
Samarium	**Sa**	**150.4**
Santalol	$C_{15}H_{24}O$	220.27
Santonin	$C_{15}H_{18}O_3$	246.22
Scandium	**Sc**	**45.1**

		O=16
Scopolamine (Hyoscine)	$C_{17}H_{21}O_4N$	303.26
“ Hydrobromide	$C_{17}H_{21}O_4NHBr.3H_2O$	438.24
“ “ anhydrous	$C_{17}H_{21}O_4NHBr$	384.19
Silenium	Se	79.2
Silicon	Si	28.1
Silicon Oxide (Silica)	SiO_2	60.10
Silver	Ag	107.88
Silver Chloride	AgCl	143.34
“ Cyanide	AgCN	133.89
“ Iodide	AgI	234.80
“ Nitrate	$AgNO_3$	169.89
“ Nitrite	$AgNO_2$	153.89
“ Oxide	Ag_2O	231.76
“ Sulphate	Ag_2SO_4	311.82
“ Sulphide	Ag_2S	247.82
Sodium	Na	23.00
Sodium Acetate	$NaC_2H_3O_2.3H_2O$	136.08
“ “ anhydrous	$NaC_2H_3O_2$	82.03
“ Arsenate	$Na_2HAsO_4.7H_2O$	312.08
“ “ anhydrous	Na_2HAsO_4	185.97
“ Arsenite (Metarsenite)	$NaAsO_2$	129.96
“ Benzoate	$NaC_7H_5O_2$	144.08
“ Benzosulphinide (see Gluside, Soluble)		
“ Bicarbonate	$NaHCO_3$	84.01
“ Biphosphate	$NaH_2PO_4.H_2O$	138.07
“ “ anhydrous	NaH_2PO_4	120.06
“ Bisulphite	$NaHSO_3$	104.07
“ Bitartrate	$NaHC_4H_4O_6.H_2O$	190.08
“ Borate	$Na_2B_4O_7.10H_2O$	381.76
“ “ anhydrous	$Na_2B_4O_7$	201.60
“ Bromate	$NaBrO_3$	150.92
“ Bromide	NaBr	102.92
“ Cacodylate	$Na(CH_3)_2AsO_2.3H_2O$	214.07
“ “ anhydrous	$Na(CH_3)_2AsO_2$	160.02
“ Carbonate	$Na_2CO_3.10H_2O$	286.17
“ “ anhydrous	Na_2CO_3	106.01
“ “ Monohydrated	$Na_2CO_3.H_2O$	124.02
“ Chlorate	$NaClO_3$	106.46
“ Chloride	NaCl	58.46
“ Citrate	$Na_3C_6H_5O_7.2H_2O$	294.10
“ “ anhydrous	$Na_3C_6H_5O_7$	258.07
“ Cobaltic Nitrate	$Co_2(NO_2)_6 6NaNO_2.H_2O$	826.05
“ Cyanide	NaCN	49.01
“ Dimethylaminoazo-benzene-sulphonate (see Methyl Orange)		
“ Glycerophosphate, anhydrous	$Na_2C_3H_7PO_6$	216.11
“ Hydroxide	NaOH	40.01
“ Hypochlorite	NaOCl	74.46
“ Hypophosphite	$NaPH_2O_2.H_2O$	106.07
“ “ anhydrous	$NaPH_2O_2$	88.06
“ Hyposulphite (see Sodium Thiosulphate)		
“ Indigotindisulphonate	$Na_2C_{16}H_8O_2N_2(SO_3)_2$	466.28
“ Iodide	NaI	149.92
“ Lactate	$NaC_3H_5O_3$	112.06
“ Nitrate	$NaNO_3$	85.01
“ Nitrite	$NaNO_2$	69.01
“ Nitro-Prusside	$Na_2Fe(NO)(CN)_5.2H_2O$	297.95
“ Oxalate	$Na_2C_2O_4$	134.01
“ Perborate	$NaBO_3.4H_2O$	153.96
“ “ anhydrous	$NaBO_3$	81.90
“ Phenolsulphonate (Sulphocarbolate)	$NaC_6H_4OH.SO_3.2H_2O$	232.16
“ “ anhydrous	$NaC_6H_4OH.SO_3$	196.13
“ Phosphate, Dibasic	$Na_2HPO_4.12H_2O$	358.24
“ “ “ anhydrous	Na_2HPO_4	142.05
“ Pyrophosphate	$Na_4P_2O_7.10H_2O$	446.24
“ “ anhydrous	$Na_4P_2O_7$	266.08
“ Salicylate	$NaC_7H_5O_3$	160.08
“ Sulphate	$Na_2SO_4.10H_2O$	322.22
“ “ anhydrous	Na_2SO_4	142.06
“ Sulphide	$Na_2S.9H_2O$	240.20

		0=16
Sodium Sulphide anhydrous	Na_2S	78.06
“ Sulphite	$Na_2SO_3.7H_2O$	252.17
“ “ anhydrous	Na_2SO_3	126.06
“ Sulphoncarbolate (see Sodium Phenolsulphonate)		
“ Tartrate	$Na_2C_4H_4O_6.2H_2O$	230.08
“ “ anhydrous	$Na_2C_4H_4O_6$	194.05
“ Tetraborate (Sodium Borate)	$Na_2B_4O_7.10H_2O$	381.76
“ Theobromine	$NaC_7H_7O_2N_4$	202.12
“ Thiosulphate (Hypopsulphite)	$Na_2S_2O_3.5H_2O$	248.20
“ “ anhydrous	$Na_2S_2O_3$	158.12
“ Tungstate	$Na_2WO_4.2H_2O$	330.03
Sparteine	$C_{15}H_{26}N_2$	234.30
“ Sulphate	$C_{15}H_{26}N_2H_2SO_4.5H_2O$	422.46
“ “ anhydrous	$C_{15}H_{26}N_2H_2SO_4$	332.38
Stannic Chloride	$SnCl_4$	260.54
“ Sulphide	SnS_2	182.82
Stannous Chloride	$SnCl_2.2H_2O$	225.65
“ “ anhydrous	$SnCl_2$	189.62
“ Sulphide	SnS	150.76
Strontium	**Sr**	87.63
Strontium Bromide	$SrBr_2.6H_2O$	355.57
“ “ anhydrous	$SrBr_2$	247.47
“ Carbonate	$SrCO_3$	147.64
“ Chloride	$SrCl_2.6H_2O$	266.65
“ “ anhydrous	$SrCl_2$	158.55
“ Iodide	$SrI_2.6H_2O$	449.57
“ “ anhydrous	SrI_2	341.47
“ Lactate	$Sr(C_3H_5O_3)_2.3H_2O$	319.79
“ “ anhydrous	$Sr(C_3H_5O_3)_2$	265.74
“ Salicylate	$Sr(C_7H_5O_3)_2.2H_2O$	397.81
“ “ anhydrous	$Sr(C_7H_5O_3)_2$	361.78
“ Sulphate	$SrSO_4$	183.69
Strychnine	$C_{21}H_{22}O_2N_2$	334.30
“ Nitrate	$C_{21}H_{22}O_2N_2HNO_3$	397.31
“ Sulphate	$(C_{21}H_{22}O_2N_2)_2H_2SO_4.5H_2O$	856.75
“ “ anhydrous	$(C_{21}H_{22}O_2N_2)_2H_2SO_4$	766.67
Sucrose (Sugar)	$C_{12}H_{22}O_{11}$	342.24
Sugar, Cane (see Sucrose)		
“ Grape (see Glucose)		
“ Milk (see Lactose)		
Sulphonethylmethane (Diethylsulphonmethylethylmethane)	$C_8H_{18}O_4S_2$	242.30
Sulphonmethane Diethylsulphon-dimethylmethane)	$C_7H_{16}O_4S_2$	228.28
Sulphur	**S**	32.06
Sulphur Dioxide	SO_2	64.06
“ Trioxide	SO_3	80.06
Tantalum	**Ta**	**181.5**
Tellurium	**Te**	**127.5**
Terbium	**Tb**	**159.2**
Terebene	$C_{10}H_{16}$	136.18
Terpin Hydrate	$C_{10}H_{18}(OH)_2.H_2O$	190.23
Tetraiodo-fluorescein (see Iodeosin)		
Tetraiodopyrrol (see Iodol)		
Tetramethylthionine Chloride (see Methylthionine Chloride)		
Thallium	**Tl**	**204.0**
Theobromine	$C_7H_8O_2N_4$	180.13
Theophylline	$C_7H_8O_2N_4.H_2O$	198.15
Thiosinamine (see Allyl-sulphocarbromide)		
Thorium	**Th**	**232.15**
Thulium	**Tm**	**169.8**
Thymol	$C_{10}H_{14}O$	150.16
“ Iodide (Dithymol-diiodide)	$(C_{10}H_{12}O)_2I_2$	550.13
Thyroxin	$C_{11}H_{10}O_3NI_3$	584.90
Tin	**Sn**	**118.7**
Tin Salts (see under Stannic and Stannous)		
Titanium	**Ti**	**48.1**
Toluene (Methyl Benzene, Toluol)	$C_6H_5CH_3$	92.10
Trinitrophenol (Picric Acid)	$C_6H_3O_7N_3$	229.08
Trioxymethylene (see Paraformaldehyde)		

		O=16
Tungsten	W	184.0
Uranium	U	238.2
Uranium Nitrate (Uranyl Nitrate)	$UO_2(NO_3)_2.6H_2O$	502.31
“ “ anhydrous	$UO_2(NO_3)_2$	394.22
Vanadium	V	51.0
Vanillin	$C_8H_8O_3$	152.10
Water	H_2O	18.016
Xenon	Xe	130.2
Xylene (Xylol, Dimethyl-benzene)	$C_6H_4(CH_3)_2$	106.12
Ytterbium (Neoytterbium)	Yb	173.5
Yttrium	Yt	89.33
Zinc	Zn	65.37
Zinc Acetate	$Zn(C_2H_3O_2)_2.2H_2O$	219.47
“ “ anhydrous	$Zn(C_2H_3O_2)_2$	183.44
“ Bromide	$ZnBr_2$	225.21
“ Carbonate (Normal, not U. S. P.)	$ZnCO_3$	125.38
“ Chloride	$ZnCl_2$	136.29
“ Iodide	ZnI_2	319.21
“ Oxide	ZnO	81.37
“ Perborate, anhydrous	$Zn(BO_3)_2$	183.17
“ Phenolsulphonate (Sulphocarbolate)	$Zn(C_6H_4.OH.SO_3)_2.8H_2O$	555.76
“ “ anhydrous	$Zn(C_6H_4.OH.SO_3)_2$	411.63
“ Phosphide	Zn_3P_2	258.19
“ Sulphate	$ZnSO_4.7H_2O$	287.54
“ “ anhydrous	$ZnSO_4$	161.43
“ Sulphide	ZnS	97.43
“ Sulphocarbolate (see Zinc Phenolsulphonate)		
“ Valerate (Valerianate)	$Zn(C_5H_9O_2)_2.2H_2O$	303.60
Zirconium	Zr	90.60

Alcoholometric Table (U. S. P. X.)

Temperature 15.56° C. (60.4° F.)

PERCENTAGE BY VOLUME					PERCENTAGE BY WEIGHT				
Per ‖ cent. vol.	Corresponding per cent. wt.	Sp. gr. app.* in air $\frac{15.56^\circ}{15.56^\circ}$	Corr.† of sp. gr. for barometer (100 mm.)	Fractional‡ per cent.	Per cent. wt.	Corresponding per cent. vol.	Sp. gr. app.* in air $\frac{15.56^\circ}{15.56^\circ}$	Corr.† of sp. gr. for barometer (100 mm.)	Fractional‡ per cent.
§0	0.000	1.00000	0.000000	0.0667	0	0.000	1.00000	0.000000	0.0532
1	0.795	0.99850	0.000000	0.0680	1	1.257	0.99812	0.000000	0.0543
2	1.593	0.99703	0.000000	0.0690	2	2.510	0.99628	0.000000	0.0565
3	2.392	0.99558	0.000001	0.0714	3	3.758	0.99451	0.000001	0.0588
4	3.194	0.99418	0.000001	0.0730	4	5.002	0.99281	0.000001	0.0610
5	3.998	0.99281	0.000001	0.0746	5	6.243	0.99117	0.000001	0.0641
6	4.804	0.99149	0.000001	0.0781	6	7.479	0.98961	0.000001	0.0671
7	5.612	0.99021	0.000001	0.0813	7	8.712	0.98812	0.000002	0.0680
8	6.422	0.98898	0.000002	0.0833	8	9.943	0.98665	0.000002	0.0700
9	7.234	0.98778	0.000002	0.0840	9	11.169	0.98523	0.000002	0.0719
10	8.047	0.98659	0.000002	0.0855	10	12.393	0.98384	0.000002	0.0746
11	8.862	0.98542	0.000002	0.0877	11	13.613	0.98351	0.000003	0.0769
12	9.679	0.98428	0.000002	0.0901	12	14.832	0.98120	0.000003	0.0775
13	10.497	0.98317	0.000003	0.0917	13	16.047	0.97991	0.000003	0.0800
14	11.317	0.98208	0.000003	0.0943	14	17.259	0.97866	0000.003	0.0820
15	12.138	0.98102	0.000003	0.0943	15	18.469	0.97744	0.000004	0.0840
16	12.961	0.97996	0.000003	0.0962	16	19.676	0.97625	0.000004	0.0833
17	13.786	0.97892	0.000003	0.0990	17	20.880	0.97505	0.000004	0.0826
18	14.612	0.97791	0.000004	0.1000	18	22.081	0.97384	0.000004	0.0813
19	15.440	0.97691	0.000004	0.1020	19	23.278	0.97261	0.000004	0.0806
20	16.269	0.97593	0.000004	0.1000	20	24.472	0.97137	0.000005	0.0794
21	17.100	0.97493	0.000004	0.0990	21	25.662	0.97011	0.000005	0.0781
22	17.933	0.97392	0.000004	0.0980	22	26.849	0.96883	0.000005	0.0769
23	18.768	0.97290	0.000004	0.0962	23	28.032	0.96753	0.000005	0.0752
24	19.604	0.97186	0.000005	0.0952	24	29.210	0.96620	0.000005	0.0740
25	20.443	0.97081	0.000005	0.0943	25	30.388	0.96485	0.000006	0.0719
26	21.285	0.96974	0.000005	0.0926	26	31.555	0.96346	0.000006	0.0694
27	22.127	0.96866	0.000005	0.0909	27	32.719	0.96202	0.000006	0.0667
28	22.973	0.96756	0.000005	0.0893	28	33.879	0.96052	0.000006	0.0649
29	23.820	0.96644	0.000005	0.0877	29	35.033	0.95898	0.000007	0.0633
30	24.670	0.96530	0.000005	0.0862	30	36.181	0.95740	0.000007	0.0613
31	25.524	0.96414	0.000006	0.0820	31	37.323	0.95577	0.000007	0.0595
32	26.382	0.96292	0.000006	0.0787	32	38.459	0.95409	0.000007	0.0578
33	27.242	0.96165	0.000006	0.0775	33	39.590	0.95236	0.000007	0.0565
34	28.104	0.96036	0.000006	0.0752	34	40.716	0.95059	0.000008	0.0556
35	28.971	0.95903	0.000006	0.0725	35	41.832	0.94879	0.000008	0.0546
36	29.842	0.95765	0.000007	0.0704	36	42.944	0.94696	0.000008	0.0538
37	30.717	0.95623	0.000007	0.0685	37	44.050	0.94509	0.000009	0.0521
38	31.596	0.95477	0.000007	0.0668	38	45.149	0.94317	0.000009	0.0515
39	32.478	0.95326	0.000007	0.0649	39	46.242	0.94123	0.000009	0.0508
40	33.364	0.95172	0.000007	0.0633	40	47.328	0.93926	0.000010	0.0498
41	34.254	0.95014	0.000008	0.0617	41	48.407	0.93725	0.000010	0.0488
42	35.150	0.94852	0.000008	0.0600	42	49.480	0.93520	0.000010	0.0485
43	36.050	0.94687	0.000008	0.0588	43	50.545	0.93312	0.000011	0.0476
44	36.955	0.94517	0.000009	0.0578	44	51.605	0.93102	0.000011	0.0474
45	37.865	0.94344	0.000009	0.0565	45	52.658	0.92891	0.000011	0.0469

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* Barometer 760 mm. Air one-half saturated with moisture.

‖ If temperature of observation is above 15.56° C. (60.4° F.), look for percentage correction in the following table.

† Correction subtractive if barometer is above, additive if below, 760 mm. If barometer readings are in inches reduce to millimeters by multiplying by 25.4.

‡ Corresponding with a difference in specific gravity of 0.0001.

§ The figures on this line across the page are for fractional percentages below 1.

NOTE.—The figures of these Alcoholometric Tables are based on tables issued by the U. S. Bureau of Standards.

Alcoholometric Table—*Continued.*

Percentage by Volume					Percentage by Weight				
Per cent. vol.	Corresponding per cent. wt.	Sp. gr. app. in air 15.56°/15.56°	Corr. of sp. gr. for barometer (100 mm.)	Fractional per cent.	Per cent. wt.	Corresponding per cent. vol.	Sp. gr. app. in air 15.56°/15.56°	Corr. of sp. gr. for barometer (100 mm.)	Fractional per cent.
46	38.778	0.94167	0.000009	0.0552	46	53.705	0.92678	0.000012	0.0467
47	39.697	0.93986	0.000009	0.0541	47	54.746	0.92464	0.000012	0.0461
48	40.622	0.93801	0.000010	0.0526	48	55.780	0.92247	0.000012	0.0461
49	41.551	0.93611	0.000010	0.0518	49	56.808	0.92030	0.000013	0.0457
50	42.487	0.93418	0.000010	0.0510	50	57.830	0.91811	0.000013	0.0455
51	43.428	0.93222	0.000011	0.0503	51	58.844	0.91591	0.000013	0.0446
52	44.374	0.93023	0.000011	0.0498	52	59.851	0.91367	0.000014	0.0444
53	45.326	0.92822	0.000011	0.0488	53	60.854	0.91142	0.000014	0.0444
54	46.283	0.92617	0.000012	0.0483	54	61.850	0.90917	0.000014	0.0442
55	47.245	0.92410	0.000012	0.0478	55	62.837	0.90691	0.000015	0.0441
56	48.214	0.92201	0.000012	0.0474	56	63.820	0.90464	0.000015	0.0441
57	49.187	0.91990	0.000013	0.0463	57	64.798	0.90237	0.000015	0.0441
58	50.167	0.91774	0.000013	0.0457	58	65.768	0.90010	0.000016	0.0437
59	51.154	0.91555	0.000013	0.0452	59	66.732	0.89781	0.000016	0.0435
60	52.147	0.91334	0.000014	0.0446	60	67.690	0.89551	0.000016	0.0433
61	53.146	0.91110	0.000014	0.0439	61	68.641	0.89320	0.000017	0.0431
62	54.152	0.90882	0.000014	0.0437	62	69.586	0.89088	0.000017	0.0431
63	55.165	0.90653	0.000015	0.0435	63	70.523	0.88856	0.000017	0.0427
64	56.184	0.90423	0.000015	0.0429	64	71.455	0.88623	0.000018	0.0426
65	57.208	0.90190	0.000015	0.0426	65	72.380	0.88388	0.000018	0.0426
66	58.241	0.89955	0.000016	0.0420	66	73.299	0.88153	0.000019	0.0426
67	59.279	0.89717	0.000016	0.0410	67	74.211	0.87918	0.000019	0.0426
68	60.325	0.89477	0.000016	0.0408	68	75.117	0.87683	0.000019	0.0422
69	61.379	0.89232	0.000017	0.0407	69	76.016	0.87446	0.000020	0.0422
70	62.441	0.88986	0.000017	0.0403	70	76.909	0.87206	0.000020	0.0418
71	63.511	0.88738	0.000018	0.0395	71	77.794	0.86970	0.000021	0.0417
72	64.588	0.88485	0.000018	0.0392	72	78.672	0.86730	0.000021	0.0417
73	65.674	0.88230	0.000019	0.0389	73	79.544	0.86490	0.000021	0.0417
74	66.768	0.87973	0.000019	0.0385	74	80.410	0.86250	0.000022	0.0413
75	67.870	0.87713	0.000019	0.0380	75	81.269	0.86008	0.000022	0.0413
76	68.982	0.87450	0.000020	0.0376	76	82.121	0.85766	0.000022	0.0413
77	70.102	0.87184	0.000020	0.0370	77	82.967	0.85524	0.000023	0.0412
78	71.234	0.86914	0.000021	0.0365	78	83.805	0.85281	0.000023	0.0403
79	72.375	0.86640	0.000021	0.0362	79	84.636	0.85033	0.000024	0.0408
80	73.526	0.86364	0.000021	0.0357	80	85.459	0.84788	0.000024	0.0403
81	74.686	0.86084	0.000022	0.0352	81	86.275	0.84540	0.000024	0.0402
82	75.858	0.85800	0.000022	0.0350	82	87.083	0.84291	0.000025	0.0402
83	77.039	0.85514	0.000023	0.0344	83	87.885	0.84042	0.000025	0.0398
84	78.233	0.85223	0.000023	0.0337	84	88.678	0.83791	0.000025	0.0394
85	79.441	0.84926	0.000024	0.0331	85	89.464	0.83537	0.000026	0.0392
86	80.662	0.84624	0.000024	0.0326	86	90.240	0.83282	0.000026	0.0391
87	81.897	0.84317	0.000025	0.0322	87	91.008	0.83026	0.000027	0.0386
88	83.144	0.84006	0.000025	0.0314	88	91.766	0.82767	0.000027	0.0377
89	84.408	0.83688	0.000026	0.0307	89	92.517	0.82502	0.000028	0.0380
90	85.689	0.83362	0.000026	0.0300	90	93.254	0.82239	0.000028	0.0372
91	86.989	0.83029	0.000027	0.0291	91	93.982	0.81970	0.000028	0.0367
92	88.310	0.82685	0.000027	0.0282	92	94.700	0.81697	0.000029	0.0362
93	89.652	0.82330	0.000028	0.0272	93	95.407	0.81421	0.000029	0.0358
94	91.025	0.81963	0.000028	0.0262	94	96.103	0.81142	0.000030	0.0353
95	92.423	0.81581	0.000029	0.0252	95	96.787	0.80859	0.000030	0.0348
96	93.851	0.81184	0.000030	0.0240	96	97.457	0.80572	0.000030	0.0342
97	95.315	0.80769	0.000030	0.0229	97	98.117	0.80280	0.000031	0.0334
98	96.820	0.80333	0.000031	0.0214	98	98.759	0.79981	0.000031	0.0328
99	98.381	0.79865	0.000031	0.0200	99	99.386	0.79676	0.000032	0.0322
100	100.000	0.79365	0.000032		100	100.000	0.79365	0.000032	

Temperature Corrections (U. S. P. X.)

For volume per cent. of Alcohol by the foregoing Alcoholometric Table

Temp. C. 15.56°	Observed Per cent.—Alcohol by volume											
	1	2	3	4	5	6	7	8	9	10	13	14
	Subtract from observed per cent. of alcohol											
16	0.04	0.04	0.05	0.05	0.05	0.05	0.05	0.06	0.06	0.06	0.07	0.08
17	0.14	0.14	0.16	0.16	0.16	0.17	0.17	0.19	0.20	0.21	0.24	0.29
18	0.25	0.25	0.27	0.27	0.27	0.29	0.31	0.33	0.35	0.37	0.42	0.49
19	0.36	0.36	0.38	0.39	0.40	0.43	0.45	0.48	0.51	0.54	0.61	0.69
20	0.48	0.48	0.50	0.52	0.54	0.57	0.60	0.64	0.67	0.71	0.80	0.91
21	0.60	0.61	0.63	0.65	0.68	0.71	0.75	0.80	0.84	0.89	0.99	1.12
22	0.73	0.75	0.77	0.79	0.83	0.86	0.91	0.97	1.02	1.07	1.19	1.35
23	0.86	0.89	0.91	0.94	0.98	1.02	1.08	1.14	1.20	1.26	1.40	1.58
24	1.00	1.04	1.06	1.10	1.14	1.20	1.25	1.32	1.38	1.45	1.61	1.81
25		1.19	1.22	1.26	1.30	1.36	1.41	1.49	1.57	1.65	1.82	2.04
26		1.35	1.38	1.43	1.47	1.54	1.60	1.68	1.76	1.85	2.04	2.28
27		1.52	1.55	1.61	1.65	1.73	1.79	1.88	1.96	2.06	2.27	2.52
28		1.69	1.73	1.78	1.84	1.91	1.99	2.08	2.17	2.28	2.50	2.76
29		1.87	1.91	1.96	2.03	2.10	2.19	2.28	2.38	2.50	2.73	3.00
30			2.09	2.15	2.22	2.30	2.39	2.49	2.60	2.72	2.97	3.25
31			2.27	2.34	2.41	2.50	2.60	2.70	2.82	2.85	3.21	3.51
32			2.45	2.54	2.61	2.71	2.82	2.92	3.05	3.18	3.46	3.77
33			2.63	2.74	2.81	2.92	3.04	3.15	3.28	3.42	3.71	4.03
34			2.82	2.95	3.02	3.14	3.27	3.39	3.52	3.66	3.96	4.29
35				3.16	3.24	3.36	3.49	3.63	3.76	3.91	4.22	4.55

Temp. C. 15.56°	Observed per cent.—Alcohol by volume											
	16	18	20	22	24	26	28	30	32	34	37	40
	Subtract from observed per cent. of alcohol											
16	0.10	0.12	0.13	0.14	0.15	0.16	0.17	0.18	0.19	0.19	0.19	0.18
17	0.33	0.38	0.42	0.46	0.50	0.54	0.57	0.59	0.60	0.60	0.59	0.58
18	0.56	0.65	0.73	0.79	0.84	0.89	0.95	0.99	1.00	1.01	1.00	0.98
19	0.80	0.91	1.02	1.11	1.19	1.27	1.33	1.39	1.40	1.41	1.41	1.39
20	1.04	1.18	1.32	1.44	1.54	1.64	1.72	1.79	1.81	1.82	1.81	1.79
21	1.28	1.45	1.61	1.76	1.88	2.00	2.10	2.18	2.21	2.22	2.22	2.19
22	1.53	1.73	1.91	2.07	2.21	2.35	2.47	2.57	2.60	2.63	2.63	2.59
23	1.78	2.00	2.21	2.39	2.55	2.71	2.84	2.95	3.00	3.03	3.03	3.00
24	2.04	2.28	2.51	2.71	2.88	3.06	3.21	3.34	3.40	3.44	3.44	3.40
25	2.29	2.56	2.81	3.03	3.22	3.41	3.58	3.73	3.80	3.84	3.85	3.80
26	2.55	2.83	3.11	3.35	3.56	3.77	3.95	4.11	4.20	4.25	4.26	4.21
27	2.80	3.11	3.41	3.68	3.91	4.13	4.32	4.50	4.59	4.65	4.67	4.62
28	3.06	3.38	3.71	4.00	4.25	4.49	4.70	4.88	4.99	5.05	5.07	5.02
29	3.32	3.66	4.01	4.33	4.60	4.85	5.06	5.26	5.38	5.46	5.48	5.43
30	3.58	3.94	4.31	4.65	4.94	5.21	5.43	5.64	5.77	5.86	5.89	5.84
31	3.85	4.22	4.61	4.97	5.28	5.56	5.80	6.01	6.16	6.26	6.29	6.24
32	4.12	4.51	4.92	5.30	5.62	5.91	6.16	6.39	6.54	6.65	6.70	6.65
33	4.40	4.80	5.22	5.62	5.95	6.26	6.50	6.76	6.92	7.04	7.10	7.05
34	4.67	5.09	5.54	5.94	6.29	6.62	6.90	7.13	7.30	7.44	7.51	7.46
35	4.94	5.39	5.86	6.27	6.63	6.97	7.26	7.50	7.67	7.83	7.91	7.86

Temperature Corrections—*Continued.*

For volume per cent. of Alcohol by the foregoing Alcoholometric Table

Temp. C. 15.56°	Observed per cent.—Alcohol by volume											
	43	46	49	52	55	58	61	64	67	70	73	76
	Subtract from observed per cent. of alcohol											
16	0.18	0.18	0.17	0.17	0.16	0.16	0.16	0.16	0.16	0.15	0.15	0.14
17	0.57	0.56	0.55	0.53	0.52	0.51	0.50	0.49	0.48	0.47	0.46	0.45
18	0.97	0.95	0.93	0.90	0.88	0.86	0.85	0.83	0.82	0.80	0.79	0.76
19	1.37	1.34	1.30	1.27	1.25	1.22	1.19	1.17	1.14	1.12	1.11	1.08
20	1.76	1.72	1.68	1.64	1.61	1.57	1.54	1.51	1.48	1.45	1.42	1.39
21	2.15	2.11	2.06	2.02	1.98	1.94	1.90	1.85	1.82	1.79	1.75	1.70
22	2.55	2.50	2.44	2.39	2.34	2.29	2.24	2.20	2.16	2.12	2.07	2.02
23	2.94	2.89	2.82	2.76	2.71	2.66	2.60	2.55	2.50	2.46	2.39	2.33
24	3.34	3.28	3.21	3.14	3.07	3.01	2.95	2.90	2.84	2.79	2.72	2.65
25	3.74	3.67	3.60	3.52	3.44	3.37	3.31	3.24	3.18	3.13	3.05	2.97
26	4.14	4.07	3.98	3.89	3.81	3.74	3.67	3.59	3.53	3.47	3.38	3.29
27	4.55	4.47	4.37	4.27	4.18	4.10	4.02	3.95	3.87	3.80	3.71	3.62
28	4.95	4.86	4.76	4.65	4.56	4.48	4.39	4.31	4.22	4.14	4.04	3.95
29	5.35	5.26	5.15	5.04	4.93	4.84	4.75	4.66	4.75	4.48	4.38	4.27
30	5.75	5.66	5.53	5.41	5.30	5.20	5.11	5.01	4.91	4.82	4.71	4.59
31	6.15	6.06	5.92	5.79	5.67	5.57	5.48	5.37	5.27	5.17	5.05	4.93
32	6.56	6.46	6.32	6.19	6.05	5.95	5.84	5.73	5.62	5.51	5.39	5.26
33	6.96	6.85	6.72	6.57	6.43	6.32	6.20	6.09	5.97	5.86	5.73	5.59
34	7.36	7.25	7.12	6.96	6.81	6.69	6.56	6.44	6.32	6.21	6.07	5.92
35	7.76	7.65	7.51	7.35	7.19	7.06	6.93	6.80	6.68	6.56	6.41	6.25

Temp. C. 15.56°	Observed per cent.—Alcohol by volume										
	79	82	84	86	88	90	92	94	96	98	100
	Subtract from observed per cent. of alcohol										
16	0.13	0.13	0.13	0.13	0.12	0.12	0.11	0.10	0.10	0.09	0.08
17	0.44	0.42	0.41	0.41	0.39	0.38	0.36	0.33	0.31	0.27	0.24
18	0.74	0.71	0.70	0.69	0.66	0.63	0.60	0.56	0.52	0.46	0.40
19	1.04	1.00	0.98	0.96	0.93	0.89	0.85	0.79	0.73	0.65	0.57
20	1.34	1.30	1.28	1.24	1.20	1.15	1.09	1.02	0.94	0.85	0.74
21	1.66	1.60	1.57	1.53	1.47	1.42	1.34	1.26	1.16	1.05	0.92
22	1.97	1.90	1.86	1.82	1.75	1.69	1.60	1.50	1.39	1.26	1.09
23	2.27	2.20	2.15	2.10	2.03	1.96	1.86	1.75	1.61	1.46	1.27
24	2.58	2.50	2.45	2.39	2.31	2.23	2.12	1.99	1.84	1.67	1.45
25	2.89	2.81	2.75	2.68	2.60	2.50	2.38	2.23	2.07	1.88	1.63
26	3.21	3.11	3.05	2.96	2.89	2.78	2.64	2.48	2.31	2.10	1.82
27	3.52	3.42	3.35	3.27	3.17	3.05	2.91	2.74	2.54	2.31	2.00
28	3.84	3.73	3.65	3.57	3.46	3.33	3.18	2.99	2.78	2.53	2.19
29	4.16	4.04	3.96	3.86	3.74	3.61	3.45	3.25	3.02	2.75	2.38
30	4.47	4.34	4.26	4.16	4.03	3.89	3.72	3.51	3.26	2.98	2.58
31	4.79	4.66	4.56	4.46	4.32	4.18	3.99	3.77	3.51	3.21	2.78
32	5.12	4.98	4.88	4.77	4.62	4.46	4.27	4.03	3.76	3.45	2.99
33	5.45	5.30	5.19	5.07	4.92	4.75	4.54	4.30	4.01	3.68	3.19
34	5.77	5.62	5.51	5.38	5.22	5.03	4.82	4.56	4.26	3.92	3.40
35	6.09	5.94	5.82	5.69	5.52	5.32	5.09	4.82	4.52	4.15	3.61

Acid and Alkali Tables.

U.S.

Specific gravity.—The term "specific gravity" in the tables which follow represents the quotient obtained by dividing the weight of a volume of the liquid by the weight of an equal volume of distilled water, both measured at the same temperature and weighed in air with brass weights. The tables include specific gravity figures for 25° C., the official temperature and also for 15° C.

Percentage.—The percentage strength of acetic, hydrochloric, nitric, and sulphuric acids and of ammonia water can be calculated from their specific gravity by reference to the tables. For the determination of the percentage by the specific gravity, it is preferable to take the specific gravity at the temperature for which figures are given in the tables, at 25° or 15° C. If it is found inconvenient to determine it at these temperatures, the specific gravity may be taken at the prevailing room temperature and the correction for the specific gravity at standard temperature made from the figures in column 4 and the per cent. of acid or ammonia water ascertained from columns 2 (or 3) and 5 in the following manner:

Example: A sample of dilute sulphuric acid has an apparent specific gravity at 21° C. (room temperature), by a pycnometer standardized at 25° C., of 1.1457. The correction for 4° C. (subtractive) is $0.000561 \times 4 = 0.0022$ (from column 4). The corrected specific gravity, $1.1457 - 0.0022 = 1.1435$. The nearest lower figure in column 2 is 1.1400, showing (column 1) 20 per cent. of acid. For the fractional per cent., multiply the difference ($1.1435 - 1.1400 = 0.0035$, taken as 35) by 0.0132 (column 5); the product is 0.462. The strength is therefore 20.462 per cent.

Normality.—Column 6 shows the "normality,"—*i.e.*, the neutralizing power of the acid or alkali. If the figure in this column is 2.74, one volume of the acid diluted with water to make 2.74 volumes will be of "normal" strength. It is therefore easy by the aid of these figures to prepare volumetric solutions of approximately any desired strength $\left(\frac{N}{1}, \frac{N}{10}, \frac{N}{40}, \text{etc}\right)$, from an acid or alkali or known percentage strength. For accurate work such solutions must of course be standardized by the usual methods. (See Volumetric Solutions).

The chief use, however, of the normality column is for the determination directly by titration of the percentage strength of an acid or alkali of unknown specific gravity.

Example: 1 cc. (accurately measured) of a sample of acetic acid of unknown strength is found to require for neutralization 4.62 cc. of normal potassium hydroxide V.S. The nearest lower figure in column 6 is 4.465, corresponding with 26 per cent. For the fractional per cent., multiply the difference ($4.620 - 4.465 = 0.155$, taken as 15.5) by 0.0565 (column 7). The product is 0.8757. The strength is therefore 26.87+ per cent.

Acetic Acid

Per cent. $HC_2H_3O_2$	Sp. gr. app. $\frac{25° C.}{25° C.}$	Sp. gr. app. $\frac{15° C.}{15° C.}$	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils	Per cent. = 0.01 mil normal KOH.
‡0	1.0000	1.0000	0.00018	0.0714	0.000	0.0599
1	1.0014	1.0015	0.00019	0.0714	0.167	0.0602
2	1.0028	1.0030	0.00020	0.0714	0.333	0.0595
3	1.0042	1.0045	0.00022	0.0714	0.501	0.0599
4	1.0056	1.0060	0.00023	0.0714	0.668	0.0595
5	1.0070	1.0075	0.00024	0.0769	0.836	0.0592
6	1.0083	1.0090	0.00025	0.0714	1.005	0.0592
7	1.0097	1.0105	0.00026	0.0714	1.174	0.0588
8	1.0111	1.0120	0.00028	0.0769	1.344	0.0588
9	1.0124	1.0135	0.00029	0.0714	1.514	0.0588
10	1.0138	1.0150	0.00030	0.0769	1.684	0.0585
11	1.0151	1.0165	0.00031	0.0714	1.855	0.0585
12	1.0165	1.0179	0.00033	0.0769	2.026	0.0581
13	1.0178	1.0193	0.00034	0.0769	2.198	0.0581
14	1.0191	1.0208	0.00036	0.0769	2.370	0.0581
15	1.0204	1.0222	0.00037	0.0769	2.542	0.0578
16	1.0217	1.0236	0.00038	0.0833	2.715	0.0578
17	1.0229	1.0251	0.00040	0.0769	2.888	0.0575
18	1.0242	1.0265	0.00041	0.0833	3.062	0.0575
19	1.0254	1.0279	0.00043	0.0833	3.236	0.0571
20	1.0266	1.0293	0.00044	0.0769	3.411	0.0571
21	1.0279	1.0307	0.00045	0.0833	3.586	0.0571
22	1.0291	1.0320	0.00046	0.0833	3.761	0.0571
23	1.0303	1.0333	0.00048	0.0833	3.936	0.0568
24	1.0315	1.0346	0.00049	0.0833	4.112	0.0568
25	1.0327	1.0359	0.00050	0.0909	4.288	0.0565
26	1.0338	1.0372	0.00051	0.0833	4.465	0.0565
27	1.0350	1.0384	0.00053	0.0909	4.642	0.0565
28	1.0361	1.0397	0.00054	0.0909	4.819	0.0565
29	1.0372	1.0409	0.00055	0.0909	4.996	0.0562
30	1.0383	1.0421	0.00056	0.0909	5.174	0.0562
31	1.0394	1.0433	0.00057	0.1000	5.352	0.0562
32	1.0404	1.0445	0.00059	0.0909	5.530	0.0559
33	1.0415	1.0456	0.00060	0.1000	5.709	0.0559
34	1.0425	1.0468	0.00062	0.1000	5.888	0.0559
35	1.0435	1.0479	0.00063	0.1000	6.067	0.0559
36	1.0445	1.0490	0.00064	0.1000	6.246	0.0559
37	1.0455	1.0501	0.00065	0.1111	6.425	0.0559
38	1.0464	1.0511	0.00066	0.1000	6.604	0.0556
39	1.0474	1.0522	0.00067	0.1111	6.784	0.0556
40	1.0483	1.0532	0.00068	0.1111	6.964	0.0556
41	1.0492	1.0542	0.00069	0.1111	7.144	0.0552
42	1.0501	1.0552	0.00070	0.1111	7.325	0.0552
43	1.0510	1.0561	0.00070	0.1250	7.506	0.0552
44	1.0518	1.0571	0.00071	0.1111	7.687	0.0552
45	1.0527	1.0580	0.00072	0.1250	7.868	0.0549
46	1.0535	1.0589	0.00073	0.1250	8.050	0.0552
47	1.0543	1.0598	0.00074	0.1250	8.231	0.0552
48	1.0551	1.0607	0.00075	0.1429	8.412	0.0552
49	1.0558	1.0616	0.00076	0.1250	8.593	0.0549
50	1.0566	1.0624	0.00077	0.1429	8.775	0.0552

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* Add if the temperature is above, subtract if it is below the standard.
† Corresponding with a difference in specific gravity of 0.0001.
‡ The figures on this line across the page are for fractional percentages below 1.

Acetic Acid—Continued

Per cent. $HC_2H_3O_2$	Sp. gr. app. 25° C./25° C.	Sp. gr. app. 15° C./15° C.	Correction of specific gravity for 1° C.	Fractional per cent.	Normality. 1 mil requires normal KOH mils	Per cent. = 0.01 mil normal KOH.
51	1.0573	1.0632	0.00077	0.1429	8.956	0.0549
52	1.0580	1.0640	0.00078	0.1429	9.138	0.0552
53	1.0587	1.0647	0.00079	0.1667	9.319	0.0549
54	1.0593	1.0655	0.00079	0.1429	9.501	0.0549
55	1.0600	1.0662	0.00080	0.1667	9.683	0.0549
56	1.0606	1.0669	0.00081	0.1667	9.865	0.0549
57	1.0612	1.0675	0.00081	0.1667	10.047	0.0549
58	1.0618	1.0682	0.00082	0.1667	10.229	0.0549
59	1.0624	1.0688	0.00083	0.2000	10.411	0.0549
60	1.0629	1.0694	0.00084	0.2000	10.593	0.0549
61	1.0634	1.0700	0.00084	0.2000	10.775	0.0549
62	1.0639	1.0706	0.00085	0.2000	10.957	0.0552
63	1.0644	1.0711	0.00086	0.2500	11.138	0.0549
64	1.0648	1.0716	0.00086	0.2500	11.320	0.0552
65	1.0652	1.0721	0.00087	0.2500	11.501	0.0552
66	1.0656	1.0726	0.00087	0.2500	11.682	0.0549
67	1.0660	1.0730	0.00088	0.2500	11.864	0.0552
68	1.0664	1.0734	0.00089	0.2500	12.045	0.0552
69	1.0668	1.0738	0.00089	0.3333	12.226	0.0552
70	1.0671	1.0742	0.00090	0.3333	12.407	0.0556
71	1.0674	1.0746	0.00090	0.5000	12.587	0.0556
72	1.0676	1.0749	0.00091	0.5000	12.767	0.0559
73	1.0678	1.0751	0.00092	1.0000	12.946	0.0559
74	1.0679	1.0753	0.00092	1.0000	13.125	0.0559
75	1.0680	1.0755	0.00093	1.0000	13.304	0.0562
76	1.0681	1.0756	0.00093	......	13.482	0.0562
77	1.0681	1.0757	0.00094	......	13.660	0.0562
78	1.0681	1.0757	0.00094	......	13.838	0.0565
79	1.0681*	1.0757	0.00095	1.0000	14.015	0.0565
80	1.0680	1.0757	0.00096	0.5000	14.192	0.0571
81	1.0678	1.0756	0.00096	0.5000	14.367	0.0571
82	1.0676	1.0755	0.00097	0.5000	14.542	0.0575
83	1.0674	1.0753	0.00097	0.3333	14.716	0.0578
84	1.0671	1.0751	0.00098	0.2500	14.889	0.0581
85	1.0667	1.0748	0.00099	0.2500	15.061	0.0585
86	1.0663	1.0745	0.00099	0.2000	15.232	0.0592
87	1.0658	1.0740	0.00100	0.1667	15.401	0.0592
88	1.0652	1.0735	0.00101	0.1667	15.570	0.0599
89	1.0646	1.0729	0.00102	0.1250	15.737	0.0602
90	1.0638	1.0722	0.00103	0.1111	15.903	0.0610
91	1.0629	1.0714	0.00103	0.1111	16.067	0.0617
92	1.0620	1.0705	0.00103	0.0833	16.229	0.0629
93	1.0608	1.0695	0.00104	0.0833	16.388	0.0637
94	1.0596	1.0683	0.00104	0.0714	16.545	0.0654
95	1.0582	1.0669	0.00105	0.0588	16.698	0.0676
96	1.0565	1.0653	0.00106	0.0526	16.846	0.0694
97	1.0546	1.0634	0.00106	0.0455	16.990	0.0709
98	1.0524	1.0613	0.00107	0.0400	17.131	0.0746
99	1.0499	1.0589	0.00108	0.0357	17.265	0.0781
100	1.0471	1.0562	0.00109	......	17.393	......

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* Below this point the specific gravity diminishes as the strength of the acid increases.

NOTE: If the specific gravity of the acid is greater than 1.045, mix some of the acid with an equal weight of water and take the specific gravity of the mixture, then multiply the corresponding percentage taken from the table by two. It is better, however, to determine the strength of any sample of acetic acid by its normality.

To find the volume per cent. of official Acetic Acid (36 per cent.) multiply the "normality" by 16.01. For the volume per cent. of Acetic Acid ($HC_2H_3O_2$), multiply the "normality" by 5.751. For the volume per cent. of official Diluted Acetic Acid (6 per cent.), multiply the "normality" by 99.5.

Table of Percentage and Specific Gravity of Hydrochloric Acid.
U. S. P. X.

Per cent. HCl	Sp. gr. app. 25° C./25° C.	Sp. gr. app. 15° C./15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils.	Per cent. = 0.01 mil normal KOH.
‡0	1.0000	1.0000	0.00018	0.0203	0.000	0.0362
1	1.0049	1.0050	0.00018	0.0204	0.276	0.0360
2	1.0098	1.0099	0.00019	0.0204	0.554	0.0357
3	1.0147	1.0149	0.00020	0.0205	0.834	0.0355
4	1.0196	1.0198	0.00020	0.0206	1.116	0.0352
5	1.0245	1.0247	0.00021	0.0207	1.400	0.0345
6	1.0293	1.0296	0.00022	0.0207	1.690	0.0344
7	1.0341	1.0346	0.00023	0.0208	1.981	0.0341
8	1.0389	1.0395	0.00024	0.0209	2.274	0.0339
9	1.0437	1.0444	0.00025	0.0210	2.569	0.0336
10	1.0485	1.0493	0.00027	0.0210	2.867	0.0332
11	1.0532	1.0542	0.00029	0.0211	3.168	0.0329
12	1.0580	1.0591	0.00030	0.0211	3.472	0.0327
13	1.0627	1.0640	0.00032	0.0212	3.778	0.0325
14	1.0674	1.0689	0.00034	0.0211	4.086	0.0322
15	1.0722	1.0738	0.00036	0.0211	4.397	0.0318
16	1.0769	1.0788	0.00038	0.0210	4.711	0.0316
17	1.0817	1.0837	0.00039	0.0209	5.027	0.0313
18	1.0865	1.0886	0.00041	0.0209	5.346	0.0311
19	1.0912	1.0936	0.00043	0.0209	5.668	0.0308
20	1.0960	1.0986	0.00045	0.0207	5.993	0.0306
21	1.1009	1.1036	0.00047	0.0205	6.320	0.0303
22	1.1057	1.1086	0.00049	0.0203	6.650	0.0300
23	1.1107	1.1137	0.00051	0.0202	6.983	0.0298
24	1.1156	1.1189	0.00053	0.0200	7.319	0.0295
25	1.1206	1.1241	0.00055	0.0201	7.658	0.0292
26	1.1256	1.1293	0.00057	0.0202	8.000	0.0290
27	1.1305	1.1344	0.00059	0.0203	8.345	0.0288
28	1.1355	1.1395	0.00061	0.0203	8.692	0.0287
29	1.1404	1.1446	0.00062	0.0203	9.041	0.0284
30	1.1453	1.1497	0.00064	0.0202	9.393	0.0281
31	1.1503	1.1548	0.00066	0.0203	9.749	0.0280
32	1.1532	1.1599	0.00068	0.0203	10.106	0.0278
33	1.1601	1.1650	0.00069	0.0203	10.466	0.0275
34	1.1651	1.1700	0.00070	0.0203	10.829	0.0274
35	1.1700	1.1751	0.00072	0.0209	11.194	0.0272
36	1.1748	1.1800	0.00073	0.0212	11.561	0.0271
37	1.1795	1.1848	0.00074	0.0216	11.930	0.0270
38	1.1841	1.1895	0.00075	0.0220	12.301	0.0267
39	1.1886	1.1941	0.00076	0.0221	12.675	0.0266
40	1.1931	1.1986	0.00077	......	13.051	......

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* Add if the temperature is above, subtract if it is below, the standard.
† Corresponding with a difference in specific gravity of 0.0001.
‡ The figures on this line across the page are for fractional percentages below 1.

NOTE: To find the per cent. of chlorine, multiply the per cent. of Hydrochloric Acid by 0.9724.

For the volume per cent. of official Hydrochloric Acid (32 per cent.), multiply the "normality" by 9.895. For the volume per cent. of official Diluted Hydrochloric Acid (10 per cent.), multiply the "normality" by 34.88.

Table showing percentage of HNO_3 in Nitric Acid of different densities. U. S. X.

Per cent. HNO_3	Sp. gr. app. 25° C./25° C.	Sp. gr. app. 15° C./15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils.	Per cent. = 0.01 mil normal KOH.
‡0	1.0000	1.0000	0.000180	0.0182	0.000	0.0629
1	1.0055	1.0056	0.000191	0.0185	0.159	0.0621
2	1.0109	1.0111	0.000201	0.0185	0.320	0.0617
3	1.0163	1.0165	0.000210	0.0185	0.482	0.0606
4	1.0217	1.0221	0.000215	0.0182	0.647	0.0602
5	1.0272	1.0277	0.000228	0.0182	0.813	0.0595
6	1.0327	1.0334	0.000255	0.0179	0.981	0.0588
7	1.0383	1.0392	0.000278	0.0175	1.151	0.0585
8	1.0440	1.0451	0.000299	0.0175	1.322	0.0575
9	1.0497	1.0510	0.000319	0.0172	1.496	0.0568
10	1.0555	1.0570	0.000335	0.0172	1.672	0.0568
11	1.0613	1.0630	0.000355	0.0169	1.848	0.0559
12	1.0672	1.0690	0.000374	0.0169	2.027	0.0556
13	1.0731	1.0751	0.000393	0.0169	2.207	0.0546
14	1.0790	1.0812	0.000415	0.0167	2.390	0.0543
15	1.0850	1.0874	0.000436	0.0167	2.574	0.0532
16	1.0910	1.0937	0.000455	0.0161	2.762	0.0529
17	1.0972	1.1000	0.000474	0.0161	2.951	0.0524
18	1.1034	1.1064	0.000492	0.0159	3.142	0.0518
19	1.1097	1.1128	0.000512	0.0161	3.335	0.0510
20	1.1159	1.1192	0.000530	0.0161	3.531	0.0508
21	1.1221	1.1256	0.000550	0.0159	3.728	0.0503
22	1.1284	1.1321	0.000569	0.0161	3.927	0.0495
23	1.1346	1.1385	0.000588	0.0159	4.129	0.0493
24	1.1409	1.1449	0.000604	0.0156	4.332	0.0488
25	1.1473	1.1514	0.000618	0.0156	4.537	0.0478
26	1.1537	1.1580	0.000635	0.0154	4.746	0.0476
27	1.1602	1.1647	0.000651	0.0156	4.956	0.0472
28	1.1668	1.1714	0.000666	0.0154	5.168	0.0465
29	1.1734	1.1781	0.000682	0.0154	5.383	0.0461
30	1.1800	1.1848	0.000696	0.0154	5.600	0.0459
31	1.1866	1.1916	0.000714	0.0149	5.818	0.0450
32	1.1933	1.1985	0.000727	0.0147	6.040	0.0448
33	1.2001	1.2054	0.000742	0.0149	6.263	0.0441
34	1.2068	1.2123	0.000763	0.0147	6.490	0.0439
35	1.2135	1.2191	0.000786	0.0152	6.718	0.0435
36	1.2201	1.2260	0.000810	0.0152	6.948	0.0431
37	1.2267	1.2329	0.000830	0.0149	7.180	0.0427
38	1.2334	1.2397	0.000849	0.0152	7.414	0.0424
39	1.2400	1.2464	0.000865	0.0152	7.650	0.0420
40	1.2466	1.2531	0.000879	0.0154	7.888	0.0418
41	1.2531	1.2598	0.000895	0.0154	8.127	0.0415
42	1.2596	1.2665	0.000915	0.0156	8.368	0.0412
43	1.2660	1.2731	0.000932	0.0156	8.611	0.0408
44	1.2724	1.2797	0.000952	0.0156	8.856	0.0405
45	1.2788	1.2862	0.000973	0.0159	9.103	0.0403
46	1.2851	1.2927	0.000992	0.0161	9.351	0.0402
47	1.2913	1.2991	0.001011	0.0161	9.600	0.0397
48	1.2975	1.3055	0.001032	0.0161	9.852	0.0395
49	1.3037	1.3119	0.001053	0.0164	10.105	0.0394
50	1.3098	1.3182	0.001076	0.0169	10.359	0.0392
51	1.3157	1.3243	0.001085	0.0169	10.614	0.0389
52	1.3216	1.3304	0.001115	0.0175	10.871	0.0389
53	1.3273	1.3363	0.001134	0.0179	11.128	0.0389
54	1.3329	1.3421	0.001154	0.0182	11.385	0.0389
55	1.3384	1.3477	0.001173	0.0185	11.643	0.0386

* Add if the temperature is above, subtract if it is below, the standard.

† Corresponding with a difference in specific gravity of 0.0001.

‡ The figures on this line across the page are for fractional percentages below 1.

Table showing percentage of HNO_3 in Nitric Acid of different densities (Continued).

Per cent. HNO_3	Sp. gr. app. 25° C. / 25° C.	Sp. gr. app. 15° C. / 15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils.	Per cent. = 0.01 mil normal KOH.
56	1.3438	1.3533	0.001191	0.0192	11.902	0.0385
57	1.3490	1.3587	0.001211	0.0196	12.162	0.0385
58	1.3541	1.3640	0.001229	0.0200	12.422	0.0383
59	1.3591	1.3692	0.001250	0.0204	12.683	0.0383
60	1.3640	1.3742	0.001269	0.0208	12.944	0.0383
61	1.3688	1.3792	0.001287	0.0213	13.205	0.0382
62	1.3735	1.3841	0.001305	0.0213	13.467	0.0377
63	1.3782	1.3890	0.001321	0.0213	13.732	0.0376
64	1.3829	1.3938	0.001338	0.0213	13.998	0.0373
65	1.3876	1.3987	0.001352	0.0208	14.266	0.0372
66	1.3924	1.4035	0.001365	0.0213	14.535	0.0369
67	1.3971	1.4083	0.001372	0.0213	14.806	0.0369
68	1.4018	1.4131	0.001382	0.0213	15.077	0.0366
69	1.4065	1.4179	0.001389	0.0213	15.350	0.0365
70	1.4112	1.4226	0.001397	0.0213	15.624	0.0362
71	1.4159	1.4273	0.001404	0.0217	15.900	0.0361
72	1.4205	1.4320	0.001412	0.0222	16.177	0.0360
73	1.4250	1.4366	0.001419	0.0227	16.455	0.0361
74	1.4294	1.4411	0.001427	0.0233	16.732	0.0365
75	1.4336	1.4454	0.001439	0.0278	17.006	0.0372
76	1.4372	1.4491	0.001442	0.0286	17.275	0.0372
77	1.4407	1.4527	0.001454	0.0303	17.544	0.0373
78	1.4440	1.4561	0.001469	0.0323	17.812	0.0372
79	1.4471	1.4595	0.001491	0.0333	18.081	0.0373
80	1.4501	1.4627	0.001515	0.0333	18.349	0.0372
81	1.4531	1.4659	0.001542	0.0333	18.618	0.0373
82	1.4561	1.4691	0.001564	0.0345	18.886	0.0372
83	1.4590	1.4721	0.001577	0.0345	19.155	0.0372
84	1.4619	1.4751	0.001583	0.0345	19.424	0.0372
85	1.4648	1.4780	0.001580	0.0345	19.693	0.0369
86	1.4677	1.4809	0.001578	0.0333	19.964	0.0366
87	1.4707	1.4838	0.001573	0.0345	20.237	0.0362
88	1.4736	1.4867	0.001569	0.0345	20.513	0.0364
89	1.4765	1.4895	0.001562	0.0333	20.788	0.0368
90	1.4795	1.4924	0.001553	0.0400	21.060	0.0377
91	1.4819	1.4949	0.001564	0.0435	21.325	0.0377
92	1.4842	1.4973	0.001575	0.0500	21.590	0.0377
93	1.4862	1.4994	0.001586	0.0526	21.855	0.0377
94	1.4881	1.5015	0.001597	0.0556	22.120	0.0377
95	1.4899	1.5033	0.001608	0.0588	22.385	0.0350
96	1.4916	1.5053	0.001631	0.0357	22.671	0.0344
97	1.4944	1.5083	0.001658	0.0270	22.962	0.0340
98	1.4981	1.5123	0.001683	0.0217	23.256	0.0336
99	1.5027	1.5171	0.001708	0.0175	23.554	0.0330
100	1.5084	1.5230	0.001732	......	23.857	......

NOTE: To find the per cent. of N_2O_5, multiply the per cent. of HNO_3 by 0.85703. To find the per cent. of NO_3, multiply the per cent. of HNO_3 by 0.98397. To find the volume per cent. of official Nitric Acid (68 per cent.), multiply the "normality" by 6.633. For the volume per cent. of official Diluted Nitric Acid (10 per cent.), multiply the "normality" by 59.81.

Table of Percentage and Specific Gravity of Sulphuric Acid. U. S. X.

Per cent. H_2SO_4	Sp. gr. app. 25° C. / 25° C.	Sp. gr. app. 15° C. / 15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils.	Per cent. = 0.01 mil normal KOH.
‡0	1.0000	1.0000	0.000180	0.0147	0.000	0.0488
1	1.0068	1.0070	0.000200	0.0152	0.205	0.0483
2	1.0134	1.0139	0.000221	0.0154	0.412	0.0476
3	1.0199	1.0206	0.000241	0.0152	0.622	0.0469
4	1.0265	1.0274	0.000262	0.0152	0.835	0.0465
5	1.0331	1.0342	0.000282	0.0149	1.050	0.0459
6	1.0398	1.0411	0.000302	0.0147	1.268	0.0452
7	1.0466	1.0480	0.000323	0.0147	1.489	0.0446
8	1.0534	1.0550	0.000343	0.0145	1.713	0.0441
9	1.0603	1.0621	0.000363	0.0145	1.940	0.0437
10	1.0672	1.0692	0.000384	0.0143	2.169	0.0429
11	1.0742	1.0764	0.000404	0.0143	2.402	0.0424
12	1.0812	1.0836	0.000424	0.0139	2.638	0.0420
13	1.0884	1.0909	0.000444	0.0141	2.876	0.0413
14	1.0955	1.0983	0.000464	0.0139	3.118	0.0410
15	1.1027	1.1057	0.000484	0.0135	3.362	0.0403
16	1.1101	1.1132	0.000500	0.0135	3.610	0.0398
17	1.1175	1.1207	0.000516	0.0135	3.861	0.0392
18	1.1249	1.1283	0.000531	0.0133	4.116	0.0388
19	1.1324	1.1360	0.000546	0.0132	4.374	0.0385
20	1.1400	1.1437	0.000561	0.0132	4.634	0.0377
21	1.1476	1.1515	0.000574	0.0130	4.898	0.0375
22	1.1553	1.1593	0.000586	0.0128	5.166	0.0368
23	1.1631	1.1671	0.000599	0.0128	5.438	0.0365
24	1.1709	1.1750	0.000611	0.0128	5.712	0.0360
25	1.1787	1.1830	0.000623	0.0127	5.990	0.0356
26	1.1866	1.1910	0.000633	0.0127	6.271	0.0351
27	1.1946	1.1991	0.000642	0.0125	6.556	0.0347
28	1.2026	1.2072	0.000651	0.0123	6.844	0.0342
29	1.2107	1.2153	0.000661	0.0123	7.136	0.0338
30	1.2188	1.2235	0.000670	0.0122	7.432	0.0334
31	1.2270	1.2318	0.000676	0.0122	7.731	0.0330
32	1.2352	1.2401	0.000682	0.0120	8.034	0.0327
33	1.2435	1.2484	0.000688	0.0119	8.340	0.0322
34	1.2519	1.2568	0.000694	0.0119	8.651	0.0318
35	1.2603	1.2653	0.000699	0.0118	8.965	0.0314
36	1.2688	1.2738	0.000702	0.0118	9.283	0.0311
37	1.2773	1.2823	0.000704	0.0116	9.605	0.0307
38	1.2859	1.2909	0.000707	0.0116	9.931	0.0303
39	1.2945	1.2996	0.000709	0.0115	10.261	0.0299
40	1.3032	1.3083	0.000712	0.0114	10.595	0.0296
41	1.3120	1.3171	0.000715	0.0112	10.933	0.0292
42	1.3209	1.3260	0.000717	0.0111	11.276	0.0288
43	1.3299	1.3350	0.000720	0.0110	11.623	0.0285
44	1.3390	1.3441	0.000723	0.0110	11.974	0.0281
45	1.3481	1.3533	0.000726	0.0108	12.330	0.0278
46	1.3574	1.3626	0.000731	0.0108	12.690	0.0273
47	1.3667	1.3721	0.000736	0.0105	13.056	0.0270
48	1.3762	1.3816	0.000741	0.0103	13.426	0.0266
49	1.3859	1.3913	0.000747	0.0103	13.802	0.0263
50	1.3956	1.4011	0.000753	0.0102	14.182	0.0260
51	1.4054	1.4110	0.000759	0.0100	14.567	0.0256
52	1.4154	1.4210	0.000765	0.0100	14.958	0.0253
53	1.4254	1.4311	0.000771	0.0098	15.354	0.0249
54	1.4356	1.4413	0.000777	0.0097	15.755	0.0246
55	1.4459	1.4516	0.000784	0.0096	16.162	0.0243

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* Add if the temperature is above, subtract if it is below, the standard.

† Corresponding with a difference in specific gravity of 0.0001.

‡ The figures in this line across th age are for fractional percentages below 1.

Table of Percentage and Specific Gravity of Sulphuric Acid. U. S. X. —Continued.

Per cent. H_2SO_4	Sp. gr. app. 25° C. / 25° C.	Sp. gr. app. 15° C. / 15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils.	Per cent. = 0.01 mil normal KOH.
56	1.4563	1.4621	0.000790	0.0095	16.574	0.0239
57	1.4668	1.4726	0.000795	0.0094	16.992	0.0236
58	1.4774	1.4832	0.000800	0.0093	17.415	0.0234
59	1.4881	1.4939	0.000805	0.0093	17.843	0.0230
60	1.4989	1.5048	0.000810	0.0092	18.277	0.0228
61	1.5098	1.5157	0.000816	0.0091	18.716	0.0225
62	1.5208	1.5267	0.000822	0.0091	19.161	0.0222
63	1.5318	1.5379	0.000828	0.0090	19.612	0.0219
64	1.5429	1.5491	0.000834	0.0089	20.068	0.0217
65	1.5541	1.5603	0.000841	0.0088	20.529	0.0214
66	1.5654	1.5717	0.000848	0.0088	20.996	0.0211
67	1.5768	1.5831	0.000856	0.0088	21.469	0.0209
68	1.5882	1.5946	0.000864	0.0087	21.947	0.0207
69	1.5997	1.6062	0.000872	0.0087	22.431	0.0204
70	1.6112	1.6178	0.000880	0.0085	22.920	0.0202
71	1.6229	1.6295	0.000888	0.0085	23.416	0.0200
72	1.6346	1.6413	0.000897	0.0085	23.917	0.0197
73	1.6464	1.6531	0.000906	0.0085	24.424	0.0196
74	1.6582	1.6650	0.000915	0.0085	24.935	0.0193
75	1.6700	1.6769	0.000924	0.0085	25.452	0.0192
76	1.6817	1.6888	0.000934	0.0085	25.972	0.0190
77	1.6935	1.7006	0.000947	0.0086	26.498	0.0189
78	1.7051	1.7124	0.000963	0.0087	27.027	0.0188
79	1.7166	1.7240	0.000976	0.0088	27.558	0.0188
80	1.7279	1.7355	0.000987	0.0090	28.090	0.0187
81	1.7390	1.7467	0.000999	0.0093	28.624	0.0188
82	1.7497	1.7575	0.001011	0.0096	29.156	0.0188
83	1.7601	1.7680	0.001022	0.0101	29.687	0.0190
84	1.7700	1.7780	0.001034	0.0109	30.213	0.0193
85	1.7792	1.7873	0.001046	0.0115	30.732	0.0195
86	1.7879	1.7959	0.001043	0.0127	31.244	0.0199
87	1.7958	1.8038	0.001040	0.0139	31.747	0.0203
88	1.8030	1.8110	0.001035	0.0154	32.240	0.0207
89	1.8095	1.8174	0.001030	0.0172	32.724	0.0211
90	1.8153	1.8231	0.001022	0.0196	33.198	0.0216
91	1.8204	1.8282	0.001032	0.0217	33.662	0.0220
92	1.8250	1.8327	0.001043	0.0256	34.116	0.0225
93	1.8289	1.8365	0.001053	0.0303	34.561	0.0230
94	1.8322	1.8397	0.001064	0.0385	34.995	0.0235
95	1.8348	1.8422	0.001074	0.0526	35.420	0.0244
96	1.8367	1.8440	0.001064	0.1111	35.830	0.0256
97	1.8376	1.8448	0.001054	......	36.221	0.0274
98	1.8372	1.8445	0.001064	0.0555	36.586	0.0297
99	1.8354	1.8427	0.001070	0.0270	36.923	0.0336
100	1.8317	1.8391	0.001074	......	37.221	......

Note that the specific gravity diminishes in acids of more than 97.5 per cent. strength as the percentage increases.

NOTE: To find the per cent. of SO_3, multiply the per cent. of H_2SO_4 by 0.81629. To find the per cent. of SO_4 multiply the per cent. of H_2SO_4 by 0.97941. To find the volume per cent. of official Sulphuric Acid (94 per cent.), multiply the "normality" by 2.857. For the volume per cent. of official Diluted Sulphuric Acid (10 per cent.), multiply the "normality" by 46.10.

To find the weight in grammes of H_2SO in 100 mils, multiply the specific gravity by the per cent. of H_2SO_4.

Table of Percentage and Specific Gravity of Ammonia. U. S. P. X.

Per Cent. NH_3	Sp. gr. app. $\frac{25^\circ \text{ C.}}{25^\circ \text{ C.}}$	Sp. gr. app. $\frac{15^\circ \text{ C.}}{15^\circ \text{ C.}}$	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal HCl mils.	Per cent. = 0.01 mil normal HCl.
‡0	1.00000	1.00000	0.00017	0.0227	0.000	0.0172
1	0.99560	0.99573	0.00018	0.0230	0.583	0.0173
2	0.99126	0.99151	0.00020	0.0233	1.160	0.0175
3	0.98696	0.98735	0.00021	0.0236	1.733	0.0176
4	0.98272	0.98324	0.00023	0.0239	2.301	0.0178
5	0.97854	0.97918	0.00024	0.0240	2.864	0.0179
6	0.97437	0.97517	0.00026	0.0243	3.422	0.0181
7	0.97025	0.97121	0.00028	0.0246	3.976	0.0182
8	0.96618	0.96730	0.00029	0.0249	4.525	0.0184
9	0.96216	0.96344	0.00030	0.0252	5.069	0.0185
10	0.95819	0.95964	0.00032	0.0267	5.609	0.0186
11	0.95445	0.95604	0.00033	0.0270	6.146	0.0188
12	0.95074	0.95249	0.00035	0.0273	6.679	0.0189
13	0.94708	0.94898	0.00036	0.0276	7.207	0.0190
14	0.94346	0.94551	0.00037	0.0279	7.732	0.0192
15	0.93987	0.94208	0,00039	0.0282	8.253	0.0193
16	0.93633	0.93869	0.00040	0.0286	8.770	0.0195
17	0.93283	0.93533	0.00042	0.0289	9.283	0.0196
18	0.92937	0.93202	0.00043	0.0292	9.793	0.0198
19	0.92594	0.92874	0.00045	0.0295	10.299	0.0199
20	0.92255	0.92550	0.00046	0.0295	10.801	0.0200
21	0.91916	0.92230	0.00047	0.0299	11.300	0.0202
22	0.91581	0.91914	0.00049	0.0301	11.796	0.0204
23	0.91249	0.91601	0.00050	0.0307	12.287	0.0205
24	0.90923	0.91292	0.00052	0.0309	12.776	0.0206
25	0.90599	0.90987	0.00053	0.0317	13.262	0.0207
26	0.90286	0.90685	0.00055	0.0321	13.744	0.0209
27	0.89974	0.90385	0.00057	0.0324	14.223	0.0210
28	0.89665	0.90087	0.00058	0.0326	14.699	0.0212
29	0.89358	0.89791	0.00059	0.0329	15.171	0.0213
30	0.89054	0.89498	0.00060	0.0339	15.640	0.0214
31	0.88759	0.89212	0.00061	0.0353	16.108	0.0214
32	0.88476	0.88938	0.00062	0.0368	16.575	0.0215
33	0.88204	0.88674	0.00063	0.0382	17.040	0.0215
34	0.87942	0.88421	0.00064	0.0394	17.505	0.0216
35	0.87688	0.88176	0.00064	......	17.968	......

* Add if the temperature is above, subtract if it is below, the standard.

† Corresponding with a difference in specific gravity of 0.0001.

‡ The figures in this line across the page are for fractional percentages below **1.**

NOTE: To find the per cent. of NH_4 multiply the per cent. of NH_3 by 1.0592. To find the volume per cent. of official Ammonia Water (10 per cent.) multiply the "normality" by 17.83. For the volume per cent. of official Stronger Ammonia Water (28 per cent.), multiply the "normality" by 6.803.

RELATIONS BETWEEN THERMOMETERS.

In *Fahrenheit's* thermometer, the freezing point of water is placed at 32°, and the boiling point at 212°, and the number of intervening degrees is 180.

The *centigrade* or *Celsius's* thermometer, which is now recognized in the U. S. Pharmacopœia and has been adopted generally by scientists, marks the freezing point *zero*, and the boiling point 100°.

In *Réaumur's* thermometer the freezing point is at *zero*, and the boiling point at 80°.

In *De Lisle's* thermometer, used in Russia, the graduations begins at the boiling point, which is marked *zero*, while the freezing point is placed at 150°.

From the above statement, it is evident that 180 degrees of Fahrenheit are equal to 100° of the Centigrade, 80° of Réaumur, and 150° of De Lisle; or 1 degree of the first is equal to $\frac{5}{9}$ of a degree of the second, $\frac{4}{9}$ of a degree of the third, and $\frac{5}{6}$ of a degree of the last. It is easy, therefore, to convert the degrees of one into the equivalent number of degrees of the other; but in ascertaining the corresponding points upon the different scales, it is necessary to take into consideration their different modes of graduation. Thus, as the zero Fahrenheit is 32° below the point at which that of the Centigrade and of Réaumur is placed, this number must be taken into account in the calculation.

1. If any degree on the *Centigrade* scale, either above or below zero, be multiplied by 1.8 the result will, in either case, be the number of degrees above or below 32° or the freezing point of *Fahrenheit*.
2. The number of degrees between any point of *Fahrenheit's* scale and 32°, if divided by 1.8, will give the corresponding point on the *Centigrade*.

Thermometric Equivalents.

(U. S. P. X)

Centigrade and Fahrenheit Scales.

$$\frac{9}{5}\,\text{C.}^\circ + 32 = \text{F.}^\circ$$

C.°	F.°	C.°	F.°	C.°	F.°	C.°	F.°	C.°	F.°
—20	—4	21	69.8	61	141.8	101	213.8	141	285.8
—19	—2.2	22	71.6	62	143.6	102	215.6	142	287.6
—18	—0.4	23	73.4	63	145.4	103	217.4	143	289.4
—17	1.4	24	75.2	64	147.2	104	219.2	144	291.2
—16	3.2	25	77.	65	149.	105	221.	145	293.
—15	5.	26	78.8	66	150.8	106	222.8	146	294.8
—14	6.8	27	80.6	67	152.6	107	224.6	147	296.6
—13	8.6	28	82.4	68	154.4	108	226.4	148	298.4
—12	10.4	29	84.2	69	156.2	109	228.2	149	300.2
—11	12.2	30	86.	70	158.	110	230.	150	302.
—10	14.	31	87.8	71	159.8	111	231.8	151	303.8
— 9	15.8	32	89.6	72	161.6	112	233.6	152	305.6
— 8	17.6	33	91.4	73	163.4	113	235.4	153	307.4
— 7	19.4	34	93.2	74	165.2	114	237.2	154	309.2
— 6	21.2	35	95.	75	167.	115	239.	155	311.
— 5	23.	36	96.8	76	168.8	116	240.8	156	312.8
— 4	24.8	37	98.6	77	170.6	117	242.6	157	314.6
— 3	26.6	38	100.4	78	172.4	118	244.4	158	316.4
— 2	28.4	39	102.2	79	174.2	119	246.2	159	318.2
— 1	30.2	40	104.	80	176.	120	248.	160	320.
0—	32.	41	105.8	81	177.8	121	249.8	161	321.8
1	33.8	42	107.6	82	179.6	122	251.6	162	323.6
2	35.6	43	109.4	83	181.4	123	253.4	163	325.4
3	37.4	44	111.2	84	183.2	124	255.2	164	327.2
4	39.2	45	113.	85	185.	125	257.	165	329.
5	41.	46	114.8	86	186.8	126	258.8	166	330.8
6	42.8	47	116.6	87	188.6	127	260.6	167	332.6
7	44.6	48	118.4	88	190.4	128	262.4	168	334.4
8	46.4	49	120.2	89	192.2	129	264.2	169	336.2
9	48.2	50	122.	90	194.	130	266.	170	338.
10	50.	51	123.8	91	195.8	131	267.8	171	339.8
11	51.8	52	125.6	92	197.6	132	269.6	172	341.6
12	53.6	53	127.4	93	199.4	133	271.4	173	343.4
13	55.4	54	129.2	94	201.2	134	273.2	174	345.2
14	57.2	55	131.	95	203.	135	275.	175	347.
15	59.	56	132.8	96	204.8	136	276.8	176	348.8
16	60.8	57	134.6	97	206.6	137	278.6	177	350.6
17	62.6	58	136.4	98	208.4	138	280.4	178	352.4
18	64.4	59	138.2	99	210.2	139	282.2	179	354.2
19	66.2	60	140.	100	212.	140	284.	180	356.
20	68.								

Thermometric Equivalents—*Continued.*

Fahrenheit to Centigrade Scales.

$$(\text{F.}^\circ - 32) \times \frac{5}{9} = \text{C.}^\circ$$

F.°	C.°	F.°	C.°	F.°	C.°	F.°	C.°	F.°	C.°
0	—17.78	61	16.11	121	49.44	181	82.78	241	116.11
1	—17.22	62	16.67	122	50.	182	83.33	242	116.67
2	—16.67	63	17.22	123	50.56	183	83.89	243	117.22
3	—16.11	64	17.78	124	51.11	184	84.44	244	117.78
4	—15.56	65	18.33	125	51.67	185	85.	245	118.33
5	—15.	66	18.89	126	52.22	186	85.56	246	118.89
6	—14.44	67	19.44	127	52.78	187	86.11	247	119.44
7	—13.89	68	20.	128	53.33	188	86.67	248	120.
8	—13.33	69	20.56	129	53.89	189	87.22	249	120.56
9	—12.78	70	21.11	130	54.44	190	87.78	250	121.11
10	—12.22	71	21.67	131	55.	191	88.33	251	121.67
11	—11.67	72	22.22	132	55.56	192	88.89	252	122.22
12	—11.11	73	22.78	133	56.11	193	89.44	253	122.78
13	—10.56	74	23.33	134	56.67	194	90.	254	123.33
14	—10.	75	23.89	135	57.22	195	90.56	255	123.89
15	— 9.44	76	24.44	136	57.78	196	91.11	256	124.44
16	— 8.89	77	25.	137	58.33	197	91.67	257	125.
17	— 8.33	78	25.56	138	58.89	198	92.22	258	125.56
18	— 7.78	79	26.11	139	59.44	199	92.78	259	126.11
19	— 7.22	80	26.67	140	60.	200	93.33	260	126.67
20	— 6.67	81	27.22	141	60.56	201	93.89	261	127.22
21	— 6.11	82	27.78	142	61.11	202	94.44	262	127.78
22	— 5.56	83	28.33	143	61.67	203	95.	263	128.33
23	— 5.	84	28.89	144	62.22	204	95.56	264	128.89
24	— 4.44	85	29.44	145	62.78	205	96.11	265	129.44
25	— 3.89	86	30.	146	63.33	206	96.67	266	130.
26	— 3.33	87	30.56	147	63.89	207	97.22	267	130.56
27	— 2.78	88	31.11	148	64.44	208	97.78	268	131.11
28	— 2.22	89	31.67	149	65.	209	98.33	269	131.67
29	— 1.67	90	32.22	150	65.56	210	98.89	270	132.22
30	— 1.11	91	32.78	151	66.11	211	99.44	271	132.78
31	— 0.56	92	33.33	152	66.67	212	100.	272	133.33
32	0.	93	33.89	153	67.22	213	100.56	273	133.89
33	0.56	94	34.44	154	67.78	214	101.11	274	134.44
34	1.11	95	35.	155	68.33	215	101.67	275	135.
35	1.67	96	35.56	156	68.89	216	102.22	276	135.56
36	2.22	97	36.11	157	69.44	217	102.78	277	136.11
37	2.78	98	36.67	158	70.	218	103.33	278	136.67
38	3.33	99	37.22	159	70.56	219	103.89	279	137.22
39	3.89	100	37.78	160	71.11	220	104.44	280	137.78
40	4.44	101	38.33	161	71.67	221	105.	281	138.33
41	5.	102	38.89	162	72.22	222	105.56	282	138.89
42	5.56	103	39.44	163	72.78	223	106.11	283	139.44
43	6.11	104	40.	164	73.33	224	106.67	284	140.
44	6.67	105	40.56	165	73.89	225	107.22	285	140.56
45	7.22	106	41.11	166	74.44	226	107.78	286	141.11
46	7.78	107	41.67	167	75.	227	108.33	287	141.67
47	8.33	108	42.22	168	75.56	228	108.89	288	142.22
48	8.89	109	42.78	169	76.11	229	109.44	289	142.78
49	9.44	110	43.33	170	76.67	230	110.	290	143.33
50	10.	111	43.89	171	77.22	231	110.56	291	143.89
51	10.56	112	44.44	172	77.78	232	111.11	292	144.44
52	11.11	113	45.	173	78.33	233	111.67	293	145.
53	11.67	114	45.56	174	78.89	234	112.22	294	145.56
54	12.22	115	46.11	175	79.44	235	112.78	295	146.11
55	12.78	116	46.67	176	80.	236	113.33	296	146.67
56	13.33	117	47.22	177	80.56	237	113.89	297	147.22
57	13.89	118	47.78	178	81.11	238	114.44	298	147.78
58	14.44	119	48.33	179	81.67	239	115.	299	148.33
59	15.	120	48.89	180	82.22	240	115.56	300	148.89
60	15.56								

Reduction of Apparent to True Specific Gravity (U. S. P. X)

viz.: $\frac{25^\circ\text{ C.}}{25^\circ\text{ C.}}$ in air to $\frac{25^\circ\text{ C.}}{25^\circ\text{ C.}}$ in vacuum.

Weights of Brass, Sp. gr. 8.4. Barometer 760 mm.

Sp. gr. apparent.	Correction.	Sp. gr. apparent.	Correction.
0.6	+0.000471	1	0.000000
0.7	+0.000353	2	−0.001177
0.8	+0.000235	3	−0.002355
0.9	+0.000118	4	−0.003532
1.0	0.000000	5	−0.004709
1.1	−0.000118	6	−0.005887
1.2	−0.000235	7	−0.007064
1.3	−0.000353	8	−0.008241
1.4	−0.000471	9	−0.009418
1.5	−0.000589	10	−0.010596
1.6	−0.000706	11	−0.011773
1.7	−0.000824	12	−0.012950
1.8	−0.000942	13	−0.014128
1.9	−0.001060	14	−0.015305
2.0	−0.001177	15	−0.016482

Formula for deriving above correction: Subtract algebraically the apparent specific gravity from 1.000 and multiply the remainder by 0.0011773. It is additive for specific gravities below, subtractive for those above, 1.000.

NOTE: The correction for reducing true to apparent specific gravity is found by subtracting algebraically 1.000 from the true specific gravity and multiplying the remainder by the factor 0.0011765. It is subtractive for specific gravities below, additive for those above, 1.000.

Calibration of Pycnometers.

Apparent Weight in Air of Distilled Water filling "100 Gm." Pycnometer at Various Temperatures.

Barometer 760 mm.† Coefficient of Expansion of Glass 0.000025. Air ½ saturated.

Temperature of water.* C.	Basis $\frac{15^\circ\text{ C.}}{4^\circ\text{ C.}}$ in vacuo. (Density) 100 cc. Wt. in air.	Basis $\frac{20^\circ\text{ C.}}{4^\circ\text{ C.}}$ in vacuo. 100 cc. Wt. in air.	Basis $\frac{15^\circ\text{ C.}}{15^\circ\text{ C.}}$ in vacuo. Wt in air.	Basis $\frac{20^\circ\text{ C.}}{20^\circ\text{ C.}}$ in vacuo. Wt. in air.	Basis $\frac{25^\circ\text{ C.}}{25^\circ\text{ C.}}$ in vacuo. Wt. in air.	Basis $\frac{15^\circ\text{ C.}}{15^\circ\text{ C.}}$ in air. Wt. in air.	Basis $\frac{15.56^\circ\text{ C.}}{15.56^\circ\text{ C.}}$ in air. (Alcohol Standard) Wt. in air.	Basis $\frac{20^\circ\text{ C.}}{20^\circ\text{ C.}}$ in air. Wt. in air.	Basis $\frac{25^\circ\text{ C.}}{25^\circ\text{ C.}}$ in air. (Official) Wt. in air.
15° C.	99.8050	99.7925	99.8923	99.9690	100.0726	100.0000	100.0070	100.0750	100.1768
16° C.	99.7923	99.7798	99.8795	99.9563	100.0598	99.9873	99.9943	100.0622	100.1640
17° C.	99.7784	99.7659	99.8656	99.9424	100.0459	99.9734	99.9804	100.0483	100.1501
18° C.	99.7634	99.7510	99.8506	99.9274	100.0309	99.9584	99.9654	100.0333	100.1351
19° C.	99.7474	99.7349	99.8345	99.9113	100.0148	99.9423	99.9493	100.0172	100.1189
20° C.	99.7302	99.7177	99.8194	99.8941	99.9975	99.9251	99.9321	100.0000	100.1017
21° C.	99.7120	99.6995	99.7991	99.8759	99.9793	99.9068	99.9138	99.9817	100.0834
22° C.	99.6927	99.6802	99.7798	99.8565	99.9600	99.8874	99.8944	99.9623	100.0641
23° C.	99.6724	99.6599	99.7595	99.8362	99.9396	99.8671	99.8741	99.9420	100.0437
24° C.	99.6511	99.6366	99.7382	99.8149	99.9183	99.8458	99.8528	99.9207	100.0224
25° C.	99.6288	99.6164	99.7159	99.7926	99.8959	99.8235	99.8305	99.8983	100.0000
26° C.	99.6056	99.5931	99.6926	99.7693	99.8726	99.8003	99.8173	99.8750	99.9767
27° C.	99.5813	99.5689	99.6684	99.7450	99.8483	99.7761	99.7831	99.8507	99.9524
28° C.	99.5562	99.5438	99.6432	99.7199	99.8231	99.7509	99.7579	99.8255	99.9271
29° C.	99.5302	99.5177	99.6172	99.6937	99.7970	99.7247	99.7317	99.7994	99.9010
30° C.	99.5032	99.4908	99.5902	99.6667	99.7700	99.6976	99.7046	99.7724	99.8739
31° C.	99.4754	99.4630	99.5623	99.6388	99.7421	99.6697	99.6767	99.7445	99.8460
32° C.	99.4467	99.4343	99.5336	99.6102	99.7133	99.6410	99.6480	99.7157	99.8172
33° C.	99.4172	99.4048	99.5041	99.5806	99.6837	99.6114	99.6184	99.6861	99.7876
34° C.	99.3868	99.3744	99.4737	99.5502	99.6533	99.5810	99.5880	99.6557	99.7572
35° C.	99.3557	99.3433	99.4425	99.5190	99.6221	99.5498	99.5568	99.6245	99.7259

* If temperature of air is above that of the water, add for each degree centigrade 0.00041; if below, subtract the same amount.

† If barometer (corrected for temperature) is above 760 mm., subtract for each 10 mm. 0.0014; if below, add the same amount (see page 550, column 5).

NOTE: When extreme exactness is required, the counterpoise of the flask should be of the same kind of glass as that of which the flask is made.

Calibration of Glass Measuring Apparatus.

Apparent weight in air of distilled water filling a 100 cc. flask at different temperatures. Barometer (corrected for temperature) 760 mm. Coefficient of cubical expansion of glass taken as 0.000025. It is assumed that the weights used are brass and that water and air (one-half saturated with moisture) are at the same temperature.

Temperature.*	Flask holds 100 cc. at 15° C.	Flask holds 100 cc. at 20° C.	Flask holds 100 cc. at 25° C. U. S. P. Standard.	Correction for 10 cc. Barometer above or below 760 mm.†
15° C.	99.8050	99.7925	99.7801	0.00142
16° C.	99.7923	99.7798	99.7673	0.00141
17° C.	99.7784	99.7659	99.7535	0.00141
18° C.	99.7634	99.7510	99.7385	0.00140
19° C.	99.7474	99.7349	99.7224	0.00140
20° C.	99.7302	99.7177	99.7052	0.00140
21° C.	99.7120	99.6995	99.6870	0.00139
22° C.	99.6927	99.6802	99.6678	0.00139
23° C.	99.6724	99.6599	99.6475	0.00138
24° C.	99.6511	99.6386	99.6262	0.00138
25° C.	99.6288	99.6164	99.6039	0.00137
26° C.	99.6056	99.5931	99.5807	0.00137
27° C.	99.5813	99.5689	99.5564	0.00136
28° C.	99.5562	99.5438	99.5313	0.00136
29° C.	99.5302	99.5177	99.5053	0.00136
30° C.	99.5032	99.4908	99.4783	0.00135
31° C.	99.4754	99.4630	99.4505	0.00135
32° C.	99.4467	99.4343	99.4218	0.00134
33° C.	99.4172	99.4048	99.3924	0.00134
34° C.	99.3868	99.3744	99.3620	0.00133
35° C.	99.3557	99.3433	99.3309	0.00133

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*If temperature of air is above that of the water, add for each degree centigrade, 0.00041; if below, subtract the same amount.

†Barometer correction additive if reading is below 760 mm., subtractive if above.

Note: When extreme exactness is required the counterpoise of the flask should be of the same kind of glass as that of which the flask is made.

Weights and Volume Relations.

Specific gravity true 25° C. / 25° C.	Specific volume.	Weight of 1 U. S. gallon in pounds avoirdupois in air.	Weight of 100 fluidounces in ounces avoirdupois.	Weight of 1 fluidounce in grains.	Volume in U. S. gallons of 100 pounds avoirdupois.	Volume in fluidounces of 100 ounces avoirdupois.	Volume in fluidounces of 1000 grains.
0.70	1.4286	5.816	72.70	318.0	17.195	137.56	3.144
0.71	1.4085	5.899	73.74	322.6	16.953	135.62	3.100
0.72	1.3889	5.982	74.78	327.1	16.717	133.73	3.057
0.73	1.3699	6.065	75.82	331.7	16.487	131.90	3.015
0.74	1.3514	6.149	76.86	336.2	16.264	130.11	2.974
0.75	1.3333	6.232	77.90	340.8	16.047	128.38	2.934
0.76	1.3158	6.315	78.94	345.3	15.836	126.69	2.896
0.77	1.2987	6.398	79.98	349.9	15.630	125.04	2.858
0.78	1.2821	6.481	81.02	354.5	15.429	123.43	2.821
0.79	1.2658	6.565	82.06	359.0	15.233	121.87	2.786
0.80	1.2500	6.648	83.10	363.6	15.043	120.34	2.751
0.81	1.2346	6.731	84.14	368.1	14.857	118.85	2.717
0.82	1.2195	6.814	85.18	372.7	14.675	117.40	2.684
0.83	1.2048	6.897	86.22	377.2	14.496	115.99	2.651
0.84	1.1905	6.981	87.26	381.8	14.325	114.60	2.620
0.85	1.1765	7.064	88.30	386.3	14.157	113.25	2.589
0.86	1.1628	7.147	89.34	390.9	13.992	111.93	2.559
0.87	1.1494	7.230	90.38	395.4	13.831	110.65	2.529
0.88	1.1364	7.314	91.42	400.0	13.673	109.39	2.500
0.89	1.1236	7.397	92.46	404.5	13.520	108.16	2.472
0.90	1.1111	7.480	93.50	409.1	13.369	106.95	2.445
0.91	1.0989	7.563	94.54	413.6	13.222	105.78	2.418
0.92	1.0870	7.646	95.58	418.2	13.078	104.62	2.391
0.93	1.0753	7.730	96.62	422.7	12.937	103.50	2.366
0.94	1.0638	7.813	97.66	427.3	12.799	102.40	2.341
0.95	1.0526	7.896	98.70	431.8	12.666	101.32	2.316
0.96	1.0417	7.979	99.74	436.4	12.532	100.26	2.292
0.97	1.0309	8.063	100.78	440.9	12.403	99.23	2.268
0.98	1.0204	8.146	101.82	445.5	12.276	98.21	2.245
0.99	1.0101	8.229	102.86	450.0	12.152	97.22	2.222
1.00	1.0000	8.312	103.90	454.6	12.031	96.24	2.200
1.02	0.9804	8.479	105.98	463.7	11.794	94.36	2.157
1.04	0.9615	8.645	108.06	472.8	11.567	92.54	2.115
1.06	0.9434	8.812	110.14	481.9	11.349	90.79	2.075
1.08	0.9259	8.978	112.22	491.0	11.138	89.11	2.037
1.10	0.9091	9.144	114.31	500.1	10.936	87.49	2.000
1.12	0.8929	9.311	116.39	509.2	10.740	85.92	1.964
1.14	0.8772	9.477	118.47	518.3	10.552	84.41	1.929
1.16	0.8621	9.644	120.55	527.4	10.370	82.96	1.896
1.18	0.8475	9.810	122.63	536.5	10.194	81.55	1.864
1.20	0.8333	9.977	124.71	545.6	10.024	80.19	1.833
1.22	0.8197	10.143	126.79	554.7	9.859	78.87	1.803
1.24	0.8065	10.309	128.87	563.8	9.700	77.60	1.774
1.26	0.7937	10.476	130.95	572.9	9.546	76.37	1.746
1.28	0.7813	10.642	133.03	582.0	9.396	75.17	1.718
1.30	0.7692	10.809	135.11	591.1	9.252	74.01	1.692
1.32	0.7576	10.975	137.19	600.2	9.111	72.89	1.666
1.34	0.7463	11.142	139.27	609.3	8.975	71.80	1.641
1.36	0.7353	11.308	141.35	618.4	8.843	70.75	1.617
1.38	0.7246	11.475	143.43	627.5	8.715	69.72	1.594
1.40	0.7143	11.641	145.51	636.6	8.590	68.72	1.571
1.42	0.7042	11.807	147.59	645.7	8.469	67.75	1.549
1.44	0.6944	11.974	149.67	654 8	8.352	66.81	1.527
1.46	0.6849	12.140	151.75	663.9	8.237	65.90	1.506
1.48	0.6757	12.307	153.83	673.0	8.126	65.01	1.486

Weights and Volume Relations—*Continued.*

Specific gravity true $\frac{25^\circ \text{C.}}{25^\circ \text{C.}}$	Specific volume.	Weight of 1 U. S. gallon in pounds avoirdupois in air.	Weight of 100 fluidounces in ounces avoirdupois.	Weight of 1 fluidounce in grains.	Volume in U. S. gallons of 100 pounds avoirdupois.	Volume in fluidounces of 100 ounces avoirdupois.	Volume in fluidounces of 1000 grains.
1.50	0.6667	12.473	155.92	682.1	8.017	64.13	1.466
1.52	0.6579	12.640	158.00	691.2	7.912	63.29	1.447
1.54	0.6494	12.806	160.08	700.3	7.809	62.47	1.428
1.56	0.6410	12.973	162.16	709.4	7.709	61.67	1.410
1.58	0.6329	13.139	164.24	718.5	7.611	60.89	1.392
1.60	0.6250	13.305	166.32	727.6	7.516	60.13	1.374
1.62	0.6173	13.472	168.40	736.7	7.423	59.38	1.357
1.64	0.6098	13.638	170.48	745.8	7.332	58.66	1.341
1.66	0.6024	13.805	172.56	754.9	7.244	57.95	1.325
1.68	0.5952	13.971	174.64	764.1	7.158	57.2	1.309
1.70	0.5882	14.138	176.72	773.2	7.073	56.59	1.293
1.72	0.5814	14.304	178.80	762.3	6.991	55.93	1.278
1.74	0.5747	14.470	180.88	791.4	6.911	55.29	1.264
1.76	0.5682	14.637	182.96	800.5	6.832	54.66	1.249
1.78	0.5618	14.803	185.04	809.6	6.755	54.04	1.235
1.80	0.5556	14.970	187.12	818.7	6.680	53.44	1.222
1.82	0.5495	15.136	189.20	827.8	6.607	52.85	1.208
1.84	0.5435	15.302	191.28	836.9	6.535	52.28	1.195
1.86	0.5376	15.469	193.36	846.0	6.465	51.72	1.182
1.88	0.5319	15.636	195.44	855.1	6.396	51.17	1.170
1.90	0.5263	15.802	197.53	864.2	6.328	50.63	1.157
1.92	0.5208	15.968	199.61	873.3	6.262	50.10	1.145
1.94	0.5155	16.135	201.69	882.4	6.198	49.58	1.133
1.96	0.5102	16.301	203.77	891.5	6.135	49.08	1.122
1.98	0.5051	16.468	205.85	900.6	6.073	48.58	1.110
2.00	0.5000	16.634	207.93	909.7	6.012	48.09	1.100

Equivalents of Weights and Measures.

Metric, Avoirdupois and Apothecaries.

Note—The values given for the relation of weight to measure and *vice versa*, are for water at the temperature of 4° C. (39.2° F.) *in vacuo*. For ordinary, practical purposes these values may be used without correction.

Weights.						Metric Weight and Measure Gm. or cc.*	Measures.		
Grains.	Apothecaries.		Avoirdupois.				Fluid.		Fluidounces and fractions.
	oz.	grains.	lbs.	oz.	grains.		ounces.	minims.	
15432.4	32	72.4	2	3	119.9	1000	33	391.1	33.815
15360.0	32	.....	2	3	47.5	995.311	33	314.9	33.656
15060.5	31	180.5	2	2	185.5	975.906	33	.....	33
15046.5	31	166.5	2	2	171.5	975	32	465.3	32.969
14880.0	31	.....	2	2	5.0	964.208	32	290.1	32.604
14660.7	30	260.7	2	1	223.2	950	32	59.5	32.124
14604.1	30	204.1	2	1	166.6	946.333	32	.....	32
14400.0	30	.....	2	..	400.0	933.104	31	265.2	31.553
14274.9	29	354.9	2	..	274.9	925	31	133.7	31.279
14147.8	29	227.8	2	..	147.8	916.760	31	.....	31
14000.0	29	80.0	2	..	.....	907.185	30	324.6	30.676
13920.0	29	.....	1	15	357.5	902.001	30	240.4	30.501
13889.1	28	449.1	1	15	326.6	900	30	207.9	30.433
13691.4	28	251.4	1	15	128.9	887.187	30	.....	30
13562.5	28	122.5	1	15	.....	878.835	29	344.4	29.718
13503.3	28	63.3	1	14	378.3	875	29	282.2	29.588
13440.0	28	.....	1	14	315.0	870.897	29	215.6	29.449
13235.0	27	275.0	1	14	110.0	857.614	29	.....	29
13125.0	27	165.0	1	14	.....	850.486	28	364.3	28.759
13117.5	27	157.5	1	13	430.0	850	28	356.4	28.742
12960.0	27	.....	1	13	272.5	839.794	28	190.8	28.397
12778.6	26	298.6	1	13	91.1	828.041	28	.....	28
12731.7	26	251.7	1	13	44.2	825	27	430.6	27.897
12687.5	26	207.5	1	13	.....	822.136	27	384.1	27.800
12480.0	26	.....	1	12	230.0	808.690	27	165.9	27.346
12345.9	25	345.9	1	12	95.9	800	27	24.9	27.052
12322.3	25	322.3	1	12	72.3	798.469	27	.....	27
12250.0	25	250.0	1	12	.....	793.787	26	404.0	26.842
12000.0	25	.....	1	11	187.5	777.587	26	141.1	26.294
11960.1	24	440.1	1	11	147.6	775	26	99.1	26.206
11865.9	24	345.9	1	11	53.4	768.896	26	.....	26
11812.5	24	292.5	1	11	.....	765.437	25	423.8	25.883
11574.3	24	54.3	1	10	199.3	750	25	173.3	25.361
11520.0	24	.....	1	10	145.0	746.484	25	116.2	25.242
11409.5	23	369.5	1	10	34.5	739.323	25	.....	25
11375.0	23	335.0	1	10	.....	737.088	24	443.7	24.924
11188.5	23	148.5	1	9	251.0	725	24	247.5	24.516
11040.0	23	.....	1	9	102.5	715.380	24	91.4	24.190
10953.1	22	393.1	1	9	15.6	709.750	24	.....	24
10937.5	22	377.5	1	9	.....	708.738	23	463.6	23.966
10802.6	22	242.6	1	8	302.6	700	23	321.7	23.670
10560.0	22	.....	1	8	60.0	684.277	23	66.5	23.139
10500.0	21	420.0	1	8	.....	680.389	23	3.4	23.007
10496.7	21	416.7	1	7	434.2	680.177	23	.....	23
10416.8	21	336.8	1	7	354.3	675	22	396.0	22.825
10080.0	21	.....	1	7	17.5	653.173	22	41.7	22.087
10062.5	20	462.5	1	7	.....	652.039	22	23.3	22.049
10040.4	20	440.4	1	6	415.4	650.604	22	.....	22
10031.0	20	431.0	1	6	406.0	650	21	470.2	21.980
9645.2	20	45.2	1	6	20.2	625	21	64.4	21.134
9625.0	20	25.0	1	6	.....	623.690	21	43.2	21.090
9600.0	20	.....	1	5	412.5	622.070	21	16.8	21.035
9584.0	19	464.0	1	5	396.5	621.031	21	.....	21

*Note—By the "cc." in this table is meant the one-thousandth part of the liter or a milliliter (ml).

Equivalents of Weights and Measures—*Continued.*

Weights.						Metric Weight and Measure	Measures.		
Grains.	Apothecaries.		Avoirdupois.				Fluid.		Fluidounces and fractions.
	oz.	grains.	lbs.	oz.	grains.	Gm. or cc.*	ounces.	minims.	
9259.4	19	139.4	1	5	71.9	600	20	138.6	20.289
9187.5	19	67.5	1	5	.....	595.340	20	63.0	20.131
9127.6	19	7.6	1	4	377.6	591.458	20	.....	20
9120.0	19	.....	1	4	370.0	590.966	19	472.0	19.983
8873.6	18	233.6	1	4	123.6	575	19	212.9	19.444
8750.0	18	110.0	1	4	.....	566.991	19	82.8	19.173
8671.2	18	31.2	1	3	358.7	561.885	19	.....	19
8640.0	18	.....	1	3	327.5	559.863	18	447.2	18.932
8487.8	17	327.8	1	3	175.3	550	18	287.1	18.598
8312.5	17	152.5	1	3	.....	538.641	18	102.7	18.214
8214.8	17	54.8	1	2	339.8	532.312	18	.....	18
8160.0	17	.....	1	2	285.0	528.759	17	422.3	17.880
8102.0	16	422.0	1	2	227.0	525	17	361.3	17.753
7875.0	16	195.0	1	2	.....	510.291	17	122.5	17.255
7758.5	16	78.5	1	1	321.0	502.739	17	.....	17
7716.2	16	36.2	1	1	278.7	500	16	435.6	16.907
7680.0	16	.....	1	1	242.5	497.656	16	397.5	16.828
7437.5	15	237.5	1	1	.....	481.942	16	142.4	16.297
7330.4	15	130.4	1	..	330.4	475	16	29.8	16.062
7302.1	15	102.1	1	..	302.1	473.167	16	.....	16
7200.0	15	.....	1	..	200.0	466.552	15	372.6	15.776
7000.0	14	280.0	1	..	.....	453.592	15	162.3	15.338
6944.6	14	224.6	..	15	382.1	450	15	104.0	15.217
6845.7	14	125.7	..	15	283.2	443.594	15	.....	15
6720.0	14	.....	..	15	157.5	435.449	14	347.8	14.725
6562.5	13	322.5	..	15	.....	425.243	14	182.2	14.379
6558.8	13	318.8	..	14	433.8	425	14	178.2	14.371
6389.3	13	149.3	..	14	264.3	414.021	14	.....	14
6240.0	13	.....	..	14	115.0	404.345	13	322.9	13.673
6172.9	12	412.9	..	14	47.9	400	13	252.4	13.526
6125.0	12	365.0	..	14	.....	396.893	13	202.0	13.421
5932.9	12	172.9	..	13	245.4	384.448	13	.....	13
5787.1	12	27.1	..	13	99.6	375	12	326.6	12.681
5760.0	12	.....	..	13	72.5	373.242	12	298.1	12.621
5687.5	11	407.5	..	13	.....	368.544	12	221.9	12.462
5476.6	11	196.6	..	12	226.6	354.875	12	.....	12
5401.3	11	121.3	..	12	151.3	350	11	400.8	11.835
5280.0	11	.....	..	12	30.0	342.138	11	273.3	11.569
5250.0	10	450.0	..	12	.....	340.194	11	241.7	11.504
5020.2	10	220.2	..	11	207.7	325.302	11	.....	11
5015.5	10	215.5	..	11	203.0	325	10	475.1	10.990
4812.5	10	12.5	..	11	.....	311.845	10	261.6	10.545
4800.0	10	.....	..	10	425.0	311.035	10	248.4	10.518
4629.7	9	309.7	..	10	254.7	300	10	69.3	10.144
4563.8	9	243.8	..	10	188.8	295.729	10	.....	10
4375.0	9	55.0	..	10	.....	283.495	9	281.4	9.586
4320.0	9	.....	..	9	382.5	279.931	9	223.6	9.466
4244.0	8	403.9	..	9	306.4	275	9	143.5	9.299
4107.4	8	267.4	..	9	169.9	266.156	9	.....	9
3937.5	8	97.5	..	9	.....	255.146	8	301.3	8.628
3858.1	8	18.1	..	8	358.1	250	8	217.8	8.454
3840.0	8	.....	..	8	340.0	248.828	8	198.7	8.414
3651.0	7	291.0	..	8	151.0	236.583	8	.....	8
3500.0	7	140.0	..	8	.....	226.796	7	321.1	7.669
3472.3	7	112.3	..	7	409.8	225	7	292.0	7.608
3360.0	7	.....	..	7	297.5	217.724	7	173.9	7.362
3194.7	6	314.7	..	7	132.2	207.010	7	.....	7

* NOTE—By the "cc." in this table is meant the one-thousandth part of the liter or a milliliter (ml.)

Equivalents of Weights and Measures—*Continued.*

Weights.						Metric Weight and Measure Gm. or cc.*	Measures.		
Grains.	Apothecaries.		Avoirdupois.				Fluid.		Fluidounces and fractions.
	oz.	grains.	lbs.	oz.	grains.		ounces.	minims.	
3086.5	6	206.5	. .	7	24.0	200	6	366.2	6.763
3062.5	6	182.5	. .	7	. . . . .	198.447	6	341.0	6.710
2880.0	6	. . . . .	. .	6	255.0	186.621	6	149.0	6.311
2738.3	5	338.3	. .	6	113.3	177.437	6	. . . . .	6
2700.7	5	300.7	. .	6	75.7	175	5	440.4	5.918
2625.0	5	225.0	. .	6	. . . . .	170.097	5	360.9	5.752
2400.0	5	. . . . .	. .	5	212.5	155.517	5	124.2	5.259
2314.9	4	394.9	. .	5	127.4	150	5	34.7	5.072
2281.9	4	361.9	. .	5	94.4	147.865	5	. . . . .	5
2187.5	4	267.5	. .	5	. . . . .	141.748	4	380.7	4.793
1929.0	4	9.0	. .	4	179.0	125	4	108.9	4.227
1920.0	4	. . . . .	. .	4	170.0	124.414	4	99.4	4.207
1825.5	3	385.5	. .	4	75.5	118.292	4	. . . . .	4
1750.0	3	310.0	. .	4	. . . . .	113.398	3	400.6	3.835
1543.2	3	103.2	. .	3	230.7	100	3	183.1	3.381
1440.0	3	. . . . .	. .	3	127.5	93.310	3	74.5	3.155
1388.9	2	428.9	. .	3	76.4	90	3	20.8	3.043
1369.1	2	409.1	. .	3	56.6	88.719	3	. . . . .	3
1312.5	2	352.5	. .	3	. . . . .	85.049	2	420.4	2.876
1234.6	2	274.6	. .	2	359.6	80	2	338.5	2.705
1157.4	2	197.4	. .	2	282.4	75	2	257.3	2.536
1080.3	2	120.3	. .	2	205.3	70	2	176.2	2.367
960.0	2	. . . . .	. .	2	85.0	62.207	2	49.7	2.104
925.9	1	445.9	. .	2	50.9	60	2	13.9	2.029
912.8	1	432.8	. .	2	37.8	59.146	2	. . . . .	2
875.0	1	395.0	. .	2	. . . . .	56.699	1	440.3	1.917
771.6	1	291.6	. .	1	334.1	50	1	331.5	1.691
617.3	1	137.3	. .	1	179.8	40	1	169.2	1.353
480.0	1	. . . . .	. .	1	42.5	31.1035	1	24.9	1.052
463.0	. .	. . . . .	. .	1	25.5	30	1	6.9	1.014
456.380	. .	. . . . .	. .	1	18.88	29.5729	1	. . . . .	1
437.5	. .	. . . . .	. .	1	. . . . .	28.350	. .	460.15	0.959
385.8	. .	. . . . .	. .	. .	. . . . .	25	. .	405.78	0.845
308.6	. .	. . . . .	. .	. .	. . . . .	20	. .	324.62	0.676
154.3	. .	. . . . .	. .	. .	. . . . .	10	. .	162.31	0.338
15.4324	. .	. . . . .	. .	. .	. . . . .	1	. .	16.23	0.0338
1	. .	. . . . .	. .	. .	. . . . .	0.06480	. .	1.0517	0.0022
0.9508	. .	. . . . .	. .	. .	. . . . .	0.06161	. .	1	0.0021

*Note—By the "cc." in this table is meant the one-thousandth part of the liter or a milliliter (ml).

Equivalents of Weights and Measures—*Continued.*

From 480 Grains down.

Grains.	Metric Weight and Measure Gm. or cc.*	Minims (of Water at 4° C.)	Grains.	Metric Weight and Measure Gm. or cc.*	Minims (of Water at 4° C.)
480 [1 ℥	31.103	504.8	240 [4 ʒ	15.552	252.4
478.4	31	503.2	231.5	15	243.5
475.4	30.805	500	228.2	14.786	240.0
463.0	30	486.9	218.75 ½ av. oz.	14.175	230.1
456.4	29.573	480 [1 f℥	216.1	14	227.2
450	29.160	473.3	210	13.608	220.9
447.5	29	470.7	200.6	13	211.0
437.5 [1 av. oz.	28.350	460.2	199.7	12.938	210.0
432.1	28	454.5	185.2	12	194.8
427.9	27.725	450			
420 [7 ʒ	27.216	4:417	180 [3 ʒ	11.664	189.3
416.7	27	438.2	171.1	11.090	180.0
401.2	26	422.0	169.8	11	178.5
399.3	25.876	420	154.3	10	162.3
390	25.272	410.2	150	9.720	157.8
385.8	25	405.8	142.6	9.242	150.0
380.3	24.644	400	138.9	9	146.1
370.8	24.028	390	123.5	8	129.8
370.4	24	389.5			
360 [6 ʒ	23.328	378.6	120 [2 ʒ	7.776	126.2
354.9	23	373.3	114.1	7.393	120.0
342.3	22.180	360	109.375 [¼ av oz	7.087	115.0
339.5	22	357.1	108.0	7	113.6
330	21.384	347.1	100	6.480	105.2
324.1	21	340.9	95.1	6.161	100.0
313.8	20.331	330	92.6	6	97.4
308.6	20	324.6	80	5.184	84.1
			77.2	5	81.2
			76.1	4.929	80.0
			61.7	4	64.9
300 [5 ʒ	19.440	315.5	60 [1 ʒ	3.888	63.1
293.2	19	308.4	57.0	3.697	60.0
285.2	18.483	300	54.6875 [⅛ av. oz.	3.544	57.5
277.8	18	292.2	47.5	3.081	50.0
270	17.496	284.0	50	3.240	52.6
262.4	17	275.9	46.3	3	48.7
256.7	16.635	270	42.8	2.772	45.0
246.9	16	259.7	40	2.592	42.1
			38.0	2.464	40.0
			33.3	2.156	35.0
			30.9	2	32.5

*NOTE—By the "cc." in this table is meant the one-thousandth part of the liter or a milliliter (ml).

Equivalents of Weights and Measures—*Continued.*

From 30 Grains down.		
Grains.	**Metric Weight and Measure** **Gm. or cc.***	Minims (of water at 4° C.)
30 [½ ʒ	1.944	31.55
28.52	1.848	30
23.77	1.540	25
20	1.296	21.04
19.02	1.232	20
15.4324	1	16.23
15	0.972	15.78
14.26	0.924	15
14	0.907	14.72
13.31	0.863	14
13	0.842	13.67
12.36	0.801	13
12	0.778	12.63
11.41	0.739	12
11	0.713	11.57
10.46	0.678	11
10	0.648	10.52
9.51	0.616	10
9	0.583	9.46
8.56	0.554	9
8	0.518	8.41
7.72	0.5	8.12
7.61	0.493	8
7	0.454	7.37
6.66	0.431	7
6	0.389	6.31
5.70	0.370	6
5	0.324	5.26
4.75	0.308	5
4	0.259	4.20
3.80	0.246	4
3	0.194	3.15
2.85	0.185	3
2	0.130	2.11
1.90	0.123	2
1	0.06480	1.0518
0.9508	0.06161	1

Weights from 5 Grains down.		
Grams.	Grains.	
	In decimal fractions.	In common fractions.
0.324	5	5
0.292	4.5	4½
0.259	4	4
0.227	3.5	3½
0.194	3	3
0.162	2.5	2½
0.130	2	2
0.097	1.5	1½
0.065	1	1
0.0607	0.9375	$\frac{15}{16}$
0.0583	0.90	$\frac{9}{10}$
0.0567	0.8750	⅞
0.0526	0.8125	$\frac{13}{16}$
0.0518	0.80	$\frac{4}{5}$
0.0486	0.75	¾
0.0445	0.6875	$\frac{11}{16}$
0.0405	0.6250	$\frac{5}{8}$
0.0364	0.5625	$\frac{9}{16}$
0.0324	0.5	½
0.0283	0.4375	$\frac{7}{16}$
0.0259	0.40	$\frac{2}{5}$
0.0243	0,3750	⅜
0.0202	0.3125	$\frac{5}{16}$
0.0162	0.25	¼
0.0121	0.1875	$\frac{3}{16}$
0.0081	0.1250	⅛
0.0040	0.0625	$\frac{1}{16}$
0.0032	0.05	$\frac{1}{2}$
0.0026	0.04	$\frac{1}{25}$
0.0022	0.033	$\frac{1}{30}$
0.0018	0.0278	$\frac{1}{36}$
0.0016	0.025	$\frac{1}{40}$
0.0013	0.02	$\frac{1}{50}$
0.0011	0.0167	$\frac{1}{60}$
0.0010	0.0156	$\frac{1}{64}$
0.0006	0.01	$\frac{1}{100}$
0.0005	0.0078	$\frac{1}{128}$
0.0004	0.0062	$\frac{1}{160}$
0.0003	0.0048	$\frac{1}{210}$
0.0002	0.0031	$\frac{1}{320}$
0.0001	0.0016	$\frac{1}{640}$

Note—By the "cc." in this table is meant the one-thousandth part of the liter or a milliliter (ml).

Equivalents of Linear Measures.

Metric to English.

Centimeters.	Inches.	Centimeters.	Inches.	Millimeters.	Inches.	
					In decimal fractions.	In 32ds.
150	59.06	55	21.65	25.4	1	32/32
145	57.09	53.3	21	25	0.98	..
140	55.12	50.8	20	24.0	0.94	..
139.7	55	50	19.69	23.8	0.94	30/32
135	53.15	48.3	19	23.0	0.91	29/32
130	51.18	45.7	18	22.2	0.88	28/32
127.0	50	45	17.72	22.0	0.87	..
125	49.21	43.2	17	21.0	0.83	..
120	47.24	40.6	16	20.6	0.81	26/32
115	45.28	40	15.75	20	0.79	..
114.3	45	38.1	15	19.1	0.75	24/32
110	43.31	35.6	14	19.0	0.75	..
105	41.34	35	13.78	18.0	0.71	..
101.6	40	33.0	13	17.5	0.69	22/32
100	39.37	30.5	12	17.0	0.67	..
99.1	39	30	11.81	16.0	0.63	..
96.5	38	27.9	11	15.9	0.62	20/32
95	37.40	25.4	10	15	0.59	..
94.0	37	25	9.84	14.3	0.56	18/32
91.4	36	22.9	9	14.0	0.55	..
90	35.43	20.3	8	13.0	0.51	..
88.9	35	20	7.87	12.7	0.50	16/32
86.4	34	17.8	7	12.0	0.47	..
85	33.46	15.2	6	11.1	0.44	14/32
83.8	33	15	5.91	11.0	0.43	..
81.3	32	12.7	5	10	0.39	..
80	31.50	10.2	4	9.5	0.38	12/32
78.7	31	10	3.94	9	0.35	..
76.2	30	9	3.54	8.7	0.34	11/32
75	29.53	8	3.15	8	0.31	..
73.7	29	7.6	3	7.9	0.31	10/32
71.1	28	7	2.76	7.1	0.28	9/32
70	27.56	6	2.36	7	0.28	..
68.6	27	5.1	2	6.4	0.25	8/32
66.0	26	5	1.97	6	0.24	..
65	25.59	4	1.57	5.6	0.22	7/32
63.5	25	3	1.18	5	0.20	..
61.0	24	2.54	1	4.8	0.19	6/32
60	23.62	2	0.79	4	0.16	..
58.4	23	1	0.39	3.2	0.12	4/32
55.9	22			3	0.12	..
				2.4	0.09	3/32
				2	0.08	..
				1.6	0.06	2/32
				1	0.04	..
				0.8	0.03	1/32
				0.1	0.0039	..

Equivalents of Linear Measures.

English to Metric.

Feet.	Meters.	Centimeters.	Inches	Millimeters.	Inches fractions.	Inches decimal fractions.	Millimeters.
25	7.620	762.0	34	863.6	$\frac{16}{16}$	1.000	25.40
24	7.315	731.5	33	838.2	$\frac{15}{16}$	0.9375	23.81
23	7.010	701.0	32	812.8	$\frac{7}{8}$	0.8750	22.22
22	6.706	670.6	31	787.4	$\frac{13}{16}$	0.8125	20.64
21	6.401	640.1	30	762.0	$\frac{6}{8}$	0.7500	19.05
20	6.096	609.6	29	736.6	$\frac{11}{16}$	0.6875	17.46
19	5.791	579.1	28	711.2	$\frac{5}{8}$	0.6250	15.88
18	5.486	548.6	27	685.8	$\frac{9}{16}$	0.5625	14.29
17	5.182	518.2	26	660.4	$\frac{1}{2}$	0.5000	12.70
16	4.877	487.7	25	635.0	$\frac{7}{16}$	0.4375	11.11
15	4.572	457.2	24	609.6	$\frac{3}{8}$	0.3750	9.52
14	4.267	426.7	23	584.2	$\frac{5}{16}$	0.3125	7.94
13	3.962	396.2	22	558.8	$\frac{1}{4}$	0.2500	6.35
12	3.658	365.8	21	533.4	$\frac{3}{16}$	0.1875	4.76
11	3.353	335.3	20	508.0	$\frac{1}{8}$	0.1250	3.18
10	3.048	304.8	19	482.6	$\frac{1}{16}$	0.0625	1.59
9	2.743	274.3	18	457.2	$\frac{1}{32}$	0.03125	0.79
8	2.438	243.8	17	431.8	$\frac{1}{64}$	0.01562	0.40
7	2.134	213.4	16	406.4	$\frac{1}{100}$	0.01000	0.25
6	1.829	182.9	15	381.0	$\frac{1}{200}$	0.00500	0.127
5	1.524	152.4	14	355.6	$\frac{1}{320}$	0.00312	0.08
4	1.219	121.9	13	330.2	$\frac{2}{3}$	0.667	16.93
3	0.9144	91.44	12	304.8	$\frac{1}{3}$	0.333	8.47
2	0.6096	60.96	11	279.4	$\frac{4}{5}$	0.800	20.32
1	0.3048	30.48	10	254.0	$\frac{3}{5}$	0.600	15.24
0.9	0.2743	27.43	9	228.6	$\frac{2}{5}$	0.400	10.16
0.8	0.2438	24.38	8	203.2	$\frac{1}{10}$	0.100	2.54
0.7	0.2134	21.34	7	177.8			
0.6	0.1829	18.29	6	152.4			
0.5	0.1524	15.24	5	127.0			
0.4	0.1219	12.19	4	101.6			
0.3	0.0914	9.144	3	76.2			
0.2	0.0610	6.096	2	50.8			
0.1	0.0305	3.048	1	25.4			

Table for Converting Metric Quantities in Pharmaceutical Processes to Quantities in the Avoirdupois System.

Table I—Grams to grains, etc. (Product measured).

Grams per liter.	Grains per fluidounce.		Grains, etc., per pint.		Grains, etc., per gallon.		
	Ounces avoir.	Grains.	Ounces avoir.	Grains.	Pounds avoir.	Ounces avoir.	Grains.
1	..	0.46	..	7.3	..	..	58.4
2	..	0.91	..	14.6	..	..	116.8
3	..	1.37	..	21.9	..	..	175.3
4	..	1.83	..	29.2	..	..	233.7
5	..	2.28	..	36.5	..	..	292.1
6	..	2.74	..	43.8	..	..	350.5
7	..	3.19	..	51.1	..	..	408.9
8	..	3.65	..	58.4	..	1	30.0
9	..	4.10	..	65.7	..	1	88.0
10	..	4.56	..	73.0	..	1	147.0
20	..	9.13	..	146.0	..	2	293.0
30	..	13.69	..	219.1	..	4	3.0
40	..	18.26	..	292.1	..	5	149.0
50	..	22.82	..	365.1	..	6	296.0
60	..	27.38	1	0.6	..	8	5.0
70	..	31.95	1	73.7	..	9	152.0
80	..	36.51	1	146.7	..	10	299.0
90	..	41.08	1	219.7	..	12	8.0
100	..	45.64	1	292.7	..	13	154.0
200	..	91.28	3	148.0	1	10	309.0
300	..	136.92	5	3.0	2	8	26.0
400	..	182.56	6	296.0	3	5	180.0
500	..	228.20	8	151.0	4	2	334.0
600	..	273.84	10	6.0	5	0	51.0
700	..	319.47	11	299.0	5	13	204.0
800	..	365.11	13	154.0	6	10	360.0
900	..	410.75	15	10.0	7	8	76.0
1000	1	18.89	16	302.0	8	5	231.0

Example: To make 1 gallon.

Soap Liniment.

Soap	60 Gm.	(Table I)	8 oz.	5 grs.
Camphor	45 Gm.	" " 40 Gm.	5 oz.	149 grs.
		5 Gm.		292.1 grs.
Oil of Rosemary	10 cc.	(Table II)	1 fl. oz.	134 min.
Alcohol	700 cc.	" " 5 pts.	9 fl. oz.	288 min.
Water, sufficient to make	1000 cc.		or 1 gallon	

Table for Converting Metric Quantities in Pharmaceutical Processes to Quantities in Apothecaries Measures.

Table II—Cc. to minims, etc. (Product Measured).

Cc. per liter.	Minims per fluidounce.	Minims, etc., per pint.		Minims, etc., per gallon.		
		Fl. oz.	Minims.	Pints.	Fl. oz.	Minims.
1	0.48	..	7.68	..	..	61
2	0.96	..	15.36	..	..	123
3	1.44	..	23.04	..	..	184
4	1.92	..	30.72	..	..	246
5	2.40	..	38.40	..	..	307
6	2.88	..	46.09	..	..	369
7	3.36	..	53.76	..	..	430
8	3.84	..	61.44	..	1	12
9	4.32	..	69.12	..	1	73
10	4.80	..	76.80	..	1	134
20	9.60	..	153.60	..	2	269
30	14.40	..	230.40	..	3	403
40	19.20	..	307.20	..	5	58
50	24.00	..	384.00	..	6	192
60	28.80	..	460.80	..	7	326
70	33.60	1	57.60	..	8	461
80	38.40	1	134.40	..	10	115
90	43.20	1	211.20	..	11	250
100	48.00	1	288.00	..	12	384
200	96.00	3	96.00	1	9	288
300	144.00	4	384.00	2	6	192
400	192.00	6	192.00	3	3	96
500	240.00	8	.....	4	..	...
600	288.00	9	288.00	4	12	384
700	336.00	11	96.00	5	9	288
800	384.00	12	384.00	6	6	192
900	432.00	14	192.00	7	3	96
1000	480.00	16	.....	8	..	...

Table for Converting Metric Quantities in Pharmaceutical Processes to Quantities in Apothecaries Weights.

Table III—Parts per 1000 to Grains, etc., per Pound Avoirdupois.

Grams per kilograms.	Grains and apothecaries ounces per pound avoirdupois.		Grains and ounces avoirdupois per pound avoirdupois.	
	Ounces.	Grains.	Ounces.	Grains.
1	..	7	..	7.0
2	..	14	..	14.0
3	..	21	..	21.0
4	..	28	..	28.0
5	..	35	..	35.0
6	..	42	..	42.0
7	..	49	..	49.0
8	..	56	..	56.0
9	..	63	..	63.0
10	..	70	..	70.0
20	..	140	..	140.0
30	..	210	..	210.0
40	..	280	..	280.0
50	..	350	..	350.0
60	..	420	..	420.0
70	1	10	1	52.5
80	1	80	1	122.5
90	1	150	1	192.5
100	1	220	1	262.5
200	2	440	3	87.5
300	4	180	4	350.0
400	5	400	6	175.0
500	7	140	8	....
600	8	360	9	262.5
700	10	100	11	87.5
800	11	320	12	350.0
900	13	60	14	175.0
1000	14	280	16	....

Example: To make 1 pound avoirdupois.

Camphor Liniment

Camphor..........................	200 Gm.	(Table III)................	3 oz.	87.5 grs.
Cottonseed Oil......................	800 Gm.	" "	12 oz.	350.0 grs.
To make.......................	1000 Gm.		or 1 pound avoirdupois	

AVOIRDUPOIS WEIGHT.

Pound.		Ounces.		Drachms.		Troy Grains.
℔ 1	=	16	=	256	=	7000
		oz. 1	=	16	=	437.5
				dr. 1		gr. 27.34375

Relative Value of Troy and Avoirdupois Weights.

Pound.		Pounds.		Pound.	Ounces.	Grains.
1 Troy	=	0.822857 Avoirdupois	=	0	13	72.5
1 Avoirdupois	=	1.215277 Troy	=	1	2	280

APOTHECARIES OR WINE MEASURE.

Gallon.		Pints.		Fluidounces.		Fluidrachms.		Minims.		Cubic Inches.
Cong. 1	=	8	=	128		1024	=	61440	=	231
	=	O 1	=	16	=	128	=	7680	=	28.875
				f℥ 1	=	8	=	480	=	1.8047
						fʒ 1	=	♏ 60	=	.2256

IMPERIAL MEASURE.

Adopted by the British Pharmacopœia.

Gallon.		Pints.		Fluidounces.		Fluidrachms.		Minims.
1	=	8	=	160	=	1280	=	76800
		1	=	20	=	160	=	9600
				1	=	8	=	480
						1	=	60

The Imperial Standard Troy weight, at present recognized by the British laws, corresponds with the Apothecaries' weight in pounds, ounces, and grains; but differs from it in the division of the ounce, which according to the former scale, contains twenty pennyweights, each weighing twenty-four grains.

Relative Value of Apothecaries' and Imperial Measure.

Apothecaries' Measure.		**Imperial Measure.**			
		Pints.	Fluidounces.	Fluidrachms.	Minims.
1 gallon	=	6	13	2	23
1 pint	=		16	5	18
1 fluidounce	=		1	0	20
1 fluidrachm	=			1	2.5
1 minim	=				1.04

Imperial Measure.		**Apothecaries' Measure.**				
		Gallon.	Pints.	Fluidounces.	Fluidrachms.	Minims.
1 gallon	=	1	1	9	5	8
1 pint	=		1	3	1	38
1 fluidounce	=				7	41
1 fluidrachm	=					58
1 minim	=					0.96

Relative Value of Weights and Measures in Distilled Water at 25° C. (77° F.).

1. Value of Apothecaries' Weight in Apothecaries' Measure.

				Pints.	Fluidounces.	Fluidrachms.	Minims.
1 pound	=	0.79188319 pint	=	0	12	5	21.6629
1 ounce	=	1.0558489 fluidounces	=	0	1	0	26.8975
1 drachm	=	1.0558489 fluidrachms	=	0	0	1	3.3509
1 scruple	=			0	0	0	21.1170
1 grain	=			0	0	0	1.0558

2. Value of Apothecaries' Measure in Apothecaries' Weight.

				℔	℥	ʒ	℈	Gr.		Grains.
1 gallon	=	10.1025000 pounds	=	10	1	1	2	10.4	=	58190.400
1 pint	=	1.2628125 pounds	=	1	3	1	0	13.80	=	7273.8000
1 fluidounce	=	0.94710937 ounce	=	0	0	7	1	14.61	=	454.6125[1]
1 fluidrachm	=	0.94710937 drachm	=	0	0	0	2	16.83	=	56.8266
1 minim	=	0.94710937 grain	=							.9471

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[1] The weight of a fluidounce of water at 25° C. (77° F.) according to the Table of Weight and Volume Relations in the U. S. Pharmacopœia IX is 454.6 grains.

3. Value of Avoirdupois Weight in Apothecaries' Measure.

				Pints.	Fluidounces.	Fluidrachms.	Minims.
1 pound	=	0.96235805 pint	=	0	15	3	10.9098
1 ounce	=	0.96235805 fluidounce	=	0	0	7	41.9319

4. Value of Apothecaries' Measure in Avoirdupois Weight.

1 gallon = 8.312914285 pounds.
1 pint = 1.039114285 pounds.
1 fluidounce = 1.039114285 ounces.

5. Value of Imperial Measure in Apothecaries' and Avoirdupois Weights.

Imperial Measure.		Apothecaries' Weight.						Avoirdupois Weight.			Grains.		Cubic Inches.
1 gallon	=	12 ℔	1 ℥	6 ʒ	2 ℈	0 gr.	=	10 ℔	0 oz.	=	70,000	=	277.27384
1 pint	=	1	6	1	2	10	=	1	4	=	8,750	=	34.65923
1 fluidounce	=			7	0	17.5	=		1	=	437.5	=	1.73296
1 fluidrachm	=				2	14.69	=				54.69	=	0.21662
1 minim	=										.91	=	0.00361

In converting the weights of liquids heavier or lighter than water into measures, or conversely, a correction must be made for specific gravity. In converting weights into measures‘ the calculator may proceed as if the liquid were water, and the obtained measure will be to the true measure *inversely* as the specific gravity. In the converse operation, of turning measures into weights, the same assumption may be made, and the obtained weight will be to the true weight *directly* as the specific gravity.

Drops

Small quantities of liquid medicines are often administered by *drops*, each of which is often considered equivalent to a minim, or the sixtieth part of a fluidrachm. The drop of water and of aqueous fluids is, sometimes, about that size; but the same is by no means the case with all medicinal liquids, and the drop even of the same liquid varies much in bulk, according to the circumstances under which it is formed. This is, therefore, an uncertain mode of estimating the quantity of liquids, and should be superseded where minim measures can be had. Certain rules, however, influence the formation of drops, which will enable us to form some notion of their probable relative number, in the same amount of liquid when possessed of the requisite data. Thus, the heavier the liquid, the smaller, other things being equal, is the size of the drops, and the greater their number in a given measure. The drop of chloroform, for example, which is a very heavy liquid, is very small, much smaller than that of alcohol or ether. The greater or less viscidity and greater or less mobility of the liquid have much influence, the former in increasing, the latter in diminishing the size of the drops. The adhesiveness of liquids, which opposes their disposition to leave the surface from which they fall, requires a greater mass to overcome it, and consequently augments the size of the drop. The rapidity of the movement acts in a contrary direction, and the drop from a full bottle should be less than from one more or less emptied. The broader the surface from which they fall, the greater is their size. The drops from a thick-lipped bottle are larger than from one with thin lips.

The results stated in the table below were obtained by Stephen L. Talbot. They may be relied on as accurate, and in most cases correspond with the results obtained by Durand and Procter (see *A. J. P.*, i, 169; 1865, p. 389; 1880, p. 337), but should be considered as indicating only the relative number of drops afforded by the several liquids mentioned under the specific conditions of the experiment with the preparations then official. While modifications in some of the methods of making the preparations and while under other circumstances than those of Talbot's experiments, entirely different results might be obtained as relates to each liquid the matter is of so much interest that, in the absence of any later data of the kind, it has been felt to be worthy of preservation as at least an approximate indication of the size of a "drop".

TABLE EXHIBITING THE NUMBER OF DROPS IN A FLUIDRACHM OF DIFFERENT LIQUIDS, WITH THE WEIGHT IN GRAINS AND GRAMMES.

Name.	Drops in fʒi (60 m.)	Weight of fʒi.		Name.	Drops in fʒi (60 m).	Weight of fʒi.	
		in gr.	in Gm.			in gr.	in Gm.
Acetum Scillæ	68	57	3.69	Sodæ Chlorinatæ	63	62	4.01
Acidum Aceticum	108	58	3.75	Zinci Chloridi	89	88	5.70
Aceticum Dilutum	68	55	3.56	Oleoresina Aspidii	130	52	3.36
Hydrochloricum	70	65	4.21	Capsici	120	51	3.30
Hydrochlor, Dilutum	60	56	3.62	Cubebæ	123	52	3.36
Hydrocyanicum Dilutum	60	54	3.49	Oleum			
Lacticum	111	66	4.27	Amygdalæ Amaræ	115	55	3.56
Nitricum	102	77	4.98	Amygdalæ Expres	108	48½	3.14
Nitricum Dilutum	60	58	3.62	Anisi	119	54	3.49
Nitrohydrochloricum	76	66	4.27	Bergamottæ	130	46	2.98
Phosphoricum Dilutum	59	57	3.69	Cari	132	50	3.24
Sulphuricum	128	101	6.54	Caryophylli	130	57	3.69
Sulphuricum Aromaticum	146	53	3.43	Cinnamomi	126	53½	3.46
Sulphuricum Dilutum	60	58½	3.79	Copaibæ	123	49½	3.20
Æther	176	39	2.52	Cubebæ	125	51	3.30
Alcohol	146	44	2.85	Fœniculi	125	53	3.43
Dilutum	137	49	3.17	Gaultheriæ	125	62	4.01
Aque	60	55	3.56	Juniperi	148	49	3.17
Ammoniæ Fortior	66	50	3.24	Lavandulæ	138	52	3.36
Destillata	60	53½	3.46	Limonis	129	47	3.04
Balsamum Peruvianum	101	60	3.88	Menthæ Piperitæ	129	50	3.24
Bromum	250	165	10.69	Ricini	77	51½	3.33
Chloroformum	250	80	5.18	Rosæ	132	47	3.04
Copaiba	110	51	3.30	Rosmarini	143	50	3.24
Creosotum	122	56½	3.66	Sassafras	133	58	3.75
Fluidextractum Belladonnæ	156	57	3.69	Terebinthinæ	136	45½	2.94
Buchu	150	47½	3.07	Tiglii	104	50	3.24
Cimicifugæ	147	48	3.11	Spiritus Ætheris Compositus	148	45	2.91
Cinchonæ	138	58	3.75	Ætheris Nitrosi	146	47	3.04
Colchici	158	55	3.56	Ammoniæ Aromaticus	142	48	3.11
Digitalis	134	62	4.01	Camphoræ	143	47	3.04
Ergotæ	133	60	3.88	Chloroformi	150	48	3.11
Gelsemii	149	49	3.14	Menthæ Piperitæ	142	47	3.04
Glycyrrhizæ	133	61	3.95	Syrupus	65	72	4.66
Hyoscyami	160	59	3.82	Acaciæ	44	73	4.73
Ipecacuanhæ	120	60	3.88	Ferri Iodidi	65	77	4.98
Rhei	158	61	3.95	Scillæ	75	74	4.79
Sarsaparillæ Compositum	134	60	3.88	Scillæ Compositus	102	70	4.53
Senegæ	137	62	4.01	Senegæ	106	70	4.53
Uvæ Ursi	137	60	3.88	Tinctura Aconiti	146	46	2.98
Zingiberis	142	48	3.11	Belladonnæ	137	53	3.43
Glycerinum	67	68	4.40	Benzoini Composita	148	48	3.11
Hydrargyrum	150	760	49.24	Cantharidis	131	51	3.33
Liquor Acidi Arsenosi	75	56	3.62	Cinchonæ Composita	140	49	3.17
Ammonii Acetatis	57	55	3.56	Digitalis	128	53	3.43
Arseni et Hydrargyri Iodidi	58	55	3.56	Ferri Chloridi	150	53	3.43
Ferri Chloridi	71	72	4.66	Iodi	148	47	3.04
Ferri Subsulphatis	73	83	5.37	Nucis Vomicæ	140	44	2.85
Ferri Tersulphatis	83	72	4.66	Opii	130	52	3.49
Iodi Compositus	63	59	3.82	Opii Camphorata	130	52	3.36
Plumbi Subacetatis	74	70	4.53	Valerianæ	130	52	3.36
Potassii Hydroxidi	62	58	3.75	Veratri Viridis	145	46	2.98
Potassii Arsenitis	57	55	3.56	Zingiberis	144	46	2.98

TABLES SHOWING SPECIFIC GRAVITY CORRESPONDING WITH DEGREES OF HYDROMETERS.

Baumé's hydrometer is still largely employed. In this instrument the specific gravity of distilled water is assumed as the zero of the descending scale in relation to fluids heavier than itself, and as ten on the ascending scale in relation to lighter fluids. In the following tables the specific gravity of liquids is given corresponding with the several degrees of this hydrometer. The first column of specific gravities is taken from the French Codex. The second column is based on the calculations of Huss. The third column was calculated by Henry Pemberton of Philadelphia, in 1851. The figures in this column correspond with the degrees of the hydrometers formerly prepared by W. H. Pile.

FOR LIQUIDS LIGHTER THAN WATER.
(Baumé's hydrometer.)

Degree of hydrometer.	Specific Gravity.			Degree of hydrometer.	Specific Gravity.		
	By Baumé.				By Baumé.		
10	1.000	1.0000	1.0000	44	0.809	0.8047	0.8045
11	0.993	0.9930	0.9929	45	0.804	0.8001	0.8000
12	0.986	0.9861	0.9859	46	0.800	0.7956	0.7954
13	0.979	0.9792	0.9790	47	0.795	0.7911	0.7909
14	0.973	0.9724	0.9722	48	0.791	0.7866	0.7865
15	0.966	0.9657	0.9655	49	0.787	0.7821	0.7821
16	0.960	0.9591	0.9589	50	0.783	0.7777	0.7777
17	0.953	0.9526	0.9523	51	0.778	0.7733	0.7734
18	0.947	0.9462	0.9459	52	0.774	0.7689	0.7692
19	0.941	0.9399	0.9395	53	0.770	0.7646	0.7650
20	0.935	0.9336	0.9333	54	0.766	0.7603	0.7608
21	0.929	0.9274	0.9271	55	0.762	0.7560	0.7567
22	0.923	0.9212	0.9210	56	0.758	0.7518	0.7526
23	0.917	0.9151	0.9150	57	0.754	0.7476	0.7486
24	0.911	0.9091	0.9090	58	0.750	0.7435	0.7446
25	0.905	0.9032	0.9032	59	0.746	0.7394	0.7407
26	0.900	0.8974	0.8974	60	0.742	0.7354	0.7368
27	0.894	0.8917	0.8917	61	0.738	0.7314	0.7329
28	0.889	0.8860	0.8860	62	0.735	0.7275	0.7290
29	0.883	0.8804	0.8805	63	0.731	......	0.7253
30	0.878	0.8748	0.8750	64	0.727	......	0.7216
31	0.872	0.8693	0.8695	65	0.724	......	0.7179
32	0.867	0.8638	0.8641	66	0.720	......	0.7142
33	0.862	0.8584	0.8588	67	0.716	......	0.7106
34	0.857	0.8531	0.8536	68	0.713	......	0.7070
35	0.852	0.8479	0.8484	69	0.709	......	0.7035
36	0.847	0.8428	0.8433	70	0.706	......	0.7000
37	0.842	0.8378	0.8383	71	0.702	......	0.6965
38	0.837	0.8329	0.8333	72	0.699	......	0.6930
39	0.832	0.8281	0.8284	73	0.696	......	0.6896
40	0.827	0.8233	0.8235	74	0.692	......	0.6863
41	0.823	0.8186	0.8187	75	0.689	......	0.6829
42	0.818	0.8139	0.8139	76	0.686	......	0.6796
43	0.813	0.8093	0.8092	77	0.682	......	0.6763

The following formulas, furnished by Pile, may prove useful by enabling any one to calculate the sp. gr. corresponding with the several degrees of Baumé's hydrometer, and, conversely, the degree of Baumé corresponding with the sp. gr.

1. *For Liquids lighter than Water.*—The following formulas give the sp. gr. as represented in the first column in the foregoing table; or, the specific gravity being known, give the corresponding degree of Baumé.

$$\frac{144}{\text{B}^\circ + 134} = \text{sp. gr.; and } \frac{144}{\text{sp. gr.}} - 134 = \text{B}^\circ.$$

The following formulas apply to the third column of specific gravities.

$$\frac{140}{\text{B}^\circ + 130} = \text{sp. gr.; and } \frac{140}{\text{sp. gr.}} - 130 = \text{B}^\circ.$$

2. *For Liquids heavier than Water.*—For the first column, $\frac{144}{144 - \text{B}^\circ} = \text{sp. gr.}$, and $144 - \frac{144}{\text{sp. gr.}} = \text{B}^\circ$; for the third, $\frac{145}{145 - \text{B}^\circ} = \text{sp. gr.}$, and $145 - \frac{145}{\text{sp. gr.}} = \text{B}^\circ$.

FOR LIQUIDS HEAVIER THAN WATER.

(Baumé's hydrometer.)

Degree of hydrometer.	Specific Gravity.			Degree of hydrometer.	Specific Gravity.		
	By Baumé.				By Baumé.		
0	1.000	1.0000	1.0000	38	1.359	1.3559	1.3551
1	1.007	1.0070	1.0069	39	1.372	1.3686	1.3679
2	1.014	1.0141	1.0139	40	1.384	1.3815	1.3809
3	1.022	1.0213	1.0211	41	1.398	1.3947	1.3942
4	1.029	1.0286	1.0283	42	1.412	1.4082	1.4077
5	1.036	1.0360	1.0357	43	1.426	1.4219	1.4215
6	1.044	1.0435	1.0431	44	1.440	1.4359	1.4356
7	1.052	1.0511	1.0507	45	1.454	1.4501	1.4500
8	1.060	1.0588	1.0583	46	1.479	1.4645	1.4646
9	1.067	1.0666	1.0661	47	1.485	1.4792	1.4795
10	1.075	1.0745	1.0740	48	1.501	1.4942	1.4949
11	1.083	1.0825	1.0820	49	1.516	1.5096	1.5104
12	1.091	1.0906	1.0902	50	1.532	1.5253	1.5263
13	1.100	1.0988	1.0984	51	1.549	1.5413	1.5425
14	1.108	1.1071	1.1008	52	1.566	1.5576	1.5591
15	1.116	1.1155	1.1153	53	1.583	1.5742	1.5760
16	1.125	1.1240	1.1240	54	1.601	1.5912	1.5934
17	1.134	1.1326	1.1328	55	1.618	1.6086	1.6111
18	1.143	1.1414	1.1417	56	1.637	1.6264	1.6292
19	1.152	1.1504	1.1507	57	1.656	1.6446	1.6477
20	1.161	1.1596	1.1600	58	1.676	1.6632	1.6666
21	1.171	1.1690	1.1693	59	1.695	1.6823	1.6860
22	1.180	1.1785	1.1788	60	1.715	1.7019	1.7058
23	1.190	1.1882	1.1885	61	1.736	1.7220	1.7261
24	1.199	1.1981	1.1983	62	1.758	1.7427	1.7469
25	1.210	1.2082	1.2083	63	1.779	1.7640	1.7682
26	1.221	1.2184	1.2184	64	1.801	1.7856	1.7901
27	1.231	1.2288	1.2288	65	1.823	1.8082	1.8125
28	1.242	1.2394	1.2393	66	1.847	1.8312	1.8354
29	1.252	1.2502	1.2500	67	1.872	1.8548	1.8589
30	1.261	1.2612	1.2608	68	1.897	1.8790	1.8831
31	1.275	1.2724	1.2719	69	1.921	1.9038	1.9079
32	1.286	1.2838	1.2831	70	1.946	1.9291	1.9333
33	1.298	1.2954	1.2946	71	1.974	1.9548	1.9595
34	1.309	1.3072	1.3063	72	2.002	1.9809	1.9863
35	1.321	1.3190	1.3181	73	2.031	2.0073	2.0139
36	1.334	1.3311	1.3302	74	2.059	2.0340	2.0422
37	1.346	1.3434	1.3425	75	2.087	2.0610	2.0714

Gay-Lussac's centesimal alcoholmeter is applicable only to alcohol. The scale of this instrument is divided into 100 unequal degrees, the zero corresponding to pure water, and 100° to absolute alcohol ; and every intermediate degree expresses the percentage of pure alcohol, by measure, contained in the liquors examined. Thus, when the instrument stands at 40° in any alcoholic liquid, it indicates that 100 measures of the liquid contain 40 of pure alcohol and 60 of water. But, as it was graduated for the temperature of 59° of Fahrenheit, the liquors to be tested should be brought to that temperature. *Tralles's centesimal alcoholmeter* is the one used by the U. S. Government in gauging the strength of spirit, and is generally employed in this country by distillers and wholesale dealers in the purchase and sale of alcoholic liquors. The scale of this instrument is, like Gay-Lussac's, divided into 100 unequal parts, each corresponding to the percentage by volume of pure alcohol contained in the liquors examined. As the sp. gr. of water is considered as unity at its temperature of greatest density, 39.8° F., and the degrees of this scale are calculated for 60° F., the zero, corresponding to the density of water, will represent a sp. gr. of .9991.

The table of Tralles on page 1752 gives the percentage of alcohol *by volume* corresponding with the specific gravity. Under the heading of Alcohol tables (see page 1757), a table of the percentage by weight corresponding with the sp. gr. is given. By means of these tables, in connection with the alcoholmeter, every problem that can arise in reference to the strength of spirituous liquors can be solved ; and by the appended table, giving the value of Baumé's degrees in those of Tralles, the facility is still further extended.

Sikes's hydrometer is used in Great Britain in the collection of the excise revenue : it is a brass instrument having a spherical bulb, with a weight at the bottom to make it float upright ; the stem is divided into twenty parts, and every other division numbered, from 0 to 10. A series of nine weights are furnished with the instrument, numbered from 10 to 90 ; these are to be added to the weight at the bottom to cause the hydrometer to sink, so that a reading may be had on the graduated scale ; this reading added to the number on the weight employed, gives a figure which indicates the strength of the spirit by referring to a table which accompanies the instrument.

Jones's hydrometer is similar to Sikes's, but by many is regarded as an improvement on it.

PART III

SECTION II

NATIONAL FORMULARY

The National Formulary, published by the American Pharmaceutical Association, was originally planned as a convenience for druggists by providing them with standardized formulas for preparations called for either by the laity or by physicians. Under the Federal law of 1906 it became a legal standard for medicines in the United States. This change in its status has led to some modification in the character of the N. F.; it has been divided in two parts: first a collection of formulas of the same type as originally composed the book, and second a description of such crude drugs employed in these formulas as are not recognized by the Pharmacopœia, with tests for their quality. This second part of the N. F., being essentially of the same category as the Pharmacopœial descriptions, has been included in Part I of the present work. The galenicals of the N. F., being of less importance, are given only in abstract in this place.

ACETUM AROMATICUM. N. F.

Aromatic Vinegar [Acet. Arom.]

It contains the volatile oils of lavender, rosemary, juniper, peppermint, cinnamon, lemon and clove, dissolved in alcohol, acetic acid and water, and is used as a stimulating inhalant.

ACIDUM NITROHYDROCHLORICUM. N. F.

Nitrohydrochloric Acid [Acid. Nitrohydrochl.]

Nitromuriatic Acid; Aqua Regia.

This differs materially from the acid of the same name which is official in the Br. It is made by mixing eighteen parts of nitric and eighty-two parts of hydrochloric acids. It is a golden yellow, fuming liquid with a chlorinous odor; it becomes lighter in color when kept, but only the golden fluid should be dispensed. The N. F. directs that unless it immediately liberates iodine from aqueous solution of potassium iodide it should not be dispensed. For description of chemical and therapeutic properties see *Acidum Nitrohydrochloricum*, Part I.

Dose, three to five minims (0.2–0.3 cc.).

ACIDUM NITROHYDROCHLORICUM DILUTUM. N. F.

Diluted Nitrohydrochloric Acid [Acid. Nitrohydrochl. Dil.]

Diluted Nitromuriatic Acid.

This represents approximately 22 per cent. of the nitrohydrochloric acid, N. F.

Dose, fifteen to thirty minims (1–2 cc.).

AMPULLÆ.

Ampules

These are small, hermetically sealed containers which are filled with a sterile solution of a medicinal agent intended for hypodermic injection. In our opinion the name is an unfortunate one as it applies to the container rather than the contents; the British name, for the corresponding preparation, of *Injectiones Hypodermicæ* seems more appropriate.

The amount of solution in each is a little more than 1 cc. (except one which is 2 cc.); this is to allow for the small amount of liquid which inevitably remains in the container when the physician fills his syringe from it.

AMPULLÆ CAFFEINÆ SODIO BENZOATIS. N. F.

Ampules of Caffeine Sodio-Benzoate [Ampul. Caf. Sod.-Benz.]

Each ampule represents 0.5 Gm. (eight grains) of the U. S. P. caffeine sodio-benzoate in sterile distilled water.

Dose, one ampule.

AMPULLÆ CAMPHORÆ.

Ampules of Camphor

Each ampule contains 0.2 Gm. (three grains) of camphor dissolved in cottonseed oil. It is used as a circulatory stimulant.

Dose, one ampule.

AMPULLÆ EMETINÆ HYDROCHLORIDI. N. F.

Ampules of Emetine Hydrochloride [Ampul. Emet. Hydrochl.]

Each ampule contains 0.03 Gm. (one-half grain) of emetine hydrochloride. It is used in the treatment of dysentery.

Dose, one ampule.

AMPULLÆ IODI. N. F.

Ampules of Iodine

Iodine Swabs.

This is a solution of 3.5 per cent. of iodine and 2.5 per cent. of potassium iodide, in 70 per cent. alcohol. It is intended as a surgical antiseptic, being of a more desirable strength for this purpose than the U. S. tincture of iodine.

AMPULLÆ QUININÆ ET UREÆ HYDROCHLORIDI. N. F.

Ampules of Quinine and Urea Hydrochloride [Ampul. Quin. Et Urea Hydrochl.]

Each contains 0.5 Gm. of quinine and urea hydrochloride. It affords a convenient method of obtaining the therapeutic action of quinine by hypodermic injection and is especially employed in pneumonia.
Dose, one ampule.

AMPULLÆ QUININÆ DIHYDROCHLORIDI. N. F.

Ampules of Quinine Dihydrochloride [Ampul. Quin. Dihydrochl.]

Each ampule contains 0.5 Gm. of the acid hydrochloride of quinine, the acidity of the solvent being regulated by titration. It is intended for the hypodermic administration of quinine, especially in severe cases of malarial fever.
Dose, one ampule.

AMPULLÆ SODII CACODYLATIS. N. F.

Ampules of Sodium Cacodylate [Ampul. Sod. Cacodyl.]

Each ampule contains 0.3 Gm. (five grains) of sodium cacodylate.
Dose, one ampule.

AQUA HAMAMELIDIS. N. F.

Hamamelis Water [Aq. Hamam.]

Witch Hazel Water; Distilled Extract of Witch Hazel.

This is a popular, but useless, embrocation made by distillation of hamamelis twigs. It contains a trace of volatile oil but no therapeutically active substance; even the alcohol present is in too small a proportion to exert any beneficial action.

AQUA PHENOLATA. N. F.

Phenolated Water [Aq. Phenol.]

Carbolic Acid Water; Phenolis Soluto, *P. I.*

This is a 2 per cent. solution of phenol in distilled water and is used as a lotion, gargle, etc.

CAFFEINÆ SODIO-SALICYLAS. N. F.

Caffeine Sodio-Salicylate [Caff. Sod.-Sal.]

This powder contains equal parts of caffeine and sodium salicylate. It is used for the same purposes as the caffeine sodio-benzoate (see Part I). The *dose* is three grains (0.2 Gm.).

CATAPLASMA KAOLINI. N. F.

Cataplasm of Kaolin [Catapl. Kaolin.]

This is a mixture of kaolin, glycerin, boric acid, thymol and oils of peppermint and wintergreen. It is used as a substitute for poultices. It should be applied as hot as can be comfortably endured.

CERATUM CAMPHORÆ. N. F.

Camphor Cerate [Cerat. Camph.]

Camphorated Ointment.

This preparation is composed of 10 per cent. of camphor liniment in a cerate base.

CERATUM PLUMBI SUBACETATIS. N. F.

Cerate of Lead Subacetate [Cerat. Plumb. Subacet.]

Goulard's Cerate.

This well-known cerate contains 20 per cent. of Goulard's extract mixed with a cerate base containing a little camphor. It is used as an astringent and sedative dressing.

CERATUM RESINÆ COMPOSITUM. N. F.

Compound Rosin Cerate [Cerat. Resin. Co.]

Deshler's Salve.

This popular cerate contains rosin, yellow wax, suet, turpentine, and linseed oil. It is used as a stimulating dressing.

CHARTA POTASSII NITRATIS. N. F.

Potassium Nitrate Paper [Chart. Pot. Nit.]

This is made by saturating unsized paper in a strong solution of potassium nitrate and drying. It is used in asthma by burning it and inhaling the smoke.

CHLORAL CAMPHORATUM. N. F.

Camphorated Chloral [Chloral Camph.]

A eutectic mixture of equal parts of hydrated chloral and camphor, used as a local anodyne and counter-irritant.

COLLODIUM BITUMINIS SULPHONATI. N. F.

Collodion of Sulphonated Bitumen [Collod. Bitum. Sulphon.]

Ichthyol Collodion.

This contains 10 per cent. of sulphonated bitumen in flexible collodion. It does not seem to us a very efficacious way of applying ichthyol.

COLLODIUM SALICYLICUM COMPOSITUM. N. F.

Compound Salicylic Collodion [Collod. Sal. Co.]

Corn Collodion; Collodium Salicylatum Compositum.

It contains salicylic acid, extract of cannabis, and flexible collodion. Used for the removal of corns.

COLLODIUM STYPTICUM. N. F.

Styptic Collodion [Collod. Stypt.]

This is a 20 per cent., by weight, solution of tannic acid in flexible collodion. It is used as a styptic application to cuts and small wounds.

CONFECTIO ROSÆ. N. F.

Confection of Rose [Confect. Ros.]

It is used principally as a pill excipient or vehicle. (See *Confectio Rosæ Gallicæ*, Part I.)

CONFECTIO SENNÆ. N. F.

Confection of Senna [Confect. Senn.]

This is very similar to the Br. confection of senna (see Part I).
Dose, sixty grains, 4 Gm., representing six grains of senna and nine and a half grains of cassia fistula.

CURATIO PARAFFINI. N. F.

Paraffin Dressing [Curat. Paraf.]

Paraffin Film.

Under this peculiar title is a paraffin softened by the addition of white petrolatum and olive oil, and containing 1 per cent. of resorcinol and 2 per cent. of eucalyptol. It is intended as a local application for burns.

DENTIFRICIUM. N. F.

Dentifrice [Dentif.]

Tooth-powder; Oxidizing Tooth-powder.

This tooth-powder contains soap, sugar and flavoring, prepared chalk, precipitated calcium carbonate and 5 per cent. of sodium perborate; because of the abrasive properties of precipitated calcium carbonate it would have been better, in our opinion, to have substituted for it an increase in the amount of chalk.

DENTILINIMENTUM ACONITI COMPOSITUM. N. F.

Compound Dental Liniment of Aconite [Dentilin. Aconit. Co.]

This contains 36 per cent. of menthol and 13.5 per cent. of chloroform in tincture of aconite. It is a powerful counter-irritant and local anesthetic, used in neuralgic conditions of the gums and in toothache. It should not be confounded with the compound liniment of aconite which is used externally.

DENTILINIMENTUM ACONITI ET IODI COMPOSITUM. N. F.

Compound Dental Liniment of Aconite and Iodine [Dentilin. Aconit. et Iod. Co.]

Refrigerant Counter-irritant.

This contains 2.2 per cent. of each of menthol and iodine and 16.5 per cent. of chloroform dissolved in tincture of aconite. It is used for similar properties to the above but is less actively counter-irritant but more antiseptic.

ELIXIR ALETRIDIS COMPOSITUM. N. F.

Compound Elixir of Aletris [Elix. Aletrid. Co.]

This contains, in each fluidrachm, 3¾ minims of the fluidextracts of aletris, mitchella, helonias and caulophyllum with 1⅞ minims of viburnum opulus. As none of these drugs are of much value and as the quantities present are ridiculously minute it is evident that the elixir is of no great use. It is intended for dysmenorrhea.

Dose, one to four fluidrachms (4–15 cc.).

ELIXIR AMMONII BROMIDI. N. F.

Elixir of Ammonium Bromide [Elix. Ammon. Brom.]

It is made with ammonium bromide and a diluted and sweetened aromatic elixir. It contains 5 grains of ammonium bromide in 1 fluidrachm of finished elixir.

The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR AMMONII VALERATIS. N. F.

Elixir of Ammonium Valerate [Elix. Ammon. Valer.]

Elixir Ammonii Valerianatis, *N. F. III.*

This preparation is made with ammonium valerate and chloroform dissolved in aromatic elixir, colored with cudbear and flavored with vanilla. It contains 2 grains of ammonium valerate in 1 fluidrachm of finished elixir.

The *dose* is one fluidrachm (4 cc.).

ELIXIR AMYGDALÆ COMPOSITUM. N. F.

Compound Elixir of Almond [Elix. Amygdal. Co.]

This is a flavoring elixir of very low alcoholic strength (5 per cent.) containing oil of bitter almond, vanillin, and orange flower water as the essential ingredients.

ELIXIR ANISI. N. F.

Elixir of Anise [Elix. Anis.]

This is a misnamed elixir containing a very low proportion of alcohol. It contains anethol, oil of fennel, spirit of bitter almond, alcohol, syrup and water. Used as a vehicle.

ELIXIR AROMATICUM RUBRUM. N. F.

Red Aromatic Elixir [Elix. Arom. Rub. Red Elixir]

This is the U. S. P. aromatic elixir colored red with cudbear.

ELIXIR AURANTII AMARI. N. F.

Elixir of Bitter Orange [Elix. Aurant. Amar.]

Elixir Curassoa; Elixir of Curaçao.

This is an improvement upon the former elixir of Curaçao. It contains oil of bitter orange, tincture of bitter orange peel, and orange flower water as the flavoring constituents.

ELIXIR BISMUTHI. N. F.

Elixir of Bismuth [Elix. Bismuth.]

This elixir is made from glycerite of bismuth, glycerin, distilled water, and aromatic elixir, and each teaspoonful represents the equivalent of 3 grains (0.19 Gm.) of bismuth sodium tartrate. This is used as an intestinal astringent, but does not possess the therapeutic virtues of the insoluble bismuth salts.

The *dose* is one fluidrachm (4 cc.).

ELIXIR BROMIDORUM QUINQUE. N. F.

Elixir of Five Bromides [Elix. Bromid. Quinq.]

What the advantage is of having five different salts of hydrobromic acid in combination, is not very obvious; they are sodium, potassium, calcium, lithium and ammonium bromides. The total quantity of bromide present is 15 grains in each fluidrachm.

Dose, one fluidrachm (4 cc.).

ELIXIR BROMIDORUM TRIUM. N. F.

Elixir of Three Bromides [Elix. Tri. Brom.]

This elixir contains in each fluidrachm 4½ grains each of ammonium, potassium and sodium bromides.

The *dose* is one fluidrachm (4 cc.).

ELIXIR BUCHU. N. F.

Elixir of Buchu [Elix. Buchu]

It contains fluidextract of buchu, alcohol, and aromatic elixir. About 7½ grains of buchu are represented by 1 fluidrachm of finished elixir.

The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR BUCHU COMPOSITUM. N. F.

Compound Elixir of Buchu [Elix. Buchu Co.]

Compound fluidextract of buchu is used instead of the simple fluidextract. About 15 minims of compound fluidextract of buchu are represented in 1 fluidrachm of finished elixir.

The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR BUCHU ET POTASSII ACETATIS. N. F.

Elixir of Buchu and Potassium Acetate [Elix. Buchu et Pot. Acet.]

This elixir contains 5 grains of potassium acetate and the equivalent of 7½ grains of buchu in 1 fluidrachm of finished elixir. It is used in cystitis with acid urine.

The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR BUCHU, JUNIPERI ET POTASSII ACETATIS. N. F.

Elixir of Buchu, Juniper and Potassium Acetate [Elix. Buchu, Junip. et Pot. Acet.]

Each fluidrachm of this represents 8½ minims of fluidextract of buchu, half that quantity of juniper and about 3 grains of potassium acetate. The proportion of active ingredients is so small that one is forced to the conclusion that the most potent substance, in this elixir, is the alcohol.

Dose, one to four fluidrachms (4–15 cc.).

ELIXIR CALCII ET SODII GLYCEROPHOSPHATUM. N. F.

Elixir of Calcium and Sodium Glycerophosphates [Elix. Calc. et Sod. Glycerophos. Elixir Glycerophosphatum, N. F. III]

This elixir contains 1 grain of sodium glycerophosphate and ½ grain calcium glycerophosphate in each fluidrachm.

The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR CALCII LACTOPHOSPHATIS. N. F.

Elixir of Calcium Lactophosphate [Elix. Calc. Lactophos.]

This elixir contains about ½ grain of calcium phosphate in 2 fluidrachms of finished elixir.

The *dose* is two to six fluidrachms (8–22 cc.).

ELIXIR CARDAMOMI COMPOSITUM. N. F.

Compound Elixir of Cardamom [Elix. Card. Co.]

This is a new elixir of low alcoholic strength (9 per cent.) and pleasantly flavored with cardamom. It is used as a vehicle and flavoring agent.

ELIXIR CARNIS ET FERRI. N. F.

Elixir of Beef and Iron [Elix. Carn. et Ferr.]

Replacing Vinum Carnis et Ferri, *N. F. IV.*

There is little material difference between this and the formerly official wine, except in flavor. It contains about 2 grains of beef extract and half a grain of iron and ammonium citrate in each fluidrachm, the menstruum being 20 per cent. of alcohol. The old preparation was enormously abused; let us hope the change in flavor will lessen its popularity as a tipple.

Dose, two to six fluidrachms (8–23 cc.).

ELIXIR CASCARÆ SAGRADÆ. N. F. Elixir Rhamni Purshianæ, N. F. III

Elixir of Cascara Sagrada [Elix. Cascar. Sagr.]

An advantageous change in the formula of this is the substitution of aqueous elixir of glycyrrhiza in the place of aromatic elixir. It is a mixture of equal parts of aromatic fluidextract of cascara and elixir of glycyrrhiza.

The *dose* is one-half to one fluidrachm (2–4 cc.).

ELIXIR CASCARÆ SAGRADÆ COMPOSITUM. N. F. Elixir Rhamni Purshianæ Compositum, N. F. III

Compound Elixir of Cascara Sagrada [Elix. Cascar. Sagr. Co. Laxative Elixir]

It contains about 7½ minims of aromatic fluidextract of cascara to each fluidrachm in addition to small amounts of senna and juglans. It is used as a laxative.

The *dose* is one to three fluidrachms (4–11 cc.).

ELIXIR CATARIÆ ET FOENICULI. N. F.

Elixir of Catnep and Fennel [Elix. Catar. et Foenic.]

This contains 10 per cent. of the fluidextract of catnep with 1.75 per cent. of sodium bicarbonate and traces of oils of fennel and spearmint. It is intended as a carminative for infants.

Dose, for an infant ten to thirty minims (0.6–2 cc.).

ELIXIR CATHARTICUM COMPOSITUM. N. F.

Compound Cathartic Elixir [Elix. Cathart. Co.]

This elixir represents, in each fluidrachm, about 7½ grains of frangula together with 5½ of senna and 3 of rhubarb, and is flavored with peppermint and aromatic elixir.

The *dose* is from one to three fluidrachms (4–12 cc.).

ELIXIR CHLORIDORUM. N. F.

Elixir of Chlorides [Elix. Chlorid.]

Elixir of Four Chlorides.

This complex elixir contains in each fluidrachm about 1-64th grain of bichloride of mercury, 1-100th grain of arsenic trioxide and ¾ grain of ferric chloride and 5 minims of diluted hydrochloric acid. Such heterogeneous mixtures are much better reserved for extemporaneous prescription.

Dose, one to two fluidrachms (4–8 cc.).

ELIXIR CINCHONÆ ALKALOIDORUM. N. F. Elixir Cinchonæ, N. F. III

Elixir of Cinchona Alkaloids [Elix. Cinchon. Alk.]

Elixir Calisaya, Alkaloidal.

This elixir is now made from the alkaloids instead of the bark direct, and is simply a solution of cinchona alkaloids in aromatic elixir colored with cudbear. It contains about 1 grain of quinine sulphate and ½ grain each of cinchonidine and cinchonine sulphates in 1 fluidounce of finished elixir. It is used as a bitter, especially in conjunction with more active drugs.

The *dose* is two to four fluidrachms (8–15 cc.).

ELIXIR CINCHONÆ ALKALOIDORUM ET FERRI. N. F. Elixir Cinchonæ et Ferri, N. F. III

Elixir of Cinchona Alkaloids and Iron [Elix. Cinchon. et Ferr.]

Ferrated Elixir of Calisaya, Alkaloidal.

This elixir contains 4 grains of soluble ferric phosphate in 2 fluidrachms of finished elixir. It is used as a chalybeate tonic.

The *dose* is two to four fluidrachms (8–15 cc.).

ELIXIR CINCHONÆ ALKALOIDORUM, FERRI, BISMUTHI ET STRYCHNINÆ. N. F. Elixir Cinchonæ, Ferri, Bismuthi et Strychninæ, N. F. III

Elixir of Cinchona Alkaloids, Iron, Bismuth and Strychnine [Elix. Cinchon., Ferr., Bism. et Strych.]

Elixir of Calisaya, Alkaloidal, with Iron, Bismuth and Strychnine.

This irrational elixir contains 1–100th of a grain of strychnine sulphate, in each fluidrachm dissolved in elixir of cinchona alkaloids, iron and bismuth.

The *dose* is one fluidrachm (4 cc.).

ELIXIR CINCHONÆ ALKALOIDORUM, FERRI ET BISMUTHI. N. F.

Elixir of Cinchona Alkaloids, Iron and Bismuth [Elix. Cinchon., Ferr. et Bism.]

Elixir of Calisaya, Alkaloidal, with Iron and Bismuth.

This polypharmaceutical preparation contains 3¾ minims of glycerite of bismuth, about 3½ grains of soluble ferric phosphate, in 2 fluidrachms of finished elixir.

The *dose* is two fluidrachms (8 cc.).

ELIXIR CINCHONÆ ALKALOIDORUM, FERRI ET STRYCHNINÆ. N. F. Elixir Cinchonæ, Ferri et Strychninæ, N. F. III

Elixir of Cinchona Alkaloids, Iron and Strychnine [Elix. Cinchon., Ferr. et Strych.]

Elixir of Calisaya, Alkaloidal, with Iron and Strychnine.

This elixir contains 1–100th of a grain of strychnine sulphate and 2 grains of soluble ferric phosphate in 1 fluidrachm of finished elixir, and is used as a bitter tonic.

The *dose* is one to three fluidrachms (4–11 cc.).

ELIXIR CORYDALIS COMPOSITUM. N. F.

Compound Elixir of Corydalis [Elix. Coryd. Co.]

This elixir contains about 3 grains of potassium iodide in 1 fluidrachm of finished elixir, with small quantities of the fluidextracts of corydalis, stillingia, xanthoxylum and blue flag.

The *dose* is one fluidrachm (4 cc.).

ELIXIR ERIODICTYI AROMATICUM. N. F.

Aromatic Elixir of Eriodictyon [Elix. Eriodict. Arom.]

Aromatic Elixir of Yerba Santa; Elixir Corrigens.

This elixir is made from fluidextract of eriodictyon, syrup and compound elixir of taraxacum. It is used chiefly as a vehicle for disguising the taste of quinine sulphate and other bitter substances.

The *dose* is one fluidrachm (4 cc.).

ELIXIR EUPHORBIÆ COMPOSITUM. N. F.

Compound Elixir of Euphorbia [Elix. Euphorb. Comp.]

Antiasthmatic Elixir.

Each fluidrachm of this contains 3 minims of fluidextract of euphorbia, 0.4 minims of fluidextract of lobelia, 2 grains each of sodium bromide and iodide and 0.5 minim of spirit of nitroglycerine.

Dose, from one to two fluidrachms (4–8 cc.).

ELIXIR FERRI PYROPHOSPHATIS, QUININÆ ET STRYCHNINÆ. N. F.

Elixir of Ferric Pyrophosphate, Quinine and Strychnine [Elix. Ferr. Pyrophos., Quin. et Strych.]

This elixir differs from the formerly official elixir of iron, quinine and strychnine phosphates in containing soluble ferric pyrophosphate instead of phosphate, while the quinine in the former elixir is replaced by quinine sulphate. It contains 1–125th grain of strychnine, ½ grain of quinine sulphate, and 2 grains of soluble ferric pyrophosphate in 1 fluidrachm of finished elixir.

The *dose* is one to three fluidrachms (4–11 cc.).

ELIXIR FERRI, QUININÆ ET STRYCHNINÆ. N. F.

Elixir of Iron, Quinine and Strychnine [Elix. Ferr., Quin. et Strych.]

Elixir Triplex.

This elixir contains about 1 grain of ferric chloride, ½ grain quinine hydrochloride, and 1–100th grain of strychnine sulphate in 1 fluidrachm of finished elixir. It is used as a chalybeate tonic.

The *dose* is one to two fluidrachms (4–8 cc.).

ELIXIR GENTIANÆ. N. F.

Elixir of Gentian [Elix. Gent.]

It is made from fluidextract of gentian and is flavored with compound spirit of cardamom, but instead of being detannated by the ferric hydroxide process, compatibility with iron is achieved by the use of sodium citrate as an ingredient. It contains too small an amount of gentian to be therapeutically efficient. It is, however, often of service as a vehicle.

The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR GENTIANÆ ET FERRI. N. F. Elixir Gentianæ cum Tinctura Ferri Chloridi, N. F. III

Elixir of Gentian and Iron [Elix. Gent. et Ferr.]

Elixir of Gentian with Tincture of Ferric Citro-chloride.

Tincture of Citro-chloride of Iron, N. F., is used in this preparation along with the simple elixir of gentian. It represents ¾ of a grain of ferric chloride and nearly 2 grains of gentian in 1 fluidrachm. It is used as a bitter tonic.

The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR GENTIANÆ ET FERRI PHOSPHATIS. N. F.

Elixir of Gentian and Ferric Phosphate [Elix. Gent. et Ferr. Phosph.]

Elixir Gentianæ Ferratum.

This elixir represents 1 grain of soluble ferric phosphate and about 2 grains of gentian in 1 fluidrachm of the finished elixir. It is used as a chalybeate and tonic.

The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR GENTIANÆ GLYCERINATUM. N. F.

Glycerinated Elixir of Gentian [Elix. Gent. Glycerin.]

It contains small amounts of gentian and taraxacum in a sweetened and flavored sherry wine. The last is its most active ingredient.

The *dose* is two to four fluidrachms (8–15 cc.).

ELIXIR GLYCEROPHOSPHATUM COMPOSITUM. N. F.

Compound Elixir of Glycerophosphates [Elix. Glycerophos. Co.]

Compound Solution of Glycerophosphates.

This new elixir contains the glycerophosphates of sodium, calcium, iron, manganese with quinine, and strychnine. It represents about 2½ grains of combined glycerophosphates, 1–160th grain of strychnine and 1–20th grain of quinine in each fluidrachm.

The *dose* is two to four fluidrachms (8–15 cc.).

ELIXIR GLYCYRRHIZÆ AQUOSUM. N. F.

Aqueous Elixir of Glycyrrhiza [Elix. Glycyrrh. Aq.]

Aqueous Elixir of Licorice.

This is a new non-alcoholic flavoring elixir containing fluidextract of licorice, compound spirit of cardamom, and orange flower water as the principal ingredients.

ELIXIR GUARANÆ. N. F.

Elixir of Guarana [Elix. Guar.]

This elixir is made from fluidextract of guarana, aromatic elixir and compound elixir of taraxacum. About 12 grains of guarana are represented in 1 fluidrachm of finished elixir. Its effects are similar to those of caffeine.

The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR GUARANÆ ET APII. N. F.

Elixir of Guarana and Celery [Elix. Guaran. et Apii.]

This represents in each fluidrachm 18 minims each of the fluidextracts of guarana and celery.

Dose, two to four fluidrachms (8–15 cc.).

ELIXIR HELONIADIS COMPOSITUM. N. F.

Compound Elixir of Helonias [Elix. Heloniad. Co.]

This contains in each fluidrachm $1^{4}/_{5}$ minims each of fluidextracts of helonias, caulophyllum and viburnum opulus and $7^{1}/_{5}$ minims of mitchella. It is used in dysmenorrhea.

Dose, one to four fluidrachms (4–15 cc.).

ELIXIR HYDRANGEÆ ET LITHII. N. F.

Elixir of Hydrangea and Lithium [Elix. Hydrang. et Lith.]

Each fluidrachm of this elixir represents 24 grains of hydrangea, and 1½ grains each of lithium benzoate and salicylate.

Dose, one to four fluidrachms (4–15 cc.).

ELIXIR HYDRASTIS COMPOSITUM. N. F.

Compound Elixir of Hydrastis [Elix. Hydrast. Co.]

Alkaline Elixir.

This contains in each fluidrachm 1 minim of the fluidextracts of hydrastis, oats and xanthoxylum with traces of ginger, gentian and sodium bicarbonate. The most active ingredient is the alcohol.

Dose, one to four fluidrachms (4–15 cc.).

ELIXIR MANACÆ COMPOSITUM. N. F.

Compound Elixir of Manaca [Elix. Manac. Co.]

Each fluidrachm of this elixir represents 9½ grains of manaca and 13 grains of combined salicylates (sodium, potassium, and lithium). It is intended for cases of rheumatism.

Dose, one fluidrachm (4 cc.).

ELIXIR PEPSINI. N. F.

Elixir of Pepsin [Elix. Pepsin.]

This elixir is made from the glycerite of pepsin, hydrochloric acid and aromatic elixir. It represents about 1 grain of pepsin in 1 fluidrachm of finished preparation. It is improbable the pepsin retains its enzymic activity in the presence of so much alcohol as is in this elixir. It affords, however, a useful vehicle for certain salts, as the iodides or bromides.

The *dose* is two to four fluidrachms (8–15 cc.).

ELIXIR PEPSINI, BISMUTHI ET STRYCHNINÆ. N. F.

Elixir of Pepsin, Bismuth and Strychnine [Elix. Pepsin., Bism. et Strych.]

This elixir contains 1–100th of a grain of strychnine, ½ grain of pepsin and 7½ minims of glycerite of bismuth in 1 fluidrachm of finished preparation. It is an irrational combination.

The *dose* is one to three fluidrachms (4–11 cc.).

ELIXIR PEPSINI COMPOSITUM. N. F.

Compound Elixir of Pepsin [Elix. Pepsin. Co.]

Compound Digestive Elixir.

The most important differences between this and the simple elixir of pepsin are the color and flavor. It is a pleasant vehicle.

ELIXIR PEPSINI ET BISMUTHI. N. F.

Elixir of Pepsin and Bismuth [Elix. Pepsin. et Bism.]

This elixir contains about ½ grain of pepsin and 7½ minims of glycerite of bismuth in 1 fluidrachm of finished preparation.
The *dose* is two fluidrachms (8 cc.).

ELIXIR PEPSINI ET RENNINI COMPOSITUM. N. F.

Compound Elixir of Pepsin and Rennin [Elix. Pepsin. et Rennin. Co.]

Essentia Pepsini; Essence of Pepsin.

This elixir contains pepsin, rennin, and lactic acid. It is used chiefly as a vehicle.
The *dose* is two fluidrachms (8 cc.).

ELIXIR PHOSPHORI. N. F.

Elixir of Phosphorus [Elix. Phosphor.]

This elixir contains 1–64th of a grain of phosphorus in 1 fluidrachm of the finished preparation, and is flavored with compound spirit of orange and oil of anise. It affords an elegant and efficacious mode of exhibiting this remedy.
The *dose* is one-half to one fluidrachm (2–4 cc.).

ELIXIR PHOSPHORI ET NUCIS VOMICÆ. N. F.

Elixir of Phosphorus and Nux Vomica [Elix. Phosphor. et Nuc. Vom.]

About 2 minims of tincture of nux vomica and about 1–64th of a grain of phosphorus are represented in 1 fluidrachm of the finished elixir.
The *dose* is one-half to one fluidrachm (2–4 cc.).

ELIXIR POTASSII BROMIDI. N. F.

Elixir of Potassium Bromide [Elix. Pot. Brom.]

This elixir contains about 10 grains of potassium bromide in 1 fluidrachm of the finished preparation, and is used as a nerve sedative. Preparations of this type are better left to extemporaneous prescription.
The *dose* is one to two fluidrachms (4–8 cc.).

ELIXIR SABAL ET SANTALI COMPOSITUM. N. F.

Compound Elixir of Sabal and Sandalwood [Elix. Sabal et Santal. Co.]

Compound Elixir of Saw Palmetto and Sandalwood.

This represents in each fluidrachm 15 grains each of sabal, triticum, and corn-silk, with 4 minims of fluidextract of sandalwood. It is used in cystitis.
Dose, one to two fluidrachms (4–8 cc.).

ELIXIR SODII BROMIDI. N. F.

Elixir of Sodium Bromide [Elix. Sod. Brom.]

About 10 grains of sodium bromide are represented in 1 fluidrachm of finished elixir.
The *dose* is one to two fluidrachms (4–8 cc.).

ELIXIR SODII SALICYLATIS. N. F.

Elixir of Sodium Salicylate [Elix. Sod. Sal.]

Five grains of sodium salicylate are represented in 1 fluidrachm of the finished elixir. It is intended for an antirheumatic but is not a very happy combination.
The *dose* is one to three fluidrachms (4–11 cc.).

ELIXIR SODII SALICYLATIS COMPOSITUM. N. F.

Compound Elixir of Sodium Salicylate [Elix. Sod. Sal. Co.]

This new elixir contains in each fluidrachm about five grains of sodium salicylate, and one grain of potassium iodide with nearly one minim of fluidextract of gelsemium and two of cimicifuga. Such polypharmaceutical mixtures had better been left to extemporaneous prescription.
The *dose* is one to two fluidrachms (4–8 cc.).

ELIXIR TARAXACI COMPOSITUM. N. F.

Compound Elixir of Taraxacum [Elix. Tarax. Co.]

This elixir is made from fluidextracts of taraxacum, wild cherry and glycyrrhiza, with the tinctures of sweet orange peel and cinnamon, compound tincture of cardamom and aromatic elixir. It is used mainly as a vehicle to cover the taste of bitter substances.
The *dose* is two fluidrachms (8 cc.).

ELIXIR TERPINI HYDRATIS. N. F.

Elixir of Terpin Hydrate [Elix. Terpin. Hyd.]

This elixir contains terpin hydrate, tincture of sweet orange peel, spirit of bitter almond, alcohol, glycerin, and syrup. About 1 grain of terpin hydrate is contained in 1 fluidrachm of the finished preparation.
The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR TERPINI HYDRATIS ET CODEINÆ. N. F.

Elixir of Terpin Hydrate and Codeine [Elix. Terpin. Hyd. et Codein.]

This elixir contains about 1 grain of terpin hydrate and about ⅛ grain of codeine in 1 fluidrachm of the finished preparation. It is a much misused mixture.
The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR TERPINI HYDRATIS ET CREOSOTI COMPOSITUM. N. F.

Compound Elixir of Terpin Hydrate and Creosote [Elix. Terpin. Hyd. et Creosot. Co.]

Each fluidrachm represents ¼ grain of terpin hydrate, ¼ minim of creosote and ½ grain each of the glycerophosphates of calcium and sodium. These proportions are so small that a fluidounce of the elixir would contain scarcely a therapeutic dose. It contains 20 per cent. of alcohol.
The official *dose* is given as one fluidrachm (4 cc.), which is ridiculous.

ELIXIR TONGÆ ET SALICYLATUM. N. F.

Elixir of Tonga and Salicylates [Elix. Tong. et Salicyl.]

This is an imitation of a widely advertised proprietary nostrum. Each fluidrachm represents 8 grains of tonga, 2 of cimicifuga, 4 of sodium salicylate, 1–100th of pilocarpine nitrate and 1–500th of colchicine. It is intended for cases of chronic rheumatism and is the type of " shot-gun " that was more popular a generation ago.

Dose, one to three fluidrachms (4–11 cc.).

ELIXIR VANILLINI COMPOSITUM. N. F.

Compound Elixir of Vanillin [Elix. Vanil. Co.]

This new elixir, intended for a palatable vehicle, contains compound spirit of vanillin and is colored with tincture of caramel.

ELIXIR VIBURNI OPULI COMPOSITUM. N. F.

Compound Elixir of Viburnum Opulus [Elix. Viburn. Opul. Co.]

About 5 grains each of viburnum opulus and aletris and 10 grains of trillium with compound elixir of taraxacum are represented in 1 fluidrachm of the finished elixir. It is probably destitute of therapeutic virtues.

The *dose* is one to four fluidrachms (4–15 cc.).

ELIXIR VIBURNI PRUNIFOLII. N. F.

Elixir of Viburnum Prunifolium [Elix. Viburn. Prun.]

Elixir of Black Haw.

This elixir is made from fluidextract of viburnum prunifolium, compound tincture of cardamom, and aromatic elixir, and contains about 7½ grains of viburnum prunifolium in 1 fluidrachm of the finished preparation.

The *dose* is one to four fluidrachms (4–15 cc.).

EMPLASTRUM FUSCUM CAMPHORATUM. N. F.

Camphorated Brown Plaster [Emp. Fusc. Camph.]

Camphorated Mother Plaster.

This plaster is made from red oxide of lead, olive oil, yellow wax and camphor, and is used as a protective in inflamed conditions of the skin or subcutaneous tissues.

EMPLASTRUM SAPONIS. N. F.

Soap Plaster [Emp. Sapon.]

This is merely lead plaster with 10 per cent. of dried soap incorporated with it by the aid of a little water. The formula of the U. S. VIII is used, unchanged.

EMULSA. N. F.

Emulsions

In the National Formulary preference is given to acacia as the emulsifying agent, although other emulsifying agents are not ignored, as exemplified in the preparation of the numerous emulsions of cod liver oil. It is recommended that emulsions, being prone to deteriorate on standing, should be freshly prepared when needed. The following flavoring agents are suggested as being acceptable for cod liver oil, the choice being left to the prescriber:

a.	Oil of Betula	4	cc.
b.	Oil of Betula	2	cc.
	Oil of Sassafras	2	cc.
c.	Compound Spirit of Orange	1.5	cc.
d.	Oil of Betula	2	cc.
	Oil of Bitter Almond	0.25	cc.
	Oil of Coriander	0.25	cc.
e.	Oil of Betula	1.50	cc.
	Oil of Sassafras	1.50	cc.
	Oil of Bitter Almond	0.25	cc.
f.	Oil of Betula	2.5	cc.
	Oil of Bitter Almond	2.5	cc.

EMULSUM OLEI MORRHUÆ CUM HYPOPHOSPHITIBUS. N. F.

Emulsion of Cod Liver Oil with Hypophosphites [Emul. Ol. Morrh. c. Hypophos.]

This emulsion contains 50 per cent. of cod liver oil. Each dessertspoonful contains 1½ grains of calcium hypophosphite and ¾ grain each of sodium and potassium hypophosphites with sufficient flavoring.

The *dose* is two to four fluidrachms (8–15 cc.).

EMULSUM OLEI MORRHUÆ CUM MALTO. N. F.

Emulsion of Cod Liver Oil with Malt [Emul. Ol. Morrh. c. Malt.]

This emulsion contains 30 per cent. of cod liver oil with about 55 per cent. of extract of malt. It affords one of the most acceptable preparations of cod liver oil.

The *dose* is four fluidrachms (15 cc.).

EMULSUM OLEI MORRHUÆ CUM VITELLO. N. F.

Emulsion of Cod Liver Oil with Egg [Emul. Ol. Morrh. c. Vitel.]

This emulsion contains 50 per cent. cod liver oil with glycerite of yolk of egg, syrup of tolu and flavoring. It is used as a tonic.

The *dose* is four fluidrachms (15 cc.).

EMULSUM OLEI RICINI. N. F.

Emulsion of Castor Oil [Emul. Ol. Ricin.]

This emulsion contains 35 per cent. of castor oil, with tincture of vanilla, syrup and water. It is used as a cathartic.

The *dose* is one and one-half fluidounces (45 cc.).

EMULSUM PETROLATI. N. F. Emulsum Petrolei, N. F. III

Emulsion of Petrolatum [Emul. Petrolat.]

This emulsion contains about 22.5 per cent. each, of white petrolatum, and expressed oil of almond, with acacia, tragacanth and syrup, tincture of lemon peel and water.

The *dose* is one-half to one fluidounce (8–15 cc.).

EXTRACTUM CONII. N. F.

Extract of Conium [Ext. Conii.]

Extract of conium yields not less than 1.8 per cent. nor more than 2.2 per cent. of coniine. This extract is prepared with diluted alcohol, a small quantity of diluted hydrochloric acid being added previous to the evaporation of the percolate. An assay is provided.

The *dose* is one-half grain (0.03 Gm.).

EXTRACTUM ERGOTÆ AQUOSUM. N. F.

Aqueous Extract of Ergot [Ext. Ergot. Aq.]

Ergotin, *P. I.*

This extract is prepared by percolating the powdered ergot, using chloroform water as menstruum, reducing to proper consistency by means of careful heat, and adding an equal weight of alcohol, and after allowing it to stand for three days, it is then filtered and the filtrate reduced to a pilular consistence. For reasons pointed out elsewhere (see *Ergota*, Part I) it does not represent the therapeutic virtues of ergot.

The *dose* is three grains (0.2 Gm.).

EXTRACTUM EUONYMI. N. F.

Extract of Euonymus [Ext. Euonymi]

Powdered Extract of Euonymus.

One gramme of the extract represents four grammes of euonymus. It is prepared by exhausting the powdered drug with diluted alcohol, evaporating to dryness, and diluting with starch.

"Caution.—It has been stated that the absorption of euonymus in the gastro-intestinal tract is uncertain and irregular. To avoid possible toxic or cumulative action, the physician should carefully guard the dosage and determine in each case the tolerance of the patient and regulate the dosage accordingly." *N. F.*

The *dose* is two grains (0.125 Gm.).

EXTRACTUM FERRI POMATUM. N. F.

Ferrated Extract of Apples [Ext. Ferr. Pomat.]

Ferri Malas Crudus; Crude Malate of Iron.

This extract is made from iron wire, fresh apple juice and water, and is used as a chalybeate.

The *dose* is ten grains (0.65 Gm.).

EXTRACTUM GENTIANÆ. N. F.

Extract of Gentian [Ext. Gentian.]

This is made by percolating with water and evaporating to dryness. It is used as a bitter stomachic. The practice of employing this extract as a pill mass is to be deprecated as it is not medicinally inert.

Dose, two to five grains (0.12–0.3 Gm.).

EXTRACTUM HÆMATOXYLI. N. F.

Extract of Hematoxylon [Ext. Hæmatox.]

This extract is prepared by exhausting the rasped drug with boiling water and evaporating the extract to dryness.

The *dose* is ten to thirty grains (0.6–2.0 Gm.).

EXTRACTUM HYDRASTIS. N. F.

Extract of Hydrastis [Ext. Hydrast.]

Powdered Extract of Hydrastis; Extract of Golden Seal.

It is made with a menstruum of alcohol acidulated with tartaric acid and "yields not less than 9 per cent. nor more than 11 per cent. of ether soluble alkaloids."

Dose, five to ten grains (0.3–0.6 Gm.).

EXTRACTUM IGNATIÆ. N. F.

Extract of Ignatia [Ext. Ignat.]

Powdered Extract of Ignatia.

Extract of ignatia yields not less than 5.4 per cent. nor more than 6.6 per cent. of the combined alkaloids of ignatia. It is prepared by exhausting the powdered drug with 75 per cent. alcohol, evaporating to dryness, weighing, and assaying at this stage, and finally diluting to the proper standard with starch.

The *dose* is one-fourth to three-fourths of a grain (0.015–0.045 Gm.).

EXTRACTUM KRAMERIÆ. N. F.

Extract of Krameria [Ext. Kramer.]

Powdered Extract of Krameria.

One gramme of the extract represents four grammes of krameria. It is prepared by exhausting the powdered drug with cold water. The percolate is then heated to boiling, strained, and the strained liquid evaporated to dryness and sufficient dried starch added as diluent.

The *dose* is five to ten grains (0.3–0.6 Gm.).

EXTRACTUM LEPTANDRÆ. N. F.

Extract of Leptandra [Ext. Leptand.]

Powdered Extract of Leptandra.

One gramme of the extract represents four grammes of leptandra. It is prepared by exhausting the drug with a menstruum of 75 per cent. alcohol, evaporating the percolate to dryness and diluting with dried starch.

The *dose* is from five to ten grains (0.3–0.6 Gm.).

EXTRACTUM OPII. N. F.

Extract of Opium [Ext. Opii]

Powdered Extract of Opium; Opii Extractum, *P. I.*

"Extract of Opium yields not less than 19.5 per cent. and not more than 20.5 per cent. of anhydrous morphine. One Gm. of the extract represents about 2 Gm. of Opium." *N. F.* This preparation does not differ materially from the extract of opium of the U. S. IX. (See also *Extractum Opii Siccum*, Part I.)

Dose, from one-sixth to one grain (0.01–0.06 Gm.).

EXTRACTUM SUMBUL. N. F.

Extract of Sumbul [Ext. Sumbul]

The formula for this preparation is the same as that of the U. S. IX.

The *dose* is from two to five grains (0.12–0.30 Gm.).

EXTRACTUM TARAXACI. N. F.

Extract of Taraxacum [Ext. Tarax.]

This preparation is the same as that formerly recognized by the U. S. IX under the same title.

The *dose* is from fifteen to sixty grains (1–4 Gm.).

FERRI OXIDUM SACCHARATUM. N. F.

Saccharated Ferric Oxide [Ferr. Oxid. Sacch.]

Soluble Ferric Oxide; Ferrum Oxydatum Saccharatum; Eisenzucker, *G.*

Saccharated ferric oxide contains the equivalent of not less than 2.8 per cent. of Fe. In the preparation of this product, freshly precipitated ferric hydroxide is dissolved in a heavy sugar syrup by the addition of a small quantity of sodium hydroxide. This solution is then evaporated on a water bath and enough sugar added to bring it to the desired weight. An assay process is given.

Dose, thirty grains (2 Gm.).

FLUIDEXTRACTA. N. F.

Fluidextracts

The fluidextracts of the N. F., like those of the U. S. P., are mostly made according to one of four type processes. These processes are essentially the same as those of the U. S. P. (see Part I). Fluidextracts should be stored in amber-colored bottles protected from sunlight and extremes of temperature. (See also *Fluidextracta*, Part I.)

FLUIDEXTRACTUM ACONITI. N. F.

Fluidextract of Aconite [Fldext. Aconit.]

This is made with a menstruum of three volumes of alcohol and one volume of water. " When assayed biologically, the minimal lethal dose of Fluidextract of Aconite should be not greater than 0.00004 cc. for each Gm. of body weight of guinea-pig." *N. F.* For description of the method of assay see under *Aconitum*, Part I.

The use of this preparation is not to be recommended because it is so highly toxic that slight errors in dosage or manipulation may have serious effects.

The *dose* is one minim (0.06 cc.).

FLUIDEXTRACTUM ADONIDIS. N. F.

Fluidextract of Adonis [Fldext. Adonid.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum.

The *dose* is two to five minims (0.12–0.30 cc.).

FLUIDEXTRACTUM ALETRIDIS. N. F.

Fluidextract of Aletris [Fldext. Aletrid.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM ANGELICÆ RADICIS. N. F.

Fluidextract of Angelica Root [Fldext. Angel. Rad.]

Prepared by using 5 volumes of alcohol with one of water as the menstruum.

The *dose* is thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM APII FRUCTUS. N. F.

Fluidextract of Celery Fruit [Fldext. Apii Fruct.]

Prepared by using alcohol as the menstruum. In order to remove any separated oil, after permitting the fluidextract to stand, filter it through an alcohol-wetted filter, rejecting the final few cc. remaining on the filter with the oil.

The *dose* is from twenty to sixty minims (1.3–4 cc.).

FLUIDEXTRACTUM APOCYNI. N. F.

Fluidextract of Apocynum [Fldext. Apocyn.]

Prepared by using three volumes of water as menstruum I, and three volumes of alcohol and two volumes of water as menstruum II. It may be assayed by the method described under *Digitalis* (Part I). The increase in the proportion of alcohol, over that of the U. S. VIII, is an advantage.

" CAUTION.—It has been stated that the absorption of apocynum in the gastro-intestinal tract is uncertain and irregular. To avoid an accumulation of the drug or toxic action, the physician should carefully guard the dosage and determine in each case the tolerance of the patient." *N. F.*

The *dose* is from five to fifteen minims (0.3–1.0 cc.).

FLUIDEXTRACTUM ARALIÆ. N. F.

Fluidextract of Aralia [Fldext. Aral.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum. It is used as an alterative.

The *dose* is thirty minims (2 cc.).

FLUIDEXTRACTUM ARNICÆ. N. F. Fluidextractum Arnicæ Florum, N. F. III

Fluidextract of Arnica [Fldext. Arnic.]

Prepared by using two volumes of alcohol with one of water as the menstruum.

The *dose* is from one to three minims (0.06–0.2 cc.).

FLUIDEXTRACTUM ASCLEPIADIS. N. F.

Fluidextract of Asclepias [Fldext. Asclepiad.]

Prepared by using diluted alcohol as the menstruum. It is used as a diaphoretic, emetic, and cathartic.

The *dose* is from twenty to sixty minims (1.2–4.0 cc.).

FLUIDEXTRACTUM AVENÆ SATIVÆ. N. F.

Fluidextract of Avena Sativa [Fldext. Aven. Sativ.]

This is prepared with a menstruum consisting of two volumes of alcohol and one of water.

The official *dose* is one fluidrachm (4 cc.) but larger amounts can be safely given.

FLUIDEXTRACTUM BAPTISIÆ. N. F.

Fluidextract of Baptisia [Fldext. Baptis.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum.

The *dose* is fifteen minims (1 cc.)

FLUIDEXTRACTUM BERBERIDIS. N. F.

Fluidextract of Berberis [Fldext. Berberid.]

Prepared by using diluted alcohol as the menstruum. It is used as an astringent tonic and cathartic.

The *dose* is from ten to thirty minims (0.6–2 cc.).

FLUIDEXTRACTUM BOLDI. N. F.

Fluidextract of Boldo [Fldext. Boldi]

Prepared by using alcohol as the menstruum. It is used as an alterative and tonic.

The *dose* is from five to eight minims (0.3–0.5 cc.).

FLUIDEXTRACTUM BUCHU COMPOSITUM. N. F.

Compound Fluidextract of Buchu [Fldext. Buchu Co.]

Prepared by using four volumes of alcohol and one volume of water as the menstruum. Each fluidrachm represents 37½ grains of buchu and 7½ grains each of cubeb, juniper and uva ursi.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM CALENDULÆ. N. F.

Fluidextract of Calendula [Fldext. Calend.]

Prepared by using two volumes of alcohol with one of water as the menstruum.

Dose, (official) fifteen minims (1 cc.).

FLUIDEXTRACTUM CALUMBÆ. N. F.

Fluidextract of Calumba [Fldext. Calumb.]

Prepared by using one volume of glycerin, two volumes of alcohol, and one volume of water as menstruum.

The *dose* is from ten to thirty minims (0.6–2.0 cc.).

FLUIDEXTRACTUM CASTANEÆ. N. F.

Fluidextract of Chestnut Leaves [Fldext. Castan.]

Prepared by using boiling water as the menstruum and adding ten volumes of glycerin and twenty volumes of alcohol being added as a preservative. It is used as an astringent.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM CATARIÆ. N. F.

Fluidextract of Catnep [Fldext. Catar.]

Prepared by using three volumes of alcohol and four volumes of water as the menstruum.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM CAULOPHYLLI. N. F.

Fluidextract of Caulophyllum [Fldext. Caulophyl.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum.

The *dose* is from five to ten minims (0.3–0.6 cc.).

FLUIDEXTRACTUM CHIMAPHILÆ. N. F.

Fluidextract of Chimaphila [Fldext. Chimaphil.]

Prepared by using diluted alcohol as the menstruum. It is used chiefly for its effects on the mucous membrane of the bladder and urethra.

The *dose* is thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM CHIONANTHI. N. F.

Fluidextract of Chionanthus [Fldext. Chionanth.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum.

The *dose* is thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM CHIRATÆ. N. F.

Fluidextract of Chirata [Fldext. Chirat.]

Prepared by using diluted alcohol as the menstruum. It is used as a tonic and febrifuge.

The *dose* is from ten to twenty minims (0.6–1.2 cc.).

FLUIDEXTRACTUM COCILLANÆ. N. F.

Fluidextract of Cocillana [Fldext. Cocillan.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum.

The *dose* is from ten to twenty minims (0.6–1.2 cc.).

FLUIDEXTRACTUM COFFEÆ. N. F. Fluidextractum Coffeæ Tostæ, N. F. III

Fluidextract of Coffee [Fldext. Coff.]

Prepared by using 65 cc. of glycerin, 250 cc. of alcohol, and 685 cc. of water as menstruum I, and one volume of alcohol and three volumes of water as menstruum II.

The *dose* is thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM COLCHICI CORMI. N. F.

Fluidextract of Colchicum Corm [Fldext. Colch. Corm.]

"One hundred cc. of fluidextract of colchicum corm yields not less than 0.31 Gm. nor more than 0.39 Gm. of colchicine." *N. F.* Prepared by using a menstruum of two volumes of alcohol and one volume of water. After assaying adjust the volume of the finished product to conform with the required standard. An assay is provided in the text.

The *dose* is from two to eight minims (0.12–0.50 cc.).

FLUIDEXTRACTUM CONDURANGO. N. F.

Fluidextract of Condurango [Fldext. Condurango]

Prepared by using diluted alcohol as the menstruum. It is used as an alterative and stomachic.

The *dose* is one fluidrachm (4 cc.).

FLUIDEXTRACTUM CONVALLARIÆ RADICIS. N. F.

Fluidextract of Convallaria Root [Fldext. Conval. Rad.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum.

The *dose* is from five to ten minims (0.3–0.6 cc.).

FLUIDEXTRACTUM COPTIS. N. F.

Fluidextract of Coptis [Fldext. Copt.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is thirty minims (2 cc.).

FLUIDEXTRACTUM CORNI. N. F. Fluidextractum Cornus, N. F. III

Fluidextract of Cornus [Fldext. Corni]

Prepared by using 150 cc. of glycerin and 850 cc. of diluted alcohol as menstruum I, and diluted alcohol as menstruum II.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM CORYDALIS. N. F.

Fluidextract of Corydalis [Fldext. Corydal.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum.

The *dose* is from ten to twenty minims (0.6–1.2 cc.).

FLUIDEXTRACTUM CUBEBÆ. N. F.

Fluidextract of Cubeb [Fldext. Cubeb.]

Prepared by using alcohol as the menstruum.

The *dose* is from fifteen to thirty minims (1–2 cc.).

FLUIDEXTRACTUM CYPRIPEDII. N. F.

Fluidextract of Cypripedium [Fldext. Cypriped.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is from fifteen to thirty minims (1–2 cc.).

FLUIDEXTRACTUM DAMIANÆ. N. F.
Fluidextractum Turneræ, N. F. III

Fluidextract of Damiana [Fldext. Damian.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is attributed, but probably erroneously so, with aphrodisiac powers.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM DIGITALIS. N. F.

Fluidextract of Digitalis [Fldext. Digit.]

This is made with a menstruum consisting of five volumes of alcohol and one of water. "When assayed biologically the minimal lethal dose should not be greater than 0.0006 cc. of the Fluidextract, or the equivalent in Fluidextract of 0.000,000,5 Gm. of ouabain for each Gm. of body weight of frog." *N. F.* For method of assay see under *Tinctura Digitalis*, Part I.

The *dose* is from one-half to one and a half minims (0.03–0.10 cc.).

FLUIDEXTRACTUM DIOSCOREÆ. N. F.

Fluidextract of Dioscorea [Fldext. Dioscor.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is one fluidrachm (4 cc.).

FLUIDEXTRACTUM DROSERÆ. N. F.

Fluidextract of Drosera [Fldext. Droser.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM DULCAMARÆ. N. F.

Fluidextract of Bittersweet [Fldext. Dulcam.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM ECHINACEÆ. N. F.

Fluidextract of Echinacea [Fldext. Echin.]

Prepared by using four volumes of alcohol and one volume of water as the menstruum.

The *dose* is from ten to thirty minims (0.6–2.0 cc.).

FLUIDEXTRACTUM EUONYMI. N. F.

Fluidextract of Euonymus [Fldext. Euonym.]

Prepared by using diluted alcohol and one volume of water as the menstruum.

The *dose* is eight minims (0.5 cc.).

"CAUTION.—It has been stated that the absorption of euonymus in the gastro-intestinal tract is uncertain and irregular. To avoid possible toxic or cumulative action of the drug, the physician should carefully determine in each case the tolerance of the patient and regulate the dosage accordingly." *N. F.*

Dose, five to ten minims (0.3–1.2 cc.).

FLUIDEXTRACTUM EUPATORII. N. F.

Fluidextract of Eupatorium [Fldext. Eupator.]

Prepared by using diluted alcohol as a menstruum.

The *dose* is thirty minims (2 cc.).

FLUIDEXTRACTUM EUPHORBIÆ. N. F.

Fluidextract of Euphorbia [Fldext. Euphorb. Pilul.]

Prepared by using diluted alcohol as the menstruum. The change of name (formerly it was *Fluidextractum Euphorbiæ Piluliferæ*) is, in our opinion, unfortunate as other species of Euphorbia—with very different medicinal properties—are used in medicine.

The *dose* is thirty minims (2 cc.).

FLUIDEXTRACTUM FRANGULÆ. N. F.

Fluidextract of Frangula [Fldext. Frang.]

In this preparation water is used as the extracting menstruum but 25 per cent. of alcohol is added to the finished fluidextract as a preservative.

The *dose* is from ten to twenty minims (0.6–1.2 cc.).

FLUIDEXTRACTUM FUCI. N. F.

Fluidextract of Fucus [Fldext. Fuci]

Prepared by using three volumes of alcohol and one volume of water as the menstruum.

The *dose* is ten minims (0.6 cc.).

FLUIDEXTRACTUM GALEGÆ. N. F.

Fluidextract of Galega [Fldext. Galeg.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is one fluidrachm (4 cc.).

FLUIDEXTRACTUM GELSEMII. N. F.

Fluidextract of Gelsemium [Fldext. Gelsem.]

Prepared with a menstruum of 4 volumes of alcohol and one of water.

Dose, from one-half to three minims (0.03–0.2 cc.).

FLUIDEXTRACTUM GENTIANÆ. N. F.

Fluidextract of Gentian [Fldext. Gentian.]

Made with a menstruum of diluted alcohol.

Dose, from ten to twenty minims (0.6–1.2 cc.).

FLUIDEXTRACTUM GERANII. N. F.

Fluidextract of Geranium [Fldext. Geran.]

Prepared by using one volume of glycerin, six volumes of alcohol and one volume of water as menstruum I, and three volumes of alcohol and two volumes of water as menstruum II. It is used as an astringent and styptic.

The *dose* is from fifteen to thirty minims (1–2 cc.).

FLUIDEXTRACTUM GOSSYPII CORTICIS. N. F.

Fluidextract of Cotton Root Bark [Fldext. Gossyp. Cort.]

Prepared by using alcohol as the menstruum.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM GRINDELIÆ. N. F.

Fluidextract of Grindelia [Fldext. Grindel.]

This is made with a menstruum of three volumes of alcohol and one volume of water.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM GUARANÆ. N. F.

Fluidextract of Guarana [Fldext. Guaran.]

"One hundred cc. of Fluidextract of Guarana yields not less than 3.6 Gm. and not more than 4.4 Gm. of anhydrous caffeine." *N. F.* It is made with a menstruum of three volumes of alcohol with one of water.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM HAMAMELIDIS FOLIORUM. N. F.

Fluidextract of Hamamelis Leaves [Fldext. Hamamel. Fol.]

Prepared by using one volume of glycerin, three volumes of alcohol, and five volumes of water as menstruum I, and one volume of alcohol and two volumes of water as menstruum II.

The *dose* is from fifteen to thirty minims (1–2 cc.).

FLUIDEXTRACTUM HELONIADIS. N. F.

Fluidextract of Helonias [Fldext. Helon.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is thirty minims (2 cc.).

FLUIDEXTRACTUM HUMULI. N. F.

Fluidextract of Hops [Fldext. Humul.]

Prepared by using five volumes of alcohol and three volumes of water as the menstruum. It is used as a nerve sedative.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM HYDRANGEÆ. N. F.

Fluidextract of Hydrangea [Fldext. Hydrang.]

Prepared by using three volumes of alcohol and two volumes of water as the menstruum.

The *dose* is thirty minims (2 cc.).

FLUIDEXTRACTUM IRIDIS VERSICOLORIS. N. F.

Fluidextract of Blue Flag [Fldext. Iris Vers. Fluidextractum Iridis, N. F. III]

Prepared by using alcohol as the menstruum.

The *dose* is from ten to thirty minims (0.6–2 cc.).

FLUIDEXTRACTUM JALAPÆ. N. F.

Fluidextract of Jalap [Fldext. Jalap.]

Prepared by mixing the drug with clean sand and using alcohol as the menstruum. "One hundred cc. of Fluidextract of Jalap yields not less than 6.5 Gm. and not more than 7.5 Gm. of the resin of Jalap." *N. F.*

The *dose* is from ten to twenty minims (0.6–1.3 cc.).

FLUIDEXTRACTUM JUGLANDIS. N. F.

Fluidextract of Juglans [Fldext. Jugland.]

Prepared by using 100 cc. of glycerin, 500 cc. of alcohol and 400 cc. of water as menstruum I, and diluted alcohol as menstruum II. It is used as a cathartic.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM JUNIPERI. N. F.

Fluidextract of Juniper Berries [Fldext. Junip.]

Prepared by using four volumes of alcohol with one of water as the menstruum. It is used as a diuretic.

The *dose* is one fluidrachm (4 cc.).

FLUIDEXTRACTUM KAVÆ. N. F.

Fluidextract of Kava [Fldext. Kav.]

Prepared by using three volumes of alcohol and two volumes of water as the menstruum.

The *dose* is fifteen minims (1 cc.).

FLUIDEXTRACTUM KOLÆ. N. F.

Fluidextract of Kola [Fldext. Kol. Fluidextractum Sterculiæ, N. F. III]

Prepared by using two volumes of alcohol and one volume of water as the menstruum. "One hundred cc. of Fluidextract of Kola yields not less than 0.85 Gm. and not more than 1.15 Gm. of caffeine." *N. F.*

The *dose* is one fluidrachm (4 cc.).

FLUIDEXTRACTUM KRAMERIÆ. N. F.

Fluidextract of Krameria [Fldext. Kramer.]

Prepared by using one volume of glycerin, five volumes of alcohol and four volumes of water as menstruum I, and diluted alcohol as menstruum II.

The *dose* is from fifteen to forty-five minims (1–3 cc.).

FLUIDEXTRACTUM LAPPÆ. N. F.

Fluidextract of Lappa [Fldext. Lapp.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM LEPTANDRÆ. N. F.

Fluidextract of Leptandra [Fldext. Leptand.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum.

The *dose* is from fifteen to thirty minims (1–2 cc.).

FLUIDEXTRACTUM LOBELIÆ. N. F.

Fluidextract of Lobelia [Fldext. Lobel.]

This is prepared with a mixture of 50 cc. of acetic acid, 500 cc. of alcohol and 450 cc. of water as menstruum I and diluted alcohol as menstruum II.

The *dose* is one to two minims (0.06–0.12 cc.).

FLUIDEXTRACTUM LUPULINI. N. F.

Fluidextract of Lupulin [Fldext. Lupulin.]

It is made with alcohol as the menstruum.

The *dose* is from five to ten minims (0.3–0.6 cc.).

FLUIDEXTRACTUM MANACÆ. N. F.

Fluidextract of Manaca [Fldext. Manac.]

This is prepared with a mixture of three volumes of alcohol and one of water as the menstruum.

The *dose* is from ten to thirty minims (0.6–1 cc.).

FLUIDEXTRACTUM MATICO. N. F.

Fluidextract of Matico [Fldext. Matic.]

Prepared by using three volumes of alcohol and one volume of water, as directed by the U. S. P. VIII, as the menstruum.

The *dose* is one fluidrachm (4 cc.).

FLUIDEXTRACTUM MEZEREI. N. F.

Fluidextract of Mezereum [Fldext. Mezer.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is used as a rubefacient.

FLUIDEXTRACTUM MITCHELLÆ. N. F.

Fluidextract of Mitchella [Fldext. Mitchel.]

This is prepared with diluted alcohol as the menstruum.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM NUCIS VOMICA. N. F.

Fluidextract of Nux Vomica [Fldext. Nuc. Vom.]

"One hundred cc. of Fluidextract of Nux Vomica yields not less than 2.37 Gm. and not more than 2.63 Gm. of the alkaloids of Nux Vomica." *N. F.* It is prepared with a menstruum of three volumes of alcohol with one of water.

The *dose* is from one to two minims (0.06–0.12 cc.).

FLUIDEXTRACTUM PAREIRÆ. N. F.

Fluidextract of Pareira [Fldext. Pareir.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is from thirty to sixty minims (1–2 cc.).

FLUIDEXTRACTUM PHYTOLACCÆ. N. F.

Fluidextract of Phytolacca [Fldext. Phytolac.]

Prepared by using diluted alcohol, as the menstruum.

The *dose* is from ten to thirty minims (0.6–2.0 cc.) as an emetic, and one to five minims (0.06–0.30 cc.) as an alterative.

FLUIDEXTRACTUM PRUNI VIRGINIANÆ. N. F.

Fluidextract of Wild Cherry [Fldext. Prun. Virg.]

Prepared by using 200 cc. of glycerin and 400 cc. of water as the macerating menstruum, then percolating with a menstruum of 250 cc. of alcohol and 150 cc. of water and continuing with one volume of alcohol and three volumes of water as the menstruum.

The *dose* is one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM QUASSIÆ. N. F.

Fluidextract of Quassia [Fldext. Quass.]

Prepared by using one volume of alcohol and two volumes of water, as the menstruum. This affords an excellent means of obtaining the effects of quassia. It has the advantage over the tincture of not requiring so large an amount of alcohol.

The *dose* is from five to fifteen minims (0.3–1.0 cc.).

FLUIDEXTRACTUM QUERCUS. N. F.

Fluidextract of Quercus [Fldext. Querc.]

Prepared by using 100 cc. of glycerin, 500 cc. of alcohol and 400 cc. of water as menstruum I, and diluted alcohol as menstruum II.

The official *dose* is fifteen minims (1 cc.) but it is rarely used internally.

FLUIDEXTRACTUM RHAMNI CATHARTICÆ. N. F.

Fluidextract of Rhamnus Cathartica [Fldext. Rham. Cathart.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is fifteen minims (1 cc.).

FLUIDEXTRACTUM RUBI. N. F.

Fluidextract of Rubus [Fldext. Rubi]

Prepared by using diluted alcohol as the menstruum. It is used as an intestinal astringent.

The *dose* is from fifteen to thirty minims (1–2 cc.).

FLUIDEXTRACTUM RUMICIS. N. F.

Fluidextract of Rumex [Fldext. Rumic.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is from fifteen to sixty minims (1–4 cc.).

FLUIDEXTRACTUM SABAL. N. F.

Fluidextract of Sabal [Fldext. Sabal]

Prepared with a menstruum of four volumes of alcohol with one of water.

The *dose* is from ten to twenty minims (0.6–1.2 cc.).

FLUIDEXTRACTUM SANGUINARIÆ. N. F.

Fluidextract of Sanguinaria [Fldext. Sanguin.]

Prepared by using 50 cc. of hydrochloric acid, 200 cc. of water and 750 cc. of alcohol as menstruum I, and three volumes of alcohol and one volume of water as menstruum II. The former process used citric, instead of hydrochloric, acid.

The *dose* is from one to five minims (0.06–0.3 cc.).

FLUIDEXTRACTUM SANTALI ALBI. N. F.

Fluidextract of Sandal Wood [Fldext. Santal. Alb.]

This is made with a menstruum of alcohol.

Dose, one fluidrachm (4 cc.).

FLUIDEXTRACTUM SARSAPARILLÆ COMPOSITUM. N. F.

Compound Fluidextract of Sarsaparilla [Fldext. Sarsap. Co.]

This is practically the same as the compound fluidextract of the U. S. IX and contains sarsaparilla, licorice, sassafras and mezereum. It is made with a mixture of 100 cc. of glycerin, 500 cc. of alcohol and 400 cc. of water as menstruum I and diluted alcohol as menstruum II.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM SCOPARII. N. F.

Fluidextract of Scoparius [Fldext. Scopar.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is from ten to fifteen minims (0.6–1 cc.).

FLUIDEXTRACTUM SCUTELLARIÆ. N. F.

Fluidextract of Scutellaria [Fldext. Scutellar.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is from fifteen minims to one fluidrachm (1–4 cc.).

FLUIDEXTRACTUM SENECIONIS. N. F.

Fluidextract of Senecio [Fldext. Senecion.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum.

The *dose* is one fluidrachm (4 cc.).

FLUIDEXTRACTUM SERPENTARIÆ. N. F.

Fluidextract of Serpentaria [Fldext. Serpentar.]

Prepared by using four volumes of alcohol and one volume of water as the menstruum.

The *dose* is from fifteen to thirty minims (1–2 cc.).

FLUIDEXTRACTUM SOLANI. N. F.

Fluidextract of Solanum [Fldext. Solan.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum.

The *dose* is one fluidrachm (4 cc.).

FLUIDEXTRACTUM STILLINGIA. N. F.

Fluidextract of Stillingia [Fldext. Stilling.]

This is made with a menstruum of diluted alcohol.

The *dose* is from fifteen to forty-five minims (1–3 cc.).

FLUIDEXTRACTUM STILLINGIÆ COMPOSITUM. N. F.

Compound Fluidextract of Stillingia [Fldext. Stilling. Co.]

Prepared by using diluted alcohol as the menstruum. It contains stillingia, corydalis, iris, sambucus, chimaphila, coriander, and xanthoxylum berries. It is a relic of therapeutic superstition.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM STRAMONII. N. F.

Fluidextract of Stramonium [Fldext. Stramon.]

"One hundred cc. of fluidextract of stramonium yields not less than 0.22 Gm. nor more than 0.28 Gm. of the alkaloids of stramonium." *N. F.* Prepared by using four volumes of alcohol and one volume of water as the menstruum. An assay is provided in the text.

The *dose* is one minim (0.05 cc.).

FLUIDEXTRACTUM TARAXACI. N. F.

Fluidextract of Taraxacum [Fldext. Tarax.]

Made with a menstruum of alcohol, water and glycerin.

Dose, from two to four fluidrachms (8–15 cc.).

FLUIDEXTRACTUM THUJÆ. N. F.

Fluidextract of Thuja [Fldext. Thuj.]

Prepared by using alcohol as the menstruum.

The *dose* is from fifteen to forty-five minims (1–3 cc.).

FLUIDEXTRACTUM THYMI. N. F.

Fluidextract of Thyme [Fldext. Thym.]

Prepared by using 100 cc. of glycerin, 250 cc. of alcohol and 650 cc. of water as menstruum I, and one volume of alcohol and three volumes of water as menstruum II.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM TONGÆ. N. F.

Fluidextract of Tonga [Fldext. Tong.]

This is prepared with a mixture of one volume of alcohol with three of water as the menstruum.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM TRIFOLII. N. F.

Fluidextract of Trifolium [Fldext. Trifol.]

Prepared by using diluted alcohol as the menstruum. It is without therapeutic virtue.

The *dose* is one fluidrachm (4 cc.).

FLUIDEXTRACTUM TRIFOLII COMPOSITUM. N. F.

Compound Fluidextract of Trifolium [Fldext. Trifol. Co.]

This represents 21.5 per cent. each of trifolium, glycyrrhiza, and berberis with half that quantity of cascara amarga, lappa, phytolacca, stillingia, and 3 per cent. of xanthoxylum. What is to be hoped from such a conglomeration of useless remedies is a conundrum.

The official *dose* is given as one fluidrachm (4 cc.).

FLUIDEXTRACTUM TRILLII. N. F.

Fluidextract of Trillium [Fldext. Trill.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM TRITICI. N. F.

Fluidextract of Triticum [Fldext. Tritic.]

This is prepared with an aqueous menstruum to which is added 20 per cent. of alcohol as a preservative.

The *dose* is from two to four fluidrachms (8–15 cc.).

FLUIDEXTRACTUM VALERIANÆ. N. F.

Fluidextract of Valerian [Fldext. Valer.]

Prepared by using four volumes of alcohol and one volume of water as the menstruum.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM VERBASCI FOLIORUM. N. F.

Fluidextract of Mullein Leaves [Fldext. Verbasc. Fol.]

Prepared by using diluted alcohol as the menstruum.

The *dose* is from one to two fluidrachms (4–8 cc.).

FLUIDEXTRACTUM VIBURNI OPULI. N. F.

Fluidextract of Viburnum Opulus [Fldext. Viburn. Opul.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM VIBURNI PRUNIFOLII. N. F.

Fluidextract of Viburnum Prunifolium [Fldext. Viburn. Prun.]

This is made with a mixture of two volumes of alcohol and one of water as the menstruum.

The *dose* is from thirty to sixty minims (2–4 cc.).

FLUIDEXTRACTUM XANTHOXYLI. N. F.

Fluidextract of Xanthoxylum [Fldext. Xanthox.]

This is made with a menstruum of three volumes of alcohol and one of water.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

FLUIDEXTRACTUM ZEÆ. N. F.

Fluidextract of Zea [Fldext. Zea.]

Made with diluted alcohol.

The *dose* is from one to three fluidrachms (4–12 cc.).

FLUIDGLYCERATA. N. F.

Fluidglycerates

Fluidglycerates are intended to be of the same drug strength as fluidextracts. They contain approximately 50 per cent., by volume, of glycerin and no alcohol. Fluidglycerates made from drugs that do not require either an acid or an alkaline menstruum may be prepared by a general process which embodies maceration, percolation, and evaporation to a given volume. The preparation is then allowed to stand for a few days, and the clear portion decanted and the remainder strained.

FLUIDGLYCERATUM CASCARÆ SAGRADÆ. N. F.

Fluidglycerate of Cascara Sagrada [Fldglycer. Casc. Sagr.]

Prepared from cascara sagrada according to the general process.

The *dose* is ten to twenty minims (0.6–1.2 cc.).

FLUIDGLYCERATUM CASCARÆ SAGRADÆ AROMATICUM. N. F.

Aromatic Fluidglycerate of Cascara Sagrada [Fldglycer. Casc. Sagr. Arom.]

Prepared from cascara sagrada by removing its bitter taste with calcium oxide and subsequently flavoring with fluidglycerate of licorice and oils of fennel, clove, and cinnamon.

The *dose* is from fifteen to thirty minims (1–2 cc.).

FLUIDGLYCERATUM GLYCYRRHIZÆ. N. F.

Fluidglycerate of Glycyrrhiza [Fldglycer. Glycyrrh. Fluidglycerate of Licorice]

Prepared from glycyrrhiza (licorice) by the general process. It is used as a flavoring agent.

FLUIDGLYCERATUM KRAMERIÆ. N. F.

Fluidglycerate of Krameria [Fldglycer. Kramer.]

Prepared from krameria by the general process.

The *dose* is from fifteen to thirty minims (1–2 cc.).

FLUIDGLYCERATUM RHEI. N. F.

Fluidglycerate of Rhubarb [Fldglycer. Rhei]

Prepared from rhubarb by the general process.

The *dose* is from fifteen to thirty minims (1–2 cc.).

FORMALDEHYDUM CRESOLATUM. N. F.

Cresolated Formaldehyde [Formal. Cresol.]

This is a mixture of 40 parts of orthocresol (see *Cresol*, Part I) with 60 parts of solution of formaldehyde. It is used as a disinfectant.

GARGARISMA GUAIACI COMPOSITUM. N. F.

Compound Gargle of Guaiac [Garg. Guaiac. Co.]

This gargle contains 10 per cent. each of ammoniated tincture of guaiac and compound tincture of cinchona, 20 per cent. of clarified honey, and 4 per cent. of potassium chlorate, and oil of peppermint enough to flavor. Used as a local stimulant for the throat.

GLYCERITUM BISMUTHI. N. F.

Glycerite of Bismuth [Glycer. Bism.]

"One hundred millilitres of glycerite of bismuth yields not less than 12.5 Gm. of bismuth oxide and not more than 13.5 of bismuth oxide (Bi_2O_3) corresponding to about 40 Gm. of Bismuth and Sodium Tartrate." *N. F.* It is made from bismuth subnitrate, nitric acid, tartaric acid, sodium bicarbonate, glycerin, and distilled water. It is used in making other preparations containing bismuth. An assay is provided in the text. As the bismuth in this compound is in a soluble form it does not represent the virtues of bismuth subnitrate which are largely due to the insolubility of that salt.

GLYCERITUM PEPSINI. N. F.

Glycerite of Pepsin [Glycer. Pepsin.]

Five grains of pepsin are represented by 1 fluidrachm of the finished glycerite. The menstruum is acidulated water and glycerin.

The *dose* is forty-five minims (3 cc.).

GLYCERITUM PICIS PINI. N. F.

Glycerite of Tar [Glycer. Pic. Liq.]

Glyceritum Picis Liquidæ, *N. F. IV.*

This glycerite is made from tar, magnesium carbonate, glycerin, alcohol and water. The medicinal virtues of about 4 grains of tar are represented in 1 fluidrachm of the finished glycerite.

The *dose* is one fluidrachm (4 cc.).

GLYCERITUM TRAGACANTHÆ. N. F.

Glycerite of Tragacanth [Glycer. Trag.]

This glycerite contains about 12.5 per cent. of tragacanth with glycerin and water. It is prepared in the form of a thick homogeneous paste. It is used as an excipient for pills.

GLYCERITUM VITELLI. N. F.

Glycerite of Egg Yolk [Glycer. Vitell. Glyconin]

This is a mixture of egg yolk, 45 per cent., and glycerin, 55 per cent. Used as a emulsifying agent.

GLYCEROGELATINA. N. F.

Glycerogelatins

Glycerogelatins originated with Doctor Unna and are soft masses which melt at the temperature of the body. They contain gelatin, glycerin, water and the medicament, and are used in *skin diseases.*

GLYCEROGELATINUM ACIDI SALICYLICI. N. F.

Salicylic Acid Glycerogelatin [Glycerogel. Acid. Salicyl.]

This preparation contains 35 per cent. of glycerin and 10 per cent. of salicylic acid in glycerinated gelatin vehicle. Used as an antiseptic and keratoplastic.

GLYCEROGELATINUM IODOFORMI. N. F.

Iodoform Glycerogelatin [Glycerogel. Iodof.]

This preparation contains 15 per cent. of glycerin, and 10 per cent. of iodoform in glycerinated gelatin vehicle.

GLYCEROGELATINUM ZINCI DURUM. N. F.

Firm Zinc Glycerogelatin [Glycerogel. Zinc. Dur.]

This preparation contains 25 per cent. of glycerin, and 10 per cent. of zinc oxide in 30 per cent. glycerinated gelatin vehicle. Used as a local sedative and protective.

GLYCEROGELATINUM ZINCI MOLLE. N. F.

Soft Zinc Glycerogelatin [Glycerogel. Zinc. Mol.]

This preparation contains 35 per cent. of glycerin and 10 per cent. of zinc oxide in 20 per cent. of glycerinated gelatin vehicle. Used as an astringent and protective.

GOSSYPIUM STYPTICUM. N. F.

Styptic Cotton [Gossyp. Stypt.]

It is made by impregnating purified cotton with diluted solution of ferric chloride, glycerin and water. It should be kept in well closed containers. It is used as a local styptic.

INFUSUM BRAYERÆ. N. F.

Infusum of Brayera [Inf. Brayer.]

This infusion, which must be freshly prepared, is made with 6 per cent. of the drug in boiling water.

The *dose* is eight fluidounces (250 cc.).

INFUSUM GENTIANÆ COMPOSITUM. N. F.

Compound Infusion of Gentian [Inf. Gent. Co.]

This elixir contains 3 per cent. of gentian, flavored with coriander, and bitter orange peel. It is used as a tonic, and is made by percolation.

The *dose* is from one to four fluidrachms (4–15 cc.).

INFUSUM ROSÆ COMPOSITUM. N. F.

Compound Infusion of Rose [Inf. Ros. Co.]

This preparation which deserves a larger use on account of its pleasant flavor and beautiful color is made from red rose, diluted sulphuric acid, sugar and water. It is used as a vehicle or mild astringent.

The *dose* is three fluidounces (100 cc.).

INFUSUM SENNÆ COMPOSITUM. N. F.

Compound Infusion of Senna [Inf. Senn. Co.]

This is the same as the former preparation of the U. S. IX. It represents 6 per cent. of senna and 12 per cent. each of manna and magnesium sulphate.

The *dose* is four fluidounces (120 cc.).

INUNCTUM MENTHOLIS. N. F.

Menthol Inunction [Inunct. Menthol.]

The necessity for the peculiar name of this ointment is not apparent. It is simply a 5 per cent. ointment of menthol in hydrous wool-fat.

INUNCTUM MENTHOLIS COMPOSITUM. N. F.

Compound Menthol Inunction [Inunct. Menthol. Co.]

This preparation contains 5 per cent. of menthol and 10 per cent. of methyl salicylate in hydrous wool fat. It is counter-irritant as well as locally anesthetic.

LAC FERMENTATUM. N. F.

Fermented Milk [Lac. Ferment. Kumyss]

This well known dietetic preparation is made from fresh cow's milk, compressed yeast, and sugar, properly fermented, and is used as a food for invalids.

The *dose* is eight fluidounces (250 cc.).

LAVATIO ORI. N. F.

Mouth Wash [Lavat. Ori]

This is a sweetened aromatic solution of soap colored with fuchsin. Its therapeutic virtues are not very obvious.

LINIMENTUM ACONITI ET CHLOROFORMI. N. F.

Liniment of Aconite and Chloroform [Lin. Aconit. et Chlorof.]

This preparation contains 4.5 per cent. fluidextract of aconite and 12.5 per cent. of chloroform in a mixture of alcohol and soap liniment. It must not be confused with the dental liniment of aconite.

LINIMENTUM AMMONIÆ. N. F.

Ammonia Liniment [Lin. Ammon.]

Hartshorn Liniment; Volatile Liniment.

This is the same as the former preparation of the U. S. IX. It is used externally as a rubefacient.

LINIMENTUM BELLADONNÆ. N. F.

Belladonna Liniment [Lin. Bellad.]

This is, like the former preparation of the U. S. IX, a 5 per cent. solution of camphor in fluidextract of belladonna.

LINIMENTUM CALAMINÆ. N. F.

Calamine Liniment [Lin. Calam.]

This contains 8 per cent. each of prepared calamine and zinc oxide suspended in lime liniment.

LINIMENTUM OPII COMPOSITUM. N. F.

Compound Liniment of Opium [Lin. Opii Co.]

Canada Liniment.

This liniment contains 10 per cent. of tincture of opium, 22 per cent. of oil of turpentine and 35 per cent. of ammonia water, with camphor, alcohol and oil of peppermint, made into a somewhat permanent emulsion with fresh egg albumen. It is used as a stimulating anodyne application.

LINIMENTUM SAPONATO-CAMPHORATUM. N. F.

Camphorated Soap Liniment [Lin. Sapon.-Camph.]

Solid Opodeldoc.

This liniment contains freshly prepared sodium stearate made by combining monohydrated sodium carbonate and stearic acid, perfumed with camphor, oils of thyme and rosemary and ammonia water. It is a useless survival of a former fad.

LINIMENTUM SAPONIS MOLLIS COMPOSITUM. N. F.

Compound Liniment of Soft Soap [Lin. Sapon. Mol. Co.]

Tinctura Saponis Viridis Composita.

There is no change in this preparation which was formerly classed as compound tincture of green soap. It contains soft soap, oil of cade, and alcohol.

LINIMENTUM SINAPIS COMPOSITUM. N. F.

Compound Liniment of Mustard [Lin. Sinap. Co.]

This preparation contains 3 per cent. of volatile oil of mustard, with fluidextract of mezereum, camphor, castor oil, and alcohol. It is an active rubefacient.

LINIMENTUM TEREBINTHINÆ. N. F.

Turpentine Liniment [Lin. Terebinth.]

Kentish Ointment.

This differs materially from the *Linimentum Terebinthinæ* of the Br. (see Part I). It is used as a stimulating application to burns and ulcers.

LINIMENTUM TEREBINTHINÆ ACETICUM. N. F.

Acetic Turpentine Liniment [Lin. Terebinth. Acet.]

Linimentum Album; Stokes' Liniment; St. John Long's Liniment.

This liniment contains 40 per cent. of oil of turpentine, fresh egg, oil of lemon, acetic acid and rose water. It is a powerful counter-irritant.

LIQUOR ALUMINI ACETATIS. N. F.

Solution of Aluminum Acetate [Liq. Alum. Acet.]

Liquor Burowii; Burow's Solution.

"An aqueous solution containing not less than 4.5 and not more than 5.5 Gm. of neutral aluminum acetate [$Al(C_2H_3O_2)_3 = 204.10$] in each 100 cc." *N. F.* It is made by the reactions between lead acetate and aluminum sulphate in aqueous solution. A process of assay is also given in the text. It should be noted that this differs from the solution of aluminum acetate of the N. F. III which is now known as the solution of the subacetate. It is astringent and antiseptic.

LIQUOR ALUMINI SUBACETATIS. N. F.

Solution of Aluminum Subacetate [Liq. Alum. Subacet.]

"An aqueous solution containing not less than 7.5 Gm. and not more than 8 Gm. of basic aluminum acetate [$Al(C_2H_3O_2)_2OH = 162.08$] in each 100 cc." *N. F.* It is made from aluminum sulphate, acetic acid, precipitated calcium carbonate and water. An assay process is also given in the text. This preparation corresponds closely to the *Liquor Alumini Acetici* of the German Pharmacopœia. It is an active germicide, as well as astringent, and is used both as a gargle and as a surgical dressing. It should generally be diluted with from 4 to 8 parts of water.

LIQUOR ANTISEPTICUS. N. F.

Antiseptic Solution [Liq. Antisept.]

This is a hydro-alcoholic solution containing 2.5 per cent. of boric acid with traces of thymol, eucalyptol, menthol and methyl salicylate. While it possesses feeble antiseptic properties, it is chiefly useful to flavor mouth-washes.

LIQUOR AROMATICUS ALKALINUS. N. F.

Alkaline Aromatic Solution [Liq. Aromat. Alk.]

Liquor Antisepticus Alkalinus, *N. F. IV.*

This solution contains 2 per cent. each of sodium borate and potassium bicarbonate with small amounts of thymol, eucalyptol and methyl salicylate and is sweetened with glycerin and colored with cudbear.

LIQUOR AURI ET ARSENI BROMIDI. N. F.

Solution of Gold and Arsenic Bromide [Liq. Aur. et Arsen. Brom.]

This is a reddish-brown solution resulting from the interaction between arsenic trioxide, bromauric acid and bromine. It was at one time lauded as a remedy for diabetes but probably owes any value it may possess chiefly to the arsenic in it.

The *dose* is from two to five minims (0.12–0.3 cc.).

LIQUOR BISMUTHI. N. F.

Solution of Bismuth [Liq. Bism.]

This solution is made from glycerite of bismuth, alcohol, and distilled water. About 3 grains of bismuth and sodium tartrate are represented in 1 fluidrachm of the finished solution. It is used as an intestinal astringent, but does not possess the therapeutic virtues of the insoluble bismuth salts.

The *dose* is one fluidrachm (4 cc.).

LIQUOR CALCIS SULPHURATÆ. N. F.

Solution of Sulphurated Lime [Liq. Calc. Sulphurat.]

Solution of Oxysulphuret of Calcium; Vleminckx' solution; Vleminckx' Lotion.

This solution is made by boiling together lime, sublimed sulphur and water. It is used as an external application in skin diseases.

LIQUOR CARMINI. N. F.

Solution of Carmine [Liq. Carmin.]

This solution is made from carmine, ammonia water, glycerin and water. It is used as a red coloring solution.

LIQUOR CHLORI COMPOSITUS. N. F.

Compound Solution of Chlorine [Liq. Chlor. Co.]

Chlorine Water.

This is "an aqueous solution containing, when freshly made, a mixture of chlorine and chlorine oxides equivalent to about 0.35 Gm. of available chlorine in each one hundred cc." *N. F.* It is made by reacting upon potassium chlorate with hydrochloric acid and then dissolving the products of the reaction in cold distilled water; this is practically identical with the U. S. P. VIII process. It is used as an intestinal antiseptic.

The *dose* is one fluidrachm (4 cc.).

LIQUOR COCCI. N. F.

Liquor Coccineus, N. F. III

Cochineal Color [Liq. Cocci]

This solution is made from cochineal, potassium carbonate, alum, potassium bitartrate, alcohol, glycerin, and water. Like the solution of carmine, it is used to color preparations red.

LIQUOR FERRI ALBUMINATI. N. F.

Solution of Albuminized Iron [Liq. Ferr. Albumin.]

Solution of Albuminate of Iron; Solution of Ferric Albuminate.

The formula for this preparation has been materially altered. It is now made by dissolving albuminized iron (see *Ferri Albuminatum*, Part I) in an aromatic vehicle. It is a clear yellowish-brown liquid, containing 5 per cent. of albuminized iron, or about $^2/_5$ of a grain of metallic iron in the form of albuminate, in 1 fluidrachm of the finished solution.

The *dose* is from two to four fluidrachms (8–15 cc.).

LIQUOR FERRI CITRATIS. N. F.

Solution of Ferric Citrate [Liq. Ferr. Cit.]

This is "an aqueous solution containing ferric citrate corresponding to not less than 8.75 Gm. of metallic iron (Fe) in each 100 cc." *N. F.* It is a dark reddish-brown liquid with an acid reaction. It is made from solution of ferric sulphate, citric acid, ammonia water, and water. A process of assay is given in the text.

The *dose* is ten minims (0.6 cc.).

LIQUOR FERRI PEPTONATI. N. F.

Solution of Peptonized Iron [Liq. Ferr. Pepton.]

It is made from pepsin, fresh egg albumen, hydrochloric acid, solution of ferric oxychloride, alcohol, and sodium citrate made up into a pleasantly flavored preparation with oil of orange, acetic ether, and vanillin, using glycerin, syrup and distilled water. It contains 1.75 per cent. of peptonized iron—equivalent to about $^2/_5$ of a grain of metallic iron—in 1 fluidrachm of the finished solution.

The *dose* is from two to four fluidrachms (8–15 cc.).

LIQUOR FERRI PEPTONATI ET MANGANI. N. F.

Solution of Peptonized Iron and Manganese [Liq. Ferr. Pepton. et Mangan.]

Solution of Iron Peptonate and Manganese.

This preparation is made from the same ingredients and in a similar manner to the foregoing preparation with the addition of soluble manganese citrate.

The *dose* is two fluidrachms (8 cc.).

LIQUOR FERRI SALICYLATIS. N. F.

Solution of Ferric Salicylate [Liq. Ferr. Salicyl. Salicylated Mixture of Iron]

This preparation contains sodium salicylate, tincture of ferric citro-chloride, ammonium carbonate, citric acid, methyl salicylate, glycerin, and distilled water. Each fluidrachm is equivalent to about 7½ grains of sodium salicylate and 7½ minims of tincture of ferric citro-chloride. It has been recommended for cases of chronic rheumatism complicated with anemia.

The *dose* is from one to two fluidrachms (4–8 cc.).

LIQUOR FERRI SUBSULPHATIS. N. F.

Solution of Ferric Subsulphate [Liq. Ferr. Subsulph.]

Monsel's Solution; Solution of Basic Ferric Sulphate.

This is "an aqueous solution containing basic ferric sulphate corresponding to not less than 20 Gm. and not more than 22 Gm. of Fe in each 100 cc." It is essentially similar to the preparation formerly recognized by the U. S. IX, although the proportion of ingredients used in its manufacture is somewhat different. The ferrous sulphate is partially oxidized to the ferric condition by boiling with nitric acid, but the amount of sulphuric acid being insufficient to form a normal sulphate, the resulting salt has the approximate composition, $5Fe_2(SO_4)_3.Fe_2(OH)_6$. It forms a reddish-brown acid liquid. It is a valuable astringent and styptic.

The *dose* is from one to three minims (0.06–0.20 cc.).

LIQUOR HYDRASTINÆ COMPOSITUS. N. F.

Compound Solution of Hydrastine [Liq. Hydrastin. Co.]

Colorless Hydrastine Solution.

This preparation contains 0.3 per cent. each of the chlorides of hydrastine, aluminum, calcium, and magnesium with 0.1 per cent. of potassium chloride in solution in glycerin and water. It owes its activity chiefly to the hydrastine.

The *dose* is from one to two fluidrachms (4–8 cc.).

LIQUOR HYPOPHOSPHITUM COMPOSITUS. N. F.

Compound Solution of Hypophosphites [Liq. Hypophos. Co.]

This solution represents in each fluidrachm ⅛ grain quinine, 1–250th of a grain of strychnine and ¼ grain of iron, with calcium, potassium, sodium, and manganese hypophosphites.

The *dose* is one to four fluidrachms (4–15 cc.).

LIQUOR IODI ET ZINCI PHENOLSULPHONATIS. N. F.

Solution of Iodine and Zinc Phenolsulphonate. [Liq. Iodi et Phenolsul.]

Pyorrhea Astringent.

This contains 15 Gm. each of zinc phenolsulphonate and potassium iodide with 20 Gm. of iodine in 100 cc. "This solution should be recently prepared when dispensed." *N. F.* It is used locally.

LIQUOR IODI PHENOLATUS. N. F. Liquor Iodi Carbolatus, N. F. III

Phenolated Solution of Iodine [Liq. Iod. Phenol.]

Carbolized Solution of Iodine; Boulton's Solution; French Mixture.

This solution is made from compound solution of iodine, liquefied phenol, glycerin, and water. The direction to expose it to sunlight until it is decolorized destroys much of its therapeutic value. It represents about 0.5 per cent. of phenol. It is used externally.

LIQUOR PANCREATINI. N. F.

Solution of Pancreatin [Liq. Pancreat.]

Liquor Pancreaticus; Pancreatic Solution.

This solution is made from pancreatin, sodium bicarbonate, glycerin, compound spirit of cardamom, alcohol, purified talc and water. About 1 grain of pancreatin is represented in 1 fluidrachm of the finished solution. It is used as a digestive.

The *dose* is one to four fluidrachms (4–15 cc.).

LIQUOR PEPSINI. N. F.

Solution of Pepsin [Liq. Pepsin.]

This solution contains glycerite of pepsin, hydrochloric acid, glycerin and water. "One cc. of this solution will digest 10 Gm. of egg albumen, carrying out the test according to the details of the U. S. P. X assay under *Pepsinum.*" *N. F.* It is too weak to be of therapeutic value.

The *dose* is from two to four fluidrachms (8–15 cc.).

LIQUOR PEPSINI ANTISEPTICUS. N. F.

Antiseptic Solution of Pepsin [Liq. Pepsin. Antisept.]

This solution represents 5 per cent. of pepsin with traces of menthol, eucalyptol and methyl salicylate. It is much stronger than the preceding; "One-tenth cc. of this solution will digest 10 Gm. of egg albumen when carrying out the test according to the details of the U. S. P. X assay under *Pepsinum.*" *N. F.* It is used externally in the treatment of old sores to assist their healing.

LIQUOR PEPSINI AROMATICUS. N. F.

Aromatic Solution of Pepsin [Liq. Pepsin. Arom.]

This solution of pepsin is flavored with cinnamon, pimenta and clove. About 1 grain of pepsin is represented in 1 fluidrachm of finished solution. It is used as a digestive. "One-fourth cc. of the solution digests 10 Gm. of egg albumen, carrying out the test according to the details of the U. S. P. under *Pepsinum.*" *N. F.*

The *dose* is from two to four fluidrachms (8–15 cc.).

LIQUOR PHOSPHATUM ACIDUS. N. F.

Acid Solution of Phosphates [Liq. Phos. Acid. Solution of Acid Phosphates]

This is now made by dissolving calcium and magnesium carbonate in phosphoric acid and water. It represents 7¼ grains of dibasic calcium phosphate in each fluidrachm.

The *dose* is one fluidrachm (4 cc.).

LIQUOR PHOSPHATUM COMPOSITUS. N. F.

Compound Solution of Phosphates [Liq. Phos. Co.]

This is a polypharmacal preparation containing the phosphates of ammonium, calcium, iron, potassium, and sodium held in aqueous solution by the use of glycerin and citric acid. It is used for making the compound syrup of phosphates.

LIQUOR PHOSPHORI. N. F.

Solution of Phosphorus [Liq. Phosphor.]

Thompson's Solution of Phosphorus.

This solution is made from phosphorus, dehydrated alcohol, spirit of peppermint and glycerin. It represents 0.07 per cent. of phosphorus. It is used as a tonic and stimulant in nervous diseases.

The *dose* is from ten to fifteen minims (0.6–1.0 cc.).

LIQUOR PICIS CARBONIS. N. F.

Coal Tar Solution [Liq. Pic. Carbon.]

Liquor Carbonis Detergens.

This preparation, sometimes known by the name of *Liquor Carbonis Detergens,* is made by digesting 200 Gm. of coal tar and 100 Gm. of soap bark with enough alcohol to make 1000 cc. It is used externally in skin diseases.

LIQUOR PLUMBI SUBACETATIS DILUTUS. N. F.

Diluted Solution of Lead Subacetate. [Liq. Plumb. Subacet. Dil.]

Lead Water.

This is a mixture of 35 parts of solution of lead subacetate with 965 parts of water. It is too weak to be of any real value. It is used locally.

LIQUOR POTASSII IODIDI. N. F.

Solution of Potassium Iodide [Liq. Pot. Iod.]

Saturated Solution of Potassium Iodide.

"An aqueous solution containing not less than 97 Gm. and not more than 103 Gm. of KI (166.02) in each 100 cc." *N. F.*

The *dose* is from five to ten minims (0.3–0.6 cc.) or more.

LIQUOR PROCAINÆ HYDROCHLORIDI.

Solution of Procaine Hydrochloride [Liq. Procain. Hydroch.]

Dental Anesthetic Solution.

This solution contains 2 Gm. of procaine hydrochloride in each 100 cc. of 0.9 per cent. sodium chloride solution, a little thymol being present as a preservative. The N. F. has a note that "to each cc. of this solution add 9.95 cc. of solution of Epinephrine Hydrochloride just before employing hypodermically" but such a memorandum seems to us an infringement on the prerogatives of the physician.

LIQUOR SODÆ ET MENTHÆ. N. F.

Solution of Soda and Mint [Liq. Sod. et Menth.]

Mistura Sodæ et Menthæ; Soda Mint.

This preparation contains sodium bicarbonate, aromatic spirit of ammonia and spearmint or peppermint water. Each fluidrachm contains 3 grains of the bicarbonate and 0.6 minim of aromatic spirit of ammonia. It is used as an antacid and carminative.

The *dose* is from two to four fluidrachms (8–15 cc.).

LIQUOR SODII ARSENATIS. N. F.

Solution of Sodium Arsenate [Liq. Sod. Arsenat.]

" An aqueous solution containing not less than 0.975 Gm. and not more than 1.025 Gm. of Na_2HAsO_4 (185.97) in each 100 cc." *N. F.* This is the same as the solution formerly official in the U. S. IX.

The *dose* is from three to eight minims (0.2–0.5 cc.).

LIQUOR SODII ARSENATIS, PEARSONII. N. F.

Pearson's Solution of Sodium Arsenate [Liq. Sod. Arsen. Pearson.]

Liquor Arsenicalis Pearsonii.

This preparation should not be confounded with the preceding Liquor Sodii Arsenatis, which is ten times stronger than Pearson's solution. It contains about ⅙ per cent. of crystallized sodium arsenate, or about ⅒ per cent. of anhydrous sodium arsenate. Whenever it is prescribed or dispensed, the name " Pearson " should be specified, to avoid serious mistakes.

The *dose* is from twenty to thirty minims (1–2 cc.).

LIQUOR SODII BORATIS COMPOSITUS. N. F.

Compound Solution of Sodium Borate [Liq. Sod. Bor. Co.]

Dobell's Solution.

This solution contains about 1.5 per cent. each of sodium borate and sodium bicarbonate and 0.3 per cent. of phenol, with glycerin and water. It is widely used as a cleansing wash in inflammations of the nose and pharynx.

LIQUOR SODII CITRATIS. N. F.

Solution of Sodium Citrate [Liq. Sod. Cit.]

Mistura Sodii Citratis; Potio Rivierii.

This solution is made with 2 per cent. of citric acid and 2.5 per cent. of sodium bicarbonate in distilled water. It should be freshly prepared. The amount of sodium citrate formed, about 1.5 grains for each fluidrachm, is so small that the solution has scarcely any effect beyond that of a mildly saline drink.

The *dose* is officially given as two fluidrachms (8 cc.) but it would require upwards of an ounce to exercise any therapeutic effect.

LIQUOR SODII PHOSPHATIS COMPOSITUS. N. F.

Compound Solution of Sodium Phosphate [Liq. Sod. Phos. Co.]

This preparation contains sodium phosphate crystals, citric acid, glycerin, and distilled water. Each cc. represents 1 gramme of crystallized sodium phosphate. It is used as a laxative.

The *dose* is from one to two fluidrachms (4–8 cc.).

LOTIO ALBA VETERINARIA. N. F.

Veterinary White Lotion [Lot. Alb. Vet.]

This preparation is the result of the reaction between zinc sulphate (23 Gm.) and lead acetate (30 Gm.) in 1000 cc. of water.

LOTIO AMMONIACALIS CAMPHORATA. N. F. Aqua Sedativa, N. F. III

Ammoniated Camphor Wash [Lot. Ammon. Camph.]

Aqua Sedativa; Sedative Water; Eau Sedative de Raspail.

This is an aqueous solution containing 6 per cent. each of sodium chloride and ammonia water, with 10 per cent. spirit of camphor.

LOTIO CALAMINÆ. N. F.

Calamine Lotion [Lot. Calam.]

This preparation contains 8 Gm. each of prepared calamine and zinc oxide in 100 cc. of lime water with a little glycerin.

LOTIO CALAMINÆ COMPOSITUM. N. F.

Compound Calamine Lotion [Lot. Calam. Co.]

This is a 10 per cent. solution of liquefied phenol in calamine lotion.

LOTIO FLAVA. N. F.

Yellow Lotion [Lot. Flav.]

Yellow Wash; Aqua Phagedænica Flava.

It is made with 0.3 per cent. of corrosive mercuric chloride in lime water slightly diluted with water. The mercury is present as a yellow hydroxide in the finished preparation. It is used externally in skin diseases. It is slightly weaker than the corresponding preparation of the Br. (See *Lotio Hydrargyri Flava,* Part I.)

LOTIO NIGRA. N. F.

Black Lotion [Lot. Nigr.]

Black Wash; Aqua Phagedænica Nigra.

It is made with 0.875 per cent. (formerly 0.75 per cent.) of mild mercurous chloride in lime water slightly diluted with water. The mercury is largely present as a black suboxide. It is used externally in skin diseases. It exceeds in strength the similar Br. preparation (see *Lotio Hydrargyri Nigra,* Part I).

LOTIO PLUMBI ET OPII. N. F.

Lotion of Lead and Opium [Lot. Plumb. et Opii.]

Lead and Opium Wash.

It contains, in each 100 cc., 1.75 grammes of lead acetate and 3.5 grammes of tincture of opium. It is used as an astringent and sedative external application.

MAGMA BISMUTHI. N. F.

Bismuth Magma [Magma Bism.]

Milk of Bismuth.

This is practically the same as the preparation formerly recognized by the U. S. IX. It contains "not less than 5.6 Gm. of Bi_2O_3 in each 100 cc., corresponding to not less than 7 Gm. of bismuth subnitrate in each 100 cc." *N. F.*

The *dose* is from one to two fluidrachms (4–8 cc.).

MASSA COPAIBÆ. N. F.

Mass of Copaiba [Mass. Copaib.]

Solidified Copaiba.

This is a combination of copaiba with a hydrated magnesium oxide reduced to a pilular consistence. It represents about 94 per cent. of copaiba.

The *dose* is from fifteen to thirty grains (1–2 Gm.).

MEL ROSÆ ET SODII BORATIS. N. F.

Honey of Rose and Sodium Borate [Mel. Ros. et Sod. Bor.]

Honey of Rose with Borax.

This preparation is made with borax, glycerin, and honey of rose. It is used as an astringent application.

MEL SODII BORATIS. N. F.

Honey of Sodium Borate [Mel. Sod. Bor.]

Mel Boracis; Honey and Borax.

This preparation is made with borax, glycerin, and clarified honey. It is used as a local application in sore throat.

MENTHOL CAMPHORATUM. N. F. Campho-Menthol, N. F. III

Camphorated Menthol [Menthol. Camph.]

Camphor and Menthol.

Equal parts by weight of camphor and menthol with a small proportion of alcohol added. Applied locally in *neuralgia*.

MISTURA ADSTRINGENS. N. F. Mistura Adstringens et Escharotica, N. F. III

Astringent Mixture [Mist. Adstring.]

Villate's Mixture.

This preparation is made from solution of lead subacetate, copper sulphate, zinc sulphate and diluted acetic acid. It should be well shaken before dispensing to insure the even distribution of the precipitated lead sulphate. It is used externally as an astringent and escharotic.

MISTURA CARMINATIVA. N. F.

Carminative Mixture [Mist. Carminat.]

Dalby's Carminative.

It is made from magnesium carbonate, potassium carbonate, tincture of opium, oils of caraway, fennel, and peppermint, with syrup and water. It contains 1–40th of a grain of opium in 10 minims of the finished mixture.

The *dose* for an infant is from five to ten minims (0.3–0.6 cc.).

MISTURA CHLORALIS ET POTASSII BROMIDI COMPOSITA. N. F.

Compound Mixture of Chloral and Potassium Bromide [Mist. Chloral. et Pot. Brom. Co.]

Chloral and Bromide Compound.

This preparation represents about 12 grains each of hydrated chloral and potassium bromide, and ⅛ grain each of the extracts of cannabis and hyoscyamus in each fluidrachm of the finished mixture.

The *dose* is one fluidrachm (4 cc.).

MISTURA CHLOROFORMI ET MORPHINÆ COMPOSITA. N. F.

Compound Mixture of Chloroform and Morphine [Mist. Chlorof. et Morph. Co.]

Mistura Chloroformi et Cannabis Indicæ Composita, *N. F. III;* Chloroform Anodyne.

This preparation contains chloroform, ether, tincture of cannabis, tincture of capsicum, morphine sulphate, oil of peppermint, glycerin, water, and alcohol. About 7½ minims of chloroform, 11 minims of tincture of cannabis, 1½ minims of tincture of capsicum, 1–7th of a grain of morphine sulphate, are represented in 1 fluidrachm of the finished mixture. It should not be confounded with chlorodyne (see *Tinctura Chloroformi et Morphinæ Composita*, Part I), which is a much stronger preparation.

The *dose* is from thirty to sixty minims (2–4 cc.).

MISTURA COPAIBÆ. N. F.

Copaiba Mixture [Mist. Copaib.]

Lafayette Mixture.

This preparation contains copaiba, spirit of nitrous ether, compound tincture of lavender, solution of potassium hydroxide, syrup, and mucilage of acacia. There is 7½ minims each of copaiba and sweet spirit of niter in one fluidrachm.

The *dose* is from two to four fluidrachms (8–15 cc.).

MISTURA COPAIBÆ ET OPII. N. F.

Mixture of Copaiba and Opium [Mist. Copaib. et Opii.]

Chapman's Mixture.

This preparation contains double the proportions of copaiba and spirit of nitrous ether in the above, and in addition two minims of tincture of opium in each fluidrachm. It is used in *gonorrhea*.

The *dose* is from one to two fluidrachms (4–8 cc.).

MISTURA MAGNESIÆ, ASAFŒTIDÆ ET OPII. N. F. Mistura Magnesiæ et Asafœtidæ, N. F. III

Mixture of Magnesia, Asafetida and Opium [Mist. Mag., Asafœt. et Opii.]

Dewee's Carminative.

This preparation contains 5 per cent. magnesium carbonate, 7.5 per cent. tincture of asafetida, 1 per cent. tincture of opium, with sugar and water. It is used as an anodyne and carminative.

The *dose* is from two to four fluidrachms (8–15 cc.).

MISTURA OLEO-BALSAMICA. N. F.

Oleo-Balsamic Mixture [Mist. Ol.-Balsam.]

Hoffmann's Balsam.

This preparation contains 0.4 per cent. each of the oils of lavender, thyme, lemon, nutmeg, and cinnamon, with eugenol, balsam of Peru, and alcohol. Its greatest value lies in its pleasant odor.

MISTURA OPII ET CHLOROFORMI COMPOSITA. N. F.

Compound Mixture of Opium and Chloroform [Mist. Opii et Chlorof. Co.]

Squibb's Diarrhea Mixture.

This preparation contains 20 per cent. each of tincture of opium and spirit of camphor, with tincture of capsicum, chloroform and alcohol.

The *dose* is from thirty to forty minims (2–2.6 cc.).

MISTURA OPII ET RHEI COMPOSITA.

Compound Mixture of Opium and Rhubarb [Mist. Opii et Rhei Co.]

Sun Cholera Mixture.

This preparation contains 10 per cent. each of tincture of capsicum and tincture of rhubarb, and 20 per cent. each of tincture of opium, spirit of camphor, and spirit of peppermint, dissolved in alcohol.

The *dose* is from twenty to forty minims (1.3–2.5 cc.).

MISTURA PECTORALIS, STOKES. N. F.

Stokes' Expectorant [Mist. Pect. Stokes]

Each fluidrachm of this preparation represents, approximately, 1 grain of ammonium carbonate, 2 minims each of fluidextracts of squill and senega, and 10 minims of paregoric dissolved in water and syrup of tolu. It is used as an expectorant.

The *dose* is one fluidrachm (4 cc.).

MISTURA RHEI ALKALINA. N. F. Syrupus Rhei et Potassii Compositus, N. F. III

Alkaline Mixture of Rhubarb [Mist. Rhei Alk.]

Elixir Rhei Alkalinum; Neutralizing Cordial.

This preparation contains in each fluidrachm 1 minim of fluidextract of rhubarb, ½ minim of fluidextract of hydrastis and 1 grain of potassium carbonate.

The official *dose* is given as one fluidrachm (4 cc.) but this is evidently intended for infants; the adult dose would be one or two fluidounces (15–30 cc.).

MISTURA RHEI COMPOSITA. N. F. Mistura Rhei et Sodæ, U. S. P. VIII

Compound Mixture of Rhubarb [Mist. Rhei Co.]

Mixture of Rhubarb and Soda.

Each fluidrachm of this contains approximately 1 minim of fluidextract of rhubarb, ⅙ minim of fluidextract of ipecac and 2 grains of sodium bicarbonate and 2 minims of spirit of peppermint.

The *dose* given by the N. F. is one fluidrachm (4 cc.) which is obviously intended for infants.

MUCILAGO CHONDRI. N. F.

Mucilage of Chondrus [Mucil. Chondr.]

Mucilage of Irish Moss.

This preparation contains 3 per cent. of Irish moss in water. It is used as an emulsifying agent and demulcent.

MUCILAGO SASSAFRAS MEDULLÆ. N. F.

Mucilage of Sassafras Pith [Mucil. Sassaf. Medul.]

This preparation contains 3 grammes of sassafras pith in each 100 cc. It is a bland mucilage used principally in eye lotions and should always be freshly prepared.

The *dose* is four fluidrachms (15 cc.).

MULLÆ. N. F.

Mulls

Steatins; Salve Mulls.

The mulls or salve mulls are very stiff ointments spread upon soft muslin (mull) similar to a plaster. The base is usually suet or lard, but wax or even lead plaster are used in some of the members of the group. They are usually made in a wholesale manner, by machinery, but the N. F. gives formulas for the retail preparation of several.

MULLA ACIDI SALICYLICI. N. F.

Salicylic Acid Mull [Mull. Ac. Salicyl.]

Unguentum Salicylatum Extensum.

This preparation contains 10 per cent. of salicylic acid with a mixture of benzoinated suet and benzoinated lard.

MULLA CREOSOTI SALICYLATA. N. F.

Salicylated Creosote Mull [Mull. Creosot. Salicyl.]

Unguentum Creosoti Salicylatum Extensum.

This preparation contains 10 per cent. of salicylic acid and 20 per cent. of creosote in a mixture of benzoinated suet and yellow wax.

MULLA HYDRARGYRI CHLORIDI CORROSIVI. N. F.

Corrosive Mercuric Chloride Mull [Mull. Hydrarg. Chlor. Corros.]

Unguentum Hydrargyri Chloridi Corrosivi Extensum.

This preparation contains 0.2 per cent. of corrosive sublimate in a mixture of benzoinated suet, benzoinated lard, and alcohol.

MULLA ZINCI. N. F.

Zinc Mull [Mull. Zinc.]

Unguentum Zinci Extensum.

This preparation is made with zinc oxide, 10 per cent., in a mixture of benzoinated suet and benzoinated lard.

NEBULA AROMATICA. N. F.

Aromatic Oil Spray [Nebul. Arom.]

Aromatol.

This preparation contains phenol, menthol, thymol, camphor, benzoic acid, eucalyptol, oil of cinnamon, oil of clove and methyl salicylate in small proportions, in solution in light liquid petrolatum. It is used in the form of a nebula, or spray.

NEBULA EUCALYPTOLIS. N. F.

Eucalyptol Spray [Nebul. Eucalyptol.]

This preparation contains 5 per cent. of eucalyptol in solution in light liquid petrolatum.

NEBULA MENTHOLIS. N. F.

Menthol Spray [Nebul. Menthol.]

This preparation consists of a solution of 2 per cent. of menthol in light liquid petrolatum.

NEBULA MENTHOLIS COMPOSITA. N. F.

Compound Menthol Spray [Nebul. Menthol. Co.]

This preparation contains 1 per cent. each of menthol and camphor, with smaller amounts of methyl salicylate, eucalyptol, and oil of cinnamon in solution in light liquid petrolatum.

NEBULA THYMOLIS. N. F.

Thymol Spray [Nebul. Thymol.]

This preparation contains 1 per cent. of thymol in solution in light liquid petrolatum.

ODONTALGICUM. N. F.

Toothache Remedy [Odontalg.]

This weirdly named mixture preparation is a mixture of 1 part of oil of cinnamon, 2 parts of phenol and 3 parts of methyl salicylate. It is intended for local application to carious teeth.

OLEA INFUSA. N. F.

Infused Oils [Ol. Inf.]

The formula for these is a general one. They are made by moistening the air dried drug with alcohol and ammonia water and infusing with warm sesame oil; they are of 10 per cent. strength.

OLEATUM QUININÆ. N. F.

Oleate of Quinine [Oleat. Quin.]

This preparation contains 25 per cent. of quinine in oleic acid and is used as a local anesthetic.

OLEATUM VERATRINÆ. N. F.

Oleate of Veratrine [Oleat. Veratrin.]

This preparation contains 2 per cent. of veratrine in equal parts of olive oil and oleic acid, and is used as an anodyne and rubefacient. It should be used cautiously on account of the danger of systemic poisoning.

OLEOSACCHARA. N. F.

Oil-sugars

Elæosacchara.

The N. F. gives a general formula for triturating any prescribed oil (2 per cent.) with sugar. What the need is of such a title is not apparent.

OLEORESINA CUBEBÆ. N. F.

Oleoresin of Cubeb [Oleores. Cubeb.]

This is prepared by exhausting cubeb with alcohol and evaporating the extract. It is a dark greenish-brown liquid whose consistency varies according to the relative proportions of oil and resin in the original drug. After standing for some time it deposits a waxy and crystalline precipitate which should be rejected, only the liquid portion being used.

Dose, from five to ten minims (0.3–0.6 cc.).

OLEUM ÆTHEREUM. N. F.

Ethereal Oil [Ol. Æther.]

This is a "volatile liquid consisting of equal volumes of ether and of heavy oil of wine," prepared by distillation of alcohol with sulphuric acid. It is transparent, nearly colorless, has a specific gravity of 0.905 at 25° C., a peculiar aromatic odor, and a pungent taste. Preserve in small glass-stoppered bottles in a cool place. It is used in the preparation of compound spirit of ether (Hoffmann's anodyne).

OLEUM HYOSCYAMI COMPOSITUM. N. F.

Compound Oil of Hyoscyamus [Ol. Hyosc. Co.]

Balsamum Tranquillans.

This preparation is made from 0.2 per cent. of the oils of lavender, peppermint, rosemary, and thyme, with infused oil of hyoscyamus. It is used as an anodyne.

OLEUM PHENOLATUM. N. F.

Phenolated Oil [Ol. Phenol.]

Oleum Carbolatum; Carbolized Oil.

It is made by dissolving 5 per cent. of phenol in olive oil. Used externally.

OLEUM PHOSPHORATUM. N. F.

Phosphorated Oil [Ol. Phosphorat.]

This preparation is made by dissolving 1 Gm. of phosphorus in 90 times its weight of expressed oil of almond with the aid of water bath heat and adding to this solution enough ether to make 100 Gm. "It is a clear, yellowish liquid, having the odor of phosphorus and of ether, and free from undissolved particles." *N. F.* It affords an excellent means of administering phosphorus.

The *dose* is one minim (0.05 cc.).

OLEUM RICINI AROMATICUM. N. F.

Aromatic Castor Oil [Ol. Ricin. Arom.]

This is castor oil flavored with gluside (0.05 per cent.), oils of clove and cinnamon, vanillin, coumarin, and alcohol.

The *dose* is from one-half to one fluidounce (15–30 cc.).

OXYMEL SCILLÆ. N. F.

Oxymel of Squill [Oxymel Scill.]

This preparation is made from 1 part of vinegar of squill and 2 parts of clarified honey. Used as an expectorant.

The *dose* is one fluidrachm (4 cc.).

PASTÆ DERMATOLOGICÆ. N. F.

Dermatologic Pastes

These preparations are ointment-like mixtures of starch, dextrin, zinc oxide, sulphur, calcium carbonate, or other medicinal substances made into a paste with glycerin, soft soap, petrolatum, etc., medicated with antiseptic or astringent agents and used in the practice of dermatologists.

PASTA BETANAPHTHOLIS. N. F.

Betanaphthol Paste [Past. Betanaphthol.]

Pasta Naphtholis Lassar; Lassar's Naphthol Paste.

This preparation contains 10 per cent. of betanaphthol, 50 per cent. of sulphur, 20 per cent. of petrolatum, and 20 per cent. of soft soap.

PASTA DEXTRINATA. N. F.

Dextrinated Paste [Past. Dextrin.]

This preparation contains 33 per cent. white dextrin, 33 per cent. glycerin and water. It is used as a vehicle.

PASTA RESORCINOLIS FORTIS. N. F.

Strong Resorcinol Paste [Past. Resorcin. Fort.]

Lassar's Stronger Resorcinol Paste.

This preparation contains 20 per cent. of resorcinol, zinc oxide, and starch, together with 40 per cent. of light liquid petrolatum.

PASTA RESORCINOLIS MITIS. N. F.

Mild Resorcinol Paste [Past. Resorcin. Mit.]

Lassar's Mild Resorcinol Paste.

This preparation contains 10 per cent. of resorcinol with 25 per cent. each of zinc oxide and starch, and 40 per cent. of light liquid petrolatum.

PASTA ZINCI. N. F.

Zinc Paste [Past. Zinc.]

Lassar's Zinc Paste.

This preparation contains 2 per cent. of salicylic acid, 24 per cent. of zinc oxide and starch, and 50 per cent. of petrolatum. Used as an antiseptic and protective in skin diseases.

PASTA ZINCI MOLLIS. N. F.

Soft Zinc Paste [Past. Zinc Moll.]

Unna's Soft Zinc Paste.

This preparation contains 25 per cent. each of zinc oxide, precipitated calcium carbonate, linseed oil, and solution of calcium hydroxide (lime water).

PASTA ZINCI SULPHURATA. N. F.

Sulphurated Zinc Paste [Past. Zinc. Sulphur.]

Unna's Sulphurated Zinc Paste.

This preparation contains 15 per cent. of zinc oxide, 10 per cent. of precipitated sulphur, 5 per cent. of purified siliceous earth, and 70 per cent. of benzoinated lard. It is used as an antizymotic and protective.

PEPSINUM SACCHARATUM. N. F.

Saccharated Pepsin [Pepsin. Sacchar.]

This preparation is a 10 per cent. triturate of pepsin with sugar of milk.

The *dose* is from thirty to sixty grains (2–4 Gm.).

PETROXOLINA MEDICATA. N. F.

Medicated Petroxolins.

These are made by dissolving the indicated medicinal substances in liquid petroxolin. Contrary to a common belief, liquid petroxolin does not readily penetrate the skin and the chief use of these preparations is as local remedies.

PETROXOLINUM BETANAPHTHOLIS. N. F.

Betanaphthol Petroxolin [Petrox. Betanaphthol.]

This preparation is a 10 per cent. fresh solution of betanaphthol in liquid petroxolin.

PETROXOLINUM BITUMENIS SULPHONATI. N. F.

Sulphonated Bitumen Petroxolin

This contains 10 per cent. of ichthyol in liquid petroxolin.

PETROXOLINUM CADINUM. N. F.

Cade Petroxolin [Petrox. Cadin.]

This preparation is a 25 per cent. mixture of oil of cade and liquid petroxolin.

PETROXOLINUM CHLOROFORMI CAMPHORATUM. N. F.

Camphorated Chloroform Petroxolin [Petrox. Chlorof. Camph.]

This is a solution of 25 per cent. each of chloroform and camphor in liquid petroxolin.

PETROXOLINUM CREOSOTI. N. F.

Creosote Petroxolin [Petrox. Creosot.]

This is a mixture of creosote 20 per cent., and olive oil 5 per cent., in liquid petroxolin. It is used as an antiputrescent and antiseptic.

PETROXOLINUM EUCALYPTOLIS. N. F.

Eucalyptol Petroxolin [Petrox. Eucalyptol.]

This is a 20 per cent. solution of eucalyptol in liquid petroxolin.

PETROXOLINUM GUAIACOLIS. N. F.

Guaiacol Petroxolin [Petrox. Guaiacol.]

This is a mixture of guaiacol 20 per cent., olive oil 5 per cent., and liquid petroxolin.

PETROXOLINUM HYDRARGYRI. N. F.

Mercury Petroxolin [Petrox. Hydrarg. Mercury Petrox]

This preparation contains 30 per cent. of mercury extinguished with 13 per cent. of hydrous wool fat and 2 per cent. oleic acid, and solid petroxolin added to make 100 parts.

PETROXOLINUM IODI. N. F.

Iodine Petroxolin [Petrox. Iod. Iodine Petrox, 10 per cent.]

This contains 10 Gm. of iodine in 100 cc. of liquid petroxolin.

PETROXOLINUM IODI DILUTUM. N. F.

Diluted Iodine Petroxolin [Petrox. Iod. Dil. Iodine Petrox, 5 per cent.]

This preparation is a solution of 5 per cent. iodine in liquid petroxolin.

PETROXOLINUM LIQUIDUM. N. F.

Liquid Petroxolin [Petrox. Liq.]

Petrolatum Saponatum Liquidum; Liquid Petrox.

This preparation is made from light liquid petrolatum, oleic acid, stronger ammonia water, and 15 per cent. alcohol and perfumed with oil of lavender. It is a yellowish-brown liquid, miscible with ether, chloroform, petroleum benzin or acetone and producing an emulsion-like mixture when added to twice its volume of water. It is used as a basis for various medicated petroxolins.

PETROXOLINUM MENTHOLIS. N. F.

Menthol Petroxolin [Petrox. Menthol.]

This preparation contains 10 Gm. of menthol in 100 cc. of liquid petroxolin. It is used as a local anesthetic.

PETROXOLINUM METHYLIS SALICYLATIS. N. F.

Methyl Salicylate Petroxolin [Petrox. Methyl. Sal.]

This preparation is a solution of methyl salicylate, 20 per cent., in liquid petroxolin. It is used as an antirheumatic.

PETROXOLINUM PHENOLIS. N. F.

Phenol Petroxolin [Petrox. Phenol.]

This preparation is a 5 per cent. solution of phenol in liquid petroxolin.

PETROXOLINUM PHENOLIS CAMPHORATUM. N. F.

Camphorated Phenol Petroxolin [Petrox. Phenol. Camph.]

This contains 12.5 per cent. phenol and 37.5 per cent. camphor in liquid petroxolin.

PETROXOLINUM SPISSUM. N. F.

Solid Petroxolin [Petrox. Spiss.]

Petrolatum Saponatum Spissum; Solid Petrox.

This preparation is a mixture of 35 per cent. white wax, 20 per cent. light liquid petrolatum, 32 per cent. oleic acid, 3 per cent. oil of lavender, 5 per cent. alcohol, and 5 per cent. stronger ammonia water. It is used as a vehicle for ointments.

PETROXOLINUM SULPHURATUM. N. F.

Sulphurated Petroxolin [Petrox. Sulphur.]

This preparation is a mixture of 3 per cent. sublimed sulphur, 37 per cent. linseed oil, 30 per cent. oleic acid, in liquid petroxolin.

PETROXOLINUM SULPHURATUM COMPOSITUM. N. F.

Compound Sulphurated Petroxolin [Petrox. Sulphur. Co.]

This preparation is made from 10 per cent. sulphurated petroxolin, 10 per cent. oil of cade, 0.3 per cent. thymol, 3 per cent. eucalyptol, 30 per cent. oil of turpentine, and liquid petroxolin.

PHENOL IODATUM. N. F.

Iodized Phenol [Phenol. Iodat.]

This is made from iodine 20 per cent., phenol 60 per cent., and glycerin. It is an active germicide.

PILULÆ. N. F.

Pills

Pills are globular or ovoid dosage forms of medicinal substances intended for internal administration. Each pill weighs not less than 0.06 Gm., nor more than 0.5 Gm. If they weigh less than 0.06 Gm. and more than 0.02 Gm. each they are known as "*Granules*"; if the weight is less than 0.02 Gm., they are usually designated as "*Parvules.*" The ingredients are massed by the aid of selected excipients.

For the extemporaneous coating of pills by the pharmacist, formulas and working directions for the following methods are supplied: gelatin, sugar, cocoa, tolu, silver, and salol coatings. For the coating of the so-called "enteric pills," the use of salol is recommended. (See also *Pilulæ*, Part I.)

PILULÆ ALOES ET ASAFŒTIDÆ. N. F.

Pills of Aloe and Asafetida [Pil. Aloe et Asafœt.]

Each pill contains about 1½ grains each of aloe and asafetida.

The *dose* is one or two pills.

PILULÆ ASAFŒTIDÆ ET FERRI. N. F.

Pills of Aloe and Iron [Pil. Aloe et Ferr.]

Each pill contains about 1 grain each of aloe and exsiccated ferrous sulphate.

The *dose* is one or two pills.

PILULÆ ALOES ET MASTICHES. N. F.

Pills of Aloe and Mastic [Pil. Aloe et Mastich.]

Lady Webster Dinner Pill.

Each pill contains about 2 grains of aloe and ⅔ grain of mastic.
The *dose* is one pill.

PILULÆ ALOES ET MYRRHÆ. N. F.

Pills of Aloe and Myrrh [Pil. Aloe et Myrrh.]

Each pill contains about 1 grain of myrrh and 2 grains of aloe.
The *dose* is one pill.

PILULÆ ALOES ET PODOPHYLLI COMPOSITÆ. N. F.

Compound Pills of Aloe and Podophyllum [Pil. Aloe et Podoph. Co.]

Janeway's Pills.

Each pill contains about 1 grain of aloe, ½ grain of resin of podophyllum and ¼ grain each of extracts of belladonna and nux vomica.
The *dose* is one pill.

PILULÆ ALOES, HYDRARGYRI ET PODOPHYLLI. N. F.

Pills of Aloe, Mercury and Podophyllum [Pil. Aloe, Hydrarg. et Podoph.]

Pilulæ Triplices; Pilula Triplex; Triplex Pills.

Each pill contains about 2 grains of aloe, 1 grain of mass of mercury and ¼ grain of resin of podophyllum.
The *dose* is one pill.

PILULÆ ALOINI COMPOSITÆ. N. F.

Compound Pills of Aloin [Pil. Aloin Co.]

Each pill contains about ½ grain of aloin, ⅛ grain of resin of podophyllum and ¼ grain of extract of belladonna.
The *dose* is one pill.

PILULÆ ALOINI, STRYCHNINÆ ET BELLADONNÆ. N. F.

Pills of Aloin, Strychnine and Belladonna [Pil. A., S. et B.]

Each pill contains about ⅕ grain of aloin, ⅛ grain of extract of belladonna and 1–125th grain of strychnine.
The *dose* is one or two pills.

PILULÆ ALOINI, STRYCHNINÆ ET BELLADONNÆ COMPOSITÆ. N. F.

Compound Pills of Aloin, Strychnine and Belladonna [Pil. A., S. et B. Co.]

These are the same as the preceding with the addition of ½ grain of cascara sagrada in each pill.
The *dose* is one or two pills.

PILULÆ ANTIPERIODICÆ. N. F.

Antiperiodic Pills [Pil. Antiperiod.]

Warburg's Pills.

Each pill contains 2 grains of aloes, ½ grain of rhubarb, ½ grain of angelica seed, ¼ grain each of inula, of saffron, and fennel, ⅛ grain of zeodoary root, of cubeb, myrrh, agaric and camphor, and 1½ grains of quinine sulphate, with a sufficient quantity of extract of gentian to form a mass.
The *dose* is one to three pills one to three times daily.

PILULÆ ANTIPERIODICÆ SINE ALOE. N. F.

Antiperiodic Pills without Aloes [Pil. Antiperiod. s. Aloe.]

Warburg's Pills without Aloes.

The formula is similar to that for the preceding pill, but the extract of aloes is omitted.
The *dose* is one to three pills.

PILULÆ CATHARTICÆ VEGETABILES. N. F.

Vegetable Cathartic Pills [Pil. Cathart. Veget.]

Each pill contains 1 grain compound extract of colocynth, ½ grain extract of hyoscyamus, ⅓ grain of resin of jalap, and ¼ grain each of extract of leptandra and resin of podophyllum.
The *dose* is two pills.

PILULÆ DIGITALIS, SCILLÆ ET HYDRARGYRI. N. F.

Pills of Digitalis, Squill and Mercury [Pil. Digit., Scill. et Hydrarg.]

Niemeyer Pills for Dropsy; Guy's Pills.

Each pill contains 1 grain each of digitalis, squill, and mass of mercury with clarified honey. Used as a diuretic. They must be carefully distinguished from Niemeyer's pill for *phthisis* (see *Pilulæ Opii Digitalis et Quininæ*).
The *dose* is one pill.

PILULÆ FERRI IODIDI. N. F.

Pills of Ferrous Iodide [Pil. Ferr. Iod.]

Blancard's Pills.

These are essentially the same as the pills of the U. S. IX. Each pill represents 1 grain of ferrous iodide.
Dose, one to three pills.

PILULÆ FERRI, QUININÆ, ALOES ET NUCIS VOMICÆ. N. F.

Pills of Iron, Quinine, Aloes and Nux Vomica [Pil. Ferr., Quin., Aloe et Nuc. Vom.]

Pilulæ Quadruplices; Quadruplex Pills; Pilulæ Ferri et Quininæ Compositæ.

Each pill contains 1 grain each of dried ferrous sulphate, quinine sulphate, and aloes, ¼ grain of extract of nux vomica, and enough extract of gentian to mass.
The *dose* is one pill.

PILULÆ FERRI, QUININÆ, STRYCHNINÆ ET ARSENI FORTIORES. N. F. Pilulæ Metallorum, N. F. III

Stronger Pills of Iron, Quinine, Strychnine and Arsenic [Pil. Ferr., Quin., Strych. et Arsen. Fort.]

Pilulæ Metallorum; Metallic Pills; Pilulæ Metallorum Amaræ; Bitter Metallic Pills.

Each pill contains 1 grain each of reduced iron and quinine sulphate, and 1–20th grain each of

strychnine and arsenic trioxide, massed with clarified honey.
The *dose* is one pill.

PILULÆ FERRI, QUININÆ, STRYCHNINÆ ET ARSENI MITES. N. F.

Mild Pills of Iron, Quinine, Strychnine, and Arsenic [Pil. Ferr., Quin., Strych. et Arsen. Mit.]

Aitken Tonic Pills.

Each pill contains ⅔ grain of reduced iron and 1 grain of quinine sulphate, and one-fiftieth grain each of strychnine and arsenic trioxide massed with clarified honey.
The *dose* is one pill.

PILULÆ LAXATIVÆ COMPOSITÆ. N. F.

Compound Laxative Pills [Pil. Lax. Co.]

Each pill contains ⅕ grain aloin, 1–125th grain strychnine, ⅛ grain extract of belladonna leaves, 1–16th grain of ipecac, licorice and syrup to mass. Used as a laxative.
The *dose* is one or two pills.

PILULÆ OPII, DIGITALIS ET QUININÆ N. F.

Pills of Opium, Digitalis, and Quinine [Pil. Opii, Digit. et Quin.]

Niemeyer Pills for Phthisis.

Each pill contains ⅕ grain of opium and 1 grain each of digitalis and quinine.
The *dose* is one pill.

PILULÆ OPII ET CAMPHORÆ. N. F.

Pills of Opium and Camphor [Pil. Opii et Camph.]

Each pill contains 1 grain of powdered opium and 2 grains of camphor.
The *dose* is one pill.

PILULÆ OPII ET PLUMBI. N. F.

Pills of Opium and Lead [Pil. Opii et Plumb.]

Each pill contains 1 grain of powdered opium and 1 grain of lead acetate.
The *dose* is one pill.

PILULÆ RHEI. N. F.

Pills of Rhubarb [Pil. Rhei]

Each pill contains 3 grains of rhubarb and 1 grain of soap.
The *dose* is one pill.

PILULÆ RHEI COMPOSITÆ. N. F.

Compound Pills of Rhubarb [Pil. Rhei Co.]

These are practically the same as the compound rhubarb pills of the U. S. IX; each pill contains, approximately, 2 grains of rhubarb, 1½ of aloes and 1 grain of myrrh.
The *dose* is two or three pills.

PULVIS ACETANILIDI COMPOSITUS. N. F.

Compound Acetanilid Powder [Pulv. Acetan. Co.]

A mixture of acetanilid, 70 Gm., caffeine, 10 Gm., and sodium bicarbonate, 20 Gm.
The *dose* is five grains (0.3 Gm.).

PULVIS ALOES ET CANELLÆ. N. F.

Powder of Aloes and Canella [Pulv. Aloe et Canell.]

Hiera Picra.

It contains 80 per cent. of purified aloes and 20 per cent. of powdered canella.
The *dose* is five grains (0.3 Gm.).

PULVIS ANTIMONIALIS. N. F.

Antimonial Powder [Pulv. Antimon.]

James' Powder.

A mixture of antimony oxide, 33 per cent., and precipitated calcium phosphate, 67 per cent.
The *dose* is three grains (0.2 Gm.).

PULVIS ANTISEPTICUS. N. F.

Antiseptic Powder [Pulv. Antisept.]

Soluble Antiseptic Powder; Pulvis Antisepticus Solubilis.

This is practically a mixture of 86.6 parts of boric acid and 12.5 parts of zinc sulphate perfumed with traces of salicylic acid, phenol, eucalyptol, menthol and thymol.

PULVIS AROMATICUS. N. F.

Aromatic Powder [Pulv. Arom.]

This is the same as the article formerly recognized by the U. S. IX. It is a mixture of 35 parts each of cinnamon and ginger with 15 parts each of cardamom and nutmeg.
The *dose* is from ten to twenty grains (0.6–1.2 Gm.).

PULVIS AROMATICUS RUBEFACIENS. N. F.

Rubefacient Spice Powder [Pulv. Arom. Rubefac.]

Consists of clove, 30 per cent., Saigon cinnamon, 30 per cent., ginger, 20 per cent., and capsicum, 20 per cent.
"NOTE.—When rubefacient spice powder is needed for *Spice Poultice*, place the required quantity in a flat muslin bag and moisten it with either diluted alcohol or vinegar, previously heated." *N. F.*
It is used only externally and should not be confused with the preceding preparation.

PULVIS CRETÆ AROMATICUS. N. F.

Aromatic Powder of Chalk [Pulv. Cret. Arom.]

It contains 8 per cent. of cinnamon, 6 per cent. of nutmeg, 3 per cent. of clove, 2 per cent. of cardamom seed, 25 per cent. of prepared chalk and 56 per cent. of sugar. It is used in *diarrhea*.
The *dose* is thirty to sixty grains (2–4 Gm.).

PULVIS CRETÆ ET OPII AROMATICUS, N. F. Pulvis Cretæ Aromaticus cum Opio, N. F. III

Aromatic Powder of Chalk and Opium [Pulv. Cret. et Opii Arom.]

This is aromatic chalk powder containing 2.5 per cent. of powdered opium.
The *dose* is from ten to thirty grains (0.6–2 Gm.).

PULVIS HYDRARGYRI CHLORIDI MITIS ET JALAPÆ. N. F.

Powder of Mild Mercurous Chloride and Jalap [Pulv. Hydrarg. Chlor. Mit. et Jalap.]

Calomel and Jalap.

This is a mixture of 34 Gm. of mild chloride of mercury and 66 Gm. of jalap.

The *dose* is ten grains (0.65 Gm.).

PULVIS MYRICÆ COMPOSITUS. N. F.

Compound Powder of Bayberry [Pulv. Myric. Co.]

Composition Powder.

It contains 60 per cent. of bayberry bark, 30 per cent. of ginger, 5 per cent. of capsicum, and 5 per cent. of clove.

The *dose* is fifteen grains (1 Gm.).

PULVIS PANCREATINI COMPOSITUS. N. F.

Compound Pancreatin Powder [Pulv. Pancreat. Co.]

Peptonizing Powder.

This is a mixture of 20 Gm. of pancreatin and 80 Gm. of sodium bicarbonate. Twenty-five grains of this powder are sufficient to peptonize 1 pint of fresh cow's milk. Used for preparing "predigested" foods.

PULVIS RHEI ET MAGNESIÆ ANISATUS. N. F.

Anisated Powder of Rhubarb and Magnesia [Pulv. Rhei et Magnes. Anis.]

Compound Anise Powder.

It contains 35 per cent. of powdered rhubarb and 65 per cent. of heavy magnesia, with anethol and alcohol. It is laxative and carminative.

The *dose* for infants is five grains (0.3 Gm.).

PULVIS TALCI COMPOSITUS. N. F.

Compound Powder of Talc [Pulv. Talc. Co.]

Boro-Salicylated Powder of Talc; Pulvis Talci Salicylicus.

It contains 3 per cent. of salicylic acid, 10 per cent. of boric acid, and 87 per cent. of talc, all in very fine powder.

SALIA EFFERVESCENTIA. N. F.

Granular Effervescent Salts

Two general processes are given for preparing effervescent salts, the one to be used being determined by the quantity of material taken. The products, however, from both processes should be identical. The citric acid should be uneffloresced crystals, powdered immediately before using; the other ingredients should be dried at a temperature not exceeding 50° C. The granulation is performed in an oven or on a water bath. The dry granular powder is passed through a No. 6 tinned-iron sieve, and immediately transferred to dry bottles of containers, and hermetically sealed.

SAL CAROLINUM FACTITIUM. N. F.

Artificial Carlsbad Salt [Sal. Carol. Fact.]

Two forms of this mixture are described. The first, a dry amorphous form, contains 2 Gm. of potassium sulphate, 18 Gm. of sodium chloride, 36 Gm. of sodium bicarbonate and 100 Gm. of sodium sulphate dried to a constant weight of about 100 Gm., there being a loss of a corresponding amount of water. The second form is crystalline; it contains the same ingredients in a crystallized state, making a total of about 180 Gm.

The *dose* would be about one or two drachms (4–8 cc.) but it is rarely used except in the effervescent form (see below).

SAL CAROLINUM FACTITIUM EFFERVESCENS. N. F.

Effervescent Artificial Carlsbad Salt [Sal. Carol. Fact. Eff.]

It contains 26.6 per cent. of artificial Calsbad salt, with sodium bicarbonate, tartaric acid, and citric acid.

The *dose* is from one to two drachms (4–8 Gm.).

SAL KISSINGENSE FACTITIUM. N. F.

Artificial Kissingen Salt [Sal Kissingen. Fact.]

It is made from 1.7 parts of potassium chloride, 35.7 parts of sodium chloride, 12 parts of magnesium sulphate and 10.7 parts of sodium bicarbonate. Twenty-four grains of this salt dissolved in 6½ fluidounces of water represents an equal volume of Kissingen water (Rakoczi).

SAL KISSINGENSE FACTITIUM EFFERVESCENS. N. F.

Effervescent Artificial Kissingen Salt [Sal Kissingen. Fact. Eff.]

It contains 40 per cent. of artificial Kissingen salt, with sodium bicarbonate, tartaric acid, and citric acid.

The *dose* is eighty grains (5.5 Gm.).

SAL LITHII CITRATIS EFFERVESCENS. N. F.

Effervescent Salt of Lithium Citrate [Sal. Lith. Cit. Eff.]

Lithii Citras Effervescens (*U. S. P. VIII*); Effervescent Lithium Citrate.

This preparation contains 5 per cent. lithium citrate, and is prepared according to the general formula. It is used as an antilithic and diuretic.

The *dose* is two drachms (8 Gm.).

SAL MAGNESII SULPHATIS EFFERVESCENS. N. F.

Effervescent Magnesium Sulphate [Sal. Mag. Sulph. Eff.]

Magnesii Sulphas Effervescens.

This represents 50 per cent. of Epsom salt with sodium bicarbonate, citric and tartaric acids.

The *dose* is usually about one-half an ounce (15 Gm.).

SAL POTASSII BROMIDI EFFERVESCENS COMPOSITUM. N. F.

Compound Effervescent Salt of Potassium Bromide [Sal Pot. Brom. Eff. Co.]

Pulvis Potassii Bromidi Effervescens cum Caffeina; Effervescent Potassium Bromide with Caffeine.

This preparation contains 0.8 per cent. caffeine, 8.3 per cent. potassium bromide, and 4.2 per cent.

lithium carbonate with sodium bicarbonate and citric and tartaric acids.

The *dose* is from one to three drachms (4–11 Gm.).

SAL VICHYANUM FACTITIUM. N. F.

Artificial Vichy Salt [Sal Vichy. Fact.]

This is a mixture of 846 Gm. of sodium bicarbonate, 38.5 Gm. of potassium carbonate, 80 Gm. of magnesium sulphate and 77 Gm. of sodium chloride. "A solution of 1 Gm. of this preparation in 200 cc. of water is similar to an equal volume of Vichy water (Grande Grille Spring) in its main constituents." *N. F.*

SAL VICHYANUM FACTITIUM EFFERVESCENS. N. F.

Effervescent Artificial Vichy Salt [Sal Vichy. Fact. Eff.]

It contains 25 per cent. artificial Vichy salt, with sodium bicarbonate, tartaric acid, and citric acid. Seven grains of this powder dissolved in 6½ fluidounces of water represents an equal volume of Vichy water (Grande Grille). an antacid.

The *dose* is from one to two drachms.

SEVUM BENZOINATUM. N. F.

Benzoinated Suet [Sev. Benz.]

Prepared by digesting suet with 3 per cent. of powdered benzoin.

SOLUTIO MASTICHES CHLOROFORMICA COMPOSITA. N. F.

Compound Chloroformic Solution of Mastic [Sol. Mastic. Chlorof. Co.]

Pulp Capping Varnish.

A solution of 3 per cent. each of mastic and balsam of Peru in chloroform. It is used in dentistry.

SOLUTIO RESINÆ CHLOROFORMICA. N. F.

Chloroformic Solution of Rosin [Sol. Resin. Chlorof.]

A 20 per cent. solution of rosin in chloroform. "Preserve in amber-colored, cork-stoppered bottles." *N. F.* It is used as a dental varnish.

SPECIES EMOLLIENTES. N. F.

Emollient Species [Spec. Emoll. Emollient Cataplasm]

It is made from equal parts of althæa leaves, mallow leaves, melilot, matricaria, and linseed. Emollient; used for making an emollient poultice, by adding to it a suitable quantity of hot water.

SPECIES LAXATIVÆ. N. F.

Laxative Species [Spec. Lax.]

Species Laxantes; St. Germain Tea.

It contains 40 per cent. of cut senna, 25 per cent. of elder flowers, 12.5 per cent. of bruised fennel, 12.5 per cent. of bruised anise, and 10 per cent. of potassium bitartrate.

The *dose* is from twenty to sixty grains (1.3–4 Gm.).

SPECIES PECTORALES. N. F.

Pectoral Species [Spec. Pect.]

Species ad Infusum Pectorale; Breast Tea.

It contains 8 parts of althæa, peeled, 4 parts of coltsfoot leaves, 3 parts of Russian glycyrrhiza, peeled, 2 parts of anise, 2 parts of mullein flowers, and 1 part of orris root. Used as a pectoral.

The *dose* is one drachm (4 Gm.).

SPIRITUS ACIDI FORMICI. N. F.

Spirit of Formic Acid [Sp. Ac. Formic.]

Spiritus Formicarum; Spirit of Ants.

It contains 4 per cent. of formic acid in alcohol and distilled water.

The *dose* is one fluidrachm (4 cc.).

SPIRITUS ÆTHERIS. N. F.

Spirit of Ether [Sp. Æth.]

Hoffmann's Drops.

An alcoholic solution of ether (32.5 per cent.).

The *dose* is from one to two fluidrachms (4–8 cc.).

SPIRITUS ÆTHERIS COMPOSITUS. N. F.

Compound Spirit of Ether [Sp. Æth. Co.]

Hoffmann's Anodyne.

This preparation contains 2.5 per cent. ethereal oil in a solution of ether in alcohol (1:2).

The *dose* is from one to two fluidrachms (4–8 cc.).

SPIRITUS AMMONIÆ ANISATUS. N. F.

Anisated Spirit of Ammonia [Sp. Ammon. Anis.]

Liquor Ammoniæ Anisatus; Anisated Solution of Ammonia.

This preparation is a solution of anethol, 3 per cent., in a mixture of 20 per cent. ammonia water in alcohol.

The *dose* is from fifteen minims to forty-five minims (1–3 cc.).

SPIRITUS AMYGDALÆ AMARÆ. N. F.

Spirit of Bitter Almond [Sp. Amygd. Amar.]

A 10 per cent. solution of the oil of bitter almond in 80 per cent. alcohol. "This spirit is intended for medicinal use; it must not be used for flavoring foods." *N. F.*

Dose, from three to eight minims (0.2–0.5 cc.).

SPIRITUS CARDAMOMI COMPOSITUS N. F.

Compound Spirit of Cardamom [Sp. Card. Co.]

It is made from the oils of cardamom, orange, cinnamon, clove, and caraway, and anethol dissolved in alcohol. Used for flavoring.

SPIRITUS MYRCIÆ COMPOSITUS. N. F.

Compound Spirit of Myrcia [Sp. Myrciæ Co.]

A hydroalcoholic solution of oils of bay, orange, and allspice. It resembles *Bay Rum.*

SPIRITUS ODORATUS. N. F.

Perfumed Spirit [Sp. Odorat.]

Aqua Cologniensis; Cologne Water.

A hydroalcoholic solution of oil of bergamot, lemon, rosemary, lavender, orange flowers, and acetic ether. Used as a perfume.

SPIRITUS OLEORUM VOLATILIUM. N. F.

Spirits of Volatile Oils

Any spirit of a volatile oil for which no specific formula is provided may be prepared by dissolving 6.5 parts of the oil in 93.5 parts of alcohol.

SPIRITUS SINAPIS. N. F.

Spirit of Mustard [Sp. Sinap.]

This spirit contains 2 per cent. of volatile oil of mustard in alcohol. Used as a counter-irritant.

SPIRITUS VANILLINI COMPOSITUS. N. F.

Compound Spirit of Vanillin [Sp. Vanil. Co.]

This preparation contains vanillin, 20 per cent., oil of orange, 5 per cent., oil of cardamom, 1 per cent., and oil of cinnamon, 0.5 per cent., in alcohol. Used as a flavoring agent.

STILI MEDICAMENTORUM. N. F.

Stili Dilubiles, N. F. IV

Paste Pencils; Unna Pencils.

These are preparations in the form of a pencil the medicinal agent incorporated in a paste made from starch, dextrin, tragacanth, sugar, and water. They are rolled into cylinders 5 mm. thick and 5 cm. long. They are used in dermatological practice. The N. F. gives one formula as exemplar (see succeeding article).

STILI ACIDI SALICYLICI. N. F.

Salicylic Acid Pencil [Stil. Acid. Salicyl.] Dilub.]

Stilus Acidi Salicylici Dilubilis.

These pencils contain 10 per cent. of salicylic acid, with tragacanth, starch, dextrin, sugar, and distilled water.

SULPHURIS IODIDUM. N. F.

Sulphur Iodide [Sulphur. Iod.]

Prepared by fusing together 20 Gm. washed sulphur and 80 Gm. of iodine. An assay process is included. It occurs in brittle masses having a crystalline fracture and a grayish-black, metallic luster. Almost insoluble in water; soluble in about 60 parts of glycerin; very soluble in carbon disulphide. Alcohol, ether, or an aqueous solution of potassium iodide dissolves the iodine, leaving the sulphur. Continued boiling with water vaporizes all of the iodine, leaving about 20 per cent. of sulphur as a residue. It is used externally.

SUPPOSITORIA BOROGLYCERINI. N. F.

Suppositories of Boroglycerin [Suppos. Boroglycer.]

The suppositories contain glycerinated gelatin, glycerin, and glycerite of boroglycerin, 30 per cent.

SYRUPUS ALLII. N. F.

Syrup of Garlic [Syr. Allii]

Prepared from garlic (20 per cent.), sugar, and diluted acetic acid.

The *dose* is one fluidrachm (4 cc.).

SYRUPUS ALTHÆÆ. N. F.

Syrup of Althæa [Syr. Althæ.]

Prepared from althæa (5 per cent.), and contains 10 per cent. of glycerin and 3 per cent. of alcohol.

"Preserve the syrup in well-stoppered, completely filled bottles, in a cool place." *N. F.*

The *dose* is one fluidrachm (4 cc.).

SYRUPUS AMMONII HYPOPHOSPHITIS. N. F.

Syrup of Ammonium Hypophosphite [Syr. Ammon. Hypophos.]

One fluidrachm (4 cc.) of this syrup contains two grains (0.125 Gm.) of ammonium hypophosphite. It is flavored with compound spirit of vanillin.

The *dose* is from one to two fluidrachms (4–8 cc.).

SYRUPUS ASARI COMPOSITUS. N. F.

Compound Syrup of Asarum [Syr. Asar. Co.]

It is made from asarum root, alcohol, cochineal, potassium carbonate, fluidextract of ipecac, sugar, and water. About 3.5 grains of asarum and ⅙ grain of ipecac are represented by 1 fluidrachm of finished syrup.

The *dose* is given in the N. F. as one fluidrachm (4 cc.) but an adult would require from one-half to one fluidounce (15–30 cc.) to produce any obvious effect.

SYRUPUS BROMIDORUM. N. F.

Syrup of the Bromides [Syr. Bromidor.]

It is made from potassium, sodium, ammonium, calcium, and lithium bromides, tincture of vanilla, compound tincture of cudbear, compound syrup of sarsaparilla and syrup. About 15 grains of the mixed bromides are contained in 1 fluidrachm of the finished syrup. Used as a nerve sedative.

The *dose* is one fluidrachm (4 cc.).

SYRUPUS CACAO. N. F.

Syrup of Cocoa [Syr. Cacao]

Syrup of Chocolate; Chocolate Syrup.

This is a pleasant flavoring agent made of chocolate, tincture of vanilla and sugar.

SYRUPUS CALCII ET SODII HYPOPHOSPHITUM. N. F.

Syrup of Calcium and Sodium Hypophosphites [Syr. Calc. et Sod. Hypophos.]

About 2 grains each of calcium and sodium hypophosphites, with hypophosphorous acid, sugar and water, are contained in 1 fluidrachm of the finished syrup.

The *dose* is from one to four fluidrachms (4–15 cc.).

SYRUPUS CALCII HYPOPHOSPHITIS. N. F.

Syrup of Calcium Hypophosphite [Syr. Calc. Hypophos.]

It is made from calcium hypophosphite, hypophosphorous acid, sugar, and water. About 2 grains of calcium hypophosphite are contained in 1 fluidrachm of the finished syrup.

The *dose* is from one to four fluidrachms (4-15 cc.).

SYRUPUS CALCII IODIDI. N. F.

Syrup of Calcium Iodide [Syr. Calc. Iodid.]

It is made from iodine, iron wire, precipitated calcium carbonate, sugar, distilled water, and syrup. About 5 grains of calcium iodide are contained in 1 fluidrachm of the finished syrup. This may be used for the same purpose as the other iodides, but is by some believed to be especially valuable in *asthma*.

The *dose* is from one-half to one fluidrachm (2-4 cc.).

SYRUPUS CALCII LACTOPHOSPHATIS. N. F.

Syrup of Calcium Lactophosphate [Syr. Calc. Lactophos.]

The formula for this is the same as that of the U. S. IX. It contains the equivalent of about 1.5 grains of calcium phosphate in each fluidrachm.

The *dose* is from two to four fluidrachms (8-15 cc.).

SYRUPUS CALCII LACTOPHOSPHATIS ET FERRI. N. F. Syrupus Calcii Lactophosphatis cum Ferro, N. F. III

Syrup of Calcium Lactophosphate and Iron [Syr. Calc. Lactophos. et Ferr.]

It is made from ferrous lactate, potassium citrate, water, and syrup of calcium lactophosphate. About ½ grain of ferrous lactate is contained in 1 fluidrachm of the finished syrup.

The *dose* is from one to four fluidrachms (4-15 cc.).

SYRUPUS CINNAMOMI. N. F.

Syrup of Cinnamon [Syr. Cinnam.]

It is made from cinnamon, alcohol, sugar, and cinnamon water. It represents 10 per cent. of the water soluble constituents of cinnamon. It is chiefly used as a flavoring agent.

The official *dose* is one fluidrachm (4 cc.).

SYRUPUS ERIODICTYI AROMATICUS. N. F.

Aromatic Syrup of Eriodictyon [Syr. Eriodict. Arom.]

Aromatic Spirit of Yerba Santa; Syrupus Corrigens.

This represents 3.2 per cent. of fluidextract of eriodictyon, flavored with compound tincture of cardamom, the oils of sassafras, lemon, and clove, alcohol, sugar, and water. Used as a vehicle, especially for quinine.

The *dose* is two fluidrachms (8 cc.).

SYRUPUS FERRI, QUININÆ ET STRYCHNINÆ PHOSPHATUM. N. F.

Syrup of the Phosphates of Iron, Quinine, and Strychnine [Syr. Ferr., Quin. et Strych. Phos.]

Easton's Syrup.

Each fluidrachm of this contains approximately 1.2 grains of soluble iron phosphate, 1.6 of quinine phosphate, and 1-60th of a grain of strychnine phosphate.

The *dose* is from one to two fluidrachms (4-8 cc.).

SYRUPUS FERRI SACCHARATI SOLUBILIS. N. F.

Syrup of Soluble Saccharated Iron [Syr. Ferr. Sacch. Sol.]

Syrupus Ferri Oxydati Solubilis; Syrup of Saccharated Oxide of Iron; Syrup of Soluble Oxide of Iron.

It is made from distilled water and syrup. About ¾ grain of metallic iron is represented in one fluidrachm of this syrup.

The *dose* is from one to three fluidrachms (4-12 cc.).

SYRUPUS FICORUM COMPOSITUS. N. F.

Compound Syrup of Figs [Syr. Ficor. Co.]

This unfortunately named syrup is prepared from figs, fluidextract of senna, aromatic fluidglycerate of cascara sagrada, oil of fennel, spirit of peppermint, sugar, and water. Each fluidrachm represents 12 grains of senna and 4.5 minims of fluidglycerate of cascara.

The *dose* is from one to two fluidrachms (4-8 cc.).

SYRUPUS GLYCYRRHIZÆ. N. F.

Syrup of Glycyrrhiza [Syr. Glycyrrh.]

Syrup of Licorice.

It is made from fluidglycerate of licorice and syrup. About 15 grains of glycyrrhiza root are represented in 1 fluidrachm of the finished syrup. It is used as a vehicle.

The *dose* is two fluidrachms (8 cc.).

SYRUPUS HYPOPHOSPHITUM. N. F.

Syrup of Hypophosphites [Syr. Hypophos.]

The formula for this is the same as that of the U. S. IX. It contains in each fluidrachm approximately 2.7 grains of calcium hypophosphite and 0.9 grains of each of sodium and potassium hypophosphites.

The *dose* is from two to four fluidrachms (8-15 cc.).

SYRUPUS HYPOPHOSPHITUM COMPOSITUS. N. F.

Compound Syrup of Hypophosphites [Syr. Hypophos. Co.]

One fluidrachm of this preparation contains 2 grains of calcium hypophosphite, one grain each of potassium and sodium hypophosphites, ⅛ grain each of ferric and manganese hypophosphites, 1-16th grain of quinine, and 1-140th grain of strychnine with sodium citrate, diluted hypophosphorous acid, in a vehicle of glycerin and syrup. It is a widely prescribed, but useless, concoction.

The *dose* is two to four fluidrachms (8-15 cc.).

SYRUPUS IODOTANNICUS. N. F.

Syrup of Iodotannin [Syr. Iodotan.]

This syrup is made from 0.27 per cent. of iodine and 0.54 per cent. of tannin. As the iodine undergoes chemical change, the syrup does not represent the therapeutic virtue of free iodine.

The *dose* is one fluidrachm (4 cc.).

SYRUPUS IPECACUANHÆ ET OPII. N. F.

Syrup of Ipecac and Opium [Syr. Ipecac. et Opii.]

Syrup of Dover's Powder.

It is made from the tincture of ipecac and opium, with spirit of cinnamon, cinnamon water, and syrup. Five grains of Dover's powder are represented by 1 fluidrachm of finished syrup.

The *dose* is one fluidrachm (4 cc.).

SYRUPUS KRAMERIÆ. N. F. (U. S. P. VIII)

Syrup of Krameria [Syr. Kramer.]

This is made with 45 per cent. fluidextract of krameria and syrup.

The *dose* is one fluidrachm (4 cc.).

SYRUPUS MANNÆ. N. F.

Syrup of Manna [Syr. Mann.]

This syrup contains about 12.5 per cent. of manna with sugar, alcohol, and water.

The *dose* is two fluidrachms (8 cc.).

SYRUPUS PHOSPHATUM COMPOSITUS. N. F.

Compound Syrup of the Phosphates [Syr. Phos. Co.]

Chemical Food.

This syrup represents 50 per cent., by volume, of compound solution of the phosphates in a vehicle of glycerin and syrup colored with cudbear.

The apparently grandiose synonym is not so fanciful as it would seem for the composition contains the essential bases, calcium, potassium, sodium and iron, as well as the equally essential phosphoric acid radical. As, however, it is difficult to conceive of a condition, short of actual starvation, in which there would be a lack of all of these mineral elements the composition is not one which seems to us to be scientifically desirable.

The *dose* is from one to two fluidrachms (4–8 cc.).

SYRUPUS PHOSPHATUM CUM QUININA ET STRYCHNINA. N. F. Syrupus Hydrochlorophosphatum, N. F. III

Syrup of Phosphates with Quinine and Strychnine [Syr. Phos. c. Quin. et Strych.]

Compound Syrup of Hydrochlorophosphates.

One fluidrachm of this syrup represents ¼ grain of quinine hydrochloride, 1–125th grain of strychnine nitrate with 30 minims of compound solution of the phosphates.

The *dose* is from one to two fluidrachms (4–8 cc.).

SYRUPUS PINI ALBÆ COMPOSITUS. N. F.

Compound Syrup of White Pine [Syr. Pin. Alb. Co.]

Syrupus Pini Strobi Compositus, *N. F. IV.*

This syrup is made from white pine bark, wild cherry bark, aralia, balsam poplar buds, sanguinaria, sassafras, cudbear, chloroform, oil of sassafras, sugar, alcohol, water, and syrup.

The *dose* is from one to two fluidrachms (4–8 cc.).

SYRUPUS PINI ALBÆ COMPOSITUS CUM MORPHINA. N. F.

Compound Syrup of White Pine with Morphine [Syr. Pin. Strob. c. Morph.]

Syrupus Pini Strobi Compositus, *N. F. IV.*

This syrup is made by dissolving 0.4 Gm. of morphine sulphate in 1000 cc. of compound syrup of white pine. It contains, therefore, about one-fortieth grain of morphine in each fluidrachm. It is an undesirable preparation as being not only of little therapeutic value but of encouraging the improper use of morphine.

The *dose* is from one-half to two fluidrachms (2–8 cc.).

SYRUPUS QUINIDINÆ. N. F.

Syrup of Quinidine [Syr. Quinid.]

Bitterless Syrup of Quinidine.

It is made from quinidine, oil of orange, and syrup. About 2 grains of quinidine is contained in 1 fluidrachm of finished syrup. Shake well before dispensing.

The *dose* is from one to two fluidrachms (4–8 cc.).

SYRUPUS RHAMNI CATHARTICÆ. N. F.

Syrup of Rhamnus Cathartica [Syr. Rham. Cathart.]

Syrup of Buckthorn Berries; Syrupus Spinæ Cervinæ.

This syrup contains 20 per cent. of fluidextract of buckthorn berries with 0.02 per cent. each of oils of fennel and cinnamon in syrup.

The *dose* is from one to two fluidrachms (4–8 cc.).

SYRUPUS ROSÆ. N. F.

Syrup of Rose [Syr. Ros.]

This syrup is made with 12.5 per cent. of fluidextract of rose and 1 per cent. diluted sulphuric acid. It is used as a flavoring vehicle.

SYRUPUS RUBI. N. F.

Syrup of Rubus [Syr. Rubi]

This syrup contains 25 per cent. of fluidextract of rubus with syrup. It is used as an astringent.

The *dose* is from one to two fluidrachms (4–8 cc.).

SYRUPUS RUBI IDÆI. N. F.

Syrup of Raspberry [Syr. Rubi Id.]

This is made with raspberry juice and sugar. It is heated to the boiling point and filtered while hot. "Preserve the product in well-stoppered bottles in a cool dark place." *N. F.* It is used as a flavoring agent.

SYRUPUS SENNÆ AROMATICUS. N. F.

Aromatic Syrup of Senna [Syr. Senn. Arom.]

It is made from fluidextract of senna, jalap, rhubarb, cinnamon, clove, nutmeg, oil of lemon, sugar, and diluted alcohol. About 7½ grains of senna, 3 grains of jalap, and 1 grain of rhubarb are contained in 1 fluidrachm of finished syrup.

The *dose* is two fluidrachms (8 cc.).

SYRUPUS STILLINGIÆ COMPOSITUS. N. F.

Compound Syrup of Stillingia [Syr. Stilling. Co.]

It is made from compound fluidextract of stillingia, sugar, and water. About 15 minims of compound fluidextract of stillingia are represented by 1 fluidrachm of the finished syrup. A useless relic of ancient superstition.

The official *dose* is one fluidrachm (4 cc.).

SYRUPUS THYMI. N. F.

Syrup of Thyme [Syr. Thymi]

This is a mixture of 20 parts of fluidextract of thyme and 80 parts of simple syrup.

The *dose* is from one to two fluidrachms (4–8 cc.).

SYRUPUS THYMI COMPOSITUS. N. F.

Compound Syrup of Thyme [Syr. Thymi Co.]

Each fluidrachm of this contains about 2 grains of ammonium bromide in syrup of thyme.

The *dose* is from one to two fluidrachms (4–8 cc.).

SYRUPUS TRIFOLII COMPOSITUS. N. F.

Compound Syrup of Trifolium [Syr. Trifol. Co.]

This contains 30 per cent. of the compound fluidextract of trifolium flavored with oils of sassafras and anise and methyl salicylate.

The *dose* is from two to four fluidrachms (8–15 cc.).

TABELLÆ. N. F.

Tablets

These are discs of two classes; tablet triturates and compressed tablets. The former are made by triturating together the active ingredient with sugar or some other diluent and moistening with some volatile liquid which permits the tablets to be molded into the desired shape and subsequently dried. They are friable and dissolve or disintegrate rapidly when dropped into water. The compressed tablets consist chiefly or wholly of active substances compressed into form by means of dyes. They are harder and less friable than the triturates and more slowly soluble. (See *Pilulæ*, Part I.)

TABELLÆ CARBONIS ANIMALIS. N. F.

Tablets of Animal Charcoal [Tab. Carb. Anim.]

Replacing Trochisci Carbonis Ligni, *N. F. IV.*; Tablets of Charcoal.

These are compressed tablets each containing 0.3 Gm. (4.6 grains) of animal charcoal.

Dose, one or two tablets.

TABELLÆ HYDRARGYRI CHLORIDI MITIS. N. F.

Tablets of Mild Mercurous Chloride [Tab. Hydrarg. Chlor. Mit.]

Calomel Tablets.

These are compressed tablets each of which contains ⅒ grain (0.0065 Gm.) of calomel colored pink with carmine.

Dose, ten to thirty tablets, usually in divided doses.

TABELLÆ PHENOLPHTHALEINI. N. F.

Tablets of Phenolphthalein [Tab. Phenolphthal.]

Replacing Trochisci Phenolphthaleini, *N. F. IV.*

Each of these contains about 1 grain (0.06 Gm.) of phenolphthalein. They are flavored with cinnamon and cocoa.

The *dose* is one or two tablets.

TABELLÆ SANTONINI. N. F.

Tablets of Santonin [Tab. Santonin.]

Replacing Trochisci Santonini, *N. F. IV.*

Each of these compressed tablets contains about ½ grain (0.03 Gm.) of santonin, flavored with vanilla and cocoa. "Caution: Because of the pleasant flavor of these tablets and the possibility of their being mistaken for candy, it is advisable to order only a very few at a time, preferably not more than three, since 0.13 Gm. of santonin has caused the death of a child." *N. F.*

The *dose* is from one to four tablets for an adult.

TABELLÆ SANTONINI COMPOSITÆ. N. F.

Compound Tablets of Santonin [Tab. Santonin. Co.]

Replacing Trochisci Santonini Compositi, *N. F. IV.*

Each of these contains about ½ grain each of santonin and calomel, flavored with vanilla and cocoa. The same caution applies as in the case of santonin tablets.

The *dose* for an adult is one to four tablets.

TABELLÆ SODII BICARBONATIS. N. F.

Tablets of Sodium Bicarbonate [Tab. Sod. Bicarb.]

Replacing Trochisci Sodii Bicarbonatis, *N. F. IV.*; Soda Mint Tablets.

Each of these compressed tablets contains about 4 grains (0.25 Gm.) of sodium bicarbonate with 1–20th of a minim (0.003 cc.) of oil of peppermint.

The *dose* is from one to four tablets or more, as required.

TABELLÆ SULPHURIS ET POTASSII BITARTRATIS. N. F.

Tablets of Sulphur and Potassium Bitartrate [Tab. Sulph. et Pot. Bitart.]

Replacing Trochisci Sulphuris et Potassii Bitartratis, *N. F. IV.*

Each tablet contains about 3 grains (0.2 Gm.) of washed sulphur and 1 grain (0.06 Gm.) of potassium bitartrate, flavored with oil of orange.

The *dose* is from five to ten tablets.

TINCTURÆ. N. F.

Tinctures

The tinctures of the N. F., like those of the U. S. P., are made by one of two processes. Those of potent drugs are of 10 per cent. strength, corresponding to the International Protocol; the others are of various concentrations.

TINCTURA ALOES. N. F.

Tincture of Aloe [Tr. Aloe.]

This is the same as the tincture of aloe of the U. S. IX. It represents 10 per cent. of aloe.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

TINCTURA ALOES ET MYRRHÆ. N. F.

Tincture of Aloes and Myrrh [Tr. Aloe et Myrrh.]

This tincture is made with 10 per cent. each of aloes, myrrh, and licorice in a menstruum of three volumes of alcohol with one of water.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

TINCTURA AMARA. N. F.

Bitter Tincture [Tr. Amar.]

Stomachic Tincture; Bitter Stomachic Drops; Stomach Drops.

It is made from gentian, centaury, bitter orange peel and zedoary, two volumes of alcohol, and one volume of water, being used as the menstruum. It is a bitter tonic.

The *dose* is thirty minims (2 cc.).

TINCTURA ANTIMONII. N. F.

Tincture of Antimony [Tr. Antimon.]

Replacing Vinum Antimonii, N. F. IV.

This contains 0.4 per cent. of the antimony and potassium tartrate in a menstruum of water and alcohol, colored with caramel and flavored with acetic ether. "Tincture of antimony may be dispensed, when Vinum Antimonii (Wine of Antimony) is ordered." *N. F.*

Dose, from ten to thirty minims (0.6–2 cc.).

TINCTURA ANTIPERIODICA. N. F.

Antiperiodic Tincture [Tr. Antiperiod. Warburg's Tincture]

This tincture is made from rhubarb, angelica fruit, elecampane, saffron, fennel, gentian, zedoary, cubeb, myrrh, camphor, white agaric, black pepper, cinnamon, ginger, quinine bisulphate, and extract of aloes, three volumes of alcohol, and two volumes of water, being used as the menstruum. About 9 grains of quinine bisulphate are contained in 1 fluidounce of finished tincture.

Dosage.—The dosage of Warburg's tincture depends on the kind used—whether with aloes or without—and the intended purpose, and varies from one fluidrachm (4 cc.) to four fluidrachms (16 cc.). The larger quantity is given when Doctor Warburg's original directions are followed for administering the remedy in remittent fevers, which were as follows: "One-half ounce to be given alone without dilution, after the bowels have been evacuated by any convenient purgative, all drink being withheld. After three hours, another half ounce is to be given." It is an antiperiodic.

TINCTURA ANTIPERIODICA SINE ALOE. N. F.

Antiperiodic Tincture without Aloes [Tr. Antiperiod. s. Aloe. Warburg's Tincture without Aloes]

This is made as directed under *Tinctura Antiperiodica,* omitting the extract of aloes.

For dosage, see *Tinctura Antiperiodica.*

TINCTURA ARNICÆ. N. F.

Tincture of Arnica [Tr. Arnic.]

This represents 20 per cent. of arnica in a menstruum of diluted alcohol. It is used chiefly externally.

Dose, from ten to twenty minims (0.6–1.2 cc.).

TINCTURA AROMATICA. N. F.

Aromatic Tincture [Tr. Arom.]

This tincture is made from cinnamon, ginger, galangal, clove and cardamom, two volumes of alcohol, and one volume of water being used as the menstruum. It is used as a carminative and aromatic.

The *dose* is thirty minims (2 cc.).

TINCTURA BRYONIÆ. N. F.

Tincture of Bryonia [Tr. Bryon.]

This tincture is made by maceration and subsequent percolation, using 10 per cent. bryonia and alcohol. It is used as an alterative and hydragogue cathartic.

The *dose* is one fluidrachm (4 cc.).

TINCTURA CACTI GRANDIFLORI. N. F.

Tincture of Cactus Grandiflorus [Tr. Cact. Grand.]

This tincture is made from 50 per cent. cactus grandiflorus and alcohol by maceration and expression and further percolation of this marc. It is supposed by some to act as a regulator of cardiac arrythmias.

The *dose* is fifteen minims (1 cc.).

TINCTURA CALENDULÆ. N. F.

Tincture of Calendula [Tr. Calend.]

This tincture is made by maceration with 20 per cent. calendula and alcohol. Used as an antiseptic and discutient.

TINCTURA CAPSICI ET MYRRHÆ. N. F.

Tincture of Capsicum and Myrrh [Tr. Capsic. et Myrrh. Hot Drops. Thomsonian Number Six]

It is made from capsicum, myrrh, nine volumes of alcohol, and one volume of water being used as the menstruum. It is a powerful gastric stimulant and carminative.

The *dose* is thirty minims (2 cc.).

TINCTURA CIMICIFUGÆ. N. F.

Tincture of Cimicifuga [Tr. Cimicif.]

This tincture is made by maceration and subsequent percolation with alcohol. It contains 20 per cent. of cimicifuga. Used as an alterative and sedative.

The *dose* is one fluidrachm (4 cc.).

TINCTURA CINNAMOMI. N. F.

Tincture of Cinnamon [Tr. Cinnam.]

This is essentially the same as the tincture of the U. S. IX, representing 20 per cent. of cinnamon.

Dose, from one-half to two fluidrachms (2–8 cc.).

TINCTURA COCCULI INDICI. N. F.

Tincture of Cocculus Indicus [Tr. Coccul. Ind.]

This tincture is made from 10 per cent. powdered fishberries with diluted alcohol by maceration and subsequent percolation.

This tincture is used almost exclusively for external application to destroy parasites.

TINCTURA COLCHICI CORMI FORTIOR. N. F.

Stronger Tincture of Colchicum Corm

Replacing Vinum Colchici Cormi, N. F. IV.

This represents 40 per cent. of colchicum corm in a menstruum of one volume of alcohol and two of water. "One hundred cc. of Stronger Tincture of Colchicum Corm yields not less than 0.126 Gm. and not more than 0.154 Gm. of colchicine." *N. F.*

"Note: Stronger Tincture of Colchicum Corm may be dispensed when Vinum Colchici Cormi is ordered."

Dose, from five to ten minims (0.3–0.6 cc.).

TINCTURA CROCI. N. F.

Tincture of Saffron [Tr. Croc.]

This tincture is made from saffron, 10 per cent., in diluted alcohol, prepared by maceration and subsequent percolation. Used as coloring and flavoring agent.

TINCTURA CUBEBÆ. N. F.

Tincture of Cubeb [Tr. Cubeb.]

This tincture is made from cubeb, 20 per cent., in alcohol, by maceration and subsequent percolation. Used as a diuretic and carminative.

The *dose* is one fluidrachm (4 cc.).

TINCTURA DELPHINII. N. F.

Tincture of Larkspur [Tr. Delphin.]

This tincture is made from 10 per cent. larkspur seed in alcohol, made by maceration and subsequent percolation.

This tincture is rarely used internally, but is commonly employed externally to destroy body vermin.

TINCTURA FERRI CHLORIDI ÆTHEREA. N. F.

Ethereal Tincture of Ferric Chloride [Tr. Ferr. Chlor. Æth.]

Bestuscheff's Tincture. Lamotte's Drops.

It is made from solution of ferric chloride, ether, and alcohol. Used as a chalybeate.

The *dose* is thirty minims (2 cc.).

TINCTURA FERRI CITRO-CHLORIDI. N. F.

Tincture of Ferric Citro-Chloride [Tr. Ferr. Citro-Chlor.]

Tasteless Tincture of Ferric Chloride. Tasteless Tincture of Iron.

This tincture contains 35 per cent. of solution of ferric chloride with sodium citrate, alcohol and water. Used as a chalybeate.

The *dose* is eight minims (0.5 cc.).

TINCTURA FERRI POMATA. N. F.

Tincture of Ferrated Extract of Apples [Tr. Ferr. Pomat.]

Tinctura Ferri Malatis Crudi. Tincture of Crude Malate of Iron.

This tincture is made from ferrated extract of apples, alcohol, and cinnamon water. Used as a chalybeate.

The *dose* is one fluidrachm (4 cc.).

TINCTURA GALLÆ. N. F.

Tincture of Nutgall [Tr. Gall.]

This tincture is made from nutgall, 20 per cent., and glycerin, 10 volumes, in alcohol. Made by maceration, instead of the percolation of the U. S. P. VIII. The menstruum was not changed. Used as an astringent.

The *dose* is one fluidrachm (4 cc.).

TINCTURA GUAIACI. N. F.

Tincture of Guaiac [Tr. Guaiac]

This, like the tincture of the U. S. IX, represents 20 per cent. of guaiac in alcoholic menstruum.

Dose, one fluidrachm (4 cc.).

TINCTURA GUAIACI AMMONIATA. N. F.

Ammoniated Tincture of Guaiac [Tr. Guaiac Ammon.]

This is similar to the tincture of the U. S. IX and represents 20 per cent. of guaiac in a menstruum of aromatic spirit of ammonia.

Dose, from one to two fluidrachms (2–4 cc.).

TINCTURA GUAIACI COMPOSITA. N. F.

Compound Tincture of Guaiac [Tr. Guaiac. Co.]

Dewee's Tincture of Guaiac.

This tincture is made from guaiac, potassium carbonate and pimenta, in a menstruum of diluted alcohol. Used for rheumatism, and as an emmenagogue.

The *dose* is one fluidrachm (4 cc.).

TINCTURA HUMULI. N. F.

Tincture of Hops [Tr. Humul.]

This tincture is made from hops, 20 per cent., in diluted alcohol. Made by maceration and subsequent percolation. Used as a sedative and bitter tonic.

The *dose* is one fluidrachm (4 cc.).

TINCTURA HYDRASTIS. N. F.

Tincture of Hydrastis [Tr. Hydrast.]

Tincture of Golden Seal.

This, like the tincture of the U. S. IX, represents 20 per cent. of hydrastis. "One hundred cc. of Tincture of Hydrastis yields not less than 0.36 Gm. and not more than 0.44 Gm. of the ether-soluble alkaloids of hydrastis." *N. F.*

Dose, from one to two fluidrachms (4–8 cc.).

TINCTURA IGNATIÆ. N. F.

Tincture of Ignatia [Tr. Ignat.]

This tincture is made from ignatia, 10 per cent., alcohol, eight volumes, and water, one volume. An assay is provided in the text which states that 100 cc. of the tincture should yield not less than 0.18 Gm. nor more than 0.22 Gm. of alkaloids of ignatia. Its uses are similar to those of Tincture of Nux Vomica.

The *dose* is ten minims (0.6 cc.).

TINCTURA IODIDORUM. N. F.

Tincture of Iodides [Tr. Iodidor.]

Replacing Tinctura Iodi Decolorata; Decolorized Tincture of Iodine.

Although this replaces the former decolorized tincture of iodine the formula differs importantly in that potassium iodide is used in the place of sodium thiosulphate. It is practically a solution of potassium and ammonium iodides in dilute alcohol. It is used externally but is of little value.

TINCTURA IODI FORTIOR. N. F.

Stronger Tincture of Iodine [Tr. Iod. Fort.]

Tincture Iodi Churchill; Churchill's Tincture of Iodine.

This tincture contains 16.5 Gm. of iodine and 3.3 Gm. of potassium iodide in each 100 cc. The solvent is about 70 per cent. alcohol.

TINCTURA IPECACUANHÆ. N. F.

Tincture of Ipecac [Tr. Ipecac.]

Replacing Vinum Ipecacuanhæ, N. F. IV.

"One hundred cc. of Tincture of Ipecac yields not less than 0.135 Gm. and not more than 0.165 Gm. of the ether-soluble alkaloids of Ipecac." *N. F.* It is made by diluting the fluidextract, and represents 10 per cent.

"Tincture of Ipecac may be dispensed when Vinum Ipecacuanhæ (Wine of Ipecac) is ordered." *N. F.*

Dose, from ten to twenty minims (0.6–1.2 cc.).

TINCTURA IPECACUANHÆ ET OPII. N. F.

Tincture of Ipecac and Opium [Tr. Ipecac. et Opii]

Tincture of Dover's Powder.

This tincture is made from tincture of deodorized opium, fluidextract of ipecac, and diluted alcohol, representing 10 per cent. each of deodorized opium and ipecac.

The *dose* is from five to ten minims (0.3–0.6 cc.).

TINCTURA JALAPÆ. N. F.

Tincture of Jalap [Tr. Jalap.]

This tincture is made from 20 per cent. of jalap, with alcohol and water.

The *dose* is one fluidrachm (4 cc.).

TINCTURA JALAPÆ COMPOSITA. N. F.

Compound Tincture of Jalap [Tr. Jalap. Co.]

It is made from 12.5 per cent. of jalap and 3.0 per cent. of scammony, with alcohol and water.

The *dose* is one fluidrachm (4 cc.).

TINCTURA OPII CROCATA. N. F.

Tincture of Opium with Saffron [Tr. Opii Crocat.]

Sydenham's Laudanum; Tinctura Opii Crocata, *P. I.*

This tincture is made from granulated opium, saffron, cinnamon, and clove, by maceration and subsequent percolation with diluted alcohol. An assay is provided. "One hundred cc. of tincture of opium with saffron contains not less than 0.95 Gm. and not more than 1.05 Gm. of anhydrous morphine." *N. F.*

The *dose* is from five to ten minims (0.3–0.6 cc.).

TINCTURA OPII ET GAMBIR COMPOSITA. N. F.

Compound Tincture of Opium and Gambir [Tr. Opii et Gambir Co.]

Tinctura Pectoralis, *N. F. IV;* Guttæ Pectorales; Pectoral Drops; Bateman's Pectoral Drops.

This is made with a menstruum of diluted alcohol. Each fluidrachm represents approximately 2.4 minims of tincture of opium, 3.6 minims of compound tincture of gambir and 0.22 grain of camphor. It is intended for infants.

The *dose* for an infant is from ten to fifteen minims (0.6–1 cc.).

TINCTURA PASSIFLORÆ. N. F.

Tincture of Passion Flower [Tr. Passiflor.]

This is a 20 per cent. tincture of passion flower made with diluted alcohol.

The *dose* is from ten to thirty minims (0.6–1.2 cc.).

TINCTURA PERSIONIS. N. F.

Tincture of Cudbear [Tr. Persion.]

This tincture is made from cudbear (10 per cent.), with a menstruum of three volumes of alcohol and one of water. Used as a bright red coloring agent.

TINCTURA PERSIONIS COMPOSITA. N. F.

Compound Tincture of Cudbear [Tr. Persion. Co.]

This tincture is made from cudbear (1.5 per cent.), and caramel (10 per cent.), with a mixture of one volume of alcohol and two of water as the menstruum. Used as a brownish-red coloring agent.

TINCTURA PULSATILLÆ. N. F.

Tincture of Pulsatilla [Tr. Pulsatil.]

This tincture is made from 10 per cent. pulsatilla, using as a menstruum three volumes of alcohol, and one volume of water.

The *dose* is thirty minims (2 cc.).

TINCTURA QUASSIÆ. N. F.

Tincture of Quassia [Tr. Quass.]

This is the same as the tincture of quassia U. S. IX. It represents 20 per cent. of quassia.

The *dose* is from one-half to one fluidrachm (2–4 cc.).

TINCTURA QUILLAJÆ. N. F.

Tincture of Quillaja [Tr. Quillaj.]

This tincture is made from 20 per cent. of quillaja, extracted with boiling water, the liquid concentrated and 35 per cent. of alcohol added. Used chiefly as an emulsifying agent.

TINCTURA RHEI AQUOSA. N. F.

Aqueous Tincture of Rhubarb [Tr. Rhei Aq.]

This tincture is made from 10 per cent. rhubarb, with potassium carbonate, cinnamon water, alcohol, and water.

The *dose* is from one to two fluidrachms (4–8 cc.).

TINCTURA RHEI DULCIS. N. F.

Sweet Tincture of Rhubarb [Tr. Rhei Dulc.]

This tincture contains 10 per cent. rhubarb, flavored with licorice, anise, cardamom seed and glycerin, in a hydroalcoholic menstruum. Used as a laxative and carminative.

The *dose* is from one to two fluidrachms (4–8 cc.).

TINCTURA RHEI ET GENTIANÆ. N. F.

Tincture of Rhubarb and Gentian [Tr. Rhei et Gent.]

This tincture is made with a menstruum of diluted alcohol. Each fluidrachm represents about 4 grains of rhubarb and 1 grain of gentian.

The *dose* is from one to two fluidrachms (4–8 cc.).

TINCTURA SABAL ET SANTALI. N. F.

Tincture of Saw Palmetto and Santal [Tr. Sabal. et Santal.]

This tincture is made with a menstruum of four volumes of alcohol and one of water. Each fluidrachm represents 12 grains of sabal and 3.75 grains of sandal wood.

The *dose* is one fluidrachm (4 cc.).

TINCTURA SANGUINARIÆ. N. F.

Tincture of Sanguinaria [Tr. Sanguin.]

This is made in a similar manner to the tincture of sanguinaria U. S. IX. It represents 10 per cent. of bloodroot.

The *dose* is from fifteen to forty-five minims (1–3 cc.).

TINCTURA SERPENTARIÆ. N. F.

Tincture of Serpentaria [Tr. Serpent.]

This tincture is made from 20 per cent. serpentaria and two volumes of alcohol and one volume of water as the menstruum.

The *dose* is from one to two fluidrachms (4–8 cc.).

TINCTURA SUMBUL. N. F.

Tincture of Sumbul [Tr. Sumbul]

This tincture is made from 10 per cent. sumbul with two volumes of alcohol and one volume of water.

The *dose* is from one to three fluidrachms (4–11 cc.).

TINCTURA VANILLÆ. N. F.

Tincture of Vanilla [Tr. Vanill.]

This tincture is made by first extracting the drug with alcohol, then drying and grinding the residue with sucrose and percolating this with a hydroalcoholic menstruum. It represents about 19 per cent. of vanilla. It is used as a flavoring agent.

TINCTURA VIBURNI OPULI COMPOSITA. N. F.

Compound Tincture of Viburnum [Tr. Viburn. Opul. Co.]

This tincture is made with a menstruum of glycerin, alcohol, and water. It contains in each fluidrachm about 2 grains each of viburnum opulus and dioscorea and $\frac{3}{5}$ grain of scutellaria and is flavored with cinnamon and cloves.

The *dose* is officially given as one fluidrachm (4 cc.) but a fluidounce (30 cc.) would contain less than one-half an average dose of the combined ingredients.

TINCTURÆ ÆTHEREÆ. N. F.

Ethereal Tinctures

In the general formula for ethereal tinctures the quantity of drug is 10 per cent. A menstruum of one volume of ether and two volumes of alcohol is used. Percolate in the usual manner, but with proper precautions to avoid evaporation.

TINCTURÆ MEDICAMENTORUM RECENTIUM. N. F.

Tinctures of Fresh Drugs

In the general formula for tinctures of fresh drugs 50 per cent. of the fresh drug is macerated with alcohol.

TROCHISCI EUCALYPTI GUMMI. N. F.

Troches of Eucalyptus Gum [Troch. Eucalypt. Gum]

Troches of Red Gum; Red Gum Lozenges.

Each of these contains about 1 grain (0.06 Gm.) of eucalyptus gum.

TROCHISCI ULMI. N. F.

Troches of Elm [Troch. Ulmi]

Each troche contains three grains (0.2 Gm.) of elm, flavored with methyl salicylate. Used as a demulcent.

UNGUENTUM BITUMINIS SULPHONATI. N. F.

Ointment of Sulphonated Bitumen [Ung. Bitum. Sulphon.]

Ichthyol Ointment.

This represents 10 per cent. of sulphonated bitumen in petrolatum.

UNGUENTUM CALAMINÆ. N. F.

Calamine Ointment [Ung. Calamin.]

Unguentum Calaminare; Turner's Cerate.

It contains 17 parts of calamine, with 83 parts of ointment. This sedative protective ointment has properties similar to those of the ointment of zinc oxide, over which it has the advantage of being a pinkish color and hence not so conspicuous when applied to the skin.

UNGUENTUM CAMPHORÆ. N. F.

Camphor Ointment [Ung. Camph.]

It contains 22 per cent. of camphor, with white wax and lard.

UNGUENTUM CAPSICI. N. F.

Ointment of Capsicum [Ung. Capsic.]

It represents 5 per cent. of the oleoresin of capsicum in a base of petrolatum and paraffin.

UNGUENTUM FUSCUM. N. F.

Brown Ointment [Ung. Fusc.]

Unguentum Matris; Mother's Salve.

It contains 50 per cent. of camphorated brown plaster, with olive oil and suet, equal parts.

UNGUENTUM HYDRARGYRI CHLORIDI MITIS. N. F.

Ointment of Mild Mercurous Chloride [Ung. Hydrarg. Chlor. Mit.]

Calomel Ointment; Prophylactic Ointment.

This contains 30 Gm. of calomel with 70 Gm. of white petrolatum.

UNGUENTUM HYDRARGYRI NITRATIS. N. F.

Ointment of Mercuric Nitrate [Ung. Hydrarg. Nit.]

Citrine Ointment.

It is made in the same manner as the citrine ointment of the U. S. IX by the interaction between mercury and nitric acid. It differs somewhat from the corresponding British preparation (see Part I.).

UNGUENTUM HYDRARGYRI OXIDI RUBRI. N. F.

Ointment of Red Mercuric Oxide [Ung. Hydrarg. Oxid. Rub.]

This ointment is made with red mercuric oxide, 10 per cent., water, hydrous wool fat and petrolatum.

UNGUENTUM IODI DENIGRESCENS. N. F.

Stainless Iodine Ointment [Ung. Iod. Denig.]

This is made by dissolving iodine in oleic acid and incorporating with a base of petrolatum and paraffin. It represents 5 per cent. of iodine although it may be questioned whether the therapeutic virtues of this are altered by the manipulations.

UNGUENTUM PICIS COMPOSITUM. N. F.

Compound Tar Ointment [Ung. Pic. Co.]

This represents 4 per cent. of oil of tar, 2 per cent. of tincture of benzoin and 3 per cent. of zinc oxide in a base of yellow wax, lard, and cottonseed oil.

UNGUENTUM PLUMBI IODIDI. N. F.

Ointment of Lead Iodide [Ung. Plumb. Iod.]

This ointment is made from lead iodide, 10 per cent., and benzoated lard, 90 per cent.

UNGUENTUM POTASSII IODIDI. N. F.

Ointment of Potassium Iodide [Ung. Pot. Iod.]

This ointment should be freshly made with 10 Gm. potassium iodide, 1 Gm. sodium thiosulphate, 9 Gm. of water, and 80 Gm. benzoinated lard.

UNGUENTUM RESORCINOLIS COMPOSITUM. N. F.

Compound Resorcinol Ointment [Ung. Resorcin. Co.]

It contains 6 per cent. each of resorcinol, zinc oxide, bismuth subnitrate, and rectified oil of birch tar, with petrolatum, anhydrous wool fat, and glycerin.

UNGUENTUM SINAPIS. N. F.

Mustard Ointment [Ung. Sinap.]

Ointment of Oil of Mustard.

It represents 0.2 per cent. of oil of mustard in a base of lard and white wax.

UNGUENTUM STRAMONII. N. F.

Stramonium Ointment [Ung. Stramon.]

This is made in a similar manner to the stramonium ointment of the U. S. IX. It represents 10 per cent. of the extract of stramonium.

UNGUENTUM SULPHURIS ALKALINUM. N. F.

Alkaline Sulphur Ointment [Ung. Sulphur. Alk.]

This ointment is made with 20 Gm. sublimed sulphur, 10 Gm. of potassium carbonate, 5 cc. water, and 65 Gm. benzoinated lard.

UNGUENTUM SULPHURIS COMPOSITUM. N. F.

Compound Sulphur Ointment [Ung. Sulphur. Co.]

Wilkinson's Ointment; Hebra's Itch Ointment.

It contains 10 per cent. of precipitated calcium carbonate, 15 per cent. of sublimed sulphur, 15 per cent. of oil of cade, with soft soap and lard.

UNGUENTUM VERATRINÆ. N. F.

Veratrine Ointment [Ung. Veratrin.]

This ointment is made with veratrine, 4 Gm., expressed oil of almond, 6 Gm., and benzoinated lard, 90 Gm.

UNGUENTUM ZINCI STEARATIS. N. F.

Ointment of Zinc Stearate [Ung. Zinc Stear.]

This ointment is made with zinc stearate, 50 Gm., and white petrolatum, 50 Gm. The U. S. P. VIII directed the incorporation of the melted zinc stearate, while the N. F. IV directs the incorporation of the zinc stearate without heat.

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